1. Regulation and Interregional Collaborations in Academia, Government and Industry

Abstract no. 1

The Development， Regulatory Policy， and Public Reimbursement of NRICM-101 (臺灣清冠一號) During COVID-19 Pandemic in Taiwan

1. Prof Yi-Tsau Huang

Institute of Tradtional Medicine, National YangMing ChiaoTung University

The COVID-19 pandemic caused by the virus SARS-CoV-2 has had devastating effects on global health (mortality and morbidity), economics and social life since year 2020. Several effective vaccines and anti-COVID-19 drugs (e.g., Paxlovid) have played important roles in alleviating the scale of pandemic and/or reducing the possibility of disease progression to severity. In this report, in my previous capacity of Director General, Department of Chinese Medicine and Pharmacy, Ministry of Health and Welfare, I trace the story of NRICM-101 as a herbal formulation for symptom relief in infected patients through its development, policy, regulation and public reimbursement during COVID-19 Pandemic in Taiwan. NRICM-101 (臺灣清冠一號) consists of 10 herbs: Scutellaria Root (Scutellaria baicalensis, 黃芩), Heartleaf Houttuynia (Houttuynia cordata, 魚腥草), Indigowoad Root (Isatis indigotica, 板藍根), Fineleaf Nepeta (Nepeta tenuifolia, 荊芥), Saposhnikovia Root (Saposhnikovia divaricata, 防風), Mulberry Leaf (Morus alba, 桑葉), Peppermint Herb (Mentha haplocalyx, 薄荷), Mongolian Snakegourd Fruit (Trichosanthes kirilowii, 瓜蔞), Magnolia Bark (Magnolia officinalis, 厚朴) and baked Liquorice Root (Glycyrrhiza glabra, 甘草). The NRICM-101 decoction was used in the first clinical observational study conducted mainly at the Tri-Service General Hospital (a tertiary medical center) during March-April 2020, the results of which were later published in Biomedicine & Pharmacotherapy 2021, Vol. 133, doi.org/10.1016/j.biopha.2020.111037, with in vitro assays suggesting pharmacological effects such as inhibiting (a) the spike protein/ACE2 interaction, (b) 3CL protease activity, (c) viral plaque formation, and (d) production of cytokines interleukin (IL)-6 and tumor necrosis factor (TNF)-α. The Traditional Chinese Medicine Treatment Guidelines (including NRICM-101 for symptom relief in mild COVID-19 cases) for COVID-19 were developed based on research by the National Research Institute of Chinese Medicine (NRICM, Ministry of Health and Welfare, Taiwan) led by Director Yi-Chang Su and finalized on March 31, 2020. These guidelines serve as the basis for Chinese medicine treatment for COVID-19 in Taiwan. In view of overwhelming mortality and morbidity worldwide, but not in Taiwan, Dr. Y-C Su initiated the idea of encouraging the good-manufacturing-practice (GMP) phytoceutical companies in Taiwan to manufacture concentrated powder formula of NRICM-101 for export instead of decoction. The expert review of the first export license of concentrated powder formula of NRICM-101 was convened in August 2020, with "indication (適應症)" - exogenous seasonal epidemic (外感時疫), and "efficacy (效能) claims- relieving exterior syndrome and dispersing Lung Qi (解表宣肺)、clearing heat-

toxin (清熱解毒), relaxing the chest and removing phlegm (寬胸化痰), regulating stomach and lowering Qi (和胃降氣)", all in traditional Chinese medicine terms, with issuance of first license in September. Between Sept. 2020 and Feb. 2021, the export value of NRICM-101 reached 100 million NTD (equivalent to 3.3 million USD or 20% of annual export revenue of Chinese herbal products from Taiwan). The expert review of the first emergency use authorization (EUA) of NRICM-101 concentrated powder was convened in April 2021, with the same indications and efficacy claims, and issuance of first EUA license as a prescription drug in May 2021. A propensity score-matched analysis of multicenter retrospective study retrieved data by Prof. Su's group showed that of 302 patients (151 received NRICM101 and 151 did not) included in the analysis to assess relative risks during the 30-day observation period, no endpoint occurred in the patients receiving NRICM101 plus usual care while 14 (9.27%) in the group receiving only usual care were intubated or admitted to ICU (Tseng et al., Pharmacological Research, Volume 184, October 2022, DOI: 10.1016/j.phrs.2022.106412). From January 2022 onwards, patients quarantined at home or elsewhere in Taiwan and diagnosed with COVID-19 infection via a virtual appointment by doctors can obtain a digital prescription of NRICM-101 concentrated powder paid by the Government from the Special Budget for Epidemic Prevention. It is estimated that until June 2023, among a total of 10 to 11 million Taiwanese have been infected by the virus SARS-CoV-2, around 18% (1.8 million) have been prescribed with the NRICM-101 concentrated powder paid by the Government. The 14 export licenses of NRICM-101 concentrated powder have reached more than 60 nations worldwide. In the latter half of 2023, a prospective, randomized, double-blind, placebo-controlled clinical trial of NRICM-101 sponsored by Sun Ten Pharmaceutical Co. (順天堂藥廠) was conducted in about 240 patients in 2 medical centers in Taiwan. The expert review of the first drug license of concentrated powder formula of NRICM-101 was convened in April 2024, with "indication (適應症)" - exogenous seasonal epidemic (外感時疫), and "efficacy (效能) claims- relieving exterior syndro

Abstract no.2

The Neglected Government-Academia Collaboration in Renowned TCM Doctor Research in Taiwan

1. Prof Hen-Hong Chang, China Medical University, Taichung

2. Dr Yen-Chieh Wu, China Medical University, Taichung

3. Dr Daniel Chen, China Medical University Hospital, Taichung

Loss of focus on the clinical experiences of renowned TCM doctors (RCMDs) is a worrying problem in Taiwan. Given the specialized nature of TCM, policy formulation in this field heavily relies on academic insights. However, Taiwan's academia has conducted relatively few studies or projects on RCMDs, which were undertaken by the Committee on Chinese Medicine and Pharmacy of the Department of Health, Executive Yuan. To be specific, Prof. Hen-Hong Chang conducted the project "Establishment of the TCM Expert File" in 2006. Together with Prof. Shu-Ling Yang, Prof. Chang completed another project "The bicoastal experience exchanges of preservation of Chinese medicine literature and academic inheritance of traditional Chinese medicine" subsequently. Similarly, Prof. Jung-Nien Lai also completed a project "Inheriting the Experiences from Veteran Practitioners of Traditional Chinese Medicine" in 2008. Their recommendations included formulation of TCM policy, establishment of RCMD recognition criteria, modernization research of TCM, and RCMDs serving as internship mentors. On top of that, the project "The Digital Archives for the Systems of Acupuncture and Chinese Medicine of Present Age," was accomplished by Dr. Ching-Wen Chen and his team. They built a website that preserves the valuable experiences and interview videos of several RCMDs of acupuncture. In conclusion, there have only been four projects about RCMDs so far, most of which are still in the preliminary text editing phase. We believe that some RCMDs might have lost follow-up. What's worse, the authorities concerned have not taken further action in response to these suggestions. The collaboration between the government and academia in this area needs to be re-emphasized. Keywords Academia, Government, Renowned TCM doctor, Taiwan.

Abstract no.3

Enhancing Interdisciplinary Healthcare Education through a Virtual Chinese Medicine Clinic

1. Dr Yuen Shan Ho, The Hong Kong Polytechnic University, Hong Kong SAR

Background: The rapid development of Chinese Medicine (CM) in Hong Kong has highlighted the need for innovative educational strategies, especially to prepare students for collaborative practice in the forthcoming CM hospital. Set to begin phased operations in 2025, this hospital aims to extend its services through District Health Centers, focusing on integrative primary healthcare. A key aspect of this initiative is interdisciplinary training for CM and nursing students, fostering a collaborative ethos that promises enhanced patient care. Methods: Traditional challenges such as large-class teaching and conflicting schedules among students from different majors have impeded effective clinical placements. This has led to reduced engagement, particularly in non-core subjects perceived as less critical. To address this, we implemented a flipped classroom approach in a collaborative project involving two universities offering CM courses to distinct student groups. This approach utilized online discussions and case studies to facilitate the collaborative design and implementation of patient care plans, thereby transforming the learning experience and enriching the educational journey for both CM and nursing students. Results: Despite initial challenges, the integration of virtual clinical placements with online discussions and case studies has demonstrated significant empirical evidence of increased student engagement and participation. This approach effectively overcomes logistical barriers and provides a comprehensive and sustainable model for interdisciplinary healthcare education in CM and nursing. Conclusion: As the healthcare landscape continues to evolve, this educational paradigm ensures that students are well-equipped for collaborative and patient-centered practice in the dynamic field of Chinese Medicine. The success of this virtual clinic model underscores its potential as a valuable tool for future interdisciplinary training. Keywords: Interprofessional, Teaching, Learning, Nurse, Online

Acknowledgment: This work is supported by the Teaching Development Grant from the University Grants Committee of the Hong Kong Special Administrative Region, China (Project No. LTG22-25/IICA/18) awarded to YSH.

Abstract no.4

Quality Control of TCM Herbs and Herbal Preparations in Taiwan and Taiwan Herbal Pharmacopeia

1. Prof Yuan-Shiun Chang, China Medical University, Taichung

2. Dr Yu-Ling Ho, Hungkuang University, Taichung

Quality Control of TCM Herbs and Herbal Preparations in Taiwan and Taiwan Herbal Pharmacopeia Yu Ling HO1 and Yuan Shiun CHANG2* 1Department of Nursing, Hungkuang University, Taichung 433, Taiwan 2*Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, College of Chinese Medicine, China Medical University, Taichung 404, Taiwan E-mail: yschang0404@gmail.com Traditional Chinese Medicine has been very popular in Taiwan in the past. TCM was incorporated in the National Insurance since 1995. Currently, TCM only accounts for less than 4% of total National Health Insurance annual budget. By September 2006, all herbal pharmaceutical companies in Taiwan were upgraded to GMP standard. Currently there are 79 GMP herbal pharmaceutical companies in Taiwan and are moving toward CGMP standard. In this paper, the compilation of both Chinese and English version of Taiwan Herbal Pharmacopeia (THP) (II, III, IV), Color Illustrations of THP will be covered. The recently published Color Illustrations of THP 2nd edition provided color photos of the plants, crude herbs and the decoction pieces of 355 herb species covered in THP IV. A totoal of 1118 color photos were provided including 523 photos of the plants and 595 photos of the crude herbs and decoction pieced. The method development of microscopic identification, TLC and HPLC will be introduced.The safety limit of sulfur dioxide residue, heavy metal contents, Organochlorine pesticide residues and aflatoxins in the herbs and herbal preparations will also be discussed. The regulations and quality control practice of Chinese medicine in Taiwan will also be introduced including the application of herbal preparation licenses. The authors also like to share some of the works they did in the Hong Kong Chinese Materia Medica Standard Project since 2011. The work in USP Botanical Dietary Supplements and Herbal Medicine Expert Committee and EDQM TCM Working Party, European Pharmacopeia will also be shared.

Abstract no.5

The key issues for research and development of sustainable niche health products for primary healthcare

1.Kelvin Chan

As the COVID-19 pandemic progressed, it became apparent that people infected during the pandemic experienced mild to moderate respiratory distress and recover without the need for any special treatment and the disease progressed more severely in the elderly and in individuals with accompanying chronic diseases, such as cardiovascular disease, diabetes, chronic respiratory disease and cancer. Recent observations during the COVID-19 pandemic period indicated the public relied on reliable herbal medicines, supplements and functional foods to strengthen their immune systems and their anti-inflammatory functions to reduce the symptoms produced. However, only products with assured quality can provide confidence to the public to use them. The present paper deals with these issues and provides the processes of research and development that are required to guaranteed the outcomes of the products that can sustain their position in the market as niche brand of their kind.

Nowadays, products from natural sources such as herbal extracts, medicinal plants, mineral origins, and extracts from animal sources (some milks products) have been used as dietary supplements, nutraceuticals to improve health, prevent chronic diseases, increase life expectancy, or support the structure or functions of the body. Publications from scientific journals have been kept as references for nutraceuticals and other health products and have received considerable interest due to potential nutrition, safety and therapeutic effects. Plenty of these ‘me-too’ products are available to the public sector. Safety, efficacy and risks of drug-health-products-interactions remains the key concerns of the health authorities.

My collective views on the current situation are to aim for collaboration between academic institute, manufacturing body, regulatory advisory body, and most importantly financial investment body. I shall detail various approaches with illustrations to produce sustainable health products.

2. TCM Diagnosis，Preventive Medicine & Healthcare

Abstract no.6

A multi-center cross-sectional study of Chinese Herbal Medicine-Drug adverse reactions using active surveillance in Singapore's Traditional Chinese Medicine clinics.

1. Dr Linda Lidan Zhong, Nanyang Technological University, Singapore

2. Mr Chester Yan Jie Ng, Nanyang Technological University, Singapore

Background: This study aimed to investigate the rates and causality of patient-reported adverse events (AEs) associated with concomitant Chinese Herbal Medicine (CHM) and Western Medicine prescription drug (WMPD) consumption through active surveillance in Singapore's Traditional Chinese Medicine (TCM) clinics. Methods: A cross-sectional study was conducted at five TCM clinics across Singapore from 8th May till 8th July 2023. Patients were screened to determine rates of CHM and WMPD consumption, and then interviewed if an AE was reported. An expert committee assessed the AE reports to determine causality. Along with descriptive statistics, odds ratios were calculated to determine AE occurrence likelihoods for patients who consumed both CHM and WMPD compared to CHM consumption alone. Results: 1028 patients were screened and 62.65% of them reported concurrent CHM-WMPD consumption. Patients who consumed CHM and WMPD were 3.65 times more likely to experience an AE as compared to CHM consumption alone. 18 AE reports were adjudicated, with most AEs deemed unlikely due to CHM consumption. Conclusions: A large proportion of patients consumed CHM and WMPD concurrently, thus increasing their risk of experiencing AEs compared to those consuming CHM only. Active surveillance is applicable for detecting AEs, collecting data for causality assessment, and analysis.

Abstract no.7

The Clinical Significance of Tongue Movements in Predicting Outcomes of Ischemic Stroke

1. Prof Lun-Chien Lo, China Medical University, Taichung

2. Mr Yung-Sheng Huang, China Medical University, Taichung

3. Dr Po-Chi Hsu, China Medical University, Taichung

4. Prof Hen-Hong Chang, China Medical University, Taichung

5. Dr Tsung-Chieh Lee, Changhua Christian Hospital, Changhua

6. Prof John Y. Chiang, National Sun Yat-Sen University, Kaohsiung

Tongue deviation (TD) and non-retroflex tongue (non-RT) are observed in patients with stroke, of which severity might be related. This study surveyed the character between RT and TD of ischemic stroke patients. 308 subjects were collected through inpatient wards at Stroke Center of Changhua Christian Hospital in Taiwan, from August 2010 to July 2013. The tongue images and the angle of tongue deviation were acquired by the automatic tongue diagnosis system. Data such as NIHSS score, Barthel Index and tongue deviation angles were gathered. One-Way ANOVA followed by multiple linear regression analysis were employed to examine variables and to determine the NIHSS of the patients. 59 patients with TD (angle 6.40 ± 7.84 degrees) and 249 patients without TD (9.72 ± 8.91 degrees) were identified. In conclusion, there is no significant difference in admission days, NIHSS score, and Barthel Index between TD and non-TD groups. Only non-RT groups showed statistical significance (p-value = 0.001). This study demonstrates that non-RT is more clinically meaningful than TD to detect the severity and prognosis of patients with ischemic stroke. The ability to maneuver tongue retroflex can serve as a simple and reliable method to survey the severity of stroke.

Abstract no.8

The Association Between Ventilator Weaning Difficulty and Pulse Diagnosis Parameters

1. Dr Mei-Yao Wu, China Medical University, Taichung
2. Mr Shih-Chien Cheng, China Medical University, Taichung
3. Dr Chih-Ching Yen, Professor, China Medical University, Taichung

Background: Prolonged weaning patients in Respiratory Care Centers focus on weaning off the ventilator. Clinical assessment of weaning difficulty utilizes Maximum Inspiratory Pressure (PImax) and the Rapid Shallow Breathing Index (RSBI). PImax ≥ -20 cmH2O indicating muscle weakness, and RSBI ≥ 105 indicating rapid shallow breathing. Both parameters suggest a lower probability of successful weaning from the ventilator. We aimed to evaluate the correlation between PImax, RSBI and traditional Chinese medicine (TCM) pulse signals. Methods: We enrolled 20 patients (70.4 years old, 60% male) from September 1, 2023, to January 31, 2024, at "China Medical University Hospital" in Taiwan. Pulse waves were assessed using pulse sphygmology, and the correlation between PImax, RSBI and pulse signals was analyzed by logistic regression. Results: Patients with PImax ≥ -20 cmH2O or RSBI ≥ 105 had a higher proportion of lung qi deficiency (57% vs. 15%, p = 0.052 and 67% vs. 0%, p = 0.001) (Table 1). Patients with RSBI < 105 were more likely to have kidney channel heat excess (91% vs. 22%, p = 0.005). PImax negatively correlated with the pulse pressure of right chi (kidney, correlation coefficient = -0.474, R^2 = 0.225), while RSBI negatively correlated with the pulse pressures of right cun (lung, -0.633, R^2 = 0.400), right guan (spleen/stomach, -0.764, R^2 = 0.583), left cun (heart, -0.607, R^2 = 0.368), and left chi (kidney, -0.521, R^2 = 0.272) (Figure 1). Conclusions: RSBI ≥ 105 is indicative of deficiency of lung qi, lung yin, spleen/stomach yin, heart yin, and kidney yin in patients facing difficulty in ventilator weaning. PImax ≥ -20 cmH2O reflects higher severity of kidney yin deficiency. Future research with larger samples is needed to establish TCM indices for assessing the success rate of ventilator weaning in patients undergoing prolonged ventilator use.

Abstract no.9

Predicting TCM Patterns in PCOS Patients: An Exploration of Feature Selection Methods and Multi-label Machine Learning Models

1. Prof Zhaoxia Xu, Shanghai University of Traditional Chinese Medicine, Shanghai

2. Ms Jiekee Lim, Shanghai University of Traditional Chinese Medicine, Shanghai

Background: Traditional Chinese Medicine (TCM) offers individualized treatment for Polycystic Ovary Syndrome (PCOS) through pattern differentiation, but the subjectivity of TCM diagnoses can lead to inconsistent outcomes. Integrating machine learning (ML) offers an objective basis to support TCM diagnoses. This study aims to evaluate various feature selection techniques and multi-label ML algorithms to develop an effective predictive model for the classification of TCM patterns in PCOS patients, thereby enhancing diagnostic standardization and treatment personalization. Methods: The study utilized a dataset comprising 432 patients with PCOS, exhibiting one or more of five TCM patterns. Feature selection started with Variance Thresholding (VT), followed by a comparison of five advanced techniques: Statistical Analysis Test, Recursive Feature Elimination with Cross-Validation (RFECV), Least Absolute Shrinkage and Selection Operator Regression, BorutaShap, and ReliefF. To ascertain the most effective model for predicting PCOS TCM patterns, four ML algorithms—Support Vector Machine, Logistic Regression, Extreme Gradient Boosting (XGBoost), and Artificial Neural Networks—were evaluated against the identified feature set. Results: VT reduced the feature count from 224 to 174. RFECV emerged as the most effective feature selection method, identifying 67 key features. XGBoost emerged as the top-performing model, demonstrating superior testing accuracy (0.7870), F1 score (0.9519), and Hamming loss (0.0481) with RFECV-optimized features. Conclusions: The RFECV-XGBoost model proved effective in classifying TCM patterns in PCOS. It emphasizes the necessity of precise feature selection and the significant capabilities of ML in advancing TCM pattern diagnostics, offering a significant stride toward enhancing precise and personalized healthcare in biomedical studies.

Abstract no.10

Analysis of Gut Microbiota and Traditional Chinese Medicine Constitution in Systemic Sclerosis Patients

1. Prof Hen-Hong Chang, China Medical University, Taichung

2. Prof Yu-Pei Chen, Tainan Hospital, Ministry of Health and Welfare, Tainan

3. Dr Ang-Jun Liu, Tainan Hospital, Ministry of Health and Welfare, Tainan

Objective: This study aims to analyze the gut microbiota composition of patients with systemic sclerosis (SSc) using 16S ribosomal RNA (rRNA) gene sequencing to identify differences in microbial communities compared to healthy controls. Methods: The study utilized raw sequencing data from both Illumina and PacBio platforms, which were cleaned using Trimmomatic and Cutadapt tools to remove primer and adaptor sequences. Quality control was performed, and amplicon sequence variants (ASVs) were identified using the DADA2 pipeline. Taxonomic assignment was conducted, and the composition and diversity of the gut microbiota were analyzed through various methods, including absolute abundance tables, heatmaps, and ordination techniques such as PCA, PCoA, and NMDS. Statistical analyses including ANOSIM, MRPP, and Adonis were employed to assess community composition differences among groups, and differential abundance analysis was conducted using Welch's t-test, Kruskal-Wallis test, and other methods. Results: Significant differences were observed in the gut microbiota composition between SSc patients and healthy controls. The results indicated a distinct microbial community structure in SSc patients, with variations in the relative abundance of specific taxa. Key findings include differences in the Firmicutes/Bacteroidetes (F/B) ratio and the presence of certain biomarkers identified through LEfSe analysis. Additionally, core microbiome analysis revealed specific taxa shared among SSc patients that could be potential indicators of disease status. Conclusions: The gut microbiota of SSc patients shows significant alterations compared to healthy individuals, highlighting the potential role of microbial dysbiosis in the pathogenesis of systemic sclerosis. These findings provide a basis for further research into microbiome-based diagnostics and therapeutic strategies for SSc.

Abstract no.11

Developing YIV-111: A Formulation Targeting NF-κB and TGF-β Signaling for Effective Fibrosis Treatment

1.Prof Yung-Chi Cheng, Yale University, New Haven

2. Dr Wing Lam, Yale University, New Haven

3. Dr Yu Wu, Yale University, New Haven

4. Dr Xiao-Qin Zhong, Yale University, New Haven

5. Dr Fu-Lan Guang, Yale University, New Haven

6. Dr Shwu-Huey Liu, Yiviva, New York

7. Mr William Cheng, Yiviva, New York

8. Mr Pei-Kwen Cheng, Yiviva, New YorkFibrosis is a chronic disease characterized by the excessive accumulation of extracellular matrix proteins, including collagen, which can occur in various tissues such as the liver, kidney, and lung, and is usually accompanied by inflammation. While TGF-β signaling is known to play a key role in fibrosis, selective agents targeting TGF-β signaling alone have not yielded satisfactory results. Our study explores the influence of other cell signaling pathways on TGF-β signaling, proposing a multiple-target strategy for more effective fibrosis treatment. We investigated the crosstalk between different cell signaling pathways and TGF-β signaling. Our findings show that TNF-α and IL-1β can enhance TGF-β-induced SMAD2/3-mediated transcriptional activity in A549 and HEK293 cells. Knockout of TAK1 or NF-κB (p65) genes diminished the potentiation effect of TNF-α or IL-1β on TGF-β-induced luciferase activity. Additionally, TNF-α and IL-1β potentiated TGF-β-induced epithelial-to-mesenchymal transition (EMT) in A549 cells, evidenced by further down-regulation of E-Cadherin and up-regulation of LOXL2. In animal models, co-treatment with bleomycin and LPS resulted in higher expression of fibrosis- and inflammation-associated genes, such as Col1a1, Vimentin, SMA, TGF-β, and TNF-α than bleomycin alone. This supports the idea that inflammation could promote fibrosis progression, while targeting both TGF-β and NF-κB signaling simultaneously could offer an effective strategy for treating fibrosis. Using our STAR (Signal, Transduction, Activity, and Response) Drug Discovery Platform, which evaluates the effects of over 300 medicinal plant extracts on more than 30 signaling pathways, we identified herbs that impact IL-1β-NF-κB, TNFα-NF-κB, and TGF-β-SMAD2/3-mediated transcriptional activity. We further validated their inhibitory effects on COX2, ICAM, TGM2, and LOXL2 protein expression induced by IL-1β, TNF-α, and/or TGF-β in cell cultures. These herbs affected SMAD3-P, IKKα/β-P, p65-P, and p65 nuclear translocation differently in cell cultures, indicating varied mechanisms in inhibiting TGF-β and NF-κB pathways. Combining herbs with different mechanisms may lead to synergistic effects. Importantly, several herbs improved fibrosis and inflammation induced by bleomycin and LPS co-treatment in animal models. Interestingly, these herbs exhibited different specificities in targeting fibrosis and inflammation in various organs, suggesting their potential use as single agents or in combination to create specific formulations for treating or preventing fibrosis in different organs. In conclusion, NF-κB signaling enhances TGF-β signaling and accelerates fibrosis

progression. We have identified herbs that simultaneously target both pathways. These herbs will be the key ingredients of YIV-111, which aims to offer a promising approach for treating fibrosis-associated diseases. With a good safety profile from their traditional use as food and health-promoting agents in China and other regions, YIV-111 could also be used preventively against fibrosis-associated diseases. Financial support: This work was supported by Yiviva and a research gift from the National Foundation for Cancer Research, USA.

Abstract no.12

Exploring hepatic fibrosis screening via deep learning analysis of tongue images

1. Prof Bao-Guo Sun, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
2. Dr Xiao-Zhou Lu, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
3. Dr Hang-Tong Hu, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
4. Prof Wei Li, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
5. Dr Jin-Feng Deng, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
6. Prof Li-Da Chen, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
7. Dr Mei-Qing Cheng, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
8. Dr Hui Huang, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
9. Mr Wei-Ping Ke, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou
10. Prof Wei Wang, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou

Background: Tongue inspection, an essential diagnostic method in Traditional Chinese Medicine (TCM), has the potential for early-stage disease screening. This study aimed to evaluate the effectiveness of deep learning-based analysis of tongue images for hepatic fibrosis screening. Methods: A total of 1083 tongue images were collected from 741 patients and divided into training, validation, and test sets. DenseNet-201, a convolutional neural network, was employed to train the AI model using these tongue images. The predictive performance of AI was assessed and compared with that of FIB-4, using real-time two-dimensional shear wave elastography as the reference standard. Results: The proposed AI model achieved an accuracy of 0.845 (95% CI: 0.79–0.90) and 0.814 (95% CI: 0.76–0.87) in the validation and test sets, respectively, with negative predictive values (NPVs) exceeding 90% in both sets. The AI model outperformed FIB-4 in all aspects, and when combined with FIB-4, the NPV reached 94.4%. Conclusion: Tongue inspection, with the assistance of AI, could serve as a first-line screening method for hepatic fibrosis.

Abstract no.13

Yange Ganoderma lucidum inheritance and innovation， research on the efficacy components of new traditional Chinese medicine，and exploration of technical solutions and technical routes for new drug research and development

1. Prof Hua-Ying Li , 北京扬格灵芝健康产业研究院有限公司, Beijing

1,The historical evolution and modern inheritance of Yange Lingzhi traditional Chinese medicine 2,The chemical composition of the main active ingredients of Yange Ganoderma lucidum traditional Chinese medicine 3,Preliminary analysis of the functional components of Ganoderma lucidum 4,Saponins (saponins) are based on the structure and efficacy of saponin combinations 5,Ganoderma lucidum sterols have a special protective effect on cell membrane structure during antioxidant processes 6,The important molecular structure of ganoderic acid and the irreplaceable important functions of triterpenoid ligands in the structural repair of cells, DNA and RNA, especially in the contribution of radiation resistance 7,New ideas and feasible technical routes arising from the combination of modern molecular biology and biochemistry in the research and development of new traditional Chinese medicine and health care products 8,The new products of Yange Ganoderma lucidum are technologically advanced and improve the physiological and psychological functions of consumers 9,Yangge Ganoderma lucidum achievement transformation, new industry formation and market and consumption highlights experience and exploration 10,A little experience in the modern scientific research and scientific research of traditional Chinese medicine

Abstract no.14

Investigating the acute and sub-acute toxicity of medicinal Cuscuta chinensis Lam plant

1. Prof 艾克白尔 买买提,新疆医科大学, 乌鲁木齐

Cuscuta chinensis Lam. had received growing attention as a traditional medicinal herb widely used for treating female impotence, abortion, male reproductive system disease and cardiovascular diseases, respectively. However, despite the centuries-long use of C. chinensis in traditional chinese medicine, information regarding its toxicity profile is still obscure.Moreover, its systematic and target-organ toxicity profile,overall safety and side effects have not yet been determined. Therefore,studies involving safety validation for clinical uses are urgently needed. Given this, the current study aims to examine the acute toxicity and a four weeks toxicity of water extract of C. chinensis (CLW) in (ICR) mice model.The acute toxicity test results revealed an LD 50 of over 5000 mg/kg for CLW. Similarly, no CLW-related mortality and severe toxicities were experienced in the sub-acute study. However, the treatment of CLW had a reducing effect on body weight of both male and female mice, and feed intake in female mice at the all tested doses (1250, 2500 and 5000 mg/kg). Moreover, significant effects in organ coefficients of brain, liver, lung, testis and thymus became apparent due to CLW mainly at the 2500 and 5000 mg/kg. The hematological analysis result showed a significant decrease in platelets, lymphocytes, and hematocrit. In contrast, a significant increase in the neutrophils was observed in the CLW treated groups (2500 and 5000 mg/kg). Biochemical test results showed a significant increase in aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase levels while decreasing albumin, total cholesterol and triglyceride levels after treatment of CLW mostly at the doses of 2500 and 5000 mg/kg. Mild liver toxicity in both sexes treated with 5000 mg/kg of CLW was recorded in the histopathological analysis. Overall, our results suggested that CLW is safe at its dose lower than 1250 mg/kg, although liver toxicity from daily use may be a matter of concern.

Abstract no.15

Monitoring Radial Arterial Pulse Harmonics in Hospice Patients Using Wrist Blood Pressure Monitors

1. Prof 育誠 郭, Taipei Medical University, Taipei

The study of end-of-life phenomena has always been a worthy topic of exploration, especially given the significant role pulse diagnosis plays in traditional Chinese medicine for end-of-life diagnosis. However, diagnostic methods described in ancient document lack scientific quantification, making it challenging to directly inherit them in modern practice. Recently, using wrist blood pressure monitors, we tracked radial arterial pulse harmonics in hospice patients during their last 30 days before death, revealing significant physiological changes as death approached. We used wrist blood pressure monitors connected to the internet cloud to non-invasively measure the radial arterial pulse in 780 end-stage data over 30 days. The pulse waveforms were transformed into several Fourier harmonics, and these data were compared with results from healthy subjects serving as the control group. Although there were no notable differences in diastolic or systolic blood pressure, we noted significant increases in the magnitude, variation, and amplitude of harmonics' phases. All harmonic variances exhibited a notable escalation during the last 30 days. Notably, we found that the higher the harmonic, the more pronounced the variation. A discernible pattern emerged during the final 20, 15, 10, and 5 days. Within this brief five-day interval, there was a substantial wave-like surge in all harmonic variances, indicating a critical and distinctive physiological phenomenon during the dying process. To conclude, we used wrist blood pressure monitors connected to the internet to track blood pressure waves and found that the stability of the pulse waveform's components decreased gradually, showing significant instability in the five days before the patients' passing. This highlights the potential of telehealth devices in understanding physiological changes during the dying process, showcasing their importance in telemedicine.

Abstract no.16

Traditional Chinese Medicine (TCM) Treatment for serous otitis media with hearing impairment

1. Mr Pingchang Lin 2. Gondon Chen

A ten years old male suffered from bilateral otitis media for one month, combined with hydrops and hearing loss. After one month of antibiotic treatment, the hydrops persisted and his hearing was impaired. The otolaryngologist informed him that surgery might be necessary, so his father led him to our TCM clinic. The chief complaint was pain in both ears and strange sounds, as well as symptoms of nasal allergy such as cough and nasal congestion.

Before came to our clinic, the patient had taken to the otolaryngology department for examination and confirmed that he had bilateral otitis media combined with acute sinusitis. The condition of effusion accumulation in both ears was as follows: The right ear was full of effusion and the left ear was half full of effusion. He stopped taking any western medicine and asked for TCM treatment, while continued to go to the otolaryngology department for examination to confirm the effect of TCM. Ten days later, the effusion in the right ear disappeared completely, but the effusion in the left ear was filled up completely. The TCM prescription was adjusted three times based on the clinical manifestation. The treatment was focus on using Qi to improve physical function by many ways, including foods and herbs. Cang Er Sang and Jing Jie Lian Qiao Tang and other herbs were used and adjusted by clinical response . After one month of TCM treatment, the patient's bilateral middle ear effusion had completely resolved, and his hearing had returned to normal.

Abstract no.17

Paeonol ameliorates diabetic nephropathy by promoting TFEB-mediated lysosome biogenesis and lipophagy

1. Dr Liang Peng, China-Japan Friendship Hospital, Beijing

2. Dr Sinan Ai, China-Japan Friendship Hospital, Beijing

Diabetic nephropathy (DN) is a significant clinical and public health burden worldwide, underscoring the urgent need for more effective therapeutic options. Renal tubular lipid accumulation leads to cell injury and dysfunction, thereby contributing to DN progression, suggesting that alleviation of renal tubular lipid accumulation is a potential therapeutic strategy for treating DN. Here, we report that paenol (PAE), a natural phenolic compound, alleviates renal tubular lipid accumulation in glucolipotoxicity treated HK-2 cells and DN progression in high fat diet and streptozotocin induced mice. Mechanistically, PAE directly binds to RHEB, functioning as an mTOR suppressor, thereby activating TFEB to promote lysosome biogenesis and lipophagy, subsequently alleviating renal tubular lipid accumulation and DN progression. Together, these findings suggest that PAE holds promise as a therapeutic agent for DN, with a unique mechanism of activating renal TFEB-mediated lipophagy.

Abstract no.18

中医药治疗多囊卵巢综合征伴胰岛素抵抗机制的研究进展

1. Dr 虹丽 吕, 成都中医药大学, 成都

摘要：多囊卵巢综合征（polycystic ovary syndrome,PCOS）是以排卵稀发、无排卵,高雄激素血症及胰岛素抵抗（insulin resistance,IR）为特征的育龄期妇女常见的内分泌疾病之一，是育龄期妇女月经不调,不孕等疾病的主要诱因，其中约有超过半数的 PCOS 患者伴随着不同程度的胰岛素抵抗。现阶段，对于多囊卵巢综合征合并胰岛素抵抗（PCOS-IR）的认识多从遗传、慢性炎症反应、环境等因素入手，临床治疗多在生活方式干预基础上，口服避孕药以及双胍类、噻唑烷二酮类等药物。中医认为该病病因包括“湿”“痰”“瘀”，涉及肝、脾、肾三脏。临床上治以补肾疏肝健脾，佐以祛痰、利湿、化瘀，在治疗上具有效果突出、运用灵活、费用较小、成功率高等特点。但由于中医大样本研究的缺乏，说服力度低，一定程度上限制了中医药优势的发挥。该文从中医的角度，对 PCOS-IR 的病因病机以及治疗采用大数据研究，进行整理综述，以期为探索 PCOS-IR 的中医药疗法提供一定的思路。 Abstract: Polycystic ovary syndrome (PCOS) is a common endocrine disease in women of reproductive age characterized by sparse ovulation, anovulation, hyperandrogenemia and insulin resistance（IR）, and it is the main cause of irregular menstruation, infertility and other diseases in women of reproductive age, and more than half of PCOS patients are accompanied by different degrees of insulin resistance. At this stage, the understanding of polycystic ovary syndrome combined with insulin resistance（PCOS-IR）is mostly based on genetic, chronic inflammatory response, environmental and other factors, and clinical treatment is mostly based on lifestyle intervention, oral contraceptives, and drugs such as biguanides and thiazolidinediones. According to Chinese medicine, the causes of the disease include "dampness", "phlegm" and "stasis", involving the liver, spleen and kidney. Clinical treatment is based on tonifying the kidney, dredging the liver and strengthening the spleen, supplemented by expelling phlegm, inducing dampness and resolving blood stasis, which is characterized by outstanding effect, flexible application, small cost and high success rate in treatment. However, due to the lack of large-sample studies in TCM, the persuasive strength is low, which limits the advantages of TCM to a certain extent. This article is an organized review of the etiology and pathogenesis of PCOS-IR and its treatment using big data research from the perspective of Chinese medicine, with a view to providing certain ideas for exploring Chinese medicine therapies for PCOS-IR.

Abstract no.19

Traditional Chinese Medicine for Renal Fibrosis by Regulating Macrophages

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2. 博 庞, 天津中医药研究院附属医院, 天津

Renal fibrosis is the main pathological feature of various chronic kidney diseases to end stage renal disease, which mainly includes glomerular sclerosis, tubular atrophy, chronic inflammation and fibrosis of the interstitial and sparse blood vessels. The occurrence and development mechanism of renal fibrosis is complex, involving many aspects, including the activation of inflammation caused by kidney injury, the release of growth factors and other pro-fibrotic mediators, myofibroblast activation, parenchymal cell phenotypic change and irreversible loss. A large number of studies had shown that macrophages played an important role in the process of renal fibrosis progression. It can participate in the progression of fibrosis through various mechanisms such as inflammatory response, polarization and myofibroblast transdifferentiation. When the kidney is slightly damaged, macrophages penetrate the injury site to remove necrotic cells and help the tissue restore its original structure, while when the kidney is severely or repeatedly damaged, macrophages infiltrate the damaged site in large numbers and persist, leading to chronic inflammation and fibrosis. The accumulation of macrophages was significantly associated with glomerular sclerosis, interstitial fibrosis and tubular atrophy. In terms of treatment, Western medicine has no good methods, while traditional Chinese medicine has the advantage of multi-component and multi-target action. In recent years, Chinese medicine scholars have continued to explore and study, and found that Chinese medicine is quite effective in regulating macrophages to improve kidney fibrosis.

Abstract no.20

The Probiotic SYP-B4138 Intervention in NAFLD Rats: Insights from Blood Biochemical Indicators and Gut Microbiota

1. Dr Xin Wu, Shenyang Pharmaceutical University, Shenyang

2. Ms Lingxuan Li, Shenyang Pharmaceutical University, Shenyang

3. Ms Yunkun Zhang, Shenyang Pharmaceutical University, Shenyang

4. Mr Guang Yang, Shenyang Pharmaceutical University, Shenyang

Non-alcoholic fatty liver disease (NAFLD) is closely related to insulin resistance, which may or may not be accompanied by diabetes mellitus, obesity, metabolic syndrome, dyslipidemia. Probiotics have the potential to enhance host immunity, moderate insulin resistance, making them a promising novel strategy for comprehensive management of NAFLD. To examine the intervention effect of different doses of probiotic SYP-B4138 on NAFLD in rats, we administered the probiotic at concentrations of 108 and 1010 CFU/mL via gavage for 16 weeks after establishing the NAFLD model with a high-fat diet (HFD). Serum ALT and AST levels were measured to indicate liver damage. TC, TG, HDL-C and HDL-C profiles were examined for lipid-lowering effects. The cecum contents were analyzed by 16S rRNA amplicon sequencing. Our research reveals that SYP-B4138 significantly reduces serum ALT and AST levels by 62.8% ($p<0.0001$) and 50.8% ($p<0.0001$), respectively, and decreases lipid paramenters such as TC and TG by 27.0% ($p<0.01$) and 35.1% ($p<0.01$). Additionally, SYP-B4138 appears to improve insulin resistance and alleviate NAFLD pathology in rats to a ceitain degree, with correlations observed between these changes and gut microbiota composition, including Firmicutes, Bacteroidota and Actinobacteriota. In summary, the probiotic SYP-B4138 appears to alleviate the histopathological manifestations of NAFLD histopathology by modulating the gut microbiota, accompanying decreases in transaminase and lipid levels, and improvements in insulin resistance.

Abstract no.21

Postbiotics: A New Frontier in Microbiome Research and Health Science

1. Dr Xin Wu, Shenyang Pharmaceutical University, Shenyang
2. Ms Yulin Hong, Shenyang Pharmaceutical University, Shenyang
3. Mr Zhenyu Liu, Shenyang Pharmaceutical University, Shenyang

Postbiotics, a concept that has recently garnered significant attention in both academia and the industry, has emerged as a key focus of modern health science research. As a novel class of food additive and nutritional supplement, postbiotics provide a novel approach to modulate the gut microbiota and positively influnce host health through their unique mechanisms of action. Originating from further advancements in probiotic and prebiotic research, postbiotics represent a novel domainwithin microbiome studies with potential applications in health and disease. Probiotics are live microorganisms that provide beneficial effects to the host, while prebiotics serve as nourishment for these microbes. Postbiotics include various advantageousl by-products generated during the metabolic processes of probiotics, including enzymes, peptides, organic acids, short-chain fatty acids, cell wall components, and other metabolic products. These components are generated during the probiotics' intake of prebiotics, during long-term storage or processing (such as pasteurization, baking), or through metabolic processes. The current mainstream methods for deactivating postbiotic can be broadly divided into two major categories: thermal treatment methods (pasteurization, sterilization, ohmic heating) and non-thermal treatment methods (pulsed electric fields, ultrasonication, radiation, and supercritical carbon dioxide). To fully leverage the efficacy of postbiotics after their inactivation process, it is essential to identify an appropriate inactivation method for each strain.

Abstract no.22

Combining network pharmacology and transcriptomics to investigate the mechanisms of Yujiang paidu decoction in the treatment of chronic rhinosinusitis with nasal polyps

1. Ms Yujie Li, Chongqing Mecial Univversity, Chongqing

Background: Yujiang Paidu decoction (YJPD) has demonstrated clinical efficacy in the treatment of chronic rhinosinusitis. However, the effects and mechanisms of the YJPD on chronic rhinosinusitis with nasal polyps (CRSwNP) remain unclear. Purpose: This study aimed to elucidate the potential mechanism of action of YJPD in the treatment of CRSwNP based on network pharmacology, transcriptomics and experiments. Methods: A CRSwNP mouse model was established using ovalbumin (OVA) and staphylococcus aureus enterotoxin B (SEB) for 12 weeks and the human nasal epithelial cell (HNEpC) model was induced with IL-13 in vitro. Behavioral tests, scanning electron microscopy (SEM), Micro-CT and pathological change of nasal tissues were observed to investigate the therapeutic effects of YJPD. Network pharmacology and transcriptomics were launched to explore the pharmacological mechanisms of YJPD in CRSwNP treatment. Finally, An ELISA, immunofluorescence, RT-qPCR, Western blotting and Tunel were performed for validation. Results: Different doses of YJPD intervention effectively alleviated rubbing and sneezing symptoms in CRSwNP mice. Additionally, YJPD significantly reduced abnormal serological markers, structural damage of the nasal mucosa, inflammatory cell infiltration, goblet cell increases, and inhibited OVA-specific IgE levels and the secretion of Th2 cytokines such as IL-4, IL-5, and IL-13. Moreover, transcriptomics and network pharmacology analyses indicated that YJPD may exert anti-inflammatory and anti-apoptotic effects by inhibiting the MAPK/AP-1 signaling pathway. The experimental findings supported this conclusion, which was further corroborated by similar results observed in IL13-induced HNEpCs in vitro. Conclusions: YJPD could alleviate inflammatory status and epithelial apoptosis by inhibiting aberrant activation of MAPK/AP-1 signaling pathway. This finding provides a strong basis for using YJPD as a potential treatment in CRSwNP.

3. Natural Products I (Cancer, Virus and Immunoregulation)

Abstract no.23

Preparation and pharmacodynamics of osimertinib co-loaded astragaloside IV liposomes (LPs-OSI/AS)

1. Dr Le le Zhang, Chengdu University, Chengdu
2. Ms Mi Li, Chengdu University, Chengdu
3. Ms Du-Juan Zhang, Chengdu University, Chengdu
4. Ms Jia-Xin Shi, Chengdu University, Chengdu
5. Dr Feiya Sheng, Chengdu University, Chengdu

Epidermal growth factor receptor (EGFR) mutations are the second most common oncogenic driver event in non-small cell lung cancer (NSCLC). The potent irreversible third-generation epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKI) osimertinib specifically targets EGFR mutations. However, as the other EGFR-TKIs, osimertinib will inevitably develop acquired resistance, which limits its efcacy on the treatment of EGFR-mutated NSCLC patients. Astragalus is a Chinese herbal medicine with anti-inflammatory, immune-enhancing effects, can enhance the activity of chemotherapeutic drugs and reduce their toxicity. It has also been reported that Astragaloside (AS) can increase sensitize cancer cells to drug resistance and reverse chemical medicine resistance, but the effect of AS on EGFR-TKI resistance in NSCLC has not been reported in detail. However, AS has a poor solubility and the solubility of AS affect its use. Therefore, it is necessary to explore a safe and efficient drug carrier system for AS, so AS to improve the solubility of AS and enhance the therapeutic effect of AS. Liposome, as a common drug carrier, is well recognised as effective drug delivery systems, with a range of products approved, including follow on generic products, and it has shown great power in drug delivery and disease treatment. Drug encapsulation in liposome has the effect of delaying drug release. In this study, we intend to construct osimertinib-Astragaloside co-carrying liposomes (Lps-OSI/AS) to establish a reliable co-delivery vector for the study of the combined use of OSI and AS. Moreover, We also conducted in vivo and in vitro pharmacokinetics studies of the constructed Lps-OSI/AS system. The expectation is that it will possess specific clinical significance in the treatment of patients with EGFR-TKI resistant NSCLC.

Abstract no.24

Xanthocillin X dimethyl ether demonstrates an anti-proliferative effect on triple-negative breast cancer by depleting mitochondrial heme

1. Dr Wenzhe Ma, Macau University of Science and Technology, Macao SAR

Triple-negative breast cancer (TNBC) poses a substantial therapeutic conundrum due to the lack of specific targeted therapies. This research investigated the therapeutic efficacy of xanthocillin X dimethyl ether (XanDME), a naturally derived isocyanide, against TNBC. To decipher the underlying mechanism, we initially established that XanDME forms a direct bond with hemin, the oxidized variant of heme, in vitro, thereby affirming previous findings. This interaction results in the diminution of intracellular regulatory heme. We further ascertained that XanDME relocates into the mitochondria, where it engages with vital hemoproteins, specifically cytochromes. The association of XanDME with mitochondrial cytochromes interrupts the electron transport chain (ETC), curtails the functionality of mitochondrial complexes, and deactivates mitochondrial respiration. The inhibitory impact of XanDME on mitochondrial function significantly contributes to its anti-TNBC effects, as evidenced both in vitro and in vivo. Our research highlights the potential of XanDME as a therapeutic agent against TNBC, necessitating additional investigations.

Abstract no.25

MO38: A Novel BRD4 Inhibitor with Potent Anti-Tumor Activity

1. Dr Wenzhe Ma, Macau University of Science and Technology, Macao SAR
2. Mr Zifeng Huang, Macau University of Science and Technology, Macao SAR
3. Mr Tong Chu, Macau University of Science and Technology, Macao SAR

Abstract MO38 is a novel small molecule, extracted from the leaves of Magnolia Officinalis, exhibiting remarkable anti-tumor ability. As a key member of the Bromodomain and Extraterminal (BET) protein family, BRD4 plays a critical role in the progression of cancer by orchestrating the expression of oncogene and maintaining genome stability. The synergistic application of Cellular thermal shift assay (CETSA), molecular docking, and Biolayer interferometry assay (BLI) collectively demonstrated the strong and persistent binding affinity of MO38 to BRD4, highlighting a robust molecular interaction. Through RNA-sequencing (RNA-seq) analysis, it was revealed that MO38 induces cell cycle arrest, disrupts the G2/M DNA damage checkpoint, and disturbs homologous recombination (HR) repair mechanisms. Notably, overexpression of BRD4 was found to rescue the MO38-induced apoptosis, DNA damage, and the loss of G2/M DNA damage checkpoint activation. This research demonstrates that MO38 suppresses the activity of BRD4, subsequently leading to downregulation of MYC transcription, induction of DNA damage, abolition of the G2/M DNA damage checkpoint, and impairment of HR repair, all of which converge to triggering apoptosis. Moreover, in vivo experimentation has demonstrated that MO38 can effectively suppresses tumor proliferation, further confirming its therapeutic promise. Collectively, these findings highlight the potential of MO38 as a novel and potent BRD4 inhibitor, suggesting promising prospects for its application in developing targeted anti-tumor therapies that specifically target BRD4. Acknowledgement This study was funded by the Science and Technology Development Fund, Macau SAR (File no. 0105/2022/A2 and 006/2023/SKL).

Abstract no.26

Screening of Natural Inhibitors against the Papain-like Protease of SARS-CoV-2: A Comprehensive Approach Utilizing LCMS-based Dereplication

1. Mr JORIM UJANG, SARAWAK BIODIVERSITY CENTRE, KUCHING

The Papain-like Protease (PLPro) of SARS-CoV-2 has emerged as a promising target for antiviral therapeutics due to its critical role in viral replication and immune evasion. In this study, a comprehensive screening effort is aimed at identifying novel inhibitors of PLPro from Natural Product Library at the Sarawak Biodiversity Centre. To streamline this process, we have integrated Liquid Chromatography Mass Spectrometry (LCMS)- based dereplication for compound identification to expedite the discovery process. Leveraging 711 crude extracts and 2,844 pre-fractionated extracts obtained from diverse plant sources, we implemented a rigorous selection process. This method entailed a stringent cutoff strategy that combined z-prime analysis with a 2-standard deviation threshold to pinpoint potential hits. Screening for Papain-like Protease inhibitor yielded 81 active extracts out of 3,555 crude and pre-fractionated samples, sourced from 34 plant species, demonstrating activity against the virus. The mass spectrometry data from these 81 active extracts were analysed using Target Analysis Screening Software (TASQ) against a library of 239 antiviral compounds. The dereplication process predicted 59 known antiviral compounds among 62 active extracts. Meanwhile, 19 active extracts did not correspond to the antiviral compound library, indicating the possible presence of novel compounds warranting further investigation. From this study, Phaius tankervilleae was found to exhibit potent activity against SARS-CoV-2 PLPro (96% inhibition at 50 μg/mL) with predicted bioactive compound, tryptanthrin via TASQ analysis. The ability to identify a known compound, tryptanthrin in Phaius tankervilleae, which has been reported to inhibit SARS-CoV-2's PLPro, demonstrate that the methodology is reliable and could enable novel anti PLPro compounds to be discovered.

Abstract no.27

Calotropis gigantea (L.) Dryand. Stem bark extracts ameliorate spleen pathology in N-Nitrosodiethylamine-induced hepatocellular carcinoma in rats

1. Dr Piyarat Srisawang, Naresuan University, Phitsanulok
2. Mr Seksan Phopaed, Naresuan University, Phitsanulok

Spleen (脾; pí) is one of five vital solid organs in traditional Chinese medicines and plays a crucial role in the regulation of hemofiltration, purification, and immunity. Spleen Qi (气; qì) deficiency leads to various morbidities. Patients with HCC are associated with spleen pathology due to portal hypertension, cancer development, and metastasis. Calotropis gigantea (L.) Dryand. stem bark extracts (CG) have revealed a variety of anticancer mechanisms, but the protective effects on the spleen in HCC rats are still unclear. Therefore, the current study aims to investigate the protective effects of the dichloromethane (CGD) and the ethyl acetate (CGE) fractions of CG on the spleen pathological changes of N-Nitrosodiethylamine (DNEA)-induced HCC in the Sprague-Dawley rats over a 12-week experimental period. Metformin was considered a positive control. CG diminished the levels of liver injury and biliary tract function biomarkers, including AST, ALT, and ALP in serum. In liver morphohistology, decreased inflammatory foci, collagen deposition, and HCC markers Ki-67. CG demonstrated interesting effects on the spleen via improved spleen enlargement and percent spleen weight index. Improved the prominence of white pulp, adequate trabecula septa, and splenic sinuses proliferation. Decreased the PSR-positive area and expression of proinflammatory cytokines, including TNF-α and α-SMA in the spleen tissue. Moreover, there was a decrease in ROS accumulation. CG exhibited protective effects, alleviating the severity of HCC progression. Especially ameliorates oxidative stress, inflammation, and fibrosis of the spleen in the NDEA-induced HCC rat. This model may be advantageous as one of the potential anticancer agents as well as for relieving the spleen pathology caused by HCC progression. This research was funded by the Agricultural Research Development Agency (Public Organization) [Grant NO. CRP6505030030 and CRP6305031420], the graduate thesis funding from the Faculty of Medical Science, Naresuan University, Phitsanulok, Thailand [Grant NO. 65062454], and Center of Excellence for Innovation in Chemistry (PERCH-CIC) [Grant NO. NUPMEM65/65-001]. Key Words: Spleen, Hepatocellular carcinoma, N-Nitrosodiethylamine, Metformin, Calotropis gigantea (L.) Dryand. stem bark extract

Abstract no.28

Calotropis gigantea (L.) Dryand. stem bark extract exhibited a protective effect against hepatocellular carcinoma in rats induced with diethylnitrosamine

1. Dr Piyarat Srisawang, Naresuan University, Phitsanulok
2. Ms Pattaraporn Chaisupasakul, Naresuan University, Phitsanulok

Hepatocellular carcinoma (HCC) is a cause of cancer deaths globally. Conventional treatments including radiotherapy and chemotherapy have limited effectiveness, as they damage normal cells and cause adverse effects. Calotropis gigantea (C. gigantea) has been used in traditional Chinese and Ayurvedic medical treatments for various diseases, including cancer. This study aimed to investigate the anti-cancer effect of the C. gigantea stem bark extract ethyl acetate fraction (CGEtAc) in vitro and HCC rat model. MTT assay was used to investigate cell viability. Annexin V/Propidium iodide was used to measure apoptosis. In animal model, male Sprague-Dawley rats were injected of DEN via intraperitoneal injections (i.p.) to induce HCC and subsequently treated with CGEtAc low dose 2 mg/kg/BW (CGEtAcL) and CGEtAc high dose 4 mg/kg/BW (CGEtAcH) i.p. 3 times per week for 12 weeks followed by DEN injection. Histopathological examinations, including H&E staining, while immunohistochemistry evaluated hepatocyte proliferation via Ki-67 expression. CGEtAc enhanced cytotoxic effect with an IC50 of 805.10±64.35 µg/mL and enhanced apoptosis in HepG2 cells. In HCC rat, neither CGEtAcL nor CGEtAcH administration altered body weight or liver weight compared to HCC groups. CGEtAcL and CGEtAcH treatment resulted in the improvement of hepatic damages, as evidenced by the reduction in levels of AST and ALT compared to the HCC group. Histological evaluation confirmed the amelioration of hepatic necrosis, inflammation, and proliferation of liver cancer cells, as indicated by the suppressed expression of Ki-67. These findings highlight the potential of CGEtAc as a preventive agent for liver cancer in future clinical therapy. This study was funded by the Agricultural Research Development Agency (Public Organization) [Grant NO. CRP6505030030 and CRP6305031420], SP and PS received grant supported from National Science Research and Innovation Fund (NSRF) of Thailand [Grant NO. R2564B007], AW [Grant NO. R2564B033]. SP, PS and DP received partial support from the Global and Frontier Research University Fund, Naresuan University [Grant NO. R2567C003]. Key Words: Hepatocellular carcinoma, HepG2, diethylnitrosamine, Calotropis gigantea stem bark ethyl acetate fraction, Apoptosis

Abstract no.29

Potential Applications of Calotropis gigantea (L.) Dryand. Stem Bark Extract in Anticancer Therapy: In Vitro and In Vivo Models

1. Dr Piyarat Srisawang, Naresuan University, Phitsanulok

The pharmacological use of Calotropis gigantea (L.) Dryand. (C. gigantea) in traditional medicine has been well-documented, with scientific studies highlighting its various parts' specific anticancer potential due to its rich content of cardenolides and other secondary metabolites. Our research focused on the therapeutic applications of the stem bark of C. gigantea. Validating the ethnopharmacological efficacy of C. gigantea offers advantages in cancer treatment and enriches existing knowledge, potentially supporting future clinical applications. Utilizing its stem bark is particularly noteworthy, as it does not interfere with agricultural processes or the market demand for the plant's flowers in Thailand. We investigated the secondary metabolites in various extract fractions of C. gigantea and their anticancer properties. The ethanolic extract (CGEtOH) had the highest calotropin content, the dichloromethane extract (CGDCM) had significantly levels of triterpenoid, flavonoid, and the cardenolide calactin, the ethyl acetate extract (CGEtOAc) contained the highest total cardiac glycoside and phenolic content, and the water extract (CGW) had the highest alkaloid content. CGDCM and CGEtOAc demonstrated greater anticancer potency in HCT116 cells compared to HT-29 cells. Combining CGDCM with 5-fluorouracil at sub-IC50 concentrations resulted in a synergistic apoptotic effect in HCT116 cells, mediated by the induction of reactive oxygen species and the suppression of ATP production. CGDCM also showed potent anticancer effects against HepG2 cells and enhanced activity when combined with doxorubicin (DOX) at sub-IC50 concentrations. In vivo, CGDCM combined with DOX demonstrated a potent anticancer effect against diethylnitrosamine-induced hepatocellular carcinoma in rats, reducing apoptosis-induced inflammation, fibrosis, and hepatocarcinogenesis. These findings provide foundational scientific knowledge supporting the use of C. gigantea extracts for further animal studies, reducing the occurrence of cancers originating from various organs, and mitigating complications in high-risk diseases, including diabetes. Ultimately, this research advances the potential for clinical anticancer applications. Funding: This work was supported by National Science Research and Innovation Fund (NSRF) of Thailand [Grant NO. R2564B007 to SP and PS], the Agricultural Research Development Agency (Public Organization), Thailand [Grant NO. CRP6505030030 and PRP6605031530 to SP and PS]. Some parts of this work were published in these references: Winitchaikul T. et. al., PLoS One. 2021 Aug 3;16(8): e0254392. doi: 10.1371/journal.pone.0254392. Sawong S. et al.,

Scientific Reports. 2022 Jul 15;12(1):12151. doi: 10.1038/s41598-022-16321-0. Key Words: Calotropis gigantea (L.) Dryand., Stem bark, Cancer, Diethylnitrosamine

Abstract no.30

Bioassay guided isolation of caffeoylquinic acids from the leaves of Ilex pubescens Hook. et Arn. and investigation of their anti-influenza mechanism

1. Prof Pang-Chui Shaw, The Chinese University of Hong Kong, Hong Kong SAR
2. Dr Fan Wang, The Chinese University of Hong Kong, Hong Kong SAR

Influenza virus infects millions of people every year around the world, greatly threatening global health. Emergence of resistant strains urges us to develop more new anti-influenza agents. Ilex pubescens belongs to Aquifoliaceae family, and has been traditionally used in China to clear heat and treat cold. In Southern China, it is a common herbal tea ingredient for heat clearance and anti-inflammation. Our results showed that 50% ethanol extract of Ilex pubescens leaves was effective against influenza virus infected cells. Based on bio-assay guided isolation, eight caffeoylquinic acids (CQAs) with anti-influenza activities were obtained and identified from this plant. They were found to inhibit neuraminidase (NA) of influenza virus. Tyr 100, Gln 412 and Arg 419 were found to be important for 3,4,5-TCQA and NA interaction. In addition, 3,4,5-TCQA downregulated the immune responses in H292 cells, and reduced the cytokine production in Pr8-infected cells, through toll like receptor (TLR) signaling pathway. 3,4,5-TCQA also showed synergistic effect against influenza virus with oseltamivir acid. This work provided scientific evidence on the use of Ilex pubescens for treating influenza virus infection, and laid the foundation for the development of CQA derivatives as potential antiviral agents.

Abstract no.31

Baicalein as a Potential Therapeutic Agent for Rheumatoid Arthritis: Enhancing Treg Cell Function and Alleviating Inflammation

1. Prof Xing-Xing Fan, Macau University of Science and Technology, Macao SAR
2. Mr Ren-Jie Zhao, Macau University of Science and Technology, Macao SAR

Abstract Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by synovial inflammation and cartilage damage. Dysfunctional regulatory T cells (Tregs) have been emphasized in RA development and progression, contributing to the breakdown of immune tolerance. This study explores the potential of baicalein, a natural flavonoid derived from Scutellaria baicalensis, to restore the function of Treg cells by increasing the expression of Foxp3, maintaining immune tolerance, and subsequently alleviating RA symptoms. In vitro experiments showing baicalein's ability to increase Foxp3 expression in CD4+ T cells. Highlighting the concentration-dependent nature of this effect, its potential implications in enhancing Treg cell population and functionality are examined. Furthermore, an animal study was conducted on adjuvant-induced arthritis (AIA) rats. Administering celiac baicalein (10mg/kg), significantly reduced foot swelling and bone damage, indicating the therapeutic potential of baicalein in RA. This study represents a significant advancement in understanding the therapeutic potential of baicalein in RA treatment. By enhancing Treg cell function via increased Foxp3 expression in CD4+ T cells, baicalein shows promise in alleviating inflammation and reducing the severity of RA symptoms. Further research into the mechanisms and clinical applications of baicalein is warranted to translate these findings into effective therapeutic options for patients with RA. Acknowledgments This work was funded by the Macau Science and Technology Development Fund project (Grant no. 0058/2020/A2) granted to Dr. Xing-Xing Fan.

Abstract no.32

Brevilin A exhibits anticancer activity against hepatocellular carcinoma through targeted inhibiting FEN1

1. Dr Guo-Qing Chen, Hong Kong Polytechnic University Shenzhen Research Institute, Shenzhen
2. Mrs Jia-Wen Chen, Hong Kong Polytechnic University Shenzhen Research Institute, Shenzhen
3. Prof Sibao Chen, Hong Kong Polytechnic University Shenzhen Research Institute, Shenzhen

Since hepatocellular carcinoma (HCC) is one of the most prevalent cancers and the primary cause of cancer-related mortality, it is very essential to find novel, efficient treatments. Brevilin A (BA), a sesquiterpene lactone compound derived from the traditional Chinese medicine Elephantopus scaber, has demonstrated anticancer effects in various cancers, including lung, gastric, and triple-negative breast cancers. Therefore, the anticancer effects of BA in HCC deserve further exploration. In our study, we initially investigated the anti-HCC activities of BA both in vivo and in vitro. BA significantly reduces HCC cell viability and proliferation while inducing apoptosis and G2/M phase cell cycle arrest. RNA sequencing and subsequent analysis revealed flap endonuclease 1 (FEN1) as a potential major target of BA in HCC treatment. Further bioinformatics study indicated that FEN1, a structure-specific nuclease required for DNA replication and repair, is highly expressed in HCC. The high expression of FEN1 is strongly related to a worse prognosis and shorter survival time in HCC patients, implying that FEN1 may be a suitable therapeutic target. We also performed molecular dynamics simulations, surface plasmon resonance (SPR), and cellular thermal shift assay (CETSA) to demonstrate the interaction between BA and FEN1. After confirmed that BA binds to FEN1, we use the enzyme-linked immunosorbent assay (ELISA) to show that this binding inhibits FEN1 activity. Furthermore, BA was discovered to reduce FEN1 expression in HCC cells, and overexpression of FEN1 reduced BA's effects on cell viability, proliferation, apoptosis, and cell cycle, emphasizing the importance of FEN1 in BA's anti-HCC mechanism. In conclusion, our findings suggest that BA exerts its anti-HCC actions by targeting FEN1. Future research will focus on understanding how the BA-FEN1 interaction influences FEN1 expression to produce anti-HCC effects, as well as investigating the downstream pathways involved.

Abstract no.33

Molecular mechanism of autophagy induced by pseudopodiosgenin in colorectal cancer cells

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Pseudoprotodioscin (PPD), an effective ingredient of Dioscorea spongiosa J. Q. Xi,M. Mizuno etW. L. Zhao, has been reported that exerted its antitumor potential in endometrial cancer. However, the effect and molecular mechanism of PPD in colon cancer are largely unknown. Here, we found that PPD induced cell death and suppressed cell proliferation in colon cancer cells. We demonstrated that autophagy was the predominant method that contributed to PPD-induced cell death of colon cancer in vitro and vivo for the first time. The levels of AMPK, p-AMPK, PERK, p-PERK, GRP78 were examined using western blot. In order to detect the relationship between PPD-induced autophagy and AMPK pathway, cells were treated with different concentrations of PPD to detect the expression level of autophagy protein, cell proliferation protein LC-3B, Beclin-1, p-mTOR. PPD could induced remarkable increases in Annexin V/PI positive cells in a dose dependent manner. In addition,westernblot assays suggested that PPD treatment increased caspase-dependent apoptosis, as it induced higher levels of cleaved-caspase 3, cleaved-caspase 9 and Bax compared to individual treatments PPD increased the levels of p-PERK and phosphorylated , as well as the protein levels of GRP78 and CHOP. PPD also induced AMPK activation in colon cell. PPD treatment significantly inhibited tumor growth in mice bearing HCT116 tumor xenografts. PPD treatment activated AMPK and promoted apoptosis in vivo. The treatment with PPD did not significantly affect the mice weight. In summary, the results of this study show that PPD inhibits the proliferation, migration of CRC cells in vitro and in vivo, as well as promoting the apoptosis of CRC cells, with no obvious toxicity to normal cells and organs. The results also reveal that PPD activates AMPK pathway to induce endoplasmic reticulum stress in CRC cells, which is a possible mechanism for the pharmacological effects of PPD on CRC cells.

Abstract no.34

Huang Zhi Duo Tang Alleviated Osimertinib Resistance in LAD Cells by Targeting Ferroptosis-associated lncRNA TFAP2A-AS1/GPX4 Axis

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#: Contributed equally. *: Correspondence should be addressed to Shanshan Wu, wushsh@gdmu.edu.cn Drug resistance poses a significant challenge in tumor treatment, particularly in lung adenocarcinoma (LAD). Ferroptosis, a novel type of cell death, has emerged as a promising approach for overcoming drug resistance, but the specific mechanisms remain unclear. This study investigates the role of ferroptosis-associated long non-coding RNAs (lncRNAs) in Osimertinib-resistant LAD cells. Using bioinformatics and machine learning algorithms (SVM-RFE, RF, GLM), lncRNA TFAP2A-AS1 was identified as significant in both ferroptosis and LAD. Its localization was confirmed via FISH assays and RT-qPCR. Osimertinib-resistant LAD cells (H1975/OR, PC9/OR) were established by chronic exposure of gradually increasing osimertinib doses. Various methods (MTT, colony formation, flow cytometry) were used to validate the biological functions of TFAP2A-AS1. Simultaneously, MOE2022 docking revealed potential small molecules targeting TFAP2A-AS1 truncations (406-597nt and 784-1133nt). Three core ferroptosis-related lncRNAs (TFAP2A-AS1, LINC01281, LINC00592) were identified first. TFAP2A-AS1 expression was significantly higher in osimertinib-resistant LAD cells and tissues. High TFAP2A-AS1 expression correlated with increased osimertinib resistance while knocking down its expression increased sensitivity to osimertinib. Treatment with ferroptosis inhibitor Erastin enhanced osimertinib sensitivity in LAD cells. Additionally, TFAP2A-AS1 overexpression decreased lipid ROS, ferrous ion, MDA, and GSH levels. TFAP2A-AS1 was found to bind with GPX4, a key ferroptosis regulator via RNA pull down assay. Using MOE2022 docking, two truncated forms of TFAP2A-AS1 demonstrated favorable binding affinities with Huang Zhi Duo Tang and quercetin. The 406-597nt form showed stable binding with Huang Zhi Duo Tang, and the 784-1133nt form interacted favorably with quercetin. Conclusively, lncRNA TFAP2A-AS1 induces osimertinib resistance in LAD cells by hindering ferroptosis through its interaction with GPX4. Targeting TFAP2A-AS1 with compounds like Huang Zhi Duo Tang and quercetin could overcome osimertinib resistance, suggesting a promising therapeutic strategy for LAD treatment. Further research into TFAP2A-AS1's mechanisms is essential for developing advanced therapeutic strategies for osimertinib-resistant LAD.

Abstract no.35

Uncover the Anticancer Potential of Lycorine

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Abstract Background: Natural products have a long history in drug discovery. Lycorine (LYC) is an alkaloid derived from Amaryllidaceae plants, demonstrating significant pharmacological potential. LYC and its hydrochloride form, lycorine hydrochloride (HLYC), have shown outstanding anticancer effects both in vitro and in vivo. Purpose: This review aims to comprehensively summarize recent research advancements regarding the anticancer potential for the clinical utilization of LYC and HLYC. It intends to elucidate current research limitations, optimization strategies, and future research directions to guide clinical applications. Methods: Various databases were systematically searched for relevant articles using keywords such as lycorine, cancer, pharmacokinetics, and toxicity. The retrieved literature was then categorized and summarized to provide an overview of the research advancements in the anticancer potential of LYC and HLYC, covering anticancer activities and mechanisms, direct binding targets, pharmacokinetics, toxicity, and potential clinical application. Results: LYC and HLYC have demonstrated significant anticancer activities against various types of cancer both in vitro and in vivo, employing diverse mechanisms such as inducing cell cycle arrest, triggering cellular senescence, regulating programmed cell death, inhibiting angiogenesis, suppressing metastasis, and modulating immune system. Furthermore, pharmacokinetic profiles and toxicity data are summarized. Additionally, this review discusses the druggability, limitations, optimization strategies, and target identification of lycorine, offering insights for future preclinical studies. Conclusion: The anticancer effects and safety profile of LYC and HLYC suggest promising potential for clinical applications. Optimization methods such as structural modifications and formulation adjustments for LYC and HLYC are expected to enhance their druggability. Keywords: lycorine, lycorine hydrochloride, anticancer mechanism, target, pharmacokinetics Acknowledgements This study was supported by the Science and Technology Development Fund, Macau SAR (File No. 0015-2022-A1 and 005/2023/SKL) and the Internal Research Grant of the State Key Laboratory of Quality Research in Chinese Medicine, University of Macau (File No. SKL-QRCM-IRG2023-011).

Abstract no.36

A novel polysaccharide with a galactose backbone from the processed Polygonati Rhizoma: Structural characterization and mechanisms of macrophage immunomodulatory activity

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This study isolated and characterized a purified polysaccharide (SRP-1) with a galactose backbone from processed Polygonati Rhizoma with black beans. The Mw of SPR-1 was 36,22 Da, which was mainly composed of galactose (61.9%), glucose (27.5%), and galacturonic acid (10.6%). The SPR-1 consists of a main chain and two branched chains, where the main chain was [(4)-β-D-Galp-(1]9→4,6)-β-D-Galp-(1→4)-α-D-GalpA-(1→4)-α-D-GalpA-(1→4)-α-D-Glcp-(1→4,6)-α-D-Glcp-(1→4)-α/β-D-Glcp, the two branched chains were R1: β-D-Galp-(1→3)-β-D-Galp-(1→ the →4,6)-β-D-Galp-(1→ of main chain via O-6, R2: α-D-Glcp-(1→6)-α-D-Glcp-(1→ connected to the →4,6)-α-D-Glcp-(1→ of main chain via O-6. Immunomodulatory assays showed that SPR-1 not only induced the secretion of nitrous oxide and cytokines (i.e. IL-1β and TNF-α), but also promoted the phagocytic activity of cells, suggesting that SPR-1 possessed immunomodulatory activity. Furthermore, molecular docking and isothermal titration calorimetry analysis further indicated that SPR-1 exhibited a strong binding affinity to the MD2 with the equilibrium dissociation constant (KD) of 18.8 μM. It was suggested that SPR-1 activated an innate immune response by promoting Toll-like receptor 4 signaling and downstream responses. Our research demonstrated that the SPR-1 has a promising candidate from PRWB for the TLR4 agonist to induce an effective immune response, and also provided an easily accessible way that can be used for PR deep processing.

Abstract no.37

In vitro investigations of the potential natural products as B7-H3 inhibitors in breast cancer

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Breast cancer has become the most frequent and the leading lethal cancer in women globally. Immune checkpoint molecule B7-H3 is considered as a promising target for breast cancer immunotherapy because it could downregulate immune response and participate in the occurrence and metastasis of breast cancer. In this study, we investigated the relationship between the B7-H3 gene and anti-tumor immunity in breast cancer and developed a method for identifying natural compounds with B7-H3 inhibitory activities. Bioinformatic analysis showed that the mRNA levels of the B7-H3 gene in tumor samples were significantly elevated in the cohorts from the GEO and TCGA databases ($P < 0.001$). The xCell and TISIDB databases showed that B7-H3 levels were positively related to the infiltration of macrophages, monocytes, T helper (Th)1 cells and Th2 cells, and showed a negative correlation with the infiltrating levels of CD8+ cytotoxic T cells. For the screening of potential B7-H3 inhibitors in breast cancer, human MCF-7 breast cancer cell line was subjected to B7-H3 inhibitor screening because of its significant expression (MFI = 1802.67 ± 85.2, $P < 0.001$). Human breast cancer MCF-7 cells were treated with eight compounds (combretastatin A4, resveratrol, piceatannol, polydatin, dihydroartemisinin, astragaloside IV, artemether, and artesunate) with non-toxic concentrations. Among the eight compounds, dihydroartemisinin and artesunate significantly decreased the expression of B7-H3 on MCF-7 cells upon 48h treatment ($P < 0.01$), and the values of MFI fold change to control were 0.51 ± 0.1 and 0.45 ± 0.1, respectively. Furthermore, dihydroartemisinin and artesunate showed concentration-dependent inhibitory effects on B7-H3 expression. This study demonstrated the relationship between B7-H3 gene expression and anti-tumor immunity in breast cancer, and developed a screening method for compounds with inhibitory effects on B7-H3 expression. Among eight natural products, dihydroartemisinin and artesunate could significantly reduce the B7-H3 expression of MCF-7 cells (both $p < 0.05$).

Abstract no.38

Development of the Immunopharmacognostic Interventions against prostate cancer.

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3. Ms Tzu-Ting Su, Academia Sinica, Taipei
4. Dr Shen-Chieh Wang, Academia Sinica, Taipei
5. Mr Tai-Yang Chen, Academia Sinica, Taipe
6. Ms Ju-I Chang, Academia Sinica, Taipei
7. Ms Sravya Mandava, Academia Sinica, Taipei
8. Prof Pei-Wen Hsiao, Academia Sinica, Taipei

The most challenge for treating prostate cancer (PCa) is the high incident rate (65~75%) of bone metastasis. The feature of PCa as the “cold” immune landscape contributes to less or even no responsiveness of immunotherapies for metastatic PCa. Therefore, PCa remains a challenge as a target for immunotherapies to achieve a decent responsive rate. Phyto-Y is a semi-purified plant extract from a medicinal Asteraceae plant. However, whether and how Phyto-Y can elicit tumor immunogenicity and recognition remains unclear. The results showed that Phyto-Y caused a significant reduction on cell viability of RM1 cells by MTT assay. HMGB1 and ATP release, the markers for immunogenic cell death (ICD), was found significantly increased in test RM1 cells by Phyto-Y monotreatment and further enhanced in the presence of Docetaxel. Besides, we observed Phyto-Y significantly increased autophagic vacuoles and sequestosome 1, indicating autophagy was induced by Phyto-Y in RM1 cells. Next, we test whether tumor cell lysates (TCL) collected from Phyto-Y-treated RM1 cells can incite better DC-T immune responses. We found the Phyto-Y resultant TCL increased CD86 expression in DC, increased T lymphocyte cytotoxic activity and retarded the tumor growth in RM1 tumor models. On the other hand, Phyto-Y in vivo treatment decreased suppressive markers and increased MHCII expression in intratumoral DC population. To sum up, this study is to address the potential development of a full-defined phyto-candidates (Phyto-Y as a lead example here) as an immunopharmacognostic Interventions through eliciting tumor immunogenicity, regulating immune status of primary and bone metastatic tumor microenvironment, and thus synergizing immunotherapies, i.e. cancer vaccine & cell therapy, against metastatic PCa.

Abstract no.39

Therapeutic Effect of Traditional Chinese Medicine Formula on Pulmonary Fibrosis Animal Model

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Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death globally, primarily due to airway inflammation, cause chronic cough, airway restriction, leading to a decline in lung function, with no specific curative treatment currently available. Oxidative stress and oxidative/antioxidant imbalance play crucial roles in the pathogenesis and progression of COPD. Our research team previously conducted studies on the traditional Chinese medicine formula SS-1 using cell models, animal models, and human clinical trials. The results showed its potential in treating pulmonary fibrosis, demonstrating multiple effects such as immune modulation, anti-inflammatory, and anti-fibrotic properties, particularly in autoimmune disease dry syndrome. In this study, antioxidant experiments (DPPH, Folin-assay) were performed to test the antioxidant capacity of SS-1, and in cell models, SS-1 was validated for its antioxidant activity, cell toxicity, and anti-inflammatory capabilities against the oxidative stress induced by LPS in macrophages. The therapeutic efficacy of SS-1 was evaluated in a pulmonary fibrosis animal model, and metabolomics analysis was applied to investigate the impact of this Chinese herbal formula on the metabolism of pulmonary tissues in fibrotic mice, as well as its potential mechanisms of action.

Abstract no.40

A study on the effect of medicinal plant-derived extracts on dendritic cellmediated immune responses.

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4. Ms Tzu-Ting Su, Academia Sinica, Taipei

5. Prof Lie-Fen Shyur, Academia Sinica, Taipei

Dendritic cells play a crucial role in the immune system, responsible for initiating immune responses and guiding immune cells to combat infections and diseases. Pharmacologically active ingredients in herbal medicines have long been regarded as a rich source of therapeutic leads in drug discovery on the basis of the anecdotal and historic practical experiences. The presented study is to explore immunotherapeutic leads in drug discovery from active ingredients in phytomedicines, to provide an immunotherapeutic intervention via targeting key antigen-presenting cells, specifically dendritic cells. Our preliminary results showed that the one of medicinal plant-derived extracts – Phyto-X significantly enhanced the maturation and key cytokines secretion of dendritic cells and promoted the subsequent activation and proliferation of effector T cells. Our study provides important information for exploring the applications of medicinal plant-derived extracts for immunomodulatory supplements.

Abstract no.41

Discovery of Salvianolic acid C as a novel SIRT5 inhibitor with potential application in tumor immunotherapy

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Abstract: Sirtuin 5 (SIRT5) is believed to modulate metabolic activities and signal transduction of the cell by regulating lysine post-translational modification (PTM) of proteins. Unraveling how SIRT5 regulates anti-tumor immunity may reveal new opportunities for anti-tumor therapeutics. Sirt5-KO C57BL/6 mice exhibited better tumor control in B16F10 melanoma model. Through scRNA-seq of B16F10 tumor-infiltrating CD45+ immune cells, we found a novel CD8 T cell subpopulation characterized by high expression of type I interferon gene signature (IFN-I hi CD8 T cells) was specifically enriched in Sirt5-KO mice. The intratumoral CD8 T cells in Sirt5-KO mice had superior functionality and lower terminal exhaustion. Antibody depletion revealed that slower tumor growth of Sirt5-KO mice was mediated by CD8 T cells. We screened a library of 1871 natural compounds derived from traditional Chinese medicine for SIRT5 inhibitors using bio-layer interferometry (BLI) high-throughput screening. We discovered Salvianolic acid C (SalC) as a novel inhibitor of SIRT5 enzymatic activity. It had binding affinity to recombinant human SIRT5 with a dissociation constant (KD) of 35.06 μM. Its IC50 for inhibiting SIRT5 desuccinylase activity was 21.95 μM. Cellular Thermal Shift Assay (CETSA) confirmed that it was cell-permeable and bound to SIRT5 protein in THP-1 cells. Molecular docking revealed that salvianolic acid C binds to the histidine 158 residue of SIRT5, critical for its enzymatic function. This study, for the first time, unravels that SIRT5 deficiency augments anti-tumor immunity by regulating CD8 T cells. SalC, a polyphenolic compound from Danshen, is identified as a SIRT5 inhibitor for the first time. This work will further our understanding of the physiological and pathological function of SIRT5 and provide rationale for establishing SIRT5 as a therapeutic target in certain cancers.
Keywords: SIRT5; tumor; CD8 T cells; type I interferon; salvianolic acid C Acknowledgement: Funded by Macau Science and Technology Development Fund (FDCT 048/2018/A2; 0113/2023/RIA2)

Abstract no.42

Shentong Zhuyu Decoction Alleviates Gouty Arthritis Through Inhibiting MAPK/NLRP3/IL-1β Signaling Pathway

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OBJECTIVE: Gouty arthritis (GA) is an acute, intense inflammation of the joints with severe pain, redness and swelling as the main clinical manifestation. In clinical practice, this greatly affects the quality of life of patients. Shentong-Zhuyu decoction (STZYD) is a classical traditional Chinese medicine (TCM) formula with centuries of clinical experience and has a wide range of pharmacological activities such as anti-inflammatory and antioxidant effects. Previous studies have shown that STZYD can improve GA symptoms, but its main pharmacological mechanism is not yet clear. Methods: STZYD was administered orally in monosodium urate (MSU)-induced GA mice. The degree of paw swelling, paw remission latency, inflammatory cell infiltration and inflammatory cytokine production were assessed in different groups of mice. The mechanism of STZYD in the treatment of GA was investigated by network pharmacological analysis, combined with Western blot validation. Results: Oral administration of STZYD reduced paw swelling and improved thermal latency of paw withdrawal in GA mice, accompanied by a reduction of inflammatory cell infiltration in paw tissue. Hematoxylin Eosin (H&E) staining of kidney and liver tissue showed that STZYD was safer than colchicine. In addition, STZYD reduced the number of M1-like macrophages and the mRNA and protein levels of interleukin-1β (IL-1β), interleukin 6 (IL-6), and tumor necrosis factor-α (TNF-α) in the foot of GA mice. Network pharmacological analysis suggested that the mitogen-activated protein kinase/nucleotide-binding oligomerization domain-like receptor family containing pyridine domain 3 (MAPK/NLRP3) pathway may be a target of STZYD to inhibit macrophage activation; indeed, Western blot results confirmed that STZYD inhibited the phosphorylation of P38, extracellular regulated protein kinases 1/2 (ERK1/2) and c-JunN-terminalkinase (JNK), and reduced NLRP3, caspase-1 and active IL-1β in the paw tissue of GA mice levels. Conclusion: STZYD attenuates joint inflammation in MSU-induced gouty arthritis in mice by a mechanism related to inhibition of the MAPK/NLRP3/IL-1β signaling pathway. Keywords: Gouty arthritis; Shentong Zhuyu decoction; Network pharmacology analysis; Pharmacological mechanism

Abstract no.43

Identification of a novel proteasome inhibitor Xerophenone H and its anticancer effect on lung cancer

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Introduction: Polycyclic polyisoprenylated acyl resorcinols (PPAPs) exhibit a unique chemical structure and a diverse range of pharmacological activities. This study identified a novel PPAP, Xerophenone H (XeH), derived from the fruit peel of Garcinia multiflora Champ. ex Benth. (Clusiaceae), which demonstrated significant anti-lung cancer effect. The objective of this study is to evaluate the anticancer effects of XeH on lung cancer and to elucidate the mechanism by which XeH induces cell death in lung cancer cells. Materials and Methods: The in vivo efficacy of XeH was evaluated using a subcutaneous tumour model. XeH-induced cell death was confirmed using methods including Transmission Electron Microscope (TEM). The anticancer mechanism of XeH was further explored using RNA-seq. Simultaneously, the target of XeH action was confirmed using molecular docking and cellular thermal shift assay (CETSA) experiments. Results: XeH inhibited the growth of a wide range of cancer cells. A subcutaneous tumour model confirmed the in vivo anticancer effect and reliable safety profile of XeH. Phenotypically, XeH treatment induced apoptosis and paraptosis in lung cancer cells. Mechanistically, XeH was idenitified to inhibit proteasome activity and induce protein aggregate formation by interacting with PSMB5. Conclusions: XeH, as a novel proteasome inhibitor, exhibits anti-lung cancer activity both in vitro and in vivo. XeH directly interacts with the proteasome subunit PSMB5, thereby inhibiting the ubiquitin-proteasome degradation pathway, leading to apoptosis and paraptosis in lung cancer cells. Acknowledgements： This study was supported by the Science and Technology Development Fund, Macau SAR (File No. 0015-2022-A1 and 005/2023/SKL), and University of Macau (File No. MYRG-GRG2023-00160-ICMS-UMD).

Abstract no.44

Berberine triggers the ablation of immunosuppression on tumor microenvironment and enhances the anti-tumor efficacy

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The tumor microenvironment (TME) consists of a heterogeneous tumor and immune cells, which cause the occurrence and progression of tumors. Therefore, identifying effective agents to strengthen host anti-tumor immune response is deeply in need. In this study, we found that berberine(BBR) could significantly promoted the increase of pro-inflammatory M1 macrophage, while decreased the anti-inflammatory M2 subset, which subsequently induced T-cell activation and its tumor killing ability. In vivo study further demonstrated that berberine could remarkably inhibit the tumor size and prolong the overall survival time of animals. Furthermore, our previous studies have shown that tumor vaccine Pseudomonas aeruginosa mannose-sensitive-hemagglutinin (PA-MSHA) injection is able to promote T-cell activation in vitro and in vivo. Thus, we took it as an adjuvant to further stimulate anti-tumor response of berberine. The combination treatment dramatically improved the killing efficacy of berberine in tumors. Taken together, the combination of PA-MSHA and BBR is a potential strategy to improve the clinical response rate for non-small cell lung cancer treatment. Acknowledgements: This work was funded by FDCT project grant to Dr. Xing-Xing Fan (File no. 0038/2023/RIB2)

Abstract no.45

Prosapogenin CP4 exacerbates mitophagy to induce apoptosis by regulating AMPK-mTOR and PINK1/Parkin pathways in non-small cell lung cancer

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Non-small cell lung cancer (NSCLC) remains a leading cause of cancer-related deaths, necessitating novel therapeutic agents. This study investigated the anti-cancer effects and mechanisms of Prosapogenin CP4 (PCP4) from Anemone rivularis. PCP4 was identified for its ability to inhibit A549 cell proliferation and activate autophagy. In vitro assays showed PCP4 significantly inhibited proliferation, invasion, and migration of A549 and H1299 cells, while sparing normal MRC-5 cells. Mechanistically, PCP4 induced mitochondrial damage, characterized by increased fragmentation, reduced mass, decreased membrane potential, and elevated ROS production, leading to apoptosis through caspase activation and Bax-dependent pathways. Additionally, PCP4 activated mitophagy via the AMPK-mTOR and PINK1/Parkin signaling pathways, enhancing autophagic flux. Moreover, the inhibition of mitophagy by specific inhibitors partly reversed the apoptosis induced by PCP4. In vivo, PCP4 treatment significantly reduced tumor growth in A549-bearing mice by promoting apoptosis and mitophagy without causing systemic toxicity. In conclusion, this study presents that PCP4 identified from Anemone rivularis exerts its anti-cancer effects by inducing excessive mitophagy via the AMPK-mTOR and PINK1/Parkin pathways, which further promote cell apoptosis in NSCLC. These findings suggest that PCP4 exerts its anti-cancer effects in NSCLC, highlighting its potential as a therapeutic agent for lung cancer.

Abstract no.46

Natural small-molecules reduce the drug resistance of renal cell carcinoma mediated by Xeroderma Pigmentosum Complementation Group C (XPC) deficiency

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2. Dr Ruihong Chen, Guangdong Medical University, Dongguan

Renal cancer is insensitive to radiotherapy or most chemotherapies. While the loss of the XPC gene was correlated with drug resistance in colon cancer, the expression of XPC and its role in the drug resistance of renal cancer have not yet been elucidated. In this study, we discovered that XPC gene expression was significantly reduced in renal cancer tissue compared with its adjacent tissue. Clinical analysis of TCGA database also identified the downregulated level of XPC gene in renal tumor tissue of stage IV patients with cancer metastasis, which was also correlated with their lower survival rate. 6 natural small-molecules derived from herbal plants including tectorigenin, pinostilbene, D-pinitol, polygalasaponin F, atractylenolide III and astragaloside II significantly enhanced XPC expression in two renal cancer cell types. Combinational treatment of the identified natural compound with the treatment of FDA-approved drug, further confirmed the up-regulation of XPC gene expression can sensitize the two types of XPC-KD drug-resistant renal cancer cells towards the FDA-approved drugs. Mechanistic study confirmed that GSTP1/ROS axis was activated in drug resistant XPC-KD renal cancer cells. Therefore, the identified active natural small molecules may work as an adjuvant therapy for circumventing the drug-resistant phenotype in renal cancer via enhancement of XPC expression. Keywords: Drug-resistance; Natural small-molecules; Renal cancer; XPC; GSTP1 FDCT project code: 0124/2022/A; 002/2023/ALC; 0081/2021/A

Abstract no.47

Evaluating the efficacy of chlorogenic acid and its containing herbal extracts to impede multi-variants of SARS-CoV-2 and H1N1 viral infection.

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3. Dr Chun-Tang Chiou, National Research Institute of Chinese Medicine, Ministry of Health and Welfare, Taipei

COVID-19 and Influenza are common upper respiratory tract infectious diseases that cause massive numbers of cases and mortality globally. Moreover, these viruses constantly produce variants, leading to the potential loss of vaccine efficacy. As a result, using herbal medicine as an intervention for viral infections provides an alternative route of protection. Chlorogenic acid is a common active ingredient in herbs or foods used to combat COVID-19 or Influenza. However, whether chlorogenic acid can be used as an indicator to predict the plant extracts with anti-upper respiratory tract viral infection activity remains to be tested. The aim of the study is to compare the anti-viral infection activities of chlorogenic acid with two herbal extracts (Green coffee bean extract and Echinacea purpurea extract) against SARS-CoV-2 variants and H1N1 viruses. For the SARS-CoV-2 model, An ELISA-based trimeric spike protein binding assay, viral infection assay and molecular docking studies were employed. Plaque assay was used to evaluate for H1N1 viral infection. As a result, antibodies blocked spike protein binding with variants up to Omicron BA.2. Contrastingly, chlorogenic acid blocked binding with all variants of concerns except for the Delta variant. Green coffee bean and E. purpurea extracts provided full spectrum of blocking activity against all variants. Molecular docking results suggested that the binding of 3-CQA to Omicron BA.1, BA.2, and BA.4 but not δ spike protein causes steric hindrance and blocks the interactions between RBD and ACE2. The H1N1 plaque assay demonstrated that both chlorogenic acid and E. purpurea extracts can intervene in the infection of H1N1, but only chlorogenic acid affected post-infection. Green coffee bean extract did not provide any anti-viral activity against H1N1. In conclusion, phyto-materials appear to provide a wider spectrum of protection against viral infections. Chlorogenic acid, as an indicator, is more consistent in anti-SARS-CoV-2 activity than in anti-H1N1 activity. Key words: SARS-CoV-2, H1N1, chlorogenic acid, Echinacea purpurea, green coffee beans, COVID-19, Influenza, upper respiratory tract infectious diseases

Abstract no.48

Investigating the effect and mechanism of Blestriarene C against triple-negative breast cancer

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2. Mr YAJIE LU, Sichuan University, Chengdu

Abstract Background: Breast cancer is one of the leading causes of death among worldwide, especially for women. Particularly, triple negative breast cancer (TNBC) with lack of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 expression, tends to be more aggressive and metastatic compared to other types of breast cancer. It is notable that nature compounds from Chinese medicine gradually exert their significance in cancer treatment. Blestriarene C (BC) could be isolated from herb, Baiji. Based on our previous data, it is interesting to find that BC could inhibit breast cancer. The effect of BC on TNBC remains unknown. Objective: To investigate the effect and mechanism of action of BC against TNBC. Methods: The suppressive effects of BC on TNBC were investigated using CCK-8, transwell, and wound healing assays. Differential expression genes (DEGs) and proteins (DEPs) were screened through transcriptomics and proteomics, followed by KEGG pathway enrichment. Core genes were identified via dual-omics analysis and validated. Fe2+ assay was used to explore the effect of BC on ferroptosis in TNBC. Results: BC inhibited the proliferation, invasion, and migration of TNBC cells. Omics analysis combined with KEGG pathways indicated that the action of BC action on TNBC is enriched in ferroptosis, consistent with Fe2+ assay results. SESN2 was identified as the core gene mediating BC's therapeutic effects. Conclusion: BC suppresses TNBC in vitro, potentially through ferroptosis-related signaling pathways. Keywords: Blestriarene C, Triple negative breast cancer, Multi-Omics, Ferroptosis

Abstract no.49

Huangqi-Guizhi-Wuwu decoction restain immune tolerance and reducing inflammatory response to prevent collagen-induced arthritis.

1. Prof qianqian liang, Shanghai University of Traditional Chinese Medicine, Shanghai

Background:Rheumatoid arthritis (RA) is a common autoimmune disease characterized by erosive arthritis and multiple organ complications. The stage characterized by months or even years of autoimmune reactions and an increase in the concentration and range of autoantibodies, inflammatory cytokines, and chemokines before joint disease is called Pre-RA. At present, the means of intervening in the Pre-RA stage to inhibit the development of RA are not yet mature. HGWD has a certain alleviating effect on arthritis swelling in CIA mice, but research on its inhibition of arthritis development by regulating immune tolerance is limited. Purpose:The aim of this study is to explore the mechanism of HGWD in preventing the development of arthritis in CIA mice by restraining immune tolerance. Methods:Divide DBA/1 mice into normal group, model group, low-dose and high-dose HGWD. Oral administration of HGWD was administered after the first immunization in collagen induced arthritis mice until the second immunization was stopped. Observation of B lymphocytes, germinal center B cells, regulatory T cells, and helper T cells in mouse spleen and peripheral lymph nodes using flow cytometry to determine whether HGWD can reshape immune homeostasis. IL-17 was detected using Q-pcr and ELISA kits, IgG, Detect inflammatory factors and autoantibodies such as IgM to observe whether HGWD can inhibit inflammatory reactions and reduce the production of autoantibodies. Observe whether arthritis can be alleviated through arthritis scoring and pathological staining of mouse ankle joints. Results:The results indicate that HGWD can inhibit the proliferation of germinal center B cells, activate regulatory T cells and tolerance dendritic cells, inhibit helper T cells17, and thus regulate immune homeostasis. Additionally, HGWD can also reduce IL-17 and IL1-β ,IgG, and IgM. Conclusion:This study suggests that HGWD can inhibit the development of arthritis during the Pre-RA stage by reshaping immune homeostasis and inhibiting inflammatory responses.

Abstract no.50

Sphondin efficiently blocks HBsAg production and cccDNA transcription through promoting HBx degradation

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ABSTRACT Hepatitis B surface antigen (HBsAg) loss and seroconversion, which is considered as functional cure of chronic HBV infection, is rarely achieved even after long-term antiviral treatments. Therefore, new antiviral strategies interfering with other HBV replication steps are required, especially those that could efficiently inhibit HBsAg production. Here, we identified novel anti-HBV compounds that could potently block HBsAg expression from cccDNA by screening a natural compound library derived from Chinese traditional medical plants by a novel screening strategy. The combination of ELISA assay detecting the HBsAg and real-time PCR detecting HBV RNAs as indicator for cccDNA transcriptional activity were used. The antiviral activity of a candidate compound and underlying mechanism were evaluated in HBV-infected cells and a humanized liver mouse model. Herein, we selected a highly effective low-cytotoxic compound sphondin, which could effectively inhibit both intracellular HBsAg production and HBV RNAs levels. Moreover, we found that sphondin markedly inhibited cccDNA transcriptional activity without affecting cccDNA level. Mechanistic study found sphondin preferentially bound to HBx protein by residue Arg72, which led to increased 26S proteasome-mediated degradation of HBx. Sphondin treatment significantly reduced the recruitment of HBx to cccDNA, which subsequently led to inhibition of cccDNA transcription and HBsAg expression. The absence of HBx or R72A mutation potently abrogated the antiviral effect induced by sphondin in HBV-infected cells. Collectively, sphondin may be considered as a novel and natural antiviral agent directly targeting HBx protein, which effectively inhibited cccDNA transcription and HBsAg expression. ACKNOWLEDGMENTS This work was supported by National Natural Science Foundation of China (Grant No. 81861168035, 81922011 and 81871656 to JC, 82304994 to FR); National key research and development program (2022YFA1303600 to ALH); Creative Research Group of CQ University (CXQT19016 to JC); Chongqing Natural Science Foundation (cstc2018jcyjAX0114 to JC); Natural Science Foundation Project of Chongqing (cstc2019jscx-dxwtBX0020 to JC); Chongqing Natural Science Foundation (CSTB2022NSCQ-MSX1560 to FR); China Postdoctoral Science Foundation (2023T160770, 2021MD703920 to FR).

Abstract no.51

β-Elemene induced ferroptosis via TFEB-mediated GPX4 degradation in EGFR wide-type non-small cell lung cancer

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Introduction:β-Elemene (β-ELE), derived from Curcuma wenyujin, has anticancer effect on non-small cell lung cancer (NSCLC). However, the potential target and detail mechanism were still not clear. TFEB is the master regulator of lysosome biogenesis. Ferroptosis, a promising strategy for cancer therapy could be triggered via suppression on glutathione peroxidase 4 (GPX4). Weather TFEB-mediated lysosome degradation contributes to GPX4 decline and how β-ELE modulates on this process are not clear. Objectives:To observe the action of β-ELE on TFEB, and the role of TFEB-mediated GPX4 degradation in β-ELE induced ferroptosis. Methods:Surface plasmon resonance (SPR) and molecular docking were applied to observe the binding affinity of β-ELE on TFEB. Activation of TFEB and lysosome were observed by immunofluorescence, western blot, flow cytometry and qPCR. Ferroptosis induced by β-ELE was observed via lipid ROS, a labile iron pool (LIP) assay and western blot. A549TFEB KO cells were established via CRISPR/Cas9. The regulation of TFEB on GPX4 and ferroptosis was observed in β-ELE treated A549WT and A549TFEB KO cells, which was further studied in orthotopic NOD/SCID mouse model. Results:β-ELE can bind to TFEB, notably activate TFEB, lysosome and transcriptional increase on downstream gene GLA, MCOLN1, SLC26A11 involved in lysosome activity in EGFR wild-type NSCLC cells. β-ELE increased GPX4 ubiquitination and lysosomal localization, with the increase on lysosome degradation of GPX4. Furthermore, β-ELE induced ferroptosis, which could be promoted by TFEB overexpression or compromised by TFEB knockout. Genetic knockout or inactivation of TFEB compromised β-ELE induced lysosome degradation of GPX4, which was further demonstrated in orthotopic NSCLC NOD/SCID mice model.

Abstract no.52

OGG1 inhibitor TH5487 suppresses Th17 cell differentiation and exhibits anti-arthritic effect in AIA rats

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2. Dr Linna Wang, Macau, Macau University of Science and Technology, Macao SAR

Rheumatoid arthritis (RA) is a chronic and progressive autoimmune disease, with 0.5-1% global incidence. The pathogenesis of RA has not been fully clarified, but sustained oxidative stress definitely involved. Guanine in DNA is easily susceptible to oxidation to form 7,8-dihydro-8-oxoguanine (8-oxoG) which is recognized and excised by OGG1. Accumulating evidence revealed that OGG1 is closely related to immune and inflammatory responses. In the present study we found that the enzymatic activity of OGG1 was demonstrated to increase in both RA patients and AIA rats as evidenced by the increased serum concentration of 8-oxoG. Downregulation or inhibition of OGG1 both suppressed the proinflammatory cytokines in LPS-stimulated cell model. Additionally, knockdown of OGG1 significantly attenuated the arthritic condition in AIA mode with decreased production of proinflammatory cytokines, increased proportion of Tregs and decreased proportion of Th17 cells, suggesting a critical role of OGG1 in experimental arthritic model. Similarly, OGG1 inhibitor TH5487 exhibited excellent anti-arthritic effect in AIA rats. RNA sequencing revealed that Th17 cell differentiation was the predominant pathway regulated by TH5487 treatment. The in vitro Th17 polarizing experiment verified that TH5487 suppressed the differentiation of Th17 cells in a dose dependent manner. However, the effect of TH5487 on Th17 differentiation is OGG1-independent since TH5487 also inhibited the differentiation of Th17 in OGG1-null naïve CD4 T cells. By analyzing the relevant 21 genes, we found that TH5487 may inhibit Th17 cell differentiation through targeting Lymphocyte-specific protein tyrosine kinase (LCK), inhibiting the phosphorylation of Zeta chain of T cell receptor associated protein kinase 70 (ZAP70) and suppressing the expression of Interferon regulatory factor 4 (IRF4). Altogether, TH5487 may be a promising small molecule in treating RA through inhibiting OGG1 mediated inflammatory pathways and T cell receptor signaling.

Abstract no.53

Immunomodulatory Effects of a 5' tRF derived from Ganoderma lucidum via Activating MDA5

1. Long-Bo Bai, 2. Kai-Yue Cao, 3. Zhi-Hong Jiang*

Ganoderma lucidum (Ganoderma) is a traditional Chinese herbal medicine known for its immunomodulatory functions. Although the bioactivity of triterpenes and polysaccharides from Ganoderma has been extensively studied, RNA components enriched in Ganoderma remain largely unexplored. Our previously studies revealed tRNA fragments (tRFs) derived from nature exhibit pharmacological activities through regulating the expression of human genes. However, the immunomodulatory of Ganoderma tRFs still remains unclear. In this study, we conducted a Ganoderma tRF library through next-generation sequencing. Bioactivity screening hit a 5' tRF-Gln mimic in double-stranded form termed LZ11 significantly upregulate the release of nitric oxide (NO) in RAW264.7 cells, as well as upregulating immune factors IL6, IL10, NOS, and TNF-α. Mechanistically, LZ11 sequence-specific activates Melanoma Differentiation-Associated protein 5 (MDA5), leading to the phosphorylation of transcription factor interferon regulatory factor 3 (p-IRF3) and subsequent promotion of type-I interferon (IFN-β) release, resulting in triggering innate immune responses. MDA5 knockdown by siRNA significantly dysregulated the expressions of MDA5/p-IRF3/IFN-β axis, as well as the release of NO in RAW264.7 cells. In a cyclophosphamide-induced immunosuppressive mice model, intravenous injection of LZ11 dose-dependently (50 μg/kg and 200 μg/kg) increased spleen and thymus index. A notable upregulation of MDA5 in these immune-related organs was observed in LZ11-treated mice, consistent with in vitro results. Furthermore, LZ11 reversed the decline of neutrophils, lymphocytes, hemoglobin, hematocrit, and red blood cell distribution width induced by cyclophosphamide. In summary, a tRF derived from Ganoderma was revealed to exhibit bioactivities via activating RNA-binding protein, which is different from current knowledge that tRFs silencing diseases-related genes. Moreover, this work suggests that Ganoderma tRFs with immunomodulatory effects should not be neglected, which benefits the design and development of small nucleic acid therapeutics.

Keywords: Ganoderma lucidum, tRF, Immunomodulatory, MDA5

Abstract no.54

The unique processing of traditional Chinese medicine as the key to its efficacy: A multi-omics approach to reveal the differences in medical components and molecular mechanisms between Rehmanniae Radix and Rehmanniae Radix Praeparata in the treatment of Alzheimer's disease

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Abstract: Currently, Alzheimer’s disease (AD), a progressive neurological disorder that causes memory decline and cognitive dysfunction, increasingly threatens human health. Rehmanniae Radix Praeparata (RRP) is derived from the steamed or wine-steamed Scrophulariaceae plant, Rehmannia glutinosa Libosch. (RR). RR and RRP show promise in the treatment of AD, yet the variations in medical components and their mechanisms of action against AD remain unclear. Therefore, this study initially used APP/PS1 mice as AD animal models and used UPLC-QE-MS/MS, network pharmacology, proteomics, 16S rRNA sequencing to investigate differences in the medical components and mechanisms of action of RR and RRP in treating AD. UPLC-QE-MS/MS screening revealed that ajugol was the effective medicinal component of RR for AD treatment, and isoacteoside was that of RRP. Integrated multi-omics analyses predicted the involvement of the neuroinflammatory pathway, apoptosis pathway, and autophagy pathway in the mechanisms of the two ingredients for AD treatment. Subsequent in vivo and in vitro experiments confirmed that RR and its active component, ajugol, primarily modulated the TLR/NF-κB/NLRP3 neuroinflammatory pathway and Bcl-2/Bax/Cytochrome C/Caspase-3 apoptosis pathway, whereas RRP and its active component isoacteoside predominantly affected the LC3-II/P62/p-mTOR/mTOR autophagy pathway. These components collectively improved cognitive deficits in ICR mice, reduced Aβ plaque deposition in brain tissue, and diminished BV2 microglial cell cytotoxicity in the inflammation model, thereby ameliorating the progression of AD. This study systematically elucidated the distinctions in the medical components and biological mechanisms of RR and RRP in treating AD, revealing that the unique processing of TCM is key to its efficacy. Keywords: Rehmannia glutinosa Libosch.; material basis of therapeutic efficacy; progressive neurological disorder; neuroinflammation; apoptosis; autophagy

4. Polychemical Activities and Mechanism StudyI (Neurological, Metabolic, Renal and Cardiovascular Diseases)

Abstract no.55

Cerebral ischemic injury impairs autophagy and exacerbates cognitive impairment in APP/PS1 mice

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Autophagy plays a pivotal role in the pathogenesis and progression of Alzheimer's disease (AD). Oxidative stress and neuroinflammation involved in autophagy are associated with cerebral ischemia-induced exacerbation of cognitive deficits in AD. However, the mechanisms underlying this impairment remain elusive. Memory capacity of APP/PS1 mice and wild-type (WT) mice was assessed using the Morris water maze test. Nissl staining, immunohistochemistry, RT-qPCR, ELISA, and Western blotting were used to study the degree of Aβ deposition, oxidative stress, neuroinflammation, and neuronal and synaptic loss after cerebral ischemia. Autophagy levels in brain tissue were assessed by RT-qPCR, Western blotting, immunofluorescence, and transmission electron microscopy. Differential proteins in the hippocampus after cerebral ischemia occurring in APP/PS1 were analyzed by label free proteomics and RT-qPCR was used to verify differential gene expression. Cerebral ischemia aggravated cognitive impairment in APP/PS1 mice by worsening neuronal and synaptic loss through damage to intracellular autophagy, increased oxidative stress, and neuroinflammation. Notably, cerebral ischemia interfered with mitochondrial and nuclear transport functions in APP/PS1 transgenic mice, thereby aggravating cognitive deficits. Attention to cellular transport functions may be a target for preventing AD progression. In summary, the results suggest that autophagy is impaired in APP/PS1 mice compared to WT mice, and oxidative stress and neuroinflammation caused by cerebral ischemia exacerbate autophagy damage and are responsible for cognitive decline. Label-free proteomics demonstrated imbalance of mitochondrial transport and nucleus transport functions exacerbated cognitive deficits. Thus, improving autophagy and the restoration of organelle transport may be a target for the prevention and treatment of dementia.

Abstract no.56

Ganoderma lucidum alleviates Aβ1-42-induced Alzheimer's disease in vitro and in vivo via suppression of neuroinflammation

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Background: Alzheimer's disease (AD) is a neurodegenerative disorder with a high prevalence among the elderly, usually characterized by memory loss, cognitive impairment and mental abnormalities. Ganoderma lucidum, a medicinal fungus with a long history of consumption, has received widespread attention for its therapeutic potential in AD. Objective: To investigate the protective effects of Ganoderma lucidum on mice and cell models of AD as well as the understanding mechanisms. Method: Aggregated Aβ1-42 was injected intraventricularly in the lateral ventricle to induce an AD mouse model, and after two weeks of gavage treatment with Ganoderma lucidum ethanol extracts (3.2 mg/kg/d and 12.8 mg/kg/d), the changes in cognitive functions of the mice were assessed by the Morris water maze test (MWM). Mice were executed and brain tissues were collected after MWM, and the expression of inflammatory factors interleukin-6 (IL-6), interleukin-1β (IL-1β), interleukin-10 (IL-10), and tumor necrosis factor-α (TNF-α), silent information regulator (SIRT1) gene, and glutathione peroxidase 4 (GPX4) were assessed in the hippocampus of mice by RT-qPCR analysis. ELISA kits were used to detect TNF-α, IL-6 levels. Carbon clearance test was used to test the functional changes of mouse macrophages. In vitro experiments, immunofluorescence staining was performed on Aβ1-42-treated RAW246.7 cells to detect NF-κB p65 position. Result: MWM results showed that Ganoderma lucidum extract significantly improved cognitive dysfunction and memory loss in AD model mice. Ganoderma lucidum treatment significantly inhibited the expression of Aβ1-42-induced hippocampal inflammatory factors IL-6, IL-1β, IL-10, and TNF-α, decreased the levels of TNF-α and IL-6, and increased the expression of SIRT1 and GPX4 in mice. The high dose group of Ganoderma lucidum extract significantly enhanced Aβ1-42-induced macrophage function. Furthermore, Ganoderma lucidum extract treatment significantly attenuated Aβ1-42-induced nuclear translocation of NF-κB p65 and p-NF-κB p65 in RAW246.7 cells. Conclusion: In summary, Ganoderma lucidum extract can improve learning and memory functions in Aβ1-42-induced AD model mice, down-regulate the levels of hippocampal inflammatory factors in Aβ1-42-induced AD mice, increase the expression of SIRT1 and GPX4, and improve neuroinflammation. It also enhanced macrophage function and inhibited NF-κB activation. Keywords: Ganoderma lucidum; Alzheimer's disease; Aβ1-42; Neuroinflammation; Mechanisms

Abstract no.57

Sojae semen germinatum and its isoflavones alleviate overactive bladder via regulating calcium signaling pathway and inflammatory pathway

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Abstract The pathogenesis of overactive bladder (OAB) involves damage to the detrusor and / or urothelium. Our previous results found that Sojae semen germinatum (SSG) water extract can effectively improve OAB symptoms in rats with benign prostate hyperplasia (an OAB model with urothelium layer injury) [1], but its therapeutic effect on the detrusor injury is still unclear. In this study, our results of urodynamics, H&E staining and Masson staining showed that SSG can effectively improve the symptoms of severe OAB in SHR rats (an OAB model with detrusor injury). Proteomics and phosphoproteomics indicated that SSG can significantly downregulate the calcium signaling pathway and inflammatory pathway in SHR bladder. We confirmed that PGE2, an OAB biomarker, can upregulate the Arachidonic acid metabolism-mediated PLCβ1/MLCK/p-MLC pathway and NF-κB/IL-1α/cPLA2 pathway by binding to EP1 and EP4 receptors in bladder smooth muscle cells (BSMC), respectively, thereby affecting the further development of detrusor overactivity (DO) and inflammation, which may be responsible for the molecular pathogenesis of SHR bladder. DARTS, CETSA and molecular docking analysis showed that daidzein and genistein, two active ingredients of SSG, directly bound to cPLA2, EP1and EP4 receptors, and down-regulated above-mentioned PGE2-actviated pathways in BSMC. Effects of SSG on these two pathways were also confirmed by Western blotting. In conclusion, SSG and its two active compounds daidzein and genistein alleviated DO by inhibiting the excitatory effect of PGE2 on EP1/PLCβ1/MLCK/p-MLC pathwa and reduced inflammation progression of detrusor by inhibiting PGE2-activated EP4/NF-κB/IL-1α/cPLA2 pathway. Acknowledgement: This study was supported by National Key R&D Program of China (No. 2021YFE0202700). Reference [1] M. Cheng, Y. Qiang, Y. Wu, X. Tong, Y. Tie, Z. Sun, S. Guan, L. Xu, P. Xu, X. Li, M. Xue, X. Zhou*. Multi-omic approaches provide insights into the molecular mechanisms of Sojae semen germinatum water extract against overactive bladder. Food Research International. 2024, 175: 113746.

Abstract no.58

Salvianolic Acid B Alleviates Cardiac Remodeling by Improving Cardiac Lymphangiogenesis in cTnTR141W Transgenic Mice with Dilated Cardiomyopathy

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Background： Dilated cardiomyopathy (DCM) is an idiopathic primary myocardial disease. Salvianolic acid B (SalB) is the active ingredient of Salvia miltiorrhiza Bunge, which is used in the treatment of myocardial remodeling of DCM. Our previous research observed aberrant cardiac lymphangiogenesis in DCM patients, and SalB promotes the proliferation and migration of lymphatic endothelial cells (LECs). This study aims to elucidate the mechanism that SalB alleviates cardiac remodeling by improving lymphangiogenesis in cTnTR141W transgenic mice with DCM. Methods： cTnTR141W transgenic mice were randomly divided into the model group, the AAV9-VEGF-C (the cardiomyocyte-specific VEGF-C overexpression adeno-associated virus) group, the SalB group, the LCZ696 group, and the non-transgenic littermates were used as age-matched Wild-type (WT) controls. Cardiac remodeling and cardiac lymphatic were observed by echocardiography, HE staining, Masson staining, WGA staining, Wholemount staining, and Western blot (VEGF-C and VEGFR-3 proteins). Results: Compared with the WT group, the values of ejection fraction (EF) and fractional shortening (FS) were decreased ($P<0.01$), the cross-sectional area of cardiomyocytes was increased ($P<0.05$), interstitial fibrosis was increased ($P<0.0001$), and the epicardial lymphatic vessels decreased ($P<0.01$), accompanied with the down-regulating of VEGF-C and VEGFR-3 proteins in hearts of cTnTR141W mice ($P<0.001$). Following overexpressed VEGF-C in the heart, the areas of epicardial lymphatics were increased ($P<0.001$), the area of cardiomyocytes was decreased ($P<0.05$), and the interstitial fibrosis and perivascular fibrosis were alleviated ($P<0.001$) along with improved cardiac function ($P<0.001$). After intervention with SalB or LCZ696, the area of cardiomyocytes was significantly diminished ($P<0.001$), interstitial and

perivascular fibrosis was alleviated ($P<0.0001$), cardiac function was improved ($P<0.05$), and the area of epicardial lymphatics was increased ($P<0.05$) accompanied by the up-regulating of VEGF-C and VEGFR-3 proteins. Conclusion: Decreased cardiac lymphatics and cardiac remodeling are observed in cTnTR141W transgenic mice with DCM, and SalB could alleviate cardiac remodeling by improving cardiac lymphangiogenesis in cTnTR141W transgenic mice. It might be a potential therapeutic measure for DCM to promote lymphangiogenesis.

Abstract no.59

A novel botanical supplement improves physical performance，ameliorates muscle atrophy and immune senescence in aging mice

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4. Dr Yu-Ling Lin, Academia Sinica, Taipei

This study identifies the herbal extract from a Lamiaceae family plant (designated MO) which enhances physical performance, muscle strength and endurance in aged mice. In aged mice, the MO supplementation increased the content of Type I slow-twitch muscle fibers, which are known to support aerobic metabolism and fatigue resistance, enabling the maintenance of longer-term contractions, a key for stabilization and postural control. The expression of PGC-1a, GHR, GSK3β genes involved in fiber switch, mitochondria biogenesis, and/or energy-associated in aged mouse muscles were upregulated in MO-treated mouse muscles. In vitro study further showed that MO promoted the myogenic differentiation and myotube formation, and improved the TNFα-induced atrophy in young and aged mouse myoblast cells, indicating that MO can effectively improve muscle damage caused by inflammaging, subsequently promoting myogenesis in the elderly. Notably, MO revealed an immune modulatory effect, activating B cells and inducing B cell differentiation into memory cells, as well as improving humoral immunosenescence by reducing the ABC population and inhibiting ABC inflammation in aged mice. In summary, this study demonstrates the novel anti-aging activity of MO via ameliorating immune senescence and inflammaging.

Abstract no.60

Schisandra chinensis Lignans exert antidepressant effects by targeting cannabinoid receptor type-1 to regulate the level of brain-derived neurotrophic factor

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The current study aimed to illustrate the mechanism of Schisandra chinensis Lignans (SCL) played a neuroprotective effects to achieve antidepression. Chronic unpredictability mild stimulation (CUMS) was used to construct the mice model of depressive-like behaviors. The results of behavioral pharmacology showed that SCL improved the depressive-like behaviors of CUMS-induced mice. In-depth studies proved SCL increased the levels of synaptic plasticity protein PSD95 and brain-derived neurotrophic factor (BDNF), and reduced the expression of apoptotic proteins to exert neuroprotective effects. The afore-mentioned results were associated with the positive regulation of tPA-BDNF by SCL, in turn to activate TrkB-MEK-ERK-PKA-CREB and PI3K-AKT to improve neuronal injury. Based on the physiological role of cannabinoid receptor type-1 (CB1R) in neuroprotection, we added CB1R antagonist AM251 to the CUMS model in the subsequent studies. The results demonstrated that AM251 could antagonize the improvement of SCL on depressive-like behaviors, and inhibit the tPA-BDNF pathway, further inactivating TrkB and PI3K-AKT pathways to reverse the neuroprotective effect of SCL. Overall, SCL mediated CB1R to activate tPA-BDNF pathway to regulate BDNF level, and then the increased BDNF stimulated the TrkB and PI3K-AKT pathways to play the neuroprotective effects. Acknowledgements This project was supported by the National Natural Science Foundation of China (82173961). Keywords: Schisandra chinensis Lignans, brain-derived neurotrophic factor, cannabinoid receptor type-1, neuroprotection

Abstract no.61

Hericium erinaceus Mycelium and Erinacine A Attenuate Reinstatement of Ketamine-Seeking Behaviors in Rats

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Rationale: Recreational ketamine use has surged in popularity in recent years. Research has shown that Hericium erinaceus (HE) mycelium can reduce the motivation for self-administered ketamine in rats. This study further investigated whether HE mycelium and its major component, erinacine A, could acutely or repeatedly reduce the reinstatement of ketamine-seeking behaviors. Method: The reinstatement model of drug relapse was employed. Male Sprague-Dawley rats were trained to self-administer intravenous ketamine (0.5 mg/kg/infusion). After the extinction of reinforced responding, the rats received an oral dose of HE mycelium before the reinstatement of ketamine or food seeking to assess the acute effects of HE mycelium. Additionally, HE mycelium and erinacine A were administered daily for 14 days after the rats reached stable self-administration of ketamine, followed by extinction and reinstatement. Their long-lasting effects were determined by assessing the reinstatement again after 14 days of abstinence. Results: Both acute and repeated administration of HE mycelium and erinacine A significantly reduced the reinstatement of ketamine-seeking behaviors. However, there were no long-term beneficial effects of repeated treatment on reinstatement after abstinence for 14 days. Conclusions: The results indicate that HE mycelium can attenuate the reinstatement of ketamine-seeking behavior, likely due to erinacine A. These findings suggest that HE mycelium supplementation might reduce the relapse risk in patients with ketamine use disorder. Acknowledgement: This work was supported by Grape King Bio (C09-003), National Science and Technology Council, Taiwan (108-2314-B-400 -034 -MY3), and National Health Research Institutes (NP-109-PP-05)

Abstract no.62

Semen Sojae Praeparatum improves anxiety in mice by inhibiting HPA axis hyperactivity and modulating gut microbiota

1. Prof Weiming Wang, Southern Medical University, Guangzhou

2. Dr Qixin Yang, Southern Medical University, Guangzhou

Semen Sojae Praeparatum (SSP) is a functional food from fermented black soybeans used in folk medicine to treat psychiatric diseases. While its efficacy in treating depression and menopausal syndromes has been well-established, research on its potential to alleviate anxiety disorders remains limited. This study, therefore, sought to elucidate the anxiolytic properties and mechanisms of action of SSP. Research demonstrated that mice administered with high concentrations of SSP displayed enhanced exploratory behavior in both the elevated plus maze and open field tests, as well as diminished hippocampal cell damage. These observations suggest that SSP effectively mitigates anxiety in mice, with concentration-dependent efficacy.Moreover, SSP was observed to reduce the expression levels of neuronal nitric oxide synthase (nNOS), corticotropin-releasing hormone (CRH), and its receptor CRFR at both the protein and mRNA levels. This reduction implies that SSP may exert its anxiolytic effects by dampening the hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis in anxious mice. Additionally, these findings indicate that anxiety can induce dysbiosis in the gut microbiota of mice. SSP was found to modulate this microbiota, specifically by decreasing the Firmicutes to Bacteroidetes ratio and by enhancing the abundance of Bacteroidetes, Ruminococcaceae, and Bacilli. Collectively, this study provides evidence that SSP possesses anxiolytic effects, potentially through the inhibition of HPA axis overactivity and the modulation of gut microbiota, thereby offering a promising avenue for the treatment of anxiety disorders.

Abstract no.63

UVB protection mechanisms of artocarpin isolated from Artocarpus altilis heartwood

1. Prof Jarupa Viyoch, Naresuan University, Phitsanulok

Apoptosis, a vital process in multicellular organisms, including skin, helps regulate tissue homeostasis and eliminate cells with potentially abnormal genetic material. In the skin's epidermal layer, keratinocytes are the primary cells involved. However, controlled apoptosis of keratinocytes can be disrupted by UV radiation. A few seconds of UV exposure can lead to an overproduction of free radicals, which damage essential molecules such as lipid membranes, receptor proteins, second messenger molecules, and DNA. This damage triggers apoptotic signals, including the expression of p-p38 MAPK, and creates an imbalance between cell proliferation and apoptosis. Recently, natural substances have garnered attention for their potential in protecting skin against the harmful effects of UV radiation. In this study, we focused on Artocarpus altilis (breadfruit), which contains artocarpin as a major active compound. Artocarpin is known for its interesting biological properties, including antioxidation, anti-inflammation, antimicrobial activity, inhibition of melanogenesis, anti-wrinkle effects, and 5α-reductase inhibition. However, the potential mechanisms of artocarpin in UVB-irradiated human keratinocyte cells have not been studied. In particular, the mechanisms underlying its protective effects against UVB-induced damage to cellular components related to apoptosis remain unclear. We found that keratinocyte cells pretreated with artocarpin (3.1 µg/mL) before exposure to UVB (55 mJ/cm²) exhibited intracellular antioxidation against both ROS and RNS. Additionally, artocarpin reduced the expression of p-p38 and caspase-3. It also inhibited the secretion of TNF-α, a prominent marker linked to apoptosis, and suppressed the activation of the Fas receptor. Overall, artocarpin demonstrated anti-apoptotic activity involving both intrinsic and extrinsic pathways. The antioxidation, anti-lipid peroxidation, and anti-inflammatory properties of artocarpin suggest it is an effective natural active ingredient for dermopharmaceutical products, particularly in sun protection formulations.

Abstract no.64

Pharmacodynamic mechanism of Chinese medicine to improve fatty liver or aging

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The incidence of metabolism-associated fatty liver disease is increasing year by year, and there is a trend of rejuvenation. Traditional Chinese medicines (TCM) have significant effects in improving fatty liver, but the target and pathway of action are not clear. Population aging in China has become an increasingly serious social problem, and aging and other related diseases continue to cause serious economic and psychological burdens to families. It is urgent to slow down aging and prevent aging-related diseases. Traditional Chinese medicine (TCM) plays a unique role in improving fatty liver and anti-aging. Therefore, the present work will elucidate the efficacy and potential mechanism of action of Chinese medicines in improving fatty liver and/or aging.

Abstract no.65

Mechanism study on the regulation of renal tissue metabolism reprogramming and improvement of renal fibrosis by Shenxikang granules

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Abstract: Objective: Observing the effects of Shenxikang granules on renal function, inflammatory factors, and HIF-a/HK-2 pathway in UUO rats, and exploring its mechanism of regulating renal fibrosis.Method：Prepare UUO rat models and divide them into model group, positive control group, and Shenxikang granules group; Set as a sham surgery group, with 6 mice in each group.The model group and sham surgery group received oral administration of deionized water, the positive control group received oral administration of benazepril hydrochloride tablets, and the SXK granules group received oral administration of traditional Chinese medicine for 4 consecutive weeks. Detect the expression of renal function and signaling factors in each group.Result:The sham surgery group showed no abnormalities in renal tissue, while the model group showed a significant increase in blue collagen fibers in renal tissue; In the Shenxikang granules group, the deposition of blue collagen was significantly reduced.Compared with the sham surgery group, the model group had creatinine, urea nitrogen, and uric acid in their blood; IL-18, TNF-a, IL-1 β, and MCP-1 proteins in serum; The expression levels of pyruvate, lactate, ATP, HIF-1a, HK-2, and a-SMA proteins in renal tissue were all upregulated ($P<0.05$, $P<0.01$).Compared with the model group, the levels of pyruvate, lactate, ATP, HIF-1a, HK-2, TGF-1β, and a-SMA in the SXK group were all down regulated ($P<0.01$, $P<0.05$);Conclusion:The improvement of renal fibrosis in UUO model by Shenxikang granules may be related to the regulation of metabolic reprogramming. Keywords: Shenxikang granules; UUO model; Metabolic reprogramming;

Abstract no.66

Investigation of the indirect mechanism of lignans derived from Sambucus williamsii Hance on osteoporosis and exploring of new TPH-1 Inhibitors

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The bone protective effects of a lignan rich fraction from Sambucus williamsii Hance (SWH), a folk herbal medicine traditionally used to treat bone fractures and joint diseases in China, have been demonstrated in our previous animal studies. However, the pharmacokinetics study showed that the levels of lignan in serum were too low to be detected. A metabolomics study revealed that serotonin synthesis was involved in the actions of SWH. Since gut-derived serotonin (5-HT) contributes to bone deficits, we hypothesize that lignans from SWH might exert bone protective effect by suppressing serotonin synthesis. Sprague-Dawley (SD) rats were employed to evaluate the effects of the lignan fraction from SWH, and the serum levels of 5-HT and kynurenine as well as the genes and proteins related to the 5-HT signaling pathway, were determined. Subsequently, the targets of lignan acting in intestine were identified using molecular docking, surface plasmon resonance, and protein activity in vitro, and were further verified in ovariectomized mice. The results showed that the lignan fraction lowered the level of serum serotonin, inhibited the gene and protein expressions of tryptophan hydroxylase-1 (TPH-1) in the intestine, and modulated the serotonin-related signaling pathway in bone. In addition, several inhibitors that suppressed the synthesis of serotonin were identified from the lignans fraction of SWH. We concluded that lignans exerted bone protective effects through direct actions in serotonin synthesis and indirect modulation in bone formation.

Abstract no.67

Effect of stem cells and their secretome with Traditional Chinese Medicine on promotion of severe burn wound healing

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2. Dr Wing Sum Siu, The Chinese University of Hong Kong, Hong Kong SAR

Either stem cells, their secretome or a Traditional Chinese Medicine (TCM) herbal oral formula, namely NF3, have been proven effective to promote diabetic wound ulcer healing in our institute. This study aims to evaluate the effects of local injected stem cells, secretome, oral NF3, and their combinations on promoting burn wound healing. Adipose tissue derived stem cells (ADMSCs) were isolated from male GFP-transgenic SD rats. Secretome was obtained by harvesting the culture medium of the ADNSCs through centrifugation and concentration. A third-degree burn wound was created on the dorsal back of SD rats by scalding them with a pre-heated stainless-steel bar at 100°C. Rats were divided into six groups: (1) intradermal injection (id) of ADMSCs, (2) secretome (id), (3) 0.9% saline (id) (Control group), (4) oral treatment with NF3, (5) combination of ADMSCs with NF3, (6) combination of secretome and NF3. At various endpoints, the size of the wound was measured, serum was collected for the biomarker analysis, and skin autopsies were collected for the histological and gene expression analyses. Preliminary results have shown that the treatment groups exhibited smaller wound sizes compared wiht the Control group between Day 14 and Day 28. Additionally, the expression of the Col1a1 gene, which is associated with wound healing, was generally upregulated in the treatment groups compared with the Control group starting from Day 7. The preliminary results suggest that the administration of ADMSCs, secretome, NF3, and their combinations holds potential for promoting burn wound healing. Further analysis and investigation are necessary to validate these findings and understand the underlying mechanisms.

Abstract no.68

Xiaochaihutang regulates exon-specific transcription of Bdnf by H3K18 acetylation in the hippocampus of mice to ameliorates depression-like behaviors induced by chronic social defeat stress

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Introduction: Depression is one of the prevalent and persistent mental diseases characterized by symptoms such as anhedonia, anxiety, and desperation. Although Xiaochaihutang (XCHT) upregulated hippocampal BDNF level in depressive mice and rats has been proved in our previous study, its underlying mechanism needs further clarification. Objectives: To assess the mechanisms of XCHT on regulating hippocampal BDNF expression in mice induced by CSDS. Methods: Adult C57BL/6J mice were subjected to chronic social defeat stress (CSDS) for 10 consecutive days to establish depression model. Treatment of XCHT (2.3, 7 and 21 g/kg, intragastric administration) for consecutive 3 weeks, the behavior tests were sequentially performed to investigate the antidepressant effect of XCHT induced by CSDS. Then, Golgi staining, immunofluorescence, immunoblotting, real time fluorescence quantitative polymerase chain reaction and chromatin immunoprecipitation were used to study the underlying mechanism of XCHT's regulation on hippocampal BDNF expression. Results: XCHT significantly improved anhedonia, social avoidance, recognition memory impairment, as well as anxiety/depression-like behavior in mice induced by CSDS. Meanwhile, XCHT markedly promoted neuronal complexity and dendritic spine maturation in the hippocampus of mice. Furthermore, XCHT reversed CSDS-induced reduction of the number of hippocampal BDNF+ cells and increased hippocampal BDNF protein and mRNA levels through upregulating specific Bdnf exons I, IV and VI. Notably, XCHT increased Bdnf transcripts through upregulating of histone H3K18 acetylation at Bdnf promoters. Conclusion: XCHT may increase the transcripts of specific Bdnf exons I, VI and VI by upregulating the H3K18 acetylation at corresponding Bdnf promoters to increase the level of BDNF expression, further promote neuronal plasticity in hippocampus, finally ameliorate anxiety/depression-like behavior in mice induced by CSDS. Keywords: Xiaochaihutang; Chronic social defeat stress; Depression; Brain-derived neurotrophic factor; Epigenetic modification

Abstract no.69

Gastrodin alleviates mitochondrial dysfunction by regulating SIRT3-mediated TFAM acetylation in vascular dementia

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Abstract Background: Mitochondrial dysfunction is key to the pathogenesis of vascular dementia (VaD). Sirtuin-3 (SIRT3), an essential member of the sirtuins family, has been proven to be a critical sirtuin in regulating mitochondrial function. The phenolic glucoside gastrodin (GAS), a bioactive ingredient from Gastrodiae Rhizome (known in Chinese as Tian ma) demonstrates significant neuroprotective properties against central nervous system disorders; however, the precise mechanisms through which GAS modulates VaD remain elusive. Purpose: This study aims to investigate whether GAS confers a protective role against VaD, and to figure out the underlying molecular mechanisms. Methods：A bilateral common carotid artery occlusion (BCCAO)-mediated chronic cerebral hypoperfusion (CCH) VaD rat model and a hypoxia model using HT22 cells were employed to investigate pharmacological properties of GAS in mitigating mitochondrial dysfunction. A SIRT3 agonist resveratrol (RES), a SIRT3 inhibitor 3-TYP and SIRT3-knockdown in vitro were used to explore the mechanism of GAS in association with SIRT3. The ability of SIRT3 to bind and deacetylate TFAM was detected by immunoprecipitation assay, and TFAM acetylation sites were further validated using mass spectrometry. Results：GAS increased SIRT3 expression and ameliorated mitochondrial structure, mitochondrial respiration, mitochondrial dynamics along with upregulated mitochondrial transcription factor A (TFAM), mitigating oxidative stress and senescence. Comparable results were noted with the SIRT3 agonist RES, indicating an impactful neuroprotection played by SIRT3. Specifically, the attenuation of SIRT3 expression through knockdown techniques or exposure to the SIRT3 inhibitor 3-TYP in HT22 cells markedly abrogated GAS-mediated mitochondrial rescuing function. Furthermore, our findings elucidate a novel facet: SIRT3 interacted with and deacetylated TFAM at the K5, K7, and K8 sites. Decreased SIRT3 is accompanied by hyper-acetylated TFAM. Conclusion：The present results were the first to demonstrate that the SIRT3/TFAM pathway is a protective target for reversing mitochondrial dysfunction in VaD. The findings suggest that GAS-mediated modulation of the SIRT3/TFAM pathway, a novel mechanism, could ameliorate CCH-induced VaD, offering a potentially beneficial therapeutic strategy for VaD. Keywords：Gastrodin, Mitochondria, Vascular dementia, SIRT3, TFAM acetylation

Abstract no.70

P9 protein produced by Akkermansia muciniphila improves metabolic phenotype in obese mice by regulating GLP-1 and GDF15

1. Dr Tongxi Zhuang, Shanghai University of Traditional Chinese Medicine, Shanghai

Abstract: Obesity has emerged as a worldwide metabolic disease, given its rapid growth in global prevalence. Recently, Akkermansia muciniphila (A. muciniphila) has been found to have a good improvement effect on obesity, insulin resistance, and liver fat accumulation as a gut symbiotic bacterium. P9, a protein secreted by A. muciniphila, was reported to interact with intercellular adhesion molecule 2 (ICAM-2) and induce glucagon-like peptide-1 (GLP-1) secretion and brown adipose tissue thermogenesis. In our study, we found that P9 treatment alleviated dietary-induced dyslipidemia and IR in obese mice in a dose-dependent manner and improved glucose and insulin tolerance, and energy expenditure. RGS treatment significantly reduced lipid deposition and induced GLP-1 secretion. Furthermore, significant inhibition of food intake in mice was observed in the early stage of P9 intervention, which is closely related to the upregulation of appetite regulatory factor Growth Differentiation Factor 15 (GDF15) levels. In vitro, the result indicate that P9 can upregulate the transcription level of GDF15 in intestinal HCT-116 cells. Further, P9 can bind to NUFIP2 protein and promote the phosphorylation level of PERK, activate downstream chop signaling pathways, and ultimately increase GDF15 levels in intestinal cells. In all, our results indicate that P9 protein can simultaneously promote the upregulation of GLP-1 and GDF15 levels in mice, which significantly alleviate HFD-induced obesity and insulin resistance. In db/db mice, P9 intervention showed similar weight loss effect in combination with GLP-1 and GDF15 recombinant protein. These findings demonstrate that P9 is a considerably effective treatment of obesity. Keywords：Akkermansia muciniphila; Obesity; P9; glucagon-like peptide-1 (GLP-1); Growth Differentiation Factor 15 (GDF15). Acknowledgement: This work is financially sponsored by multiple Natural Science Foundations of China and China Postdoctoral Science Foundation. We are grateful to all colleagues who have contributed to the experiment.

Abstract no.71

A novel herbal formula attenuates bladder functional loss in pelvic ischemia induced overactive bladder rat

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5. Dr Chi Man Koon, The Chinese University of Hong Kong, Hong Kong SAR

[Background] Overactive bladder is a common syndrome characterized by urinary urgency, usually accompanied by frequency and nocturia, with or without urge urinary incontinence. Discovery of novel and effective therapies remains a significant clinical demand. [Objectives] A novel herbal formula (YSN) consisting of Sojae semen germinatum (Da-Dou-Huang-Juan), Puerariae Lobatae Radix (Gegen), Alpinia Oxyphylla fructus (Yan-Yi-Zhi-Ren) was selected to investigate its therapeutic efficacy and underlying mechanisms on overactive bladder. [Methods] The chronic bladder ischemia induced overactive bladder rat model was established by arterial endothelial injury (AI) of bilateral common iliac arteries combined with high cholesterol diet. The sham group received sham operation and a regular diet. Orally administration of the water extract of YSN for 8 weeks, the arteries were collected for H&E staining. The bladder blood flow was measured by Full-field laser perfusion imager. The bladder was also processed for organ bath investigation and immunohistochemistry staining. [Results] High dose of YSN significantly attenuated the ischemia accompanied by decreased arterial wall thickness of the common iliac arteries and increased bladder blood flow when compare with the AI group. Organ bath analysis data showed that bladder contractile responses to potassium chloride, carbachol and electrical field stimulation were improved by YSN compared with the AI group. Mechanistically, YSN attenuated the vascular damage induced overactive bladder by inhibiting 8-OHdG expression. [Summary] Our results suggest that YSN may serve as a potential agent for treatment of overactive bladder. Acknowledgement: The work was supported by Mainland-Hong Kong Joint Funding Scheme project of Innovation and Technology Commission, Hong Kong (Project No.: MHP/039/20).

Abstract no.72

Mechanisms of the dilator action of a novel herbal formula used for overactive bladder

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[Introduction] Pelvic ischemia during to ageing may lead to impaired lower urinary tract perfusion and play an important role in the development of bladder dysfunctions of detrusor overactivity and overactive bladder (OAB). Improved circulation in the region would be a good way to improve the situation. [Objectives] A novel herbal formula (Yishenning,YSN) consisting of Sojae semen germinatum, Puerariae Lobatae Radix, Alpinia Oxyphylla fructus were selected to investigate its vasodilative activity and underlying mechanisms on iliac artery. [Methods] Iliac artery from rats will be cut into rings and mounted in organ bath. After equilibration, rings will be then pre-contracted with thromboxane A2 mimetic, U46619 to establish stable contractile tone. Vasodilation of atrial rings will be tested for the involvement of endothelium by comparing the vasodilative activity with or without endothelium, involvement of potassium channel by using different type of potassium channel inhibitors and involvement of calcium channel by sequential increase of calcium ion. [Results] The vasodilative activities of YSN was found to be both endothelium-dependent and endothelium independent. For endothelium-independent pathways, YSN exerted its vasodilator actions through an inwardly rectifying K+ channels (KIR), a voltage-activated K+ channels (KV) and a large-conductance Ca2+-activated K+ channels (BKCa). In addition, YSN could inhibit the vasoconstriction action of sequential increase of calcium ion. [Summary] Our results suggest that the vasodilator effect of YSN was both endothelium-dependent and endothelium-independent, mediated by decreasing the influx of Ca2+ by calcium channel inhibition and increasing the influx of K+ by opening of a KIR , Kv and BKCa potassium channels. Acknowledgement: The work was supported by Mainland-Hong Kong Joint Funding Scheme project of Innovation and Technology Commission, Hong Kong (Project No.: MHP/039/20).

Abstract no.73

The effect of active components of Citri Reticulatae Semen on neuronal function and motor ability of A53T- αSyn-Tg mice

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Parkinson's disease (PD) is the fastest-growing neurodegenerative disease globally, significantly burdening society. Long-term use of anti-Parkinsonian drugs often leads to reduced efficacy and increased drug toxicity and tolerance, highlighting the need for new treatments. Plant extracts offer natural, safe, and accessible therapeutic options. Citri Reticulatae Semen (CRS), a common traditional Chinese herb, is known for its antioxidant, anti-inflammatory, and analgesic properties. However, its potential therapeutic effects on PD remain underexplored. This study investigates the effects of CRS active components on neuronal function and motor ability in A53T-αSyn-Tg mice, aiming to provide new insights into PD treatment. In this experiment, 10-month-old B6129SF2/J mice (n=10) served as controls, and A53T-αSyn-Tg mice (n=30) were divided into control, model, high-dose CRS, and low-dose CRS groups. Oral administration was conducted for 8 weeks, followed by Y maze, open field, and rotarod behavioral tests. Transcriptome sequencing of striatal tissues suggested that CRS active components might prevent PD through the IP3Rs-MCU calcium axis. Immunofluorescence and electron microscopy showed neuronal function improvement in CRS-treated mice. qPCR and immunoblotting assessed the expression levels of autophagy-related proteins LC3, P62, and p70S6K in the striatum. Further studies revealed that CRS significantly improved the expression of IP3Rs, GRP75, and VDAC1 in rotenone-induced PC12 cells. We hypothesize that CRS can alleviate neuronal dysfunction and motor symptoms in PD model mice by enhancing the IP3Rs-GRP75-VDAC1 pathway. We will use siRNA technology to knock down GRP75 expression to further validate our hypothesis. Additionally, we will investigate the pharmacokinetics of CRS active components in PD model mice, including absorption, distribution, metabolism, and excretion (ADME). This research aims to provide references for preventing and treating neurodegenerative diseases, particularly in developing natural drugs, while enriching the pharmacological activity and efficacy research foundation of traditional Chinese medicine.

Abstract no.74

Therapeutic effects of Huang-Lian Jie-Du decoction on diabetes mellitus complicated with ischemic stroke

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4. Mr Hui Peng, Guangdong Pharmaceutical University, Guangzhou

Objective: This study aimed to investigate the therapeutic effects of Huanglian Jiedu decoction (HLJDD) on diabetes mellitus complicated with ischemic stroke (DIS) in rats. Methods: Male SD rats were induced with T2DM via a high-fat diet with multiple injections of low-dose treptozotocin (STZ) as well as the cerebral ischemic injury was established using the MCAO method. The rats were randomly divided into groups: model (Mod), HLJDD low-dose (HDL, 1.5 g/kg), HLJDD high-dose (HDH, 6 g/kg), positive control (NDP, nimodipine), and normal control (Con). After 7 days of intragastric administration, the rats' neurological function was assessed using the Longa score, the infarct area was measured by TTC staining, and the brain tissue pathology was examined by HE and Nissl staining. ELISA kits were employed to detect the levels of inflammatory cytokines lipopolysaccharide (LPS) and interleukin-1β (IL-1β) in the blood and brain tissues to further investigate the mechanisms of HLJDD in DIS. Results: HLJDD was able to reduce neurological deficit scores and decrease the area of brain infarction. HE and Nissl staining indicated after oral administration with HLJDD, the pathological damage in the rat brain tissue was improved to varying degrees, showing a clear dose-dependent relationship. There was also a noticeable increase in the number of Nissl bodies in brain tissue. Compared to the Mod group, the levels of LPS and IL-1β in the brain tissue and blood of rats in the HLJDD group were reduced. Conclusion: HLJDD exhibited significant therapeutic effects and reduced systemic inflammation in DIS rats.

Abstract no.75

Oenothera biennis water extract inhibits the NLRP3 inflammasome by activating microglial autophagy via the AMPK-PI3K/AKT/mTOR pathway in Alzheimer's disease

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Background: Alzheimer's disease (AD) is characterized by cognitive decline and neuropathological features such as amyloid-beta (Aβ) plaques and neurofibrillary tangles. Neuroinflammation, particularly as mediated by the NLRP3 inflammasome in microglial cells, plays a critical role in AD progression. Oenothera biennis water extract (OWE) has demonstrated anti-inflammatory and antioxidant properties, and this study explores its potential neuroprotective effects in AD. Methods and results: BV-2 cells were used to investigate the effects of OWE on the NLRP3 inflammasome and autophagy activation. Various assays, including MTT, Western blot, immunofluorescence, Hoechst/PI staining, YO-PRO-1/Eth-D2 staining, and real-time phagocytosis assays, were conducted. The in vivo effects of OWE on autophagy, cognitive function, and neuropathological changes were further evaluated using C. elegans and 3xTg-AD mouse models. Through extensive screening of a natural herbal library using LPS/Nigericin-stimulated BV-2 cells, we found that OWE significantly enhanced cell survival and inhibited the NLRP3 inflammasome by downregulating its component proteins and suppressing pyroptosis. Similar protective effects were observed in Aβ1-42-stimulated BV-2 cells, where OWE reduced inflammasome activity and modulated microglial phagocytic function. Additionally, OWE protected neuronal PC-12 cells from inflammatory damage. Further mechanistic studies revealed that OWE activated autophagy by regulating the AMPK-PI3K/AKT/mTOR signaling pathway. While the autophagy inhibition reversed the effects of OWE on NLRP3 inflammasome inhibition and pyroptosis. In C. elegans models, OWE enhanced autophagy and reduced Aβ toxicity, as indicated by increased GFP::LGG-1 puncta formation in DA2123 worms and decreased paralysis and cell death in CL4176 worms. Moreover, OWE demonstrated neuroprotective effects in 3xTg-AD mice by improving cognitive functions and reducing inflammatory markers through autophagy induction. Conclusion: OWE presents significant neuroprotective effects in AD by inhibiting the NLRP3 inflammasome and enhancing autophagy via the AMPK-PI3K/AKT/mTOR pathway. These findings underscore the potential of OWE as a multi-targeted therapeutic agent for mitigating neuroinflammation and neuronal damage in AD.

Abstract no.76

A dual-targeting approach to discover Gaultheria leucocarpa for inhibiting amyloid-beta fibrillization and enhancing the degradation of pathogenic proteins via mitophagy in Alzheimer's disease

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3. Mrs 悦 张, Southwest Medical University, Luzhou

Background: Alzheimer's disease (AD) is characterized by the accumulation of amyloid-beta (Aβ) and neuronal toxicity. Effective treatments targeting Aβ fibrillization and the degradation of pathogenic proteins are urgently needed. This study aims to discover and evaluate the efficacy of Gaultheria leucocarpa in inhibiting Aβ fibrillization and promoting the degradation of pathological proteins via mitophagy. Method: We conducted ThT fluorescence assays to screen various herbal extracts for their ability to inhibit Aβ fibril formation. Further investigations included cell viability assays in PC-12 cells treated with Aβ peptides, GFP-LC3 puncta formation, and LC3-I/II conversion analyses. We also explored the underlying mechanisms of GPF-induced mitophagy through the AMPK/ULK1 and PI3K/AKT/mTOR pathways, confirmed by the use of specific inhibitors. The effects of GPF were validated in Caenorhabditis elegans (C. elegans) AD models. Results: Gaultheria leucocarpa extract (GE), particularly its fraction GPF, significantly inhibited Aβ fibril formation, as shown by ThT fluorescence assays. GPF improved cell viability in PC-12 cells treated with Aβ peptides and fibrils. Additionally, GPF enhanced mitophagic activity, as evidenced by increased GFP-LC3 puncta formation, LC3-II/I ratio, and the co-localization of GFP-LC3 with MitoTracker-Red. Mechanistically, GPF activated mitophagy through the AMPK/ULK1 pathway while inhibiting the PI3K/AKT/mTOR pathway. GPF also promoted the degradation of APP and Tau proteins via autophagy. In C. elegans, GPF enhanced mitophagy, reduced Aβ deposits, delayed paralysis, improved food perception deficits, and reduced oxidative stress. Conclusion: Gaultheria leucocarpa, particularly its GPF fraction, offers a dual-targeting approach by inhibiting Aβ fibrillization and enhancing the degradation of pathogenic proteins through mitophagy. These findings suggest its potential therapeutic application in mitigating AD pathology and warrant further investigation into its bioactive compounds and molecular mechanisms. Keywords: Dual-targeting approach; Gaultheria leucocarpa; Alzheimer's disease; amyloid-beta; mitophagy; Caenorhabditis elegans

Abstract no.77

Tangshen Formula Ameliorates Non-Alcoholic Fatty Liver Disease via SIRT1-Mediated Activation of Lipophagy

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Background: Non-alcoholic fatty liver disease (NAFLD) has emerged as the most common chronic liver disease worldwide, contributing significantly to the rising incidences of cirrhosis and hepatocellular carcinoma. Reducing hepatic lipid accumulation is crucial for NAFLD management, but current therapeutic options remain limited, necessitating the development of effective treatments. Tangshen Formula (TSF), a traditional Chinese medicine compound developed from the clinical experiences of veteran practitioners, consists of seven herbal components, including Astragalus and Rehmannia. Previous clinical and experimental studies have demonstrated TSF's efficacy in correcting dyslipidemia and ameliorating renal lipid deposition in diabetic nephropathy. However, the therapeutic effects and underlying mechanisms of TSF in NAFLD remain unclear. Objective: This study aims to evaluate the effects of TSF on lipid metabolism disorders in NAFLD and elucidate its molecular mechanism in promoting hepatic lipophagy via SIRT1 activation. Methods: We established a liver-specific SIRT1 knockout mouse model and induced NAFLD in mice through a high-fat diet, followed by 16 weeks of TSF treatment via gavage. Additionally, a palmitic acid (PA)-induced lipid overload HepG2 cell model was utilized to assess TSF intervention. The pharmacological mechanisms of TSF were investigated using Western blot, immunofluorescence, and transmission electron microscopy. Results: In vitro experiments revealed significant lipid accumulation, autophagosome accumulation, and autophagy flux blockade in PA-induced HepG2 cells, characterized by elevated p62 levels and decreased LC3-II levels. TSF treatment markedly upregulated SIRT1 expression, restored TFEB-mediated lysosome biogenesis, facilitated autophagosome-lysosome fusion, and ameliorated impaired lipophagy. In the high-fat diet-induced NAFLD mouse model, TSF significantly alleviated hepatic steatosis, evidenced by reduced lipid vacuoles and inflammatory cell infiltration in liver tissues. TSF also upregulated hepatic SIRT1 expression, promoted TFEB-mediated autophagy-lysosome pathways, and restored impaired autophagy flux. Conversely, liver-specific SIRT1 knockout mice exhibited blocked TSF-induced lipophagy and nullified therapeutic effects on hepatic steatosis. Conclusion: TSF ameliorates NAFLD by activating SIRT1, which promotes TFEB-mediated autophagy-lysosome pathways and drives lipophagy. These findings suggest that TSF is a potential therapeutic strategy for NAFLD. 精简摘要，不超过 300 个 words ChatGPT Title: Tangshen Formula Ameliorates Non-Alcoholic Fatty Liver Disease via SIRT1-Mediated Activation of Lipophagy Background: Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease globally, leading to cirrhosis and liver cancer. Effective treatments are limited, necessitating new therapeutic options. Tangshen Formula (TSF), a traditional Chinese medicine compound with seven herbal components, has shown promise in correcting dyslipidemia and reducing renal lipid deposition in diabetic nephropathy. However, its effects and mechanisms in treating NAFLD are not well understood. Objective: To evaluate the impact of TSF on lipid metabolism in NAFLD and uncover the molecular mechanism of SIRT1-

mediated activation of lipophagy. Methods: A liver-specific SIRT1 knockout mouse model was developed, and NAFLD was induced using a high-fat diet, followed by 16 weeks of TSF treatment via gavage. Additionally, a palmitic acid (PA)-induced HepG2 cell model was used to assess TSF intervention. Western blot, immunofluorescence, and transmission electron microscopy were employed to investigate TSF's pharmacological mechanisms. Results: In PA-induced HepG2 cells, lipid accumulation, autophagosome accumulation, and blocked autophagy flux were observed, marked by increased p62 and decreased LC3-II levels. TSF treatment upregulated SIRT1, restored TFEB-mediated lysosome biogenesis, facilitated autophagosome-lysosome fusion, and improved impaired lipophagy. In NAFLD mice, TSF significantly reduced hepatic steatosis, lipid vacuoles, and inflammatory cell infiltration. TSF also increased hepatic SIRT1 expression, promoted TFEB-mediated autophagy-lysosome pathways, and restored autophagy flux. In contrast, SIRT1 knockout mice showed blocked TSF-induced lipophagy and no therapeutic effects on hepatic steatosis. Conclusion: TSF improves NAFLD by activating SIRT1, promoting TFEB-mediated autophagy-lysosome pathways, and enhancing lipophagy. TSF is a potential therapeutic strategy for NAFLD.

Abstract no.78

Licochalcone B Enhances Autophagy and Ubi-degradation of α-synuclein through FBXL16-dependent Mechanism

1. Prof Betty Law, Macau University of Science and Technology, Macao SAR

Licochalcone B Enhances Autophagy and Ubi-degradation of α-synuclein through FBXL16-dependent Mechanism Jianhui Wu1, Zhikang Wang 1, Vincent Kam-Wai Wong1, Betty Yuen-Kwan Law1* State Key Laboratory of Quality Research in Chinese Medicine (Macau University of Science and Technology), Taipa, Macao, P. R. China; * Correspondence to Betty Yuen-Kwan Law, Email: yklaw@must.edu.mo Parkinson's disease is the second most common neurodegenerative disease and has an increased incidence associated with age. While the etiology and pathogenesis of PD are not fully elucidated. With the increasing aged population worldwide, there is a gr- owing need to develop new pharmacological strategies and targets for PD. Ubiquitination（Ubi） is the major degradation pathway for the clearance of endogenous and overexpressed levels of α-synuclein in the living mouse brain. Selective autophagy is able to degrade large and heterogeneous cytosolic material, including aggregated proteins, organelles, and molecular machines. Substrate labels recognized by the autophagic machinery are more diverse and include Ubi. In this study, overexpression of FBXL16 in SH-SY5Y cells reduced mutant α-synuclein accumulation. Therefore, a co-expression vector of FBXL16 promoter and luciferase reporter gene was constructed for screening the active ingredients of traditional Chinese medicine. It was found that Licochalcone B(LCB) increased the transcriptional activity of FBXL16. In addition, PCR array experiments revealed that LCB may enhance autophagy and remove misfolded proteins by activating the AMPK/SIRT1 pathway. LCB exerted a protective role in transgenic PD mice by enhancing ubiquitylation and autophagic degradation of disease protein, which finally improved the behavioral ability of transgenic PD mice. LCB able to alleviate the symptoms and may be advocated as a natural preventive supplement for PD. Key words: Ubiquitination, Autophagy, FBXL, Parkinson’s disease Acknowledgement: This research was funded by grants from the Macao Science and Technology Development Fund 002/2023/ALC and 006/2023/SKL.

Abstract no.79

Tangshen Formula Reduces Lipid Accumulation in NAFLD Mice by Modulating Lipophagy

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Objective: To investigate the potential mechanisms by which the Chinese herbal compound Tangshen Formula (TSF) regulates autophagy to improve lipid deposition in mice with nonalcoholic fatty liver disease (NAFLD). Methods: A NAFLD mouse model was established through a high-fat diet, and post-modeling, the mice were administered TSF via gavage. Changes in triglycerides (TG), total cholesterol (TC), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels were monitored. Liver tissue lipid deposition was examined using Hematoxylin-Eosin (HE) and Oil Red O staining. Expression levels of autophagic marker LC3B-I/II, autophagy substrate p62, silent information regulator 1 (SIRT1), and the key upstream molecule of autophagy, mTOR, were analyzed by Western blot. Results: TSF significantly reduced serum levels of TG, TC, ALT, and AST in NAFLD model mice and markedly improved lipid deposition in liver tissues. Western blot analysis revealed that TSF significantly upregulated the expression of autophagy protein LC3BII and SIRT1, and significantly decreased the expression of phosphorylated mTOR and p62. Conclusion: TSF significantly alleviates lipid deposition in the livers of NAFLD model mice, potentially through mechanisms involving the regulation of the SIRT1 and mTOR-mediated autophagy pathway.

Abstract no.80

The analgesic effect and mechanism of the active components screening from Corydalis Rhizoma by P2X3 receptors

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The study was aimed to screen Corydalis Rhizoma for anti-central sensitization active components and investigate and clarify the pharmacological mechanism and therapeutic efficacy of the active ingredient Cavidine (CAV) in the treatment of chronic pain. First, cell membrane immobilized chromatography was used to screen the active ingredients in Corydalis Rhizoma. Spare nerve injury (SNI) model and complete Freund's adjuvant (CFA) mice model were constructed to identify the analgesic effect of CAV. RNA-seq and bioinformatics analyses were used to explore the potential targets of CAV in CFA mice and SNI mice. HE staining was used to observe the infiltration of inflammatory cells in the dorsal root ganglion (DRG) and spinal cord of CFA mice and SNI mice. WB and qPCR were used to detect the expression of inflammatory factors TNF-α, IL-1β and IL-6 in DRG (dorsal root ganglion) and spinal cord. In vitro and in vivo models were used to study the effect and mechanism of CAV on microglial activation in SNI models and CFA mice.

Abstract no.81

Kuoxin Decoction Promotes Cardiac Lymphangiogenesis in Doxorubicin-Induced Dilated Cardiomyopathy Rats and in Vitro

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BACKGROUND: Dilated cardiomyopathy (DCM) is a primary myocardial disorder characterized by ventricular dilation and impaired contractility, which is a significant cause of heart failure. The cardiac lymphatic system, particularly through lymphangiogenesis, plays a crucial role in cardiovascular diseases. Kuoxin Decoction (KXD) is a traditional Chinese medicine prescription used to treat DCM, specifically addressing lymphangiogenesis deficiency. This study investigated the effects of KXD on cardiac lymphangiogenesis in a doxorubicin (DOX)-induced DCM rats model and its influence in lymphatic endothelial cells (LECs). METHODS: In vivo experiments were initially conducted using DOX-induced DCM rats, with the rats being divided into control, model, low-dose KXD, medium-dose KXD, high-dose KXD, and Captopril groups. Echocardiography was used to measure the heart function. Histological evaluations including hematoxylin and eosin (HE) and Masson's staining were performed to assess structural integrity and fibrotic status. Immunohistochemical staining was utilized to determine the expression of LYVE-1 and Prox-1 in the cardiac tissue. Western blot analysis was carried out to detect the expression of VEGFR-3 and NRP2 in the myocardial tissue.Subsequent in vitro experiments were performed using LECs under normal conditions and in a model of injured LECs induced by the VEGFR-3 receptor kinase inhibitor MAZ51. Cell viability was assessed using the CCK8 method, cell migration was evaluated using the scratch method, and mRNA and protein expression levels of VEGF-C, VEGF-D, VEGFR-3, and NRP2 were measured using qPCR and Western blot, respectively. RESULTS： The results showed that KXD improved cardiac function, reduced myocardial fibrosis, and increased key lymphangiogenesis mediators such as VEGFR-3, LYVE-1, and Prox-1 ($P < 0.01$) in DOX-induced DCM rats. In vitro experiments demonstrated that KXD enhanced LECs proliferation and motility ($P < 0.01$), raised VEGF-C, VEGFR-3, and NRP2 expression, and elevated the VEGF-C / VEGF-D ratio ($P < 0.05$). CONCLUSION: KXD may enhance cardiac lymphangiogenesis in DOX-induced DCM rats, improve cardiac function, and boost LECs proliferation and migration, possibly through the VEGFC/D-VEGFR3/NRP2 axis. ACKNOWLEDGEMENT This research was funded by the National Natural Science Foundation of China (81873264, 82004319).

Abstract no.82

Meta-analysis of Clinical Efficacy and "Disease-Symptom-Formula" Associated Mechanism Investigation of Shangke Jiegu Tablet Against Bone Fracture

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ABSTRACT Aim: To systematically evaluate the clinical efficacy of Shangke Jiegu Tablets in the intervention of bone fracture, and to elucidate its pharmacological mechanisms against this disease from the perspective of "Disease-Symptom-Formula" association. Methods: The published research literatures associated with the intervention of bone fractures using Shangke Jiegu Tablets were retrieved from Chinese databases (CNKI, Wanfang and VIP databases) and English databases (PubMed, Cochrane Library and EMbase), covering the period from the inception of the databases to January 2024. Then, the risk assessment tools were used to evaluate the quality of all the enrolled literatures, and the clinical efficacy of Shangke Jiegu Tablets against bone fractures was evaluated by Stata 16.0 software. After collecting the putative targets of Shangke Jiegu Tablets and the fracture-related genes from ETCM 2.0 database and GEO database, our "drug target-disease gene" interaction network was constructed and the topological features were calculated. In addition, the key network targets of Shangke Jiegu Tablets against bone fractures were screened due to their topological importance, and the involved biological functions were analyzed by enrichment analysis based on the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway database, which were also experimentally validated. Results A total of 14 articles were incorporated into the Meta-analysis, encompassing a cumulative sample size of 1,293 cases, indicating an overall response rate of Shangke Jiegu Tablets for bone fracture therapy (RR=1.24, 95%CI: 1.18-1.31, P<0.001). Mechanistically, the clinical efficacy of Shangke Jiegu Tablets against bone fractures were associated with various functional modules including bone injury healing, nerve and blood system regulation, and immune-inflammation regulation. Notably, the candidate network targets of the Huoxue Huayu and Xiaozhong Zhitong efficacy groups of this prescription were found to be involved into the phosphatidylinositol 3-kinase /protein kinase B pathway, vascular smooth muscle contraction, and NOD-like receptor signaling pathways which may contribute to the dredging of meridians, dissipation of stasis, maintenance of immune-inflammation system balance, regulation of bone metabolism balance, and ultimately the breaking of blood stasis and promotion of muscle and bone connectivity. The candidate network targets of the Xujin Jiegu and the Qingre Jiedu efficacy groups were revealed to play a role in enhancing liver qi, facilitating cardiac blood circulation, dilating blood vessels, and alleviating heartburn through modulating the circulatory system, reversing the immune-inflammation imbalance, and regulating the material and energy metabolism. Moreover, the candidate network targets of the Huoxue Huayu, Xiaozhong Zhitong, Xujin Jiangu, and Qingre Jiedu efficacy groups were involved into modulating the nervous system to promote the circulation of qi and blood, and improving metabolic processes. Experimentally, the administration of Shangke Jiegu Tablets effectively promoted the bone trabecular growth and callus remodeling, shortened the fracture healing time, enhanced the muscle strength and improved the mechanical properties of the affected limbs, mainly by accelerating the process of endochondral ossification, decreasing the number of osteoclasts, increasing the level of bone growth factor, and improving the indicators of

bone metabolism. Conclusion The current study offer an evidence that Shangke Jiegu Tablets may promote bone fracture healing through regulating the blood circulation system and the nervous system, reversing the immune-inflammation imbalances, maintaining the bone and energy metabolism homeostasis, as well as its comprehensive effects including the dissipation of blood stasis, the promotion of blood circulation, the alleviation of swelling and pain, the regeneration of muscles and bones, and the clearance of heat and detoxification. These findings may offer guidance for the clinical rational application of Shangke Jiegu Tablets in bone fracture therapy. Key words: Shangke Jiegu Tablet; Bone Fracture; Meta-Analysis; Network Pharmacology; Clinical Efficacy; “Disease-Symptom-Formula” Association

Abstract no.83

Bushen Huoxue Formula Alleviates Inflammation and Interstitial Fibrosis in Chronic Kidney Disease by Inhibiting the NLRP3/GSDMD/Caspase-1 Signaling Pathway

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Background: With increasing incidence and mortality, chronic kidney disease (CKD) has become a global concern. Nod-like receptor family pyrin domain containing 3 (NLRP3) inflammasome activation induces pro-inflammatory cytokines interleukin (IL)-1β and IL-18, promotes gasdermin D (GSDMD)-mediated pyroptosis, and accelerates renal fibrosis, leading to end-stage renal disease (ESRD). The Bushen Huoxue Formula (BSHXF) has shown promising clinical efficacy; however, its underlying mechanisms remain unclear. Objective: This study investigates the effects and mechanisms of BSHXF on mice with CKD based on the NLRP3/GSDMD/Caspase-1 signaling pathway. Methods: Six-week-old male C57BL/6 Mice were fed a 0.25% adenine diet for 4 weeks to establish CKD models. They were then randomly divided into CKD, and BSHXF groups, respectively receiving double-distilled water,and BSHXF via gavage for 6 weeks. Blood serum samples were collected to measure serum creatinine (SCr) and blood urea nitrogen (BUN) for renal function evaluation. Kidney tissues were harvested for histological sectioning, protein, and RNA extraction. HE staining assessed pathological changes, while Masson staining,fibronectin (FN) and α-smooth muscle actin (α-SMA)expression evaluated tubulointerstitial fibrosis. IL-18 and IL-1β expression measured inflammation, and NLRP3, GSDMD, and Caspase-1 levels determined pyroptosis activation. Results: In the CKD model, Scr and BUN levels were significantly elevated. Renal tissues exhibited inflammatory cell infiltration, glomerular atrophy, tubular dilation, cast formation, and increased tubulointerstitial fibrosis. BSHXF treatment resulted in decreased Scr and BUN levels, amelioration of renal histopathological damage, inhibition of NLRP3/GSDMD/Caspase-1 pathway activation, and reduced levels of inflammation and fibrosis. Conclusion: In summary,BSHXF inhibits the NLRP3/GSDMD/Caspase-1 signaling pathway in adenine-induced CKD micec models, thereby protecting renal function and exhibiting anti-inflammatory, antifibrotic, and anti-pyroptotic effects. Traditional Chinese medicine should receive broader attention and application. Keywords: Bushen Huoxue Formula, CKD, NLRP3,GSDMD,Caspase-1

Abstract no.84

Spatial metabolomics combined with PK-PD modeling to investigate the pharmacological material basis and mechanism of Tangshen formula in treating diabetic kidney disease by regulating TCA cycle homeostasis imbalance

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Diabetic kidney disease (DKD) is a severe microvascular complication of diabetes, characterized biochemically by abnormal renal energy metabolism. Recent studies suggest that changes in the tricarboxylic acid (TCA) cycle metabolites are closely associated with kidney damage in DKD. Our research group has previously confirmed that after treatment with Tangshen formula, the abundance of TCA cycle metabolites in the serum of DKD patients increases, preliminarily indicating the relevance of Tangshen formula treatment to the regulation of TCA metabolism. Therefore, we propose a scientific hypothesis: the pharmacologically active components of Tangshen formula exert therapeutic effects on DKD by regulating the imbalance of the renal TCA cycle. This project aims to first apply targeted metabolomics analysis to study the changes in the content of TCA cycle intermediates in the kidneys, and then use Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) to screen for high-exposure components of Tangshen formula in the kidneys. Based on these two sets of results, spatial metabolomics research will be conducted using mass spectrometry imaging technology, further combined with Pharmacokinetics-Pharmacodynamics (PK-PD) modeling to clarify the correlation and dynamic changes among drug exposure, TCA cycle metabolites, and renal function indicators, revealing the regulation of TCA cycle homeostasis imbalance as a key mechanism by which Tangshen formula treats DKD.

Abstract no.85

Jianpi Huogu Formula promotes angiogenesis-osteogenesis coupling to ameliorate on steroid-induced necrosis of the femoral head in rats

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Jianpi Huogu Formula(JPHGF) is a product of traditional Chinese medicine prescription that has been effective in steroid-induced necrosis of the femoral head (SNOFH) clinically for many years. Nevertheless, the pharmacological effects and mechanisms of JPHGF ameliorating SNOFH needed to be better defined. In this study, a rat model of SNOFH induced by glucocorticoid and lipopolysaccharide was established to observe the effects of JPHGF on angiogenesis-osteogenesis coupling of SNOFH and the regulatory mechanism by oxidation of lipid metabolome and transcriptome. The results showed that JPHGF can reduce the histopathological and imaging changes of femoral head in rats of SNOFH, improve microvascular circulation, blood lipids, blood rheology and coagulation abnormalities, and effectively treat SNOFH, which was related to the modulation of oxidized lipids metabolism such as arachidonic acid, linoleic acid and unsaturated fatty acids. In addition, JPHGF can also down-regulate 4-HDHA by decreasing 5-LO expression in femoral head and decrease PPARγ, then up-regulate the VEGF-Notch1-Noggin signaling pathway to promote the angiogenesis-osteogenesis coupling of the femoral head of SNOFH rats. The study preliminarily revealed the scientific connotation of "treatment from the spleen" of SNOFH from the perspective of lipid metabolism regulating angiogenesis-osteogenesis coupling and provided experimental basis for clinical medication.

Abstract no.86

Network pharmacology analysis reveals the active compounds and the potential mechanisms underlying the antidepressant effects of herbal formulation Banxia-Houpo Decoction

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Introduction: The chemical complexity and mechanistic elusiveness largely limited the global acceptance of Chinese medicines as the treatment for increasingly prevalent depression. The aim of the present research is to reveal the active compounds and the potential mechanisms underlying the antidepressant effects of herbal formulation Banxia-Houpo Decoction (BHD). Materials and Methods: We analyzed the chemical composition of ethanolic BHD extract and identified 64 compounds by UPLC-QTOF-MS. The prediction and screening of potential depression-related targets were performed using Similarity Ensemble Approach (SEA), the Search Tool for Interactions of Chemicals (STITCH), SwissTargetPrediction, Therapeutic Target Database (TTD), Comparative Toxicogenomics Database (CTD), PharmGKB, DisGeNET, and GeneCards. Gene Ontology (GO) and the Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathway Enrichment of selected targets were performed using the online bioinformatics tool DAVID at http://david.ncifcrf.gov. Results: As result, the top enriched KEGG pathway was the serotonin pathway involving 11 targets (i.e., APP, HTR7, MAOA, CASP3, HTR1A, HTR2B, HTR1B, MAPK1, HTR2C, HTR2A, and SLC6A4). In parallel, six compounds (i.e., luteolin, N-nornuciferine, scutellarin, roemerine, baicalein, and 6-shogaol) from the 5 herbal ingredients of BHD were identified as the corresponding active compounds. Conclusions: Our results suggest that the six active compounds may contribute to the antidepressant activity of the herbal formulation BHD via regulating the serotonin pathway.

Abstract no.87

Establishment of a platform for the liver toxicity evaluation induced by Traditional Chinese Medicine injections

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Objectives: Traditional Chinese medicine (TCM) injection, a sterile preparation (solution, powder, concentrated solution, emulsions, etc.) made from traditional Chinese medicine and a meant for injection into the human body is widely used in clinical applications due to its characteristics of rapid effect. Yet many serious adverse drug reactions (ADRs) related to TCM injections have been brought out due to the limited mechanistic research. Liver cancer is one of the indications of TCM injections and many ADRs related to TCM injections occurred in the liver. Thus, we try to establish a reliable platform for the evaluation of the impact of TCM injections on the liver. Methods: An in-house cohort of forty TCM preparations was adopted and their impact on the proliferation and viability of the normal liver cell lines (NLC) and liver cancer cell lines (HCC) was evaluated. To recapitulate the pathological process of HCC, a spontaneous HCC model induced by hydrodynamic delivery of oncogenic genes (HDTVi) was established and TCM preparations was injected together with the oncogenes to evaluate the impact of the selected TCM preparations in the acceleration or deceleration of HCC. Results: Taking a 50% increase or decrease as a significant impact on the cells, we identified two preparations (TCMinh) which reduced HCC cell proliferation while didn't affect/promote NLC growth in all four dilutions. In the meantime, two preparations which exhibited significant toxic effect to NLC only (TCMpro) was also included for further animal study. Our results showed that two TCMinh showed significantly tumor shrinking effect and only one TCMpro exhibited consistent promoting effect in tumor development. Conclusions: These results suggest a reliable animal model in evaluation of TCM injections in HCC treatment as well as liver toxicity in the aspect of liver cancer development. Our findings may contribute to the re-evaluation and better management of TCM injections.

5. Bioinformatics and AI Applications in TCM

Abstract no.88

Data construction and systemic analysis of Pu-Ji-Fang by machine learning and wound healing related formula development

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Abstract: When an external wound becomes infected, it often presents with cellulitis, tissue suppuration, and wound ulceration. In recent years, numerous studies have highlighted the beneficial therapeutic effects of traditional Chinese medicine (TCM) in trauma medicine. With thousands of years of clinical experience and data accumulation, TCM offers valuable insights. Many medical texts detail the efficacy, properties, and appropriate dosages of individual Chinese herbs. This project utilizes Pu-Ji-Fang (普濟方) as its foundation and constructs a database of Chinese medicine formulas for data exploration and correlation confirmation. Specifically, we focus on trauma drugs suitable for experimentation and establish drug association modules. We organize data from the Jin-Chuang-Phylum, Zhang-Chuang-Phylum, and Chih-Chuang-Phylum, comprising 490 formulas across six volumes. Correlation analysis reveals two clusters of trauma medicines categorized as oral medication and external application. Cell biology experiments and signaling pathway analyses aim to confirm the formulas' ability to promote the cell growth rate of fibroblasts. Ultimately, these studies aim to achieve several objectives: (1) Combine the traditional Chinese medicine theory of the emperor and minister with modern data mining and machine learning techniques to identify potential candidate drugs from traumatic formulae. This could pave the way for future product development. (2) Systematically analyze the 61,000 formulas recorded in Pu-Ji-Fang for various diseases, pinpointing core modules and suggesting relevant drug recommendations. (3) Establish a systematic platform integrating ancient Chinese medicine knowledge with Western medicine, facilitating comprehensive herbal database construction for drug cocktail therapy in basic research and clinical applications. (Some of results were published in 2024; PMID: 38584602) Acknowledgement: IHMed IVF Center.

Abstract no.89

Using Artificial Graph Neural Network to Mechanism Elucidation for Validating Traditional Practices and Developing Evidence Based Cancer Therapies of Traditional Chinese Medicine

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Traditional Chinese Medicine (TCM) offers a wealth of experience in cancer treatment, but its wider acceptance is hampered by a lack of understanding of how TCM formulas work on a molecular level. Here, artificial graph neural networks (GNNs) emerge as a powerful tool for mechanism elucidation, bridging the gap between traditional practices and developing evidence-based cancer therapies. Beyond Traditional Methods: Traditional mechanism elucidation relies on expert knowledge and databases, with limited ability to discover hidden connections. GNNs offer a data-driven approach: Learning from Big Data: GNNs analyze vast datasets of: TCM Formulas: Composition (herbs, chemical compounds), known bioactivities. Cancer Networks: Proteins, genes, and their interactions forming pathways involved in cancer development. Network Representation: Both TCM formulas and cancer networks are represented as interconnected nodes in a graph. Formulas become nodes with features like herb type, chemical compounds, and known activities. Similarly, cancer networks are represented as nodes (proteins, genes) connected by edges indicating their interactions. GNNs Decipher TCM Mechanisms: Feature Learning: GNNs analyze features of nodes (TCM formulas and cancer network elements) and their connections within the network. This allows them to learn how TCM compounds might influence the cancer network. Target Identification and Pathway Prediction: By analyzing the learned data, GNNs can predict: Target Molecules: Specific proteins or genes within the cancer network most likely to be influenced by a particular TCM formula. Affected Pathways: The pathways most likely to be affected by the TCM formula, providing insights into its potential therapeutic mechanisms. Revolutionizing TCM with GNNs: Unveiling Hidden Connections: GNNs can reveal previously unknown interactions between TCM and cancer, leading to the discovery of novel therapeutic targets and mechanisms. Enhanced Accuracy: Trained on vast amounts of data, GNNs can potentially predict target molecules and affected pathways with greater accuracy compared to traditional methods. Integration with Other Techniques: GNNs can be combined with molecular docking simulations to gain a deeper understanding of how TCM formulas interact with cancer cells at the molecular level. Challenges and the Road Ahead: Data Quality and Standardization: GNNs require large, high-quality, and standardized datasets on TCM formulas, their components, and cancer pathways. Ensuring data accuracy is crucial. Interpretability of GNN Models: Understanding how GNNs arrive at their predictions can be challenging. Research is ongoing to develop more interpretable models for better understanding of the identified mechanisms. Collaboration is Key: Effective utilization of GNNs requires collaboration between data scientists, TCM practitioners, and cancer biologists. Data scientists build the models, TCM practitioners provide expertise on formulas, and cancer biologists interpret the results within a biological context. Conclusion: Artificial Graph Neural Networks offer a transformative approach for mechanism elucidation in TCM cancer therapies. By leveraging their ability to learn complex relationships from data, GNNs can accelerate the discovery of novel therapeutic mechanisms

and pave the way for the development of evidence-based TCM cancer therapies. This collaborative approach holds immense potential for unlocking the full potential of TCM and revolutionizing cancer treatment.

Abstract no.90

Construction of a TCM Intelligent Syndrome Differentiation Model for Diabetic Kidney Disease Based on Large Language Model Knowledge Extraction Technology

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Objective Research on knowledge extraction technology for diabetic kidney disease based on large language models, and construction of intelligent syndrome differentiation models in traditional Chinese medicine. Methods Construct a database of traditional Chinese medicine information for diabetic kidney disease cases, write prompt words to guide the large language model to achieve case extraction, adopt a variety of machine learning models to establish a traditional Chinese medicine syndrome differentiation model, and use five-fold cross-validation to evaluate the model. Evaluation indicators include Accuracy, Precision, Recall, and F1. Results The large language model can accurately extract medical records from the literature and output them in the format indicated by the prompt words. By combining the standardization and unification of symptoms and four diagnostic information, a dataset with multi-dimensional input variables of traditional Chinese medicine four diagnostic information was successfully obtained, and the output was a total of 9 items of traditional Chinese medicine syndrome types of diabetic kidney disease. The fitting effects of the 5 machine learning models are relatively good, among which the SVM model has the highest indicators, which are 0.94, 0.92, 0.91, and 0.92 respectively. Conclusion The large language model can accurately extract medical records and output them in a standardized manner. The traditional Chinese medicine syndrome differentiation model of diabetic kidney disease based on SVM should have good diagnostic ability, which can verify the feasibility of applying artificial intelligence to the construction and clinical application of traditional Chinese medicine syndrome differentiation models for diabetic kidney disease, and has a high accuracy rate.

Abstract no.91

Discovery of Novel Anti-Cancer Inhibitors using Machine Learning and Molecular Docking Approach

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2. Mr Hailong Zhang, Macao Polytechnic University, Macao SAR

Abstract EGFR and BRAF targets are leading therapeutical targets for anti-cancer treatment in pharmaceutical industry. The present study is to develop novel models to predict bioactivity for EGFR and BRAF inhibitors and to uncover critical substructural groups for designing new drugs of EGFR and BRAF targets. The results showed that Random Forest (RF) model demonstrated the best performance for bioactive prediction of both EGFR and BRAF targets. The RF models of BRAF and EGFR targets showed the accuracy and AUC were 93%, 0.96, and 90%, 0.96, respectively. The study showed it was critical to properly increase element of chlorine or fluorine in the inhibitor structures of both BRAF and EGFR targets. In addition, the present study was the first one to discover EGFR and BRAF inhibitors exhibited same priority in selecting Halogen, which was fluorine>chlorine>bromine. The molecular docking showed the docking S scores of the molecules were -6.79 and -8.13 in EGFR and BRAF proteins, respectively. Globally, our study is the first one to uncover that forming hydrogen bond may be a key factor for affecting selecting priority of fluorine>chlorine>bromine in the structures by using molecular ducking. Our findings indicate the preferable number of the group of NH should be selected in the range from 2 to 3 and fluorine should be selected in the range from 1 to 2 for inhibitor structures of both BRAF and EGFR targets.

Abstract no.92

UPLC-qToF-MS Coupled with Cell Phenotype Screening of American Aconitum

1. Prof Edward Kennelly, The City University of New York, The Bronx

Aconitum plants have been widely used as traditional medicine in Asian countries for centuries, including the well-known fuzi, the lateral root of Aconitum carmichaelii. However, there are few records about how American Aconitum has been used medicinally, despite its phylogenetic closeness to medicinally important Asian species. This study aims to explore bioactive compounds in American Aconitum using a systematic molecular network strategy integrating both mass spectrometric data and a high-throughput phenotype screening assay known as cell painting. The chemical profiles of different parts of two American Aconitum species were obtained by ion mobility spectrometry technique and compared with non-American Aconitum species. Image analysis and feature extraction were performed on four different concentrations of Aconitum extracts assayed in cell painting, resulting in 2,090 unique morphological features per extract. In conjunction with the TargetMol library of 4,400 compounds with known mechanisms of action, 198 unique hierarchical clusters were established after a feature selection strategy known as Fast Correlation-Based Filtering, which reduced the number of features to 429. An overall activity heuristic called the CP score was calculated for each sample. After integrating the CP score and spectrometric data, a molecular network containing higher CP scores was constructed and the compounds with high activity were targeted and being identified. The molecular network showed that American Aconitum contains several bioactive diterpenoid alkaloids.

Abstract no.93

Molecular mechanisms associated with CKP and CKI suppression of mucositis caused by radiotherapy

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Aims: This research aims to explore the mechanisms by which Compound Kushen Powder (CKP) and Compound Kushen Injection (CKI) act on irradiated intestinal mucosa to alleviate gastrointestinal mucositis (GIM) symptoms at the molecular level. The efficiency of newly developed oral dosage form CKP against radiation induced GIM will be examined, and the differential gene expression induced by CKI, CKP against GIM on rats will be explored. Methods: We employed a previously established rat model for GIM, induced through fractionated irradiation of the abdomen in Sprague Dawley (SD) rats. Utilizing this model, the efficacy of orally administered CKP in mitigating GIM was evaluated. Tissue samples from the mucosal epithelia of both the small and large intestines were collected at the onset and peak of GIM symptoms. From these samples, total RNA was extraction, followed by sequencing for transcriptome analyses. The subsequent analyses focused on identifying differential gene expression patterns and conducting pathway over-representation analyses to understand the molecular basis of CKP and CKI's therapeutic effects. Results： The results of our study demonstrated a significant amelioration of GIM symptoms in the rat model, specifically in reducing diarrhea and preventing weight loss, following the oral administration of CKP concurrent with abdominal irradiation. Transcriptome analysis revealed that both CKI and CKP influence multiple molecular pathways. The various gene expression appears to reduce apoptosis and inflammation while promoting tissue healing, thereby effectively mitigating the adverse effects of radiation-induced GIM.

Abstract no.94

Fusing Pulse and ECG Data for Coronary Heart Disease and Complications Identification

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2. Ms Leixin Hong, Shanghai University of Traditional Chinese Medicine, Shanghai

Objectives: This study aimed to explore the potential of combining wrist pulse with limb lead electrocardiogram (ECG) data to develop an identification model for coronary heart disease (CHD) and its associated comorbidities. Methods: We utilized a pulse-detecting device equipped with a pressure sensor and an ECG sensor to simultaneously collect wrist pulse and limb lead ECG signals from patients with coronary heart disease (CHD) and various comorbidities, including hypertension and diabetes. Time-domain analysis was applied to extract features such as time-domain parameters and pulse rate variability from the wrist pulse signals, as well as time-domain parameters and heart rate variability from the limb lead ECG signals. We implemented the random forest (RF) machine learning algorithm, to establish disease identification models based on these features, and evaluated their performance. Results: The results indicated that the disease identification model which incorporated features from both pulse and ECG signals, exhibited improvements of 1.99%, 3.13%, 3.78% and 3.32% in terms of accuracy, average precision, average recall and F1 value, respectively, when compared to the model based solely on pulse features. Furthermore, when compared to the ECG-based model, the results were improved by 3.99%, 3.13%, 3.78% and 3.32% respectively. Conclusions: The fusion of information from multiple sources enhances the reliability of decision-making of the system. This approach presents a novel method for managing cardiovascular diseases and offers insights into the application and promotion of wearable pulse-detecting products.

Abstract no.95

Causal relationship between volume of brain subcortical structures and bone mineral density across the life cycle: a Mendelian randomization study

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This study aims to explore the causal relationship between the volume of subcortical brain structures and bone density across the lifespan using a two-sample Mendelian randomization approach. The analysis is based on genome-wide association study (GWAS) summary data, including the subcortical brain structure volume and bone density data of European populations. The inverse variance weighted (IVW) method was employed as the primary analysis method, with horizontal pleiotropy and heterogeneity tests conducted to ensure result stability. The results indicate that an increase in genetically predicted ventral striatum volume is significantly causally associated with increased bone density in individuals over 60 years old and across the lifespan (b=2.36 x10E-04, 95%CI: 3.69x10E-05～4.34x10E-04, P=0.020). Additionally, an increase in intracranial volume is associated with increased bone density in individuals aged 45-60 years (b=1.50 x 10E-06, 95%CI: 9.84x10E-08～2.91x10E-06, P=0.036), while an increase in hippocampal volume is associated with increased bone density in individuals under 15 years old. After Bonferroni correction, an increase in thalamic volume shows a significant causal relationship with increased bone density in individuals aged 45-60 years (b=6.81x10E-04, 95%CI: 3.00x10E-04 ～ 1.06x10E-03, P=4.60x10E-04). The study concludes that the volumes of the thalamus, ventral striatum, intracranial space, and hippocampus have a causal relationship with bone density across the lifespan.

Abstract no.96

The tongue appearance of the population in plateau areas is different from that in plain areas

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Abstract: Background: Long-term residence at high altitudes (over 2400 m) can cause changes in the body's physiological state, and traditional Chinese medicine (TCM) believes that these changes may be reflected in the tongue's appearance. However, it is still unclear whether the tongue characteristics of individuals living in plateau areas (PA) differ from those in non-plateau areas (NPA). Objective: To explore the differences in tongue appearance features between residents of PA and NPA. Methods: Residents from PA and NPA were recruited for this study. Tongue images were collected using an automated tongue diagnosis system and segmented with Mask R-CNN technology. The color and texture features of the tongue were then quantitatively analyzed using Lab color space, GLCM, and GLRLM methods. Dimensionality reduction was performed on the data using t-SNE analysis, and a Random Forest Model (RFM) was constructed based on the color and texture features of the tongues from PA and NPA residents. The model's performance was evaluated using the Receiver Operating Characteristic (ROC) curve and the Precision-Recall (PR) curve. Conclusion: There are differences in the tongue characteristics between PA and NPA residents, mainly reflected in the color distribution of the tongue and tongue coating. Key words: High altitude medicine; Tongue diagnosis in Traditional Chinese Medicine; Machine learning algorithm

Abstract no.97

Automating Chinese Medicine Prescriptions Based on Pulse Pattens using Novel Equipment

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After US President Richard Nixon's visit to China in 1971, acupuncture sparked a global craze; however, the theory behind acupuncture and the meridian theory underlying traditional Chinese medicine has been incompletely understood by the scientific community. Apart from active collaboration between the U.S. NIH and Harvard University with China, the Chinese government has prioritized meridian research as a core medical topic from the 75-Plan in 1986 to the current 145-Plan. However, there were no significant results before the 115-Plan. It wasn't until the 125-Plan (2010 to 2015) that preliminary affirmative results emerged. On the other hand, Taiwan's Academia Sinica has analyzed the relationship between harmonics and meridians through blood pressure wave analysis from 1989 and has developed a digital meridian pulse diagnosis instrument for the medical use.With second harmonic generation law and conservation of energy, we conducted and verified the “Five Elements Principle”.Deriving the Radial Resonance Equation, we built the physic basis of pulse diagnosis.From the Radial Resonance Theory and pulse diagnosis principle, we design a pulse diagnosis apparatus to evaluate the excess or deficiency on meridians.In addition, through pulse diagnosis apparatus, we can analyze the pharmacological effects of acupuncture, herbs, and herbs formulae on reinforcing or reducing of meridians. Furthermore, the effect of herbs formula can be simulated by the matrix summation of individual herbs.In clinic, with Harmonic Coefficient of Variation, we can quantitatively evaluate the patients’condition.Combining the H.C.V.,Pathology and Pharmacology matrixes, we identified the indication of Chinese Medicine Bible- Shang Han Za Bing Lun.Now we know why these formulae are amazingly effective when the indication confirmed, because the pharmacological matrix of the formula is just the reverse of pathological matrix. In Chinese medicine bible Shang Han Za Bing Lun, it gives almost as many pharmacological matrixes in formulae as the possibilities of the pathological matrixes. By science, the thousand years’ secret is revealed now and we can automating Chinese Medicine prescriptions based on pulse pattens using novel equipment.

Abstract no.98

Differential analysis of two methicillin-resistant Staphylococcus aureus species based on transcriptome sequencing

1. Ms Hongsa An, China Academy of Chinese Medical Sciences, Beijing

2. Prof Yong Tan, China Academy of Chinese Medical Sciences, Beijing

In order to investigate the biosynthesis-related differential genes of two methicillin-resistant Staphylococcus aureus(MRSA) virulence, the present study was carried out using RNA-seq technology to sequence the transcriptomes of two MRSAs, "ATCC43300" and "USA300". In this study, we used "ATCC43300"and"USA300"MRSA as materials, and sequenced the transcriptomes of the two MRSA using RNA-seq technology. By analyzing the differential expression of the two different types of MRSA genes, 1,375 differentially expressed genes were identified, including 676 up-regulated genes and 699 down-regulated genes. GO (Gene Ontology) and KEGG (Kyoto Encyclopedia of Genes and Genomes) enrichment(Figure1 and Figure2) analysis of the common differential genes revealed that the two groups of common differential genes were mainly enriched in protein metabolic processes, transmembrane transporter protein activity, structural molecule activity, pyruvate metabolism, two-component system, DNA replication and the pentose phosphate pathway, and other processes. Among them, the significant changes in the expression of SepA, SspA and other genes may play an important role in the virulence expression of MRSA. This study facilitates the understanding of those specific genes associated with bacterial virulence, which may be potential targets for the development of new drugs or vaccines, thus providing us with new weapons against this superbug.

Abstract no.99

Analysis of the Mechanisms of Action of Panax notoginseng on MRSA Strains ACTT43300 and USA300

1. Mrs Yuwen Xia, China Academy of Chinese Medical Sciences, Beijing

Objective: To investigate the common and differential mechanisms of action of Panax notoginseng extract on methicillin-resistant Staphylococcus aureus (MRSA) strains ACTT43300 and USA300. Methods: RNA sequencing was used to analyze the differentially expressed genes in ACTT43300 and USA300 strains treated with Panax notoginseng extract. GO and KEGG pathway enrichment analyses were performed to reveal the key pathways commonly and differentially regulated by the extract in these strains. PPI network construction and network topology analysis were used to identify core targets of Panax notoginseng extract action. Results: After treatment with Panax notoginseng extract, 552 and 276 differentially expressed genes were identified in ACTT43300 and USA300 strains, respectively. GO and KEGG pathway enrichment analyses indicated that, in ACTT43300, the pathways for redox reactions, fatty acid metabolism, and amino acid metabolism were significantly activated, while pathways for carbohydrate metabolism, carbon metabolism, and stress response were inhibited. In USA300, redox and amino acid metabolism pathways were significantly activated, while lipid, vitamin, and polysaccharide metabolism pathways were inhibited. Conclusion: Panax notoginseng extract exerts common regulatory effects by targeting pathways related to redox reactions, amino acid metabolism, and carbohydrate metabolism. It also specifically regulates ACTT43300 by upregulating/downregulating fatty acid metabolism, carbon metabolism, and stress response, and USA300 by upregulating/downregulating lipid and vitamin metabolism. Keywords: MRSA; Panax notoginseng; antibiotic resistance; transcriptomics

Abstract no.100

A novel herb formula Four-Herb Formula showed potently anti-breast cancer effect via progesterone receptor-mediated cell proliferation

1. Dr Dong-Jie Wang, The Chinese University of Hong Kong, Hong Kong SAR

With significant advancements in breast cancer therapy, early-stage patients can achieve tumor-bearing survival and maintain a good quality of life through regular radiotherapy and chemotherapy. However, effective treatments for advanced breast cancer remain elusive. Based on classical traditional Chinese medicine (TCM) prescriptions and extensive preliminary research, we developed a novel TCM compound named "Four-Herb Formula," composed of Ganoderma lucidum, Andrographis paniculata, Eleutherococcus senticosus, and Hedyotis diffusa. In vivo and in vitro experiments indicate that "Four-Herb Formula" exhibits promising anti-breast cancer effects, although the precise mechanisms remain unclear. Using clinical databases, network pharmacology, and bioinformatics, we aim to elucidate the specific mechanisms. Identification shows andrographolide (20%) and ganoderic acid A (12%) as the main active constituents, with other excipients comprising approximately 65% (consist of sucrose, citric acid and lactose). We investigated the anti-tumor effects of the primary active ingredients through a combined medication approach. Network pharmacology identified five common targets of andrographolide and breast cancer (PGR, CDK1, CHEK1, NUDT1, and PDCD4). Lasso-Cox and WGCNA further identified PGR and CDK1 as most associated with breast cancer malignancy. Molecular docking showed andrographolide binds to PGR with an affinity of 1.12 x 10^-9 M and to CDK1 with 1.79 x 10^-6 M, indicating selective binding to PGR. Gene enrichment and pathway analysis of PGR revealed its role in regulating cell proliferation and cytoskeletal pathways, validated in single-cell data. Ganoderic acid A enhances the PGR-related pathways regulated by andrographolide, demonstrating a synergistic effect. Our study provides new insights into TCM compound mechanisms, suggesting they could serve as reference models for multi-target drug development.

Abstract no.101

Development of an effective random forest classifier for plant and animal miRNAs

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3. Mr Yihong Luo, Chinese Academy of Medical Sciences, Haidian

MicroRNAs (miRNAs) are a class of non-coding RNA molecules that are vital for the regulation of gene expression in both animals and plants. There are significant differences in the maturation, processing, and mechanisms of action of miRNAs between animals and plants. This study aims to employ machine learning techniques to classify miRNAs from animal and plant sources, with the objective of identifying the most suitable model for miRNA classification and identifying the features that distinguish animal and plant miRNAs. Firstly, we collected 37,811 animal miRNA sequences and 37,621 plant miRNA sequences to construct a miRNA sequence database. Secondly, all the miRNA sequences were encoded using a one-hot encoding scheme and randomly divided them into a training and a test set in an 8 to 2 ratio. Thirdly, we employed five different machine learning models (SVM, DT, RF, NN, and CNN) to classify the animal and plant miRNA sequences, identifying the optimal parameters and execution time for each model. Upon evaluating and comparing these five models, we concluded that Random Forest is the most suitable model for classifying animal and plant miRNAs. Finally, we discussed why Random Forest emerged as the best classifier for animal and plant miRNAs and provided an outlook for future work in this field. Results obtained from these study suggest that animal and plant miRNAs have unique features that can be distinguished.

Abstract no.102

Tongue color parameters in predicting the degree of coronary stenosis: a retrospective cohort study of 282 patients with coronary angiography

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2. Ms Li Jieyun, Shanghai University of Traditional Chinese Medicine, Shangahi

Abstract Purpose: This retrospective cohort study aimed to analyze the relationship between tongue color and coronary artery stenosis severity in 282 patients after underwent coronary angiography. Methods: A retrospective cohort study was conducted to collect data from patients who underwent coronary angiography in the Department of Cardiology, Shanghai Jiading District Central Hospital from October 1, 2023 to January 15, 2024. All patients were divided into four various stenosis groups. The tongue images of each patient was normalized captured, tongue body (TC_) and tongue coating (CC_) data were converted into RGB and HSV model parameters using SMX System 2.0. Four supervised machine learning classifiers were used to establish a coronary artery stenosis grading prediction model, including random forest (RF), logistic regression, and support vector machine (SVM). Accuracy, precision, recall, and F1 score were used as classification indicators to evaluate the training and validation performance of the model. SHAP values were furthermore used to explore the impacts of features. Results: This study finally included 282 patients, including 164 males (58.16%) and 118 females (41.84%). 69 patients without stenosis, 70 patients with mild stenosis, 65 patients with moderate stenosis, and 78 patients with severe stenosis. Significant differences of tongue parameters were observed in the four groups [TC_R (P=0.000),TC_G (P=0.003),TC_H (P=0.001) and TC_S (P=0.024),CC_R (P=0.006),CC_B (P=0.023) and CC_S (P=0.001)]. The SVM model had the highest predictive ability, with AUC values above 0.9 in different stenosis groups, and was particularly good at identifying mild and severe stenosis (AUC=0.98). SHAP value showed that high values of TC_RIGHT_R, low values of CC_LEFT_R were the most impact factors to predict no coronary stenosis; high CC_LEFT_R and low TC_ROOT_H for mild coronary stenosis; low TC_ROOT_R and CC_ROOT_B for moderate coronary stenosis; high CC_RIGHT_G and low TC_ROOT_H for severe coronary stenosis. Conclusion: Tongue color parameters can provide a reference for predicting the degree of coronary artery stenosis. The study provides insights into the potential application of tongue color parameters in predicting coronary artery stenosis severity. Future research can expand on tongue features, optimize prediction models, and explore applications in other cardiovascular diseases. Keywords：Tongue analysis, Coronary angiography, Coronary artery stenosis, Retrospective cohort study, Machine learning Conflicts of Interest The authors declare that there are no conflicts of interest. Acknowledgement This work was supported by the Shanghai Key Laboratory of Health Identification and Assessment under Grant No.21DZ2271000, and the National Natural Science Foundation of China No.82074333 and 82374336.

Abstract no.103

Understanding the self-assembly dynamics and molecular structure of mRNA lipid nanoparticles at real size: insights from the coarse-grained simulations

1. Dr Ruifeng Wang, University of Macau, Macao SAR

Messenger RNA (mRNA) encapsulated in lipid nanoparticles (LNPs) is regarded as a cutting-edge delivery technology, which play a key role in the COVID19 pandemic and vaccine development [1]. However, molecular structure of mRNA-LNPs at real size remains elusive, with discrepancies observed between different experimental results. In this study, our aim is to explore the assembly process and structural details of mRNA-LNPs at real size by coarse-grained molecular dynamic simulations. The largest system at real size (~80 nm) reaches up to ~ 6 million beads. Moreover, the impacts of different mRNA loading levels and pH changes on the structure of mRNA-LNPs are also examined. At acidic pH, cationic lipid (dilinoleylmethyl-4-dimethylaminobutyrate, MC3) and helper lipid molecules as well as mRNA are rapidly self-assembled to form spherical-like LNPs within 50 ns, with a diameter of 51.2 nm (2 mRNA) and 75.8 nm (4 mRNA). A continuous lipid phase is observed inside mRNA-LNPs by self-assembled lipids, while the aqueous solution constitutes another continuous phase. Helper lipids can form lipid rafts, distributed in the shell or core layer of LNPs. Different mRNA payloads can affect the lipid composition in the core-shell of LNPs. At neutral pH, structural changes of mRNA-LNPs slightly decreases the ability of LNPs resident mRNA. These findings offer novel insights into the assembly dynamics and molecular structure of actual sized mRNA-LNPs, which will significantly contribute to a rational design of LNPs for efficient mRNA delivery in the future. Acknowledgments: This work was supported by University of Macau Research Grant (MYRG-CRG2022-00008-ICMS) and the Macau science and technology development fund (NO.005/2023/SKL). References: [1] Suzuki Y, Ishihara H. Drug Metab Pharmacokinet 2021;41:100424 [2] Wang Wei, Ouyang Defang. Acta Pharmaceutica Sinica B 2022;12:2950-62.

Abstract no.104

An Online Platform for Screening Active Ingredients in Traditional Chinese Medicine Based on Network Proximity Principle

1. Mr 梦晨 刘, 遵义医科大学珠海校区, 珠海

Abstract： Traditional Chinese Medicine (TCM) has long played a pivotal role in healthcare, however, identifying its active ingredients remains challenging due to the complex mixture of components and intricate biological interactions. This study introduces an online platform, accessible at http://www.zmupredict.cn, designed to screen TCM active ingredients based on network proximity principle. Users can upload disease-relevant genes and TCM ingredient targets to perform network proximity calculations, assessing the proximity between the ingredient-target dataset and the disease gene dataset. The resulting proximity scores rank bioactive ingredients, and the active ingredient regulatory network can guide experimental mechanism studies. For instance, network proximity analysis predicted 18 potential bioactive ingredients in Amomum villosum for treating acute liver injury. By integrating TCM databases with advanced network pharmacology, the platform enhances the analysis of ingredient-target networks and their proximity to disease networks. This approach prioritizes bioactive ingredients, aiding in the identification of therapeutic candidates and bridging traditional knowledge with modern computational methods for efficient TCM drug discovery. Our results demonstrate the platform's capability to predict active ingredients, suggest new candidates, and elucidate network mechanisms, underscoring its value to TCM and drug discovery researchers.

Abstract no.105

Exploring the pharmacological effects of Antiviral Oral-Liquid: A study based on network pharmacology and molecular docking

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2. Ms Xinhui Yang, Shenyang Pharmaceutical University, Shenyang
3. Ms Ying Long, Shenyang Pharmaceutical University, Shenyang
4. Ms Hongfei Lv, Shenyang Pharmaceutical University, Shenyang
5. Mr Tianjun Guo, Shenyang Pharmaceutical University, Shenyang

The Chinese patent medicine KBDOL, an antiviral oral liquid, has been used to treat bacterial pharyngitis. It is thought to target common pathogens like Staphylococcus. However, its exact mechanism is not yet clear. This study aimed to evaluate KBDOL's effect on bacterial pharyngitis and confirm its bacteriostatic properties through network pharmacology and experimental methods. By using network pharmacology and molecular docking, we predicted KBDOL's effects and identified Staphylococcus aureus as its target for inhibition, which was later experimentally verified. We found 13 key targets, including SRC, STAT3, PIK3CB, etc. KEGG analysis indicated that KBDOL's therapeutic effects involve pathways related to cancer, Kaposi's sarcoma-associated herpesvirus infection, and PI3K-Akt, and that its inhibition of S. aureus may also be via these pathways. In summary, potential targets of KBDOL for treating bacterial pharyngitis have been predicted, and KBDOL has been shown to inhibit the growth of Staphylococcus aureus, providing a theoretical basis for further study of its pharmacological actions and clinical application. Keywords: antiviral oral liquid, network pharmacology, bacterial pharyngeal tonsillitis, bacteriostatic assay

Abstract no.106

Developing Artificial Intelligence Technology for Pulse Diagnosis and its Application for Cardiovascular Diseases with Traditional Chinese Medicine

1. Prof Jiangang Shen, The University of Hong Kong, Hong Kong SAR

Cardiovascular diseases (CVDs) are major disease burdens with high mortality worldwide. Due to complex pathological mechanisms of CVDs, traditional data analysis is insufficient to manage multidimensional data of CVDs, medical image interpretations, therapeutic decision-making, and disease prognosis prediction. Traditional Chinese Medicine (TCM) offers unique applications for CVDs. In TCM practice, sphygmopalpation at human wrists is used for pulse diagnosis. However, the standardization and digitalized analysis on the arterial pulse waves for pulse diagnosis are challenge task. Artificial intelligence (AI) technology facilitates the development of integrative approaches for pulse diagnosis, offering great opportunity to resolve these challenges. Hence, we have developed a pulse sensing platform for studying and digitalizing arterial pulse patterns. This platform consists of a robotic hand with three pressure-feedback-controlled robotic fingers for pulse measurement and an artificial neural network (ANN) for pulse pattern recognition. Data analyses reveal that consistent pulse patterns could be identified in selected subjects. The classification rates were 99.1% in the training process and 97.4% in testing result for these 3 basic pulse patterns. Furthermore, we developed an AI assistant pulse sensor system to record the pulse data prolife with TCM practitioners simultaneously. Furthermore, we performed a largescale multiple center clinical trials to evaluate the TCM expert consensus for diagnosis and treatment of heart failure and developed a TCM Syndrome Diagnosis Questionnaire for Heart Failure (SDQHF). Therefore, the application of AI and ML technology would create great opportunity to promote synergy between western medicine and TCM for the diagnosis and treatment of CVDs. Recent progress in artificial intelligence (AI) technology has allowed these challenges to be resolved. The AI machine learning technology facilitates the development of integrative approaches for pulse diagnosis. Hence, we have developed a pulse sensing platform for studying and digitalizing arterial pulse patterns. This platform consists of a robotic hand with three pressure-feedback-controlled robotic fingers for pulse measurement and an artificial neural network (ANN) for pulse pattern recognition. Data analyses reveal that consistent pulse patterns could be identified in selected subjects. The classification rates were 99.1% in the training process and 97.4% in testing result for these 3 basic pulse patterns. Furthermore, we developed an AI assistant pulse sensor system to record the pulse data prolife with TCM practitioners simultaneously. Furthermore, we performed a largescale multiple center clinical trials to evaluate the TCM expert consensus for diagnosis and treatment of heart failure and developed a TCM Syndrome Diagnosis Questionnaire for Heart Failure (SDQHF). Therefore, the application of AI and ML technology would create great opportunity to promote synergy between western medicine and TCM for the diagnosis and treatment of CVDs.

Abstract no.107

Analyzing the anti-inflammatory activity of Vitamin D and herbal medicine on COVID-19 infection using bioinformatic analysis， computer modelling and in vitro approaches

1. Ms 碧田 张, The Chinese University of Hong Kong, Hong Kong SAR

Introduction Herbal medicines and Vitamin D (VD) exhibit unique immunomodulatory activities against respiratory disorders. This study aims to investigate their anti-inflammatory effects on SARS-CoV-2 infection using in vitro experiments, computer modeling, and bioinformatics. Methods A cytometric bead array (CBA) assay analyzed inflammatory cytokine expression in human PBMCs and macrophages treated with VD and the traditional Chinese medicine (TCM) Astragalus membranaceus. Flow cytometry assessed macrophage differentiation after treatment with spike protein and the astragalus compound formononetin. Antioxidant activity post-herbal treatment was measured using a superoxide dismutase (SOD) assay. Calycosin's effect on inhibiting the binding between spike protein and ACE2 was evaluated. Molecular docking explored interactions between herbal compounds and key proteins like ACE2/toll-like receptor (TLR)3 in SARS-CoV-2 infection. Bioinformatics analyzed COVID-19's impact on disease progression. Results Calycosin significantly inhibited the binding between ACE2 and the SARS-CoV-2 spike protein. Spike protein treatment increased pro-inflammatory cytokine levels, while calycosin reduced these levels and increased anti-inflammatory cytokines. Inflammatory M1 macrophage proportion increased with spike protein treatment but decreased after calycosin treatment. Astragalus water extract and formononetin significantly increased SOD activity. Molecular docking simulated interactions between formononetin, calycosin, and TLR binding sites. Bioinformatic analysis indicated potential disease recurrence triggered by SARS-CoV-2 in common targets of COVID-19 and lung cancer. Formononetin and calycosin inhibited spike protein-induced IL-6 release and protein binding. Computational docking supported VD and TCM's efficacy in reducing inflammation. Conclusion/Summary TCM and VD have potent immunomodulatory effects on inflammation, supported by computational predictions. Bioinformatics indicated potential cancer recurrence pathways in SARS-CoV-2 infection. Future studies will include in vivo approaches using murine models to explore the anti-inflammatory mechanisms of VD and TCM.

Abstract no.108

A QAMS method integrated with AI analysis for quality evaluation of traditional Chinese medicine herbals: Aurantii fructus immature，as a case study

1. Dr Liangliang He, Jinan University, Guangzhou

The chromatographic fingerprint offers a systematic approach to the quality control of traditional Chinese medicine (TCM) herbals. However, it is unable to quantify components in practical applications, and the image format makes it difficult to share information between different links in the production and circulation of TCM herbals. Hence, a quantitative analysis of multi-components by single marker (QAMS) method integrated with artificial intelligence (AI) analysis based on graph neural network (GNN) is developed and applied for quality evaluation of TCM herbals, using Aurantia fructus immature (AFI) as a research example. As a result, 8 components showing multiple features were filtrated as the quality markers for AFI from 116 characterized chemicals and 112 in vivo xenobiotics of AFI, as well as the identified specificity chemicals. Subsequently, an UPLC fingerprint-based QAMS method was constructed for these 8 components within 11 minutes. Additionally, an automatic identification model for different sources of AFI by GNN analysis based on chromatographic fingerprint images was constructed and applied. This model not only achieved variety differentiation in a rapid and economical manner but also provided a probabilistic assessment of classification confidence, offering a foundation for future broad-scale AI analysis on TCM herbals. In brief, the quality evaluation method in this study enables the digital processing and image analysis of chromatographic fingerprints, which not only has practical significance for improving the quality control of AFI in a rapid and economical manner but also provides some new insights for the overall improvement of the quality control study of TCM herbals.

Abstract no.109

Cornuside protects from cognitive dysfunction through ameliorating oxidative stress and neuroinflammation via RAGE/TXNIP/ NF-κB signaling

1. Prof Wei-Ku Zhang, China-Japan Friendship Hospital, Beijing

2. Dr Fu-Lin Zhou, China-Japan Friendship Hospital, Beijing

Alzheimer's disease (AD) is a common central nervous system degenerative disease characterized by progressive cognitive dysfunction. Oxidative stress and neuroinflammation cause by Aβ have drawn attention in the prevention and treatment of AD. Cornuside, an iridoid glycoside deriving from the traditional Chinese medicine Corni Fructus, has been discovered to improve learning and memory in AD mice, however, its underlying mechanism was not fully understood. In the present study, the effect of cornuside on the learning and memory was evaluated in Aβ1-42 intracerebroventricular injected mice, and mechanisms were also investigated from the aspects of oxidative stress and neuroinflammation combined with LPS stimulated BV2 cells. Result showed that cornuside significantly ameliorated behavioural deficits. Cornuside could also promote cholinergic synaptic transmission, restoring the level of acetylcholine (ACh) in hippocampus and cortex by inhibiting the activities of acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), as well as facilitating the activity of choline acetyltransferase (ChAT). Furthermore, cornuside obviously inhibited oxidative stress level in hippocampus and cortex by inhibiting TXNIP expression, amplified as decreased malondialdehyde (MDA), increased total anti-oxidative capacity (TAOC), increased activity of superoxide dismutase (SOD) and catalase (CAT). Cornuside also reduced the activation of microglia and astrocytes, decreased the level of proinflammatory factors TNF-α, IL-6, IL-1β, iNOS and COX2 via interfering RAGE mediated IKK-IκB-NF-κB phosphorylation. Similar anti-oxidative and anti-inflammatory results were also found in LPS stimulated BV2 cells via hampering RAGE mediated TXNIP activation and NF-κB nuclear translocation. In conclusion, cornuside could bind to the RAGE directly impeding the interaction of Aβ and RAGE, and cut down the expression of TXNIP inhibiting ROS production and oxidative stress, as well as hamper NF-κB p65 mediated the infammation. Acknowledgments: National High Level Hospital Clinical Research Funding & Elite Medical Professionals Project of China-Japan Friendship Hospital (2023-NHLHCRF-CXYW-01, ZRJY2023-QM10).

Abstract no.110

Efficacy evaluation and mechanism research of Quan Duzhong capsule in relieving comorbidity of knee osteoarthritis and hypertension

1. Prof Yanqiong Zhang, China Academy of Chinese Medical Sciences, Beijing

2. Dr Zhaochen Ma, China Academy of Chinese Medical Sciences, Beijing

3. Prof Na Lin, China Academy of Chinese Medical Sciences, Beijing

Abstract: Objective To objectively evaluate the efficacy of Quan Duzhong capsule (QDZC) in relieving knee osteoarthritis (KOA) combined with hypertension (HTN), clarify its advantage intervention linkage, and thereby elucidate its intervention mechanism for comorbidities. Methods Using spontaneously hypertensive rats as experimental subjects, the modified Hulth method was used to construct a rat model of KOA combined with HTN. Related pathological and physiological indicators, including arterial blood pressure, arterial vascular pathological changes, knee joint motor function, knee joint cartilage degeneration, subchondral bone blood perfusion, and subchondral bone degradation, were detected using small animal non-invasive blood pressure meter, H&E staining, gait analysis instrument, Safranin O-Fast Green staining, Microfil, and Micro CT. Furthermore, the “herbal medicine candidate target-comorbidity related genes” interaction network was constructed using ETCM 2.0 database and Cytoscape 3.8.2 software, and the key pathological links and potential action mechanisms of QDZC in interfering with KOA combined with HTNwere mined. Finally, the mined results were experimentally verified using animal experimental biological samples through Western blot, immunohistochemistry, and other molecular biology detection. Results QDZC can significantly lower the arterial blood pressure of the comorbid rats, improve their vascular narrowing and knee joint motor function, and inhibit the degenerative changes of the affected joint cartilage. Further mechanistic exploration and validation results indicate that the QDZC can exert its therapeutic effects on comorbidities through two pathways. On the one hand, it can regulate the AHR-Wnt/β-catenin-VEGFA-Ang II signal axis in the arterial vessels of comorbidized rats, dilating the arterial vessels, not only lowering blood pressure but also increasing the blood perfusion to the subchondral bone of the knee joint, thereby inhibiting the subchondral bone ischemia and bone resorption caused by HTN, and playing a role in relieving KOA. On the other hand, QDZC can alleviate KOA by regulating the AHR-Wnt/β-catenin-RANKL-RANK-cFOS signal axis in the subchondral bone of comorbidized rats, inhibit the abnormal activation of osteoclast in subchondral bone, delay the process of bone resorption, blocking the degeneration of subchondral bone, and protect the overlying articular cartilage. Conclusion This study confirmed that the QDZC could improve pathological changes such as arterial stenosis and subchondral bone degeneration by regulating the “abnormal blood perfusion-subchondral bone ischemia” pathway mediated by the AHR-Wnt/β-catenin-VEGFA-Ang II signaling axis and the “subchondral bone degeneration” pathway mediated by the AHR-Wnt/β-catenin-RANKL-RANK-cFOS signaling axis, thereby alleviating the comorbidity. The relevant research results will provide strong experimental evidence for the promotion and application of the clinical use of QDZC to treat comorbidity, and enrich the scientific connotation of traditional Chinese medicine in treating comorbidity. Keywords: Quanduzhong capsule; Knee osteoarthritis; Hypertension; Comorbidity; Aryl hydrocarbon receptor

Abstract no.111

Cistanche tubulosa Ameliorates Microplastic-Induced Disruption of Nociceptive and Mechanosensory Behaviors in Drosophila

1. Prof Wei-Yong Lin, China Medical University, Taichung

Microplastics (MPs) can enter the body through various routes, including ingestion, inhalation, and dermal absorption. They can even traverse biological barriers like the blood-brain barrier, reaching and potentially affecting neural tissues. MPs have been shown to induce neuroinflammation, disrupt neurotransmitter systems, impair synaptic transmission, cause oxidative stress in the brain, and interfere with nervous system development and function. While a previous study demonstrated the benefits of Chinese herbal medicine (CHM) on MP-induced sperm DNA fragmentation, the ability of CHM to rescue MP-disrupted nervous system function remains unknown. In this study, we employed polystyrene MPs to induce developmental disruption, nociception (pain perception) impairment, and mechanosensory (touch perception) dysfunction in Drosophila melanogaster larvae. Notably, treatment with Cistanche tubulosa, a type of CHM, rescued nociception and mechanosensory behaviors in a dose-dependent manner, but did not significantly impact larval development. These findings suggest that Cistanche tubulosa can effectively mitigate MP-induced disruption in behaviors reflecting nervous system activity.

Abstract no.112

X-chromosome-linked miR-542-5p as a key regulator of sex disparity in rheumatoid arthritis by promoting Th17 differentiation

1. Prof Vincent Kam Wai Wong, Macau University of Science and Technology, Macao SAR

2. Dr Jiujie Yang, Macau University of Science and Technology, Macao SAR

3. Dr Zhi Li,

4. Prof Betty Yuen Kwan Law, Macau University of Science and Technology, Macao SAR

While number of studies have shown that biological sex is a risk factor in the incidence and severity of autoimmune diseases (including RA). the underlying mechanisms are still poorly understood. Given the importance of the chromosome X-linked microRNA542-5p (miR-542-5p) in modulating the infammatory process and immune cell polarization, we investigated its potential contribution in sex bias of AIA rats model. Our experimental results showed that miR-542-5p was upregulated in RA patients and animal models. Moreover, miR-542-5p was highly expressed in females with RA. Up-regulation of miR-542-5p can promote the aggravation of arthritis in AIA rats. Moreover, further animal experiments confirmed that the severe phenotype and immune response of female AIA rats may be associated with the high expression of miR-542-5p compared with male rats. Subsequently, gender-specific modulation of miR-542-5p expression showed that inhibitory expression of miR-542-5p in female AIA rats alleviated arthritic symptoms and inflammatory responses, whereas overexpression of miR-542-5p in male rats exacerbated arthritic symptoms and inflammatory responses. In vitro experiments demonstrated that miR-542-5p has the effect of promoting Th17 differentiation. Collectively, these findings underscore the involvement of miR-542-5p in modulating rheumatoid arthritis (RA) pathogenesis, while also highlighting its capacity to modulate gender-specific responses to RA through the regulation of Th17 differentiation. This delineation solidifies the pivotal role of miR-542-5p in governing gender disparities within the RA landscape. Notably, X-linked miR-542-5p emerges as a potential target for tailoring gender-specific, individualized therapeutic interventions in RA management. Key word: Rheumatoid arthritis; Gender difference；X chromosomes; MicroRNA;Th 17differentiation.

6. Natural Products II (Identification, Biotransformation, Metabolism & other Biological activities)

Abstract no.113

Inhibitory effect of Calotropis gigantea (L.) Dryand. extracts against Pseudomonas aeruginosa.

1. Ms Chanakan Chailom, Naresuan University, Phitsanulok

Nowadays, the rise of serious bacterial infections is one of the top ten global health concerns [1]. These infections can kill many people across the world. Therefore, it is essential to find alternative sources for novel and potent antimicrobial compounds against pathogenic bacteria. Crown flower, known as 牛角瓜 (niu jiao gua) or Calotropis gigantea (L.) Dryand., belongs to the Apocynaceae family and is native to several countries, including China, India, Malaysia, and Thailand. It has been used in folk medicine to treat diseases involving inflammation and infections [2]. However, there have been no reports comparing the antimicrobial activity of different parts of this plant. Therefore, this study aims to investigate the inhibitory activity against Pseudomonas aeruginosa, a pathogenic gram-negative bacterium, of ethanolic extracts from four parts of C. gigantea, including the flowers, leaves, stem bark, and latex. Each part of the plant was extracted using 50% ethanol with ultrasonic assistance. The ethanolic extracts were evaluated for their inhibitory effect on P. aeruginosa using a disc diffusion method at a dose of 2 mg/disc. The results demonstrated that every part of C. gigantea could inhibit the growth of P. aeruginosa, with the extract from the stem bark exhibiting the highest inhibition zone (8 mm). These findings indicate that C. gigantea is a promising natural resource for further isolation and purification in the development and discovery of effective and sustainable antimicrobial agents to combat P. aeruginosa infections. Keywords: Calotropis gigantea, Anti-microbial activity, Pseudomonas aeruginosa, Disc diffusion.

Abstract no.114

Quality control of Calotropis gigantea (L.) Dryand. stem bark extracts for drug development

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The extracts of Calotropis gigantea (L.) Dryand. stem barks have been reported to exhibit cytotoxicity against various cancer cell lines, demonstrating potential in drug development. However, one of the major challenges in the development of medicinal plants for drug discovery is ensuring the quality control of these extracts to maintain consistent bioactivities. Therefore, this research aimed to identify and determine the phytochemicals present in C. gigantea stem bark extracts using colorimetric assays and high-performance liquid chromatography (HPLC) with ultraviolet (UV) or mass spectrometry (MS) detectors for quality control purposes. The stem bark of C. gigantea was extracted using 95% ethanol then subsequently fractionated to obtain three fractions: dichloromethane, ethyl acetate, and water. These four samples were analyzed for their total cardiac glycoside, phenolic, and triterpenoid contents using colorimetric assays. Additionally, calactin and calotropin contents were quantified using HPLC-UV, and calactin was identified using HPLC-MS. The results revealed that one gram of these four samples contained total cardiac glycoside, phenolic, triterpenoid, calactin, and calotropin contents of approximately 34-181 mg digoxin equivalent, 4-30 mg gallic acid equivalent, 31-649 mg ursolic acid equivalent, 310-1,286 µg calactin, and 40-711 µg calotropin, respectively. The HPLC-MS was effective in identifying calactin in the extracts. In summary, the quality control of bioactive extracts from C. gigantea stem bark can be effectively performed using a variety of techniques. Nevertheless, the identification and quantitative analysis of bioactive markers in the extracts are essential to develop a specific method for the quality control of extracts from C. gigantea barks in the future to ensure the consistency and reliability of the extracts' bioactivity. Acknowledgement: This work was supported by NSRF of Thailand [Grant NO.R2564B007], ARDA [Grant NO.CRP6505030030 and PRP6605031530]. Special thanks to Professor Zhi-Hong Jiang and Professor Li-Ping Bai, Macau University of Science and Technology, Macau, for providing calotropin and calactin. Some parts of this work were published in these references: Winitchaikul T. et. al., PLoS One. 2021;16(8):e0254392. Published 2021 Aug 3. Simanurak O. et. al., Heliyon. 2023;9(7):e18013. Published 2023 Jul 7. Suknoppakit P. et. al., Heliyon. 2023;9(5):e16375. Published 2023 May 18.

Abstract no.115

Targeting PPARγ for pro-angiogenesis in ischemic bladder may be the target of compounds from Alpinia oxyphylla Frctus water extract against bladder overactivity

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Objective: Bladder ischemia can trigger bladder overactivity (OAB) which is a syndrome characterized by the urgency of urination, often accompanied by frequent urination and nocturia. Alpinia oxyphylla Frctus (Yi-Zhi-Ren, YZR, 益智仁) is often used to relieve enuresis. Our previous study have confirmed that YZR can relieved OAB symptoms in spontaneously hypertensive rats (SHR), a vascular disorder-related OAB model.[1] However, the molecular target and upstream pathways are still unknown. This study investigated the potential mechanisms of YZR and its compounds in treating OAB due to its effect on increasing bladder blood flow in SHR. Methods: After a 3-week oral administration of YZR water extract, bladder blood flow was measured and the staining experiments of bladder tissue sections including Masson and CD 31 immunofluorescent staining were carried out to observe the blood vessels and angiogenesis in SHR. An integrated approach of multi-omics including transcriptomic, proteomics, phosphoproteomics and metabolomics was applied to explore the potential mechanism of YZR, and the protein expressions were validated by Western blotting. Molecular target of compounds in YZR was confirmed by DARTS and CESTA. Results: After YZR treatment, the bladder blood flow was significantly increased. The results of Masson staining showed that the diameter of bladder vessels was larger and the number of capillaries in the urothelium was increased, which was further identified by CD 31 immunofluorescent staining. Transcriptomics and metabolomics results suggested that PPARγ played an important role in the angiogenesis of YZR. Meanwhile, the integrated analysis of proteomics and phosphoproteomics indicated that the VEGF signaling pathway was upregulated by YZR. Furthermore, the results of DARTS and CESTA found that nootkatone, the main compound of YZR, could bind with PPARγ. Conclusion: YZR water extract can increase bladder blood flow of SHR rats by dilating blood vessels and promoting bladder neovascularization to relieve OAB symptoms and nootkatone may be the active compound targeting PPARγ for pro-angiogenesis in OAB bladder. Acknowledgement: This study was supported by National Key R&D Program of China (No. 2021YFE0202700). Reference [1] Yan Tie, Zhihui Sun, Xinyi Tong, Mingchang Cheng, Yushan Wu, Zhilong Shi, Pingxiang Xu, Ming Xue, Liping Xu**, Xuelin Zhou*. Multi-Omic analysis revealed the therapeutic mechanisms of Alpinia Oxyphylla Fructus water extract against bladder overactivity in spontaneously hypertensive rats. Phytomedicine, 2024, 123: 155154.

Abstract no.116

Anti Acinetobacter baumannii activity of Macadamia integrifolia shell extract.

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Macadamia integrifolia is a popular nut with an annual global production of 230,000 tons. In the 1970s, China began cultivating macadamia in Guangdong, Yunnan, Guangxi, and Guizhou provinces. By the end of 2018, China's macadamia planting area exceeded 30% of the global total (1). However, macadamia nut production generates enormous waste, as 70% of the nut's weight is unusable. Literature indicates that M. integrifolia contains bioactive compounds with promising antimicrobial activity (2). Acinetobacter baumannii, a gram-negative bacterium causes various serious infections, including pneumonia and bloodstream infections (3). This research aims to extract bioactive compounds from macadamia shells and investigate their antimicrobial activity against A. baumannii. The shell powder of M. integrifolia was macerated in 95% ethanol with ultrasonic assistance to obtain a crude extract, followed by liquid-liquid partition using dichloromethane, ethyl acetate, and water to obtain four M. integrifolia fractions. Thin layer chromatography was used for quality control of the samples. Antimicrobial activities against A. baumannii of four fractions were evaluated by using disc diffusion method at a dose of 200 µg/disc. Colistin at the same dose was used as a positive control. The results revealed that the crude extracts along with three fractions of M. integrifolia could inhibit the growth of A. baumannii with inhibition zones ranging from 10.0 to 13.0 mm. (Colistin 18.0 mm.). Interestingly, the crude extract was the most potent These findings explore the possibility of using macadamia shell, a waste product from macadamia nut production, as a natural resource for the discovery of potent bioactive compounds with antibiotic activity against A. baumannii.

Abstract no.117

Red Yeast Rice (Monascus purpureus) Ameliorates Testicular Morphology and Sperm Quality in High-Fat Diet-Induced Dyslipidemia Rats

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Abstract Dyslipidemia is associated with male infertility, affecting both sperm quality and testicular integrity. Red yeast rice (RYR) is a traditional Chinese medicine that has been used to lower blood lipid levels. Therefore, RYR could potentially be a candidate for mitigating dyslipidemia-induced infertility. This study aimed to investigate the protective effects of RYR on male reproductive dysfunction in dyslipidemic rats. Male Wistar rats were divided into 5 groups (n=4/group): normal diet (ND), high-fat diet (HF), HF supplemented with RYR at 100 mg/kg (HF+RYR100) or 500 mg/kg (HF+RYR500), and HF with simvastatin 40 mg/kg (HF+SIM) for 12 weeks via oral gavage. Compared with the HF group, both RYR or simvastatin significantly lowered LDL (52.75±7.90, HF vs. 36.50±6.95, HF+RYR100, p=0.004; 34.00±3.74, HF+RYR500, p=0.001; 29.00±3.74, HF+SIM40, p<0.001) and total cholesterol levels (96.75±1.71, HF vs. 80.00±12.46, HF+RYR100, p=0.047; 77.00±8.83, HF+RYR500, p=0.016; 69.75±5.19, HF+SIM40, p=0.001). Moreover, RYR consumption exhibited a positive impact on the male reproductive system, especially at the dosage of 500 mg/kg/day, which increased relative testicular weight (0.31±0.02%, HF vs. 0.37±0.02%, HF+RYR500, p=0.006), reduced testicular abnormalities (p=0.023, Figure 1), and improved sperm quality by increasing sperm concentration (p=0.004, Figure 2A), and viability (p<0.001, Figure 2B), while RYR at 100 mg/kg/day could only benefit sperm viability (p<0.001, Figure 2B). These findings suggest RYR as a promising candidate for improving blood lipid profiles and male reproductive system in dyslipidemic conditions. Keywords: Dyslipidemia; Red yeast rice; Testis; Sperm quality; Male reproductive system

Abstract no.118

Extraction，structure characterization and antioxidant activity of polysaccharides from Ixeris chinensis (Thunb. ex Thunb.) Nakai

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Ixeris chinensis, a member of the Asteraceae family, has long been utilized in traditional folk medicine to alleviate ailments such as stomachaches, colds, and diarrhea. In this study, the entire herb of endive was subjected to hot water extraction, yielding a crude polysaccharide with a 40.1% extraction efficiency. Through anion-exchange column chromatography, two distinct polysaccharide fractions, ICP-1 and ICP-2, were isolated and subsequently selenated to produce ICP-1-Se and ICP-2-Se. ICP-1 was found to comprise six monosaccharides: mannose, galacturonic acid, arabinose, rhamnose, xylose, and galactose. ICP-2, consisted of five monosaccharides: galacturonic acid, mannose, rhamnose, arabinose, and galactose. Detailed characterization using GC-MS and NMR revealed the specific sugar residues in ICP-1 as →4)-D-Xylp-(1→, →3)-L-Arap-(1→, →2,3,4)-L-Manp-(1→, D-Galp-(1→, →2,4)-L-Rhap-(1→, and →4)-D-GalpA-(1→. For ICP-2, the major sugar residues were identified as →3)-L-Arap-(1→, →2,3,4)-L-Manp-(1→, D-Galp-(1→, →2,4)-L-Rhap-(1→, and →4)-D-GalpA-(1→. Scanning electron microscopy analyses provided insights into the characteristic morphology of the different polysaccharide fractions. Antioxidant activity assays demonstrated that ICP-1, ICP-2, ICP-1-Se, and ICP-2-Se exhibited significant antioxidant properties and notably inhibited tyrosinase activity. Furthermore, the neuroprotective effects of these polysaccharides were evaluated using an H2O2-induced damage model on SH-SY5Y neuronal cells. The results indicated that ICP-1, ICP-2, and ICP-1-Se conferred a protective effect against H2O2-induced neuronal cell injury, highlighting their potential therapeutic benefits. This study not only enriches our understanding of the Chinese endive's pharmacological properties but also opens new avenues for the development of innovative treatments derived from this venerable herb.

Abstract no.119

Terpenoids of hawthorn leaves and their biological activities

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Hawthorn leaves are the dried leaves of Crataegus pinnatifida Bge. var. major N. E. Br. or C. pinnatifida Bge. (Rosaceae). It has been used in traditional Chinese medicine for the treatment of cardiovascular protective, lower blood lipids, hypotensive and hypocholesterolemic. In the present work, the systematic separation of 70% alcoholic fraction of hawthorn leaves was carried out by combining various chromatographic separation techniques, and the structures of all the compounds were determined by 1D NMR, 2D NMR, HR-ESI-MS, ORD, CD spectroscopy, etc., respectively: crataegusnoside R (1), amarantholidoside V (2), icariside C3 (3), amarantholidoside IV (4), schensianolside A (5), schensianolside B (6), eucomegastigsides D (7), phoebenoside A (8),(7E,9R)-9-Hydroxy-5,7-megastigmadien-4-one-9-O-β-D-glucopyranoside (9), crataegusnoside E (10), crataegusnoside F (11), S-(−)-inalool-O-α-L-arabinofuranosyl-(1→6)-β-D-glucopyranoside (12), (6S,9R)-roseoside II (13), saussurenoid D (14), leeaoside (15), (3R, 9R)-9-O-β-D-glucopyranosides (16), icariside B2 (17), byzantionoside A (18), 3β-hydroxy-β-ionone 3-O-β-D-glucopyranoside (19), byzantionoside B (20), (6R,9R)-3-oxo-α-ionol-9-O-β-D-glucopyranoside (21), (3S,4R,7E,9S)-3,4,9-trihydroxy-5,7-megastigmadiene (22), and brucojavan 1 (23). There were 19 sesquiterpenoids and their glycosides (1-9, 13-22), 2 diterpenoid glycosides (10, 11), 2 monoterpenoid glycosides (12, 23).Compound 1 is a new compound, and compounds 2-3, 5-6, 8-9, 12, 14-16, 18 and 22 were isolated from this genus for the first time. And further explore the differences of antiplatelet aggregation activity, α-glucosidase inhibition activity and ABTS+ free radical scavenging activity of single compounds in hawthorn leaves, and classify the isolated single compounds for 3 aspects of activity screening. In the present work,it provides certain theoretical basis and data support for the in-depth study of the chemical composition and pharmacological effects of hawthorn leaves, further enriches the material basis of hawthorn leaves, and develops its potential medicinal value. Key words: the leaves of Crataegus pinnatifida, chemical composition, antiplatelet aggregation activity, α-glucosidase inhibitory activity, ABTS+ free radical scavenging activity

Abstract no.120

The erythromycin polyketide compound TMC-154 stimulates ROS generation to exert antibacterial effects against Streptococcus pyogenes

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Streptococcus pyogenes is a nearly ubiquitous human pathogen that causes a variety of diseases ranging from mild pharyngitis and skin infection to fatal sepsis and toxic heat shock syndrome. With the increasing incidence of known antibiotic resistance, there is an urgent need to find novel drugs with good antibacterial activity against S. pyogenes. The erythromycin polyketide compound TMC-154 is a secondary metabolite that is isolated from the rhizospheric fungus Clonostachys rogersoniana associated with Panax notoginseng, a famous traditional Chinese medicine known as San Qi. TMC-154 possesses remarkable broad-spectrum antibacterial activity, but its antibacterial mechanism has not been investigated thus far. In this study, proteomics coupled with bioinformatics approaches was used to explore the antibacterial mechanism of TMC-154. KEGG pathway enrichment analysis indicated that eight signaling pathways were associated with TMC-154, including oxidative phosphorylation, cationic antimicrobial peptide (CAMP) resistance, benzoate degradation, heme acquisition systems, glycine/serine and threonine metabolism, beta-lactam resistance, ascorbate and aldarate metabolism, and the phosphotransferase system (PTS). Cell biology experiments confirmed that TMC-154 could induce reactive oxygen species (ROS) generation in Streptococcus pyogenes. Moreover, TMC-154-induced antibacterial effects could be blocked by the inhibition of ROS generation with the antioxidant N-acetyl L-cysteine. In addition, TMC-154 combined with ciprofloxacin or chloramphenicol had synergistic antibacterial effects. These findings indicate the potential of TMC-154 as a promising drug for treating S. pyogenes infections and provide potential options for the treatment of S. pyogenes infections in the future.

Abstract no.121

Discovery of Anti-melanogenic Components in Persimmon (Diospyros kaki) Leaf Using LC-MS/MS-MN， AlphaFold-enabled Virtual Screening and Biological Validation

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2. Mr Jiazheng Liu, Macau University of Science and Technology, Macao SAR

Persimmon (Diospyros kaki) leaf is widely used as a Chinese herbal tea in East Asia, offering potential health benefits. Although studies have highlighted their effects on hyperpigmentation disorders, the active components remain unidentified. This study introduces a novel approach combining LC-MS/MS-based molecular networking with AlphaFold-enabled virtual screening to expedite the identification of bioactive components in persimmon leaf. A total of 105 compounds were identified by MS/MS analysis. Further, virtual screening identified five flavonoids with potential anti-melanogenic properties. Bioassays confirmed myricetin, quercetin, and kaempferol inhibited melanogenesis in human melanocytes in a dose-dependent manner. Biolayer interferometry assays revealed strong binding affinity between these flavonols and hsTYR, with KD values of 23.26 ± 11.77 μM for myricetin, 12.43 ± 0.37 μM for quercetin, and 14.99 ± 3.80 μM for kaempferol. Molecular dynamics simulations provided insights into the binding interactions of these flavonols with hsTYR, particularly highlighting the essential role of the 3-OH group on the C-ring. This study elucidates the bioactive components responsible for the anti-melanogenic effects of persimmon leaf, supporting their use in product development. Acknowledgement: This research was financially supported by the Science and Technology Development Fund, Macau SAR (File no. 0043/2020/AGJ, 0001/2023/AKP, 006/2023/SKL). We also thank the Department of Science and Technology of Guangdong Province for the support of GDST-FDCT Projects (File no. 2021A0505080007).

Abstract no.122

Antifibrotic cevanine-type alkaloids from the bulbs of Fritillaria unibracteata var. wabuensis

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The bulbs of Fritillaria have long been used in traditional Chinese medicine, known as "Beimu", for treating cough. Steroidal alkaloids are the main bioactive components present in the bulbs of Fritillaria. In this study, we isolated and identified two previously unknown cevanine-type steroidal alkaloids (1 and 2), as well as four previously undescribed cevanine-type alkaloid glycosides (3–6), and 19 known steroidal alkaloids (7–25) from the bulbs of Fritillaria unibracteata var. wabuensis. Their structures were elucidated by HRMS and NMR spectroscopic analysis, along with DP4+ NMR calculations. The compounds were evaluated for their antifibrotic activity. Results showed that compounds 2, 7–10, 14, 15, and 17 were able to downregulate fibrotic markers induced by transforming growth factor-β (TGF-β) in MRC-5 cells. Additionally, compounds 14 and 17 demonstrated dose-dependent inhibition of TGF-β-induced epithelial-mesenchymal transition (EMT) in A549 cells. Furthermore, these compounds alleviated TGF-β-induced migration and proliferation of fibroblasts, and reduced the expression of fibrotic markers such as fibronectin and N-cadherin in TGF-β-induced MRC-5 cells. This research shows the potential of cevanine-type alkaloids as natural antifibrotic agents.

Abstract no.123

Glecholimers A-B，two distinctive sesquiterpene dimers with anti-gastric cancer activity from Glechoma longituba by feature-based molecular networking

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Under the guidance of Feature-Based Molecular Networking (FBMN), Glecholimers A, and B (1-2), two sesquiterpenoid dimers polymerized in two ways by a bisabolane-type sesquiterpene and a caryophyllene and its biogenic precursor compound glecholone (3), were isolated from Glechoma Longituba (Nakai) Kupr. The absolute configurations of 1 and 2 were assigned by DP4+ and ECD experiments. Compounds 1 and 2 possessed an unprecedented chemical skeleton with a 4/9/4/6 fused ring system and the plausible biosynthetic pathways were postulated. Both had significant inhibitory activity on gastric cancer cells HGC-27 and MGC-803, especially compound 1 had less cytotoxicity on normal gastric cells GES-1. Compound 1 can promote the apoptosis of gastric cancer cells by reducing the expression levels of PCNA, PARP, and Bcl2/Bax.

Abstract no.124

Rhapontin alleviates C-reactive protein induced diabetic kidney disease through SMAD3-ACSM3 mediated ferroptosis

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Background: Accumulated evidence indicated that C-reactive protein (CRP) enhances diabetic kidney disease (DKD) via Smad3 signaling pathway[1]. Acyl-CoA synthetase medium-chain family member 3 (ACSM3) locates on the membrane of mitochondria to catalyze fatty acids[2]. Ferroptosis is one type of cell deaths, featured with iron-dependent phospholipid peroxidation[3]. This study determined whether CRP promotes DKD via Smad3-ACSM3 mediated ferroptosis and explore potential therapeutics by Chinese medicine. Methods: CRP transgenic (Tg)×db/db, CRPtg×db/dm, Smad3 knockout (KO)×db/db and Smad3 KO×db/m mice were used in the study. Differentially expressed genes in CRPtg×db/db mice were analyzed by the RNA sequencing. To evaluate protective role of ACSM3, AAVs with ACSM3 overexpression were administered into db/db mice. In vitro, HK-2 cells were treated with CRP with/without blocking of CRP receptor by CD32b antibody or treated with Smad3 inhibitor SIS3 were employed. Ferroptosis indexes were measured by IF, WB and qPCR. High through output molecular docking and cellular thermal shift assay (CETSA) were conducted to identify candidate compounds targeting ACSM3. Results: Overexpression of CRP in diabetic mice significantly enhanced ferroptosis in kidneys. The RNAseq result indicated that ACSM3 level was significantly downregulated in CRPtg×db/db mice, compared with CRPtg×db/dm mice. Interestingly, deletion of Smad3 alleviated the ferroptosis and reversed ACSM3 deficiency in diabetic kidneys. Overexpression of ACSM3 in diabetic mice led to ferroptosis alleviation in kidneys. Consistently, the ferroptosis induced by CRP in vitro were reversed by SIS3, or the blockade of CRP receptor, or the overexpression of ACSM3. Furthermore, through the high through output molecular docking prediction and CETSA, we found that Rhapontin was one of potential compounds to suppress ferroptosis by targeting ACSM3. Conclusion: Targeting Rhapontin on ACSM3 and SMAD3 have therapeutic potential for CRP induced ferroptosis in DKD.

Abstract no.125

Protective effect of active constituents from licorice on the intestine and lung

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【Purpose】 Licorice has been used as a traditional Chinese medicine with the function of tonifying deficiency of the body, especially for the deficiency of "Pi" that is considered to be closely associated with the digestive system. Therefore, we performed a series of investigations on the constitute from licorice to reveal their effect on intestinal epithelium as the intestine is an important of the digestive system. 【Methods】1. Normal intestinal epithelial cells IEC-6, Caco2, and HCoEpiC cells were used to evaluate the in vitro effect. Although the Caco2 cell line is a colorectal adenocarcinoma cell line, but it retains most of the normal function of small intestinal epithelial cells, which makes it a good cell model for the research of small intestinal cell function. 2. The stem cell from the crypt of small intestine of mice was isolated and cultured in vitro to construct the ex vivo model, which is also called intestinal organoids. This ex vivo model contains multiple types of cells like cup cells, paneth cells, and epithelial cells in intestinal epithelium, simulating in vivo development of intestinal crypts, and was used to examine the ex vivo effect of characteristic molecules from licorice. 3. FAST and antibiotic-induced injury murine models were adopted to assess the in vivo effect of licorice-derived molecules on intestinal epithelial integrity. 4. Fish experiments were performed to observed the level of non-coding RNAs in the mechanism study. 【Results】 1.We use in vitro cell model to screen the active constituents on normal intestinal cell growth and the first molecule that attracted our interests was glycyrrhetinic acid (GA), a characteristic pentacyclic triterpenoid from licorice. The results showed that GA could promote growth and enhance recovery after wounding of IEC-6 cells.Ex vivo experiments indicated that GA could promote intestinal organoid development as shown by the ration of enteroid/enterosphere on day 2 (Figure 2). Results from 48-h FAST model in SD rats indicated that 48-h FAST induced epithelial atrophy in rats and GA could partially reverse the epithelial atrophy in the model group.Mechanism studies suggested that GA exerts its effect through RNA-binding protein HuR to modulate levels of EGF, EGFR, and MEK post-transcriptionally, and thereby promote intestinal epithelial renewal .Furthermore, the effect of GA on the antibiotic-induced intestinal injury was investigated. The application/abuse of antibiotics can cause antibiotic-induced intestinal injury (AIJ), a typical clinical issue that disturbs intestinal homeostasis. However, the underlying post-transcriptional mechanism of AIJ remains unknown. In vivo results revealed the antibiotic induced epithelial injury in both the small intestine (shortened and spared mucosa) and the large intestine (injured/deformed glands, reduced number of cup cells, and evident inflammatory cell infiltration) in addition to the abnormal flora, all of which were ameliorated after GA treatment (10 and 20 μM). Mechanism studies showed that the antibiotic (500 μM) suppressed proliferation, induced a delay in restitution after wounding, and caused cell cycle arrest at the G0/G1 phase in IEC-6 and Caco-2 cells. Moreover, the expression levels of HuR and its downstream gene, occludin and cyclin D1, decreased after treatment with the antibiotic (500 μM). This HuR-caused phenomenon can be reversed by GA. 2. In addition to GA, we also found echinatin, licochalcone A, and other components to be effective regarding promoting intestinal epithelial renewal through post-transcriptional mechanism like CUPBP1 and T-UCRs. 【Discussion】

Previous studies revealed that natural molecules can induce the proliferation of IECs, and bioactive components from traditional Chinese medicines can also stimulate intestinal epithelial repair. Among them, licorice and its main components exhibited various functions in the intestine. For example, licorice aqueous extract can regulate polyamine-depleted intestinal crypt cells proliferation. But the specific effect of the individual compound on intestinal renewal so far remains unknown. Particularly, for the reason that licorice can also be used as a food or food additives in our daily diet in normal/healthy conditions, figuring out its effect on digestive mucosa is quite meaningful to understand the modulative effect of licorice on the human body. Our studies reveal for the first time that as either a commonly-used traditional Chinese medicine or a food component, using reasonable dosage of licorice or its component can be helpful to intestinal epithelial homeostasis.

Abstract no.126

Molecular mechanism of improvement of nephrotic syndrome by highly sulfonated derivatives of foraminifera glycans based on non-targeted serum metabolomics study

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OBJECTIVE: Ulva pertusa is a medicinal seaweed, which has been recorded in Gleanings from the Materia Medica 'Supplement to the Herbal Foundation', as well as the Sea Medicinal Herbs 'Herbal Foundation of Overseas Medicines'. The active component of Ulva pertusa, Ulvan polysaccharide (Ulvan, U), has various biological activities such as good antioxidant and anti-hyperlipidaemia, and the biological activity of Ulva pertusa polysaccharide can be improved by changing the molecular weight and structural modification. Therefore, high-sulfated derivative of ulvan (HU) of Ulvan polysaccharide was prepared in this study. However, due to the multi-component, multi-target and multi-pathway action characteristics of HU, its biological activity and mechanism of action in the treatment of Nephrotic Syndrome (NS) are still unclear. In the present study, we investigated the molecular mechanism by which HU ameliorates adriamycin-induced NS by serum untargeted metabolomics. METHODS: U was extracted from Ulva oryzae by aqueous alcoholic precipitation, and HU was prepared by sulfonation reaction. 6.0 mg/kg of ADR was administered into the tail vein of rats to establish the NS model, and the rats with proteinuria were randomly divided into three groups, and except for the model group, the other two groups were given U and HU (173 mg/kg/day) by gavage. Equal doses of distilled water were administered by gavage to both normal and model groups. After 6 weeks of treatment, urine, blood and kidney tissues were collected for subsequent experimental studies. Various physiological parameters were measured in serum and urine. Histological and ultrastructural analyses of the kidneys were performed using H&E, Masson and PAS. Thickening of the glomerular basement membrane and damage to the podocyte structure were observed under electron microscopy. The serum samples of rats were tested and analysed separately by LC-MS/MS method, and differential metabolites between groups were screened according to $VIP > 1$ and $P < 0.05$. The differences between serum metabolites in each group were analysed and compared to find biomarkers and their related metabolic pathways. RESULTS: HU alleviated hyperlipidaemia and hypoproteinaemia, ameliorated the infiltration of mononuclear inflammatory cells and the deposition of large amounts of collagen, and alleviated the thickening of the renal capsule, the abscesses of the glomerulus and renal capsule, and the proliferation of the glomerular thylakoid stroma. Electron microscopic observations demonstrated severe fusion of HU-reduced pedicles as well as severe thickening of the glomerular basement membrane. A total of 2881 metabolites were detected by metabolomics. 180 differential metabolites were detected in the ADR and NOR groups, of which 117 were up-regulated and 63 were down-regulated; 80 differential metabolites were detected in the ADR and HU groups, of which 31 were up-regulated and 49 were down-regulated; and 60 differential metabolites were detected in the ADR and U groups, of which 32 were up-regulated and 28 were down-regulated. under the KEEG pathway enrichment, the ADR group, the NOR group, and the HU The co-enriched pathways were glycerophospholipid metabolism, choline metabolism, fatty acid

metabolism, etc. Palmitoyl carnitine, levulinic acid carnitine, 4-methylheptadecanoyl carnitine, and PS (P-20:0/16:0) were significantly down-regulated in the HU group compared with the ADR group. CONCLUSION: HU showed excellent activity in reducing glomerulosclerosis, interstitial fibrosis and protecting the glomerular filtration barrier, thereby reducing urinary protein. The results of metabolomics analysis showed that HU improved nephrotic syndrome by regulating lipid metabolism, glycerophospholipid metabolism, choline metabolism and other pathways.
Keywords: nephrotic syndrome; algal polysaccharide; metabolomics; lipid metabolism

Abstract no.127

Aconine modulates osteoclast ferroptosis to attenuate OVX-induced cartilage endplate calcification via inhibiting NF-κB signaling

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Cartilage endplate calcification obstructs the nutrition supply of the intervertebral disc and aggravates the intervertebral disc degeneration (IVDD) progression. Emerging evidence has reported that ovariectomized (OVX) may cause bone mass loss and induced endplate calcification, thus leading to IVDD. Our previous study found that Aconine (AC), a diester alkaloid isolated from a traditional Chinese medicine Aconiti Lateralis Radix Preparata (Fuzi), effectively improved osteoporosis and suppressed osteoclast ferroptosis in ovariectomized (OVX) mice. Thus, it provokes us to explore whether AC ameliorates OVX-induced endplate calcification and endplate degeneration and its underlying molecular mechanisms. We administered intraperitoneal injections of AC to OVX mice for 8 weeks. In the results, histological staining revealed that AC ameliorated endochondral ossification in the endplate of OVX mice, thus alleviating endplate degeneration. Specifically, AC significantly suppressed abnormal endplate bone remodeling by restoring the overexpression of osteoblast markers Runx2 and Osterix, as well as osteoclast markers TRAP, RANKL, Cathepsin K, and Mmp9. Moreover, administration of AC inhibited osteoclast ferroptosis in calcified endplate through suppressing the level of phosphorylated I-κB and p65. These findings suggest that AC attenuates osteoclast ferroptosis to improve the endplate degeneration by NF-κB signaling, which could be a promising therapeutic against osteoporosis induced IVDD.

Abstract no.128

Optimal extraction of antioxidants flavonoids and phenolic acids from the leaves of Apocynum venetum L. by response surface methodology with integrated chemical profiles and bioactivity evaluation

1. Dr yang yu, Shenyang Pharmaceutical University, Shenyang

Abstract The leaf of Apocynum venetum (Luobuma in Chinese) is a common medicine and functional food that botanically from the dry leaf of Apocynum venetum L, which possess calming the liver and nerves, heat-clearing and promoting diuresis, etc. As a commonly used herbal medicine that plays an important role in anti-oxidation due to its high content of flavonoids and phenolic acids. Meanwhile, the optimal extraction process of A. venetum is closely related to its activity. In order to further develop the application of antioxidants flavonoids and phenolic acids from A. venetum leaves. In this study, an ultra-high performance liquid chromatography coupled with diode array detector, electrospray ionization, and quadrupole time-of-flight mass spectrometry technique has been established for the qualitative and quantitative analysis of 3 phenolic acids and 6 flavonoids in A. venetum. And an ultrasonic-assisted extraction condition for the maximum recovery of phenolic and flavonoid compounds with high antioxidation effect was optimized by response surface methodology. Moreover, contribution of total and individual phenolic acids and flavonoids to antioxidant was also estimated by Pearson correlation analysis. The optimum extraction conditions were as follows: ethanol concentration: 64%, extraction time: 20 min and liquid-to-solid ratio: 16:1 mL/g. The yield of three phenolic acids and six flavonoids under the optimal process was found to be 8.935 and 20.557 mg/g, which matched with the predicted values (8.755 and 20.404 mg/g) within a 95% confidence level. The results showed that the optimal extract had strong activities compared with conventional reflux extraction methods and demonstrated the flavonoids and phenolic acids of A. venetum having excellent antioxidation could be produced in an optimal extraction determined by response surface methodology. Keywords: Apocynum venetum; Flavonoids; Phenolic acids; Antioxidant activity; Response surface methodology; Pearson correlation analysis

Abstract no.129

Comparison of Chemical profiles and bioactivities of Nymphaea pubescens Willd. and Nymphaea rubra Roxb. ex Andrews

1. Ms Chayaporn Muangsawat, Naresuan University, Phitsanulok

This study compares the chemical profiles and bioactivities of two Nymphaea species: Nymphaea pubescens Willd. and Nymphaea rubra Roxb. ex Andrews. Both species, traditionally used for their medicinal properties, have not been extensively explored for their chemical composition and bioactivity profiles. Using HPLC, we found no significant differences in their chemical compositions, with comparable concentrations of key flavonoids. Antioxidant activities were assessed using DPPH and FRAP assays, revealing robust activity and strong free radical scavenging abilities in both species. Total flavonoid content showed no significant variation. Additionally, phosphodiesterase 5 inhibitory activity was evaluated, with both extracts demonstrating similar efficacy. In conclusion, N. pubescens and N. rubra exhibit analogous chemical profiles and bioactivities. These findings suggest both species can be used interchangeably in traditional and modern medicinal applications, providing a valuable basis for further pharmacological and therapeutic studies.

Abstract no.130

Mulberry Fruit Extract Provides Testicular and Spermatoprotection in High-fat Diet-fed Rats

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4. Prof Hiroki Nakata, Komatsu University, Komatsu
5. Prof Wai Chen, Curtin University, Perth
6. Prof Kroekkiat Chinda, Naresuan University, Phitsanulok
7. Prof Sirikan Chanprasert, Sirindhorn College of Public Health Suphanburi, Suphan Buri
8. Prof Yutthapong Tongpob, Naresuan University, Phitsanulok

Abstract Consuming fatty food promotes oxidative stress and low-grade inflammation, which is a major cause of decreased sperm function and male infertility. Mulberry fruit is an enriched source of anthocyanins that provide antioxidants against oxidative stress. Therefore, this study aimed to determine the testicular and spermatoprotective effects of standardized extract mulberry (SEM) in high-fat-fed rats. Male Wistar rats were divided into 5 groups (n=4/group): Normal Diet (ND), High-Fat Diet (HFD), HFD+SEM 100 mg/kg/day (HFD+SEM100), HFD+SEM 300 mg/kg/day (HFD+SEM300), and HFD+Atorvastatin 10 mg/kg/day (HFD+ATV10). After 90 days of treatment, serum lipid profiles, sperm quality, and testicular histological changes were evaluated. HFD rats had significantly increased LDL cholesterol indicating dyslipidemia. While sperm motility was comparable between groups, both SEM and ATV treatments significantly improved sperm concentration compared to HFD (p=0.003, HFD+SEM100; p=<0.001, HFD+SEM300; p=<0.001, HFD+ATV10, Figure 1). Moreover, high-dose SEM and ATV showed a trend towards improved testicular morphology, with a lower number of separation characteristics (Figure 2). In summary, SEM supplementation provides therapeutic potential against male reproductive abnormality by increasing sperm concentration and mitigating testicular caused by HFD consumption. Keywords: Mulberry; High-fat diet; Male reproductive system; Sperm quality; Testis

Abstract no.131

Anxiolytic Effect of Corilagin via Targeting 5-HTR2C for the Upregulation of BDNF/TrkB/CREB Pathway and Synaptic Plasticity

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2. Prof Vincent Kam-Wai Wong, Macau University of Science and Technology, Macao SAR

Anxiety neurosis, commonly referred to as anxiety disorders, is a brain disorder characterized by persistent anxiety, fear, tension, and disturbances in plant nervous activity and is often accompanied by motor restlessness and somatic discomfort. Anxiety disorders are among the most common mental health problems and are highly comorbid with other psychiatric disorders, such as depression. There has been a notable increase in the prevalence of anxiety disorders on a global scale amidst the COVID-19 pandemic from 2019 to 2021, resulting in enduring economic and social consequences. The etiology of anxiety disorders is multifaceted. The 'neurotrophic factor hypothesis' and the 'monoamine neurotransmitter hypotheses suggest that dysregulation of brain-derived neurotrophic factors (BDNF) and neurotransmitters may underlie the process of anxiety and depression and that the serotonergic system may play an important role in the development, expression, and control of anxiety. Despite the approval of anxiolytic drugs that target neurotrophic factors and the serotonergic system for clinical use, the effectiveness and adverse effects of current medications for anxiety disorders have proven to be inadequate, underscoring the necessity for the development of new pharmaceuticals. Nevertheless, the absence of innovative drugs based on mechanistic principles for the management of anxiety disorders on the pharmaceutical market for more than twenty years highlights the urgent need for novel mechanism-based therapies. Traditional Chinese medicine has a rich historical background and has led to significant advancements in addressing anxiety disorders. This study revealed that corilagin, a water-soluble tannin derived from the Chinese medicine Phyllanthus emblica Linn., possesses neuroprotective and antianxiety properties. In vitro experiments revealed that corilagin effectively mitigated the oxidative damage and apoptosis triggered by glutamate overstimulation in neuronal cells while also enhancing the antioxidant capacity of these cells. It can also reverse the decrease in BDNF caused by glutamate overdose, suggesting that corilagin has a neuroprotective effect. In a scopolamine-induced anxiety animal model, corilagin effectively ameliorated anxiety-related behaviors, including abnormal agitation, emotional and working memory deficits, and increased 5-HT levels in the prefrontal cortex (PFC), thereby activating the BDNF/CREB/TrkB pathway. Transcriptome sequencing analysis indicated that the anxiolytic effects of corilagin may be linked to the modulation of neuroactive ligand-receptor interactions and neural synapse function, potentially through the targeting of serotonin receptor 2C (Htr2c). Subsequent analysis of the synaptic plasticity-related proteins PSD95, synaptophysin (Syp), and Htr2c revealed that corilagin increased the protein levels of PSD95/Syp and upregulated Htr2c gene and protein expression. Adeno-associated virus (AAV)-based gene silencing studies revealed that Htr2c silencing decreased both the anti-anxiety effects of corilagin and the activation of BDNF/CREB/TrkB in the PFC and affected the levels of 5-HT but not PSD95/Syp in the PFC. The findings of our study indicated that corilagin may function as a natural small molecule within the serotonergic system, exerting anxiolytic effects by targeting Htr2c to regulate the levels of 5-HT and the BDNF/CREB/TrkB pathway in the PFC. Furthermore, the observed hepatoprotective properties and minimal

toxicity of corilagin suggest its potential as an adjunctive therapeutic agent for anxiety treatment, offering a novel approach for both the prevention and management of anxiety disorders. Keywords: Anxiety Disorders, Brain-Derived Neurotrophic Factor (BDNF), Corilagin, 5-Hydroxytryptamine, Serotonin System, 5-Hydroxytryptamine Receptor 2C

Abstract no.132

Protective effects of sweet tea Lithocarpus litseifolius on diabetic cognitive impairment

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Objective: Diabetic cognitive impairment (DCI) is a serious complication caused by damage to the central nervous system of diabetic patients. Lithocarpus litseifolius (Hance) Chun., also known as Lithocarpus polystachyus Rehd., commonly known as sweet tea, is a traditional Chinese medicine with homology of medicine and food, which integrates medicine, tea, food and sugar. L. litseifolius is rich in dihydrochalcones such as trilobatin, phloridzin and phloretin. Therefore, this study aimed to investigate the protective effects of L. litseifolius against cognitive impairment in diabetic mice. Methods: Quantitative analysis of dihydrochalcones in L. litseifolius was employed by HPLC. Additionally, 30 four-week-old male C57BL/6 mice were given a high-fat diet and intraperitoneal injection of streptozotocin (45 mg/kg). After the animals were in confirmed diabetic condition, the mice were randomly divided into the model group, L. litseifolius group (0.8g/kg), and the metformin group (400 mg/kg). 10 four-week-old male C57BL/6 mice fed with normal diet were used as the control group. After 10 weeks of L. litseifolius intervention, cognitive function was measured by Morris water maze. HE staining were used to evaluate brain pathology. Results: The HPLC results showed that L. litseifolius mainly contained dihydroflavonoids such as trilobatin, phloridzin and phloretin. The Morris water maze localization cruise and avoidance delay ($p<0.05$) showed a significant increase in the model group as compared to the control group, indicating the DCI mouse model was successfully established. The results of the water maze experiment showed that L. litseifolius could effectively improve the cognitive dysfunction of DCI mice. HE staining showed L. litseifolius improved neuronal cell morphology and increased the number of neuronal cells in DCI mice. Conclusion: L. litseifolius rich in dihydrochalcones can significantly improve the diabetic cognitive impairment . Keywords: Lithocarpus litseifolius; Sweet tea; Diabetic cognitive impairment (DCI) Funding: This research was supported by the National Natural Science Foundation of China (No. 82374177, 82074137), Guangdong Basic and Applied Basic Research Foundation (No. 2022A1515220068), Key Project of Department of Education of Guangdong Province (No. 2022ZDZX2032).
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Abstract no.133

Standardized Extract of Centella asiatica (ECa233) Mitigates High-fat Diet-Induced Sperm Dysfunction in Rats

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Abstract Background: High-fat diets negatively impact sperm quality through mechanisms involving oxidative stress and inflammation. ECa233, a standardized extract of Centella asiatica, is enriched with triterpenoids that provide antioxidant and anti-inflammation properties that could potentially mitigate male reproductive dysfunction. This study aimed to explore the effects of ECa233 on sperm quality in high-fat diet-fed rats. Methods: Male Wistar rats were divided into four groups (n=5/group): normal diet (ND), high-fat diet (HF), HF with ECa233 (100 mg/kg/day; HF+ECa100), HF with simvastatin (40 mg/kg/day; HF+SIM40). Following a 12-weeks of oral treatment, a gross assessment of testis, epididymis+vas deferens was conducted. Sperm was collected from cauda epididymis to evaluate concentration and viability. Results: HF rats exhibited dyslipidemia, evidenced by elevated total cholesterol (HF: 79.40±7.50 vs. ND: 49.40±5.86, $p<0.001$) and LDL levels (HF: 30.00±6.60 vs. ND: 12.40±5.32, $p<0.001$). Furthermore, these rats displayed male reproductive dysfunction (Figure 1), as indicated by a decrease in sperm concentration ($p<0.001$) and viability ($p<0.001$). Treatment with both ECa233 and simvastatin could alleviate dyslipidemia and improve male reproductive function by significantly reducing total cholesterol levels (HF±ECa233: 56.80±2.28, $p<0.001$; HF±SIM: 53.20±3.63, $p<0.001$) and increasing sperm concentration ($p=0.005$, HF±ECa233; $p=0.002$, HF±SIM, Figure 1A). There were no significant changes observed in LDL level (HF±ECa233: 21.20±3.70, $p=0.109$; HF±SIM: 19.80±6.65, $p=0.053$), sperm viability (HF±ECa233: $p=0.999$; HF±SIM: $p=0.056$, Figure 1B), and relative weight of testis and epididymis+vas deferens. Conclusion: ECa233 provides spermatoprotective effect, mitigating male reproductive dysfunction caused by high-fat diets. Keyword: ECa233; Dyslipidemia; Male reproductive system; Sperm quality; Infertility Acknowledgment: This work was supported by the Agricultural Research Development Agency (Public Organization) Grant number: PRP6605031550.

Abstract no.134

Review of Personalized Medicine and Pharmacogenomics of Anti-Cancer Compounds and Natural Products

1. Mrs Cai Xinyin, Shanghai University of Traditional Chinese Medicine, Shanghai

In recent years, the FDA has approved numerous anti-cancer drugs that are mutation-based for clinical use. These drugs have improved the precision of treatment and reduced adverse effects and side effects. Personalized therapy is a prominent and hot topic of current medicine and also represents the future direction of development. With the continuous advancements in gene sequencing and high-throughput screening, research and development strategies for personalized clinical drugs have developed rapidly. We elaborates the recent personalized treatment strategies, which include artificial intelligence, multi-omics analysis, chemical proteomics, and computation-aided drug design. These technologies rely on the molecular classification of diseases, the global signaling network within organisms, and new models for all targets, which significantly support the development of personalized medicine. Meanwhile, we summarize chemical drugs, such as lorlatinib, osimertinib, and other natural products, that deliver personalized therapeutic effects based on genetic mutations. We focused on personalized anti-cancer agents targeting ALK and EFGR receptors. Anaplastic lymphoma kinase (ALK) is an important molecular marker of non-small-cell lung cancer. EGFR is a member of the epidermal growth factor receptor family of ErbB receptor tyrosine kinases, which also includes BGFR, ErbB2 (HER2), ErbB3(HER3), and ErbB4(HER4). EGFR is a transmembrane receptor protein consisting of extracellular ligand-binding domains, transmembrane domains, and intracellular kinase-active domains. It also highlights potential challenges in interpreting genetic mutations and combining drugs, while providing new ideas for the development of personalized medicine and pharmacogenomics in cancer study.

Abstract no.135

Comprehensive characterization of absorbed compounds in multi-biological samples and pharmacokinetics study of 18 representative components after oral administration of YIV906 and sorafenib in rat plasma

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YIV-906 (PHY906) originated from traditional Chinese medicine prescription Huang Qin Tang, which has been widely used to alleviate symptoms of gastrointestinal tract over 1,500 years. The clinical results indicated that it could enhance anti-tumor activity and ameliorate the side effects when was used in combination with anticancer agents including sorafenib, irinotecan, and capecitabine. However, the comprehensive analysis of the absorbed bioactive constituents and the pharmacokinetic characteristics are no well studied. Moreover, it is also unclear whether YIV906 will affect the pharmacokinetic characteristics of sorafenib. In this study, a comprehensive analysis strategy was established to characterize the prototype components and metabolites of YIV906 and sorafenib in plasma and multiple tissues. Firstly, a sensitive method based on ultra-high performance liquid chromatography coupled with quadruple Exactive mass spectrometry (UHPLC-Q-Exactive-MS) combined with a multivariate data processing approach was established to analyze multi-biological samples. Secondly, UHPLC-MS/MS based Global Natural Product Social molecular networking (GNPS) were applied to screen out the unknown metabolites. In addition, a rapid UPLC-MS/MS analytical method was developed and applied to detect 18 major bioactive components in rat plasma after oral administration of YIV906 and sorafenib. The metabolic process of YIV906 and sorafenib in vivo was speculated and the differences in pharmacokinetic parameters between single and combined administration of YIV906 and sorafenib were compared. Finally, a total of 158 absorbed compounds including 59 prototype components and 99 metabolites were identified in rat plasma based on the established strategy, as well as revealed the tissue distribution characteristics of main components. The main metabolic pathways included hydroxylation, sulfation and glucuronidation. Moreover, the UPLC-MS/MS method was fully validated for its satisfactory linearity ($r \geq 0.9917$), good precisions (RSD <9.43%), and accuracy (RE: 80.22-116.35%), as well as extraction recoveries (81.51-107.01%), matrix effects (81.02–111.40%), and stability (RSD <12.97%). The pharmacokinetic results indicated that there were statistically significant differences ($P < 0.05$) in MRT(0-t), MRT(0-∞), Tmax, t1/2, Cmax, CL/F, CL/F between single and combined administration groups. This study could provide a basis for further study on the pharmacokinetic-pharmacodynamic correlation and clinical application for combination of YIV906 and sorafenib.

Abstract no.136

A novel strategy with in vivo characterization， extraction， isolation and activity evaluation for discovery of absorbed anti-inflammatory oligosaccharides from Zhu-Ling decoction

1. Prof Yi Dai, Jinan University, Guangzhou

2. Dr Xiyang Tang, Jinan University, Guangzhou

ABSTRACT Zhu-Ling decoction (ZLD), a classical traditional Chinese medicine (TCM) formula, is used for the treatment of chronic kidney diseases. However, the structure and activity of absorbed oligosaccharides (OSs) in ZLD are not clear. In this study, a novel strategy with in vivo characterization, extraction, isolation, activity evaluation was established and applied to identify absorbed anti-inflammatory OSs in ZLD. The results revealed that 30 OSs (22 reducing and 8 non-reducing OSs) and 11 OSs (7 reducing and 4 non-reducing OS) were characterized from ZLD in vitro and in vivo by using UPLC/Q-TOF-MS with PMP derivatization, respectively. Among them, a series of -1→3-β-D-Glcp-OSs were isolated and identified by HPLC-HILIC-UVD-ELSD, SPHPLC-HILIC-RID, monosaccharide composition, MS and 1D/2D-NMR spectroscopy, including laminaritriose, laminaritetraose, laminaripentaose, laminarihexaose, laminariheptaose, laminarioctaose and laminarinonaose. Moreover, the 4 non-reducing absorbed OSs were identified by comparison with reference standards, including sucrose, trehalose, raffinose and stachyose. Among them, laminaritriose, laminaritetraose and laminaripentaose significantly inhibited TNF-α and IL-6 levels in LPS-induced HK-2 cell and exerted significant anti-inflammatory effects via the NF-κB and Akt/mTOR signaling pathways. Together, the novel strategy has been realized accurate LC-MS (derivatization) guided target isolation and purification of in vivo absorbed reducing and non-reducing OSs (multiple types) from a complex system (TCM formulas) for the first time. Our work provides new perspectives on the discovery of in vivo effective substances in TCM formulas and the forms of action of polysaccharides in medicinal materials after the preparation process of TCM formulations. Keywords Zhu-Ling decoction (ZLD); Novel strategy, activity evaluation; Reducing and non-reducing absorbed OSs; -1→3-β-D-Glcp-OSs; Anti-inflammatory; NF-κB and Akt/mTOR signaling pathway Acknowledgements: The present study was supported by National Natural Science Foundation of China (82204582), and Innovation Team and Talents Cultivation Program of National Administration of Traditional Chinese Medicine (ZYYCXTU-D-202203). References: Tang, XY, et al. Carbohydrate Polymers, 2024. 342: 122422

Abstract no.137

A preliminary study on the efficacy of Bao Yuan Jing pressed tablets in replenishing qi and blood

1. Mrs Chenghao Yu, Chengdu University of Traditional Chinese Medicine, Chengdu

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Double deficiency of qi and blood is the name of the Chinese medicine syndrome, which is mainly manifested as fatigue, night sweating, insomnia, pale or yellowish color. Modern people because of life and work pressure, fast pace of life, irregular diet and rest, excessive thought and labor, spleen and stomach function decline, in the long run, will make the qi and blood biochemical lack of source, resulting in qi and blood double deficiency. Chinese medicine believes that the gas and blood deficiency is mostly due to long-term disease consumption, gas and blood injuries caused by; or first blood loss, gas with blood consumption; or first due to gas deficiency, the blood of the obstacles and the gradual decline, thus forming a gas and blood deficiency. Qi and blood is the fundamental survival of the human body, the theory of qi and blood is an important part of the theoretical system of traditional Chinese medicine, qi can generate blood, blood can carry qi, the two are rooted in each other, interdependent. A deficiency of qi results in a lack of blood, and a lack of blood results in a deficiency of qi.

Abstract no.138

Protective effect of SYP-5 against ethanol-induced gastric ulcer in mice

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3. Ms Yulin Hong, Shenyang Pharmaceutical University, Shenyang

4. Ms Xinhui Yang, Shenyang Pharmaceutical University, Shenyang

SYP-5, a natural compound from Aspergillus secondary metabolites, exhibits anti-tumor, anti-virus, anti-inflammatory activities. However, its potential for gastric ulcer treatment remains unexplored. This study aimed to investigate the protective effect of SYP-5 against ethanol-induced gastric ulcers. Methods: The rats in the treatment group received tail vein administration 100ng/kg for two consecutive days. After the last administration for 2 hours, the rats followed by oral administration of 0.1 mL/10g anhydrous alcohol, and blood and tissue samples were collected one hour later for evaluation of gastric ulcer area and protective index using Image J software. Elisa assay were used to quantify the levels of inflammatory factors, oxidative stress and Caspase-3 in gastric tissue and serum. Immunohistochemistry was also employed the expression levels of Caspase-3 and Bax. Results: SPY-5 significantly decreased gastric ulcer index and gastric remnant rate, while decreasing the expression of TNF-α, IL-6, IL-1β, MDA and Bax in serum and tissue. Additionally, it increased GSH-PX activity (an antioxidant enzyme), thereby reduce the apoptosis of gastric tissue cells in mice with ethanol-induced gastric ulcer. Conclusion: Our finding suggest that SYP-5 can protect against ethanol- induced gastric ulcer by improving oxidative stress level, suppressing inflammatory and apoptosis.

Abstract no.139

An integrated 3-M workflow for accelerated annotation of natural product: flavonoids in Daemonorops draco as a case study

1. Dr Wenxiang Fan, Shanghai University of Traditional Chinese Medicine, Shanghai

Efficient annotation of metabolites in natural products and functional foods, particularly those from resource-endangered plants lacking reference standards, is crucial for nutraceuticals development. Advanced techniques like high resolution mass spectrometry (LC-HRMS) have significantly enhanced metabolite characterization. However, challenges such as redundant spectral data, limited reference databases, and inferior structural analogs analysis hinder its broad applicability. In this study, we propose an integrated annotation strategy utilizing various computational tools, including mass defect filters (MDF), molecular fingerprints, and molecular networks (3-M strategy). We demonstrate this approach using Daemonorops draco (D. draco), a renowned yet resource-endangered natural product rich in functional flavonoids. By applying pre-defined flavonoids MDF windows, the MS1 peaks reduced by 85% (from 10,043 to 1,585) in positive mode. Subsequent de novo molecular formula annotation and molecular fingerprint-based structure elucidation were automatically performed using the SIRIUS machine learning platform. Additionally, two complementary cluster tools were incorporated, including feature-based molecular network (FBMN) and t-distributed stochastic neighbor embedding (t-SNE) molecular network, to efficiently discover novel flavonoids in D. draco. Totally, 108 flavonoids (containing flavones, flavanes, flavanones, chalcones, chalcanes, dihydrochalcones, anthocyanins, homoisoflavanes, homoisoflavanones, and isoflavones), 18 flavone derivatives, and 54 flavone oligomers were identified. Among them, 25 compounds were firstly reported in D. draco. This 3-M workflow shed light on the composition of D. draco and validate the effectiveness of our approach, which facilitated the rapid annotation and screening of subclass metabolites in complex natural products.

Abstract no.140

Chemical Compounds from the Aerial Parts of Isodon Serra and Their Cytotoxic Activities

1. Dr Guo-Yuan Zhu, Macau University of Science and Technology, Macao SAR

Isodon serra (Maxim.) Kudo, a perennial plant named “Xihuangcao” in China, is mainly distributed in Hunan, Hubei, Sichuan, Yunnan, Guangdong, Jiangxi, and Fujian provinces. As a widely used Chinese folk medicine in clinical application, I. serra has been popularly used to treat acute icteric hepatitis, arthritis, acute cholecystitis, enteritis, damp-heat dysentery, bruises, and health care. Some health-promoting Chinese patent medicine and beverages derived from this plant have been developed, such as Xihuangcao granules, Xihuangcao tea bags, Xiaoyan Lidan Tablet, and Fufangdantong Tablets, and they have significant liver and cholecyst protection and anticanner effects. In addition, I. serra is an important ingredient in Cantonese herbal tea which are used for daily health care. The whole herb of I. serra is often used as medicine, approximately 150 compounds including a variety of ent-kaurane types diterpenoids, triterpenoids, flavonoids, and phenols have been have been isolated extensively from this species over the past few decades. Previous pharmacological studies suggested that the above compounds displayed cytotoxic, anti-inflammatory, antiviral, antibacterial, antioxidant activities. As a result, With the aim of searching for more bioactive terpenoids with structurally intriguing phytochemical constituents, a ethanol extract of the aerial parts of I. serra has been investigated, which led to the isolation and characterization of five undescribed diterpenoids, serranins A−E (1−5), and four noval triterpenoids, serratic acids A−D (6−9), along with 40 known terpenoids (10−44). The planar structures of 1−9 and their relative configurations were established on the basis of extensive spectroscopic analysis. Structurally, the p-coumaric and ferulic triterpene esters, serratic acids A−D (6−9), were the unprecedented triterpenoids with a 18,19-seco ring E. Compound 26, as a isosteviol-type diterpenoid, is a noval natural product. Among them, compounds 11−13 and 19−20 have strong inhibitory effects on human lung cancer cells H1299, with IC50 values lower than 10 μM.

Abstract no.141

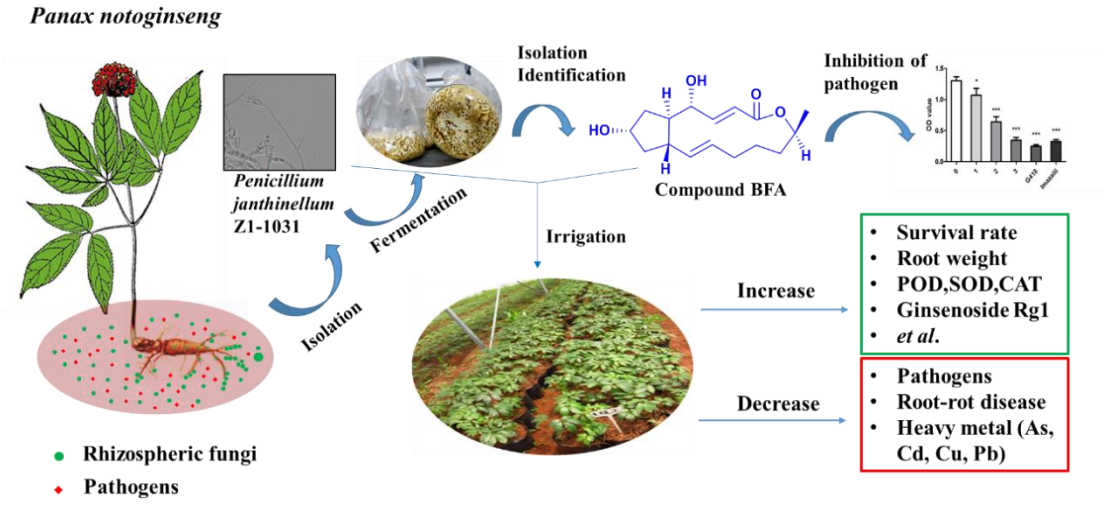
Active compound-producing Penicillium janthinellum mediates root-rot disease resistance and promotes growth of Panax notoginseng

1. Meng-Yue Zhang, 2. Ying-Ying Wu, 3. Jun Xie, Juan Chen, 4. Shu-Tian Xu, 5. Xun-Yong Zhou, 6.Yi-Xuan Zhang

Abstract：Root-rot disease caused by the plant pathogens is a major threat to Panax notoginseng cultivation. Increased concerns about the side effects of chemical pesticides have resulted in greater interest in developing biocontrol strategies against phytopathogens. The potential of the biological control fungus Penicillium sp. to suppress crop diseases under different growth conditions has been intensively discussed. However, such application for the biocontrol agent of Penicillium sp. with popular medicinal herbs, such as P. notoginseng, are rare. This study aimed to apply the selected endophytic fungus Penicillium janthinellum to control root-rot disease in vitro and in field conditions and promote plant growth. Crude extract and active compounds from ten fungal isolates of P. notoginseng were screened against root-rot pathogens Alternaria brassicicola, Cylindrocarpon destructans and Fusarium solani, where P. janthinellum and brefeldin A isolated from this strain showed strongest antagonism. Agar plating test revealed that spores of A. brassicicola and C. destructans were losing germination ability after interacted with brefeldin A (100 μg/ml). Colonization assay demonstrated that P. janthinellum could conlonize on rhizosphere of P. notoginseng and leaves in a large population. Formulations were prepared with P. janthinellum to form biocontrol agent and tested for its biocontrol activities under glasshouse. Biocontrol agent treatment where brefeldin A was detected in the treatment soil remarkably recorded the minimum disease incidence, maximum plant growth, higher Rg1 content and defense enzymes activities in root of P. notoginseng. Therefore, this study has potential to be adopted for sustainable and eco-friendly P. notoginseng cultivation.

Key words: Panax notoginseng, Penicillium janthinellum, Brefeldin A, Root-rot disease, Colonization, Plant growth promotion

Graphic Summary


Panax notoginseng
Penicillium janthinellum Z1-1031
Fermentation
Isolation
Isolation Identification
Compound BFA
Inhibition of pathogen
Irrigation
Increase
Decrease
Survival rate
Root weight
POD,SOD,CAT
Ginsenoside Rg1
et al.
Pathogens
Root-rot disease
Heavy metal (As, Cd, Cu, Pb)
Rhizospheric fungi
Pathogens

Abstract no.142

Triple Three-dimensional MS/MS Spectrum Facilitates Quantitative Ginsenosides-targeted Sub-metabolome Characterization in Notoginseng

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2. Ms Ke Zhang, Beijing University of Chinese Medicine, Beijing

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Although serving as the workhorse, MS/MS cannot fully satisfy the analytical requirements of quantitative sub-metabolome characterization. Because more information intrinsically correlates to more structural and concentration clues, here, efforts were devoted to comprehensively tracing and deciphering MS/MS behaviors through constructing triple three-dimensional (3×3D)-MS/MS spectrum. Ginsenoside-targeted metabolomics of notoginseng, one of the most famous edible medicinal plants, was employed as a proof-of-concept. Serial authentic ginsenosides were deployed to build the correlations between 3×3D-MS/MS spectra and structural/concentration features. Through assaying ginsenosides with progressive concentrations using Qtof-MS to configure 1st 3D spectrum, the generations of MS1 spectral signals, particularly multi-charged multimer anions e.g., [2M–2H]2– and [2M+2HCOO]2– ions, relied on both concentration and the amount of sugar chains. By programming progressive collision energies to the front collision cell of Qtrap-MS device to gain 2nd 3D spectrum, optimal collision energy (OCE) corresponding to the glycosidic bond fission was primarily correlated with the masses of precursor and fragment ions and partially governed by the glycosidation site. The quantitative relationships between OCEs and masses of precursor and fragment ions were utilized to build large-scale quantitative program for ginsenosides. After applying progressive exciting energies to the back collision chamber to build 3rd 3D spectrum, the fragment ion and the decomposition product anion exhibited identical dissociation trajectories when they shared the same molecular geometry. After ginsenosides-focused quantitative metabolomics, significant differences occurred for sub-metabolome amongst different parts of notoginseng. The differential ginsenosides were confirmatively identified by applying the correlations between 3×3D-MS/MS spectra and structures. Together, 3×3D-MS/MS spectrum covers all MS/MS behaviors and dramatically facilitates sub-metabolome characterization from both quantitative program development and structural identification.

7. Polychemical Activities and Mechanism StudyII(Cancer, Immunomodulation, Inflammation)

Abstract no.143

Immunomodulatory Effects of Yu-Ping-Feng Formula on Primary Sjögren's Syndrome: Interrogating the T Cell Response

1. Prof Xiang Lin, The University of Hong Kong, Hong Kong SAR

Ethnopharmacological treatments have shown beneficial effects in the clinical practice of autoimmune disorders. However, the underlying mechanism of immunomodulatory effects remains challenging, given the complicate composition of herbal medicines. Here, we developed an immunological approach to interrogate the T helper cell response. Through data mining we hypothesized that Chinese medicine formula, Yu-Ping-Feng (YPF) might be a promising candidate for treating primary Sjögren's syndrome (pSS), a common autoimmune disease manifested by exocrine gland dysfunction. We took advantage of a mouse model of experimental Sjögren's syndrome (ESS) that we previously established for YPF formula treatment. YPF therapy ameliorated the ESS pathology in mice with active disease, showing improved salivary function and decreased serum levels of autoantibodies. Phenotypic analysis suggested that both effector T and B cells were significantly suppressed. Using co-culture assay and adoptive transfer models, we demonstrated that YPF formula directly restrained effector/memory T cell expansion and differentiation into Th17 and T follicular helper (Tfh) cells, the key subsets in ESS pathogenesis. Importantly, we recruited 20 pSS patients and conducted a pilot study of 8-week therapy of YPF formula. YPF treatment effectively improved fatigue symptoms, exocrine gland functions and reduced serum IgG/IgA levels, while effector T and B cell subsets were significantly decreased. There was a trend of reduction on disease activity, but not statistically significant. Together, our findings suggested a novel approach to assess the immunomodulatory effects of YPF formula, which may be favorable for patients with autoimmune disorders.

Abstract no.144

A novel hotspot mutant p53R175H binding partner protein X stabilizes mutant p53 and promotes mutant p53 GOFs in tumorigenesis

1. Prof Wenzhe Ma, Macau University of Science and Technology, Macao SAR

Tumor-suppressor p53 is frequently mutated in various human malignancies. Mutant p53 proteins often accumulate at high concentrations in human cancers to promote cancer progression through the gain-of-function (GOF) mechanism. Although the GOFs of p53 mutants is well acknowledged, it remains an open question in research whether different p53 mutants share the same cofactors to induce GOFs. In a comprehensive proteomic screening, we identified Protein X, a cellular component that discriminates p53 variants based on their mutation status, specifically interacts with the p53 DNA-binding domain. Protein X exhibits a robust binding affinity for the p53R175H but fails to effectively bind wild-type p53 or other hotspot mutants in vivo for functional regulation. Our findings reveal that p53R175H promotes Protein X-dependent tumor metastasis by upregulating expression of pro-metastatic targets. Importantly, genetic ablation of protein X in p53R172H knock-in mice effectively reduces the metastatic potential and prolongs the survival of p53R172H mice, underscoring protein X's pivotal role in mutp53R175H-driven pathogenesis. Furthermore, we observe protein X is frequently overexpressed in many human tumors and the over-expression of protein X is associated with poor prognosis of cancer patients. Our results highlight protein X as a novel mutp53R175H-interacting partner, elucidating a pivotal mechanism by which it facilitates GOFs of mutp53 in tumor development, thus presenting protein X as a potential therapeutic target for intervention in mutp53-driven cancers.

Abstract no.145

A Formulation of Silvestrol Improves Psoriatic Skin and Suppresses IL-17A in an Imiquimod-Induced Psoriasis Mouse Model

1. Dr Nyuk Fong Kon, Sarawak Biodiversity Centre, Sarawak

Psoriasis is an autoimmune inflammatory skin disorder that causes red, itchy, flaky patches on the skin. Inflammatory cytokines such as interleukin 17 (IL-17) are elevated in the skin of psoriatic patients. The effectiveness of blocking these cytokines in psoriasis confirms their role in the pathogenesis of the condition. We have demonstrated that a natural compound silvestrol belonging to the flavaglines is an IL-17A inhibitor that has therapeutic potential for psoriasis treatment. Silvestrol is isolated from the plant Aglaia stellatopilosa which is endemic to central Borneo, Sarawak, Malaysia. Silvestrol effectively inhibited the production of inflammatory cytokines in the nanomolar range of concentrations measured by enzyme-linked immunosorbent assay (ELISA), including IL-17A, IL-17F, TNF-α and IL-12. Silvestrol was incorporated into an emulsifying ointment-based formulation and assessed for both efficacy and safety in a psoriasis model using BALB/c mice induced chemically by imiquimod (IMQ). The vehicle formulation, serving as an emollient for the symptomatic relief of dry skin conditions, effectively improved the skin outlook. Meanwhile, the formulation containing silvestrol demonstrated a significant decrease in cytokine levels of IL-17A, as observed via Luminex multiplex cytokine assay conducted on the skin of the mouse's ear. Overall, silvestrol demonstrated its potential to control inflammatory skin diseases by inhibiting IL-17A, suggesting it could be a potential therapeutic agent in psoriasis. Keywords: Psoriasis; Natural Compound; IL-17A. Acknowledgement: We express our gratitude to the Sarawak Government for their support in this project. Our appreciation also goes to Sarawak Biodiversity Centre for their contribution support.

Abstract no.146

Exploring the Mechanism of Lou Bei San in Reshaping the Immune Microenvironment of Triple-Negative Breast Cancer via the PLK1/cGAS/STING Axis

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2. Prof Yang Yu, Macau University of Science and Technology, Macao SAR

3. Prof Cun Liu, Shandong Second Medical University, Weifang

4. Prof Changgang Sun, Shandong Second Medical University, Weifang

Genomic instability is one of the hallmarks of cancer, determining its heterogeneity and response to immunotherapy. The cGAS-STING pathway, as a crucial DNA sensing mechanism, is an effective means of reshaping the tumor immune microenvironment and enhancing anti-tumor immune responses. Deficiencies in the DNA damage repair system are key components in maintaining genomic instability. Polo-like kinase 1 (PLK1), as an important regulatory factor in the DNA double-strand break (DSB) repair system, is correlated with disease progression in triple-negative breast cancer (TNBC) due to its overexpression. Studies have shown that PLK1 not only mediates the RAD51 involvement in the DSB repair process but also may regulate immune responses by phosphorylating cGAS. Traditional Chinese medicine (TCM) views genomic instability as a result of the long-standing accumulation of pathogenic factors leading to the formation of cancerous masses. The TCM principle of "treating pathogenic accumulation with dissipation" provides new insights for the intervention of genomic instability. This study focuses on the activation of immune responses by defects in the DSB repair system, the changes in the immune microenvironment induced by PLK1 regulation of the cGAS-STING axis, and the classic TCM formula Lou Bei San as the object of study. It aims to explore the effective mechanism by which TCM interventions counteract genomic instability and reshape the immune microenvironment of TNBC. This aligns with the research patterns and advantages of TCM intervention in TNBC and provides a novel perspective for studying the anti-tumor mechanisms of TCM immunomodulation.

Abstract no.147

Mechanism of Hederacolchiside A1 inhibiting human lung cancer A549 cells in vitro by PI3K/Akt/mTOR signaling pathway

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3. Prof Jin-Cai Lu, Shenyang Pharmaceutical University, Shenyang

Background：Hederacolchiside A1 (HA1), an active extract from traditional Chinese medicine herb Anemone raddeana Regel, is widely reported in cancer treatment. This study aimed to investigate the effects of HA1 on human lung cancer A549 cells and explore its mechanism through the PI3K/Akt/mTOR signaling pathway. Methods: The CCK-8 assay was used to detect the effects of HA1 on the viability of A549 cells. Chemical fluorescence methods were used to measure intracellular reactive oxygen species (ROS), mitochondrial membrane potential, cell apoptosis, and cell cycle. Western blotting was used to measure the expression levels of apoptosis-related proteins Bax, Bcl-2, Cytc, caspase3/9, and their activated forms cleaved-caspase3/9, as well as the expression levels of PI3Kp85, Akt, mTOR, and their phosphorylated proteins in the PI3K/Akt/mTOR signaling pathway. Furthermore, the antioxidant N-acetylcysteine (NAC) was used to inhibit the increase in ROS levels, and the proliferation of cells and the activity of the PI3K/Akt/mTOR pathway were measured. Results: The results showed that HA1 dose-dependently induced apoptosis and G0/G1 phase arrest in A549 cells. HA1 also significantly increased ROS levels and decreased mitochondrial membrane potential, leading to mitochondrial damage. HA1 upregulated the expression levels of apoptosis-related proteins Bax and cytochrome c in the cytoplasm, downregulated the expression levels of Bcl-2 and apoptosis-related proteins caspase3/9, and significantly increased the expression levels of their activated forms cleaved-caspase3/9. The phosphorylation levels of PI3K/Akt/mTOR were downregulated as well. Further studies found that HA1 could not inhibit the proliferation of A549 cells or suppress the activity of the PI3K/Akt/mTOR pathway when ROS was blocked by NAC. Conclusion: HA1 can inhibit the proliferation of A549 cells by blocking the G0/G1 phase and induce apoptosis by upregulating ROS levels and inhibiting the PI3K/Akt/mTOR pathway, thereby inducing apoptosis in A549 cells. Keywords: Hederacolchiside A1; A549 cells; PI3K/Akt/mTOR signaling pathway; mitochondrial apoptosis

Abstract no.148

Efficacy and mechanism in enhancing anti-PD-1 against colorectal cancer of cordyceps polysaccharides mediated by gut microbiota

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Empirical evidence has highlighted the pivotal role of the gut microbiota in modulating the efficacy of immune checkpoint inhibitors such as PD-1/PD-L1 antibodies, which has marked a pivotal shift in the therapeutic approach to colorectal cancer (CRC). Cordyceps polysaccharides (CPS) of Cordyceps sinensis may contribute to improved treatment outcomes. Our study assessed the combined therapeutic efficacy of CPS and PD-1 inhibitors in treating CRC, with a focus on their influence on the tumor's immune microenvironment and the underlying anti-cancer mechanisms, as elucidated by 16S rRNA gene sequencing. The study used three mouse models to evaluate the co-treatment's efficacy, MC38 and CT26 tumor-bearing mice, and an AOM/DSS induced CRC model. Results showed that CPS and PD-1 antibody co-treatment significantly enhanced therapeutic outcomes, modulating the immune environment, increasing CD8+ T cell infiltration and activity, and enhancing the CD8+/Treg cell ratio. In the AOM/DSS model, CPS ameliorated colon damage and upregulated gut barrier protein expression. The treatment modified the gut microbiota composition, enhancing both alpha and beta diversity, and increased the relative abundance of Lachnospira at the genus level. Additionally, fecal microbiota transplantation(FMT) and oral antibiotic treatment experiments confirmed the gut microbiota's contribution to the improved anti-colorectal cancer effects of PD-1 antibodies with CPS. In conclusion, the combination of Cordyceps polysaccharides and PD-1 inhibitors presents a novel therapeutic strategy for CRC, enhancing treatment efficacy by modulating the tumor microenvironment, amplifying immune responses, and optimizing gut microbiota.

Abstract no.149

Gegen Qinlian decoction restores the intestinal barrier in bacterial diarrhea piglets by promoting Lactobacillus growth and inhibiting the TLR2/MyD88/NF-κB pathway

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2. Mr Zhen-Ye Luo, Southern Medical University, Guangzhou

Acute bacterial diarrhea is a severe global problem with a particularly high incidence rate in children. The microecology inhabiting the intestinal mucosa is the key factor leading to diarrhea. Gegen Qinlian decoction (GQD) is used to treat bacterial diarrhea, however, its underlying mechanism remains unclear. Thus, this study aimed to clarify the restorative effect of GQD on the intestinal barrier from the perspective of gut microbiota. A Tibetan piglet model with bacterial diarrhea was established through orally administered Escherichia coli, and diarrheal piglets were treated with GQD for three days. After treatment, GQD significantly ameliorated the diarrheal symptoms. GQD decreased the levels of IL-6, LPS, and DAO, and increased SIgA, ZO-1, and occludin levels in intestinal mucosa, indicating the restoration of intestinal barrier. GQD modulated the microbial compositions inhabited on the intestinal mucosa, especially an increase of the Lactobacillus. Spearman analysis showed that Lactobacillus was the key genus of intestinal barrier-related bacteria. Bacterial culture in vitro validated that GQD directly promoted Lactobacillus growth and inhibited E. coli proliferation. Moreover, the expressions of TLR2, MyD88, and NF-κB in the colon decreased after GQD treatment. In conclusion, GQD may treat diarrhea and restore the intestinal mucosal barrier by facilitating Lactobacillus growth and inhibiting the TLR2/MyD88/NF-κB signaling pathway.

Abstract no.150

Fufang Biejia Ruangan tablet Intervenes ICC Process by Regulating FAK-Hippo cascade

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Background & Aims: Intrahepatic cholangiocarcinoma (ICC) is a lethal malignancy without effective treatment options. Research has indicated that ICC development is associated with liver fibrosis and characterized by extensive desmoplastic reactions independent of surrounding tissue fibers. Fufang Biejia Ruangan tablet (BJRG), as the first approved Chinese patent medicine for liver fibrosis, in combination with entecavir, demonstrates a significant reduction in mortality rates related to hepatitis B-induced liver fibrosis and cirrhosis. Therefore, this study aims to investigate the intervention effect of BJRG on an intrahepatic cholangiocarcinoma mouse model to explore potential mechanisms underlying BJRG's efficacy. Methods & Results: This study aims to investigate whether the administration of BJRG can effectively inhibit the progression of intrahepatic cholangiocarcinoma in an AKT-YAP mouse model. The findings demonstrate that treatment with BJRG leads to a reduction in liver tumor size and a significant improvement in overall survival rate. Immunohistochemical analysis reveals that compared to the model group, the BJRG-treated group exhibits a remarkable decrease in CK19 expression, increased apoptosis of tumor cells as indicated by KI67+, reduced collagen deposition and α-SMA expression, enhanced infiltration of F4/80+ macrophages, and modulation of the FAK-Hippo signaling pathway along with regulation of extracellular matrix. Conclusion BJRG modulates FAK via the Hippo pathway, thereby suppressing tumor cell proliferation, facilitating immune cell infiltration, and consequently regulating the extracellular matrix.

Abstract no.151

Tou Nong powder obstructs ulcerative colitis through the regulation of NF-kB/NLRP3/Caspase-1/GSDMD inflammasome pyroptotic pathway

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Tou Nong Powder (TNP), a classical Chinese medicinal formula originated from the Chinese Ming Dynasty, has been applied to treat skin ulcers in patients with deficient constitutions. According to theory of traditional Chinese medicine, colonic ulcers share similar pathological conditions with skin ulcers, and consequently, TNP has been applied to ulcerative colitis safely and effectively. To investigate whether TNP obstructs enteric inflammation in 2,4,6-trinitrobenzene sulfonic acid (TNBS) induced rats through regulation of NLRP3 inflammasome and attenuating enteric pyroptosis. In this study, network pharmacology and UPLC-Q-TOF/MS were applied to identify compounds and potential pharmacological targets. The therapeutic effects of TNP were assessed on TNBS induced experimental colitis rats using general symptoms (body weight, disease activity index, colonic weight, and length) and histopathological observation. The NF-kB/NLRP3/Caspase-1/GSDMD signaling pathway regulation was investigated by western blot and real time reverse transcription polymerase chain reaction (RT-qPCR). The results showed that TNP ameliorates the disease activity index, reverses colonic weight increase, alleviates colonic shortening and colonic histopathological injury. A decrease in tumor necrosis factor alpha (TNF-α), diamine oxidase (DAO), intercellular adhesion molecule-1 (ICAM-1), and endotoxin (ET) were detected in peripheral circulation. Moreover, TNP significantly obstructed the NF-κB/NLRP3/Caspase-1/GSDMD signaling pathway. TNP displays a promising therapeutic effect on ulcerative colitis via reducing the release of IL-18 and IL-1β and suppressing NF-κB/NLRP3/Caspase-1/GSDMD signaling pathway.

Abstract no.152

Network Pharmacology-Based Exploration of the Potential Mechanisms of the classic prescription WW for Acute Lung Injury Treatment

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5. Ms Yumiao Zhen, Jinan University, Guangzhou

Background: Acute lung injury (ALI) is a severe respiratory condition with high mortality rates and lacks effective treatments. Traditional Chinese medicine (TCM) have emerged as potential therapeutics for ALI, but their mechanisms remain largely unexplored. This study is the first to investigate the potential of the classic prescription WW, in treating ALI using a network pharmacology approach. Methods: Network pharmacology was employed to identify the active ingredients, potential targets, and signaling pathways through which WW may exert therapeutic effects on ALI. Molecular docking and experimental validation were performed to support the findings. Results: A total of 56 active chemical ingredients, 876 potential targets, and 2399 ALI-related genes were identified for WW. The analysis revealed 316 common targets between WW and ALI, 4011 GO biological processes, and 195 KEGG pathways. Molecular docking demonstrated good binding affinity between WW compounds and target proteins. In vitro and in vivo experiments indicated that WW might alleviate ALI through modulation of the RAP pathway. Conclusion: This pioneering study provides the first evidence of WW's potential therapeutic effects on ALI, potentially mediated through the RAP pathway. The network pharmacology approach, coupled with experimental validation, offers a valuable strategy for uncovering the mechanisms of TCM compounds in complex diseases like ALI. Keywords: Acute Lung Injury, Traditional Chinese Medicine, classic prescription, Network Pharmacology, RAP Pathway

Abstract no.153

Potent glycolipid inhibits neuroblastoma growth and liver metastasis through reprogramming the tumor microenvironment

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3. Dr Ya-Hui Wang, Chang Gung Memorial Hospital, Linkou

4. Dr Jen-Chine Wu, Chang Gung Memorial Hospital, Linkou

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α-Galactosylceramide (α-GalCer), a glycolipid derived from marine sponge, could stimulate invariant natural killer T cell (iNKT) cells to produce large amounts of cytokines and thus triggered strong anticancer activities in mice. However, repeated treatment of α-GalCer induced NKT cell anergy with reduced productions of IFN-γ, and IL-12 in the serum, which compromised its clinical application. Another potent glycolipid being able to activate NKT cells but without inducing anergy might provide an alternative strategy to solve the problem. In this study, anticancer effects of the potent glycolipid (PG) against cancer cells with hepatic metastatic potential were examined for the first time since liver contained a much higher percentage of iNKT cells and was a common site of metastasis at the late stage of neuroblastoma growth. PG efficiently prolonged mouse survival, suppressed neuroblastoma growth and liver metastasis, as well as induced Th1-biased cytokine productions in the liver tumor microenvironment (TME). PG stimulation also upregulated CD1d expression on myeloid-derived suppressor cells (MDSCs), which might be directly killed by PG-activated NKT cells and thus reduced the amounts of MDSCs in the TME. Moreover, NKT cells might indirectly kill CD1d-negative neuroblastoma cells through the expansion of CD4+ T, CD8+ T, and NK cells in the liver. These mechanisms might be coexisted for contribution to the better anti-cancer/metastasis activities of PG triggered in the liver TME, suggesting the potential clinical application of PG for treatment of neuroblastoma, especially for curbing liver metastasis.

Abstract no.154

Small molecule α-methylene-γ-butyrolactone， an evolutionarily conserved moiety in sesquiterpene lactones， ameliorates arthritic phenotype via interference DNA binding activity of NF-κB

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2. Dr Ke-Gang LINGHU, Guizhou Medical University, Guizhou

Sesquiterpene lactones (SLs) are the main anti-inflammatory ingredients of many traditional herbs utilized in RA treatment. α-Methylene-γ-butyrolactone (α-M-γ-B) is a core moiety that widely exists in natural SLs. This study was designed to investigate the anti-arthritic potential of α-M-γ-B as an independent small molecule in vitro and in vivo. α-M-γ-B exhibited stronger electrophilicity and anti-inflammatory effects than the other six analogs. α-M-γ-B inhibited the production of pro-inflammatory mediators via repolarizing M1 macrophages into M2 macrophages. α-M-γ-B attenuated collagen type II-induced arthritic (CIA) phenotype, restored Tregs-macrophages' balance and remodeled the synovial microenvironment via repolarizing the synovial-associated macrophages in CIA mice. Mechanistically, α-M-γ-B interfered with the DNA binding activity of NF-κB via direct interaction with the sulfhydryl in cysteine residue of NF-κB p65, which blocked the activation of NF-κB. α-M-γ-B failed to ameliorate CIA in the presence of N-acetylcysteine or when the mice were subjected to the macrophage-specific deficiency of Rela. These results suggest that α-M-γ-B has the potential to serve as an alternative candidate for treating RA.

Abstract no.155

Investigation on the influence of Hanshiyi formula on cytokine production in HUVECtert cells

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During the initial phase of the pandemic, the traditional Chinese medicine (TCM) formula Hanshiyi (HSYF) was developed for the treatment of COVID-19. HSYF consists of 20 ingredients. 16 are derived from plant material, and 4 from animal, mineral fungi, or are a mixture of fermented plant material. A clinical study involving over 700 participants found that none of those patients treated with HSYF experienced severe disease progression [1]. This project subsequently aimed to investigate the pharmacological effects of HSYF. A decoction made from the single herbs and fractions of different polarity were investigated using human umbilical vein endothelial cells (HUVECtert), which were activated by lipopolysaccharide (LPS), tumor necrosis factor (TNF), or interleukin-1β (IL-1β). The impact of HSYF and its fractions on the release of interleukin-8 was tested. The results from the ELISA suggested a mild dose-dependent immunostimulatory effect of the whole decoction. Subsequently a more detailed analysis was conducted using quantitative PCR (qPCR). On the one hand this analysis aimed to demonstrate whether HSYF exerts an immunomodulatory effect by upregulating the mRNA of Interferon α, Interferon β and MX-1. On the other hand the mRNA of OAS-1 was downregulated, and the mRNA-production of STAT1 and ISG15 was not influenced. In the tested concentration between 12.5-500 µg/ml no cytotoxicity was detected. In summary, HSYF has pharmacological effects on different molecules involved in cytokine production and regulation of the immune system. Especially MX-1 is known for antiviral activity against a wide range of different viruses like influenza, Viral Enzephalitis, Thogoto virus, HBV [2].

Abstract no.156

Andrographolide promotes lymphangiogenesis and lymphatic vessel remodeling to alleviate secondary lymphedema

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5. Mr Yunxi Han, Shanghai University of Traditional Chinese Medicine, Shanghai
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Lymphedema, a prevalent, multifaceted, and chronic ailment, is mainly managed through physical manipulation and suffers from a lack of specific pharmacological treatments. Secondary lymphedema is mainly caused by impaired lymphatic drainage. Therapeutic lymphangiogenesis is a promising strategy in the treatment of lymphedema. Andrographolide, a natural product from Andrographis paniculata, is unknown whether andrographolide promotes lymphangiogenesis to improve secondary lymphedema. By using the murine tail lymphedema model, we demonstrated that andrographolide can reduce the thickness of subcutaneous tissue in the mice's tail and enhance lymphatic drainage. Moreover, immunofluorescence staining showed that the number of capillary lymphatic vessels in the ANDRO25 group was significantly more than that in the ANDRO50 and Model groups. Near-infrared lymphography images showed that highlighted sciatic lymph nodes could be seen in the ANDRO25 and ANDRO50 groups. In vitro, andrographolide could promote the proliferation and migration of LEC. In conclusion, andrographolide enhanced the recovery of lymphatic vessels, and promoted lymphatic drainage in the murine tail lymphedema model by promoting the proliferation of lymphatic endothelial cells, thereby reducing the symptoms of lymphedema. This suggested andrographolide may be used as a potential therapeutic drug or medical food ingredient to help patients with secondary lymphedema.

Abstract no.157

Indigo Naturalis as Potential Drug in the Treatment of Ulcerative Colitis: A Comprehensive Review of Current Evidence

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2. Dr Zhen Ye, Chengdu University of Traditional Chinese Medicine, Chengdu

3. Prof Qiaobo Ye, Chengdu University of Traditional Chinese Medicine, Chengdu

Ulcerative colitis (UC) is an intractable inflammatory bowel disease that threatens the lives of patients. In light of the limited availability of therapeutic strategies, it is imperative to explore more efficient and safer drugs. Indigo naturalis (IN) is a traditional Chinese medicine that possesses many pharmacological activities, such as anti-inflammatory, antioxidant, and immunomodulatory. The treating potential of IN for UC has been proven by numerous preclinical and clinical studies in recent years. This paper aims to provide a comprehensive review of the utility and potential of IN in the treatment of UC. 'Indigo naturalis' 'Qing dai' 'Qingdai' 'Ulcerative colitis' 'UC' were used as the keywords, and the relevant literature was collected from online databases (Elsevier, PubMed, and Web of Science). We found that indirubin, indigo, isatin, tryptanthrin, and β-sitosterol are considered the key components in the treatment of UC with IN. Both preclinical and clinical studies support the efficacy of IN for UC, especially in severe UC or in those who do not respond to or have poor efficacy with existing therapies. The mechanisms of IN for UC are associated with the aryl hydrocarbon receptor pathway activation, immune regulation, oxidative stress inhibition, and the intestinal microbial modulation. However, the clinical use of IN has the risk of adverse events such as pulmonary hypertension, which suggests the necessity for its rational application. As a potential therapeutic agent for UC that is currently receiving more attention, the clinical value of IN has been initially demonstrated and warrants further evaluation (Figure 1).

Abstract no.158

Scutellarin suppresses growth of breast cancer stem cells in vitro and in vivo

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Introduction: Scutellarin is one of the active components in Scutellaria barbata D. Don (SB), also known as Ban Zhi Lian. It has shown promising anti-tumor effects. This study aimed to assess the impact of SB water extract (SBW) and scutellarin on breast cancer stem cells (BCSCs) and explore their potential as therapeutic agents for breast tumors in mice. Materials and Methods: BCSCs were isolated from human breast cancer cells (MDA-MB-231 and MDA-MB-361) and analyzed for their characteristics. The impact of varying concentrations of SBW and scutellarin on BCSCs' viability, proliferation, self-renewal, and migration abilities, along with the underlying mechanisms, were studied. The anti-tumor effects of scutellarin were evaluated in SCID/NOD mice. Inoculation and treatment protocols were performed with naïve BCSCs and pre-treated BCSCs. Results: The derived BCSCs expressed CD44, CD133, and ALDH1, confirming successful induction from MDA-MB-231 and MDA-MB-361 cells. Both SBW and scutellarin showed reductions in BCSCs' viability, proliferation, sphere and colony formation, and migration. In mice with tumors derived from naïve BCSCs, scutellarin significantly reduced tumor growth, expression of proliferative (Ki67) and stem cell markers (CD44), and lung metastasis. Pre-treatment with scutellarin also slowed tumor growth. Western blot results indicated involvement of the Wnt/β-catenin, NF-κB, and PTEN/Akt/mTOR signaling pathways in scutellarin's inhibitory effects. Conclusions: This study demonstrated for the first time that SB water extract and scutellarin can reduce the proliferation and migration of BCSCs in vitro. Scutellarin exhibited novel inhibitory activities in BCSCs progression. These findings suggest that Scutellaria barbata water extract, particularly scutellarin, may have potential as adjuvants for reducing breast cancer recurrence (Figure 1) (1). References: 1. Ma et al. Phytomedicine, 2024. 128:155418. Figure 1. Scutellarin inhibits the growth of BCSCs and its potential mechanisms.

Abstract no.159

Artesunate covalently binds glucosylceramidase to inhibit hepatocellular carcinoma proliferation and induce apoptosis

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3. Dr Xia Mao, China Academy of Chinese Medical Sciences, Beijing
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Background: Lack of highly effective and cost-efficient targeted drugs have severely limited the clinical outcome of patients with hepatocellular carcinoma (HCC). Our previous preclinical study determined artesunate as a candidate drug for HCC and identified glucosylceramidase as one of its direct targets. Herein, we aimed to identify the covalent binding sites of glucosylceramidase with artesunate and the potential anti-HCC mechanisms, which remain unclear. Methods: The anti-HCC potentials of artesunate were evaluated based on two HCC cell lines (HepG2 and MHCC-97H) using CCK8 assay and TUNEL/Hoechst apoptosis analysis. Then, the network regulatory mechanism and the binding characteristics of artesunate against glucosylceramidase were predicted, and experimentally verified on samples from orthotopic mouse model and HCC cell lines. After that, the relevant key amino-acid residues of glucosylceramidase with binding to artesunate were identified in a series of gain-of-function and loss-of-function experiments. Results: Artesunate effectively suppressed cell viability and proliferation, and enhanced apoptosis of HCC cell lines with more sensitivity in HepG2 than MHCC-97H. The apoptosis-related glucosylceramidase-ceramide-CTSD-BID-BAX signaling was one of the key putative target pathways by which artesunate may inhibit the malignant progression of HCC. In addition, we inferred that artesunate might directly bind to the amino acids of glucosylceramidase including Y313, E340 and N396. Notably, mutations at these three sites alone and in combination largely impaired the thermal stability and binding affinities of glucosylceramidase with artesunate, and especially, abolished modulatory effects of artesunate on the above apoptosis-related targets. Conclusion: Artesunate covalently binds to Y313, E340 and N396 on glucoceramidase, thereby regulating the glucosylceramidase-ceramide-CTSD-BID-BAX axis, promoting apoptosis of HCC cells and delaying the malignant progression of HCC. These findings pave a promising way to successfully develop covalent drug for targeting GBA proteins, open up new opportunities for anti-HCC drug discovery. Key words: Hepatocellular carcinoma, Artesunate, Glucosylceramidase, Covalent binding site, Apoptosis

Abstract no.160

Study on the Effect and Mechanism of β-lapachone targetted NQO1-mediated Ferroptosis in anti-Resistant Non-Small Cell Lung Cancer

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The continuous emergence of EGFR in situ mutations and the coexistence of various drug resistance mechanisms have become one of the key bottlenecks in the clinical treatment of non-small cell lung cancer (NSCLC). Due to the acquired and intrinsic resistance of tumor cells to apoptosis, many preclinical and clinical research drugs have limited effects on inducing apoptosis in tumors, often leading to tumor drug resistance due to apoptosis tolerance. By inducing and activating non-apoptotic cell death, apoptosis tolerance can be avoided, drug-resistant tumors can be killed, and a possible new strategy for anti-drug-resistant NSCLC can be provided. In recent years, research has found that ferroptosis is a type of programmed cell death that is catalyzed by unstable iron ions, mediated by excessive lipid oxidation, and different from apoptosis. Ferroptosis is closely related to the occurrence and development of tumors. Compared with normal cells, tumor cells will show higher iron demand for growth. This iron dependence can make tumor cells more sensitive to ferroptosis inducers. Therefore, ferroptosis is expected to become a new way to kill drug-resistant tumors. This study aims to kill apoptosis-tolerant drug-resistant NSCLC by studying LAP-activated NQO1-dependent ferroptosis and intends to further explore the internal mechanism of LAP's anti-tumor effect from the perspective of ferroptosis through molecular biology methods. The study will construct stable knockout, high-expression, and active site mutation cell lines through CRISPR/Cas9 and other technologies to reveal the molecular targets of LAP regulating ferroptosis and evaluate the efficacy of LAP-induced ferroptosis in killing drug-resistant NSCLC.

Abstract no.161

Small molecule a-methylene-g-butyrolactone， an evolutionarily conserved moiety in sesquiterpene lactones， ameliorates arthritic phenotype via interference DNA binding activity of NF-kB

1. Prof 祥春 沈, 贵州医科大学, 安顺

Rheumatoid arthritis (RA) is an inflammatory disease accompanied by abnormal synovial microenvironment (SM). Sesquiterpene lactones (SLs) are the main anti-inflammatory ingredients of many traditional herbs utilized in RA treatment. a-Methylene-g-butyrolactone (a-M-g-B) is a core moiety that widely exists in natural SLs. This study was designed to investigate the anti-arthritic potential of a-M-g-B as an independent small molecule in vitro and in vivo. a-M-g-B exhibited stronger electrophilicity and anti-inflammatory effects than the other six analogs. a-M-g-B inhibited the production of pro-inflammatory mediators via repolarizing M1 macrophages into M2 macrophages.The transcriptome sequencing suggested that a-M-g-B regulated the immune system pathway.Consistently, a-M-g-B attenuated collagen type II-induced arthritic (CIA) phenotype, restored the balance of Tregs-macrophages and remodeled SM via repolarizing the synovial-associated macrophages in CIA mice. Mechanistically, although a-M-g-B did not prevent the trans-nucleus of NF-kB it interfered with the DNA binding activity of NF-kB via direct interaction with the sulfhydryl in cysteine residue of NF-kB p65, which blocked the activation of NF-kB. Inhibition of NF-kB reduced the M1 polarization of macrophage and suppressed the synovial hyperplasia and angiogenesis. a-M-g-B failed to ameliorate CIA in the presence of N-acetylcysteine or when the mice were subjected to the macrophage-specific deficiency of Rela. In conclusion, a-M-g-B significantly attenuated the CIA phenotype by directly targeting NF-kB p65 and inhibiting its DNA binding ability. These results suggest that a-M-g-B has the potential to serve as an alternative candidate for treating RA. The greater electrophilicity of a-Mg-B, the basis for triggering strong anti-inflammatory activity, accounts for the reason why a-M-g-B is evolutionarily conserved in the SLs by medical plants.

Abstract no.162

Verification of the anti-tumor activities of Scutellaria barbata and its bioactive marker scutellarin in colon and breast cancer preclinical models

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Scutellaria barbata D. Don (SB, also known as Banzhilian), is commonly prescribed by Chinese medicine practitioners to cancer patients. The anti-tumor activities of extracts and natural products isolated from this herb have been demonstrated in liver, breast and colorectal cancer preclinical studies [1]. Our recent study aimed to verify the efficacy of SB aqueous extract (SBW) and SB chemical marker listed in Chinese Pharmacopoeia (CP), scutellarin, in colon and breast cancer preclinical models. In colon cancer study, SBW or scutellarin were orally administered to nude mice bearing human colon HCT116 xenografts for 4 weeks. In breast cancer study, the inhibitory activities of SBW and scutellarin were evaluated in breast cancer stem cells (BCSCs), which were enriched from human breast cancer cells (MDA-MB-231 and MDA-MB-361). Besides, the anti-tumor effects of scutellarin were further evaluated in SCID/NOD mice bearing tumors generated from BCSCs. Results showed that 4-weeks treatment with CP recommended dosages of SBW (1230 mg/kg) and scutellarin (7 mg/kg) could reduce the tumor weights and tumor metastasis to lungs [2]. SBW treatments also induced significant changes in expressions of colon cancer metastasis-related proteins in tumors, such as E-cadherin, CXCR4, and Src kinase [2]. Besides, both SBW and scutellarin reduced the viability, proliferation, sphere and colony formation, and migration of BCSCs [3]. In mice with tumors derived from naïve BCSCs, scutellarin (100 mg/kg) significantly reduced tumor growth, expression of stem cell marker CD44, and lung metastasis. Western blot results of tumors suggested the involvement of Wnt/β-catenin and PTEN/Akt signaling pathways. In conclusion, both SBW and scutellarin could exert similar anti-tumor and anti-metastatic effects in colon tumor-bearing mice, while scutellarin could suppress the growth of BCSCs in vitro and in vivo. Hence, scutellarin could be regarded as a bioactive marker for quality control of Scutellaria barbata, as well as being developed as an active agent for colon and breast cancer treatment. References: [1] Wang L, et al. Journal of Ethnopharmacology. 2020, 254:112260; [2] Yue GGL, et al. Phytotherapy Research, 2021, 35(1): 361-373. [3] Ma H, et al. Phytomedicine, 2024, 128:155418.

Abstract no.163

Exploring Anti-osteoporosis Mechanisms of Bletilla striata (Thunb.) Reichb.f. using an Isothermal Thermal Proteome Profiling Strategy

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Elevated bone resorption resulting from osteoclast overactivation is a primary factor contributing to osteoporosis progression. Antiresorptive agents derived from Chinese medicine targeting osteoclast formation and function are effective strategies for managing osteoporosis. Although Bletilla striata (Thunb.) Reichb.f. is well known for its wide range of pharmacological effects such as hemostasis and anti-inflammation, its therapeutic effects on osteoporosis and underlying mechanisms remain unrevealed. In our study, we found oral administration of Bletilla striata ethanol extract (BSE, 100 and 200 mg/kg) significantly inhibited bone loss in ovariectomized (OVX)-induced osteoporosis rats, as evidenced by micro-CT and histopathology analysis. Additionally, BSE attenuated glucocorticoid-induced bone loss in osteoporotic zebrafish. Further evidence suggested that BSE (10 and 20 μg/mL) inhibited RANKL-induced the differentiation of osteoclast precursors (BMMs) to mature multinucleated osteoclasts, decreased the expression of osteoclast-specific genes and proteins, and inhibited F-actin ring formation and bone resorption. These results suggested that the anti-osteoporosis effect of BSE strongly attributed to the regulation on osteoclast activity. Furthermore, a combined strategy of isothermal thermal proteome profiling (TPP) and quantitative proteomics was applied to investigate the mechanisms of BSE against osteoclastogenesis. After a short thermal challenge (52 °C for 4 min), BSE was found to increase the thermal stability of 84 proteins while decreasing thermal stability of 139 proteins (FC > 1.5), suggesting that these proteins were the direct targets of BSE. Subsequently, TMT quantitative proteomics was employed to reveal the proteomic alterations pre- and post-BSE treatment of osteoclasts, and the differentially expressed proteins were defined as indirect protein perturbations resulting from the interaction of BSE with direct targets. The key active components bound to individual direct target were determined using molecular docking between target structure and a BSE component library. Ultimately, a “BSE-components-direct targets-indirect targets-pathways-osteoporosis” interaction network was constructed to elucidate the material basis and potential mechanisms of BSE. Collectively, these findings offer compelling support for the potential therapeutic application of BSE for managing osteoporosis. Keywords: Osteoporosis, osteoclast formation, Bletilla striata, isothermal thermal proteome profiling Acknowledgments: This work was supported by the National Natural Science Foundation of China (Grant No. 82204724). Graphical abstract

Abstract no.164

Mechanistic study of SIRT5-mediated lysine succinylation in reversing metabolic reprogramming of rheumatoid arthritis treatment

1. Mr YUANQING QU, Macau University of Science and Technology, Macao SAR

Rheumatoid arthritis (RA) is an autoimmune disease characterized by a complex etiology, with its pathological mechanisms remaining largely obscure. Our previous studies demonstrated that silencing SIRT5 would regulate protein succinylation in RA patients. In the present study, we used liquid chromatography-tandem mass spectrometry (LC-MS/MS) to quantitatively assess succinylated proteins in the synovial tissues of Sprague-Dawley (SD) rats with adjuvant-induced arthritis (AIA). Enrichment analyses were conducted using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) to elucidate the role of protein succinylation in RA and to identify potential SIRT5-mediated succinylated protein targets. Our findings revealed the identification of 1046 proteins and 4155 lysine succinylation sites in the plasmapheresis results, with 487 differentially expressed proteins and 4126 differentially expressed succinylation sites being identified. Comparative analysis of AIA synovial samples from wild-type (WT) and SIRT5 knockout (SIRT5 KO) rats indicated that 530 succinylation sites across 232 proteins were upregulated, whereas 44 succinylation sites across 41 proteins were downregulated. Bioinformatics analyses indicated significant enrichment of succinylated proteins in the tricarboxylic acid (TCA) cycle and fatty acid metabolism pathways. These results suggest that SIRT5 is implicated in various biological processes within synovial tissues and succinylation resulting from SIRT5 silencing plays a crucial role in RA progression. This study enhances the understanding of RA pathogenesis and aids in the identification of potential biomarkers for the disease. Acknowledgments：This research is supported by FDCT grants from the Macao Science and Technology Development Fund (Project code: 002/2023/ALC)

Abstract no.165

Trametinib boosts palbociclib’s efficacy in breast cancer via autophagy inhibition

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2. Mrs Yiru Pan, Southwest Medical University Luzhou
3. Mr Chi Feng, Southwest Medical University, Luzhou

Breast cancer, a predominant global health issue, requires ongoing exploration of new therapeutic strategies. Palbociclib (PAL), a well-known cyclin-dependent kinase (CDK) inhibitor, plays a critical role in breast cancer treatment. While its efficacy is recognized, the interplay between PAL and cellular autophagy, particularly in the context of the RAF/MEK/ERK signaling pathway, remains insufficiently explored. This study investigates PAL’s inhibitory effects on breast cancer using both in vitro (MCF7 and MDA-MB-468 cells) and in vivo (tumor-bearing nude mice) models. Aimed at elucidating the impact of PAL on autophagic processes and exploring the potential of combining it with trametinib (TRA), an MEK inhibitor, our research seeks to address the challenge of PAL-induced drug resistance. Our findings reveal that PAL significantly decreases the viability of MCF7 and MDA-MB-468 cells and reduces tumor size in mice while showing minimal cytotoxicity in MCF10A cells. However, PAL also induces protective autophagy, potentially leading to drug resistance via the RAF/MEK/ERK pathway activation. Introducing TRA effectively neutralized this autophagy, enhancing PAL's anti-tumor efficacy. A combination of PAL and TRA synergistically reduced cell viability and proliferation, and in vivo studies showed notable tumor size reduction. In conclusion, the PAL and TRA combination emerges as a promising strategy for overcoming PAL-induced resistance, offering a new horizon in breast cancer treatment. ◦

Abstract no.166

Study on the Effect and Mechanism of β-lapachone targetted NQO1-mediated Ferroptosis in anti-Resistant Non-Small Cell Lung Cancer

1. Ms Wenxia Tang, Wuhan Polytechnic University, Wuhan

The drug-resistance and high recurrence are the major failure reasons in treating non-small cell lung cancer (NSCLC). Ferroptosis is a recently identified regulated form of cell death with distinct molecular pathways from those of apoptosis. It is considered as a novel strategy in cancer therapy, especially in drug-resistant cancer therapy.

β-lapachone (LAP) has been described as a NQO1- bioactivatable compound. It is currently undergoing clinical evaluation for treatment of solid tumors. However, the mechanism is still unclear. Our research preliminarily found that β-lapachone could increase the labile iron level and lipid peroxidation. Furthermore, the iron chelator DFO could significantly reverse the cell death. These results indicated that LAP may induce ferroptosis in drug-resistant NSCLC cells by activating NQO1. In this proposal, we aim to investigate the mechanisms of LAP induce ferroptosis to inhibit drug-resistant NSCLC, further clarify the target of ferroptosis triggered by LAP. In addition, we will determine the anti-cancer activity of LAP in drug-resistant NSCLC xenograft mouse model and investigate whether ferroptosis is the anticancer mechanism. Our study will elucidate whether activation of ferroptosis is the anticancer mechanism of LAP. Successful completion of this study will promote the translational research of NQO1-bioactivable compound as a ferroptosis inducer, as well as provide a new direction for fighting drug resistance.

Abstract no.167

Research Progress on Anti-tumor Mechanism of Curcumin

1. Ms 红婷 管，成都中医药大学，成都

Curcumin is a kind of diketones obtained from the roots of some plants of the family Curcumin and Araceae. Current scientific research has confirmed that curcumin can induce apoptosis, control growth, inhibit transformation and invasion, control the formation of blood vessels, regulate gene expression, sensitize chemical drugs, reverse drug resistance and other functions of tumor cells by various mechanisms and methods. Therefore, it can be used for the diagnosis of endometrial cancer, liver cancer, colon cancer, stomach cancer, esophageal cancer and other cancer lesions. In this paper, the main mechanism of action of curcumin against tumor and related clinical trials were summarized in order to provide the basis for relevant scientific research.

Abstract no.168

Shuang Bailian Mixture inhibits the proliferation and induces apoptosis of esophageal cancer by regulating the PI3K/Akt/Bcl-2 pathway

1. Dr Guoxin Huang, Shantou Central Hospital, Shantou

Aim of the study: The primary objective of this investigation is to delve into whether Shuang Bailian Mixture (SBLM) possesses the capacity to inhibit the proliferation of esophageal cancer (EC) cells and simultaneously promote their apoptosis via the regulation of PI3K/Akt/Bcl-2 pathway. Materials and methods: The key constituents of SBLM were analyzed and identified utilizing ultra-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS). Leveraging the Traditional Chinese Medicine Integrative Pharmacology (TCMIP) v2.0 research platform, we predicted potential targets of SBLM and EC. In vitro cellular experiments, the effects of SBLM or its combination with cis-platinum (CP) on the proliferative potential of KYSE30 and KYSE140 cells were confirmed through the CCK-8 assay, cell clone formation assessment, flow cytometry with Annexin V-7-AAD and PI apoptosis detection kits, as well as the mitochondrial membrane potential (MMP) assay employing JC-1. Cell invasion and migration were evaluated using the wound healing assay. Subsequently, the expression of proteins related to the PI3K/Akt/Bcl-2 signaling pathway was analyzed via western blot (WB). Furthermore, the tumor growth inhibitory effects of SBLM in tumor-bearing nude mice were continuously tracked by measuring tumor volume. Results: The administration of SBLM or its combined CP treatment significantly inhibited the proliferation of EC cells, inducing marked apoptosis compared to the negative control (NC) group. The findings revealed that the optimal concentrations of SBLM for EC cell lines were IC50KYSE30=7.76 μg/ml and IC50KYSE140=36.52 μg/ml. Network pharmacology analyses predicted that the PI3K/Akt/Bcl-2 pathway might serve as the primary regulatory target of SBLM's antitumor efficacy. The intervention group significantly hindered cell proliferation, induced cell cycle arrest and apoptosis, suppressed colony formation and invasion, reduced MMP, and attenuated PI3K/Akt/Bcl-2 signaling in EC cells. Our study demonstrated that SBLM effectively retarded tumor growth in EC-bearing nude mice and attenuated PI3K/Akt/Bcl-2 signaling in these animals. WB analysis initially validated that SBLM significantly upregulated the expression of pro-apoptotic proteins, including Bad, cleaved caspase-3, and cleaved PARP, while downregulating the expression of the anti-apoptotic protein Bcl-2, as well as the phosphorylated forms of PI3K and Akt. Conclusions: SBLM exerts its antitumor effects by inhibiting the proliferation and inducing apoptosis of EC cells through inhibiting the PI3K/Akt/Bcl-2 signaling pathway.

Abstract no.169

Tripterygium Glycosides Tablet suppresses T Follicular Helper cell differentiation to ameliorate ACPA+ rheumatoid arthritis animal by modulating the glycolytic pathway

1. Dr Liting Xu, China Academy of Chinese Medical Sciences, Beijing

The study investigates the effects of Tripterygium Glycosides Tablet (TGT) on rheumatoid arthritis (RA) in an animal model induced by Porphyromonas gingivalis infected CIA mice. TGT significantly reduced the incidence, pathological damage, and bone destruction in the RA model. Additionally, TGT effectively inhibited the production of anti-citrullinated protein antibodies (ACPA), which is a key marker in RA. Antibody responses can be either T cell-dependent or independent, and T follicular helper (Tfh) cells, a subset of CD4+ T cells, are crucial in regulating these responses and maintaining self-tolerance. Excessive Tfh cells are associated with autoimmune disorders. The study further demonstrated that TGT reduced the proportion of Tfh and germinal center B (GCB) cells in the spleen of Pg+CIA-induced mice. This suggests that TGT can inhibit the function of RA-Tfh and GCB cells, indicating that Tfh-GCB cells may be targets for TGT in treating RA. Dysregulation of T cell glucose metabolism is widely reported in autoimmune diseases, and the study showed that Pg+CIA-induced mice had increased glycolytic activity in spleen CD4+ T cells, with no significant change in the pentose phosphate pathway. Oral administration of TGT corrected this glycolytic dysregulation. In summary, TGT may suppress Tfh-GCB cell differentiation by modulating the glycolytic pathway, thereby affecting the production of autoantibodies like ACPA.

Abstract no.170

The analgesic effect and mechanism action of Phaseoloidin on SNL mice

1. Ms Hanxue Wu, Fujian University of Traditional Chinese Medicine, Fuzhou

Neuropathic pain remains a significant clinical challenge. Currently, there is no good treatment strategies or drugs to treat neuropathic pain, so the treatment effects are relatively stubborn. In particular, some drugs cannot cross the blood-brain barrier(BBB), which affects the treatment of neuropathic pain with these drugs. Experimental studies have found that phaseoloidin, which is the main component of Entada phaseoloides (Linn.) Merr., has good penetrating power and can pass through the blood-brain barrier(BBB). Experiments have proved that phaseoloidin have a good analgesic and relieving effect on mechanical pain sensitivity and thermal radiation pain sensitivity threshold. Further experiments have shown that by using network pharmacology and bioinformatics analysis to identify key targets related to neuropathic pain, it was found that targets such as PPARG and EGFR play a crucial role in neuropathic pain, which provide a potential solution for the treatment of neuropathic pain.

Abstract no.171

Network pharmacology， molecular docking， and experimental evaluation of Qing-Yi Decoction in treating acute pancreatitis

1. Prof Yunfeng Cui, Tianjin Nankai Hospital, Tianjin

Background and Purpose: Macrophage infiltration and activation is a critical step during acute pancreatitis (AP). NLRP3 inflammasomes in macrophages plays a critical role in mediating pancreatic inflammatory responses. Qing-Yi Decoction（QYD）has been used for many years in clinical practice of Nankai Hospital combined with traditional Chinese and western medicine treatment of acute pancreatitis. Although QYD has a well-established clinical efficacy, little is known about its bioactive ingredients, how they interact with different therapeutic targets and the pathways to produce anti-inflammatory effects. Here, we elucidate the therapeutic effects of QYD against acute pancreatitis and reveal its mechanism of action. Methods: The main components of QYD were identified using UHPLC-Q-TOF-MS. Network pharmacology was employed to predict potential therapeutic targets and their mechanisms of action. Along with molecular docking of key bioactive compounds and targets, the signaling pathways and proteins associated with the therapeutic effects of QYT on AP were identified. C57BL/6 mice were randomly divided into control group, model group, low, medium and high dose (6, 12, 24g/kg) QYD groups, with 10 mice in each group. The therapeutic effect of QYD on cerulein-induced acute pancreatitis (CER-AP) was evaluated by histopathological score, immunohistochemistry, serum amylase, lipase and cytokines detection by ELISA. The protein expressions of HIF-1 signaling pathway, MyD88/NF-κB and NLRP3 signaling pathway were detected by Western blotting. BMDMs (bone marrow-derived macrophages) were stimulated with 1μg/mL LPS combined with 5 mmol/L adenosine triphosphate (ATP) to activate NLRP3. Inhibitory effects of the main chemical composition Wogonoside on NLRP3 inflammasomes were analysed by ELISA, Western blots and qRT-PCR. Results: Using UPLC-Q-TOF-MS, 147 compounds were identified from QYD, including Wogonoside, catechins, rhein, etc. A visualization network of QYD-compounds-key targets-pathways-AP show that QYD may modulate HIF-1 signaling pathway, VEGF signaling pathway, TNF signaling pathway and the NOD like receptor signaling pathway by targeting TNF、IL1β、AKT1 and STAT3, exerting a therapeutic effect on AP. QYD administration effectively mitigated CER-induced cytokine storm, pancreas edema and serum amylase, lipase. QYD12 mg/kg showed better effect. The protein expression levels of MyD88, NF-κB, NLRP3, ASC, Caspase-1 and GSDMD in pancreatic tissue were significantly decreased ($P<0.05$). The secretion of IL-1β, IL-6 and TNF-α in BMDMs in the Wogonoside group was significantly decreased ($P<0.01$), and the expression levels of NLRP3/Caspase-1/GSDMD pathway-related proteins were significantly decreased ($P<0.05$). NLRP3 inflammatory corpuscle assembly significantly inhibited ($P < 0.05$). Conclusion: The results of network pharmacology indicate that QYD can inhibit AP through multiple pathways and targets. This finding was validated through in vivo tests, which demonstrated that QYD can reduce AP by inhibiting NLRP3 inflammasomes via multiple signaling pathways, additionally, it should be noted that 12mg/kg was a relatively superior dose. One of the main chemical compositions Wogonoside regulated NLRP3 inflammasome activation to protect against AP. This study is the first to verify the intrinsic molecular mechanism of QYD in treating

AP by combining pharmacokinetics, network pharmacology, and animal experiments. The findings can provide evidence for subsequent clinical research and drug development.

Abstract no.172

THE INFLUENCE OF STEAMING PROCESS ON POLYSACCHARIDES AND THEIR ANTI-COLITIS ACTIVITY IN POLYGONATUM CYRTONEMA

1. Prof huijun wang, Shanghai University of Traditional Chinese Medicine, Shanghai

Polygonatum cyrtonema, commonly known as Huangjing, is a frequently used medicinal herb. It typically requires steaming and drying to enhance its therapeutic effects. Polysaccharides are an important active component in Huangjing and play a significant role in treating various diseases, such as antioxidant, anti-tumor, hypoglycaemic, and anti-colitis. However, there has been little research and reporting on how steaming affects the content, structure, and biological activity of the polysaccharides in Huangjing. To reveal the impact of the steaming process on polysaccharides, the concentration ratio of the aqueous extract was first examined. It was found that the higher the concentration ratio, the more significant the degradation of the polysaccharide yield. Subsequently, the concentration of ethanol for degreasing and the temperature for aqueous extraction were examined. It was found that 95% ethanol should be used for degreasing, and the concentration temperature should not be too high. Additionally, we tested the pH value of the aqueous extract and found that the pH decreases during the processing. Furthermore, anti-inflammatory effects were observed in mice with colitis, indicating that the steamed extract exhibited better anti-colitis activity. In summary, the differences in anti-inflammatory activity may be related to the changes in polysaccharide content and structure caused by steaming. These findings lay the foundation for exploring the processing mechanism of Huangjing.

Abstract no.173

Panax Notoginseng Saponins Ameliorate LPS-induced Acute Lung Injury by Promoting STAT6-mediated M2-like polarization in Macrophage

1. Mr Xunjiang wang, Shanghai University of Traditional Chinese Medicine, Shanghai

Background: Acute lung injury (ALI) is characterized by an exaggerated inflammatory response, which significantly raises mortality rates. At present, the availability of efficacious clinical interventions for ALI remains inadequate. Panax notoginseng saponins (PNS), the biologically active constituents derived from the herb Panax notoginseng, have demonstrated a plethora of favorable pharmacological properties. However, a comprehensive understanding of the potential therapeutic effects and the underlying molecular mechanisms of PNS in mitigating ALI necessitates further intensive investigation. Purpose: To investigate the therapeutic potential of PNS in the context of ALI, with a particular focus on elucidating whether this efficacy is associated with the modulation of M2 macrophage polarization, mediated through the upregulation of signal transducer and activator of transcription 6 (STAT6). Methods: The therapeutic efficacy of PNS was evaluated in an ALI mouse model induced by intratracheal instillation of lipopolysaccharides (LPS). This assessment encompassed metrics such as included lung field shadowing, oxygen saturation levels, pulmonary function assessment, and detailed lung pathology examination. Additionally, PNS underwent chemical profiling, and its key components were assessed in vivo in LPS-induced ALI mice for indicators of lung edema, histopathological analysis using hematoxylin and eosin staining, and quantification of pro-inflammatory factors in bronchoalveolar lavage fluid (BALF) and serum. To gain insights into the underlying molecular mechanisms, network pharmacology analysis was employed to predict the signaling pathways targeted by PNS in ALI treatment. Furthermore, flow cytometry analysis was conducted in THP-1 and bone marrow-derived macrophages (BMDM) cells to explore the regulatory impact of PNS on inflammation processes. The expression of STAT6 was meticulously investigated using quantitative real-time PCR (qRT-PCR) and western blotting techniques. To validate the role of STAT6 in mediating the protective effects of PNS against ALI, experiments were conducted using both Stat6 knockdown THP-1 cells and Stat6 knockout mice. These studies aimed to elucidate whether the therapeutic benefits of PNS in ALI are mediated through STAT6-dependent macrophage polarization signaling. Results: The PNS was primarily constituted of Notoginsenoside R1, Ginsenoside Rg1, Ginsenoside Re, and Ginsenoside Rb1, as determined by high performance liquid chromatography (HPLC). Treatment with PNS dose-dependently mitigated the LPS-induced inflammatory response in ALI mice models by down-regulating inflammatory cytokines. Further analysis revealed that the four primary constituents of PNS individually contributed to the improvement of ALI in mice, and a total of 56 potential ALI-related targets were identified. Enrichment analysis of Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways predicted that PNS exerts its protective effects against ALI by inhibiting inflammatory response signaling pathways. Both in vivo and in vitro experimental studies robustly demonstrated that PNS significantly promoted the polarization of M2 macrophages and markedly upregulated the expression of STAT6 gene and protein. Notably, this upregulation was mitigated by genetic knockdown of Stat6. Additionally, genetic knockout of Stat6 partially reversed the protective effects of PNS on ALI

and macrophage polarization, highlighting the crucial role of STAT6 in mediating the beneficial effects of PNS. Conclusion: This study demonstrated that PNS significantly alleviated LPS-induced ALI in mice and facilitated the polarization of M2 macrophages mediated by STAT6. Consequently, our findings offer compelling experimental evidence supporting the potential of PNS as a promising therapeutic candidate for the protection against ALI.

Abstract no.174

Tulipalin A suppressed the pro-inflammatory polarization of M1 macrophage and mitigated the acute lung injury in mice via interference DNA binding activity of NF-κB

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2. Dr 克刚 令狐，贵州医科大学，贵阳

3. Ms 悦婷 度，贵州医科大学，贵阳

Abstract The acute lung injury (ALI) is an inflammatory disorder accompanied with higher morbidity and mortality. The pathological mechanism of ALI has been reported to be associated with the release of inflammatory cytokines by macrophages. Sesquiterpene lactones (SLs) represent the principle anti-inflammatory components of many natural products. Tulipalin A is a natural small molecule and a conserved moiety in anti-inflammatory SLs. However, anti-inflammatory potential of Tulipalin A has not been fully disclosed. The present study aims to investigate Tulipalin A ‘s anti-inflammatory activity and underlying mechanisms in vitro and in vivo. Tulipalin A suppressed inflammatory responses in macrophages and ameliorated lipopolysaccharide (LPS)-induced ALI in mice. Mechanistically, Tulipalin A directly targets the NF-κB p65 and disrupts its DNA binding activity, thereby impeding the activation of NF-κB. Inhibition of NF-κB attenuated M1 polarization of macrophages, consequently suppressing the production of pro-inflammatory mediators and ameliorating the onset and progression of ALI. These findings suggest the potential of Tulipalin A on mitigating inflammatory disorders like ALI via targeting NF-κB p65 and disrupting its DNA binding activity. Keywords: Tulipalin A, acute lung injury, M1 polarization, macrophage, DNA binding activity, NF-κB Acknowledgment Financial support by the National Natural science foundation of china (82260801), china Postdoctoral Science Foundation(2023M730815),Excellent Young Talents Plan of Guizhou Medical University (20231 10), the Guizhou Provincial scientific and Technologic innovationBase (120231003, the High-Level linnovation Talents (No. GCC[20231048) and Youth science and Technology Talent Growth Proiect ofGuizhou Medical University (220NRC08) are aratefully acknowledaed

8. Herbal Resources (Authentication ,Cultivation, Quality Control, Manufacture, Regional Development & Endangered species)

Abstract no.175

When DNA Barcoding Fails: Analysis of Whole-Genome Addressed the Challenge in Fungal Species

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Species identification is a cornerstone of fungal research; however, traditional molecular methods face difficulties in achieving rapid and precise onsite identification, especially for closely related species. To tackle this challenge, we introduce a universal identification method called Analysis of whole-GEnome (AGE). AGE includes two key steps: bioinformatics analysis and experimental practice. Comparative genomic analysis screens species-specific target sequences, and sequencing or nonsequencing technologies confirm the results. First, AGE obtained more than 1,000,000 qualified targets for each of 13 fungal species within the phyla Ascomycota and Basidiomycota, and the sequencing and genome editing system validated the ultra-specific performance of the specific targets; especially noteworthy is the first-time demonstration of the identification potential of sequences from unannotated genomic regions. Then, AGE was applied to address the challenges posed by closely related species within the genus Aspergillus. Specific targets for each of 77 Aspergillus species were identified through bioinformatic analysis of reliable whole genome data for these species. Subsequently, the on-site detection method was developed and the results indicate that AGE has successfully achieved reliable identification of all IA-related species (Aspergillus fumigatus, A. niger, A. nidulans, A. flavus, and A. terreus) and three well-known species (A. flavus, A. parasiticus, and A. oryzae) within the Aspergillus section. In summary, AGE opens the door for the development of whole-genome-based fungal species identification and also shows promising potential as an effective tool for epidemiological research and species classification.

Abstract no.176

TaqMan Probe-Based Quantitative Real-Time PCR to Detect Panax notoginseng in Traditional Chinese Patent Medicines

1. Ms Qian Lou, Institute of Medicinal Plant Development, Beijing

Background: There has been global concern about the safety and accuracy of traditional Chinese patent medicines (TCPMs). Panax notoginseng, also known as sanqi, is an important constituent of TCPMs. However, identifying the species contained in TCPMs is challenging due to the presence of multiple ingredients and the use of various preparation processes. Objective: To detect P. notoginseng in TCPMs. Methods: A TaqMan probe-based qPCR assay was constructed and validated with DNA extracted from P. notoginseng and adulterants. In total, 75 samples derived from 25 batches of TCPMs were tested using the constructed qPCR method. Results: A TaqMan probe-based qPCR assay targeting P. notoginseng was established. The constructed qPCR assay could specifically discriminate P. notoginseng from Panax ginseng, Panax quinquefolium and Curcuma aromatica Salisb. cv. Wenyujin. The sensitivity study showed that the detectable DNA template concentration of P. notoginseng for this qPCR assay was 0.001 ng/μl. All 75 samples from TCPMs were confirmed to contain P. notoginseng by the qPCR assay. Conclusions: The qPCR method can accurately identify P. notoginseng in TCPMs and is promising as a powerful tool for quality control and market regulation.

Abstract no.177

Ethnopharmacology of five flowers herbal tea， a popular traditional beverage in Hong Kong and South China

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2. Mr Kwun Tin CHAN, The Chinese University of Hong Kong, Hong Kong SAR

Background It has been a long-standing tradition of using herbal tea for preventive and therapeutic healthcare in Hong Kong and South China and Five Flowers Tea is one of the most popular herbal teas. Based on the principle of traditional Chinese medicine, the pharmacological functions are to clear heat and dispel dampness in the body. Heat and dampness are thought to contribute to a range of health problems, especially during the hot and humid season in South China and Hong Kong. The most prevalent herbs in the formula contain bioactive compounds including flavonoids, alkaloids and terpenoids, which have a wide range of pharmacological properties including anti-inflammation, antivirus, antidiarrhoea, antibacteria, and antioxidation. However, with the composition varies widely, the ethnopharmacological benefits described may not be delivered uniformly. This study is to provide a comprehensive analysis on the composition of the Five Flowers Tea sold in Hong Kong and investigate the rationale behind the selection of herbs used in the formula. This study also provides information on the variation and quality of the Five Flowers Tea in the market. Methods Thirty-three Five Flowers Tea samples were collected from various locations in Hong Kong. The size, texture, colour and organoleptic properties were documented. Macroscopic and molecular authentication methods were employed to identify the individual components. Results Macroscopic identification revealed there were 23 herbs belonging to 18 plant families. The most prevalent herb was Bombax ceiba L., followed by Chrysanthemum morifolium. Ten adulterants and the existence of insect Lasioderma serricorne were confirmed by DNA barcoding techniques. Conclusion This study employed a comprehensive approach to authenticate the herbs in Five Flowers Tea samples collected from various locations in Hong Kong. Macroscopic and molecular methods were used to identify the herbs and adulterants. The findings revealed the varied composition in Five Flowers Tea and the occurrence of adulterants in some samples. This shows that quality assurance of Five Flowers Tea is essential for the effective use of this popular folk medicine.

Abstract no.178

New Strategies for Research on Traditional Chinese Medicine Standards

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The quality evaluation standards of traditional Chinese medicine (TCM) are crucial for ensuring the safety and efficacy of its clinical applications. Current standards provide effective quality control methods for most of TCMs. However, many commonly used herbals still have issues such as the marker components are of low content, weak specificity, and lack of correlation with bioactivity. It is urgent to establish practical, scientific, and advanced quality evaluation methods for these herbal drugs. Some commonly used medicinal materials such as Sophorae Flavescentis Radix, Achyranthis Bidentatae Radix, Phellodendri Chinensis Cortex have plenty of research on their components and pharmacology published, and their quality standard methods seemed relatively mature. However, in this study, existing quality standards of these drugs were re-evaluated and a comparative research strategy with closely related species was adopted, some interesting and valuable constituents were discovered. For example, Sophorae Flavescentis Radix and Sophorae Tonkinensis Radix et Rhizoma, both belonging to Sophora genus, contain lots of same constituents making them easily misidentified with each other. Multi-dimensional comparative research results showed that in addition to the well-known alkaloid components, a large number of differential flavonoid components with identification value were discovered existing in two species. The structures of the target compounds were identified by MS/MS2 fragmentations vis TLC/LC-ESI-MS techniques, typical compounds were guided-isolated and structurally elucidated to validate the TLC/LC-MS results (Fig.1). Lastly the appropriate components were chosen as quality-markers based on their content, specificity, measurability, and bioactivity based on literature research findings, and corresponding qualitative or quantitative methods were established for enhancing their quality standards.

Abstract no.179

A novel and sensitive dual signaling ratiometric electrochemical aptasensor based on nanoporous gold for determination of Ochratoxin A

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2. Ms Yue Wang, Macau University of Science and Technology, Macao SAR

Abstract Ochratoxin A (OTA) is a toxic pollutant in foods, and its actual detection is crucial. A novel and sensitive dual signaling ratiometric electrochemical aptasensor based on nanoporous gold (NPG) was proposed to determine OTA. NPG, with high specific surface area and conductivity, improved the sensitivity by immobilizing more aptamers. Meanwhile, the dual signaling ratiometric strategy improved the detection reproducibility through self-referencing and built-in correction. NPG and ratiometric strategy multi-amplified the dual signal changes. The sensitivity of OTA was evaluated by the ratio of methylene to ferrocene current values. Under the optimal conditions, the NPG-based aptasensor demonstrated excellent sensitivity with a wide linear range of 1 pg/mL to 2 ng/mL and the limit of detection (LOD) of 0.4 pg/mL for OTA. This developed aptasensor also effectively detected OTA in spiked Cordyceps sinensis and grape juice samples, with recovery values falling in the 98.49-108.0% range. Acknowledgement This work was supported by the Science and Technology Development Fund, Macau SAR (File Nos. 0040/2021/AGJ).

Abstract no.180

Understory Cultivation Enhances the Quality Improvement of F. hupehensis (湖北贝母) and Explores its Medicinally Advantageous Ingredients

1. Dr xiaoyue wang, Hubei Academy of Agricultural Sciences, Enshi

Fritillaria hupehensis Hsiao et K.C. Hsia (F. hupehensis) is a traditional medicinal plant native to the Hubei province of China, widely utilized for its antitussive properties. Its therapeutic applications are well-documented in the Pharmacopoeia of the People's Republic of China, 2020 edition. However, the decreasing wild populations of F.hupehensis, species degradation, and the enforcement of arable land protection policies have significantly threatened its cultivation environment. To mitigate these challenges and enhance the quality of F. hupehensis, an innovative ecological planting method has been developed, which involves cultivating F. hupehensis under Magnolia officinalis forest to mimic its natural growth conditions. This approach not only improves the quality of the herb but also reduces the need for pesticides and minimizes weeding frequency. Our preliminary studies demonstrated that F. hupehensis grown in the understory of Magnolia officinalis (U-F. hupehensis) exhibits a notable increase in alkaloid content compared to traditionally field-grown F. hupehensis (T-F.hupehensis). It suggest a significant enhancement in both yield and quality of U-F. hupehensis relative to T-F. hupehensis. Given that alkaloids are the primary active constituents of F.hupehensis, it raises crucial questions about the potential changes in the efficacy of U-F. hupehensis. What are the active ingredients driving these key changes? To address this, our study employs a network pharmacology approach. We investigated the predominant components of U-F.hupehensis, utilizing three animal models: ammonia-induced cough, phenol red secretion, and LPS-induced bronchitis. This research aims to comparatively evaluate the differences in efficacy between F. hupehensis cultivated under different conditions, elucidating the impact of forest ecological cultivation on the quality of F.hupehensis and revealing its therapeutic mechanisms in treating bronchitis diseases.

Abstract no.181

Study on the relationship between stem colors of Astragalus membranaceus and the content of active ingredients

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ABSTRACT: OBJECTIVE The relationship of isoflavones, saponins and total polysaccharides in root and stem of Astragalus membranaceus was studied METHODS The extraction process of Astragalus polysaccharide by internal boiling under reduced pressure was optimized, and the total polysaccharide content was determined by Ultraviolet-visible spectrophotometry, isoflavone content was determined by UPLC-DAD method, and saponin content was determined by HPLC-ELSD method. RESULTS The optimal extraction process of Astragalus polysaccharides was as follows: the concentration of desorption agent was 75%, the desorption time was 40 min, the solid-liquid ratio was 1:12, the extraction time was 45 min, the solid-liquid ratio of desorption agent was 1:3, the extraction temperature was 80 ℃, and the extraction times were 2 times. The contents of 4 isoflavones and 3 saponins in the root and stem of A. membranaceus with green stem were higher than A. membranaceus with purple stem.Among them, the contents of ononin, formononetin and calycosin 7-o-glucoside in stem were very significantly different ($P<0.01$), the contents of calycosin in stem were significantly different ($P<0.05$), and the contents of Astragaloside II in root were significantly different ($P<0.05$). There was no difference in total polysaccharide content in root and stem of Astragalus membranaceus with different stem color CONCLUSION The content of isoflavones and saponins in root and stem of Astragalus membranaceus were related to stem color, which provided theoretical basis for further breeding and breeding of high-quality Astragalus membranaceus.

Abstract no.182

Simultaneous determination of six components in Eucommia bark by UPLC based on deep eutectic solvent assisted ultrasonic extraction

1. Mr Kan Zhong, Shanghai University of Traditional Chinese Medicine, Shanghai

Abstract: Objectives: To establish an extraction method of Eucommia bark based on deep eutectic solvent and ultrasonic extraction, compare the quality differences between commercial salt-processed Eucommia ulmoides and the effect of different processing conditions on content. Methods: For optimiazing the extraction process, the extraction yields of geniposide, chlorogenic acid, geniposide, rosin diglucoside, syringal diglucoside, and rosin monoglucoside were taken as the index to select the deep eutectic solvent using single-factor investigation. HPLC method was employed to determine the contents of the six target compounds to analysis the difference in O、origin of Eucommia bark. The impact of changing processing conditions on the content was investigated. Results: The deep eutectic solvent composed of choline chloride and acetic acid in a molar ratio of 1:2 with a water content of 70% had the best extraction effect. The optimal extraction conditions were ultrasonic extraction for 30 minutes.The six components (geniposidic acid, chlorogenic acid, geniposide, pinoresinol diglucoside, syringin, and pinoresinol glucoside) exhibited good linear relationships 0.189~2.271(r=0.997), 0.103~1.032(r=0.996), 0.011~1.057(r=0.997), 0.016~1.569(r=0.997), 0.013~1.348(r=0.997), 0.097~0.970 mg(r=0.998), which recovery rates met pharmacopeia standards. The best processing effect was achieved at a processing temperature of 210-220℃ for 9 minutes. Conclusion: This method replaces traditional chemical reagents with deep eutectic solvents, achieving less than a 3% difference in extraction rate compared to traditional methods. The analysis method shows good accuracy, repeatability, and stability. Among the 24 batches of salt-processed Eucommia ulmoides analyzed, there were significant differences in the contents of the six components. After processing, geniposidic acid, chlorogenic acid, and geniposide decreased over time, while pinoresinol diglucoside and syringin first increased and then decreased, and pinoresinol glucoside increased over time.

Abstract no.183

Comparison of morphology and chemical compounds among various types and colors medicinal herbaceous peony (Shaoyao)

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Herbaceous peony (Paeonia lactiflora Pall., Shaoyao) is a well-known medicinal plant. Its root is the official source of Chinese materia medica, Baishao (Paeoniae Alba Radix) and Chishao (Paeoniae Rubra Radix). Varius Shaoyao flowers can be found in cultivation areas. In order to select good and genetic stable varieties of Shaoyao for cultivation, the genetic information, output and quality of medicinal parts were compared among the Shaoyao varieties. Those varieties were firstly classified into two types by the stamen, i.e., single petal flower (stamen normal) and double petal flower (petaloid stamen). The type of single petal flower was further classified by petal color, namely white (1), vivid purplish red (2), light purplish pink (3) and strong purplish red (5). Similarly, the type of double petal flower was further classified into three colors, namely white (6), pale purplish pink (7) and strong purplish pink (8). A total of 48 samples of petals and petaloid stamen of various types and colors of Shaoyao flowers were collected and determined the relative expression quantities of genes related to floral organ development and flower color by qRT-PCR. The results indicated AG and MADS2 genes were related to the petaloidying of stamen; PAL, CHS, CHI, F3H and F3'H genes were related to the colors of petals. A total of 102 herbal samples of Shaoyao roots were harvested and quantified the outputs and seven bioactive compounds (paeoniflorin, albiflorin benzoylpaeoniflorin, oxypaeoniflorin, 1,2,3,4,6-pentagalloylglucose, gallic acid and catechin) using UPLC. The results indicated the outputs and amounts of bioactive compounds were different among the eight Shaoyao varieties. In generally, the output and quality of the double petal flower type is better than that of the single petal flower type.

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Abstract no.184

Chemical constituents and anti-oxidation in stems and leaves of daylily (Huanghuacai)

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Daylily flower (Huanghua) is commonly used medicinal and edible herbs to own the effect of anti-depression, antioxidation, sedation, etc. It is also a vegetable in people's daily life. Daylily flower is derived from the flower buds of Hemerocallis citrina Baroni. After harvesting the flower buds from Daylily, the stems and leaves are abandoned without utilized. Although the chemical constituents have been studied in daylily flower, but it is not be investigated the stems and leaves. In order to fully utilize the plant resources, this study focused on studying the chemical constituents and evaluating anti-oxidation because this bioactivity related to anti-depression.

The sample of stem and leaf was extracted in 75% ethanol. The ethanolic extract was then extracted with petroleum ether. The aqueous extract was further separated by macroporous adsorbent resin and multiple column chromatography to obtain 12 pure compounds, which were identified by spectral data, namely methyl-2-hydroxy-4-O-β-D-glucopyranosyl-6-(4-hydroxyphenethyl)-3-methylbenzoate (1), methyl-2,4-dihydroxy-6-(4-O-β-D-glucopyranosyl-benzene)-3-methylbenzoate (2), methyl-2-hydroxy-4-O-β-D-glucopyranosyl-6-[2-(4-hydroxyphenethyl)ethyl]benzoate (3), 1,3-dimethoxy-5-[1-hydroxy-2-(4-hydroxyphenyl)ethyl]benzene (4), methyl 2,4-dihydroxy-6-(4-hydroxyphenethyl)-3-methylbenzoate (5), methyl 2,4-dihydroxy-6-[2-(4-hydroxyphenyl)ethyl]benzoate (6), 5-neochlorogenic acid (7), isoquercetin (8), isorhamnetin-3-O-β-D-galactoside(9), velutin (10), rutin (11) and (+)-syringaresinol (12). Compounds 1~4 were new found compounds. Moreover, all the 12 compounds were evaluated on anti-oxidation in vitro using DPPH radical and ABTS+ radical scavenging rate as indicators. Compounds 1~4 showed anti-oxidant effect. Compounds 7, 8 and 12 indicated significant antioxidant effect. Those results demonstrate the stems and leaves of Daylily should be developed antioxidation drugs and/or health foods to utilize the enrich plant resources.

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Abstract no.185

Species discrimination of Fritillaria Bulbus using PCR-CRISPR/Cas12a-based nucleic acid detection

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Abstract： Fritillaria Bulbus (FB) is a group of medicinal herbs known for their cough-relieving and asthma-relieving properties. Because of their significant medicinal and economic value, it is imperative to easily authenticate these herbs due to the prevalence of fake products in the market. In this study, we propose a nucleic acid detection method that integrates PCR amplification of target genes and CRISPR/Cas12a trans-cleavage of fluorescent reporter genes to determine the authenticity of herbs by their fluorescence values. Fritillaria Cirrhosa Bulbus (FCB) and Fritillaria Ussuriensis Bulbus (FUB) are two of the most valuable species in FB and are often used in a confusing manner, and this study distinguishes between the two species by this nucleic acid detection method. A conserved fragment from the nuclear ribosomal DNA was chosen to design crRNAs specific to these two species. Both crRNAs exhibited high sensitivity in detecting amplified genes and specificity for target species, with no cross-reactivity with the non-target species. The practicality of this method was verified by using standard medicinal materials and real samples. Compared with previously reported identification methods, this method offers the advantage of not relying on high-precision testing instruments, as well as being simple to operate and requiring a short amount of time. Compared with DNA barcoding, our method demonstrated a greater capability in detecting mixed samples, thus providing a theoretical basis for the application of CRISPR/Cas-based nucleic acid detection in verifying the authenticity of Chinese herbal medicines. Acknowledgments This study was funded by the Science and Technology Development Fund, Macau SAR (File no. 0105/2022/A2 and 006/2023/SKL).

Abstract no.186

Compositional and structural analysis of oligosaccharides in Polygonatum odoratum (Mill.) Druce through UPLC-Orbitrap-HRMS along with enzymatic technology

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Polygonatum odoratum (P. odoratum) oligosaccharides (POO) are bioactive compounds with complex structures affected by monosaccharide composition, connectivity, anomeric configurations, and branching structure. Since the precise structure of POO remains undefined, their pharmacological development and clinical application have been hindered. This study developed a strategy combining ultra-performance liquid chromatography with Orbitrap high-resolution mass spectrometry (UPLC-Orbitrap-HRMS) and enzymatic technology to elucidate oligosaccharide structures. Initially, monosaccharide constituents of free POO and polysaccharides (POP) were quantitatively analyzed using pre-column derivatization with 1-phenyl-3-methyl-5-pyrazolone (PMP) and Liquid chromatography-tandem mass spectrometry (LC-MS/MS) in dynamic multiple reaction monitoring modes. The results indicated that POO contained ten monosaccharides including fructose, mannose, glucose, galactose, ribose, rhamnose, fucose, xylose, arabinose and galacturonic acid, while an extra monosaccharide of glucuronic acid was only founded in POP. Furthermore, an oligosaccharide library containing 986 structures was built based on these 11 monosaccharides. The accurate mass values, retention time and sequence-specific fragment ion information produce highly corresponding results have been chosen for initial characterization. Due to the limitations of MS in precisely identifying isomer structures, enzymatic technology was employed to distinguish the glycosidic linkage and oligosaccharide type. Fructanase mixture, endo-1,4-β-mannanase, exo-1,3-β-D-glucanase, and amyloglucosidase were used to identify hexose-based isomers, while α-L-arabinofuranosidase and endo-1,4-β-xylanase were used for pentose-based isomers. Ultimately, 77 oligosaccharides in POO and 76 in POPO were finally identified. The study revealed that POO primarily consisted of fructooligosaccharides, and its isomers such as 1-ketose, 6-ketose, and neokestose were clarified. POP is mainly composed of galactomannan, and the branching site at α-(1→6)-galactoside in POPO was determined for the first time in P. odoratum. This method provides a rapid and accurate framework for analyzing plant oligosaccharides, establishing a theoretical foundation for further pharmacological research and potential clinical applications.

Abstract no.187

Five-layer-funnel filtering mode discovers effective components of Chinese medicine formulas: Zhishi-Xiebai-Guizhi decoction as a case study

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ABSTRACT: How to screen and identify the effective components in the complex substance system is one of the core issues in achieving the modernization of traditional Chinese medicine (TCM) formulas. However, it's still challenging to systematically screen out the effective components from the hundreds or thousands of components in a TCM formula. In this study, for the first time, an innovative five-layer funnel filtering mode stepwise integrating chemical profile, quantitative analysis, xenobiotic profile, network pharmacology and bioactivity evaluation was successfully presented to discover the effective components and implemented on a case study of Zhishi-Xiebai-Guizhi decoction (ZXG), a well-known TCM formula for coronary heart disease (CHD). First of all, the chemical profile of ZXG was systemically characterized by UHPLC-Q/TOF-MS with the detection of 201 components. Secondly, 37 representative components were quantified to comprehensively describe its content distribution characteristics by UHPLC-TQ-MS. Thirdly, among the quantified components, 24 bioavailable components were screened based on the multi-component xenobiotic profile. Fourthly, an integrated pharmacology network led to the identification of 11 crucial bioavailable components against CHD. Finally, 9 components (honokiol, magnolol, naringenin, magnoflorine, hesperidin, hesperetin, naringin, neohesperidin and narirutin) exhibiting myocardial protection in vitro were identified as effective components. Overall, this innovative strategy discovered the effective components of ZXG for the first time. It could not only significantly contribute to elucidating the therapeutic mechanism of ZXG in the treatment of CHD, but also serve as a helpful reference for the systematic discovery of effective components as well as ideal quality markers in the quality evaluation of TCM formulas. Key words: Effective components; Zhishi-Xiebai-Guizhi decoction; Traditional Chinese medicine formula; Coronary heart disease; five-layer funnel filtering mode

Abstract no.188

A Multi-dimensional Scoring Equation Orients the Discovery of Q-Markers for Traditional Chinese Medicine Prescriptions

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ABSTRACT Traditional Chinese Medicine (TCM) is an enduring healthcare system that utilizes treatments through the administration of TCM prescriptions (TCMPs). Ensuring the quality and safety of TCMPs is crucial, and the identification of quality markers (Q-markers) plays a pivotal role in effective quality control. However, discovering highly valuable Q-markers within the complex chemical composition of TCMPs poses a significant challenge. Our study developed a multi-dimensional scoring system for discovering Q-markers in TCMPs, with a focused on the classical TCMP "Shaoyao Gancao Tang (SGT)" and its modern derivatives. Initially, UPLC-Q/TOF-MS analysis was conducted to comprehensively analyze the chemical composition of SGT and its modern derivatives. Chemometrics techniques were then applied to identify representative compounds. Additionally, plasma and urine samples from orally administered rats were examined to determine the in vivo bioavailable constituents of each TCMP. The Mahalanobis-Taguchi method was combined with fingerprints to identify key contribution peaks responsible for quality fluctuations. The quality traceability of corresponding TCMP throughout the entire preparation process, including decoction, concentration, and drying, was determined by integrating UPLC-PDA fingerprinting with quantitative analysis of multi-components using single marker techniques. Finally, a novel multi-dimensional scoring equation was proposed to identify valuable Q-markers by integrating chemical specificity, in vivo bioavailability, quality fluctuation contribution, quality traceability, bioactivity, and content. Nine compounds were identified as Q-markers for modern derivatives of SGT and categorized into three levels: A-level (Glycyrrhizic acid, Albiflorin, Paeoniflorin), B-level (Liquiritin apioside, Liquiritin), and C-level (Gallic acid, Pentagalloyl glucose, Isoliquiritin apioside). This system aids in determining the importance of ingredients in TCMPs, guiding quality control practices, and ensuring consistent quality, with broader implications beyond this study. Keywords: Traditional Chinese medicine prescription; Q-marker; full-process quality control; multi-dimensional scoring system; Shaoyao Gancao Tang.

Abstract no.189

Analysis of Whole-Genome for Penicillium Species Identification

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The Penicillium genus exhibits a broad global distribution and holds substantial economic value across agriculture, medicine, industry, and food processing sectors. Timely detection of Penicillium species is crucial for disease control, industrial production, and preventing mycotoxins from entering the food chain. However, traditional methods face challenges in achieving fast and precise identification, particularly for closely related species. To address this need, we implemented a novel species identification approach called Analysis of Whole-Genome (AGE). This method involves two principal steps: first, bioinformatics analysis is used to screen Target sequences from the whole-genome of species; second, experimental verification is conducted using a combination of non-sequencing and sequencing technologies. Here, we initially constructed specific Target sequence libraries from the whole-genome of entire Penicillium species. We randomly selected seven Target sequences from libraries and successfully identified the species through Sanger sequencing and CRISPR-Cas12a technologies. Notably, based on CRISPR-Cas12a technology, AGE can achieve rapid and accurate identification of genomic DNA samples at concentrations as low as 0.01 ng/μl within 30 minutes. This approach offers high sensitivity and portability, making it suitable for on-site detection. The enhancement in diagnostic precision and speed is beneficial for applications in agricultural control, industrial production, clinical diagnostics, food and drug safety.

Abstract no.190

Effect of Jianyao Qiangji formula on lumbar spine instability-induced intervertebral disc degeneration model mice

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2. Ms 佳凡 杨，上海市中医医院，上海

【Abstract】 Objective: To observe the effect of Jianyao Qiangji formula on lumbar spine instability-induced intervertebral disc degeneration model mice. Methods: Thirty 8-week-old C57BL/6 male mice were randomly divided into the sham group, model group and Jianyao Qiangji formula group. Mice in model group and Jianyao Qiangji formula group were performed with LSI surgery. The Jianyao Qiangji formula group was given the Jianyao Qiangji formula(2.94g raw herb/mL) by gavage while the sham group and the model group were given 0.9% saline gavage. After 8 weeks of intervention, the lumbar spine tissues of mice in each group were collected. HE staining and Safranine O-Fast Green staining were performed to observe the morphology of the intervertebral discs, the height of the intervertebral discs, and the calcification defects of the cartilage endplates. Besides, the expression level of Col II, Col X, and MMP-9 was detected by immunohistochemical staining. Results: The histomorphological observation of HE and Safranine O-Fast Green staining showed that the height of intervertebral discs decreased significantly by 147±74 μm after LSI surgery ($P < 0.01$), and the calcification area of cartilage endplate increased significantly ($P < 0.01$). After the intervention of Jianyao Qiangji formula, the height of intervertebral discs increased significantly by 96±21 μm ($P < 0.05$), and the calcification area of cartilage endplate was reduced ($P < 0.05$). Immunohistochemical results showed that the expression of Col II of cartilage endplate was significantly increased ($P < 0.001$), and the expression of Col X and MMP-9 protein was decreased ($P < 0.05$). Conclusion: Jianyao Qiangji formula can ameliorate cartilage endplate calcification, inhibit extracellular matrix degradation, and thus delay intervertebral disc degeneration. Keywords: Intervertebral disc degeneration; Jianyao Qiangji formula; Cartilaginous endplate; Cartilage matrix

Abstract no.191

Uncovering the characteristics of the gut microbiota in patients with symptomatic cerebral arteries stenosis in phlegm-damp syndrome

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2. Ms Guixian Chen, Guangzhou University of Chinese Medicine, Guangzhou

Introduction: Symptomatic cerebral arteries stenosis (SCAS) is an important cause of ischemic stroke worldwide, with a greater prominence in China. Base on the "gut-microbiota-brain axis", gut microbiota may play an important and unknown role in the development of SCAS. We aimed to investigate the characteristics of gut microbiota in patients with symptomatic cerebral arteries stenosis (SCAS) in phlegm-damp syndrome. Materials and Methods: Forty-two SCAS patients in phlegm-damp syndrome and twenty-nine healthy subjects were selected to compare the clinical data and gut microbiota of the patient group in two phases and 16S RNA gene sequencing was used to search the differences of gut microbiota in subjects. Results: Compared with the healthy subjects, the community diversity was higher and the species distribution was more uniform in both acute phase and convalescent phase patients through alpha-diversity analysis. Gut microbiome beta-diversity differed between patients in the acute phase vs. non-acute phase. Specifically, patients in the acute phase were characterized by larger abundances of Sutterella. Lachnospiraceae and Agathobacter were abundant in the acute phase group (all $p < 0.05$). Conclusions: Gut dysbiosis existed in SCAS patients in the acute phase and convalescent phase. Sutterella, Lachnospiraceae and Agathobacter may be potential indicators of gut microbiota that distinguish acute and non-acute patients.

Abstract no.192

A reliable and practical identification method for the powder of cultivated ginseng，mountain cultivated ginseng and wild ginseng

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2. Prof Chongning Lv, Shenyang Pharmaceutical University, Shenyang

3. Prof Jincai Lu, Shenyang Pharmaceutical University, Shenyang

Background: Ginseng, the most famous traditional Chinese medicine, is mainly produced in northeast China. Due to the rarity of wild ginseng (WG) resources, a reliable identification method for the powder of WG, mountain cultivated ginseng (MCG) and cultivated ginseng (CG) is urgently needed. However, although there have been many studies, the currently reported identification methods still have significant deficiencies and are difficult to apply in practice. Methods: UPLC-Q/TOF-MS/MS was employed to identify ginsenosides in CG, MCG and WG. In order to explore the differences of CG, MCG and WG in ginsenoside content, UPLC-DAD was used to establish the fingerprints of 117 batches of CG, MCG and WG, and determine the content of 18 ginsenosides. Results and conclusion: The fingerprints of 117 batches of CG, MCG and WG were successfully established with the similarities of 0.826-0.999. The analysis results demonstrated that the 18 ginsenosides content in WG and MCG elevated first and then decreased with the increase of age, reaching the highest in WG with 18-19 growth years. Among the three kinds of ginseng, WG showed the highest ginsenoside content. By comparing ginseng from different producing areas, no significant difference in ginsenoside content of WG from the three provinces in northeast China was observed. Moreover, there was also no obvious difference in content of CG with five growth years from different cities and counties of Jilin Province. Most important of all, we found that the value of Rb1/R0 can be preliminarily used to distinguish CG, MCG and WG. When Rb1/R0 value is less than 2.5, we can determine the ginseng as CG, and when greater than 2.5, it can be determined to be MCG or WG. The content ratio of Rb1 and R0 is a convenient and reliable method to distinguish the powder of CG, MCG and WG.

Abstract no.193

Computer-driven formulation development of ginsenoside Rh2 ternary solid dispersion

1. Prof Defang Ouyang, University of Macau, Macao SAR

2. Ms Tianshu Lu, University of Macau, Macao SAR

Background: (20S)-Ginsenoside Rh2, a potent anticancer saponin from Panax ginseng Meyer, has poor water solubility and bioavailability, limiting its pharmaceutical applications. This study aims to develop a (20S)-Ginsenoside Rh2 formulation with enhanced solubility, dissolution rate, and bioavailability using combined computational and experimental methods. Method: The "PharmSD" model identified the optimal polymer for solid dispersion formulations. Various polymers' solubility and ternary solid dispersion dissolution were assessed. Characterization techniques included PXRD and FTIR, while molecular dynamics simulations explored the formation mechanism and interactions among the API and excipients. Cell and animal experiments evaluated the in vivo performance. Results: The "PharmSD" model identified Gelucire 44/14 as the best polymer for enhancing Rh2's dissolution rate, confirmed by experiments. Adding sodium dodecyl sulfate (SDS) to the ternary solid dispersion significantly improved dissolution rates. Characterization showed the API in an amorphous state, interacting via hydrogen bonding with SDS and Gelucire. Molecular modeling supported these findings. Cell and in vivo experiments demonstrated improved absorption and a lower efflux ratio for the modified formulation. Conclusion: This study developed an optimal ternary solid dispersion for Rh2, enhancing its solubility, dissolution rate, and bioavailability through integrated computational and experimental approaches

Abstract no.194

Machine Learning in Accelerating Microsphere Formulation Development

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2. Ms Jiayin Deng, University of Macau, Macao SAR

Abstract：Microspheres have received significant attention from the pharmaceutical and medical industries due to their excellent biodegradability and controlled-release characteristics. However, the in vitro drug release behavior of microspheres is highly influenced by the complex formulation and manufacturing factors. The traditional trial-and-error methods used in formulation development are ineffective and intractable. Thus, this research aims to utilize machine learning techniques to build a prediction model that can accelerate microsphere product development for small-molecule drugs. A dataset of 286 microsphere formulations with small-molecule drugs, including their dissolution temperature at both 37℃ and 45℃, was collected from publications and pharmaceutical companies. After comparing 14 machine learning approaches, the consensus model achieved accurate predictions for the validation set at both 37℃ and 45℃, demonstrating its predictive capability for the in vitro drug release behavior. The prediction models revealed the feature importance of formulations, providing meaningful insights into microsphere development. The experiment of microsphere formulations further validated the accuracy of the prediction models. Additionally, molecular dynamics simulations provided a microscopic view of the preparation process of microspheres. In conclusion, a prediction model for microsphere formulations of small-molecule drugs was successfully developed with high accuracy, which can accelerate microsphere product development and promote quality control in the pharmaceutical industry. Keywords: Drug release; Machine learning; Microspheres; Molecular dynamics simulation.

Abstract no.195

Analysis of Whole-Genome as a Novel Strategy for Animal Species Identification

1. Dr Yutong Gan, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing

Survival crises stalks many animals especially endangered and rare animals. Accurate species identification plays a pivotal role in animal resource conservation.In this study, we developed an animal species identification method called Analysis of whole-GEnome (AGE) which identifies species by finding species-specific sequences through bioinformatics analysis of the whole-genome and subsequently recognizing these sequences using experimental technologies. To clearly demonstrate the AGE method flow, Cervus nippon, a well-known endangered species, and its closely related species Cervus elaphus were set as model species without and with published genomes respectively. By analyzing the whole-genomes of C.nippon and C.elaphus which were obtained through next-generation sequencing and online databases, we built the specific sequence databases containing 7670140 and 570981 sequences respectively. Then the species-specificity of the specific sequences was confirmed experimentally using Sanger sequencing and the CRISPR-Cas12a system. Moreover, for 11 fresh animal samples and 35 commercially available products, our results were in 100% agreement with other authoritative identification methods, demonstrating AGE's precision and potential application. Notably, AGE found a mixture from 35 commercially available products and successfully identified it. This study broadens the horizons of species identification using whole-genome and sheds light on the potential of AGE in conserving animal resources.[1] [1] Gan, Y.; Qi, G.; Hao, L.; Xin, T.; Lou, Q.; Xu, W.; Song, J. Analysis of Whole-Genome as a Novel Strategy for Animal Species Identification. Int. J. Mol. Sci. 2024, 25, 2955. https://doi.org/10.3390/ijms25052955

Abstract no.196

UPLC-QTOF-MS-based metabolomics and biological activity comparison distinguish Coptis teeta from different regions

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2. Dr Zhuo Cheng, Minzu University of China, Beijing

Coptis teeta Wall. is an extremely endangered species in China and is mainly distributed in the Gaoligong Mountains in the Nujiang River and Dulong River watersheds in northwest Yunnan, China. Based on metabolomics and pharmacology, we first used UHPLC-QTOF-MS technology to detect the components of wild Coptis teeta in six locations including Fugong County, Gongshan County, Lushui City, Motuo County, Tengchong City and Longyang District. The key compounds were identified through standards and secondary mass spectrometry fragments, and significantly different metabolite components in different regions were found through PCA analysis, OPLS-DA analysis and S-plot analysis. Then pharmacological activities were compared (cytotoxicity, anti-inflammatory activity and anti-bacterial activity). The results showed that a total of 89 compounds were identified in Coptis teeta samples, of which 30 significantly different metabolites were screened out, mainly alkaloids and their derivatives. There are significant differences in the cytotoxicity, anti-inflammatory activity and anti-bacterial activity of Coptis teeta from different regions. Coptis teeta from Motuo County has the best cytotoxicity effect on three types of tumor cells and anti-bacterial activity against G+ bacteria. Coptis teeta from Longyang District, Tengchong City and Gongshan County has the best anti-inflammatory effects. By correlating activity differences and metabolite differences, 19 bioactive markers were screened out, mainly alkaloids such as berberine, coptisine and jatrorrhizine and their derivatives that have been proven the active effects. This study scientifically explains and evaluates the medicinal effects and differences of Coptis teeta in different traditional regions. In addition, the metabolite composition and activity differences of Coptis teeta from six regions showed three clusters, which were highly correlated with the distribution of their geographical regions, providing ideas for the classification and identification of Coptis teeta from different populations.

Abstract no.197

Coptis as the alternative to bear bile in liver diseases and cancer treatment

1. Prof Yibin Feng, The University of Hong Kong, Hong Kong SAR

Coptis as the alternative to bear bile in liver diseases and cancer treatment 黃連作為熊膽的替代品用於肝臟疾病和癌症治療 Yibin FENG School of Chinese Medicine, The University of Hong Kong, Hong Kong SAR, China Abstract: The use of Chinese Medicines originated from endangered animal species such as Bears has raised ethical concerns and become internationally controversial. We have paid efforts to search herbal alternatives that can replace and stop the use of these Chinese Medicines in the clinical practice. We did comparative studies on bear bile and other animal bile in liver disease and HCC models and found all animal bile have different chemical profiles, but similar biological activities. We further performed comparative studies on bear bile and coptis in chronic liver models and found coptis and berberine have equivalent or better anticancer effect, liver protective and anti-fibrotic effects than bear bile and UDCA. We published scientific papers that exploring possibility of Coptis to replace bear bile in treating hepatic disorders and cancers on the top journals related to Chinese Medicine, and called on the global consensus of stopping bear bile consumption in Chinese Medicine practice. Our approaches set a paradigm in Environment-friendly practice and innovation of Chinese Medicine for replacing endangered animal species. Based on our literature review and experimental studies, we have been using coptis and its formulae to treat liver diseases and various cancers as alternative of bear bile in clinical setting. In this presentation, we will present our original research and comparative studies for plant alternative of bear bile, then use some clinical cases to show the effectives of coptis and its formulae in cancer and metabolic diseases treatment, but not bear bile.

Abstract no.198

One Polysaccharide Fraction In Codonopsis tangshen Oliv：Highly Acticity In Anti-lipid Metabolism Disorder

1. Prof Huifeng Zhu, Southwest University, Chongqing

2. Mr Qianfeng Fu, Southwest University, Chongqing

Codonopsis pilosula (CP) is an herbal medicine, widely used in China. CP with highly efficacy of yiqi has been demonstrated in traditional Chinese medicine, and also it is a medicine that can be consumed as a safety food. CP often appears in the treatment of hyperlipidemia in traditional Chinese medicine. Codonopsis tangshen Oliv (CTO) is a subspecies of CP，which grows in Wushan County, Chongqing, China, and it's well-popular and widely used in traditional Chinese medicine. Codonopsis pilosula polysaccharide (CPP) is identified as a major constituent responsible for the therapeutic function of CP, such as antitumor, antimicrobial, immunoenhancing and antioxidant functions. This objective of this work we detect a new polysaccharide, Codonopsis tangshen Oliv polysaccharide (CTOP), was isolated from CTO and found to promote lipid metabolism. The results showed that CTOP significantly improved oleic acid-induced HepG2 cell hyperlipidemia model, and the lipid-lowering effect was more obvious with the increase of CTOP concentration, and the lipid-lowering effect was the most obvious at 10μm/ml. In subsequent animal high-fat feeding experiments we found that the growth as the breeding time every day to fill the stomach give CTOP 2.5 mg/kg group than other group have significantly reduce weight, is especially significant in the 21 d. Serum levels of TG, T-CHO and LDL-C were significantly lower in 2.5mg/kg simvastatin group than in high-fat diet group, and serum TG level was significantly lower in 2.5mg/kg simvastatin group than in 5mg/kg simvastatin group. HE staining of fat and liver showed that 2.5mg/kg CTOP could significantly reduce the volume of adipocytes and fat vacuoles around hepatocytes compared with the normal group. Our study found that the lipid-lowering effect of CTOP was promoted by low dose and inhibited by high dose. Ctop had a better lipid-lowering activity at the concentration of 2.5mg/kg. The result shows that CTO, as a safe traditional Chinese medicine with the same origin of medicine and food, has great potential in weight loss health care. This work was supported by traditional Chinese medicine science and technology project of Chongqing Municipal Health and Family Planning Commission (ZY201801002).

Abstract no.199

Traditional Knowledge and Efficacy Analysis of An Edible and Medicinal Plant Dimetia scandens

1. Ms 晴宇 陈, Minzu University of China, Beijing
2. Prof 春林 龙, Minzu University of China, Beijing
3. Dr 苗苗 王, Minzu University of China, Beijing

Dimetia scandens (Roxb.) R. J. Wang, locally known as Lifeisan, is not only a traditional anti-inflammatory herb in southwestern Yunnan but also a common wild vegetable. However, previous research on the anti-inflammatory and antioxidant activities of this important medicinal and edible plant has been limited. To promote the sustainable use of Dimetia scandens, this study measured the in vitro antioxidant and anti-inflammatory activities of its water and ethanol extracts. The results showed that within the range of 0-300 μg/ml, both extracts exhibited low cytotoxicity to mouse RAW 264.7 macrophages, with the ethanol extract showing better NO scavenging activity (IC50 = 100.4 ± 4.34 μg/ml) and a dose-dependent effect. Additionally, both extracts demonstrated significant ABTS+·scavenging capacity and total antioxidant activity. These findings validate the local use of Dimetia scandens as an anti-inflammatory herb. In northwestern Yunnan and surrounding areas, Dimetia scandens has the potential to be developed into new health foods, nutritional supplements, or dietary supplements, promoting local development.

Abstract no.200

The roots essential oil of Lindera communis against Methicillin-Resistant Staphylococcus aureus via a Membrane-targeting

1. Mrs Miaomiao Wang, Minzu University of China, Beijing

The roots of Lindera species have traditionally been used for their healing properties in preventing hemorrhage, providing analgesic relief, and reducing fever in Chinese folk medicine. To explore the full potential of Lindera plants, in this study, we delved into the chemicals and the assessments of antibacterial activity of the n-hexane fraction of Lindera communis roots (LCH) through the broth microdilution methods against MRSA (MIC=0.1 mg/mL). The action mode was investigated with the utilization of the DiOC2(3) probe, resazurin assay, fluorescence probe PI, SYTOX Green, the assessment of AKP activity, and in healing rat excisional wounds, respectively. Based on our findings, humulene-type sesquiterpenes, guaiane-type sesquiterpenes, and lauric acid were identified as the main chemical components of LCH, responsible for antibacterial and wound healing activities. It was speculated that it affected the growth of MRSA through morphological alterations and disrupting cell surface structures, causing membrane hyperpolarization and altering membrane integrity. This result was subsequently validated through SEM analysis of MRSA treated with LCH. LCH has exhibited remarkable effectiveness in healing rat excisional wounds, reinforcing its traditional use as a wound-healing agent. All these results indicate that LCH effectively repressed the growth of MRSA by disrupting its membrane, positioning it as a potential candidate for novel and easily accessible wound healing agents.

Abstract no.201

Phytochemistry and update clinical applications of Choerospondias axillaris: an investigation into its potential cardiovascular therapy

1. Prof Pei Luo, Macau University of Science and Technology, Macao SAR

2. Ms Qi Ye, Macau University of Science and Technology, Macao SAR

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4. Mr Yifan Tian, Southwest Minzu University, Chengdu

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7. Prof Liping Bai, Macau University of Science and Technology, Macao SAR

The fruit of Choerospondias axillaris (Roxb.) Burtt et Hill (C. axillaris) commonly known as “nansuanzao” in China, which is edible and possesses immense economic value. The dried mature fruit of C. axillaris (CF) is named Choerospondiatis Fructus (CF) in traditional Chinese medicine (TCM), which can be used to treat chest pain and heart pain. This paper provides a detailed evaluation of both traditional therapeutic application knowledge and research literature on Choerospondias axillaris (Roxb.) Burtt et Hill. Traditional application information was acquired from pertinent reports, books, and classic medical literature. Research literature on CF's chemical constituents and pharmacological activities was used to find electronic databases up to 2023. Pharmaceutical components found in CF were identified and classified based on their cardiovascular relevance. And exploring the Chinese patent medicine and prescription rules of CF for the diagnosis and treatment of cardiovascular diseases. The pharmacological effects of CF were summarized, including hemorheological effects, anti-myocardial ischemia-reperfusion injury, antiarrhythmic properties, and anti-myocardial fibrosis effects. This review aspires to provide valuable insights for therapeutic applications in cardiovascular therapies and hopefully offer a possible translation of traditional uses into contemporary medicines.

Abstract no.202

芍药非药用部位的化学成分研究

Objective Study on chemical components of the non-medicinal parts of P. lactiflora

1. Prof 志锋 张, Macau University of Science and Technology, Macao SAR
2. Ms 凌滔 田, Macau University of Science and Technology, Macao SAR
3. Mr 嘉桓 梁, Macau University of Science and Technology, Macao SAR
4. Ms 靖晨 闫, Macau University of Science and Technology, Macao SAR

Abstract Objective Study on chemical components of the non-medicinal parts of P. lactiflora. High-performance liquid chromatography (HPLC) was used to establish fingerprints of the stems and leaves of P. lactiflora.and determine the paeoniflorin, gallic acid, and benzoylpaeoniflorin etc. UHPLC-MS technology was used to detect the chemical components in stems and leaves and compare the differences in main components. Method The root, stem, and leaf of P. lactiflora were extracted by ultrasonic with 50% methanol and used HPLC to detect. HPLC method: Agilent EC-C18 column (4.6×150 mm, 4 μm); mobile phase: acetonitrile-0.1% formic acid.; Flow rate: 1.0 ml/min; Detection wavelength: 230nm and 250nm, gradient elution. The 2012 version of "Chinese Medicine Chromatographic Fingerprint Similarity Evaluation System" software was used to establish the chemical fingerprint; UHPLC-MS method: waters -HSS T3 column (2.1×100 mm, 1.8 μm); mobile phase: acetonitrile-0.1% formic acid; flow rate: 0.3 ml/min; detection wavelength: 230nm and 250nm, gradient elution. Results The HPLC chemical fingerprints of P. lactiflora stems and leaves were established, and the differences in main components were analyzed. Conclusion Fingerprints can effectively evaluate the quality of P. lactiflora from different origins. The results of quantitative analysis show that gallic acid, albiflorin, β-1,2,3,4,6-pentagalloylglucose, paeoniflorin and other effective components have significant content in stems and leaves. Provide a relevant theoretical basis for the comprehensive evaluation of the quality of P. lactiflora and make full use of non-medicinal parts of it. Keywords：Paeonia lactiflora Pall.; non-medicinal parts；fingerprints；content；chemical composition.

Abstract no.203

Bioprospecting Medicinal Plants for the Treatment of Benign Prostatic Hyperplasia through Analysis of Lontara Pabbura， an Ancient Manuscript of Buginese Traditional Medicine

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2. Mr Junaedi Junaedi, Megarezky University, South Sulawesi

Benign Prostatic Hyperplasia (BPH) commonly affects men over the age of 50, characterized by prostate tissue proliferation involving smooth muscle and epithelial cells. Current treatments include alpha-adrenergic receptor blockers and 5-alpha reductase inhibitors, which, despite effectiveness, raise concerns due to side effects, affordability, and accessibility issues. Medicinal plants offer potential alternatives, particularly in rural areas, for managing BPH, and further exploration of medicinal plants could yield additional therapeutic options. Ancient medicinal manuscripts, such as the Buginese Lontara Pabbura from South Sulawesi, Indonesia, provide valuable insights into traditional medicinal knowledge. This study analyzed the Lontara Pabbura, a handwritten manuscript obtained in microfilm form from the National Archive Institute of Indonesia. The manuscript was written in the Lontara script, an abugida script, requiring interpretation and analysis. The analysis involved consultations with a philologist, a traditional healer, and a botanist to ensure the accurate interpretation of the text. Our analysis identified a promising BPH treatment combining Curcuma longa (rhizome) and Averrhoa bilimbi (leaves), prepared through overnight water extraction in an open-air environment. This remedy has demonstrated potential for managing BPH symptoms, including urinary difficulties, as demonstrated in the manuscript by its effective treatment of kidney stones, a common symptom associated with BPH. Exploring Buginese ancient medicinal scripts may offer more accessible and affordable treatment options, providing early insights for further investigation. Future studies should explore herb-herb interactions and evaluate efficacy in BPH models.

Abstract no.204

Study on suitability regionalization of Forsythia Suspensa in Shanxi Province based on MaxEnt and ArcGIS

1. Mr 子豪 徐, 山西中医药大学, 晋中

Abstract: Objective: The purpose of this paper is to grasp the main ecological factors affecting the growth of Forsythia suspensa. It predicted the distribution of Forsythia suspensa in suitable areas in Shanxi Province, which can provide reference for the rational distribution of Forsythia suspensa resources in Shanxi Province. Method: This study used the Forsythia suspensa sample point distribution data collected in the "Fourth Survey of Chinese Medicine Resources" database in Shanxi Province, and supplemented it by searching the China Digital Herbarium and retrieving related literature records. 210 Forsythia suspensa sample points distribution data and ecological factors were added to the MaxEnt model, after running, screened out the main ecological factors and contribution rates affecting the geographical distribution of Forsythia suspensa. The geographic information system (ArcGIS) software was used to divide the ecological suitable area of Forsythia suspensa in Shanxi Province. Result: The AUC value of the established MaxEnt model was 0.908, indicating that the prediction results of the model were accurate. The model screened 23 ecological factors, including standard deviation of seasonal temperature change, vegetation type, coldest month and wettest month precipitation, etc. Among them, climate factor is the most important ecological factor affecting the distribution of Forsythia suspensa, followed by biological factor and topographic factor, soil factor has the least influence. The potential suitable areas of Forsythia suspensa in Shanxi Province are mainly distributed in the southern mountainous areas. The suitability level gradually decreases from south to north. Under the current climatic conditions, the most suitable area of Forsythia suspensa in Shanxi Province is 12 830 km2, the area of suitable area is 15 467 km2, the area of secondary suitable area is 34 410 km2, and the area of unsuitable area is 93 993 km2. Conclusion: Based on MaxEnt model and ArcGIS software, This study predicted the distribution of Forsythia suspensa suitable areas in Shanxi Province, which has certain reference value for the protection and rational distribution of Forsythia suspensa resources in Shanxi Province.

Abstract no.205

Exploration of Trisatthakula Remedy through profiling its antioxidant activity

1. Dr Pasarapa Towiwat, Chulalongkorn University, Bangkok

2. Ms Thanchanok Limcharoen, Chulalongkorn University, Bangkok

Thai traditional medicine (TTM) has a long history of using medicinal plants to treat numerous diseases, as documented in ancient medicinal scripts. TTM typically employs remedies, known as 'Pikad,' for treating diseases. Remedies containing several plants are believed to be more effective compared to those using a single plant. In the present study, an exploration of recipes in TTM was performed. The ancient remedy of Thai medicine, noted by the Ministry of Public Health Thailand, was used and further explored to find a potential remedy. From this exploration, one remedy called Trisatthakula was identified and selected. The Trisatthakula remedy consists of a combination of three medicinal plants including Nigella sativa L. (NS), Coriandrum sativum L. (CS), and Zingiber officinale Roscoe (ZO). In TTM systems, this remedy is used to treat diseases caused by the impairment of the four fire and six wind elements, characterized by symptoms such as intestinal gas excretion and vomiting. The plants mentioned in the remedy were collected and authenticated. The plants were then extracted with an ethanol solution (95%) using a Soxhlet extractor for 8 hours and subsequently dried with an evaporator at 40°C. The percentage yields obtained from the remedy, NS, CS, and ZO were 9.50, 11.55, 4.48, and 9.44 gram, respectively. The extracts were then used for further evaluation in an antioxidant assay. The remedy, with a combination ratio of 1:1:1 of NS, CS, and ZO, and each single plant extract (0, 3, 10, 30, 100, 300 µg/mL) were tested for their antioxidant activities as an initial assay using DPPH assay. The results demonstrated that the antioxidant activities (IC50) of the remedy, NS, CS, and ZO were 18.76, 29.69, 32.01, and 8.54 µg/mL, respectively. As per the results, the remedy and its individual components demonstrated the ability to suppress radicals. This study demonstrated the potential antioxidant activity of the Trisatthakula remedy and supports its use and application in Thai traditional treatments. Further evaluation in other biological and pharmacological models are required to further investigate the potentials of Trisatthakula remedy.

Abstract no.206

Cordycepin alleviates NLRP3 inflammasome activation via modulating the Ltb4r2/FXR axis and ameliorates inflammatory diseases

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3. Mr xu wang, Shanghai University of Traditional Chinese Medicine, Shanghai

Background: The involvement of the NLRP3 inflammasome plays a crucial role in various inflammatory conditions. Targeting the activation of the NLRP3 inflammasome has emerged as a significant therapeutic strategy for treating inflammasome-mediated diseases. Cordycepin, the nucleoside antibiotic extracted from fungi, demonstrates anti-inflammatory properties. Nevertheless, the precise molecular mechanisms and specific inflammatory signaling pathways remain poorly comprehended. Purpose: The study seeks to investigate the effects of cordycepin on the NLRP3 inflammasome and its underlying mechanisms, while also evaluating its potential as a therapeutic approach for inflammatory conditions associated with NLRP3 overactivation. Study design: In vitro models were established using J774A.1 cells or THP-1 cells stimulated with lipopolysaccharide (LPS) in conjunction with Nigericin or adenosine triphosphate (ATP). A sepsis model in mice was induced via cecal ligation and puncture (CLP), and a peritonitis model in mice was induced using monosodium urate (MSU). Cordycepin was administered orally. Methods: In investigating NLRP3 inflammasome activation, cells underwent diverse stimulations, with ELISA measuring interleukin-1β (IL-1β) and interleukin-18 (IL-18) concentrations in supernatants. Mechanistic analyses included cell death assays, immunoblotting, immunoprecipitation, and immunofluorescence. Cordycepin's efficacy in mitigating inflammatory diseases was assessed in mouse models of bacterial sepsis and MSU-induced peritonitis. Results: Cordycepin inhibited the secretion of IL-1β and IL-18, suppressed caspase-1 activation, reduced cell death, and blocked the formation of ASC specks after NLRP3 inflammasome activation. Additionally, cordycepin inhibited Leukotriene B4 receptor 2 (Ltb4r2), thereby inducing FXR and NLRP3 interaction, which in turn blocked the interaction between NLRP3 and acetyltransferase KAT5, ultimately inhibiting NLRP3 acetylation and suppressing NLRP3 inflammasome activation. In mouse models, cordycepin demonstrated promising therapeutic effects in treating diseases associated with excessive NLRP3 activation, including bacterial sepsis induced by CLP and peritonitis induced by MSU. Conclusion: Cordycepin inhibits Ltb4r2, inducing FXR and NLRP3 interaction. This blocks NLRP3 from binding with KAT5, inhibits NLRP3 acetylation, and suppresses the assembly and activation of the NLRP3 inflammasome. These findings suggest cordycepin as a promising inhibitor for diseases induced by excessive NLRP3 activation.

9. Natural Products III(Biosynthesis, Modification, Chemical Library and Novel New Usage)

Abstract no.207

Study on the effect of glycosaminoglycan from the mucus of giant salamander on angiogenesis and wound healing

1. Prof Qing Zhang, Southwest Hospital, Chongqing

Objective: Microcirculation disorder is an important restriction factor of refractory wound repair. In order to improve the application of giant salamander mucus in the treatment of refractory wounds, the effect and mechanism of glycosaminoglycan in giant salamander mucus in promoting wound angiogenesis were investigated. Methods: The glycosaminoglycans from skin mucus of Chinese giant salamander were extracted by alkaline protease hydrolysis. The effect of glycosaminoglycan on wound healing and repair quality were evaluated in diabetic wound models. Results: The mucous glycosaminoglycan of giant salamander could not only promote wound closure, but also improve the appearance of wound, showing excellent effect of enhanced wound repair. Compared with the untreated group, the wound healing rate of glycosaminoglycans treatment was significantly accelerated. Moreover, compared with giant salamander mucous virginal powder and alginate dressing, glycosaminoglycan treatment significantly improved the regeneration of skin appendages such as neovasculature, hair follicles and sebaceous glands in granulation tissue. Conclusion: The angiogenic effects of glycosaminoglycans in the mucus of giant salamander is the key to promote wound repair. Mucus glycosaminoglycans of giant salamander can be a promising andidate for clinical treatment of refractory wounds.

Abstract no.208

Development of mucoadhesive alginate-polyethylenimine nanoparticles containing Piper retrofractum extract

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3. Ms Chulaphan Suttakamonkul, Naresuan University, Phitsanulok
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Stomatitis, an inflammation or sore inside the mouth, can be mild and localized or severe and widespread. Piper retrofractum extract (PrE), a rich source of piperine, has anti-inflammatory effects that reduce inflammation and swelling. Thus, this study aimed to develop mucoadhesive alginate-polyethyleneimine nanoparticles (APNPs) containing PrE (PrE- APNPs) for local oral mucosa delivery to treat stomatitis. APNPs were constructed using the polyelectrolyte complexation technique employing positively charged polyethyleneimine (PEI) and negatively charged alginate (Alg), with PEG 400 as a stabilizer. Under optimal conditions, the PrE-APNPs exhibited a spherical shape with a mean particle size of ~ 200 nm and a zeta potential of ~ +44 mV. Up to 80%, drug entrapment efficiency was achieved. In vitro wash-off tests confirmed the good mucoadhesive properties of PrE-APNPs, as ~ 30% of PrE-NPs remained on the cellulose acetate membrane after 120 minutes. Therefore, PrE-APNPs show great promise as a localized treatment for stomatitis, providing excellent mucoadhesive properties and potential for improved therapeutic effectiveness. Keywords: Piper retrofractum, mucoadhesive, stomatitis, nanoparticles, polyelectrolyte complexation technique

Abstract no.209

The genomic mechanism of crocin biosynthesis in two distant species Gardenia and Crocus

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Crocins, which are highly valuable as medicines for human disorders and spices for flavoring and coloring, are biosynthesized in two distant species Gardenia jasminoides (eudicot) and Crocus sativus (monocot). We firstly assembled the chromosomal-level genome of G. jasminoides and C. sativus. And we completely deciphered the dedicated pathway of crocin biosynthesis including carotenoid cleavage dioxygenases (CCDs), aldehyde dehydrogenases, and UDP-glucosyltransferases. Comparative genomics analysis showed that the first gene participated in the crocin biosynthetic pathway from G. jasminoides, GjCCD4a, evolved from recent tandem gene duplication and neofunctionalization. While CsCCD2, from C. sativus, originated from the duplication of CsCCD1 after the Crocus-specific WGT event, and the rapid evolution of CsCCD2 gave rise to neofunctionalization to produce crocetin dialdehyde. Kingdom-wide identification and phylogenetic analysis of CCDs revealed that the crocin biosynthesis in eudicots (Gardenia) and monocots (Crocus) is independent. Furthermore, we completed in vivo production of five types of crocins in E. coli for the first time, which shed light on the industrial production of crocins.

Abstract no.210

Discovery and Characterization of a Bioactive Compound with Anti-Epileptic Activity from Acranthera multiflora

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Epilepsy, a prevalent neurological disorder with a global health impact, necessitates the exploration of innovative therapies. Numerous medicinal herbs have shown promising effects in treating epilepsy. However, the specific bioactive compounds within these herbs responsible for these therapeutic properties remain not fully understood. In this study, twenty traditional herb extracts were screened for anti-epileptic activity using pentylenetetrazole (PTZ)-induced seizure zebrafish model, resulting in the discovery of a potential candidate - Acranthera multiflora. The effectiveness of crude extracts and 26 fractions from A. multiflora in suppressing PTZ-induced seizure-like behavior in 6-dpf zebrafish larvae was measured. Our results revealed that the crude extract notably reduced hyperactive swimming induced by PTZ in zebrafish larvae. Among all fractions, the semi-purified fraction DM10-04 exhibited the most significant protective effect against PTZ-induced seizures in a dose-dependent manner. Bioassay-guided fractionation and spectroscopic elucidation of DM10-04 isolated and identified Asiatic acid, known for neuroprotective, anti-inflammatory, antioxidant, and wound healing properties. Asiatic acid (3 μg/mL) exhibited anti-epileptic activity comparable to the positive control drug, valproic acid. While further research is necessary to elucidate its antiepileptic mechanism, Asiatic acid's potential as an antiepileptic drug candidate is undeniable. This study demonstrated, for the first time, the significant anti-epileptic potential of A. multiflora and its active compound, Asiatic acid, providing a validated strategy for developing novel anticonvulsant drugs for epilepsy treatment. Keywords: Anti-epileptic, bioassay-guided fractionation, neurological disorder Acknowledgement: We would like to acknowledge the collaboration with the University of Macao and The Hong Kong Polytechnic University in this research. We express our gratitude to the Sarawak Government and Sarawak Biodiversity Centre for their support in this project.

Abstract no.211

The application of the TREM2 podocyte damage in chronic kidney disease

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Purpose The aim of this study is to explore the potential mechanism of pyroptosis-related genes in podocyte injury and its relationship with immune inflammatory response, to identify the role and mechanism of new diagnostic biomarkers in podocyte injury in chronic kidney disease in vivo and in vitro, and to provide new targets and ideas for its treatment. Methods CKD-PE-IM target genes were screened from Immport of immune gene set by downloading pyroptosis data set from GEO database and MSigDB database. western blot, immunohistochemistry and immunofluorescence were used to verify the differential abundance of target genes in vivo. The core compounds were further screened based on Coremine medical database, and the binding sites were predicted by molecular docking, which was verified in vitro. Results We finally identified TREM2 as the core target gene of CKD-PE-IM, and TREM2 was upregulated when podocytes were injured. In addition, molecular docking results showed that gallic acid and quinic acid can bind to TREM2. Conclusion Our results indicate that TREM2 is the core target gene of CKD-PE-IM, and gallic acid and quinic acid have good predictive binding efficiency with TREM2. Gallic acid is a potential drug to improve the immune and inflammatory mechanisms of CKD by affecting inflammation and podocyte pyroptosis. Keywords Podocytosis, Biomarkers, Gallic acid, TREM2

Abstract no.212

Identification of Descurainiae Semen and Lepidii Semen by thin-layer chromatography and high-performance liquid chromatography

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The traditional Chinese medicine Descurainiae Semen and Lepidii Semen (Chinese pinyin: Tinglizi) is a remedy with thousands of years of history in treating cough and asthma in China, and its traditional efficacy is to diarrhea the lungs and relieve asthma, and to move water to eliminate swelling. Modern pharmacological studies have shown that it has anti-inflammatory, antibacterial, antitumor, antitussive, antitussive, asthma, diuretic, and improves cardiovascular function. Tinglizi contain two varieties, Descurainiae Semen is the dried seeds of Descurainia sophia (L.) Webb. ex Prantl. and Lepidii Semen is the dried seeds of Lepidium apetalum Willd., they look similar in appearance, making it difficult to differentiate them. Currently, there are no qualitative and quantitative methods specified for Lepidii Semen in the existing standard. Furthermore, there is no systematic research on whether there are differences in the chemical components of these two varieties and why they exhibit such similar pharmacological effects. In this study, the same high-performance liquid (HPLC) method was used for the comparative analysis of constituents in Descurainiae semen and Lepidii semen, and their structures were identified by LC-MS, to establish their respective HPLC characteristic chromatogram. Test solutions were prepared by sonication with 50% methanol in water. The separation was performed on an NanoChrom HP AQ C-18 column (250 mm×4.6 mm, 5μm) at 35 ℃ column temperature, The flow rate was 1.0 mL·min-1, the detection wavelength was 220 nm. As a result, A total of 13 peaks were identified, 9 constituents were identified from Lepidii Semen, 4 constituents were from Descurainiae Semen, and sinapine thiocyanate was the common component in both. Additionally, desulfobenzylglucosinolate, desulfoglucoerucin and duercetin-3-O-β-D-[2-O-(6-O-sinapoyl)-β-D-glucopyranosyl]-glucopyranoside were the more abundant and characterized constituents in the Lepidii Semen, In contrast, glucocappasalin and quercetin-3-O-β-D-glucose-7-O-β-D-gentiobioside were the more abundant and characterized constituents in Descurainiae Semen. The results of this study provided references for the selection of index components in quality standard research and subsequent pharmacological studies of the two species. Keywords: Descurainiae semen; Lepidii semen; high-performance liquid chromatography; characteristic compounds

Abstract no.213

Investigation on the anti-metastatic effects of Eriocalyxin B derivative compound 38S in colon cancer

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Colorectal cancer (CRC) is the third most prevalent cancer worldwide1. Metastasis of CRC is the leading cause of CRC-related death and remains a serious problem even with Western conventional therapies2. Therefore, discovering more effective therapeutic agents for treating CRC metastasis is still urgently needed. Eriocalyxin B (EriB), a natural ent-kaurene diterpenoid isolated from Isodon eriocalyx var. laxiflora, has been demonstrated to exhibit broad spectrum anti-tumor activities including CRC3. We recently found that EriB has anti-metastatic and immunomodulatory activities in breast cancer4. Being chemically modified with improved solubility, a derivative of EriB known as compound 38S was generated. This study aimed to evaluate the anti-metastatic effect of compound 38S on colon cancer in preclinical models. The in vitro effects of compound 38S on cell proliferation, motility and migration were assessed on human colon cancer LoVo cells and murine colon 26 cells using MTT, BrdU, colony formation, scratch wound healing and transwell migration assays. The in vivo anti-metastatic effect of 38S was examined in orthotopic colon tumor-bearing mouse model. Our results demonstrated that compound 38S exhibited around 2-fold more potent cytotoxicity than EriB on LoVo and colon 26 cancer cells. Compound 38S also significantly exhibited anti-proliferative activities in these cancer cells. Besides, the motility and migration of LoVo cells and colon 26 cells could be significantly inhibited by compound 38S at 0.075-0.3 μM and 0.25-1.0 μM, respectively. Furthermore, our preliminary results showed that intraperitoneal administration of compound 38S (4 mg/kg) could suppress tumor growth, lung metastasis and expression of CD31 in colon 26 tumor-bearing mice. Compound 38S also modulated the population of T cells in lymph nodes and the cytokines levels of IL-2, IL-12, IL-10 and IFN-γ of spleen lymphocytes. This study suggested the anti-metastatic effects of compound 38S in colon cancer, and its underlying mechanisms will be investigated in the future. References: 1. Bray F, et al. CA Cancer J Clin, 2024, DOI: 10.3322/caac.21834. 2. Hui Z, et al. Signal Transduct Target Ther, 2022. 7(1): 70. 3. Riaz A, et al. Nat. Prod. Commun, 2019. 14(8): 1-9. 4. Gou L, et al. Biochem Pharmacol, 2023. 210, 115491.

Abstract no.214

Development of an Herbal Product Containing CBD and Brahmi Extracts for Stress and Anxiety Relief.

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Global trends indicate a rising incidence of stress and anxiety, with research demonstrating the effectiveness of natural products in treating these conditions. Cannabidiol (CBD), a non-psychoactive compound, and Brahmi (Bacopa monnieri) extract are known for their potential to relieve these symptoms. This research focuses on developing a herbal product containing CBD as an active ingredient and includes Brahmi extract to enhance the product's effectiveness, providing an option for stress and anxiety relief. The product is currently undergoing stability studies.

Abstract no.215

Development of Sinomenine Derivatives for Counteracting Methotrexate-resistance in Rheumatoid Arthritis

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2. Dr Jerome Pak Lam Ng, Macau University of Science and Technology, Macao SAR

Rheumatoid arthritis (RA), a systemic autoimmune disease that leads to polyarthritis of joints and disorder of multiple organs, affects around 0.5% of the world population. Current therapeutic approaches can only suppress disease progression without addressing the root cause, and long-term chemotherapy often leads to the development of drug resistance in RA. Our preliminary results found elevated expression of P-glycoprotein (P-gp) in the peripheral blood mononuclear cells (PBMCs) of RA patients, and its up-regulation was partly associated with the resistance to methotrexate (MTX), a front-line drug for treating RA. Therefore, targeting P-gp-induced drug efflux may be a promising strategy to reverse drug resistance in RA. In addition, our preliminary results also showed that the TCM-derived natural product, sinomenine, can inhibit both wild-type and mutants of P-gp overexpressing rheumatoid arthritis fibroblast-like synoviocytes (RAFLSs), whereas other known P-gp inhibitors failed to effectively inhibit mutants of P-gp. Although sinomenine is a promising compound for treating RA, its limitations such as poor bioavailability hinder its further application. Herein, we reported the structural modifications of sinomenine to improve its P-gp inhibitory effect and reverse drug resistance to MTX. In this study, a series of sinomenine derivatives was prepared from sinomenine by organic synthesis at various positions. All synthesized derivatives generally exhibited a low cytotoxicity (IC50 >100 μM) in normal cell lines. In vitro MTX-efflux model also revealed that most derivatives, especially derivative 2, had a better P-gp inhibitory effect than the parent compound sinomenine. Further in vivo study demonstrated that co-treatment of 2 with MTX obviously ameliorated arthritis conditions in P-gp transgenic AIA rat model, while cotreatment with sinomenine was ineffective to suppress drug resistance at a low dose. Extensive studies on the development of a newer generation of sinomenine derivatives are still in progress. Grant support: This project was funded by The Science and Technology Development Fund, Macau SAR (File no.: 002/2023/ALC).

Abstract no.216

Celastrol derivatives improve inflammatory arthritis in AIA rats and reduce biotoxicity

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Celastrol (CEL), a natural product isolated from herbaceous plants, is widely known as a potential drug for the treatment of rheumatoid arthritis (RA), but its high toxicity and narrow therapeutic window severely limit its clinical application. To reduce its toxicity and optimize its physicochemical properties, structural modification of CEL is an effective strategy to reduce its off-target toxicity. In this study, six CEL derivatives, especially COM5 and COM6, showed low cytotoxicity against LO2 and BEAS-2B in normal cells. And they were effective in inducing/rheumatoid arthritis fibroblast-like synoviocytes (RAFLS) to undergo autophagic death. Reduced the expression of TNF-α, IL-1β and IL-6 inflammatory factors in macrophage cells RAW264.7. Meanwhile, these two derivatives were as effective as CEL in improving the arthritic condition of AIA rats, reducing bone destruction and bone damage, and restoring immune cell homeostasis in AIA rats, but with significantly lower toxicity. What's more, our toxicity test in ICR mice showed that COM5 and COM6 are at least 10 times less toxic than the parent compound CEL, which has a good safety profile. In conclusion, these findings demonstrate that CEL derivatives possess lower in vivo and in vitro toxicity, can reduce arthritis symptoms and inflammatory responses by inducing autophagic cell death in RAFLS cells and, in AIA rats, can achieve therapeutic benefits for RA, reduce the toxicity of CEL, and increase the window of safety of the drug. Keywords: Rheumatoid arthritis; Celastrol; AIA; derivatives; acute toxicity assay. Funding information: Macao Science and Technology Development Fund, Grant/Award Numbers: 0005/2023/RIA1 and 002/2023/ALC

Abstract no.217

Lycorine attenuates microglia inflammation after cerebral ischemia by inhibiting NF-κB pathway

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Lycorine, the first active alkaloid isolated from Narcissus in 1877, is the main active alkaloid in most Amaryllidaceae plants, and its chemical molecular structure and biological function have been widely studied. In this study,we examined the anti-neuroinflammatory effects of lycorine after IS and assessed whether this effect is mediated through modulation of the NF-κB signaling. In this study, Lyc acts on LPS stimulated astrocytes in BV2 cells, and it was found that Lyc can inhibit BV2 cell polarization and reduce the level of inflammatory factors, confirming that Lyc has anti-inflammatory effects through NF-κκB pathway in vitro.Meanwhile, lyc can alleviate the symptoms of cerebral infarction in IS rat models and reduce inflammation levels. Through in vitro and in vivo experiments, it has been confirmed that Lyc can inhibit the NF - κ B signaling pathway, suppress inflammatory symptoms, alleviate cerebral ischemia, and promote disease prognosis. In summary, these findings indicate that Lyc has a good anti-inflammatory effect, which can inhibit inflammation levels by inhibiting NF - κ B, and in MCAO rats, it can achieve therapeutic benefits of IS, alleviate brain infarction rate in rats, and improve disease prognosis of IS. Meanwhile, it has expanded the modern clinical application of LYC.

Abstract no.218

Evaluation of percutaneous transdermal behavior of coumarin 6 nanogel with different properties in psoriatic skin

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Psoriasis is a chronic inflammatory skin disease with a high incidence worldwide. Percutaneous drug delivery system has become the first choice for psoriasis treatment because of its high efficiency, safety and direct targeting of the lesions. Nanomedicine can significantly improve the efficiency of percutaneous drug delivery and has been widely used in the treatment of psoriasis in recent years. Coumarin 6 (C6), as a stable fluorescent probe, is often used for visual tracking of the distribution of nanomedicine in vivo. Psoriasis causes epidermal hyperplasia of the skin and changes in the skin barrier that may result in different penetration behavior than healthy skin. In this study, C6 Poly (co-glycolic acid) (PLGA) NPs with negative charge of 50, 100 and 500 nm and positive charge of 100 nm were prepared. Utilizing carbomer gel as the drug carrier, both psoriatic skin and healthy skin were selected as models. It is intended to compare the transmission and retention of nanomedicine with different properties, and investigate the transmission behavior in pathological state, so as to guide the design of the preparation. After the in vitro transdermal experiment, frozen skin sections were prepared and observed by laser confocal scanning microscope (CLSM) to qualitatively analyze the transdermal effect of C6-PLGA-NPs. As shown in Figure 1, the skin permeability of C6-PLGA-NPs is higher than that of free drugs, while the skin permeability of small size NPs is higher than larger ones. In addition, more accumulation of large size C6-PLGA-NPs were found in psoriatic skin than that in healthy skin. Positive charged NPs had no significant effect on drug penetration. As shown in the CLSM results in Figure 2, the fluorescence of the psoriatic skin was significantly enhanced compared with that of the healthy skin, indicating that NPs group could penetrate the epidermis of the psoriatic skin to reach the dermis, while in the healthy skin more accumulated in the epidermis, further confirming that the occurrence of psoriasis enhances the permeability of the skin.

Abstract no.219

Efficiently find new compounds in Tall Gastrodia Tuber (Tianma) by combined molecular networking analysis and target separation

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Tall Gastrodia Tuber (Tianma, the tubers of Gastrodia elata Bl., TM) is a well-known Chinese materia medica with the medicinal efficacy on multiple human diseases, in particular neurological disorders. However, the bioactive compounds are not fully known in TM. This study focused on rapid and efficient finding new compounds in TM employed the modern and advanced mass-spectrometric techniques.

A new method for finding new compounds in complex chemical sample was developed by combining molecular networking (MN) analysis with targeted separation. This method included four steps. Firstly, tandem MS data were acquired in guidance of scheduled precursor lists (SPLs) containing specific MS1 features. Secondly, the potential new compounds were predicted by MN analysis. Thirdly, the predicted new compounds were targeted separated under the monitoring of retention time and mass-to-charge ratio to obtain monomeric compounds. Fourthly, the chemical structures of monomeric compounds were elucidated by MS and NMR data.

By this developed method, Tianma sample was extracted, analyzed and targeted separated. 10 new aromatic compounds were obtained and identified as (1) {1,6-di-[4'-(1-O-β-D-glucopyranosyl)benzyl],5-ethyl}citrate, (2) 1,6-di-[4-(1-O-β-D-glucopyranosyl)benzyl]isocitrate, (3) 7-[4-hydroxy-3-(4-hydroxybenzyl)benzyl] gastrodin, (4) 7-lactyl-gastrodin, (5) 6'-lactyl-gastrodin, (6) 7-O-[(4-hydroxybenzyloxy) -4-hydroxybenzyloxy]gastrodin, (8) 6'-[4-hydroxy-3-(4-hydroxybenzyl) benzyl] gastrodin, (9) 7-[4-hydroxy-3-(4-hydroxybenzyl)benzyl] gastrodin and (10) gastropolyphenol A.

The developed new method is demonstrated to be accurate and rapid to find new compounds in complex herbal sample. The optimized LC-MS/MS acquisition guided by SPLs improves the quality of data and reduces the redundancy nodes of MN, which leading to more accurate and rapid predicting new compounds.

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Abstract no.220

An Innovative Natural Nanomaterial-Based Method for Efficient Enrichment of Small RNAs

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Small RNAs, a class of non-coding RNA molecules less than 200 nucleotides in length, include ribosomal RNA fragments, tRNAs and their derived small RNA fragments (tsRNAs), miRNAs and etc. tsRNAs exhibit crucial biological activities such as regulation of gene expression, participation in immune response, and promotion of apoptosis. Thus, characterization of small RNAs would help better understand the disease pathogenesis intervened by traditional Chinese Medicine and aid in the discovery of new therapeutic targets. Unfortunately, although current methods for small RNA extraction are commercially available, their efficiency in enriching tsRNAs is too low to obtain comprehensive information, making them unsuitable for downstream investigations. To address this, our lab developed a novel method for extracting and enriching small RNAs using a natural nanomaterial. Initially, samples are lysed with a 4 M guanidine thiocyanate buffer for 10 minutes. The lysate is then incubated with the nanomaterial for 20 minutes to capture RNA molecules, followed by elution with a special buffer for 20 minutes to obtain small RNAs (<200 nt). Compared to the classical TRIzol extraction method, this new approach offers 50-fold higher efficiency in tsRNA enrichment. This method is simple, fast, cost-effective, and environmentally friendly as it does not involve toxic reagents. It can be widely applied to various samples, including plants, microorganisms, and clinical specimens. In conclusion, the new method we developed significantly benefits downstream investigations of tsRNAs and other small RNAs, thus greatly expanding their research field.

Keywords: tsRNAs, small RNAs, natural nanomaterial

Abstract no.221

Antibacterial activities analysis of secondary metabolites from Streptomyces rhizogenes SYP-A8194 isolated from Panax notoginseng

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3. Dr Meng-Yue Zhang, Shenyang Pharmaceutical University, Shenyang

Objective To investigate the secondary metabolites and their antibacterial activities of Streptomyces rhizogenes SYP-A8194 isolated from Panax notoginseng. Methods Liquid fermentation medium was employed, and a dedicated fermentation tank was utilized for the fermentation process. Subsequently, the resulting fermentation broth was extracted with ethyl acetate. The secondary metabolites of Streptomyces rhizogenes SYP-A8194 were isolated and purified using a combination of silica gel column chromatography,gel column chromatography, ODS column chromatography, reverse phase HPLC and other advanced chromatographic separation techniques. The structures of the compounds were determined through comprehensive analysis of spectral data, identified by spectral data and physical and chemical constants analysis, as well as comparison relevant literature. The antibacterial activities of the compounds were assessed, and the subsequent molecular docking studies were conducted for the compounds exhibiting significant activity. Results Ten compounds were isolated and identified from the fermentation products of Streptomyces rhizogenes SYP-A8194, and their structures were: Cyclo(D-Pro-D-Leu) (1), Cyclo(D-Pro-D-Phe) (2), N-[2-(1H-indol-3-yl)ethyl], acetamide (3), Phomolide C (4), 1,2-benzenedicarboxylic acid dibuty lester (5), Hyacinthacine B4 (6), Sargassopenilline F (7), butyl 2-methylpropyl ester (8), Estra-1,3,5(10)-trien-l7-one (9) and 7,4'-dihydroxy isoflavone (10). The antibacterial experimental results demonstrated that compound 7 exhibited the most potent bactericidal activity against Staphylococcus aureus, reaching MIC 4.2 μg/ml. The compound 7, which exhibited the highest activity, was subjected to network pharmacology and molecular docking experiments. The docking results revealed that compound 7 exhibited strong binding affinity towards heat shock protein 90 α alpha family class A member 1 Gene (HSP90AA1) with a with a remarkable binding energy of -112 kcal/mol. This suggests that compound 7 has the potential to interact with the bacterial surface and subsequently translocate into the cytoplasm. By competitively binding to heat shock proteins, it effectively impedes the processing and folding of numerous immature proteins facilitated by chaperone proteins, thereby demonstrating potent antibacterial activity. Conclusion Streptomyces rhizogenes SYP-A8194 exhibits promising research potential in the synthesis of antibacterial lead compounds. Key words: Panax notoginseng ; Streptomye sp.; Secondary metabolites; Antimicrobial activity; Heat shock proteins; Molecular docking

10. Acupuncture, Massage, Exercise, Mind & Body

Abstract no.222

Transcutaneous Auricular Vagus Nerve Stimulation Improves Gastric Emptying and Visceral Hypersensitivity in Functional Dyspepsia via Cholinergic Anti-inflammatory Pathway

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3. Dr Shaoyuan Li, China Academy of Chinese Medical Sciences, Beijing
4. Dr Bowen Feng, China Academy of Chinese Medical Sciences, Beijing
5. Dr Juan Han, China Academy of Chinese Medical Sciences, Beijing

Objective: Gastric dysmotility and visceral hypersensitivity are major pathophysiological factors of functional dyspepsia (FD). Transcutaneous auricular vagus nerve stimulation (taVNS) was recently reported to ameliorate these symptoms in patients with FD with largely unknown mechanisms. This study used a well-established rodent model of FD for evaluating whether taVNS can improve gastric emptying and visceral hypersensitivity compared with subdiaphragmatic vagus nerve stimulation (SDVNS) and exploring relevant mechanisms. Methods: A total of 60 young SD rats were subjected to gastric injection of iodoacetamide (IA) at the neonatal stage, and randomly divided into IA, taVNS, SDVNS, sham SDVNS, subdiaphragmatic vagotomy (SDV) and SDV+taVNS groups and received treatments for 2 weeks. Visceral hypersensitivity was assessed by abdominal electromyography (EMG) in response to gastric distension. After intervention, gastric and duodenal tissues were harvested for assessment of acetylcholine (ACh), motilin (MTL), nicotinic acetylcholine receptor α7 subunit (α7nAChR), Interleukin (IL)-6, IL-1β, tumor necrosis factor-α (TNF-α), nuclear factor-kappa B (NF-κB) p65, and transient receptor potential vanilloid 1 (TRPV1). Results: Compared with control rats, neonatal IA delayed gastric emptying and induced visceral hypersensitivity ($P < 0.001$). taVNS significantly improved visceral hypersensitivity and gastric emptying in IA rats ($P < 0.001$), with effects similar to SDVNS ($P > 0.05$). Promotility effect of taVNS was attributed to normalization of ACh and MTL levels. Analgesic effect of taVNS was mediated via the cholinergic anti-inflammatory pathway (CAP) reflected as enhanced release of ACh, suppression of IL-6, IL-1β, and TNF-α in duodenum and gastric TRPV1 (all $P < 0.001$). Involvement of CAP pathway was further supported by up-regulation of α7nAChR ($P < 0.001$) and down-regulation of NF-κB p65 ($P < 0.01$). Conclusion: Noninvasive taVNS improves both gastric dysmotility and visceral hypersensitivity in FD rats, with effects comparable to those of SDVNS. Its prokinetic activity and analgesic effect are attributed to the activation of CAP.

Abstract no.223

A Special Report on Acupuncture and Medicine Combination in Treating Different Types of Insomnia

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Abstract Purpose: By reviewing the literature on insomnia of different types, we can obtain the acupuncture points and prescriptions for treating each type, so that we can select appropriate treatment plans more effectively clinically and improve the quality of life and physical and mental health. Methods: Search China National Knowledge Infrastructure (CNKI) from 2013 to 2023 for the five types included in the insomnia chapter formulated according to the "Diagnostic and Efficacy Standards of Traditional Chinese Medicine Diseases and Syndromes" formulated by the State Administration of Traditional Chinese Medicine, including deficiency of the heart and spleen, deficiency of heart and gallbladder qi, and deficiency of yin and excess of fire. , phlegm-heat internal disturbance, liver stagnation transforming fire, search for "insomnia", "heart and spleen deficiency", "heart and gallbladder qi deficiency", "yin deficiency and excessive fire", "phlegm-heat internal disturbance", "liver stagnation transforming fire", "acupuncture" "needle" Clinical literature with keywords such as "acupuncture and drug combination" and "acupuncture and drug combination" were searched for relevant literature, and the literature on acupuncture and drug combination treatment for the above syndromes was summarized and summarized. Result: A total of 5 literatures were obtained on the syndrome of both the heart and spleen, and 20 acupoints were identified. The most frequently used acupoints were Xinshu and Pishu , the most commonly used prescription is Guipi tang. A total of 6 literatures were obtained on the syndrome of hyperactivity of fire due to yin deficiency, and 13 acupoints were identified. The most frequently used acupoints were Xinshu, Shenshu, Taixi, and Zhaohai, the prescriptions are Jiaotai Wan, Huanglian Ejiao Tang, Tianwang Buxin Dan, Guyuan Ningshen Tang, etc. A total of 1 literature was obtained on the syndrome of qi-deficiency of heart and gallbladder, and 9 acupoints were identified. The most frequently used acupoints were Xinshu, Danshu, Shaochong, Zhaohai, Shenmai, and Qiuxu, the prescriptions are Anshen Dingzhi Pill. A total of 2 literature were obtained on the syndrome of internal disturbance of phlegm-heat, and 7 acupoints were identified. The most frequently used acupoints were Zusanli, Zhigou, and Fenglong, the prescriptions are Jiawei Wendan Tang. A total of 8 literature were obtained on the syndrome of liver depression transforming fire, and 16 acupoints were identified. The most frequently used acupoints were Xingjian, Taiheng, Fengchi, and Zusanli, The prescriptions are Longdan Xiegan Tang and Danzhi Xiaoyao San. Overall speaking, according to literature of research statistics, Shenmen, Sanyinjiao, Baihui, Sishencong, Neiguan, and Anmian are the six acupoints most frequently used in insomnia. Conclusion: Acupuncture combined with traditional Chinese medicine treatment is more effective in improving patients' sleep quality, enhancing treatment effectiveness, and alleviating the accompanying symptoms. The combined use of both is more superior than simply using acupuncture or traditional Chinese medicine treatment alone. Both acupuncture and traditional Chinese medicine can regulate neurotransmitters and cytokines invloved in the sleeping mechanism.

Abstract no.224

The immediate modulatory effects of transcutaneous auricular vagus nerve stimulation on mild cognitive impairment by rs-fMRI

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Objective: To explore changes in brain activation patterns after immediate transcutaneous auricular vagus nerve stimulation (taVNS) on mild cognitive impairment (MCI) by resting-state fMRI (rs-fMRI). Methods: 22 MCI patients and 11 healthy controls (HCs) were enrolled into this study. Subjects in taVNS group underwent mild electric stimulation applied to the concha of their bilateral outer ears, whereas sham taVNS group received the same procedure in the scapha of their bilateral outer ears. The duration of stimulation lasted for 30 minutes. HCs group did not receive any stimulation. All MCI patients underwent rs-fMRI prior to and post the administration of stimulation, while HCs were scanned once. Data of rs-fMRI preprocessing and analysis were performed using DPABI 8.0 to calculate the fractional amplitude of low frequency fluctuations (fALFF). The rs-fMRI results of baseline were utilized to conduct one-way ANOVA. And the rs-fMRI results of before and after the stimulation were used ANCOVA. Finally, a pot hoc analysis was performed on these results to obtain differences between groups. Results: In this study, we observe that fALFF of the left anterior cingulate cortex (ACC) and right caudate in MCI patients significantly reduced compared to HCs at baseline. After stimulation, both the fALFF of the bilateral ACC in taVNS group significantly increased compared to sham taVNS group. Conclusion: Immediate taVNS modulates the function of ACC in MCI, and ACC may be the target brain regions for taVNS treatment on MCI. Keywords: mild cognitive impairment; taVNS; immediate modulatory; rs-fMRI Acknowledgment: Thanks to Beijing Municipal Natural Science Foundation (No.7212191) for its support.

Abstract no.225

Efficacy and safety of Tuina and its combination therapy in patients with knee joint sports injuries: A systematic review and meta-analysis

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Abstract: Objective: To systematically evaluate the efficacy and safety of Tuina and its combination therapy in patients with knee joint sports injuries. Methods: Eight databases at home and abroad were searched to collect data of randomized controlled trial (RCT) with respect to Tuina for knee joint sports injuries. We screened all literature and extracted data based on the inclusion and exclusion criteria. The data were analyzed using Revman 5.3 statistical software. The included literatures were assessed for methodological quality using the Physiotherapy Evidence Database Scale (PEDro). INPLASY registration number: INPLASY202170066. Results: A total of 19 eligible randomized controlled trials (RCTs) involving1670 patients were included. There were 18 studies exceeded the PEDro cut-off score of 6 (included 6). Meta-analysis showed that the overall efficacy rate of Tuina and its combination therapy was higher[OR, 6.39; 95% CI, (4.32, 9.46) ; Z = 9.27; P < 0.00001], VAS score was decreased[SMD, −2.27; 95% CI, (−3.59, −1.96) ; Z = 6.68, P < 0.00001], and LKSS score was significantly improved[SMD，1.69；95%CI, (1.18, 2.19)；Z = 6.53，P < 0.00001] compared with the control group. Conclusion: Existing evidence indicates that Tuina and its combination therapy demonstrate superior clinical efficacy and greater safety in patients with knee joint sports injuries. Key words: Tuina; knee joint sports injuries; systematic review; Meta-analysis

Abstract no.226

Manual Therapy Reduces Muscle Inflammation in Rats with Knee Osteoarthritis by Regulating PD-1/PD-L1 Pathway

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2. Mr Yifei Xu, Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai

Objective: To investigate the effectiveness of manual therapy on knee osteoarthritis (KOA) and explore the potential mechanisms underlying its beneficial effects. Design: This study combined the gene analysis and the animal experiment. The gene analysis is originated through the Gene Expression Omnibus (GEO) database. Thirty-two male Sprague-Dawley (SD) rats weighing between 180-220 g were randomly assigned to four groups: Sham group (Sh), Model group (Mo), Manual therapy group (MT), and Manual therapy Anti-PD-L1 group (MTA) on average. The KOA model was induced by monosodium iodoacetate injection. The behavioral changes of rats were assessed using the mechanical withdrawal threshold (MWT) and paw withdrawal thermal latency (PWL). In addition, the enzyme-linked immunosorbent assay (ELISA) was performed as well. Results: The gene analysis shown that the people with serious conditions of KOA have gene expression variation in the skeletal muscle around the joint. In animal study, compared with the Model group, the MWT and PWL of the Manual therapy group showed significantly increased MWT and PWL ($P < 0.05$) and significant lower the knee joint evaluation levels according to Lequesne MG ($P < 0.05$). The expression of PD-1/PD-L1 pathway is significantly correlated with the MWT and PWL, as well as the cytokines IL-10, IL-1β, IL-6, TNF-α expression in both blood and muscle. Conclusions: Manual therapy may exert analgesic effects in KOA rats by inhibiting the secretion of pro-inflammatory cytokines in muscles and blood, likely through modulation of the PD-1/PD-L1 pathway.

Abstract no.227

Electroacupuncture modifies inflammation levels and metabolites in ischemic stroke patients.

1. Dr Yu Chen Lee, China Medical University Hospital, Taichung

Introduction: This study aimed to evaluate the impact of EA in early ischemic stroke as a modulator of CHOL-t, HDL-c, and LDL-c in the blood, and its anti-inflammatory effect measured through individual levels and lipid indices before and after treatment with EA. Material and method A total of 14 patients with a first-time stroke diagnosis will be randomly assigned to one of two groups: an EA group and a sham EA group. All patients received the interventions three times a week for six sessions over two weeks. Outcome measurements included blood tests for total cholesterol, triglycerides, HDL with HDL-c cholesterol, LDL cholesterol, and LDL-c, along with the visual analog scale (VAS), the National Institutes of Health Stroke Scale (NIHSS), and the Barthel scale. index (BI)) and Friedwald formula. Results: A real EA group (5 cases) and a second sham or placebo group (5 cases). 2 patients did not complete all examinations. Our sample of patients has moderate, low HDL, and high LDL levels; average blood lipid levels: (CHOL-t (169), HDL c (40.75), LDL c (107), TG (112)) compared to ACC and AHA indices. The average blood lipid levels are: CHOL/HDL (4), LDL/HDL (3), TG/HDL (3), and LDL/BMI (5) correspond to moderate levels compared to the ACC and AHA indices. The acupuncture group had an average EA (differential formula: initial time-final time) of 1.3804 mg/dL compared to the Sham cases, which was 0.08 to 0.83. mg/dL. The Standard Deviation (σ) obtained is 0.64, comparing before and after the intervention. Conclusion: This study will help determine the effect of EA on ischemic stroke, focusing on metabolic changes early in the diagnosis. Treatment with EA could modify the risk indices (HDL-c), maintain or control (LDL-c), and generate localized reperfusion of the vascular areas involved in the stroke.

Abstract no.228

Efficacy of Laser Acupuncture Treatment on Sleep Disturbances: A Randomized Clinical Trial

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2. Prof Yu-Pei Chen, Tainan Hospital, Tainan

3. Dr Ang-Jun Liu, Tainan Hospital, Tainan

Objective: This study aimed to evaluate the effectiveness of laser acupuncture treatment on sleep disturbances in middle-aged adults through a randomized clinical trial. Methods: A one-year randomized clinical trial was conducted with participants aged 40-60 years who had sleep disturbances persisting for more than one month. Forty participants were randomly assigned to either an experimental group (n=20) or a control group (n=20). The experimental group received laser acupuncture treatment at Taichong, Shenmen, and Neiguan points twice a week for three weeks, along with sleep hygiene guidance. The control group received subcutaneous laser acupuncture at non-therapeutic points twice a week for three weeks and received sleep health guidance. All participants underwent pre-test and post-test assessments, including polysomnography (PSG) for sleep evaluation. Results: Data from physiological sleep examinations were collected and analyzed before and after the intervention. Key metrics included heart rate during various sleep stages, PLM (Periodic Limb Movement) indices, and other sleep-related physiological parameters. Conclusion: The results of this study will provide insights into the efficacy of laser acupuncture on sleep disturbances, potentially offering a non-pharmacological intervention for improving sleep quality in middle-aged adults.

Abstract no.229

Effect of Transcutaneous Auricular Vagus nerve Stimulation on Insular Subregion Functional Connectivity of Functional Dyspepsia—A fMRI Study

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2. Ms 屹 罗，中国中医科学院广安门医院，北京

Background: Brian-gut axis dysfunction is the main pathological mechanism of functional dyspepsia (FD). Studies have shown that insula is the key brain region of FD central abnormality. This study aimed to explore the regulatory effect of taVNS on the whole brain functional connectivity (FC) of the ventral anterior insula (VAI), dorsal anterior insula (DAI) and posterior insula (PI) of FD. Methods: The resting state functional magnetic resonance imaging (rs-fMRI) data of 21 FD subjects before and after 8-week transcutaneous auricular vagus nerve stimulation (taVNS) intervention and 30 healthy subjects (HC) were analyzed. Results: Before treatment, the FC values of left DAI and the left medial frontal gyrus were higher in the FD group than that in the HC group. After 8 weeks of taVNS intervention, the FC values of insula and the whole brain were widely decreased, and the main regulated insula subregions were anterior insula, including VAI and DAI, and the regulated functional connection related brain regions were mainly including middle frontal gyrus, precuneus and lingual gyrus. Conclusion: There is abnormal functional connection between anterior insula and default network in FD, and taVNS can regulate the functional connection between anterior insula and default network and visual network, which may be the potential target of taVNS in the treatment of FD.

Abstract no.230

Effects of Acupuncture on Surgical Scar-related Discomfort: A Case Report

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2. Dr Daniel Chen, China Medical University, Taichung

3. Dr Yen-Chieh Wu, China Medical University, Taichung

Acupuncture analgesia for postoperative pain is a promising treatment. Emerging evidence has shown the association between local or referred discomfort such as pain and tightness and postoperative scar. However, discussions regarding the effects of acupuncture on postoperative scar management are limited. This case report presents a case of tension relief by acupuncture in a 24-year-old male patient with a poorly healing right inguinal scar (approximately 1cm2). This patient has experienced discomfort of tightness around his right inguinal region and pelvis for one year after receiving a laparoscopic appendectomy, simultaneously combined with low back pain. The visual analogue scale (VAS) was 5 before receiving acupuncture. Acupuncture was applied to palpable tenderness points around muscles anatomically correlating to the scar tightness, such as the external oblique abdominis and rectus abdominis muscles. Traditional acupoints on the Liver and Gallbladder Meridians were also used, including LR5, GB27, and GB28. After single-time acupuncture, the patient reported tension relief (VAS=2) lasting for several days. Other effects included peristalsis improvement and backache relief. Acupuncture appears to be potentially effective in providing immediate and safe tension relief in surgical scar tightness. Randomized controlled trials using personalized acupuncture point protocols are necessary to determine their effectiveness and safety.

Abstract no.231

TRANSCUTANEOUS ELECTRICAL CRANIAL-AURICULAR ACUPOINT STIMULATION VERSUS ESCITALOPRAM FOR MILD-TO-MODERATE DEPRESSION: AN ASSESSOR-BLINDED， RANDOMIZED， NON-INFERIORITY TRIAL

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Introduction: Transcutaneous electrical cranial-auricular acupoint stimulation (TECAS) is a novel non-invasive therapy that stimulates acupoints innervated by the trigeminal and auricular vagus nerves. An assessor-blinded, randomized, non-inferiority trial was designed to compare the efficacy of TECAS and escitalopram in mild-to-moderate major depressive disorder. Method: 468 participants received two TECAS sessions per day at home (n = 233) or approximately 10 –13 mg/day escitalopram (n = 235) for 8 weeks plus 4-week follow-up. The primary outcome was clinical response, defined as a baseline-to-endpoint ≥50% reduction in Montgomery-Åsberg Depression Rating Scale (MADRS) score. Secondary outcomes included remission rate, changes in the severity of depression, anxiety, sleep and life quality. Results: The response rate was 66.4% on TECAS and 63.2% on escitalopram with a 3.2% difference (95% confidence interval [CI], 5.9% to 12.9%) in intention-to-treat analysis, and 68.5% versus 66.2% with a 2.3% difference(95% CI, 6.9% to 11.4%) in per-protocol analysis. The lower limit of 95% CI of the differences fell within the prespecified non-inferiority margin of 10% ($P \leq 0.004$ for non-inferiority). Most secondary outcomes did not differ between the two groups. TECAS-treated participants who experienced psychological trauma displayed a markedly greater response than those without traumatic experience (81.3% vs 62.1%, P = 0.013). TECAS caused much fewer adverse events than escitalopram. Conclusion: TECAS was comparable to escitalopram in improving depression and related symptoms, with high acceptability, better safety profile, and particular efficacy inreducing trauma -associated depression. It could serve an effective portable therapy for mild-to-moderate depression.

Abstract no.232

Anti-obesity Effect of Transcutaneous Auricular Vagus Nerve Stimulation via Promoting BCAA Metabolism in Brown Adipose Tissue

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Background: Obesity, characterized by excessive adipose tissue accumulation, poses significant health risks including type 2 diabetes, hypertension, and cardiovascular diseases. Modulating branched-chain amino acid (BCAA) metabolism in adipose tissue offers a potential therapeutic approach to enhance energy expenditure and combat obesity. Objective: This study aimed to investigate the anti-obesity effect of transcutaneous auricular vagus nerve stimulation (taVNS) on diet-induced obese (DIO) rats by promoting BCAA metabolism in adipose tissue. Methods: Male Sprague-dawley rats, aged 3 weeks, were acclimatized and divided into chow or high-fat diet (HFD) groups. DIO rats were further assigned to model (HFD), HFD + taVNS, and HFD + Orlistat groups. taVNS was applied through an electroacupuncture apparatus at the auricular conche (2/15 Hz, 1 mA, 30 min/d, 6times/week) for 6 weeks. Body weight, body mass index (BMI), and food intake were measured weekly. Brown adipose tissue (BAT), inguinal white adipose tissue (iWAT) and epididymal white adipose tissue (eWAT) were collected and weighed. Serum levels of norepinephrine (NE) and leptin were analyzed using enzyme-linked immunosorbent assay (ELISA). Morphological changes in adipose tissues were examined via Hematoxylin and Eosin (HE) staining, and Western Blot (WB) assessed uncoupling protein 1 (UCP1), solute carrier family 25 member 44 (SLC25A44), branched-chain ketoacid dehydrogenase kinase (BCKDK), and protein phosphatase Mg2+/Mn2+ dependent 1K (PPM1K) protein expressions to elucidate taVNS-induced adipose tissue browning mechanism. Results: 6 weeks of taVNS significantly reduced body weight, BMI, iWAT and eWAT content in DIO rats, similar to Orlistat. taVNS increased brown adipose tissue (BAT) content and elevated serum norepinephrine (NE) and leptin levels more than Orlistat. taVNS upregulated SLC25A44 and PPM1K and downregulated BCKDK, increasing UCP1 expression to promote adipose tissue browning. Conclusion: The anti-obesity effect of taVNS on high-fat-diet induced obese rats is related to BCAA metabolism in BAT. Keywords: Transcutaneous auricular vagus nerve stimulation; Obesity; Brown adipose tissue; Branched-chain amino acid

Abstract no.233

The Effects of Tai Chi Combined with Acupressure in Treating Anxiety-induced Insomnia Among College Students: A Randomized Controlled Trial

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Background: This study was to evaluate the efficacy and the optimal treating timing of Tai Chi combined with acupressure in the treatment of anxiety induced insomnia among college students in China mainland. Methods: A total of 126 eligible participants were randomly assigned to three groups: treatment group A (participants treated before sleeping), treatment group B (participants treated after sleeping), and control group C (waiting list group). The treatment groups underwent a 12-week intervention consisting of 24-step Tai Chi exercises and acupressure, while all groups received regular psychological counseling. The primary outcome were the Pittsburgh Sleep Quality Index (PSQI) and the Hamilton Anxiety Scale (HAMA). Secondary outcome included the Generalized Anxiety Disorder-7 (GAD-7) and the Insomnia Severity Index (ISI). Results: The treatment group displayed significant reductions in scale scores compared to the waiting group, and the changes in scale scores during the follow-up period were statistically different between the treatment and waiting groups ($P< 0.05$). Notably, the treatment group before bedtime displayed greater improvement compared to the treatment group after waking up ($P< 0.05$). Conclusions: Tai Chi combined with acupressure demonstrated significant efficacy in the treatment of anxiety-induced insomnia among college students. The intervention was found to be most effective when administered before bedtime. Trial registration: ClinicalTrials.gov, Identifier: ChiCTR2200057003.

Abstract no.234

Early detection of knee osteoarthritis by MRI and deep learning assessment of gait analysis: a multimodal approach

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Abstract Objectives This study aims to develop and validate a predictive model for knee osteoarthritis using MRI and gait analysis, exploring the relationship between knee imaging and gait changes for early osteoarthritis screening. Methods High-resolution MRI is used to analyze microstructural changes in the knee joint's bony and soft tissues. A deep learning model, Lateral Multilayer Perceptron Architecture (LM-UNet), is combined a Multilayer Perceptron (MLP) with a U-Net-based framework, linking local tissue features with patient phenotype. Gait analysis is conducted using the PN3 PRO wireless nine-axis MEMS sensor for precise motion data. This multimodal approach study involved 80 patients from Longhua Hospital, Shanghai University of Traditional Chinese Medicine, focusing on knee osteoarthritis's early development and identification of its biomechanical risk factors. Results This study included a total of 80 participants, each providing a set of sagittal and axial T1/T2-weighted images of the knee joint, comprising 80 slices. These data were randomly divided into training, testing, and validation sets. The LM-UNet model achieved a Dice coefficient of 0.92 and an average IoU of 88.71%. Analysis of changes in knee joint tissue characteristics and gait data before and after acupuncture revealed a significant correlation between imaging and gait mechanics. Changes in joint space width and fluid volume were associated with limb movement and joint torque parameters ($P<0.05$). Additionally, the clinical prediction model constructed using the above AI detection scheme improved the AUC from 0.648, obtained by manual delineation by doctors, to 0.849, and the accuracy from 0.677 to 0.86. Conclusions Through this study, the knee osteoarthritis diagnosis accuracy is increased by combining medical imaging segmentation with gait analysis, and a more precise approach is provided for early detection and auxiliary predictive analysis. Keywords Medical Imaging, Semantic Segmentation, Motion Capture Technology, Knee Joint References 1.Takashima Y T K, et al. Comparison of intraoperative soft tissue balance measurement between two tensor systems in total knee arthroplasty. Knee, 2020, 27(3): 1071-1077. 2.Zhai G, Wang-Sattler R, Hart D J, et al. Serum branched-chain amino acid to histidine ratio: a novel metabolomic biomarker of knee osteoarthritis. Annals of the Rheumatic Diseases, 2010, 69(6): 1227-1231.

Abstract no.235

Electroacupunture treatment for regulating musculoskeletal balance of knee osteoarthritis:a randomized multicenter double-blind clinical trial

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5. Prof 王 拥军, 上海中医药大学附属龙华医院, 上海

Abstract Objective This study aims to evaluate the effectiveness and safety of acupuncture treatment for knee osteoarthritis (KOA), focusing on WOMAC scores, MRI-detected joint effusion improvements, and clarifying the mechanisms associated with acupuncture treatment for osteoarthritis through multi-omics analysis. Methods In a multicenter, randomized, double-blind trial, 480 KOA patients were divided into an acupuncture group or a sham acupuncture group. Over 6 weeks of treatment and 24 weeks of follow-up, evaluation metrics included WOMAC scores, Lequesne indices, Lysholm scores, SF-36 scale scores, six-minute walk tests, joint effusion assessed by MRI, and peripheral blood omics analysis. Results Electroacupuncture intervention significantly improves WOMAC pain scores, joint swelling, and function in the short term, with sustained clinical efficacy and functional improvement during long-term follow-up. Electroacupuncture significantly reduces synovial inflammation and blood flow signals in joint effusion in the knee, and improves inguinal lymphadenopathy, as evidenced by ultrasound showing reduced lymph node volume and improved blood flow signals. MRI assessments demonstrate that electroacupuncture reduces inflammation in the joint cavity and infrapatellar fat pad on the sagittal plane, and improves inflammation in the infrapatellar and surrounding soft tissue spaces on the horizontal plane. Additionally, electroacupuncture enhances overall stability by ameliorating joint instability and balance issues during gait.Regression models reveal that the efficacy of electroacupuncture is closely associated with pain, cartilage defects, meniscal signal abnormalities, gait speed, knee swing angle, and functional scores. Key predictors include gait-knee height (OR, 0.93 [95% CI] 0.90-0.96, P<0.001); gait-walking speed (OR, 1.19 [95% CI] 0.34-4.16, P=0.012); WOMAC-function score (OR, 0.99 [95% CI] 0.95-1.02, P<0.001); WOMAC-pain score (OR, 1.19 [95% CI] 0.34-4.16, P<0.001); tibial cartilage thickness (OR, 6.9 [95% CI] 4.3-9.6, P=0.007); and meniscal signal intensity coefficient (OR, 10.1 [95% CI] 9.8-10.5, P=0.04). Multi-omics studies suggest that Sohingolipid, NK-Kappa B, and Calcium may be potential pathways of the electroacupuncture effect, indicating that its efficacy may be related to the regulation of neuro-smooth muscle contraction and chronic inflammatory immunity. Conclusion Electroacupuncture effectively improves clinical symptoms of pain and joint function in KOA patients, alleviates synovial inflammation, stabilizes trunk and joint stability, and slows disease progression. Correlation analysis based on imaging combined with objective outcome measures suggests that the efficacy of electroacupuncture is closely related to a comprehensive mechanical and imaging evaluation of patients' pain, cartilage defects, meniscal signal abnormalities, gait speed, knee swing angle during walking, and functional scores. Multi-omics studies indicate that the mechanisms underlying the efficacy of electroacupuncture may involve regulating vascular smooth muscle and sphingolipid-related pathways, improving

neuroimmune function, and reducing inflammatory responses and joint damage. Keywords Acupuncture, Knee osteoarthritis, WOMAC score, Joint effusion, MRI, Signaling pathways.

Abstract no.236

Mechanism Investigation of Low-Intensity Focused Ultrasound Intervention on Zusanli (ST36) Point in Sepsis Mice

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2. Dr Xiaozhuo Sun, Capital Medical University, Beijing

3. Mr Chenhao Zhao, Hebei University, Baoding

4. Prof Jiao Liu, Capital Medical University, Beijing

A research team has discovered that electroacupuncture stimulation of the Zusanli acupoint in septic mice can effectively elicit the release of catecholamines from the adrenal glands into the bloodstream, thereby achieving therapeutic effects. The discovery reveals the indirect regulation mechanism of acupuncture and moxibustion,specifically their roles inactivating the vagus nerve and adrenal network. The Low-intensity Focused Ultrasound (LIFU) ,being a non-invasive medical method, not only achieve the stimulation depth of acupuncture and moxibustion but also exerts thermal or or other mechanical effect by precisely focusing specific intensity ultrasound on targeted areas. Our team's research focuses on investigating whether LIFU can have an indirect regulatory effect on the Zusanli (ST36) acupoint in septic mice, while exploring and verifying the indirect regulatory effect of sepsis mediated by intermediate substances (IMS) through the mechanical and thermal effects of LIFU, which activate PIEZO series proteins (mechanosensory proteins) and TRPV series proteins (thermal effector proteins).

Abstract no.237

Evaluating Electroacupuncture for Cognitive Improvement in a Rat Model of Major Depressive Disorder

1. Dr Yuen Shan Ho, The Hong Kong Polytechnic University, Hong Kong SAR

Background: Cognitive impairment is a common symptom experienced by patients with Major Depressive Disorder (MDD) at various stages of the illness. Electroacupuncture (EA) has demonstrated efficacy in reducing depressive symptoms in MDD and improving cognitive function in other neurodegenerative conditions. However, its effects on cognitive symptoms specifically in MDD have not been thoroughly investigated. This study aims to evaluate the potential of EA to alleviate cognitive impairments in a rat model of MDD. Methods: Male Sprague-Dawley rats were assigned to one of three groups: (a) sham (sesame oil only), (b) corticosterone injection only (CORT only), and (c) corticosterone injection with EA (CORT+EA). To induce depressive-like behaviors and cognitive symptoms, rats received daily subcutaneous injections of corticosterone (CORT) (40 mg/kg) for 6 weeks. EA treatment began 2 weeks after the commencement of CORT administration, targeting the acupoints Baihui (DU20), Zusanli (ST36), and Yintang (EX-HN3). The burrowing test and the novel object recognition (NOR) test were conducted during the final week of treatment. Results: Although EA treatment did not reverse the corticosterone-induced adrenal gland shrinkage, the CORT+EA group exhibited significant improvements in both the burrowing and NOR tests compared to the CORT group. EA treatment enhanced daily living activities in the burrowing test and showed promise in improving cognitive function as indicated by the NOR test. Conclusion: This study suggests that EA is a viable complementary treatment within the long-term corticosterone model of MDD. EA demonstrates significant potential to mitigate cognitive dysfunction in MDD patients, warranting further exploration as a therapeutic intervention. Keywords: Corticosterone, Electroacupuncture, Cognitive dysfunction Acknowledgment: This study was supported by the Health Medical Research Fund (20212801) awarded to YSH.

Abstract no.238

Systematic Review of Acupuncture for Primary Insomnia: Efficacy， Safety， Mechanisms， and Clinical Recommendations

1. Dr Yuen Shan Ho, The Hong Kong Polytechnic University, Hong Kong SAR

Background: Primary insomnia (PI) is a growing concern in modern society. While cognitive-behavioral therapy for insomnia is the first-line recommendation, its limited availability and high costs impede widespread use. Hypnotics are frequently prescribed but come with significant risks of adverse events. This review explores acupuncture as a treatment for PI, summarizing clinical and preclinical evidence, discussing potential mechanisms, and providing recommendations for clinical practice. Methods: Clinical trials indicate that acupuncture improves subjective sleep quality, reduces fatigue, mitigates cognitive impairments, and alleviates emotional symptoms with minimal adverse events. It positively affects objective sleep parameters, including increased total sleep time, improved sleep efficiency, reduced sleep onset latency and wake after sleep onset, and enhanced sleep architecture (e.g., increasing N3% and REM%, while decreasing N1%). However, methodological shortcomings in some trials reduce the overall quality of evidence. Results: Animal studies suggest that acupuncture restores circadian rhythms in sleep-deprived rodents and improves their performance in behavioral tests. These effects may be mediated by several clinical variables and pathways, including neurotransmitters, brain-derived neurotrophic factors, inflammatory cytokines, the hypothalamic-pituitary-adrenal axis, gut microbiota, and other cellular events. Conclusion: Existing findings support acupuncture as a promising therapeutic strategy for PI, but additional high-quality trials are necessary to validate its benefits. The review underscores the potential mechanisms through which acupuncture may exert its effects, providing a comprehensive overview of its role in treating primary insomnia and offering recommendations for clinical practice. Keywords: Acupuncture, Complementary and alternative medicine, Sleep, Insomnia, Mechanisms, Melatonin, Inflammation, Microbiota Acknowledgments: This work was supported by the Shanghai Key Laboratory for Pharmaceutical Metabolite Research Project [SHZYDX2023-01] and the University's scientific research project, Shanghai Sanda University [2021zz02-yj] to FY-Z; the National Key R&D Program of China [2021YFC2501500] to WJ-Z; the Construction of Non-pharmacological TCM Treatment of Insomnia Center, Shanghai Municipal Health Commission [ZY(2021–2023)-0204-06] to YM-W; and the Health and Medical Research Fund [20212801], Health Bureau, Hong Kong SAR to YS-H.

Abstract no.239

Exploring the Mechanisms of Electroacupuncture Modulation of Gut Microbiota for the Treatment of Osteoporosis Based on the Gut-Bone Axis Theory

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Abstract: Primary osteoporosis is a prevalent metabolic bone disease characterized by decreased bone density and increased fracture risk, predominantly affecting the elderly, particularly postmenopausal women. In recent years, numerous studies have shown that gut microbiota play a crucial role in bone metabolism through various mechanisms, including the production of metabolites, immune regulation, and nutrient absorption. This discovery has led to the development of the "gut-bone axis" theory. Electroacupuncture, a traditional Chinese medical therapy, involves the application of electrical stimulation to specific acupoints to regulate the flow of Qi and blood and is widely used in the treatment of various diseases. Modern research has found that electroacupuncture not only modulates the composition of gut microbiota but also influences bone metabolism through neural, endocrine, and immune pathways. This paper, based on the "gut-bone axis" theory, reviews existing studies to explore the potential mechanisms and therapeutic value of electroacupuncture in regulating gut microbiota for the treatment of primary osteoporosis, aiming to provide a theoretical foundation and new directions for future research. Keywords: primary osteoporosis; gut-Bone Axis; electroacupuncture; gut microbiota.

Abstract no.240

Shugan Yangxue Jiedu Decoction inhibited the inflammatory reaction induced by the over-activation of the gut-brain-skin axis and ameliorated the psoriasis-like lesions induced by Imiquimod in rats

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2. Dr Zixuan Wang, Beijing Hospital of Traditional Chinese Medicin, Beijing

Abstract Background Psoriasis is a chronic disease that significantly impairs the psychosocial functioning of patients, and it is recognized as a serious psychosomatic disease. The main clinical manifestation of psoriasis is erythema and scaly skin with severe pruritus, which significantly impacts the quality of life of patients. Shugan Yangxue Jiedu decoction (SGYXJD) has been used to treat psoriasis in China for several decades, but its therapeutic mechanism is still unclear. In this study, we investigated the effects of SGYXJD on the hyperactivation of the HPA axis and intestinal microflora disturbance in an Imiquimod-induced psoriasis rat model, as well as its potential mechanisms and possible immunomodulatory effects. Method Wistar rats model of psoriasis with depression induced by IMQ and chronic unpredictable mild stress (CUMS) was established and treated with fluoxetine, methotrexate, and SGYXJD. The depression level was assessed through behavioral experiments, while the severity of psoriasis-like lesions was evaluated using the Psoriasis Area and Severity Index (PASI) and Baker score. HPA axis-related hormones and inflammatory factors were measured using ELISA and Western blot techniques. Microglia activation was assessed through immunohistochemistry. Additionally, bioinformatics analysis of the intestinal flora was conducted through metagenomic sequencing. Results SGYXJD ameliorated depressive symptoms, decreased PASI and Baker scores, and inhibited the hyperactivation of the HPA axis. In psoriasis combined with depression, rats treated with SGYXJD showed decreased levels of hormones associated with the HPA axis, reduced levels of inflammatory cytokines, decreased microglia activation in the hippocampus, and relief from the disturbance of intestinal flora. Conclusion SGYXJD can not only treat psoriasis but also relieve depression by affecting intestinal flora, regulating the HPA axis, and down-regulating the expression of inflammatory factors. SGYXJD may represent a new direction in developing immunomodulatory drugs for psoriasis, which has achieved good clinical results.

Abstract no.241

Theory of tonifying kidney and activating blood circulation acupuncture therapy for diabetic nephropathy

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Diabetic nephropathy is one of the main microvascular complications of diabetes, and is also one of the important cause of end-stage renal failure. Diabetes is the leading cause of chronic kidney disease in developed countries. The 2015 national epidemiological survey in China showed that DKD was the leading cause of CKD in hospitalized patients in China, and about 21.3% of diabetic patients were accompanied by CKD. Zhang Daning, a master of traditional Chinese medicine, found in his clinical research that patients with DKD had varying degrees of "kidney deficiency" and "blood stasis". The kidney qi was deficient, not reaching the blood vessels, there was less qi in the veins, and blood stagnation caused by stasis. Kidney invigorate the stitch in the kidney and blood stasis "is the theoretical guidance, choose: shen shu, jing men,tai xi, xue hai, dan zhong, qi hai, guan yuan, take sth as the principal thing. Prone position in shen shu, to make up for line method of fast pin 30 s, to the supine position in xue hai drainage method,dan zhong ping supplementing and reducing technique,In order to achieve tonifying the kidney and consolidating the root, invigorate the circulation of qi and modern research proves that it is the body's internal organs to acupoints in physiology and pathology in the body function of important induction point, through the acupuncture to improve kidney function. The optimal combination of tonifying kidney and activating blood acupuncture in the treatment of DKD was carried out according to the diagnostic criteria of western medicine and the key points of TCM syndrome differentiation in different stages. In order to achieve the best clinical effect, the combination of Chinese and Western medicine and acupuncture and medicine are combined.

Abstract no.242

Effect of Acupuncture in the treatment of schizophrenia with central obesity research

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3. Dr Minghui Hang, Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai

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5. Dr Jianhua Chen, Shanghai Mental Health Center, Shanghai

Objective: This study aimed to evaluate the effectiveness of acupuncture in treating schizophrenia patients with central obesity, exploring its potential as a non-pharmacological intervention given the metabolic syndrome, particularly central obesity, often accompanying schizophrenia. Method: Forty schizophrenia inpatients with central obesity (waist circumference ≥90cm for men or ≥80cm for women) from Shanghai Mental Health Center between April 2023 and April 2024 were randomly divided into a control group (n=20) and a treatment group (n=20). The treatment group received acupuncture three times weekly for 8 weeks, targeting bilateral Zusanli (S36) and Fenglong (S40). The control group received no treatment during this period but underwent the same acupuncture treatment post-study. Various parameters, including waist circumference, body weight, BMI, and cholesterol levels, were monitored and analyzed using IBM SPSS Statistics 27. Result: After 8 weeks, the treatment group showed significant reductions in body weight, waist circumference, BMI, and total cholesterol levels ($p<0.05$), while the control group did not exhibit significant changes. The treatment group's improvements were significantly greater than those of the control group across these parameters. Conclusion: This case-control study suggests that acupuncture therapy may have potential clinical value in treating schizophrenia patients with central obesity, particularly in improving body weight, BMI, waist circumference, and total cholesterol levels. The mechanism might involve regulating total cholesterol levels, warranting further research and application. Keyword: Acupuncture; Central obesity; Schizophrenia

Abstract no.243

Transcutaneous Electrical Acupoint Stimulation and Dense Cranial Electroacupuncture Stimulation for Psychiatric Sequelae and related biomarkers in Women Victims of Domestic Violence: Study Protocol for a Randomized Controlled Trial

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2. Ms Sichang YANG, The University of Hong Kong, Hong Kong SAR

Background: Domestic violence is a global problem associated with mental illness morbidity. However, a large proportion of victims of domestic violence fail to achieve a satisfactory response from first-line interventions. Dense Cranial Electroacupuncture Stimulation (DCEAS) and Transcutaneous Electrical Acupoint Stimulation (TEAS) has been demonstrated for its safety and efficacy for psychiatric disorders in previous clinical trials. We hope to combine these therapies into a both clinic-based and home-based treatment modality to improve the psychiatric outcomes of women victims of domestic violence. Methods: This is an assessor-blinded randomized controlled trial that will involve 110 patients with depression. Patients will be randomly assigned to either the treatment group or the routine care group in a 1:1 ratio. The treatment group will receive 2 sessions of DCEAS treatments and 3 sessions of TEAS treatments per week for 12 consecutive weeks. While the routine care control group will not receive any TEAS/DCEAS treatment until the end of the 12-week study. All patients participating in this study will continue their original routine care regardless of the group to which the patient is assigned. The primary outcome will be measured by Beck Depression Inventory–II (BDI-II). The secondary outcomes include 17-item Hamilton Depression Rating Scale, 10-Item Perceived Stress Scale, PTSD Check List-Civilian Version, Insomnia Severity Index, 12-Item Short Form Survey and adverse events. Two 10-ml blood samples will be collected at baseline and at the end of 12-week study, respectively, for further tests on psychiatric sequelae related biomarkers. Discussion: If effective, this new combination of interventions could have significant clinical implications for women victims of domestic violence with psychiatric sequelae. Trials registration: ClinicalTrials.gov as NCT05102253. Registered 1 November 2021 Funding: This study is funded by the Health and Medical Research Fund provided by the Government of the Hong Kong Special Administrative Region of China (Ref no: 18191451).

11. Clinical Investigation(Internationally Recognized Criteria for Clinical Trials and their Challenges)

Abstract no.244

Network pharmacology-based analysis to explore the therapeutic mechanism of Purslane in atopic dermatitis

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2. Mr Wenjie Lai, Macau University of Science and Technology, Macao SAR
3. Mr Haobin Wei, Macau University of Science and Technology, Macao SAR

Abstract Background: Portulaca oleracea L. (PO) is a widely distributed edible plant with documented medicinal properties in traditional Chinse medicine (TCM). The purslane extracts or compounds have exhibited numerous biological activities such as anti-inflammatory, antimicrobial, antiviral, anticancer properties. Atopic dermatitis (AD) is a common chronic allergic skin disease characterized by severe skin lesions and pruritus. However, the anti-inflammatory effects and AD-alleviating mechanisms of PO remains unclear. This study aimed to provide a network pharmacology-based analysis to explore the therapeutic mechanism of PO in AD treatment. Methods: The chemical ingredients in PO were retrieved using the TCMSP database and supplemented with literature search. The Swiss Target Prediction was used to predict the targets of active ingredients in PO. The disease targets were searched using “Atopic Dermatitis” as a keyword from DisGeNET and Genecards databases. The data was standardized using Uniprot. Venny 2.1.0 was employed to obtain the intersection targets of ingredients and diseases. STRING 12.0 was used for a protein-protein interaction (PPI) network profiling. DAVID was utilized for enrichment analysis of gene ontology (GO) functional annotation and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis. An online bioinformatics platform (https://www.bioinformatics.com.cn) and Cytoscape 3.10.2 were used for analysis and visualization. The chemical structures of PO ingredients were downloaded from the PubChem database. AutoDock 4.2.6 and PyMOL 3.0.1 were used for molecular docking and visualization, respectively. Results: This study screened 20 main active ingredients of PO. To further reveal potential targets of PO for AD treatment, a total of 2,185 AD-related targets were obtained from available databases, and 308 targets were also identified for PO active ingredients. The resulting 103 common targets can be considered as potential targets of PO for AD treatment. PPI network analysis showed that JAK1 and STAT3 may be the core targets for the treatment of AD. KEGG pathway enrichment analysis identified 143 signaling pathways, with the JAK1/STAT3 signaling pathway being one of the key pathways involved. Using available JAK1 inhibitors as references, one of PO active ingredients, Aurantiamide Acetate (AUA), was predicted to be a potential JAK1 inhibitor, forming hydrogen bonds with Asn1008, Arg1007 and Glu883 residues. The docking energy of JAK1 and AUA was -7.71 Kcal/mol, moderate among 11 JAK1 inhibitors. Conclusion: This study predicted the biological processes and key pathways through which PO active components intervene in AD. AUA may serve as the material basis for treating AD, acting on several core targets such as JAK1 and STAT3. This

provides a rationale for further development of AUA as a potential clinical anti-atopic dermatitis drug. Keywords: Purslane; Aurantiamide Acetate; Molecular docking; JAK/STAT signaling pathway

Abstract no.245

Activation of free fatty acid receptor 4 attenuates inflammatory responses in perivascular adipose tissue

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Background and aims: Perivascular adipose tissue (PVAT) is a special type of adipose tissue widely distributed around blood vessels in the human body. Free fatty acid receptor 4 (FFAR4) is an unsaturated fatty acid receptor widely distributed in multiple organs, specifically adipocytes and inflammatory cells in the vasculature. FFAR4 plays a role in improving vascular function and counteracting cardiovascular inflammation by mediating the signaling of unsaturated fatty acids. The aim of this study is to identify FFAR4 agonists and explore their anti-inflammatory effectiveness in PVAT. Methods: FFAR4 selective agonist TUG-891 and Oleracein E, an active compound in Portulaca oleracea L. (PO), were administrated in vitro or in vivo. In RAW264.7 cells and 3T3-L1-derived adipocytes stimulated by lipopolysaccharides (LPS), the anti-inflammatory effects of agonists at different concentrations were analyzed by qPCR and Western-blot analyses. Adipose tissue-specific Ffar4-/- mice (Adipo-Ffar4-/-) were generated by crossing Ffar4flox/flox mouse with adipose-Cre transgenic mouse. In a model of PVAT injury induced by 10% FeCl3 in mice, the regulatory effects of FFAR4 agonists TUG-891 were evaluated in the absence or presence of FFAR4. Results: In RAW264.7 cells (monocytes), Oleracein E had a significant inhibitory effect on the mRNA expression of classical inflammatory cytokines and chemokines such as MIP-1α, IL-6, IL-1β, and MCP-1. In animal experiments, mice's abdominal aorta subjected to FeCl3 injury showed significant vascular damage with reduced blood flow, while both vascular narrowness and reduced blood flow were alleviated in Ffar4flox/flox mice treated with TUG-891. Conversely, no significant modification occurred Adipo-Ffar4-/- mice. Histological analysis of damaged aorta showed significant thickening of the adventitia, which was attenuated in the Ffar4flox/flox mice, but not Adipo-Ffar4-/- mice, after administration of the FFAR4 agonist TUG-891. Conclusion: Activation of FFAR4 exerts anti-inflammatory effects and modulates vascular inflammation in PVAT. Oleracein E has anti-inflammatory properties and is a potent FFAR4 agonist. Keywords: FFAR4 agonist, Oleracein E, purslane, adipose tissue, abdominal aorta, inflammation

Abstract no.246

Using a twin herbal formula for the treatment of upper limb Lymphedema after breast cancer resection

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2. Prof Chiu Tor Wo, The Chinese University of Hong Kong, Hong Kong SAR

Background:Chronic lymphedema is a common post-resection complication in breast cancer patients,and its occurrence is related to surgical trauma,and radiation therapy. Chronic lymphedema can lead to generalized limb edema,pain,cellulitis and joint stiffness,seriously affecting the quality of life of patients. In addition, long term lymphedema can also lead to infection and skin ulceration,increasing the patient's mental burden and economic pressure. Methods: This study was conducted as a prospective self controlled clinical trial. Participants were evaluated before treatment and followed up monthly for six months. Main outcome measures were limb volume changes,quality of life (QOL) for limb lymphoma questionnaire (LYMQOL), handgrip strength test and tonometer for tissue indentation. Results: We enrolled 20 patients with breast cancer related limb lymphoma in a prospective self-controlled trial,from May 2018 to July 2023. After 6 months of treatment, affected limb volume decreased by 4.1% compared to baseline. The LYMQOL improved after treatment,especially in the symptom domain ($p=0.006$), with no changes in grip strength and tonometer measurements. Conclusion: After 6 months of treatment,the mean volume of affected limbs showed a decreasing trend,especially in the symptom domain.

Abstract no.247

A tRNA-derived fragment from Chinese yew suppresses the progression and metastasis of colorectal cancer by targeted activation of the transfer RNA-modifying enzyme TYW2

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Colorectal cancer ranks second in cancer-related deaths worldwide, and its clinical characteristics of being "prone to metastasis and recurrence" have led to an urgent need for effective targeted therapies to prevent metastasis and recurrence. Recent studies suggest that treatment strategies based on tRNA epigenetic modifications hold promise for precise treatment of CRC. For instance, wybutosine modification at the position 37th of tRNA-Phe along with its modifying enzyme TYW2 play a role in CRC cell proliferation and metastasis. Our laboratory previously constructed an exogenous tRNA fragment (tRF) library. Here, from which we identified a tRF derived from the 5′ termini of tRNAASN(GUU) of Chinese yew, with its antisense, termed HC37, upregulates the expression of TYW2 and subsequently increase wybutosine modification levels in CRC cells. In vitro, HC37 exhibits strong inhibitory effects on the proliferation, colony formation and metastasis of CRC cells. Intratumorally injection of HC37 (2.5 mg/kg) on HCT-8 xenograft nude mice exhibited tumor-suppressive effect comparable to that of taxol (5 mg/kg). Additionally, TYW2 expression was significantly higher in HC37-treated tumors compared to the control group. Mechanistically, HC37 activates double-stranded RNA sensor RIG-I to upregulate TYW2, which in turn triggers innate immune responses in CRC cells. Knockdown of TYW2 by siRNA significantly reduced the proliferation and metastasis of CRC cells caused by HC37, as well as dysregulating RIG-I. In summary, this study not only identifies a novel double-stranded RNA sequence with therapeutic potential for CRC, distinct from siRNA mechanisms that silence disease-related genes, but also providing new clues for the design and development of next-generation small nucleic acid drugs from exogenous tRF library. Furthermore, our findings highlight TYW2 as an important signaling molecule in innate immune responses, as well as a potential target for CRC drug development.

Keywords: tRNA-derived fragment, medicinal plants, TYW2, colorectal cancer

Abstract no.248

Study of respiratory infection prevention and treatment based on fusion of Chinese traditional and western medicine, and translation from bench to bedside

1.Yang Zi Feng , 2. Wang Yu Tao, 3. Ma Qing Hai, 4. Li Run Feng, 5. Chen Xiao Hong,6. Zhong Nan Shan

Traditional Chinese medicine (TCM), which has developed over thousands of years, plays an important role in epidemic control. It has displayed efficacy in relief of symptoms，reducing mortality in critically ill patients and delaying the development from mild-to-moderate disease to severe and critical illness. To explain clearly and understand the efficacy of TCM against epidemic by using modern scientific language, we have developed animal models and biomimetic models for viral respiratory tract infections (influenza, COVID-19, RSV) that mimic human symptoms, viral replication, and microenvironment. From more than 2,000 kinds of Chinese Traditional Patent Medicine, empirical prescriptions, components or monomer of TCM, a group of Chinese medicines and components, such as Lianhua Qingwen, Liushen pills, phillyrin, were identified by applying these model systems. Multi-omics analysis has revealed the molecular mechanisms of respiratory virus-host interaction and potential therapeutic targets of the TCM. One of the successful practices from bench to bedside is the discovery and translation of phillyrin. Phillyrin is an active component of Lianhua Qingwen, a commonly used TCM formula. The anti-COVID-19 activity was firstly identified in vivo and in vitro in our lab. After finishing the preclinical study and phase I and II clinical trial for COVID-19 infection treatment, it has been approved for phase III clinical trial study by the National Medical Products Administration.

In summary, prevention and treatment of respiratory infections should combined advantages of Chinese traditional and western medicine.

Abstract no.249

Lianhe Xiaozhi Ointment Improves Lipid Metabolism and Inflammation in MASLD by Regulating PPARα and Gut Microbiota

1. Prof Xiqiao Zhou，江苏省中医院，南京

Background and Aims: Lianhe Xiaozhi ointment (LXO) is an empirical formula developed by the Jiangsu Province Hospital of Chinese Medicine, which has demonstrated a noteworthy therapeutic effect on metabolic dysfunction-associated fatty liver disease (MASLD) in clinical practice. Nevertheless, the precise underlying mechanisms remain elusive. The aim of this study is to elucidate the mechanisms by which LXO alleviates metabolic disorders, utilizing both animal and cell models. Methods: The UPLC-Q-TOF-MS technology was employed to meticulously analyze the chemical components present in the water decoction and serum containing of LXO. Additionally, network pharmacology techniques were utilized to screen for the vital pharmacological components and associated biological pathways of LXO. Subsequently, a comprehensive exploration of the therapeutic efficacy and underlying mechanisms of LXO on MASLD was conducted through a rigorous combination of in vivo and in vitro high-fat model experiments. Results: The network pharmacology analysis revealed hyperoside, Magnoflorine, N-Methylisococlaurine, O-demethyl nuciferine isomer, Coclaurine, polygonoside, Tangeretin, Quercetin-3-O-β-D-glucuronide, and Narigenin as the key active ingredients in LXO responsible for treating MASLD. LXO exhibited diverse therapeutic effects on MASLD, including delaying weight gain, improving glucose and lipid metabolism disorders, reducing liver injury, mitigating liver inflammation, and alleviating gut microbiota disorders. Moreover, insights from network pharmacology and liver transcriptomics studies indicated that the PPAR signaling pathway plays a pivotal role in the treatment of MASLD with LXO. Further investigations demonstrated that LXO significantly activates liver PPARα, along with enhancing the activity and mRNA expression of key proteins involved in downstream fatty acid beta oxidation and ketone body generation. Notably, our in vitro studies also revealed that the PPARα antagonist significantly attenuated the lipid-lowering effect of LXO. Conclusions: Our study confirmed that LXO was effective for treating MASLD and has promising clinical applications. Keywords: MASLD; Traditional Chinese Medicine; PPARα; inflammation; gut microbiota. Acknowledgment:This work was supported by the Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD, 035062005002-14) and the special research project of Jiangsu Administration of traditional Chinese medicine (zt202105).

Abstract no.250

Integrative treatment for new-onset type 2 diabetes mellitus in pediatric patients in the post COVID-19 infection: A case series

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The incidence of pediatric diabetes, accompanied by diabetic ketoacidosis (DKA), has significantly increased after the COVID-19 pandemic. However, therapeutic options for children and adolescents with newly diagnosed diabetes remain constrained. This study reports three cases of achieving remission of type 2 diabetes mellitus (T2DM) in pediatric patients following COVID-19 infection, achieved through an integrated treatment approach combining Traditional Chinese Medicine (TCM) herbal medicine, berberine, and lifestyle modifications. The patients, aged 3 to 14, were diagnosed with DKA and new onset of T2DM after COVID-19 infection. Common clinical manifestations included polydipsia, polyphagia, yellow greasy tongue coating, and a wiry, rapid pulse. TCM syndrome differentiation indicated the presence of middle-Jiao damp heat pattern in these patients. Patients received the modified Huangqi-Shigao decoction, which consisted of herbs such as Huangqi, Shigao, Huanglian, Dahuang, Tianma, Zhimu, Danshen, and Xixin. Additionally, bi-daily administration of 0.4 g berberine hydrochloride tablets were prescribed, together with the routine medical cares. Changes in previous intervention included a gradual reduction in insulin regimen (3 units/day) until complete cessation. After four months of TCM treatment, all patients exhibited normal levels of HbA1c and blood glucose with the discontinuation of conventional diabetes treatment. Subsequent follow-up periods (6-9 months) showed that the patients had normal blood glucose levels, as well as the restoration of insulin sensitivity and β-cell function as evidenced by the homeostasis model assessment of insulin resistance test. This is the first report demonstrating the efficacy of an integrative treatment approach in reversing pediatric diabetes following COVID-19 infection.

Abstract no.251

Role of protein post-translational modification in myocardial ischemia-reperfusion injury

1. Dr ting chen, 湖南中医药大学, 长沙

Content (Limit 300 words): Myocardial ischemia-reperfusion injury (MIRI) caused by percutaneous coronary therapy (PCI) in cardiovascular disease (CVD) is one of the diseases with increasing mortality in heart disease that threatens human life and health. The pathogenesis of MIRI has been studied for decades, and the effects of epigenetic changes on MIRI have been extensively studied. The latest research suggests that epigenetics may be a new target for preventing or reducing MIRI. Protein post-translational modifications (PTMs), including glycosylation, crotonylation of lysine (Kcr), lactation, succinylation, acetylation, isonicotinoylation, etc., play an important role in the normal function of the cardiovascular system. Every change in protein conformation may change protein function and cause MIRI, and this process is usually reversible. The related mechanisms of MIRI, such as calcium overload, oxidative stress, mitochondrial damage, are relatively complex. In MIRI, multiple PTMs may occur simultaneously, and PTMs caused by the same protein may also have bidirectional effects. Therefore, the role of PTMs in MIRI is still worthy of further study. This paper summarizes the mechanism of six common PTMs in the occurrence and development of MIRI, and discusses related drugs and potential mechanisms, which may provide new ideas for the development of drugs to treat or alleviate MIRI, further improve the prognosis of MIRI, and reduce the mortality of cardiovascular diseases. Keywords: Myocardial ischemia-reperfusion injury; Protein post-translational modifications; Glycosylation; Lysine crotonylation; lactylation

Abstract no.252

Visual study of prognosis，glucose and lipid metabolism and tongue image parameters in patients with coronary heart disease after PCI

1. Mrs zhaoxia Xu, Shanghai University of Traditional Chinese Medicine, Shanghai

2. Ms mi zhou, Shanghai University of Traditional Chinese Medicine, Shanghai

【Abstract】Objective Many articles related to glycolipid metabolism and tongue parameter characteristics after PCI for coronary heart disease have been published, and the aim of this study is to analyse the relationship between the prognosis of patients after PCI for coronary heart disease and glycolipid metabolism and tongue parameter characteristics based on the visualisation software VOSviewer, as well as the relationship between glycolipid metabolism indexes, tongue parameter characteristics, and the prognosis of patients after PCI, and finally to outline the hotspots of the content of this research and trends. Methods Eight major Chinese and English databases (pubmed, web of science, embase, cochrane, China Knowledge, Wanfang, Wipro, China Biomedical Literature) were collected, and the time frame for searching was from the establishment of the database to the present day (12 October 2023) for relevant literature on the relationship between prognosis and glycemic and lipid metabolism and tongue characteristics of post-PCI patients with coronary artery disease, and VOSviewer software was used to analyse the keywords and other parameters of the study. VOSviewer software to summarise the keywords and other information. Results A total of 433 articles were included in the literature, and the keyword analysis suggested that the prognosis of post-PCI patients with coronary artery disease was correlated with specific indexes of glycolipid metabolism, and the research direction was mainly in the prognostic value of these indexes, while the number of literature related to the parameters of tongue features was too small, so we only did a descriptive overview. Conclusion There is a correlation between the prognosis of post-PCI patients and the parameters of glycolipid metabolism and tongue features, but there is no relevant research on the indicators of glycolipid metabolism and tongue features.

Abstract no.253

M3R-based study of the role and mechanism of catalpol in preventing olanzapine-induced lipid metabolism disorders

1. Prof Huifeng Zhu, Southwest University, Chongqing

This study investigates the effects and mechanisms of Catalpol (CAT) in preventing lipid metabolism disorders caused by Olanzapine (OLZ), based on the M3 receptor (M3R). Olanzapine is a commonly used antipsychotic drug that significantly improves the negative and positive symptoms of mental disorders. However, long-term use of Olanzapine can lead to a series of lipid metabolic diseases such as obesity and dyslipidemia in patients, which seriously affects patient medication compliance and clinical treatment outcomes. Catalpol, an active ingredient extracted from the traditional Chinese medicine Rehmannia glutinosa, has significant hypoglycemic and lipid-lowering effects.The research methods include in vivo and in vitro studies, with in vivo experiments involving animal grouping and administration, biochemical index detection, tissue section observation, and detection of the expression of AMPK and its downstream metabolic key enzymes. In vitro experiments observe the effects of Olanzapine and Catalpol on fat accumulation in LO2 cells, detect the effects of Catalpol on key enzymes of cellular fat metabolism, and explore whether Catalpol has an agonistic effect on hepatic M3Rs in rats through an M3R-silenced LO2 cell model.

Abstract no.254

Correlation between serum uric acid levels and bone mineral density in Chinese elderly: an observational study and Mendelian randomization analysis

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Research Objectives: This study aims to investigate the association between serum uric acid (SUA) levels and bone mineral density (BMD) in elderly Chinese individuals through observational study and Mendelian randomization analysis. Methods: Participants were randomly selected from two communities in Kunming and Jinshan, Shanghai, China, between January 2020 and December 2021. Clinical information, biochemical indicators, and bone density were collected from the participants. The relationship between SUA levels and BMD was assessed using a multiple linear regression model. In the Mendelian randomization study, genetic instruments for SUA were derived from GWAS data from the UK Biobank, and outcome variables were obtained from GEFFOS consortium GWAS data, which included BMD measurements of the lumbar spine, femoral neck, heel, forearm, and whole body across different age groups. Both univariable and multivariable Mendelian randomization analyses were conducted to evaluate the causal effect of SUA levels on BMD, adjusting for covariates such as smoking, alcohol consumption, physical activity, and sleep status to assess the stability of the results. Results: A total of 1575 eligible participants were included, comprising 583 men and 992 postmenopausal women. In postmenopausal women, SUA levels were significantly positively correlated with BMD at the lumbar spine and hip ($P < 0.05$). However, in elderly men, the association between SUA levels and BMD was weaker. Mendelian randomization analysis indicated a significant positive causal relationship between genetically determined SUA levels and BMD at various sites, including the heel, forearm, and whole body (age stratified: 30-45 years) ($P < 0.05$), with results remaining significant after adjusting for covariates. Conclusion: In postmenopausal Chinese women, SUA levels are positively correlated with BMD, and there is a significant positive causal relationship between genetically determined SUA levels and BMD. These findings suggest that SUA may play an active role in bone metabolism.

Abstract no.255

Early-Life Malnutrition and Increased Osteoporosis Risk in Adulthood: Findings from a Large-Scale Cross-Sectional Study

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Introduction: The association between early-life malnutrition and the risk of osteoporosis and fractures in adulthood is not well-established. This study aims to clarify this relationship. Methods: This cross-sectional analysis is part of the China Community-based Cohort of Osteoporosis (CCCO) study. Participants were categorized by birthdate into non-exposed, fetal, early childhood, mid-childhood, late childhood, and adolescence exposure groups. The non-exposure and adolescence groups were combined into an "age-matched group" for comparison. Multiple logistic regression models were used to analyze the relationship between early-life malnutrition and the risks of osteoporosis (defined as a T-score ≤ -2.5) and self-reported fractures. Findings were validated using the China Northwest Cohort (CNC). Results: The final analysis included 12,789 participants. Adjusted for covariates, individuals exposed to malnutrition during fetal and childhood stages showed a higher likelihood of developing osteoporosis compared to their age-matched counterparts. The odds ratios (ORs) for osteoporosis were 1.223 (95% CI: 1.035-1.445) for fetal, 1.208 (1.052-1.386) for early childhood, 1.249 (1.097-1.421) for mid-childhood, and 1.101 (1.001-1.210) for late childhood exposure (all P-values < 0.05). Late childhood exposure was also linked to a higher risk of fractures, with an OR of 1.155 (95% CI: 1.033-1.291, P = 0.011). Stratified analyses revealed a significant correlation between early-life malnutrition and osteoporosis risk in participants with lower educational attainment, and those who were overweight or obese. CNC data confirmed these findings. Conclusions: Early-life malnutrition adversely affects bone health, increasing the risk of osteoporosis in adulthood, particularly in women and individuals who are overweight, obese, or have lower education levels.

Abstract no.256

Treatment of Functional Dyspepsia through the Combination of Chinese Herbal Acupoint application and Paraffin therapy on Professor Tian Conghuo's "Regulating Qi Movement": A Randomized Controlled Trial

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5. Dr Tao Yang, Guang'anmen Hospital China Academy of Chinese Medical Science, Beijing
6. Dr Yinqiu Gao, Guang'anmen Hospital China Academy of Chinese Medical Science, Beijing

Abstract: Objective: The present study aims to investigate the clinical efficacy and safety of combining traditional Chinese medicine with wax therapy, drawing inspiration from Professor Tian Conghuo's "conditioning Qi Method," in the management of functional dyspepsia. This approach intends to provide clinical evidence for the integration of traditional Chinese medicine and wax therapy in treating functional dyspepsia. Methods: A total of 120 patients were randomly assigned to four groups: a combined Chinese medicine and wax therapy group (TCMPT group, 30 cases), a Chinese medicine-only group (CMT group, 30 cases), a wax therapy-only group (PT group, 30 cases), and a basic therapy-only group (MT group, 30 cases), using a number table method. The baseline treatment involved oral administration of omeprazole magnesium enteric-coated tablets, 20mg daily, for a duration of 4 weeks. The CMT group received additional herbal medication (consisting of Sichuan pepper, dried ginger, Xiangfu, and raphani seed) along with acupoint application on Zhongwan and Shenque points, thrice weekly, for 4 hours each session, over 4 weeks. The PT group underwent additional wax therapy (with a wax block placed in a wax therapy bag and positioned over the gastric duct), thrice weekly, for 20 minutes per session, over 4 weeks. The TCMPT group received both Chinese medicine application and wax therapy, where wax therapy was administered on the Chinese medicine acupoints for 20 minutes, followed by removal of the wax therapy kit and the acupoint patch after 4 hours, thrice weekly, for 4 weeks. Pre- and post-treatment comparisons were made for symptoms such as epigastric pain, early satiety, postprandial fullness and discomfort, epigastric burning, SF-36 quality of life scores, and liver-stomach disharmony scores. Clinical outcomes and safety evaluations were statistically analyzed among the four groups. Results: Following the intervention, the TCMPT group exhibited notably reduced scores in significant symptoms including epigastric discomfort, early satiation, postprandial distension and uneasiness, as well as epigastric burning sensation, compared to the MT group ($P<0.01$). Additionally, scores indicating liver and stomach dysregulation were substantially lower in the combined group compared to the MT group ($P<0.01$). The treatment efficacy in the TCMPT group stood at 93% (28/30), surpassing the 73% (22/30) achieved in the CMT group, the 70% (21/30) in the PT group, and exceeding the MT group's 50% (15/30) by a significant margin. Statistical analysis revealed a marked difference among the four groups ($F = 35.185$, $P < 0.01$). All four treatment approaches led to an improvement in physiological function, social function, and quality of life scores, with significant differences

observed post-treatment compared to pre-treatment ($P < 0.01$). Notably, the combination of TCMPT yielded significantly greater improvements in these dimensions compared to the CMT group, PT group, and MT group ($P < 0.01$). During the study, no adverse reactions attributable to the use of Chinese medicine or wax therapy were observed. In conclusion, the approach integrating Professor Tian Conghuo's "regulating Qi Method" through Chinese medicine patches and wax therapy effectively alleviates primary symptoms, ameliorates traditional Chinese medicine syndromes, and enhances the quality of life for patients with functional dyspepsia.

Abstract no.257

Traditional Chinese medicine formulas granules of dispelling dampness and eliminating phlegm in symptomatic cerebral arteries stenosis patients: A prospective exploratory intervention study

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Introduction: To determine the efficacy and safety of traditional Chinese medicine formula granules of dispelling dampness and eliminating phlegm (DDPE) in symptomatic cerebral arteries stenosis (SCAS) patients. Materials and Methods: Sixty adults diagnosed with SCAS (within 90 days of onset) and phlegm-damp syndrome were assigned to DDEP group (n=30) or control group (n=30). Formulas of DDEP were composed of Atractylodes Lancea, Magnolia Officinalis, Citrus Reticulata and other traditional Chinese herb s. Patients in DDEP group took 2 packets of DDEP formulas granules 3 times a day for 3 months. Two groups received standard drugs treatments for SCAS including antiplatelet aggregation, statins, hypoglycemic agent, and hypotensor. The primary outcome was Modified Rankin Scale(mRS) score three months after treatments. The secondary outcomes were dynamic cerebral autoregulation(dCA) indices, including phase shift and gain and recurrent events, including stroke and transient ischemic attack. Results: 1）Compared with control group, the proportion of patients with favorable outcomes (mRS≤1 at 3 months) in DDFP group was higher (P=0.07) . 2）The phase shift at low frequency band in DDFP group was higher than control group, indicating dCA was better in DDFP group than control group. 3）There was no significant difference in recurrence rate between two groups.4）In terms of safety, no serious adverse reactions were observed except for two patients in the DDFP group with slight gastrointestinal discomfort. Conclusions: Chinese medicinal formulas granules of dispelling dampness and eliminating phlegm showed the potential to improve the three-month clinical outcomes and protect dynamic cerebral autoregulation function of SCAS patients with phlegm-damp syndrome.

Abstract no.258

A Systematic Review and Meta-analysis of the Clinical Efficacy of Qingkailing in the Treatment of Influenza

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Objective To systematically evaluate the efficacy and safety of Qingkailing in the treatment of influenza and to provide evidence-based medical support for clinical use of the drug. Methods Eight Chinese and English databases, including PubMed, EMbase, Cochrane Library, Web of Science, CNKI, Wanfang,VIP and SinoMed,were systematically searched for randomized controlled trials (RCTs) of Qingkailing alone or in combination with conventional western medicines for the treatment of influenza.The risk of bias assessment tool in Cochrane Handbook and RevMan5.4 software were used to evaluate the quality of literature and Meta-analysis. Results Fifteen RCTs with 1854 patients were finally included. Compared with conventional western medicines,Qingkailing or Qingkailing+conventional western medicines increased the overall effective rate(RR=1.21,95%CI[1.13,1.30],P<0.00001),shortened the time to fever symptom remission,shortened the time to cough symptom remission,and increased the rate of 3d symptom remission,and the difference was not statistically significant in terms of the incidence rate of adverse reactions.The results of subgroup analysis showed that Qingkailing+conventional western medicine could improve the overall effective rate (RR=1.25,95%CI[1.14,1.37],P<0.00001),shorten the time of fever symptom remission,shorten the time of cough symptom remission,and improve the 3d symptom remission rate compared with conventional western medicine.Qingkailing alone also improved the overall efficiency(RR=1.14,95%CI[1.05,1.22],P=0.0009).It improved the 3d symptom relief rate,but the difference was not statistically significant in terms of time to fever symptom relief and time to cough symptom relief.In addition,there was no statistically significant difference in adverse effects between Qingkailing or Qingkailing+conventional western medicines compared with conventional western medicines (RR=1.65,95%CI(0.91,2.99),P=0.10).Conclusion Qingkailing is effective in the treatment of influenza and can accelerate symptomatic relief when used in combination with conventional western medicines, and has a better safety profile,pending a multicenter,large-sample RCT to validate its efficacy and safety.

Abstract no.259

Decreased serum adipose triglyceride lipase level is associated with renal function impairment in patients with type 2 diabetes

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Introduction Diabetic kidney disease (DKD) diagnosis is challenging. Kidney injury caused by disorders of lipid metabolism has become a research focus. Adipose triglyceride lipase (ATGL) is the rate-limiting enzyme in lipolysis and plays a crucial role in maintaining lipid metabolism balance. This study aimed to determine whether serum ATGL is a potential early biomarker of DKD. Methods 236 participants were divided into healthy control (n=59), type 2 diabetes mellitus (T2DM) (albumin to creatinine ratio (ACR) <30 mg/g) (n=80), microalbuminuria (L-DKD) (ACR 30–300 mg/g) (n=41), and macroalbuminuria (H-DKD) (ACR≥300 mg/g) (n=56) groups, and the relevant clinical data were collected. Serum ATGL, kidney injury molecule-1 (KIM-1), and tumor necrosis factor-1 (TNFR-1) levels in 236 participants were determined. Several Spearman's correlation test, receiver operating characteristic curve, multivariate logistic regression analysis, restricted cubic spline (RCS) and other methods were used to evaluate the correlation between serum ATGL levels and renal function damage in DKD. Results Serum ATGL levels were significantly lower in the T2DM, L-DKD, and H-DKD groups compared to healthy controls . Serum ATGL levels positively correlated with estimated glomerular filtration rates (eGFR) and negatively correlated with DM duration, history of hypertension and hyperlipidemia, urine ACR (UACR), 24h-urine total protein (UTP), serum creatinine (SCr), blood urea nitrogen, uric acid, TNFR-1, and KIM-1/creatinine (KIM-1/Cr) levels ($p < 0.05$). The receiver operating characteristic curve showed that ATGL had better diagnostic value for DKD (area under the curve [AUC] = 0.703). Grouping according to serum ATGL quartiles revealed that with an increase in serum ATGL levels, UACR, 24h-UTP, SCr, and TNFR-1 gradually decreased, and eGFR gradually increased. Odds ratios for elevated UACR and 24h-UTP gradually decreased, whereas eGFR gradually increased with increasing ATGL quartiles. Based on the univariate and multivariate logistic regression analyses, serum ATGL remained a protective factor against the development of DKD after adjusting for relevant confounders. The RCS suggests a nonlinear dose-effect relationship between serum ATGL and renal function parameters (UACR and eGFR) in DKD. Conclusion Serum ATGL levels are associated with impaired renal function in patients with T2DM. As ATGL levels decreased, nonlinear increases in UACR and decreases in eGFR were observed, indicating that serum ATGL can serve as a biomarker of DKD progression.

Abstract no.260

The Effectiveness and Safety of a Thai Medicinal Herbal Remedy in the Rehabilitation of Patients Due to Cerebrovascular Disease

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Thamlai-Phra-Su-Men (TPM), a traditional Thai herbal remedy from National Thai Traditional Medicine Formulary 2018 Edition, is used for rehabilitation of patients with cerebrovascular disease (CVD) due to its muscle relaxation, stress, anxiety, and pain reduction effects. However, there has not been scientifically researched regarding the efficacy and safety of TPM. Accordingly, the aims of this study were to evaluate the effectiveness and safety of TPM in rehabilitation of patients due to intermediate care for CVD. A randomized, double-blinded clinical trial in 30 CVD patients aged between 40 and 70 years was conducted. All patients received Thai Court-type massage and hot herbal compress for 1.30 h/time, twice a week. One treatment group (15 patients) received 500 mg of TPM capsules (2x2 ac every day for 20 weeks), while the other received placebos. All assessments were followed up at 10 and 20 weeks. Changes in motor power grade, the National Institute of Health Stroke Scale (NIHSS), Barthel Activities of Daily Living (ADL), EQ-5D-5L, as well as Patient Global Assessment were examined for efficacy. Clinical examinations, abnormalities in laboratory tests, and the incidence of adverse events (AEs) were assessed for safety. The efficacy outcomes of the TPM group showed significantly increased motor power in the arm since week 10 and the leg in week 20. The TPM group also improved NIHSS and ADL more than the placebo group at week 20 when compared with day 0. The ED-5D-5L levels of both groups increased significantly; the TPM group observed an increase at week 10, whereas the placebo group observed an increase at week 20. At the completion of the experiment, over 70% of the TPM group recorded ratings of "very much better" and "excellent" in terms of overall effectiveness from the global assessment, leading to statistically significant differences from the placebo groups. In terms of safety outcomes, both groups reported no severe adverse events. The liver function and renal function were within the normal range for all patients before and during the treatment. This clinical trial revealed the safety of using TPM and its efficacy in terms of increasing motor power grade, NIHSS, EQ-5D-5L, as well as Patient Global assessment, which improved the daily life activities of patients. As a result, TPM can be an alternative medicine for patients due to the intermediate care of CVD.

Abstract no.261

Clinical study of Chinese Medicine in the treatment of patients with intractable dizziness — A Randomized Controlled Trial

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Abstract: 1. Background: It has been reported that far-infrared energy is helpful in body treatment, but there are few studies of its actual use on acupoints according to the Chinese medicine. A new way of heat treatment with far-infrared energy released in a form out of a patch of thermal fabric can easily and precisely be applied. A design with the far-infrared patch and/or acupuncture is studied to treat the refractory dizziness of patients. 2. Method: A 3-group single-blind parallel randomized controlled trial is designed: acupuncture group (A), electrified far-infrared (FIR) group (B) and no electrified FIR control group (C). There are four acupoints selected on each of the left and right limbs correspondingly, namely Neiguan (PC6), Hegu (LI4), Zusanli (ST36) and Taichong (LR3). If patients are with intractable dizziness in the emergency department after drugs and otolith respositioning procedure treatment, they will be given 20 minutes of the above experimental interventional therapy according to the designed schedule on the eight acupoints in the above three groups. Baseline assessments include age, gender, height, weight, waist circumference, neck circumference, body temperature, respiration rate, pulse rate and blood pressure. Main assessments are measured by visual analog scale (VAS), dizziness handicap inventory (DHI) questionnaire, and heart rate variability (HRV). The analysis method used is one-way analysis of variation for the three groups and paired t test when comparing within two groups. 3. Result: VAS and DHI are found with statistically significant effect ($p<0.05$) within the same groups on the experimental groups A and B, but no corresponding result on the group C. HRV is found without statistically significant effect ($p>0.05$) within the same groups over the three groups correspondingly.

Abstract no.262

A Botanical Drug Development Roadmap for YIV-906

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7.Yung-Chi Cheng

YIV-906 (formerly known as PHY906, KD018), inspired by a 1800-year traditional botanical medicine formulation, is being developed as adjuvant therapy under the FDA's botanical drug guidance (IND's 138525 and 62627) to treat unmet medical needs for gastrointestinal (GI) aliments with chemotherapeutics or chemoradiation therapies. Following strict botanicas selection criteria and marker compound specifications, YIV-906 is manufactured according to robust cGMP standards, to produce the patient-friendly, fast release capsule filled with consistent drug substance. The results from more than 250 patients with liver, pancreatic, colorectal, or rectal cancers being treated with YIV-906 as pan adjuvant treatment, in combination with chemotherapeutic or chemoradiation regimens in ten phase I/II to II clinical studies at prestigious cancer research institutions, indicate YIV-906 used not only reduces the GI ailments, including diarrhea, nausea, vomiting, abdominal pain, also does not compromise the anti-cancer treatment's efficacy. By improving the quality of life, and reducing GI and skin toxicities, the therapeutic indexes of the anticancer treatments are enhanced.

The CMC behind producing a consistent drug substance and stable drug product is a major hurdle for TCM drug development. Combining scientific rigor, two generations of quality controls platforms (Phytomics and MeQC platforms), in addition to commercial chromatography, were developed and applied to YIV-906's manufacturing processes and address quality assurance. In preclinical studies the indication-specific biomarkers for YIV-906 not only confirm its batch-to-batch bioactive properties, can be used to discover new usages for its poly-target medicinal properties.

12. Polychemical Activities and Mechanism Study III (Metabolic Diseases, Systems Biology, Microbiota, Exosome, Tissue Action Specificity)

Abstract no.263

Panax notoginseng saponins alleviates colitis via the regulation of gut microbiota

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The occurrence and progression of inflammatory bowel disease (IBD) are significantly associated with gut microbiota. Panax notoginseng saponins (PNS) can be used to treat colitis and regulate intestinal microbiota. However, the mechanism behind PNS's anti-colitis effect related to intestinal microbiota remains largely unknown. This study explored the role of PNS in treating IBD and its correlation with intestinal microbiota. The results showed that PNS not only significantly alleviated colitis symptoms induced by dextran sulfate sodium (DSS) but also increased the level of tight junction proteins in the intestines of mice. Meanwhile, PNS reduced the expression of proinflammatory factors. Furthermore, fecal microbiota transplantation (FMT) experiments confirmed that PNS-reshaped intestinal microbiota had a significant effect on relieving colitis. In addition, PNS also regulated the composition and abundance of intestinal microbiota and altered bile acid metabolism, particularly by increasing the content of conjugated bile acids such as TCA and TCDCA. These changes are closely related to intestinal immune regulation. Through in vivo experiments, we found that TCA and TCDCA alleviate IBD symptoms by increasing the proportion of Treg cells and improving intestinal barrier function. In summary, this study revealed a new mechanism of PNS in treating colitis, which exerts an anti-inflammatory effect by regulating intestinal microbiota balance and bile acid metabolism, providing new insights for the treatment of IBD.

Abstract no.264

Mapping the regulatory effects of herbal organic compounds on gut bacteria

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Herbal organic compounds (HOCs) are bioactive natural products from medicinal plants and some traditional Chinese medicines (TCMs). Recently, ingestion of a few HOCs with low bioavailability has been associated with alterations in gut microbiota, but the extent of this phenomenon remains unclear. Here, we systematically screened 481 HOCs against 47 representative gut bacterial strains in vitro and found that almost one-third of the HOCs exhibited unique anticommensal activity. Quinones showed a potent anticommensal activity, while saturated fatty acids exhibited stronger inhibition of the Lactobacillus genus. Flavonoids, phenylpropanoids, terpenoids, triterpenoids, alkaloids and phenols displayed weaker anticommensal activity, but steroids, saccharides and glycosides had hardly any effect on strain growth. Notably, S-configuration HOCs demonstrated stronger anticommensal activity than R-configuration HOCs. The strict screening conditions ensured high accuracy (95%) through benchmarking validation. Additionally, the effects of HOCs on human fecal microbiota profiling were positively correlated with their anticommensal activity against bacterial strains. Molecular and chemical features such as AATS3i and XLogP3 were correlated with the anticommensal activity of the HOCs in the random forest classifier. Finally, we validated that curcumin, a polyhydric phenol with anticommensal activity, improved insulin resistance in HFD mice by modulating the composition and metabolic function of gut microbiota. Our results systematically mapped the profile of HOCs directly affecting human gut bacterial strains, offering a resource for future research on HOC-microbiota interaction, and broadening our understanding of natural product utilization through gut microbiota modulation.

Abstract no.265

Exploring the mechanisms of WenShenYang Formula for treating osteoporosis through regulating gut microbiota based on network pharmacology and molecular docking

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Abstract Background: Osteoporosis (OP) is a common systemic metabolic bone disease that greatly increases the risk of fracture. The imbalance of gut microbiota (GM) is closely related to the development of osteoporosis. WenShenYang Formula (WSYF) has a remarkable effect on OP. Therefore, it is of great interest to explore whether WSYF can treat OP through modulating GM. METHODS: A systematical network pharmacology approach, including multi-database search, bioinformatics analysis, protein-protein interaction network construction, GO and KEGG enrichment analysis and molecular docking, was used to elucidate the active components, potential targets, and signaling pathways of the WSYF treating OP through regulating GM. RESULTS: A total of 71 active components and 358 active compounds targets for WSYF were obtained by TCMSP. GeneCards and OMIM provided 730 targets related to GM and 4629 targets related to osteoporosis, respectively. Taking their intersection with the active compound targets of WSYF obtained, a total of 92 potential therapeutic targets of Wen Renyang were derived. According to the sub-network analysis of PPI, IL2、UGT1A1、HSP90AA1、FOS as the nodes with high scores in their respective sub-networks, can be considered the core targets of WSYF for treating OP through regulating GM. Functional and pathway enrichment analysis indicated that these putative targets exerted therapeutic effects on OP by regulating signaling pathways (e.g., IL-17 signaling pathway), and are involved many biological processes (e.g., xenobiotic stimulus). The molecular docking indicated that WSYF active compounds and potential therapeutic targets has a strong binding capacity. Conclusion: A variety of bioactive compounds, targets, and pathways suggested that the WSYF may play a role in treating OP through modulating GM, which provides evidence for further study of the pharmacological mechanisms of WSYF. Keywords: WenShenYang Formula, Gut microbiota, Osteoporosis, Network pharmacology, Molecular mechanism

Abstract no.266

A Meritorious Integrated Medical Regimen for Hepatic Fibrosis and Its Complications Via The Systematic Review and Meta-analysis For Dahuang Zhechong Pill Based Therapy

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Background: Hepatic fibrosis is a challenging health issue with limited treatment options, especially at the cirrhosis stage. Dahuang Zhechong pill (DHZCP) therapy has shown promise in treating hepatic fibrosis and cirrhosis. A systematic review and clinical evidence assessment of DHZCP therapy is needed to generate clinical recommendations for its efficacy in treating hepatic fibrosis. Potential indicators such as hepatic function, spleen thickness, and portal vein internal diameter should be evaluated. Methods: PubMed, the Excerpta Medica Database, the Cochrane Library, Web of Science, the WanFang Database, the Chinese Scientific Journal Database, and the Chinese National Knowledge Infrastructure database were searched to identify clinical trials. Three subgroup analyses were performed based on stages of disease, medications use, and courses of treatment. Statistical analyses were performed using Review Manager 5.4. Results: DHZCP-based therapy was effective in reducing plasma levels of hyaluronic acid, laminin, procollagen III, and IV collagen, as well as reversing abnormalities in liver enzymes and bilirubin levels. A 6-month treatment course was found to be the most beneficial. The therapy also showed potential in inhibiting hepatic stellate cell growth, reducing inflammation, and preventing extracellular matrix formation. Additionally, improvements were seen in hepatic portal hypertension and splenomegaly. Conclusion: DHZCP-based therapy has demonstrated efficacy as a treatment for hepatic fibrosis, and cirrhosis. A 6-month course of treatment is the recommended option for DHZCP-based therapy in clinical practice. The combination of DHZCP-based therapy and entecavir is a favorable treatment for hepatic cirrhosis.

Abstract no.267

Exosomal delivery of rapamycin modulates blood-brain barrier penetration and VEGF axis in glioblastoma

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Exosomes (Exos), nanosized membranous vesicles (30-160 nm), have been validated as an effective drug delivery system capable of traversing biological barriers. Mesenchymal stem cells (MSCs), due to their near-limitless self-renewal capabilities, provide a plentiful source of exosomes for clinical applications. In this study, we utilized an exosome-encapsulated rapamycin (Exo-Rapa) delivery strategy, which permits the use of smaller drug dosages to achieve effects typically seen with higher dosages, thus enhancing drug efficacy. Moreover, Exos can transport pharmaceuticals across the blood-brain barrier (BBB) to the brain, and further penetrate GL261 cells to exert their effects. Within the tumor microenvironment, Exo-Rapa is released more rapidly and efficiently at the tumor site. The acidic conditions in tumors accelerate the release of Exo-Rapa, a characteristic that may make it a promising targeted therapeutic in future cancer research. Additionally, a series of in vivo experiments have further demonstrated the permeability of Exo-Rapa across the BBB, enabling it to accumulate at tumor sites; it also ameliorates inflammatory responses in Glioblastoma multiforme (GBM) mouse models and enhances anti-tumor activity through the regulation of angiogenesis via the VEGF/VEGFRs axis. Our results indicate that MSC-derived exosomes are a potent therapeutic carrier for GBM, offering an effective strategy for enhancing drug delivery across the BBB and providing a scientific foundation for the use of exosomes in the treatment of GBM and other diseases. Dr. Neher’s Biophysics Laboratory for Innovative Drug Discovery, State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology, Macau, China b Faculty of Chinese Medicine, Macau University of Science and Technology, Macau, China Corresponding authors: Dr. Betty Yuen Kwan Law, Ph.D, Dr. Neher’s Biophysics Laboratory for Innovative Drug Discovery, State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology, Macau, China. Tel: (853) 8897-2407. E-mail Address: yklaw@must.edu.mo. Acknowledgments This research was funded by grants from the Macao Science and Technology Development Fund 002/2023/ALC,006/2023/SKL.

Abstract no.268

Panax notoginseng attenuates MRSA PSM-induced neutrophilic inflammation by inhibiting RIPK1/RIPK3/MLKL pathway

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Background: Methicillin-resistant Staphylococcus aureus (MRSA) is one of the most serious multidrug-resistant bacteria causing infections. MRSA releases the virulence factor psm, which recruits and activates neutrophils (Neu) at infection sites, inducing neutrophil necroptosis and respiratory burst (massive production of reactive oxygen species (ROS)), thereby promoting inflammatory responses. Panax notoginseng (PN), a traditional Chinese medicine with anti-inflammatory properties, can inhibit Neu-induced inflammatory reactions. This study aimed to explore the effect of PN on MRSA-induced Neu inflammation. Methods: CCK8 assay was used to detect the cytotoxicity of PN on Neu. An MRSA-infected Neu in vitro model was established, and qRT-PCR was performed to assess the impact of PN on the transcription levels of psmα1, 2, and 3 in MRSA, and the transcription levels of RIPK1, RIPK3, and MLKL in Neu. ELISA was employed to measure the protein levels of IL-1β, IL-33, MCP-1, and HMGB1. Flow cytometry was used to detect neutrophil counts and levels of ROS. Results: PN exhibited no cytotoxicity on Neu at concentrations below 0.5 mg/mL (Figure 1A). PN inhibited the expression of psmα1, 2, and 3 in MRSA. Compared to the Control group, the mRNA levels of necroptosis pathway genes RIPK1, RIPK3, and MLKL were significantly elevated in the model group. PN inhibited the transcription of all three genes. The inhibitory effect of PN on RIPK1 and RIPK3 paralleled that of the necroptosis inhibitor (Nec-1), particularly restoring RIPK1 transcription levels to those of the Control group. In the model group, the levels of inflammation-related factors were significantly elevated. PN exhibited a similar inhibitory effect on these factors as Nec-1 (Figure 1B). Compared to the model group, PN markedly reduced the expression of IL-33 and HMGB-1, with a tendency to inhibit IL-1β and MCP-1 expression (Figure 1C). The number of Neu in the model group was significantly reduced, with ROS levels markedly increased, which PN reversed (Figure 2). Conclusion: PN can inhibit the expression of MRSA virulence factors psmα1, 2, 3, and reduce Neu apoptosis and inflammatory response induced by MRSA infection by suppressing ROS production in neutrophils and the transcription levels of necroptosis pathway genes RIPK1, RIPK3, and MLKL.

Abstract no.269

Honghua Xiaoyao tablets mitigate depressive-like behaviors of premenstrual syndrome rats by reversing the dysregulation of HPA axis activation-mediated nervous-endocrine crosstalk

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Background: Premenstrual syndrome (PMS), characterized by dysphoria and physical symptoms approximately two weeks before menstruation, is a common disease among women of reproductive age worldwide. It is a lack of effective drugs for the treatment of PMS with satisfying clinical efficacies. Honghua Xiaoyao Tablets (HXTs) have been indicated to improve the psychosomatic symptoms of patients with PMS. However, its underlying pharmacological mechanisms remain unclear. Methods: The progesterone-withdrawal rat model was treated with HXT for 1 week to evaluate the pharmacological effects of this prescription for PMS. The depression-like degree was evaluated by the open field. In addition, the serum biochemistry was analyzed to assess the changes in the sex hormone and HPA-axis hormones. Following the prediction of HTX putative targets and the collection of PMS-related genes from our ETCM 2.0 database (http://www.tcmip.cn/ETCM2/front/#/), the "HXT putative target-PMS-related gene" network was constructed using the gene-gene interaction data and the network topological features of each nodes were calculated to screen the key network targets of HXT against PMS. Experimentally, the pathologic changes in the ovary and hippocampus were evaluated using hematoxylin and eosin (H&E), Nissl, and TUNEL stainings. After that, western blot, immunohistochemical staining (IHC), and immunofluorescence (IF) were performed to verify the underlying mechanisms of HXT against PMS. Results: HXT administration effectively improved ovarian function and ameliorated depressive-like behaviors in PMS rats. Our network analysis revealed that the therapeutic effects of HXT on PMS were associated with its regulation of the UBE2I-CYP19A1-ESR2-GSK3β axis. According to our experimental validation results, HXT administration effectively reversed the abnormal downregulation of UBE2I protein, which may be closely associated with the aberrant expression of CYP19A1 and estrogen depletion. Subsequently, the recovery level of estradiol rescued neuropathological changes from HPA axis activation-mediated cellular pyroptosis and inflammatory responses in the hippocampus of the PMS mice. Both IHC and western blot analyses also confirmed that HXT exerted significant neuroprotective and anti-inflammatory effects on PMS rats' hippocampus by elevating the expression of ESR2 and inhibiting the expression of GSK3β, NLRP3, Caspase-1, and GSDMD, and simultaneously suppressing the synthesis of the inflammatory factor IL-1β. Conclusion： The current study reveals that HXT may mitigate depressive-like behaviors of PMS via exerting its reproduction protective and neuroprotective effects by reversing the dysregulation of HPA axis

activation-mediated nervous-endocrine crosstalk. Fig.1. Reproduction protective and neuroprotective effects of HXT administration based on the PMS animal model. (A) Flow chart for assessing the effects of HXT based on the PMS rats. (B) The motion track in the OFT. (C) and (D) Serum levels of E2 and CORT in different groups. (E) Pathological observations of ovaries in each group with HE staining. Scale bars: 100 μm (F) Immunofluorescence for UBE2I (red) in ovaries of rats in different groups. Blue, DAPI. Scale bars: 100 μm. (G) Western blot analysis of the expression of NR5A1. (H) Ovarian index in different groups. (I) The level of AMH in the ovaries. (J) and (K) The level and activity of CYP19A1 in different groups. (L) and (M) Immunocytochemistry for the expression of ESR2 in the hippocampus. (N) Neuron numbers in the hippocampal CA3 region among the groups. (O) TUNEL staining was used to detect the pyroptosis (green) in the hippocampus. Blue, DAPI. Scale bars: 100 μm. (P) (Q) (R) (S) (T) and (U). Western blot analysis of the expression of GSK3β, Caspase-1, and GSDMD. (V) The level of IL-1β in the hippocampus. (The results are presented as the mean ±SEM. N=3 to 5 independent experiments, where each experiment was performed in duplicates or triplicates. #$p < 0.05$, ##$p < 0.01$, ###$p < 0.001$, vs. Vehicle group; *$p < 0.05$, **$p < 0.01$, ***$p < 0.01$, vs. Model group.) Fig.2. Schematic diagram of the pharmacological mechanisms of HXT administration against PMS.

Abstract no.270

Osteoking Exerts Pro-osteogenic and Anti-adipogenic Effects in Promoting Bone Fracture Healing via EGF-EGFR-HDAC1-Wnt/β-catenin Signaling

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Background: Bone fractures, as a global public health issue, often lead to disability and reduce the quality of patients' lives. Modern medicine has a very limited number of drugs with the potential to promote fracture healing. Growing number of clinical evidence shows the satisfying efficacy of Chinese patent drug Osteoking in promoting bone fracture healing. However, its therapeutic properties and the underlying mechanisms remain unclear. Methods: A rat model of tibial bone fracture was established to evaluate the pharmacological effects of Osteoking by behavioral experiments, X-ray scanning, micro-CT 3D reconstruction, histopathological staining, biomechanical testing and so on. Then, an integrated investigation combining transcriptomics profiling, network analysis and in vivo experimental validation was carried out to determine the potential targets of Osteoking in promoting bone fracture healing. Results: Osteoking treatment effectively promoted the bone trabecular growth and callus remodeling, shortened the fracture healing time, enhanced the muscle strength and improved the mechanical properties of the affected limbs, mainly by accelerating the process of endochondral ossification, decreasing the number of osteoclasts, increasing the level of bone growth factor, and improving the indicators of bone metabolism. Following the construction of the “disease gene-drug target” network and the calculation of nodes’ topological features and shortest path values, a total of 23 key network targets were screened. On the basis of the functional enrichment analysis, we hypothesized that the EGF-EGFR-HDAC1-Wnt/β-catenin axis-mediated adipogenesis-angiogenesis-osteogenesis crosstalk might be a candidate target of Osteoking against bone fracture. Experimentally, our data indicated that Osteoking treatment significantly reduced the expression levels of EGF, p-EGFR, and HDAC1 proteins and activated the Wnt/β-catenin signaling, which subsequently elevated the expression levels of VEGFA, OSX and CD31 proteins, increased the RUNX2/PPARγ ratio, decreased the RANKL/OPG ratio, and reduced the serum levels of TC, LDL-C and HDL-C. Notably, the significant negative correlations among VEGFA, OSX, TC and LDL-C levels were also verified. Conclusion: Our data indicate for the first time that Osteoking may effectively reverse the disturbance of adipogenesis-angiogenesis-osteogenesis homeostasis caused by bone fractures and also promote the fracture healing via regulating the EGF-EGFR-HDAC1-Wnt/β-catenin axis.

Abstract no.271

Loganin improves chronic unpredictable mild stress-induced depressive-like behaviors and neurochemical dysfunction

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Cornus officinalis Sieb. et Zucc., a cherished herb in traditional Chinese medicine, yields Loganin, a pivotal iridoid glycoside. Notably, Loganin has emerged as a promising antidepressant contender, having demonstrated efficacy in alleviating depression-like behaviors in mice subjected to acute stress. To further investigate its potential, we evaluated Loganin's effects on mice experiencing chronic unpredictable mild stress (CUMS), a model mimicking depressive-like states. ICR mice were subjected to the CUMS paradigm, and Loganin's therapeutic impact was gauged through a battery of behavioral assessments: sucrose preference test (SPT), forced swim test (FST), tail suspension test (TST), and open-field test (OFT). Additionally, we quantified serum levels of adrenocorticotropic hormone (ACTH) and corticosterone (CORT) using ELISA, monitored monoamine neurotransmitter levels via HPLC-ECD, and assessed brain-derived neurotrophic factor (BDNF) expression in the hippocampus through western blot analysis. Our findings revealed that CUMS indeed induced depressive-like behaviors in mice, as evidenced by the behavioral tests. Notably, Loganin administration significantly enhanced sucrose preference in SPT, reduced immobility durations in FST and TST, improved food intake, and increased locomotor activity in OFT. Mechanistically, Loganin normalized the perturbed secretion of monoamine neurotransmitters, ACTH, and CORT. Furthermore, it augmented BDNF expression in the hippocampus. In summary, Loganin exerts antidepressant-like effects in CUMS mice by modulating monoamine neurotransmitters, ACTH, CORT, and BDNF. By elevating 5-hydroxytryptamine (5-HT) and dopamine (DA) levels, mitigating hypothalamic-pituitary-adrenal (HPA) axis dysfunction, and enhancing BDNF expression, Loganin effectively ameliorates depressive-like symptoms in these mice.

Abstract no.272

Evaluation of the safety and efficacy of the combined use of FOLFOX and Patriniae Herba in colon xenograft-bearing mice

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Patriniae Herba (Bai Jiang Cao) has long been used as a medicinal herb for treating gastrointestinal disorders. In recent years, Patriniae Herba (PH) is commonly prescribed by Chinese medicine practitioners to colorectal cancer (CRC) patients. Thus, the possibility of concurrent use of PH with chemotherapeutics occurs. This study aimed to investigate whether PH aqueous extract (PHW) would interfere with the metabolism of FOLFOX, one of the first-line chemotherapy regiments for CRC patients. The anti-tumor efficacy of the combined use of PH and FOLFOX was also evaluated. Male nude mice bearing HCT116 colon xenograft were treated with FOLFOX (5-fluorouracil, folinic acid and oxaliplatin) and/or PHW for three weeks. FOLFOX was administered on day 1 every week while PHW was given by oral gavage on days 2-7 of each week. After 3-weeks treatment, blood samples were collected for determination of metabolizing enzymes/molecules of FOLFOX component drugs. For example, dihydropyrimidine dehydrogenase (DPD), serine hydroxymethyltransferase (SHMT) and cysteine, which are responsible for the catabolism or transformation of 5-fluorouracil, folinic acid and oxaliplatin, respectively. Besides, final tumor sizes were also compared in different treatment groups. Our results showed that oral administration of PHW did not significantly alter the plasma levels of DPD, SHMT and cysteine in colon xenograft-bearing mice. On the other hand, the combined PHW and FOLFOX treatment resulted in stronger inhibitory effect on HCT116 tumor growth, when compared with PHW or FOLFOX alone treatments. In conclusion, with the potent anti-tumor efficacy of PHW alone as demonstrated in our previous studies [1,2], together with the findings obtained from the present study, the beneficial potentials of combined use of PHW and FOLFOX has been scientifically verified, which supports the clinical use in colon cancer management. References: [1] Yang et al., 2023. Phytomedicine, 117:154900. [2] Yang et al., 2023. Frontiers in Chemistry, 11: 1195883. Acknowledgement: This work was supported by Food and Health Bureau of HKSAR Government, Health and Medical Research Fund (Ref: 09203106).

Abstract no.273

The mechanism action of Kernel extract of Entada phaseoloides in treating neuropathic pain

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Neuropathic pain is a type of chronic pain with limited treatment options. Entada phaseoloides (L.) Merr. is a traditional Chinese medicine that has shown potential for treating neuropathic pain. This study employed behavioral experiments to validate the pharmacological characteristics of Kernel extract of Entada phaseoloides. in treating neuropathic pain, identified the components that enter the brain and blood, and further investigated its mechanisms of action using in vivo antagonist verification, network analysis, and molecular biology methods. The results showed that Kernel extract of Entada phaseoloides effectively alleviated neuropathic pain. Its active components can Penetrates the blood-brain barrier(BBB) and exert their effects by inhibiting neuroinflammation through pathways such as suppressing microglial PPARG. The findings suggest that Kernel extract of Entada phaseoloides has the potential to treat neuropathic pain. Future research will delve deeper into its mechanisms of action to provide a theoretical foundation for the development of new therapeutic drugs.

Abstract no.274

A comprehensive review of meta-analysis and network pharmacology conducted on preclinical trials of Salvia miltiorrhiza Bunge for ulcerative colitis.

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Ethnopharmacological relevance: Salvia miltiorrhiza Bunge (SM) can enhance blood flow, alleviate stagnation, dredge meridians, relieve pain, purify the heart, eliminate restlessness, cool blood, and eliminate carbuncles. Aim of the study: The purpose of this study was to utilize a combination of meta-analysis and network analysis of experimental studies to assess the effectiveness of SM for treating ulcerative colitis (UC). Materials and methods: We conducted a comprehensive search of the PubMed, Web of Science, and Elsevier ScienceDirect databases for literature published up to December 2023. Data were extracted and analyzed using Grapher 10 and Review Manager 5.3, respectively. To synthesize the retrieved data, a random effects model was employed, and network pharmacology was conducted to validate the mechanism based on the STRING database. Results: Compared to the UC model group, the SM treatment had a more potent therapeutic effect. It was observed that the colonic histological score in the UC animal model decreased significantly [SMD = -2.35, 95% CI (-3.29, -1.42); P < 0.00001], and colon shortening was effectively reversed [WMD = 1.29, 95% CI (0.91, 1.66); P < 0.00001]. Furthermore, a notable decrease in the level of TNF-α [SMD = -4.26, 95% CI (-5.91, -2.61); P < 0.00001] was observed. In addition, network pharmacological analysis revealed that immune regulation, repair of the damaged intestinal barrier, anti-inflammation, antioxidative stress, regulation of the intestinal flora, and lipid metabolism were the main therapeutic mechanisms of SM or SM-derived active compounds in the treatment of UC. Conclusion: This study employed meta-analysis and network pharmacology to demonstrate the efficacy of SM or SM-derived active compounds in relevant preclinical investigations of UC, providing supportive evidence and novel perspectives to facilitate future investigations. Reveal novel perspectives to facilitate future investigations. However, certain limitations exist, and more rigorously designed clinical and experimental studies are needed to further confirm the findings of our study. Acknowledgements This work was funded by the Science and Technology Development Fund, Macau SAR (No.: 0098/2021/A2 and 0048/2023/AFJ), and Chinese Medicine Guangdong Laboratory(HQCML-C-2024007).

Abstract no.275

A systematic review and meta-analysis of chondroitinase ABC promotes functional recovery in rat models of spinal cord injury

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Background. To comprehensively assess the neurologic recovery potential of chondroitinase ABC (ChABC) in rats after spinal cord injury (SCI). Methods. The PubMed, Embase, ScienceDirect, Web of Science, and China National Knowledge Infrastructure databases were searched for animal experiments that evaluated the use of ChABC in the treatment of SCI up to November 2022. Studies reporting neurological function using the Basso, Beattie, and Bresnahan (BBB) scale, as well as assessments of cavity area, lesion area, and glial fibrillary acidic protein (GFAP) levels, were included in the analysis. Results. A total of 46 studies were ultimately selected for inclusion. The results of the study showed that rats with SCI that received ChABC therapy exhibited a significant improvement in locomotor function after 7 days compared with controls (32 studies, weighted mean difference (WMD) = 0.58, [0.33, 0.83], P<0.00001). Furthermore, the benefits of ChABC therapy were maintained for up to 28 days according to BBB scale. The lesion area was reduced by ChABC (5 studies, WMD = -20.94, [-28.42, -13.46], P<0.00001). Meanwhile, GFAP levels were reduced in the ChABC treatment group (8 studies, WMD = -29.15, [-41.57, -16.72], P<0.00001). Cavity area is not statistically significant. The subgroup analysis recommended that a single injection of 10 μL (8 studies, WMD = 2.82, [1.99, 3.65], P<0.00001) or 20 U/mL (4 studies, WMD = 2.21, [0.73, 3.70], P=0.003) had a better effect on improving the function. The funnel plot of the BBB scale was found to be essentially symmetrical, indicating a low risk of publication bias. Conclusions. This systematic review and meta-analysis have indicated that ChABC could improve functional recovery in rats after SCI. The mechanism exploration is mainly to use ChABC to degrade glial scar chondroitin sulfate proteoglycans (CSPGs). This degradation leads to a decrease in the formation of glial scars and promotes axonal regeneration growth and myelination.

Abstract no.276

Puerarin Modulates Hepatic Farnesoid X Receptor and Gut Microbiota in High-Fat Diet-Induced Obese Mice

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Obesity is associated with alterations in lipid metabolism and gut microbiota dysbiosis. This study investigated the effects of puerarin, a bioactive isoflavone, on lipid metabolism disorders and gut microbiota in high-fat diet (HFD)-induced obese mice. Supplementation with puerarin reduced plasma alanine aminotransferase, liver triglyceride, liver free fatty acid (FFA), and improved gut microbiota dysbiosis in obese mice. Puerarin's beneficial metabolic effects were attenuated when farnesoid X receptor (FXR) was antagonized, suggesting FXR-mediated mechanisms. In hepatocytes, puerarin ameliorated high FFA-induced sterol regulatory element-binding protein (SREBP) 1 signaling, inflammation, and mitochondrial dysfunction in an FXR-dependent manner. In obese mice, puerarin reduced liver damage, regulated hepatic lipogenesis, decreased inflammation, improved mitochondrial function, and modulated mitophagy and ubiquitin-proteasome pathways, but was less effective in FXR knockout mice. Puerarin upregulated hepatic expression of FXR, bile salt export pump (BSEP), and downregulated cytochrome P450 7A1 (CYP7A1) and sodium taurocholate transporter (NTCP), indicating modulation of bile acid synthesis and transport. Puerarin also restored gut microbial diversity, the Firmicutes/Bacteroidetes ratio, and the abundance of Clostridium celatum and Akkermansia muciniphila. This study demonstrates that puerarin effectively ameliorates metabolic disturbances and gut microbiota dysbiosis in obese mice, predominantly through FXR-dependent pathways. These findings underscore puerarin's potential as a therapeutic agent for managing obesity and enhancing gut health, highlighting its dual role in improving metabolic functions and modulating microbial communities.

Abstract no.277

Evaluation of the anti-atherosclerotic effect for Allium macrostemon Bge. polysaccharides and structural characterization of its a newly active fructan

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ABSTRACT: Allium Macrostemon Bge. (AMB) is a well-known homology of herbal medicine and food that has been extensively used for thousands of years to alleviate cardiovascular diseases. It contains a significant amount of polysaccharides, yet limited research exists on whether these polysaccharides are responsible for its cardiovascular protective effects. In this study, the anti-atherosclerosis effect of the crude polysaccharides of AMB (AMBP) was evaluated using ApoE-/- mice fed a high-fat diet, along with ox-LDL-induced Thp-1 foam cells. Subsequently, guided by the inhibitory activity of foam cells formation, a major homogeneous polysaccharide named AMBP80-1a was isolated and purified, yielding 11.1% from AMB. The molecular weight of AMBP80-1a was determined to be 10.01 kDa. AMBP80-1a was firstly characterized as an agavin-type fructan with main chains consisting of →1)-β-D-Fruf-(2→ and →1,6)-β-D-Fruf-(2→ linked to an internal glucose moiety, with →6)-β-D-Fruf-(2→ and β-D-Fruf-(2→ serving as side chains. Furthermore, the bio-activity results indicated that AMBP80-1a reduced lipid accumulation and cholesterol contents in ox-LDL-induced Thp-1 foam cell. These findings supported the role of AMBP in alleviating atherosclerosis in vivo/vitro. AMBP80-1a, as the predominant homogeneous polysaccharide in AMB, was expected to be developed as a functional agent to prevent atherosclerosis. KEY WORDS: Allium Mcrostemon Bge.; polysaccharide; anti-atherosclerosis; ApoE-/- mice; foam cell; fructan

Abstract no.278

Tangluoning intervenes in the mechanism of Trx2 deficiency mediating abnormal cholesterol metabolism in Schwann cells

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Abstract Objective: Exploring the mechanism of Tangluoning (TLN) intervention in mitochondrial thioredoxin 2 (Trx2) deficiency mediated abnormal cholesterol metabolism in Schwann cells (SCs). Methods: Western blot (WB) method was used to detect the expression of Trx2 protein and myelin basic protein (MBP) in SCs after 24 and 48 hours of Trx2 siRNA blockade intervention. The appropriate intervention time was selected for the experiment. SCs were divided into a control group, a Trx2 siRNA intervention (siRNA) group, and a Trx2 siRNA intervention+TLN drug containing serum (siRNA+TLN) group. The high content analysis method was used to detect the content and expression of MBP, cholesterol, and lanosterol synthase (LSS), 7 hydroxysteroid 17-β dehydrogenase 7 (HSD17B7), 3-β hydroxysteroid- Δ(8), Δ(7) isomerase (EBP) in SCs, as well as in the cholesterol synthesis pathway. The WB method was used to detect the protein content of lanosterol 14-alpha demethylase (CYP51A) in the Control group, siRNA group, and siRNA+TLN group. Immunofluorescence assay was used to detect the expression of LSS, HSD17B7, CYP51A, and EBP in the sciatic nerve tissue of rats in blank control (Control) group, DPN model (HG) group, positive drug control (ALA) group, and Tangluoning treatment (TLN) group. Results: The WB results showed that the expression of Trx2 and MBP in SCs was significantly reduced in the 24 hour Trx2 siRNA intervention group compared to the normal group and the 48 hour intervention group ($P<0.05$). Therefore, the subsequent Trx2 siRNA intervention time was 24 hours. The results of high connotation analysis showed that compared with the Control group, the expression of MBP in SCs of the siRNA group was significantly reduced ($P<0.01$), cholesterol content was significantly increased ($P<0.01$), and the expression of LSS, HSD17B7, and EBP was significantly increased ($P<0.01$, $P<0.05$, $P<0.01$), compared with the siRNA group, the siRNA+TLN group showed a significant increase in MBP content ($P<0.01$), a significant decrease in cholesterol content ($P<0.01$), and a significant decrease in LSS and EBP expression ($P<0.01$). The WB results showed that compared with the Control group, the expression of CYP51A in SCs in the siRNA group was significantly increased ($P<0.05$), Compared with the siRNA group, the expression of CYP51A in the siRNA+TLN group was significantly reduced ($P<0.01$). The results of immunofluorescence assay showed that compared with Control group, the expression of LSS, HSD17B7, EBP, and CYP51A in the HG group was significantly increased ($P<0.05$), compared with the HG group, the expression of LSS, HSD17B7, EBP, and CYP51A in the TLN group was significantly reduced ($P<0.01$). Conclusion: TLN can effectively reduce the abnormal increase of LSS, EBP, and CYP51A proteins in the cholesterol synthesis pathway, increase the content of MBP, and reduce the abnormal accumulation of cholesterol. This suggests that TLN has an improvement effect on the lipid metabolism abnormalities of SCs after siRNA blocking Trx2, and can also improve the demyelination of DPN rats, which has the potential to treat DPN. Acknowledgement: This study was supported by National Natural Science Foundation of China (No.82174184) and General Project of Science and Technology Plan of Beijing Municipal Commission of Education (No.KM202210025021).

Abstract no.279

Effect of paeoniflorin on TOM20 of mitochondrial import pathway in diabetic peripheral neuropathy

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Abstract: Objective：To investigate the effect of paeoniflorin (PF) on the protein involved in mitochondrial import pathway mitochondrial translocase of outer mitochondrial membrane 20 (TOM20) in the sciatic nerve of diabetic peripheral neuropathy (DPN) rats and high glucose environment of Schwann cells (SCs). Methods：RSC96 cells was used to intervene with 25, 100 and 150 mmol/L glucose for 12, 24 and 48 h, respectively, and the expressions of TOM20 and mitochondrial thioredoxin 2 (Trx2) were detected by high content analysis; Control group (25 mmol/L glucose), TOM20 siRNA group, TOM20 siRNA + paeoniflorin 24 h group, and TOM20 siRNA + paeoniflorin 48 h group were set up. After transfection with TOM20 siRNA, 10 mmol/L paeoniflorin was given for 24, 48 h, respectively, Western blotting was used to detect TOM20 and Trx2 protein expressions; Control group (25 mmol/L glucose), highglucose group (150 mmol/L glucose), and paeoniflorin group (150 mmol/L glucose + 10 mmol/L paeoniflorin) were set up, high connotation analysis was used to detect TOM20 and Trx2 protein expressions. DPN rat model was prepared and given total glucosides of paeony, immunofluorescence was used to detect TOM20 and Trx2 protein expressions in sciatic nerve of rats. Results：The results of high content analysis showed that after 12, 24h of 150 mmol/L glucose intervention, TOM20 and Trx2 protein expressions were significantly decreased ($P < 0.05, 0.01$), and there was a correlation between the expressions of the two proteins. Compared with control group, TOM20 and Trx2 protein expressions in high glucose group were significantly decreased ($P < 0.01$); Compared with high glucose group, TOM20 and Trx2 protein expressions in paeoniflorin group were significantly increased ($P < 0.01$). The results of Western blotting showed that compared with control group, TOM20 and Trx2 protein expressions in TOM20 siRNA group were significantly decreased ($P < 0.05, 0.01$); Compared with TOM20 siRNA group, TOM20 and Trx2 protein expressions were significantly increased after intervention with paeoniflorin for 24, 48 h ($P < 0.05, 0.01$). Compared with control group, TOM20 and Trx2 protein expressions were significantly decreased in sciatic nerve of rats in model group ($P < 0.01$); Compared with model group, TOM20 and Trx2 protein expressions were significantly increased in total glucosides of paeony group ($P < 0.01$). Conclusion：Paeoniflorin can effectively counteract mitochondrial oxidative stress by up-regulating the expression of TOM20 protein in SCs as well as rat sciatic nerve and promoting the mitochondrial input of Trx2, which has therapeutic potential for the treatment of DPN. Acknowledgement: This study was supported by National Natural Science Foundation of China (No.82174184)；General Project of Science and Technology Plan of Beijing Municipal Commission of Education (KM202210025021) ； Beijing Science and Technology Association Youth Talent Promotion Project (BYESS2023386)；National Natural Science Foundation of China Young Scientist Fund（82204826）.

Abstract no.280

NADH-associated Reducing Stress reduction prevent alcoholic lipid degeneration in liver

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Background & Aims:Steatosis represents a significant pathological hallmark of alcoholic liver disease (ALD), contributing to the facilitation of acetaldehyde and Reactive oxygen species (ROS)-induced hepatic injury. During alcohol metabolism, the energy metabolite nicotinamide adenine dinucleotide (NADH) plays a pivotal role in lipid peroxidation, potentially leading to lipid toxicity; however, its precise involvement in ALD remains uncertain. This study utilized acute isopropyl alcohol (IPA) and the chronic-binge (NIAAA) model to investigate the role of NADH in ALD, aiming to ascertain its potential as a therapeutic target for ALD beyond acetaldehyde and ROS.Methods:This study utilized two models: IPA (3 g/kg, twice daily for two days, resulting in exclusive NADH accumulation) and NIAAA (employing the same modeling method as previous studies, inducing simultaneous generation of both NADH accumulation and other alcohol metabolites). Liver function, lipid metabolism, and pathological indicators were observed in the model group and control group. The NADH-recycling agent Methylene blue (MB) was administered to intervene in the model group, with changes in each indicator monitored before and after intervention.Result: In comparison to the control group, the IPA group demonstrated significantly elevated levels of ALT and TG ($P<0.05$), with increasing trends observed in AST and NADH values. Oil red and HE results indicated liver steatosis and injury. Similarly, when compared to the control group, the NIAAA group exhibited significantly increased levels of ALT, AST, and TG ($P<0.05$), along with an upward trend in NADH values. The HE and oil red staining results suggested occurrences of steatosis and liver injury in the NIAAA model group. However, following administration of the MB, the detection indicators were all improved to different extents. Conclusion: The study suggests that targeting NADH could represent a novel therapeutic approach for ALD, given its association with steatosis and liver injury during alcohol metabolism.

Abstract no.281

Tangshen Formula alleviates inflammatory injury against aged diabetic kidney disease through modulating gut microbiota composition and related amino acid metabolism

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Diabetic kidney disease (DKD) is leading causes and one of the fastest growing causes of chronic kidney disease worldwide, and leads to high morbidity and mortality. Emerging evidences have revealed gut microbiota dysbiosis and related metabolism dysfunction play a dominant role in DKD progression and treatment through modulating inflammation. Our previous studies showed that Tangshen Formula (TSF), a Chinese herbal prescription, exhibited anti-inflammatory effect on DKD, but underlying mechanism that involved gut microbiota and related metabolism in aged model remained obscure. Here, leptin-deficient ob/ob mice were used to establish aged DKD model, and 16S rRNA sequence and untargeted metabolomic analyses were employed to investigate the correlation between colonic microbiota serum metabolism. The aged ob/ob mice exhibited obvious glomerular and renal tubule injury and kidney function decline in kidney, while TSF treatment significantly attenuated these abnormalities. TSF also substantially exhibited potent anti-inflammatory effect in aged ob/ob mice indicating by reduced proinflammatory factor IL-6 and TNF-α, MCP-1 and COX-2 in serum, kidney and intestine, which suggested the involvement of gut microbiota with TSF effect. The 16S rDNA sequencing of the colonic microbiome and nontargeted serum metabolomics analysis revealed significant differences in gut microbiota structure and serum metabolomic profiles between WT and ob/ob mice. Notably, TSF treatment reshaped the structure of gut microbiota and corrected the disorder of metabolism especially tryptophan metabolism and arginine biosynthesis. TSF increased Anaeroplasma and Barnesiella genera and decreased Romboutsia, Akkermansia, and Collinsella genera, and further elevated tryptophan, 5-hydroxyindoleacetate, glutamic acid, aspartate and reduced 4-hydroxy-2-quinolinecarboxylic acid, indole-3-acetic acid, xanthurenic acid, glutamine. Further correlation analysis indicated that disturbed gut microbiota was linked to tryptophan metabolism and arginine biosynthesis to suppress inflammation. Our data revealed that TSF attenuated renal inflammation in DKD model by modulating gut microbiota and related amino acid metabolism in aged DKD model, highlighting gut microbiota and related metabolism functioned as potential therapeutic

target for DKD in elderly patients.

Abstract no.282

Poricoic acid A suppresses renal fibroblast activation and interstitial fibrosis in UUO rats via up-regulating Sirt3 and promoting β-catenin K49 deacetylation

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Renal interstitial fibrosis is the common pathological process of various chronic kidney diseases to end-stage renal disease. Inhibition of fibroblast activation attenuates renal interstitial fibrosis. Our previous studies show that poricoic acid A (PAA) isolated from Poria cocos is a potent anti-fibrotic agent. In the present study we investigated the effects of PAA on renal fibroblast activation and interstitial fibrosis and the underlying mechanisms. Renal interstitial fibrosis was induced in rats or mice by unilateral ureteral obstruction (UUO). UUO rats were administered PAA (10 mg·kg-1·d-1, i.g.) for 1 or 2 weeks. An in vitro model of renal fibrosis was established in normal renal kidney fibroblasts (NRK-49F cells) treated with TGF-β1. We showed that PAA treatment rescued Sirt3 expression, and significantly attenuated renal fibroblast activation and interstitial fibrosis in both the in vivo and in vitro models. In TGF-β1-treated NRK-49F cells, we demonstrated that Sirt3 deacetylated β-catenin (a key transcription factor of fibroblast activation) and then accelerated its ubiquitin-dependent degradation, thus suppressing the protein expression and promoter activity of pro-fibrotic downstream target genes (twist, snail1, MMP-7 and PAI-1) to alleviate fibroblast activation; the lysine-49 (K49) of β-catenin was responsible for Sirt3-mediated β-catenin deacetylation. In molecular docking analysis, we found the potential interaction of Sirt3 and PAA. In both in vivo and in vitro models, pharmacological activation of Sirt3 by PAA significantly suppressed renal fibroblast activation via facilitating β-catenin K49 deacetylation. In UUO mice, Sirt3 overexpression enhanced the anti-fibrotic effect of PAA, whereas Sirt3 knockdown weakened the effect. Taken together, PAA attenuates renal fibroblast activation and interstitial fibrosis by up-regulating Sirt3 and inducing β-catenin K49 deacetylation, highlighting Sirt3 function as a promising therapeutic target of renal fibroblast activation and interstitial fibrosis.

Abstract no.283

Study on the Spectral-effect Relationship of Rhubarb tanguticum Tschirch in Vitro to Repair Intestinal Barrier Damaged by Alcohol

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Objective: To study the spectral effect relationship of Rhubarb tanguticum Tschirchin vitro to repair intestinal barrier damage caused by alcohol, and to provide evidence for the material basis of protecting intestinal barrier function. Methods: The Caco-2 cells were cultured on transwell inserts to establish a compact monolayerarchitecture.The presence of alcohol induced structural changes in the monolayer of Caco-2 cells, mimicking injury to the intestinal barrier. The TEER value, the expression of tight junction protein Occludin, and the fluorescent yellow apparent permeability coefficient (Papp) were utilized to investigate the reparative function of the intestinal barrier in 21 batches of Rhubarb tanguticum Tschirch. The spectral relationship between HPLC characteristic peaks and intestinal barrier integrity,tight junction connectivity,and permeability was analyzed using Partial Least Squares Regression (PLSR). Results: The PLSR results revealed a positive correlation between 7 out of the 30 characteristic peaks and TEER value as well as Occludin expression (partial regression coefficient > 0).Conversely, there was a negative correlation with the fluorescent yellow apparent permeability coefficient (Papp) (partial regression coefficient < 0).Peaks1,11,27(rhein),12(sennosideA),28(emodin),10,14(chrysophanol),24(aloe emodin),22,30(emodin methyl ether) exhibited variable importance projection (VIP) values greater than 1. Conclusion: The active components of Rhubarb tanguticum, including Rhein, sennoside A, emodin, chrysophanol, aloe emodin, and emodin methyl ether, play a crucial role in repairing alcohol-induced intestinal barrier damage. These findings provide a solid research foundation and scientific evidence for elucidating the material basis and mechanism underlying the protective effects of Rhubarb tanguticum Tschirch on alcohol-induced intestinal barrier damage.

Abstract no.284

Morroniside attenuates podocytes lipid deposition in diabetic nephropathy: a network pharmacology，molecular docking and experimental validation study

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Background Dysregulation of lipid metabolism is a key factor influencing the progression of diabetic nephropathy (DN). Morroniside (MOR) is a major active compound isolated from the traditional Chinese herb Cornus officinalis, our previous research found that it can improve the lipid deposition of renal tubular epithelial cells. The purpose of this study is to explore whether MOR can improve podocyte lipid deposition and its mechanism of reducing DN. Methods Initially, we used network pharmacology and bioinformatics techniques to predict the relationship between renal lipid metabolism of MOR and DN. Subsequently, the binding activity of MOR with lipid-related proteins was studied by molecular docking to determine how MOR acts through these proteins. After determining the target of MOR, animal experiments and cell tests were carried out to verify it. Results Using network pharmacology, bioinformatics, and molecular docking, target proteins for MOR treatment of DN were predicted and screened, including PGC-1α, LXRs, ABCA1, PPARY, CD36, and nephrin. It is particularly noted that MOR effectively binds to PGC-1α, while LXRs, ABCA1, PPARY and CD36 are downstream molecules of PGC-1α. Silencing the PGC-1α gene significantly reduced the therapeutic effects of MOR. Conversely, in groups without PGC-1α knockdown, MOR was able to increase the expression levels of PGC-1α and influence the expression of downstream proteins. Furthermore, through in vivo and in vitro experiments, utilizing techniques such as lipid droplet staining, PAS, MASSON staining, immunofluorescence, and Western blot, we found that MOR effectively elevated the expression levels of the podocyte protein nephrin and lipid metabolism-regulating proteins PGC-1α, PPARY, and ABCA1, while significantly inhibiting the expression of the lipid accumulation promoter CD36. Conclusion MOR can regulate the cholesterol efflux in podocytes via the PGC-1α/LXRs/ABCA1 signaling pathway, and control cholesterol intake via the PGC-1α/PPARY/CD36 signaling pathway, thereby ameliorating lipid deposition in DN.

Abstract no.285

Hepatoprotective Effects of Standardized Mulberry (Morus alba) Fruit Extract on High-Fat Diet-Induced Liver Injury in Male Wistar Rats

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Introduction: Overconsumption of high-fat food can lead to dyslipidemia and non-alcoholic fatty liver disease (NAFLD), characterized by fat accumulation and inflammation. Mulberry (Morus alba) fruit contains high anthocyanin, known for its anti-inflammatory and antioxidative properties, has not been extensively studied for its effects on NAFLD in rats. Objective: This study aimed to determine the hepatoprotective effects of mulberry fruit extract on liver damage induced by a high-fat diet. Methods: Forty-two male Wistar rats were divided into seven groups (n=6/group): normal diet (ND), high-fat diet (HF), HF with crude mulberry extract (CEM) at 100 mg/kg/day, HF with standardized mulberry extract (SEM) at 10, 100, and 300 mg/kg/day, and HF with atorvastatin (ATV) at 10 mg/kg/day. After 90 days of treatment, plasma lipid profiles and liver enzymes were measured, and the liver was examined for macroscopic and microscopic changes. Results: HF rats showed significant dyslipidemia with increased triglyceride levels compared to the ND group ($p<0.001$). Rats treated with 100 and 300 mg/kg SEM had significantly decreased triglyceride levels compared to the HF group ($p<0.0001$). The HF group exhibited paler, larger livers with increased relative liver weight. Histologically, the HF group had significant lipid accumulation ($p<0.0001$), inflammation ($p=0.0035$ for portal inflammation, $p=0.0004$ for necroinflammation), and fibrosis ($p=0.0142$). Mulberry extract treatment reduced necroinflammation ($p=0.0407$ for SEM100) and fibrosis ($p=0.0014$ for SEM10 & SEM300; $p=0.0002$ for SEM100) compared to the HF group. Conclusion: Standardized mulberry fruit extract improved lipid profiles and provided hepatoprotection in rats with high-fat diet-induced liver injury. These findings suggest that standardized mulberry fruit extract could be a potential therapeutic agent for treating NAFLD and related hepatic diseases. Keywords: Mulberry fruit extract, Morus alba, Liver injury, Hepatoprotection, NAFLD

Abstract no.286

Huang-Lian-Jie-Du-Decoction alleviates diabetes mellitus complicated with ischemic stroke through intestinal flora and metabolite SCFAs

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Objective: A previous study found that Huang-Lian-Jie-Du-Decoction (HDD) could treat Diabetes Mellitus complicated with Ischemic Stroke (DIS) and excert therapeutic effects through intestinal flora and its metabolite short-chain fatty acids (SCFAs). In this research, we verified its therapeutic effects by employing pseudo-sterile rats. Methods: A pseudo sterile diabetic ischemic stroke rat model was constructed by wire bolus method and gavage antibiotic mixture, after successful modeling, normal rats and rats with successful modeling were randomly divided into control group, model group, HDD group, pseudo sterile sham-operated group, pseudo sterile model group, pseudo sterile HDD group, and SCFAs group. The effect of intestinal flora was assessed by means of biochemical indices, pathologic sections, immunofluorescence, and SCFAs assays. Results: Compared with non-pseudo-sterile DIS rats, longa score and TTC staining revealed that HDD had a reduced effect on neurological deficits and cerebral infarction in pseudo sterile DIS rats, and pseudo sterile treatment attenuated the ability of HDD to ameliorate dyslipidemia in DIS rats. Staining of brain tissue and colon pathological sections revealed that pseudo sterility treatment attenuated the ability of HDD to alleviate neural cell damage and repair intestinal damage in DIS rats. Immunofluorescence results suggested that the aseptic treatment attenuated the ability of HDD to ameliorate neuroinflammatory cell expression and neuronal loss in brain tissue of DIS rats. After gavage of the SCFAs mixture, the above conditions were found to be improved accordingly. Conclusion: This study suggests that intestinal flora and their beneficial metabolites SCFAs play an important role in the treatment of DIS by HDD. Keywords: Huang-Lian-Jie-Du Decoction; Diabetes Mellitus complicated with Ischemic Stroke; Intestinal Flora; Short-Chain Fatty Acids Acknowledgments: This research was supported by the National Natural Science Foun dation of China (No. 82374177, 82074137), Guangdong Basic and Applied Basic Research Foundation (No. 2022A1515220068), Key Project of Department of Education of Guangdong Province (No. 2022ZDZX 2032). * Corresponding author: Dan Tang, E-mail: tdpharm@126.com

Abstract no.287

Protective effects of Huang-Qi-Ge-Gen Decoction against diabetic liver injury

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Objective: To explore the protective effects of Huang-Qi-Ge-Gen Decoction (HGD) against liver injury in diabetic mice.. Methods: The liver injury model of type 2 diabetic mice was established by high-fat diet combined with multiple injections of low-dose streptozotocin. Forty mice with successful modeling were randomly divided into five groups: normal group, model group, HGD low-dose intervention group (3 g/kg), HGD high-dose intervention group (12 g/kg), and Metformin group (300 mg/kg), with eight mice in each group.After administration with HGD in fourteen weeks, blood and liver tissue samples of mice were collected, and blood glucose and lipid indexes, liver function indexes and liver tissue pathological sections were detected and analyzed. Results: Compared with the normal group, the serum TC, TG, ALT and AST levels of mice in the model group were significantly increased; Compared with the model group, the levels of ALT and AST in the high and low dose groups of HGD and the Met group were significantly decreased. The results of HE showed that HGD could improve liver lesions, fibrosis and lipid accumulation in diabetic liver injury mice.The degree of hepatocyte steatosis was significantly reduced and fat droplet accumulation was significantly reduced in the high and low dose groups of HGD as well as the metformin group. Conclusion: The results showed that HGD could regulate the disorder of glucose and lipid metabolism and reduce the pathological damage of liver tissue, thus playing a role in protecting diabetic liver disease. Key words: Huang-Qi-Ge-Gen Decoction; diabetes; liver injury; HE staining Funding: This research was supported by the National Natural Science Foundation of China (No. 82374177, 82074137), Guangdong Basic and Applied Basic Research Foundation (No. 2022A1515220068), Key Project of Department of Education of Guangdong Province (No. 2022ZDZX2032) *Corresponding author: Dan Tang, E-mail: tdpharm@126.com

Abstract no.288

Protective effects of Phellodendron amurense against diabetic liver injury

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Objective: To elucidate the ameliorative hepatoprotective effects of Phellodendron amurense (PA) on diabetic liver injury (DLI). Methods: A diabetic mice model was induced by feeding a high-fat diet (HFD) and injecting intraperitoneally with streptozotocin (STZ) (40 mg kg-1) for five days. After the animals were in confirmed diabetic condition, they were given PA (0.75 or 3 g kg-1, i. g.), metformin (Met) (0.3 g kg-1, i. g.) for 14 weeks. The effectiveness of PA in treating DLI mice was evaluated by monitoring blood glucose and blood lipid levels, liver function, and pathological conditions. Results: (1) The levels of Fasting blood glucose (FBG) were significantly elevated in DLI mice (Mod group) compared with those in normal mice (Con group), and their levels were regressed toward the Con group after PA intervention (HBL and HBH). In addition, the model group showed disturbances in lipid metabolism, including higher levels of Total triglyceride (TG), Total cholesterol (TC), Low-density lipoprotein cholesterol (LDL-C), and these abnormalities were significantly regulated after the administration of PA .These results revealed that disorders of glucose and lipid metabolism exist in DLI mice and that they could be reduced by treatment with PA. (2) Compared with the Con group, the plasma levels of aspartate aminotransferas (AST) and alanine aminotransferase (ALT) in the Mod group significantly increased, suggesting that the liver function of DLI mice was impaired. Notably, both HBL and HBH could reduce the levels of AST and ALT, indicating that PA had a repairing effect on liver function damage in DLI mice. (3) The staining results showed that the hepatocytes in the Con group were uniform in size and clear in overall structure. In the Mod group, the hepatocytes were diffusely swollen, with loose connections, enlarged hepatic sinusoids, and a large number of fat vacuoles. In addition, the mice in the Mod group had an accumulation of collagen fibers and severe hepatocyte vacuolar degeneration, lipid deposition, and inflammatory cell infiltration. The results indicated that the liver morphology of DLI mice presented pathological damage accompanied by lipid deposition and hepatic fibrosis, which were reduced by the PA intervention. Conclusions: PA ameliorates diabetic liver injury and improves the state of liver pathological damage.
Keywords: Phellodendron amurense; diabetes mellitus; diabetic liver injury Founding: This research was supported by the National Natural Science Foundation of China (No. 82374177, 82074137), Guangdong Basic and Applied Basic Research Foundation (No. 2022A1515220068), Key Project of Department of Education of Guangdong Province (No. 2022ZDZX2032).

Abstract no.289

Lychee seed polyphenol represses retinal neovascularization with abnormal capillary via inhibiting apoptosis and the NRLP3 inflammasome in hRECs and db/db Mice

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Background: Diabetic retinopathy (DR) is the most common and serious microvascular complication. Emerging evidence indicates that NLRP3 inflammation-induced retinal endothelial cell apoptosis and high VEGF expression contributed to retinal endothelial cell destruction and BRB damage, leading to retinal haemorrhage, exudation and macular oedema. However, inhibition of VEGF inhibited neovascularization in the retinas of db/db mice. Currently, surgical treatment is the main clinical treatment for DR and there are many limitations, so the early prevention and treatment of DR are even more important. Traditional Chinese medicines (TCMs) have a history of 2000 years for human diseases, which possess the advantages of high safety and few toxicity and side effects. Our previous studies have found that the lychee seed polyphenol (LSP) exhibit the pharmacological activities, including anti-apoptosis, the improvement of insulin resistance, anti-inflammatory response, and the maintenance of BBB and BRB integrity. However, the inhibitory effect of LSP on retinal neovascularization with abnormal capillary and its mechanism of action are still unknown. In this article, we discussed the role of the NLRP3 inflammasome-mediated inflammation in apoptosis and aberrant vascular proliferation in db/db mice and human retinal microvascular endothelial cells (hRECs). Method: 10-week-old male db/db mice and male C57BL/6 wild type mice were used in this experiment. all mice were fed with normal chow diet and were randomly divided into 6 groups as follows：C57BL/6 wild type mice, db/db mice, db/db mice + LSP (50 mg/kg·d-1), db/db mice + LSP (100 mg/kg·d-1), db/db mice + LSP (200 mg/kg·d-1), and db/db mice + Met (300 mg/kg·d-1). Each group has 8 mice, and all mice were administered once daily for 6 weeks after intragastric administration. apoptosis, inflammatory factors, protein expressions and cell morphology were detected by ELISA, immunohistochemical analysis, retinal staining, biochemical analysis and Western blot methods, respectively. 200 mM glucose was used to induced in human retinal endothelial cells (hRECs) and inflammatory response. After treatment of LSP, cell viability, inflammatory factors, apoptosis, protein expressions and cell morphology were detected by flow cytometry, Hoechst/PI and Western blot methods, respectively. Result: 1.LSP ameliorates obesity, hyperglycemia, and hyperlipidemia in db/db mice. 2.LSP alleviates retinal vascular injury in db/db mice. 3.LSP inhibits the inflammatory response and improves TJs expression in db/db mice. 4.LSP inhibits cell apoptosis and VEGF expression in the retinal tissue of db/db mice. 5.In LSP inhibits HG-induced cell death in hRECs. 6.LSP suppresses the activation of NLRP3 inflammasome in HG-induced hRECs. 7.LSP inhibits cell apoptosis and VEGF expression in HG-induced hRECs. Conclusion: In summary, the current study demonstrates that LSP ameliorates DR by inhibiting the NLRP3 inflammasome, cell apoptosis, and the abnormal retinal capillary neovascularization in HG-induced hRECs and db/db mice, which provides a sound scientific basis for the clinical application of LSP in the treatment of DR.

Abstract no.290

Hederagenin inhibits mitochondrial damage in Parkinson’s disease via mitophay induction

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Abstract Background: Parkinson's disease (PD) is a neurodegenerative disorder marked by the loss of dopaminergic neurons and the formation of α-synuclein aggregates. Mitochondrial dysfunction and oxidative stress are pivotal in PD pathogenesis, with impaired mitophagy contributing to mitochondrial damage accumulation. Hederagenin (Hed), a natural triterpenoid, has shown potential neuroprotective effects, but its mechanisms of action in PD models are not fully understood. Method: We investigated the effects of Hed on 6-hydroxydopamine (6-OHDA)-induced cytotoxicity in SH-SY5Y cells, assessing cell viability, mitochondrial function, and oxidative stress markers. Mitophagy induction was evaluated using autophagy/mitophagy inhibitors and fluorescent staining techniques. Additionally, transgenic Caenorhabditis elegans (C. elegans) models of PD were used to validate the neuroprotective effects of Hed in vivo, focusing on α-synuclein aggregation, mobility, and dopaminergic neuron integrity. Results: Hed significantly enhanced cell viability in 6-OHDA-treated SH-SY5Y cells by inhibiting cell death and reducing oxidative stress. It ameliorated mitochondrial damage, evidenced by decreased mitochondrial superoxide production, restored membrane potential, and improved mitochondrial morphology. Hed also induced mitophagy, as shown by increased autophagosome formation and reduced oxidative stress, effects that were diminished by autophagy/mitophagy inhibitors. In C. elegans models, Hed could activate mitophagy and reduce α-synuclein aggregation, improve mobility, and mitigate the loss of dopaminergic neurons. RNA interference targeting mitophagy-related genes Pdr-1 and pink-1 partially reversed these benefits, underscoring the role of mitophagy in hederagenin's neuroprotective actions. Conclusion: Hed exhibits significant neuroprotective effects in both in vitro and in vivo PD models by enhancing mitophagy, reducing oxidative stress, and mitigating mitochondrial dysfunction. These findings suggest that Hed holds promise as a therapeutic agent for PD, offering a new avenue for future research and potential drug development.

Abstract no.291

The potential of herbal extracts and derived active pharmaceutical ingredients for alleviation of aging-induced immunosenescence and inflammaging

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Immunosenescence means the decrease in immune function with age. Elderly people have fewer naive T cells and more memory T cells than young adults, mainly a consequence of thymic involution. Aged T cells also show impaired proliferative and/or effector functions. The accumulation of senescent cells can cause the increase in levels of pro-inflammatory cytokines, such as TNF-α and interferon gamma (IFN-γ), resulting in the chronic inflammation in the absence of acute infection. Inflammaging is also observed with age. Therefore, many efforts have been made to eliminate senescent cells with senolytics or to modulate a proinflammatory phenotype with senostatics for alleviation of aging and age-related disorders. In this study, we isolated three herbal extracts, including X, Y, and Z, to decrease aging-induced inflammation or to improve aging-associated immunosenescence and further identify the active pharmaceutical ingredient (API) in three extracts. Splenocytes and thymocytes from young and aged mice were isolated and treated with three herbal extracts (X, Y, and Z) in vitro. The activation and proliferation status in different T cell populations were examined using flow cytometry, showing that the extract Y and Z had the higher potential to induce the activation of aged splenic T cells and to trigger T helper 2 (Th2)-biased thymic T cell proliferation. Using the same in vitro bioactivity platforms, we further identified the API in each extract contribution to their anti-aging effects. All of the three identified APIs were superior to their original extracts to induce aged T cell proliferation or to alleviate aging-induced inflammation when compared at the same concentration. These findings suggested that the three identified APIs may have the potential to alleviate aging-induced immunosenescence and inflammaging in vivo, which deserved to be examined their anti-aging effects in the age-related disease models.

Abstract no.292

Coptis inhibited epithelial–mesenchymal transition and fibrogenesis of diabetic nephropathy through lncRNA CLYBL-AS2-miR-204-5p-SNAI1 axis

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Diabetic nephropathy (DN) is one of the severe complications of diabetes.Nowadays,effective treatment for end-stage renal disease(ESRD) patients is still limited.HK-2 cells were stimulated with serum from phosphate-buffered saline(PBS) or Jiawei Shuilu Erxiandan (JSE)-treated DN mice,then long non-coding RNA (lncRNA) CLYBL-AS2 was discovered by RNA sequence, following the comparison of the serum from normal patients with DN patients to confirm the role of lncCLYBL-AS2. Next, we performed in vitro studies to explore the effect of lncCLYBL-AS2 in DN and its molecular mechanism. Coptis, as one of the components of JSE, could decrease the expression of lncCLYBL-AS2, which is increased in DN and correlated with the severity of DN. Knockdown/overexpression of lncCLYBL-AS2 inhibited/promoted the invasion and fibrogenesis of HK-2 cells. Furthermore, lncCLYBL-AS2 was negatively correlated with miR-204-4p with a positive correlation with SNAI1; eventually, CLYBL-AS2 regulated SNAI1 by binding to miR-204-5p, which accounted for the inhibition of epithelial–mesenchymal transition (EMT) and fibrogenesis. LncCLYBL-AS2 inhibited by Coptis improved EMT and fibrogenesis in HK-2 cells through miR-204-5p-SNAI1 axis, therefore, lncCLYBL-AS2 could serve as a potential diagnosis and therapeutic target for DN.

Abstract no.293

Regulation of Autophagy by Traditional Chinese Medicine Tangshen Formula to Alleviate Renal Lipid Deposition in Diabetic Kidney Disease

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Objective: Autophagy can delay the progression of diabetic kidney disease (DKD) in type 2 diabetes by alleviating renal lipotoxicity. Our previous research found that the traditional Chinese medicine compound Tangshen Formula (TSF) can improve lipid metabolism disorders in diabetic nephropathy, but its underlying mechanism remains unclear. This study aims to explore the mechanism of TSF in regulating lipid autophagy to improve renal lipid metabolism disorders in DKD. Methods: Obese DKD model mice (KK-Ay) were used in this study and randomly divided into a model group and a TSF group. Age-matched C57BL/6J mice served as the normal control. Ten mice were assigned to each group, and continuous drug administration was given for 16 weeks. Renal function indicators and renal pathological injuries were assessed in each group. Cellular lipid deposition was detected using immunohistochemical and immunofluorescence methods to explore the molecular mechanism underlying TSF's improvement of renal lipid deposition in DKD. Results: TSF treatment improved multiple biochemical markers associated with diabetic renal injury in KK-Ay mice, including body weight, blood glucose, kidney weight index, urinary albumin, serum total cholesterol (TC), and triglycerides (TG). It also mitigated renal extracellular matrix deposition and tubulointerstitial fibrosis. Additionally, TSF significantly upregulated lipid autophagy activity in the kidneys of DKD model mice and reduced renal lipid deposition. These results indicate that TSF can improve renal lipid deposition by upregulating autophagy, suggesting its potential as a promising clinical drug for treating obesity-related renal injury. Conclusion: In summary, TSF can improve renal lipid deposition by upregulating autophagy mediated by adipose triglyceride lipase (ATGL), demonstrating its potential as a promising clinical drug for treating obesity-related renal injury.

Abstract no.294

20(S)-protopanaxadiol-loaded nanomicelles ameliorate corticosterone-induced depressive behaviors in C57/BL mice

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Depression greatly affects an estimated 3.8% of the global population[1]. Herbal medicine is a rich source for effective and safe antidepressant drugs. 20(S)-protopanaxadiol (PPD) is the aglycone of the dammarane type saponins from Panax ginseng and exerts a prominent antidepressant effect in mice[2]. However, the antidepressant effects of PPD is limited by the poor water solubility (<50 ng/mL) and low oral bioavailability. Interestingly, the nano-drug delivery system holds great promise for longer half-life, flexible dosage and lower frequency. Specifically, PEG-PCL copolymers are characterized by a high biocompatibility, biodegradability, and long-circulating properties and have great potential for the delivery of poorly water-soluble or hydrophobic drugs[3]. The present study investigated the anti-depressant effects and toxic activities of PPD-loaded nanomicelles (nano-PPD) in mouse model of corticosterone-induced depression. PPD was loaded into PEG-PCL nanoparticles, yielding nano-PPD with optimal size, spherical morphology, good bioavailability, slower peak time and clearance in mice. PPD and nano-PPD were administered into corticosterone-lesioned C57BL/6 J male mice for 3 weeks. As results, PPD and nano-PPD ameliorated depressive-like behaviors in the CORT-lesioned mice, increased the travel distance in open field test and decreased the immobility time in FST and TST. Moreover, nano-PPD caused little changes in the tissue integrity and function of heart, kidney, lung, and spleen. Collectively, nano-PPD represents a translatable therapeutic opportunity against depression.