Response Modified Smart Co-Polymeric Oxaliplatin Nanoparticles for Tumor Targeted Drug Delivery

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Abstract:

The objective of the research study was to develop and characterize a biodegradable, thermo and pH dual responsive Oxaliplatin-loaded chitosan-g-poly(N-isopropylacrylamide-co-vinyl pyrrolidone) [CS-g-P(NIPAAm-co-NVP)] co-polymeric nanoparticles for tumor targeted delivery of drug. CS-g-P(NIPAAm-co-NVP co-polymer was synthesized by free radical polymerization method. Base structure of synthesized co-polymer was determined and it is characterized for the determination of its grafting ratio, particle size, PDI and LCST. Oxaliplatin was loaded in to the co-polymer by self assembly method and nanoparticles were evaluated for their particle size, polydispersity index (PDI), zeta potential, loading efficiency and in vitro drug release study. The particle size of co-polymer was 146nm with a PDI of 0.249 which indicates the homodispersity of co-polymer particles. The grafting ratio and LCST of co-polymer were 43.33% and 38.27^{0}C respectively. Drug loaded nanoparticles shows particle size of 237 nm and Zeta potential of about 58 ±12 mV that indicates good stability of nanoparticles. The drug release was very low at physiological pH and temperature conditions while the drug release rate was drastically increased at the pH and temperature conditions of tumor microenvironment. MTT assay and fluorescence microscopic study demonstrated that synthesized co-polymer was biocompatible as well as drug release and cell uptake were significantly enhanced in tumor microenvironment pH and temperature. In conclusion, the obtained nanoparticles appeared to be of great promise in tumor targeted drug delivery of oxaliplatin.

Keywords:

Oxaliplatin, thermo and pH responsive nanoparticles, chitosan-graft-poly-N-isopropylacrylamide co-polymer, tumor targeting.

Design, synthesis and their biological evaluation of (E)-N-(2-(benzo[d]thiazol-2-ylamino)-5-phenylpyridin-3-yl)-4-phenylbut-3-enamide derivetives

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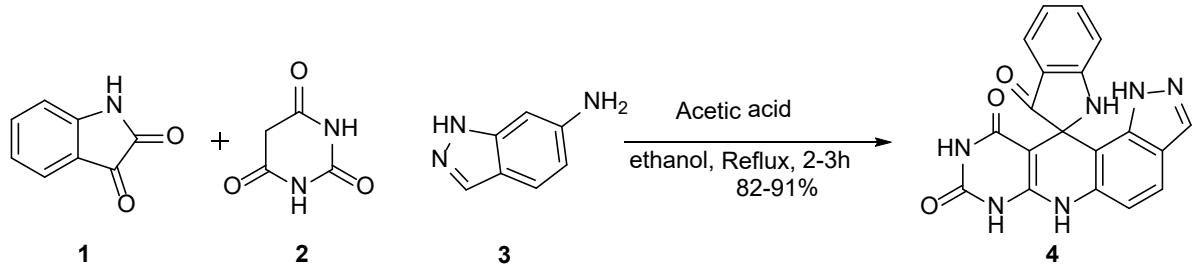
Abstract:

A series of (E)-N-(2-(benzo[d]thiazol-2-ylamino)-5-phenylpyridin-3-yl)-4-phenylbut-3-enamide derivetives were synthesized 13 derivetives and evaluated for their cytotoxicity, among all the derivetives. Most of the conjugates exhibited significant anticancer activity against some representative human cancer cell lines cytotoxicity with IC50 values of 0.96 mM and 12.4 mM against A549 human lung cancer respectively, and were comparable to E7010 as control drug.

Keywords:

E7010, Anticancer, phenylbut-3-enamide derivetives, multi step.



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Comparative Study Of Different Capsular Systems For Pulsatile Drug Release Of A Pain Relieving Drug

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Abstract:

Sustained and controlled drug delivery system release the drug at a substantially steady rate of release per unit of time. However, there are instances where maintaining a constant blood level of a drug is not desirable. In such cases a pulsatile drug delivery may be more advantageous. Pulsatile drug delivery systems (PDDS) are gaining importance as these systems deliver the drug at specific time as per the pathophysiological need of the disease resulting in improved patient therapeutic efficacy and compliance. It will be very much beneficial for opioid drugs intended to be used mainly in the therapy of pain symptoms which depend on circadian rhythms. So that, this drug delivery system will be designed to deliver the drug at such a time when it could be most needful to patient of rheumatoid arthritis and fibromyalgia

The aim of the present work was to develop a pulsatile drug delivery system based on different capsular systems with osmosis mechanism, plug systems etc. here different modifications with carried out in capsular system to achieve drug release lag time and the quality control study results were then compared. The factors influencing on lag time such as type of polymeric shell and outer coating weight will be also investigated.

Differential scanning calorimeter and Fourier transformed infrared spectroscopy study showed compatibility between drug and coating material. The surface morphology of the capsular pulsatile drug delivery system was examined by a scanning electron microscopy.

Keywords:

Sustained; Controlled; Pulsatile; Capsular; Plugs; Osmosis; Lag time.

Formulation And Evaluation Of Transdermal Patches Of Active Phyto Constituent From *Terminalia Arjuna* Bark For Anti-Diabetic Activity

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Abstract:

Conventional drug delivery system has many problems so bulk of research has now shifted from synthetic drugs to herbal drugs. This is possible because of the vast variety of bioactive molecules in the plants and their higher safety margin. This present study focused on the use of tannins and chief constituent obtained from *Terminallia arjuna*, and belonging to family combretaceae as an antioxidant agent and anti diabetic activity. The main objective of present work was to develop the trans-dermal patch of tannins using polymer blends so that minimize the side effects and maximize the therapeutic efficacy. The formulations characterized for weight variation, moisture uptake, thickness, moisture content, and folding endurance. We also evaluated anti-diabetic activity of formulations, all parameters show significant satisfactory results.

Keywords:

Tannins, Poly Vinayl Pyrollidone, Ethyl Cellulose, Transdermal Patch.

Formulation And Evaluation Of Lamivudine Nanospheres

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Abstract:

In the present research work, an attempt is being made to formulate, optimize and evaluate Lamivudine Nanospheres drug delivery system for enhancing its oral bioavailability and efficacy. Lamivudine Nanospheres were prepared with Glyceryl monostearate, HPMC K4M and Ethylcellulose for designing of nanoparticles by using Emulsion solvent evaporation technique. The prepared Nanoparticle formulations were evaluated for their Particle size distribution, Modified, Assay, zeta potential and in-vitro drug release properties. The formulation LF9 containing Lamivudine nanoparticles using combination of polymer was selected as Optimize formulation which release more than 98.9% drug in 20hrs. IR spectroscopic and DSC studies indicated that there are no drug-excipient interactions in the optimized formulation. The optimized formulation LF9 can be considered as a promising Sustained drug delivery system of Lamivudine nanoparticles providing nearly zero order drug release over a period of 20 hrs.

Keywords:

Nanospheres, Eudragit, Ethylcellulose, zeta potential, Sustained drug delivery system

Proteome-wide docking-based identification of biomolecular targets of small chemical compounds

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[3] School of Pharmacy, College of Medicine, National Taiwan University, Taipei, Taiwan

Abstract:

Identification of possible biomolecular targets of small chemical compounds is an important step for unravelling their underlying action mechanisums at the molecular level. We constructed a web server, idTarget, which can predict possible binding targets of a given small chemical molecule via a divide-and-conquer docking approach, in combination with our scoring functions based on robust regress analysis and quantum chemical models, and several other scoring functions based on machine learning and deep learning approaches. Affinity profiles of the protien targets are used to provide the confidence levels of prediction. The divide and conquer docking approach uses adatively constructed small overlapping grids to constrain the searching space, thereby achieving better docking efficiency. Unlike previous approaches that screen against only a specific class of targets or a limited number of targets, id Target screens against nearly all protein structures deposited in the Protein Data Bank (PDB), and the identified protein targets can be displayed on pathway maps curated by KEGG. We show that idTarget is able to reproduce known off target effects of drugs or drug like compounds, and the suggested new targets could be prioritiezed for further investigation.

Keywords:

Drug target, drug-like, docking, pathway analysis, machine learning, deep learning, quantum chemical calculations, structre-based drug design, druggable proteome.

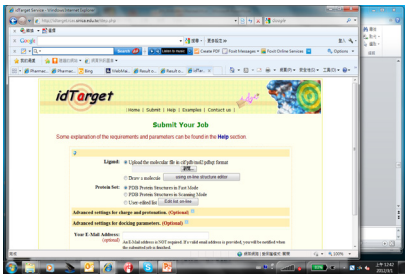

Figure 1: The submission web page of the idTarget web server (http://idtarget.rcas.sinica.edu.tw). The structure of the small chemical molecule can be either drawn directly with the molecular editor of this web server, or uploaded with the 3D molecular structure file.

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Natural Products for Sustainable Conservation of Agriculture

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Abstract:

There has been a paradigm shift in the mind-set over the time of using more environmentally benign products like sustainable agro-chemicals over synthetically derived ones given the nature of later one as hazardous and obnoxious, non biodegradable, and persistent chemicals which has posed a threat to ecology bringing about substantial degradation of soil and consequently its productivity. It demands substituting chemical-based conventional agrochemicals with more greener, eco-friendly but compatible alternatives which control pests with a great degree of efficiency, effectiveness, and efficacy, and therefore it is sustainable in action. The chemical-based agrochemicals have already brought about a lot much of ecological imbalance by substantially polluting water bodies, reducing fertility of the soil, making their way into the food cycle as bioaccumulators. Further because of their nonbiodegradability and persistent nature, and thereby subse-quently posing a threat to biodiversity. Thus, the use of natural products will continue to provide clues to new modes of action, new chemistries for the sake of conservation of agriculture and in enhancing productivity without compromising ecological balance for the generations to come.

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ISBN: 978-93-82829-66-9 Larix International Pte. Ltd

Heterotrimeric complex of p38 MAPK, PKCδ, and TIRAP is required for AP1 mediated inflammatory response.

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Abstract:

Inflammation could be described as a physiological response of the body to tissue injury, pathogen invasion, and irritants. During the inflammatory phase, cells of both the innate as well as adaptive immune system are activated and recruited to the site of inflammation. These mediators are downstream targets for the transcription factors; activator protein-1 (AP1), nuclear factor kappa light hain enhancer (NF-κB), signal transducers and activators of transcription factors (STAT1), as well as interferon regulatory factors (IRFs), which control the expression of most immunomodulatory genes. There is a significant increase in active p38 mitogen-activated protein kinase (p38MAK) immediately after lipopolysaccharide (LPS) stimulation, which results in the activation of AP-1 transcription factor and expression of proinflammatory cytokines, IL-12 and IL-23. We studied the novel mechanism of p38 MAPK activation through the formation of a heterotrimeric complex of Protein kinase C delta type (PKCδ), Toll-Interleukin 1 Receptor (TIR) Domain Containing Adaptor Protein (TIRAP), and p38 proteins. TIRAP serves as an adaptor molecule which brings PKCδ and p38 in close proximity. The complex facilitates the activation of p38MAPK by PKCδ. Therefore, we propose that disruption of the heterotrimeric complex may be a good strategy to dampen the inflammatory response.

Keywords:

Inflammation, heterotrimeric complex, AP1, NF-κB, STAT1, LPS

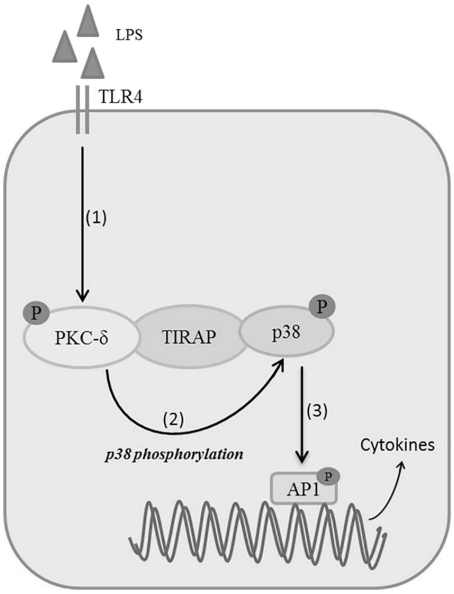

Figure 1: Heterotrimer complex of PKCδ-TIRAP-p38 mediated inflammatory response in macrophages. (1) LPS from Gram-negative bacteria stimulates TLR4 receptor in macrophages; (2) This induces the activation of the AP1 signaling pathway via heterotrimer complex of PKCδ-TIRAP-p38; (3) LPS stimulation activates PKCδ, which in result phosphory-lates p38 MAPK (4, 5) p38 MAPK activation induces AP1 transcriptional activity and ex-pression of inflammatory cytokines such as IL-12, IL-23.

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Drug repositioning as an effective therapy for Protease-Activated Receptor-2 inhibition

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Abstract:

Proteinase-activated receptor-2 (PAR-2) is a GPCR activated by both trypsin and a specific agonist peptide, SLIGKV-NH2. It has been linked to various pathologies, including pain and inflammation. Several peptide and peptidomimetic agonists for PAR-2 have been developed exhibiting high potency and efficacy. However, the number of PAR-2 antagonists is smaller. We screened the FDA library of approved compounds to retrieve novel antagonists for repositioning in the PAR-2 structure. The most efficacious compound Bicalutamide bound to the PAR-2 binding groove near the extracellular domain as observed in the insilico studies. Further, it showed reduced Ca2+ release in trypsin activated cells in a dose-dependent manner. Hence, Bicalutamide is a novel and potent PAR-2 antagonist which could be therapeutically useful in blocking multiple pathways diverging from PAR-2 signaling. Further, the novel scaffold of Bicalutamide represents a new molecular structure for PAR-2 antagonism and can serve as a basis for further drug development.

Keywords:

Drug Repositioning, inflammation, PAR-2, antagonist

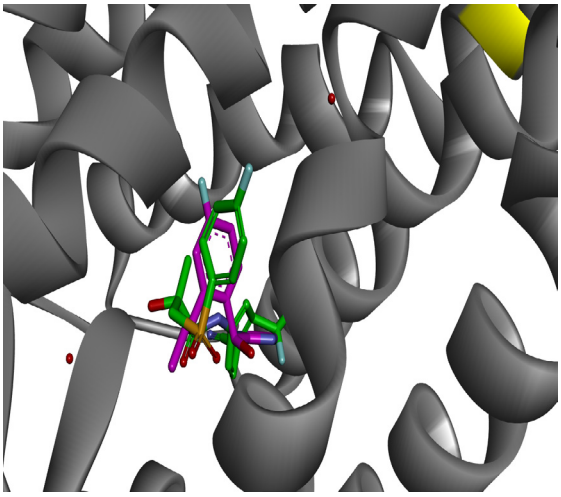

Figure 1: Comparison of docked poses of AZ8838 (magenta atom color sticks) and Bicalutam ide (green atom color sticks) in the PAR-2 binding site (grey ribbons).The small red-colored spheres are the water molecules.

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CONGENITAL DIVERGENCES: GLOBAL PANORAMA

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Abstract:

Congenital anomalies (birth defects) are structural or functional anomalies (e.g. metabolic disorders) that occur during intrauterine life and can be identified prenatally, at birth or later in life. Congenital anomalies are the major cause of new born deaths within four weeks of birth and can result in long term disability with a significant impact on individuals, families, societies and health care systems.

According to the WHO an estimated 303000 newborns die within 4 weeks of birth every year, worldwide, due to congenital anomalies. Though approximately 50% of all congenital anomalies cannot be due to a specific cause, but some known genetic, environmental and other causes or risk factors may play akey role. Consanguinity also increases the prevalence of rare genetic congenital anomalies and nearly doubles the risk for neonatal and childhood death, intellectual disability and other anomalies.

It is estimated that about 94% of severe congenital anomalies occur in low and middle income countries. An indirect determinant, this higher risk relates to a possible lack of access to sufficient, nutritious foods by pregnant women, an increased exposure to agents or factors such as infection and alcohol, or poorer access to healthcare and screening.

Preventive public health measures work to decrease the frequency of certain congenital anomalies through the removal of risk factors or the reinforcement of protective factors ensuring an adequate dietary intake of vitamins and minerals, and particularly folic acid in adolescent girls and mothers.

Screening includes obtaining family histories and carrier screening may include screening for young or advanced maternal age, as well as screening for use of alcohol, tobacco or other risks. Maternal blood can be screened for placental markers to aid in prediction of risk of chromosomal abnormalities or neural tube defects, or for free fetal DNA to screen for many chromosomal abnormalities. Many structural congenital anomalies can be corrected with paediatric surgery and early treatment can be administered to children with functional problems such as thalassaemia (inherited recessive blood disorders), sickle cell disorders, and congenital hypothyroidism.

Keywords:

Congenital anomalies, Consanguinity, chromosomal abnormalities, Down syndrome, neural tube defects, thalassaemia

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Heteronuclear Coordination Compounds With Ligands Of Carboxylic Acids And Their Biological Properties

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Tajik National University, Dushanbe, Republic of Tajikistan

Abstract:

Heteronuclear complex compounds have their own peculiarity, they can contain two or more types of metals in the internal coordination sphere and different composition and structure of the ligand, so the conditions for their formation are special. The processes of formation of heterovalent, heteronuclear complexes of iron, zinc and cobalt in the redox system Fe (II)-Fe (III)-aqueous solutions of acetic acid were studied by the method of oxidative potential. Analysis of the experimental dependences of the oxidative potential of the system (or electromotive force) on the concentration parameters: pH, pC0, pCr, pCГА, pCL - indicators of the concentration of H+, oxidized, reduced forms of the Central metal-complexing agent, metal heteroatom and ligand, respectively, at a temperature of 298 K and the ionic strength of the solution of 0.5 mol/l (NaClO4).

The compiled mathematical and chemical models have allowed using the General equations of the oxidation potential and the oxidation function of Yusupov to determine the composition of the emerging coordination compounds and the stability constant. It was found that, for example, in the presence of zinc heteroatom in the system, complexes of composition are formed: [FeL (H2O) 5]2+; [Fe2L2Zn (H2O) 14]6+; [FeIIIFeIIZnII L2 (H2O)14]5+;

[FeIIIL2(H2O)4] +; [FeIIZnIIL (H2O)9]3+ and [FeIIIFeIIL2 (H2O)10]3+. As can be seen from the structures of complexes of iron (II) iron (III) and zinc (II) in the formed coordination compounds of unique structure, i.e. a net heteronuclear complex ([Fe2IIIL2Zn (H2O)14]6+; [FeIIZnIIL (H2O)9]3+), and heterofullerenes connection [FeIIIFeIIZnIIL2(H2O)14]5+. The first two complexes contain two trivalent iron atoms and one zinc atom, but two ligands. The second complex contains one bivalent iron atom and one zinc atom, as well as one ligand in the internal coordination sphere. The third complex has a very interesting composition in terms of practical application, as in the internal coordination area are just trivalent and bivalent iron with two ligands. As you can see, this compound contains biologically active Fe (II) acetate and a ligand. With the use of modern computer programs, the maximum degree of accumulation of complexes is calculated. Based on the obtained data, their distribution diagrams on the pH scale are constructed, based on which optimal conditions for obtaining heteronuclear complexes are developed.

The complex compound [Fe III Fe II Zn II L2 (H2) 14]5+ was obtained in the form of a powder, the corresponding analyses and tests on wheat seeds of the "Vatan"variety were carried out. It was found that this complex increases the energy of germination and germination of wheat seeds, increases the growth and weight of roots and seedlings.

ISBN: 978-93-82829-66-9 Larix International Pte. Ltd

Stimulated production of oxidatively-truncated phospholipids defines a new pathway of cytokine-induced cell death

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Abstract:

TNF-α is an inflammatory cytokine, known to modulate cell survival and proliferationby the activation of NF-kB-dependent pathwaywhereassimultaneous activation of caspase regulates apoptosis.TNFα generates reactive oxygen species (ROS) required in cell death, but their molecular identity and mode of action remain undefined. We demonstrate that oxidatively truncated phospholipids connect TNFα to apoptosis. In the present study we showed that TNF-α stimulated ROS production by Nox4 in Jurkat cells that oxidized cellular polyunsaturated phospholipids. Glutathione peroxidase-4 (GPx4), which uniquely metabolizes these to non-reactive lipid alcohols, fell in TNF-α stimulated cells prior to death. Overexpression of GPx4 ameliorated, while GPx4 siRNA knockdown enhanced, apoptosis. Phospholipid hydroperoxides are unstable with fragmentation of the esterified oxidized fatty acyl chain, forming truncated phospholipds. The truncated product azelaoyl phosphatidylcholine (Az-PC)-a mitotoxic and pro-apoptotic phospholipid— accumulated after TNFα stimulation. Over-expression of GPx4 or PAFAH2 that specifically hydrolyzes oxidized phospholipids suppressed Az-PC accumulation, and each enzyme prevented TNF-α stimulated cell death. Accordingly, exogenous Az-PC bypassed the protection afforded by GPx4 over-expression. Truncated phospholipid are common effectors of stimulated apoptosis required for TNF-α cytotoxicity in HepG2 cells, and FasL induced death of Jurkat cells. Thus, cytokines stimulate ROS production that oxidizes cellular polyunsaturated phospholipids, which then fragment to mitotoxic truncated phospholipids that are required components of stimulated apoptosis.

ISBN: 978-93-82829-66-9 Larix International Pte. Ltd

Anti-proliferative effect of potential LSD1/CoREST inhibitors based on molecular dynamics model derived from its interaction with tetrahydrofolate cofactor.

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Abstract:

Targeting cancer through epigenetics is a recent era, where a specific gene is manipulated without destroying it. Lysine-specific demethylase 1 (LSD1) is one of the enzymes that are associated with chromatin for post-translational modifications, where it demethylates lysine amino acid in the chromatin H3 tail. LSD1 is associated with its corepressor protein CoREST, and utilises tetrahydrofolate as a cofactor to accept CH2 from the demethylation process. Many studies showed that inhibiting LSD1 could potentially be used to treat cancer epigenetically.

The fact that the cofactor is best bound to the active site inspired us to explore its interactions to LSD1/CoREST enzyme complex utilizing molecular dynamics simulation, which aids designing novel and potent inhibitors. Also, the conformational existence of the enzyme complex bound to the cofactor has been investigated. According to the molecular dynamics simulation study, LSD1/CoREST complex is present in open and closed conformations. Furthermore, tetrahydrofolate was found to bind to two binding subsites with different binding modes.

The model derived from the molecular dynamics simulation study and the key contacts to the active site were used in the subsequent structure based drug design and *in-silico* screening, which revealed a number of new chemical entities with a potential inhibitory effect of LSD1/CoREST complex. *In-silico* mining on National Cancer Institute (NCI) database identified 60 promising and structurally diverse inhibitors.The cytotoxic activities of these compounds were tested against different cancer cell lines with different expression modes of LSD1/CoREST complex such as leukaemia K562, prostate cancer PC3 and neuroblastoma SH-SY5Y. All compounds were also tested against normal fibroblast cells to study their selectivity against cancer cells.

Applying the abovementioned molecular modeling procedure yielded array of LSD1/CoREST inhibitors with IC_{50} < 5µM, when tested against different cancer cell lines. Three compounds inhibited the growth of PC3 prostate cells with IC_{50} = (2.68, 2.08 and 2.95µM), Four of them inhibited the growth of K562 leukaemia cells with IC_{50} = (1.20, 1.92, 2.70, and 1.20µM) and three of them inhibited the growth of SH-SY5Y neuroblastoma cells with IC_{50} = (0.27, 0.83 and 4.28µM). These compounds are excellent candidates for further optimization.

ISBN: 978-93-82829-66-9 Larix International Pte. Ltd

Chemical composition and oral toxicity assessment of *Anisophyllea boehmii* kernel oil: Potential source of new edible oil with high tocopherol content

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[2] Laboratory of Biology of Plants and Microorganisms, Department of Biology, Faculty of Science, University Mohammed First, Oujda, Morocco
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Abstract:

Anisophyllea boehmii is an indigenous and wild species in Burundi. Its fruits are edible and commercialized in local markets. This study investigates chemical quality, composition and toxicity test of A.boehmii kernel oil from two sites in eastern Burundi. Results of the present study reveal A. boehmii kernels to be an oil-rich source, yielding up to 29% of oil. Fatty acid composition analysis classifies these oils as palmitic. In fact, the main fatty acids are palmitic acid (36.47–39.55%) and oleic acid (18.83–22.21%). The analysis of minor compounds shows high tocopherols (485–657 mg kg−1), phenols (82–135 mg kg−1) and β-carotene (144–234 mg kg−1) content. The physicochemical parameters analyzed make A.boehmii kernel a source of good quality oil. Furthermore, acute oral toxicity test reveals no toxicity of A. boehmii kernel oil. Results of the present study are decisive in adoption of A.boehmii kernel oil as an alternative source of edible oil. The nutritionnal and medicianal potential of indigenous species of African Great Lake region will be discussed and challenges and opportunities in related research addressed.

Keywords:

Anisophyllea boehmii, Burundi, Fatty acids, Kernel oil, Oxidative stability, Tocopherols.

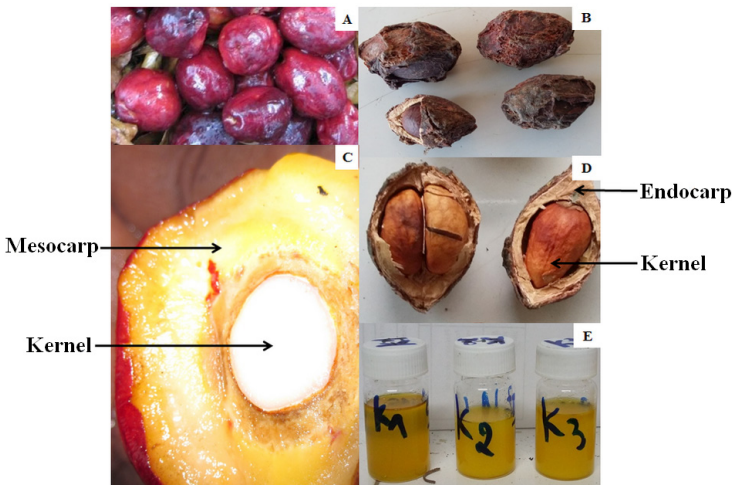

Figure 1: Anisophyllea boehmii fresh (A) and dried (B) fruits; kernels (C & D) and kernel oil (E).

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Development of Lignocellulosic Biomass Derived Nanomaterials for Applications in Nanomedicine

Jayeeta Bhaumik, Y. Nikhileshwar Reddy, Neeraj S. Thakur, Ravneet Kaur, Sanjam Chandna and Shatabdi Paul

Center of Innovative and Applied Bioprocessing Department of Biotechnology ,India

Abstract:

Agricultural biomass serves as a potential source for aromatic renewable materials. However, the biomass being generated in enormous amounts, ends up creating environment pollution due to stubble burning initiated by the farmers. Through developing biocompatible nanomaterials from such agribiomass, the agricultural waste generated every year can be reduced significantly, which will be beneficial to the environment. Lignin is present in large quantities in the agricultural biomass and is an important source of polyphenols. Moreover, lignin is known for its commendable photoprotective and antimicrobial properties. Additionally, due to the biocompatible nature and antioxidant properties of lignin, nanomaterials derived from it can be employed in various applications including biomedicine. Lignin (obtained from agricultural waste) derived nanocapsules, metallic, bimetallic and metal oxide nanomaterials were therefore developed via applying low cost and green techniques. Lignin based nanomaterials were further characterized by UV-visible spectroscopy, dynamic light scattering, transmission electron microscopy and other other analytical tools. The surface engineering of the newly derived nanomaterials was performed through functionalization with various diagnostic, therapeutic or enzyme moieties via encapsulation or conjugation chemistry. Lignin derived nanomaterials were further examined for potential antioxidant and antioxidant properties for possible biomedical applications. These lignin derived nanocomplexes is expected to reduce environmental pollution and simultaneously being applicable in versatile sectors including nanomedicine.

Keywords:

Agri-biomass, nanomaterials, Surface functionalization, antioxidant and antimicrobial potential

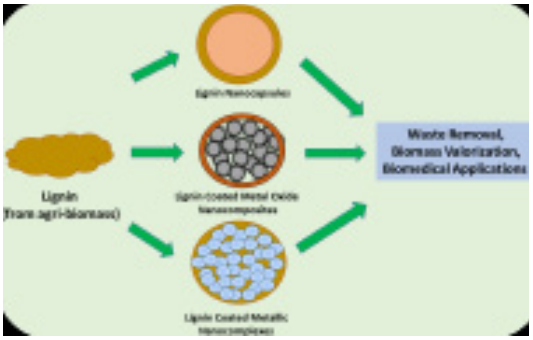

Figure 1: The schematic diagram explains thevalorization of lignocellulosic biomass via the formations of metallic, metal oxide and lignin nanoscaffolds.

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Synthesis Of Azomethines Of Anthrones And 10- Arylidene Anthrones And Testing For Anticancer And Antiaids Activity.

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Abstract:

A new series of azomethines of anthrones have been prepared by condensing anthrone with different primary amines, o-aminophenol and p-aminobenzoic acid.

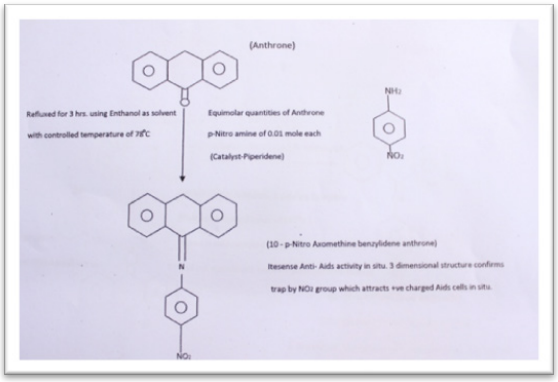
Similarly 10-Arylidene anthrones with different functional groups were synthesized using Acetic Anhydrite as well as ethanol as solvent.

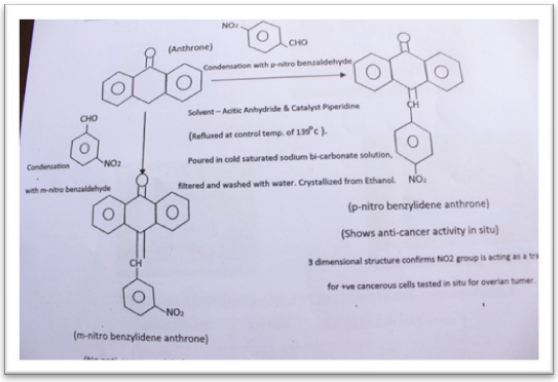
It is found that Azomethines of anthrones prepared by condensing primary amines with nitro group in p-position of aromatic ring indicate intense anticancer activity in situ as compared to other azomethines of anthrones.It is also proved that azomethin group stabilized by aromatic ring shows anti-cancer activity,but Nitro group in p-position of aromatic ring can be considered for further investigation for development of anticancer drug, after doing detailed toxici-ty studies. Similarly 10-Arylidene anthrones with Nitro group in p-position of aromatic ring shows antiaids activity *in situ*. However detailed studies of toxicity should be done before considering for further development of antiaids drugs.

This study also includes structure activity relationship and new reaction mechanism which involves bending of functional group.

Keywords:

Azomethines, 10-Arylidene, structure activity, reaction mechanism.





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Overcoming the Blood-Brain Barrier (BBB) with peptide-conjugates

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Abstract:

The blood-brain barrier (BBB) restricts the de-livery of therapeutic proteins into the brain. To increase their brain accumulation, therapeutic proteins have been conjugated to trans-BBB peptides. Most trans-BBB peptides target natural receptors on the surface of BBB cells, leading to receptor saturation or competition with natural ligands. The outcome might be the hamper of brain homeostasis. Therefore, we intented to take advantage of the adsorptive-mediated transport to get access into the brain. We have previously reported on the PepH3 peptide that is able to cross the BBB in vitro and in vivo un-conjugated and conjugated to GFP or antibody fragments. In this work, we have evaluated in vitro the capacity of PepH3 to increase the BBB translocation of an Fc domain of an IgG. To do so, we chemical conjugated PepH3 to the Fc domain via streamlined expressed protein ligation (SEPL) (Figure 1 A) to obtain a chemically well-defined Fc-PepH3 conjugate (Figure 1 B). While the Fc alone does not translocate the *in vitro* BBB model, the conjugation to PepH3 results in a translocation comparable to the well-stablished Fc5 single antibody.

Keywords:

Trans-BBB peptides, peptide-conjugates, PepH3, adsorptive-mediated transport, blood-brain barrier, therapeutic proteins, translocation, antibodies

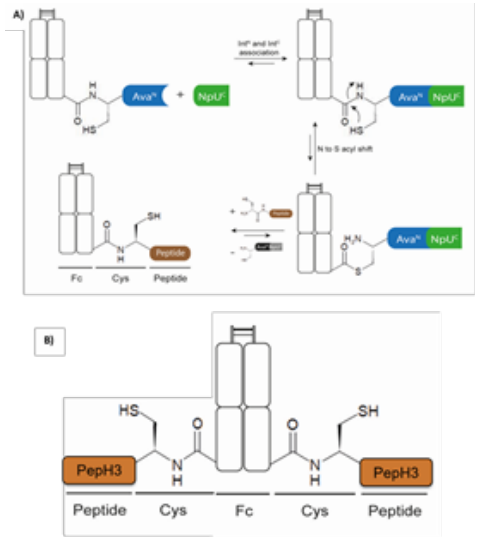

Figure 1: Figure illustrating the strategy debeloped to conjugate PepH3 to the Fc domain of an IgG. A) Scheme of the Streamlined Ex- pressed Protein Ligation (SEPL) applied in the conjugation. B) The final product obtained after the SEPL reaction with two PepH3 conjugated to the Fc domain.

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Molecular Epidemiology and Drug Sensitivity Pattern of Mycobacterium tuberculosis Strains Isolated from Pulmonary Tuberculosis Patients in and around Ambo Town, Central Ethiopia.

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Abstract:

Introduction: Tuberculosis (TB) is caused by M. tuberculosis complex and remains a major global public health problem. The epidemic remains a threat to sub-Saharan Africa, including Ethiopia, with further emergence of drug resistant TB.

Methods: A cross-sectional study was conducted involving 105 consecutive new smear positive pulmonary TB patients diagnosed at Ambo Hospital and surrounding Health Centers between May 2014 and March 2015. Sputum samples were cultured on Löwenstein-Jensen (LJ) media using standard techniques to isolate mycobacteria. Region of difference 9 (RD9)-based polymerase chain reaction (PCR) and spoligotyping was employed for the identification of the isolates at species and strain levels. The spoligotype patterns were entered into the SITVIT database to determine Octal and SIT (Spoligotyping International Typing) numbers for each strain. The sensitivity of the isolates to isoniazid (INH), rifampicin (RIF), ethambutol (ETB) and streptomycin (STM) was evaluated on LJ-medium with the indirect proportion method.

Results: Cultures were positive in 86/105 (82 %) of newly diagnosed smear positive pulmonary TB cases. All of the 86 isolates were confirmed as M. tuberculosis. The majority (76.7%) of them were clustered into seven groups while the rest (23.3%) appeared unique. The most predominant Spoligotypes were SIT53 and SIT149, consisting of 24.4% and 20.9% of the isolates, respectively. The majority (76.7%) of the M. tuberculosis isolates were susceptible to all the four drugs. Any resistance to any one of the four drugs was detected in 23.3% of the isolates. The highest proportion of any resistance was observed against isoniazid (9.3%) and ethambutol (7%). There was only a single case (1.2%) of multidrug resistant/rifampicin resistant (MDR/RR) TB.

Conclusion: The majority of the isolates were clustered suggesting on-going active transmission in the study area. Mono resistance is relatively prevalent while the magnitude of MDR/RR-TB was found to be lower than in previous studies

Keywords:

Tuberculosis, Multi drug resistance

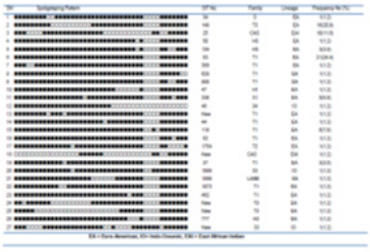

Figure 1: Spoligotype pattern of M. tuberculosis strains isolated from pulmonary tuberculosis patients in and around Ambo Town, Central Ethiopia, 2015.

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Free radicals and natural antioxidants in the cellular environment

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Abstract:

The broad field of free radicals and antioxidants covers an emerging area known as redox biology, and has been perceived as focussing around the use of antioxidant supplements to prevent a variety of human diseases. During the events of evolution, the emergence of photosynthetic system in aerobic organisms, plants in particular, generates reactive oxygen species and has opened up a paradoxical situation compelling life confront hostile environment and to be able to adapt, the redox processes have become increasingly significant. Antioxidants/free radicals permeate the entire living systems in the cellular *milieu*. Life is a balance between the two like a tug-of-war: antioxidants serve to decrease the levels of free radicals permitting them to perform useful biological functions without causing much damage. However, some damages are inevitable requiring repair systems to maintain cellular integrity and viability.

Reactive oxygen species are all over the cellular environment in aerobic microbes, plants and animals. These species protect life from various types of infections and involve in critical signaling pathways. Eventually, these species also often kill cells, tissues and organs in the end. The continual damages by these species, failing repair pathways, can cause age-related tumor development, neurodenerative diseases and several human disorders. It would have been wonderful if life had evolved entirely in the anaerobic environment, in which case, the life-spans would have been much longer and diseases would have rarely occurred.

Interestingly, several medicinal plants possess 'bio-active molecules' which can prevent several human diseases. These molecules having diversified chemical structures possess strong antioxidant profiles and encounter damaging radical species very efficiently at time scales of micro-, nano-, pico- or femto- seconds in cellular environment thereby preventing molecular damages done to the DNA and membranes. In this presentation, some of these issues shall be discussed with reference to a few medicinal plants such as turmeric and tropical ginger.

ISBN: 978-93-82829-66-9 Larix International Pte. Ltd

Development of Activity-based Reporter Gene Technology (AbRGT) for Imaging of Enzyme Activity with Exquisite Specificity in a Single Live Cell

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Abstract:

Fluorescence microscopy coupled with sub-strate-based reporter assays (both genetic and synthetic substrate) is being extensively used to monitor the function of "active en-zymes" in (patho) physiological processes. Currently available methods for imaging enzyme activity comprise substrate-based reporters and activity based fluorescent probes (ABFP). However, both the methods lack target specificity in the native cellular conditions. To overcome this limitation, we disclose the design and development of a new technology called "Activity-based Reporter Gene Technology" (AbRGT). As a proof of concept, we show that the activation of the caspase-3 enzyme in both intrinsic and extrinsic apoptosis signaling pathways can be followed with unprecedented specificity using this technology. AbRGT has further been validated using targets including another initiator (caspase-8 and -9), effector (caspase-3 and -7) caspases and cathepsin B cysteine enzymes. The same method is adopted for profiling of compounds which can inhibit caspases and cathepsin B activity. Altogether, this technology holds immense potential for applications in the area of diagnostic, screening of drugs and other therapeutic interventions.

Keywords:

Substrate-based reporter assay, ABFP, FRET, active enzyme, AbRGT, caspase, apoptosis pathway and inhibitor screening

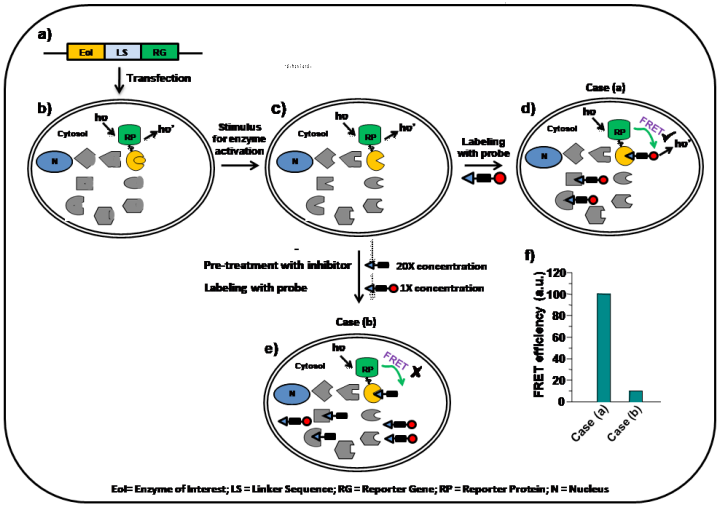

Figure 1: The concept of our technology is diagrammatically depicted in (Figure 1.) Here, the plasmid encoding enzyme-of-interest (EoI) tagged to a reporter protein (RP; FRET do-nor) (Figure 1a.) is expressed in the cell line of interest (Figure 1b.). An appropriate stimulus is given to cells for the activation of EoI (Figure 1c.) followed by incubation of cells with a cell-permeable ABFP carrying an appropriate fluorophore (FRET acceptor). Labeling of EoI by an ABFP instantaneously creates a FRET pair *in-situ* (Figure 1d.). Upon RP excitation, its fluorescence emission is absorbed by fluorophore of ABFP, resulting in quenching of RP fluorescence and simultaneous excitation and emission of ABFP at longer wave-length resulting in FRET effect (case a). Since the FRET effect extensively depends on the distance between donor and acceptor, the labeling of other enzymes by ABFP will not contribute to the FRET signal..

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Identification of novel targets and their associated pathways for Rheumatoid Arthritis using next generation sequence data analysis

Nikhil Vitthal Ghorpade[1], Snijesh.V.P[1], Monica Steffi Matchado[1], Atul Kumar[1,2] and Sachidanand Singh[1,3]

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[2]Institute for Genomics and System Biology, University of Chicago, United States
[3]Institute of Biosciences and Technology, Shri Ramswaroop Memorial University,India

Abstract:

Background: Rheumatoid Arthritis (RA) is a systemic autoimmune disease which affects different parts of the body but primarily affects synovial joint. The abnormal activities of inflammatory and immune cells are the basic hallmark of RA. The dysregulated activities of the immune related cells lead to abnormal immune response in the synovial membrane that ultimately results in cartilage destruction and bone erosion. The cells in the synovium, i.e. synovial macrophages (SM) and synovial fibroblast (SF) have been mainly focused to identify and elucidate the role of dysregulated genes in the pathophysiology of RA.

Results: We have adopted an integrated approach of transcript expression and network biology, based on theoretical graph parameters to identify significant biomarkers or targets in the pathogenesis of RA. Next Generation Sequence Data analysis using RNA-Seq technique has been implemented to identify significant Differentially Expressed Genes (DEGs) at whole genome level. Comparative analysis of the significant DEGs was performed on two different experimental conditions, i.e Rheumatoid Arthritis-Synovial Fibroblast (RA-SF) and Rheumatoid ArthritisTumor Necrosis Factor (RA-TNF) drug treatment data to find the deviation of transcripts expression levels. All the possible associations of significant DEGs were established using GeneMania to build the Rheumatoid Arthritis Gene Interactome Map (RA-GIM). Biological annotation of the interactome map gave an insight about the involvement of prominent pathways closely related to pathogenesis of RA. The downstream analysis of aforesaid integrated approaches depicted the indispensable role of TINGAL1 in the implication of arachidonic acid metabolism associated with RA.

Conclusion: TINGAL1 and c11orf48, two signature molecules were identified based on comparative genome analysis of high throughput data. The result anticipates the potential properties of identified genes as a possible target or biomarker for RA. Further validation using trials in the wet-lab, *in vitro* and *in vivo* settings, are proposed to delineate the major impact of these potential genes in the etiopathogenesis of RA

ISBN: 978-93-82829-66-9 Larix International Pte. Ltd

Sustainable synthesis of lignin-metallic/bimetallic nanocomplexes and their application as nano-antimicrobial agents

Sanjam Chandna, Ravneet Kaur, Neeraj Singh Thakur, Y. Nikhileshwar Reddy and Jayeeta Bhaumik

Center of Innovative and Applied Bioprocessing, Department of Biotechnology, India

Abstract:

Antibiotic resistance crisis is one of the most persistent issues in global public health, which is associated with lack of new antimicrobials. Therefore, the development of new and highly effective antimicrobial agents is of great interest. Lignin, which is found to be non-toxic group of complex phenolic polymers, is a major underutilized and abundant component of lignocellulosic biomass possessing antibacterial and antioxidant properties. Herein, we have synthesized a synergistic antimicrobial nanocom-plex by growing both silver and gold nano-particles in lignin matrix, which acts as a reducing, stabilizing and capping agent for the synthesis of lignin-metallic/bimetallic nano-complexes. The developed nanocomplexes were characterized using UV-visible spectroscopy, dynamic light scattering (DLS), X-Ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), electron dispersive X-ray spectroscopy (EDS), Line EDS, EDS mapping and scanning tunneling electron microscopy (STEM). The nanocomplexes were found to possess a substantial amount of phenolic and flavonoid contents, which imparted them high antioxidant properties. Lignin-metallic/bimetallic nanocomplexes were then tested for their antimicrobial activities against Gram-positive bacteria, Gram-negative bacteria and fungi. When compared with silver-lignin nanocomplexes, it was found that the lignin-bimetallic (Ag-Au) nanocomplexes possessed higher anti-oxidant and antibacterial properties. The mild preparation conditions, no use of harmful solvents and low cost of the lignin Au-Ag nanocomplexes established in this work may contribute as useful antimicrobial agents in fight against antibiotic resistance.

Keywords:

Biomass, lignin, silver, gold, bimetallic, nanocomplexes, antioxidant, antimicrobial, antibiotic resistance

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In-Vitro Anti-inflammatory activity of *Solanum xanthocarpum* by HRBC Membrane Stabilization

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[2]Millennium College of Pharmacy,India

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Abstract:

Solanum xanthocarpum herb is highly used by the rural and tribal people in curing various disorders. Natural remedies are more acceptable in the belief that they are safer with fewer side effects than the synthetic ones. Herbal formulations have growing demand in the world market. HRBC membrane stabilising assay is alternative test for determination of Anti-inflammatory active. The principal of this assay is based on osmotic presser on human RBC cell. Human erythrocyte cell suspension (10%w/w) was prepared by centrifuged RBC packed cell with normal saline (0.85%NaCl solution).When this HRBC suspension cell place in hypotonic solution lyses of erythrocyte membrane occur. Herbal extract or drug which have anti-inflammatory activity may reduce lyses process.

The aim of current research work is to evaluation of anti inflammatory activity of *Solanum xanthocarpum* by HRBC membrane stabilization method. Ethanolic acetate extract at concentration 6mg/ml showed maximum anti-inflammatory activity among all extract and concentrations, 69 % protection of HRBC in hypotonic solution. All the results were compared with standard indomethacin which showed 70 % protection. The activity may be due to the presence of one or more phytochemical constituents present in the extract. The result obtained have been supported by Photomicrographical pictures of the HRBC.

Keywords:

Anti-inflammatory, Erythrocyte cell, Hypotonicity, Membrane stabilization.

References:

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Biosynthesis Of Silver Nanoparticles Using Chamomilla Officinalis Leaf Extract

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Abstract:

Nanotechnology is manipulation of matter on an atomic, molecular, and supramolecular scale. This review focuses on the possibilities of synthesizing metallic nanoparticles using plant extracts. This approach is being actively developed in recent years as an alternative, efficient, cheap and environmentally friendly method for producing nanoparticles with the given properties.

Purpose of the study. Biosynthesis of silver nanoparticles using *Chamomilla officinalis* leaf extract and AFM study of obtained nanoparticles.

Materials and Methods: The method of Green synthesis was used to obtain silver nanoparticles. For this, extract of the train was previously obtained, after filtration, a 0.01 M solution of silver nitrate was added to it. Then they were thoroughly mixed, left for a certain time at room temperature, after which the suspension was centrifuged.

A detailed picture was visualized by a microscopic method - atomic force microscopy (AFM).

Results and discussions: Presents the results of a microscopic study of silver nanoparticles obtained using extract. It can be seen from the presented figure that silver nanoparticles with a size of 4-24 nm were predominantly obtained using the green synthesis method using the Chamomile extract. A significant amount of nanoparticles had a size of 24.5 - 30 nm.

Given that the most effective for the destruction of pathogens is a 9-15 nm silver particle having an extremely large specific surface area that increases the area of contact of silver with bacteria or viruses, significantly improving its bactericidal actions, it can be concluded that the resulting nanoparticles both with the use of *Chamomilla officinalis* extract are satisfactory.

Conclusions: From the conducted studies it can be concluded that silver nanoparticles obtained using *Chamomilla officinalis* extract have dimensions (4-24 nm) that most effectively provide bactericidal properties.

Keywords:

Nanotechnology, silver nanoparticles, AFM, extract, Green synthesis.

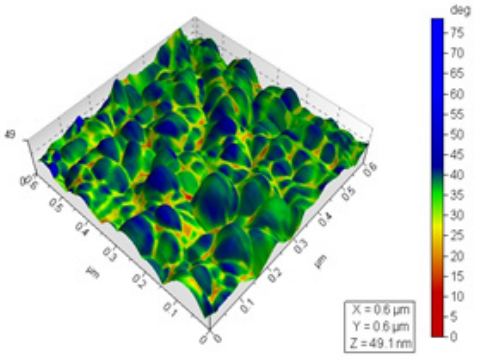

Figure 1: Microscopic examination of silver nanoparticles obtained using extract *Chamomilla officinalis* by atomic force microscopy.

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Novel Indole-fused benzo-oxazepines (IFBOs) obliterate hepatocellular carcinoma through IL-6/JAK2/STAT3 oncogenic signaling blockade

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[2]Centre of Biomedical Research, SGPGIMS Campus, India

Abstract:

Inspired by the well-documented tumor protecting ability of paullones, recently, we synthesized novel paullone-like scaffolds, indole-fused benzo-oxazepines (IFBOs), and screened them against hepatocellular carcinoma (HCC) specific Hep-G2 cells. Three of the synthesized compounds significantly attenuated the progression of HCC in vitro. By computational studies, we further discovered that IFBOs exhibited a stable binding complex with the IL-6 receptor. In this context, we investigated *in vivo* study using the nitrosodiethyl amine (NDEA)-induced HCC model, which strengthened our previous findings by showing the blockade of the IL-6 mediated JAK2/STAT3 oncogenic signaling pathway. Treatment with IFBOs showed remarkable attenuation of cellular proliferation, as evidenced through a decrease in the number of nodules, restoration of body weight, oxidative stress parameters, liver marker enzymes and histological architecture. Interestingly, using a metabolomic approach we further discovered that IFBOs can restore the perturbed metabolic profile associated with the HCC condition to normalcy. Particularly, the efficacy of T1 for an anti-HCC response was significantly better than the marketed chemotherapeutic drug, 5-fluorouracil. Altogether, these remarkable findings open up possibilities of developing IFBOs as novel future candidate molecules for plausible alternatives for HCC treatment.

Keywords:

Indole-fused benzo-oxazepines, Hepatocellular carcinoma, IL-6/JAK2/STAT3, 1H-NMR based metabolomics, drug interaction

Molecular Detection of Multidrug-resistant tuberculosis (MDR-TB) in MDR-TB Patients' Attendant in North-Western Pakistan

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Abstract:

Objective: To determine the drugs susceptibility pattern of *Mycobacterium tuberculosis* (M.TB) in multi-drug resistant tuberculosis (MDR-TB) patients' attendants in North Western, Pakistan. This study was conducted at Peshawar Tuberculosis Research Laboratory (PTRL), Provincial TB Control Program Hayatabad Medical Complex Peshawar, (KP) from August 2013 to March 2014. A cross-sectional study in which four hundred and eighty sputum samples from MDR-TB patients' attendants were processed for the detection of M.TB through Ziehl-Neelsen staining, Lowenstein-Jensen, BACTEC MGIT-960 culture, and line probe assay. Out of 480 samples, 06 (2.1%) were found positive for M.TB through Ziehl-Neelsen staining while 10 (2.8%) were positive through LJ and BACTEC MGIT-960 culture. The 10 positive samples were further subjected to drugs susceptibility testing and line probes assay test to find out rifampicin, isoniazid, streptomycin, and ethambutol resistant and it was found that 06 M.TB isolates were resistant while 4 were sensitive to rifampicin and isoniazid. Among the 6 resistant M.TB strains, 04 showed a mutation in the rpoB gene at 531, 516 and 526 codons. Majority of MDR-TB patients attendants had drug-resistant tuberculosis and the rate of drug-susceptible TB was low.

Keywords:

Assay, Multi-drug resistant tuberculosis, Sputum, Tuberculosis.

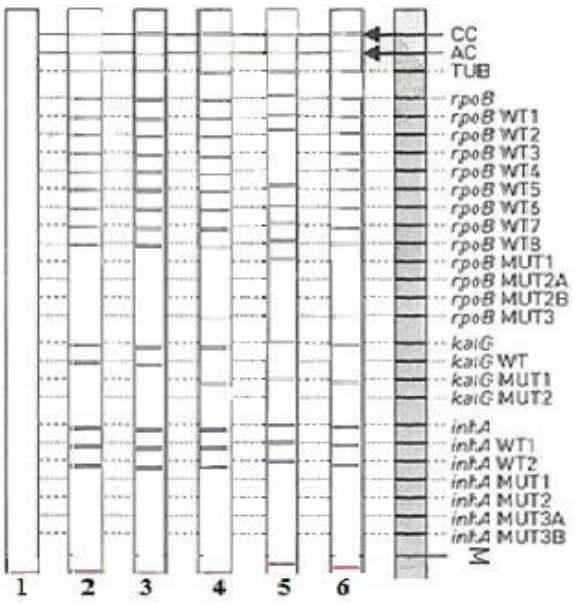

Figure 1: Representative DNA patterns of M. tuberculosis showing resistant and sensitive pattern through LPA.

ISBN: 978-93-82829-66-9 Larix International Pte. Ltd

Synthesis and In-vitro Evaluation of Novel Quinozolines as Potent EGFR Inhibitor

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Abstract:

Non small cell-lung cancer (NSCLC) cells have increased expression of EGFR, which makes them a potential target for cancer therapy. Based on molecular docking and previous reports, we designed and synthesized quinazoline derivatives as potent EGFR inhibitors. Among the derivatives, three compounds showed good antiproliferative activity against A-549 and H-1299 cells. Further more, these compounds inhibited EGFR sig-naling exhibiting diminishing p-EGFR and its downstream proteins like p-Akt, p-Erk1/2 and p-mTOR however, it did not alter the levels of EGFR, Akt, Erk1/2 and mTOR proteins. Flow cytometric analysis indicated the accumulation of cells at G1 phase suggesting induction of apoptosis, which was further confirmed by annexin V/propidium iodide staining. Our study suggested that quinazoline scaffold can be developed as novel EGFR kinase inhibitors for cancer therapy.

Keywords:

Apoptosis, Non small cell-lung cancer cells, EGFR, Quinazoline.

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Determination of optimal composition of “Ambrol” tablets

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Abstract:

One of the promising areas of pharmacy development is the expansion of the range of highly effective generic drugs. In order to achieve these goals, peripheral cough preparations are also promising objects. Development and improvement of the compositions of existing dosage forms of the most popular drugs, replacement of imported substances by representatives of local raw materials, respectively, reducing the cost of products is one of the main tasks of domestic pharmaceutical technology

We used a number of auxiliary substances that are used in the pharmaceutical industry as fillers, binders, loosening agents. More than 25 tablet formulations have been studied, differing in nature and amount of excipients. Compositions No. 1 and No. 2 contained MCC in an amount from 5% to 10%. Composition No. 3 contained 0.08% of aerosil. Compositions No. 4-6 differed in the ratio of lactose and starch, respectively). The remaining mixtures had the same composition, but differed in preparation technology. To obtain a granulate under laboratory conditions, the powder mixture was moistened with a solution of a binder, and then rubbed through a sieve with a hole diameter of 3 mm. Dried in an oven at a temperature not higher than 50 ° C to a residual moisture content of 3.5–4.5%, then rubbed through a sieve with a hole diameter of 1.5 mm. Powdered in a mortar with a plastic scoop. In industrial conditions, the tablet mass was prepared as follows: excipients and pharmaceutical substances were loaded into a granulator mixer, a solution of a binder was added and granulated for 15 minutes. The granulate was dried at a temperature of 40-50 ° C for 30 minutes, rubbed through a sieve with a hole diameter of 1.5 mm. The dusting was performed on a two conical mixer at a rotation speed of 22 revolutions per minute. Technological characteristics of the tablet mass (flowability, bulk density with compaction and without compaction) were determined by the methods of GF XII. It has been established that tablet blends with microcrystalline cellulose have the best tabletting properties. It is established that the substance of abroxol has unsatisfactory flowability, has a low bulk density. Therefore, it is impossible to produce tablets by direct compression

The technological properties of tablet blends and granules were determined in accordance with the XI State Pharmacopoeia: flowability was studied by the fixed funnel method, disintegration of the tablets was investigated using a laboratory identifier of the rotary basket in the decaying material, determination of the abrasion of the tablets was carried out in a drum-type eraser, compressive strength of the tablets was examined with a spring dynamometer, the compressive strength of the tablets was examined using a spring dynamometer, and the compressive strength of the tablets was determined using a spring dynamometer. the device with the basket, the height and diameter of the tablets were studied using calipers

It is shown that the tablets have satisfactory performance: disintegration (10.1 ± 0.32) min., Abrasion (99.22%) and compressive strength (75.9 ± 3.45) N.

Keywords:

Technological properties, fractional composition, bulk density, flowability, compressibility, compactibility.

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Formulation and Evaluation of Lovastatin Nanoparticles for Enhancing the Oral Bioavailability

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Abstract:

Lovastatin nanosuspension was formulated using solvent/anti-solvent method using probe sonication technique. Lovastatin is an anti-lipidemic drug which belongs to class of statins. It has poor oral bioavailability because of low solubility and variable dissolution rate. The main aim of this study was to enhance the solubility and dissolution rate of the drug and in turn the oral bioavailability. Nanosuspension was prepared by using HPMC K15M and Pluronic F68 as stabilizers. The formulated nanosuspension was characterized for particle size, PDI, zeta potential, surface morphology and In vitro release rate. Further, in vivo bioavailability study and stability study was also carried out. FT-IR and DSC study showed no interaction between the drug and the excipients which were used in the formulation. Optimized formulation showed particle size of 127± 0.01nm and PDI of 0.492±0.001 and zeta potential of -37.9mV which showed a good stability. Morphological study showed that the particles were in nano range. The drug content was found to be in the range of 73% - 87%. In vitro release study showed much faster release in one hour compared to the pure drug and marketed formulation. In vivo bioavailability study was carried out in wistar rats which showed improvement in bioavailability of approximately 2.5 folds compared to marketed formulation. Stability study was carried out for optimized formulation F2 which showed that formulation was more stable at 4°±2°C.

Keywords:

Lovastatin, oral bioavailability, Solubility, Nano suspension.

A Prospective Study On Detection Of Drug Interactions, Improving The Drug Safety Access And Therapeutic Outcome In A Tertiary Care Teaching Hospital.

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Abstract:

An interaction is alleged to occur once the consequences of one drug are changed by the presence of another drug, herbal medicine, food, drink or by some environmental chemical agents. [1] As per APA drug interaction is defined aschemical or physiological reaction that can occur when two different drugs are taken together. This prospective study aimed to determine the prevalence of adverse DI's events associated polypharmacy. To categorize and classify the potential DI's as the major, moderate and minor. A Prospective observational study was conducted in Santhiram medical college and general hospital, Nandyal from July 2017 to December 2017, to detect the drug interactions, improving the drug safety access and therapeutic outcome in a tertiary care teaching hospital. Clinical data collected by using case sheets to detect drug interactions in patients who are admitted in inpatient wards. A total of 108 patients were evaluated for their drug interactions, out of which four patients showed positive drug interactions. A chi-square test was used to asses, the significance levels between drug interactions and age, severity. We found the incidence of potential DDIs was higher in the age group of 61-80 years age group. Among all those 108 patients collected for the study, the incidence of interactions were observed more in male patients (58.3%) compared to female patients (41.7%).The study found the associations of potential DIs with age, sex, number of drugs per prescription. There was a direct link between polypharmacy and occurrence of DIs. To lower the frequency of potential interactions it could be necessary to make a careful selection of therapeutic alternatives, and in cases without other options, patients should be continuously monitored to identify adverse events. The study concluded that educational interventions can minimize the incidence of DIs.

Keywords:

Drug interactions, poly pharmacy, drug safety, therapeutic outcome.