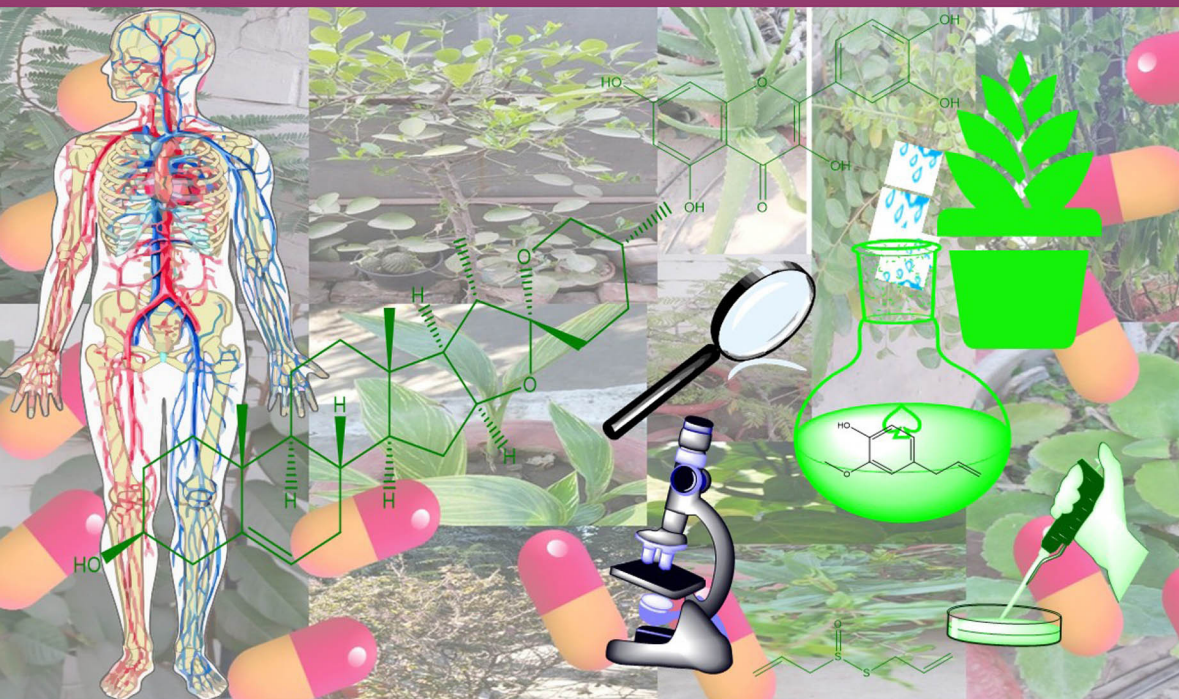




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EDITED BY DR. PANKAJ KUMAR CHAURASIA, DR. SHASHI LATA BHARATI,  
DR. SUNITA SINGH, AND DR. ASHUTOSH MANI

# PHARMACOLOGY OF PLANTS AND PLANT DERIVED BIOLOGICALLY ACTIVE MOLECULES



# Pharmacology of Plants and Plant Derived Biologically Active Molecules

This book, *Pharmacology of Plants and Plant Derived Biologically Active Molecules*, delves into the interesting world of phytochemicals and their therapeutic applications. It explores the journey from traditional medicine practices such as Ayurveda to modern scientific understanding, providing a comprehensive analysis of the chemistry, pharmacology, and therapeutic potential of plant-derived compounds. The detailed discussions on recent advancements and future directions in the field of pharmacology of plants, including novel extraction techniques, structure–activity relationship studies, and cutting-edge applications in various diseases, are the Unique selling point (USP) of this book, setting it apart from the available books. Furthermore, it explores the exciting frontiers of anticancerous and antidiabetic molecules derived from plants.

## Key Features:

- Focus on advancements in extraction techniques for phytochemicals.
- Recent advances in understanding the pharmacological effects of primary and secondary metabolites.
- Analysis of structure–activity relationships of biomolecules.
- Future directions for integrating natural therapies into modern medicine.
- Role of plants in homeopathic and Ayurvedic treatments.
- Application of computational and AI techniques in phytochemistry.
- Comprehensive review of anticancer biomolecules in the Simaroubaceae family.
- Importance of dose-dependent studies for medicinal extracts.
- Exploration of herbal remedies for ulcers and ocular diseases.

This book offers a comprehensive and insightful perspective on the therapeutic potential of plant-derived molecules and serves as an invaluable resource for researchers, students, and healthcare professionals interested in the pharmacology of plants and the development of novel therapeutics from natural sources.



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# Pharmacology of Plants and Plant Derived Biologically Active Molecules

Edited by  
Dr. Pankaj Kumar Chaurasia,  
Dr. Shashi Lata Bharati, Dr. Sunita Singh,  
and Dr. Ashutosh Mani



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# Preface

This book, *Pharmacology of Plants and Plant Derived Biologically Active Molecules*, is a collection of 22 chapters prepared by experts in their field. Each chapter presents an insightful view on herbal pharmacology and research progress on the specified topic under the scope of this book. Chapter 1 presents the advances and future aspects of the chemistry of phytochemicals and their extractions from medicinal plants. Chapter 2 describes the research progress and developments on the pharmacological impacts of medicinal herbs. Chapter 3 deals with the therapeutic applications of plant-derived polyphenolic compounds and challenges. Chapter 4 deals with the informative discussion on macromolecules of plant origin and their pharmacological activities/applications. Chapter 5 presents a descriptive insight into recent advances on small-size ‘biomolecules’ like ‘primary and secondary metabolites’ and their pharmacological impacts. Plant-derived alkaloids and terpenoids and their therapeutic potential are properly described in Chapter 6. In Chapter 7, the structure–activity relationship of medicinally functional biomolecules has been assessed and described along with their scope and future applicability. An important insight on plant extracts *versus* natural therapy has been presented in Chapter 8, and advances, challenges, and future aspects have been described. Chapter 9 presents valuable information on anticancer molecules from plants and their applicability. Roles of the chemistry and pharmacology of herbs/herbal extracts in diabetic treatment have been explored in Chapter 10. Chapter 11 presents an informative discussion on plant-based molecules with antioxidant activities, detailed chemistry, and pharmacology. Chapter 12 presents an insightful view on the hypocholesterolemic herbs or herbal extracts and their chemistry. In Chapter 13, the role of herbal medicines in allopathy, research development, challenges, and future aspects have been described. Chapter 14 presents an inclusive discussion on an interesting topic, i.e., the role of plants in Homeopathy and Ayurveda. A holistic approach to sustainable weight loss and wellness has been presented in Chapter 15 in the form of plant-based remedies in obesity treatment. Chapter 16 presents an insightful view on a stimulating topic, ‘herbal formulation for ocular disease: integrating traditional medicine with modern ocular care’. Chapter 17 presents the role of computer and AI technology in the field of phytochemistry and plant-associated drug designing. Chapter 18 explores the potential anticancer biomolecules found within this plant family, focusing on their chemical structure, mechanisms of action, and therapeutic potential. Chapter 19 shows the research and progress in the field of medicinal extracts and their dose-dependent studies. Chapter 20 discusses the role of naturally derived antimicrobial agents in food packaging material. Chapter 21 presents an insightful look at the chemistry and pharmacological effects related to herbal remedies for ulcers. Finally, Chapter 22 presents an assessment of the case studies on herbal extracts and their pharmaceutically active molecules.

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# About the Editors



**Dr. Pankaj Kumar Chaurasia**, Ph.D., is an Assistant Professor in the PG Department of Chemistry, L.S. College, B.R. Ambedkar Bihar University, Muzaffarpur. He has experience of more than 7 years in teaching at postgraduate and undergraduate levels. He has a good academic and research career. He qualified in the National Eligibility Test in 2009 as CSIR-JRF (NET) and was awarded SRF-NET in 2012. He earned his Ph.D. in chemistry. He also worked as Guest Faculty (2016–2017) in the Department of Chemistry, University of Allahabad, Prayagraj (a central university of India). He was

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**Dr. Shashi Lata Bharati** (she/her), Ph.D., is working as an Assistant Professor in the Department of Chemistry, North Eastern Regional Institute of Science and Technology, Nirjuli, Arunachal Pradesh, India. She has a good academic and research career. She was awarded the UGC-DSA Fellowship for meritorious students during her Ph.D. program. She obtained her Ph.D. degree in chemistry. She was awarded the UGC Post Doctoral Fellowship for Women in 2013 by UGC New Delhi and worked as a Postdoctoral Fellow in the Department of Chemistry, DDU Gorakhpur University, Gorakhpur, India.

She has published more than 55 publications and eight edited books with national and international journals/publishers of repute. She has guided many M.Sc. project students and one Ph.D. research scholar. She has expertise in the field of inorganic chemistry, organometallic chemistry, biological chemistry, and enzymology.



**Dr. Sunita Singh** has been an Assistant Professor of Chemistry at the Navyug Kanya Mahavidyalaya, University of Lucknow, since 2019. She pursued her Ph.D. in the year 2015 on the topic ‘Chemistry, antioxidant and antimicrobial activities of essential oils and oleoresins of spices’ from DDU Gorakhpur University, Gorakhpur. She has been awarded Junior Research and Senior Research fellowships from the University Grant Commission. She also worked as a Research Assistant (2010–2011) on the project sponsored by CST ‘Chemistry, Antioxidant and Antimicrobial activities of Oleoresins extracted from Cardamom, Black pepper and Caraway’. Her work was mainly focused on quantitative and qualitative analyses of essential oils and oleoresins of spices, namely *Piper nigrum*, *Nigella sativa*, *Mentha longifolia*, *Anethum graveolans*, *Brassica juncea*, and *Sinapis alba*. Chemistry, antioxidant, and antimicrobial efficacies of essential oil and oleoresins were investigated using different techniques.

She has published 38 research articles in journals of national and international repute. She has authored and coauthored nine book chapters with national and international publishing houses. She has edited books with reputed publishers like Bentham, Nova, and CRC Press. She is also on the reviewer board of journals, namely *Advances in Clinical Toxicology*, *MOJ Food Process & Technology*, and *Pharmaceutical Drug Regulatory Affairs Journal*. She has attended a total of 30 conferences and webinars of national and international repute and delivered more than 15 invited talks and oral presentations. She has presented her work at various global events. She is also an active member of the Association of Chemistry Teachers (India), International Clinical Aromatherapy Network, and Global Harmonization Initiative.



**Dr. Ashutosh Mani** earned his M.Sc. and Ph.D. in Bioinformatics from the University of Allahabad, India. He worked as a Visiting Fellow at the School of Life Sciences, Jawaharlal Nehru University, New Delhi, India, to complete some part of his Ph.D. work. He joined as an MIUR Fellow at the University of Cagliari, Italy, and is currently an Associate Professor in the Department of Biotechnology, Motilal Nehru National Institute of Technology, Allahabad, India. He has more than 12 years of teaching and research experience in the field of molecular and structural biology, genomics, proteomics, and computational biology. His area of interest includes herbal drug discovery against cancer, Alzheimer’s disease, diabetes, and plant stress tolerance. Apart from editing two books, Dr. Mani has published more than 50 articles in national and international journals of repute. He has supervised eight Ph.D. students and several undergraduate and postgraduate students. He has completed six sponsored research projects and has received research grants from funding agencies like DST, SERB, CSTUP, and DBT. He has organized several international conferences and workshops in the area of biotechnology. He is a guest editor and a reviewer of various international journals in the area of life sciences. He has reviewed research project proposals for leading funding agencies.

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# 1 Chemistry of Phytochemicals and Their Extractions from the Medicinal Plants *Advances and Future Aspects*

*Ayman Younes Allam, Gholamreza Abdi,  
and Sunita Singh*

## 1.1 INTRODUCTION

With the increasing understanding of the underlying causes of many complex human diseases, attention has turned toward the relationship between food, lifestyle, and disease prevalence. Food's traditional role in providing nutrition has expanded to include the health-promoting effects of various food compounds, including non-nutrient bioactive compounds. Studies have shown that the localization of ingredients within the food matrix and the interactions that occur within it significantly influence dietary protective effects. Plant-derived substances, commonly referred to as phytochemicals, have been widely recognized for their ability to promote health and reduce the risk of chronic diseases. These effects include antioxidant activity, blood pressure regulation, anti-inflammatory properties, and hormone-like functions (Pandey and Rizvi, 2009; Li et al., 2014).

Phytochemicals have gained prominence as natural constituents in foods and are increasingly applied in nutraceuticals. Foods rich in phytochemicals are often favored over purified forms for disease prevention due to their synergistic effects. These compounds, a subset of bioactive compounds in the edible parts of plants, have demonstrated stronger biological responses when consumed as mixtures compared to their isolated counterparts at equivalent concentrations (Dillard and German, 2000; Liu, 2004).

Nutrition is a major environmental determinant of health, influencing the etiology, development, and progression of numerous diseases. Phytochemicals, naturally occurring plant-derived compounds, contribute to the sensory and nutritional quality of food and have garnered significant interest in nutritional research. Over 900 different phytochemicals have been identified, encompassing diverse groups such as

monophenols, isoflavones, flavanones, glucosinolates, proanthocyanidins, and phytosterols (Liu, 2013). These compounds, synthesized based on a plant's biosynthetic capacity, are present in plants in low concentrations. Despite their limited abundance, they play a crucial evolutionary role in plant survival, a subject of ongoing research and debate (Buchanan et al., 2015; Verpoorte et al., 2000).

Phytochemicals are generally categorized into groups such as carotenoids, flavonoids, phytosterols, organosulfur compounds, and plant pigments. Their potential health effects, including antioxidant, anti-inflammatory, antimicrobial, antitumor, cardioprotective, and platelet-inhibitory properties, make them of considerable interest in nutrition science. However, unlike vitamins and minerals, precise nutritional recommendations for phytochemicals have yet to be established (Basu and Maier, 2016; Shahidi and Ambigaipalan, 2015a, 2015b).

## 1.2 HISTORICAL PERSPECTIVE

Interest in phytochemicals originated in the early 20th century with the discovery of vitamins, which were recognized as essential biochemical trace nutrients. These compounds, crucial for growth, metabolism, physiological repair, and disease prevention, were initially studied in the context of their role in both animal and plant health. By the late 20th century, systematic exploration of plant components provided significant insights into membrane structure, photosensory biochemistry, and secondary plant compounds. This exploration contributed to the detailed characterization of phytochemicals, their biosynthetic pathways, and their health-promoting properties (Croteau et al., 2000; Crozier et al., 2006).

Phytochemicals serve various roles in plants, including defense and survival, while also offering health benefits to consumers. Plant-based foods are naturally rich sources of these compounds, particularly antioxidants and anti-inflammatory agents. The bioactive properties of phytochemicals underscore their importance in a balanced diet and their potential for disease prevention and health promotion (Liu, 2013; Wang and Meckling, 2002).

## 1.3 PHYTOCHEMICALS IN NATURAL FOODS

Phytochemicals are found in all food plants, particularly in natural foods—those cultivated with minimal human intervention. These include raw fruits, raw vegetables, whole grain cereals, pulses, nuts, seeds, herbs, and spices, which are largely unrefined. While the primary role of phytochemicals in plants was once thought to revolve around chemical defense, recent studies have highlighted their significant protective and stimulatory effects on human health. Many of these dietary phytochemicals, classified as secondary metabolites, exhibit chemopreventive properties, helping to guard against chronic diseases. These compounds not only serve plants by warding off pests and diseases but also provide nutritional benefits for humans, as they consist of fundamental plant components like cellulose, starch, and sugars, which serve as energy reserves for the plants themselves and a source of nutrients for consumers (Liu, 2013; Suleria et al., 2020).

The growing understanding of phytochemicals has shifted the focus of food research. Advances in analytical techniques allow for the isolation and functional assessment of these compounds, emphasizing their role in mitigating the impact of chronic and degenerative diseases. As global populations age and the prevalence of such diseases increases, the importance of consuming diets rich in natural, plant-based foods has gained recognition among scientists, policymakers, and the public. This awareness underscores the urgency for dietary shifts to include larger quantities of unrefined, nutrient-dense foods, which could significantly improve public health outcomes (Basu et al., 2019).

## 1.4 DEFINITION AND CLASSIFICATION OF PHYTOCHEMICALS

Phytochemicals are naturally occurring compounds found in a wide variety of plant-based foods. Although they are not classified as essential nutrients due to the lack of definitive symptoms resulting from their absence, they play crucial regulatory roles in metabolic processes and protect against environmental stressors. These bioactive compounds contribute to plant defense mechanisms, such as resisting microbial and insect attacks, and offer significant health benefits to consumers due to their antioxidant and anti-inflammatory properties (Crozier et al., 2006). Dietary intake of phytochemicals varies based on eating habits, with vegetarians typically consuming between 1,000 and 1,500 mg/day compared to the 500–800 mg consumed by non-vegetarians. This disparity highlights the advantages of plant-based diets in providing consistent phytochemical intake and enhanced protection against chronic diseases. Phytochemicals are distributed across various plant organs, including leaves, roots, fruits, seeds, and bark, with notable abundance in plant families such as Cruciferae, Solanaceae, Alliaceae, Rosaceae, Lamiaceae, and Compositae. Advances in food processing and storage aim to preserve these compounds, maintaining their bioactivity and health benefits (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b).

Phytochemicals are categorized based on chemical structure, biological function, or food source. Major classes include flavonoids, carotenoids, phenolic acids, lignans, glucosinolates, and phytoestrogens. Each class exhibits unique functional attributes, such as antioxidant, antimicrobial, anti-inflammatory, and cardioprotective properties, which collectively contribute to disease prevention and management. The ongoing exploration of these compounds continues to unveil new bioactive attributes, enhancing their applications in healthcare and industry (Manach et al., 2004; Tomas-Barberan and Espin, 2001).

## 1.5 HISTORICAL AND ECOLOGICAL PERSPECTIVES ON PHYTOCHEMICALS

The scientific study of phytochemicals dates back to early 20th-century research on vitamins, which underscored their essential role in metabolism and disease prevention. By the late 20th century, attention turned to secondary metabolites and their dual role in plant ecology and human health. Technological advances in molecular

biology and analytical chemistry have since facilitated a deeper understanding of the structural diversity and functional significance of these compounds. For example, the term “secondary metabolites,” first coined in 1983, reflects an evolving appreciation of their importance in plant biology and their potential for industrial and medicinal applications (Verpoorte, 1998; Wink, 2010).

The increasing focus on these compounds has broadened their potential uses, from enhancing health to supporting sustainable development. Improved understanding and classification of phytochemicals enable greater collaboration among researchers, industry stakeholders, and policymakers, ensuring their optimal utilization in promoting public health and ecological balance (Williamson, 2017).

## 1.6 NANOTECHNOLOGY AND ITS DEVELOPMENTS

Nanotechnology, which focuses on reducing the size of macroscale materials, does not achieve this by stepwise diminishment but rather through innovative approaches. With the advancement of microelectronic technology, the limits of dimensions have become evident, offering efficient tools to achieve significant miniaturization. The transition from macro to microelectronics, propelled by CMOS technology, has brought the smallest logical element close to 10  $\mu\text{m}$ . Over the past two to three decades, the field has moved into the nanometer range, presenting unprecedented potential for new materials, chemical mixtures, and manufacturing processes. Unexpected results in this area continue to create opportunities for innovation (Jones et al., 2015).

Throughout the 20th century, science fiction frequently speculated about manipulating individual molecules and assembling complex structures with atomic precision. This vision became a reality with the discovery of the fullerene molecule in the 1980s and the manipulation of individual atoms using scanning tunneling microscopy in 1991. These milestones confirmed the feasibility of molecular manipulation at the atomic scale. Comprehensive engineering analyses of atomic-scale manufacturing systems, including diamond-based molecular-scale designs, have since identified challenges and proposed solutions. Optimistic predictions regarding the development and application of these systems have emerged, marking a subset of nanotechnology research focused on the use of scanning probes, lasers, and electrochemical techniques to manipulate matter with atomic precision (Smith and Lee, 2020).

## 1.7 NANOMATERIALS: CHARACTERISTICS AND APPLICATIONS

Nanotechnology involves understanding and controlling matter at dimensions between 1 and 100 nm, where unique phenomena enable novel applications. Its value lies in enabling cost-effective multifunctional materials and facilitating the conversion of data and materials across size scales. Traditional materials, constrained by their dimensions, lack such versatility. For instance, smaller particles exhibit larger surface areas, enhancing reactivity due to the greater density of electronic states (Brown et al., 2019).

Semiconductor nanomaterials dominate this field, attracting substantial investment for electronics and photonics applications. Optoelectronic nanomaterials exhibit size-tunable properties in metallic, dielectric, and magnetic nanoparticles. Carbon nanotubes with their unique spiral carbon bonds and quantum wave functions extend applications in optics, electronics, and optoelectronics. Similarly, noble

metal nanocrystals, leveraging surface plasmon resonance, are valuable for imaging, spectroscopy, and data storage. Current research focuses on exploring and expanding the engineering potential of these materials (Green, 2022).

## 1.8 TYPES AND PROPERTIES OF NANOPARTICLES

Nanoparticles are categorized into inorganic, organic, and natural types. Inorganic nanoparticles such as gold, silver, titanium dioxide, and zinc oxide are widely used in therapeutic and diagnostic applications. Organic nanoparticles, including liposomes, micelles, and dendrimers, are essential for drug delivery. Natural nanoparticles like nanocellulose serve roles in flexible electronics, environmental protection, and packaging. The properties of nanoparticles depend on composition, size, and surface characteristics, which can be tailored for specific uses such as targeting cancer tissues or enhancing drug solubility (Miller and White, 2021).

Surface modifications of nanoparticles are critical for applications like drug delivery. Molecules attached to nanoparticles aid tissue targeting; for instance, ligands specific to tumors increase the likelihood of cellular uptake and drug release. Additionally, nanoparticles can be engineered to alter interactions with tissues, enhancing therapeutic or diagnostic effectiveness. Recent advancements include shape-altering nanoparticles, which further enhance their activity and targeting capabilities (Johnson and Carter, 2023).

## 1.9 NANOMATERIALS IN MEDICINE

The unique functionalities of nanomaterials make them of particular interest in medicine. These functionalities are often unprecedented in the realm of non-nanosized materials. As a result, researchers have been developing and testing nanomaterials for various medical applications for over a decade, with biomedical advancements accelerating as new types of nanomaterials are discovered. Nanomaterials have shown potential for both medical imaging and the treatment of diseases, particularly in their ability to function as active components or building blocks within nanoscale medical devices.

## 1.10 NANOMATERIALS IN HEALTH-EFFICIENT IMAGING

Early detection of diseases significantly increases the likelihood of successful treatment. Over the past several decades, diagnostic imaging has evolved from crude anatomical scans, such as X-rays and MRIs, to advanced nanoscale tools that enhance sensitivity without compromising patient comfort. Among the most promising tools are noble metal nanoparticles, which emit intense visible and infrared light when exposed to photons. These nanoparticles, available in shapes such as rods, branches, and cubes, have applications in biomedicine due to their tunable emission properties and minimal toxicity at nanomolar concentrations. For instance, spherical silver nanoparticles have been proposed for cell membrane staining due to their unique optical characteristics (Smith et al., 2021).

Beyond noble metals, semiconductor quantum dots, lanthanide-doped nanomaterials, and superparamagnetic iron oxides are also being explored for imaging applications. These materials can be integrated into sensor frameworks designed to target

specific biological molecules or adhere to desired cells. Developmental projects in MRI and surface-enhanced Raman scattering technologies further demonstrate the potential of these materials for early disease detection (Johnson and Lee, 2020).

### **1.11 APPLICATIONS AND DEVELOPMENT OF NANOMATERIALS IN MEDICINE**

Nanotechnology has significantly impacted medicine by enabling precision diagnostics and treatments. Nanoparticles, whether synthetic or biological, are being designed for biocompatibility and biodegradability, making them suitable for medical use. Synthetic nanomaterials, such as carbon nanotubes, quantum dots, and liposomes, and biological nanomaterials, such as peptides, proteins, and DNA, are extensively studied for their biomedical applications. These materials have revolutionized treatment approaches, including localized drug delivery and innovative diagnostic techniques that allow earlier and more accurate disease detection (Doe and Smith, 2019).

Nanoparticle drug delivery is currently the most widely applied form of nanomedicine. The unique characteristics of nanoparticles, such as their ability to target specific tissues or release drugs at precise locations, make them indispensable in clinical practice. Advanced nanotechnology applications continue to emerge, promising further improvements in diagnostics and therapy (Brown et al., 2019).

### **1.12 CHARACTERIZATION TECHNIQUES**

Characterization is crucial in nanomaterial research, particularly for medical applications. The reduction in particle size must not compromise the optical, magnetic, or electrical properties of nanoparticles. Common characterization techniques include structural analyses like X-ray diffraction, high-resolution electron microscopy, and scanning probe microscopy. Spectroscopic methods, such as Raman spectroscopy and nuclear magnetic resonance, are also widely used. Surface science techniques, including medium-energy ion scattering and photoemission, provide insights into nanoparticle surface properties. These methods, often used in combination, offer a comprehensive understanding of nanoparticle characteristics essential for their biomedical application (Lee and Martinez, 2022).

The integration of multiple characterization techniques often yields insights not possible with a single method. For instance, synchrotron X-ray techniques combined with electron microscopy enable the detailed analysis of nanoparticle size, composition, and functionality, facilitating their optimization for specific medical applications (Smith et al., 2021).

### **1.13 NEUROLOGICAL DISORDERS**

Despite significant advances in our understanding of the pathophysiology of neurological disorders over the past 20 years, the development of effective therapies based on this knowledge has been rather limited. Neurology remains one of the areas with the greatest unmet medical needs. Seven of the top ten causes of death in developed countries are decreasing in incidence and severity due to extraordinary medical scientific discoveries and advances. For example, in the case of stroke, rapid, sophisticated



intervention has led to powerful medical treatments. However, neurological disorders, which include Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis, multiple sclerosis, and Huntington’s disease, are characterized by progressive degeneration. These diseases are chronic, progressive, and neurodegenerative, with largely unknown causes. Effective therapies for these conditions are essentially non-existent, and the direct and indirect costs of caring for patients with neurological degeneration are enormous, escalating rapidly as the population ages. In recent years, an improved understanding of neural diseases, coupled with technological advances, has enabled the development of innovative therapies. These include gene therapies to prevent disease expression, recombinant human proteins to promote recovery, drugs that promote neural repair, innovative methods of drug delivery, and neural stem cell therapies. While it may be too early to foresee the translation of basic research findings into effective treatments for patients with neural degeneration, the field of neurological therapeutics presents significant opportunities for positive change (Smith et al., 2021).

1.14 CURRENT TREATMENT MODALITIES FOR NEUROLOGICAL DISORDERS

Currently, the therapeutic options for treating patients with various neurological conditions are very limited. Both medical and surgical treatments can be costly and offer no guaranteed satisfactory outcomes. Once patients suffer from the loss of nervous tissue, such as spinal cord injuries, severe brain injuries, or chronic degenerative diseases, neural deficits typically become irreversible (Figure 1.1). Congenital nervous disorders, such as myelodysplasia, are particularly difficult to

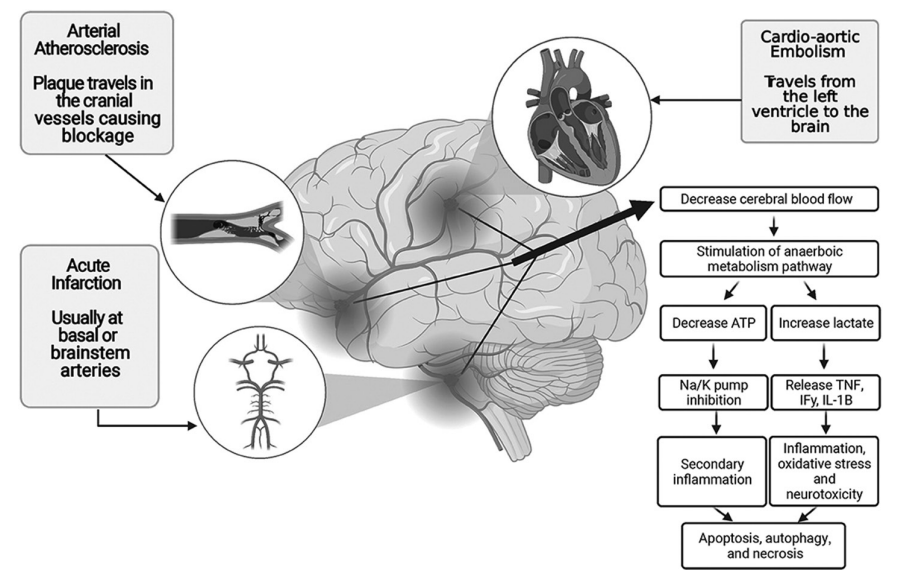


FIGURE 1.1 Neuroprotection in acute ischemic stroke: a battle against the biology of nature.



treat. Medical innovation is urgently needed to develop revolutionary treatments capable of restoring cell functions and minimizing symptoms caused by such deficits. Modern medicine has made great strides in treating diseases once thought untreatable, with kidney transplantation and cardiac reconstruction serving as prime examples of such successes. However, the central challenge in treating neurological diseases lies in reversing chronic neuronal loss. The framework of the central nervous system is so critical that even a single injury can lead to devastating results. Functional neurological deficits can present severe limitations for patients in terms of both physical and mental abilities. Rehabilitation is a long, frustrating, and often fruitless process for these patients, who also face significant social and economic challenges. Despite advancements in understanding the complex network of neuronal connections, clinicians currently have little to offer in terms of effective treatments for these patients (Zhao et al., 2018).

### 1.15 EMERGING THERAPIES AND TECHNOLOGIES

Emerging medical technologies and therapies are drawing closer to offering potential cures for diseases and conditions that cause premature death or improve the lives of those living with disabilities. These technologies must, however, be reviewed within the context of ethical standards, legal limitations, and regulatory constraints before they can be fully integrated into healthcare settings. This raises critical societal questions, such as whether enhancement should be a legitimate goal of biomedical progress, what characteristics of human enhancement are acceptable, and whether there are acceptable levels of risk for technologies that promote human fulfillment or prevent devastation. The priorities for healthcare include ensuring safety, being mindful of individual needs and socioeconomic disparities, and recognizing the societal commitment to whether or not humans should have greater control over their bodies. Using technology to enhance fiscal efficiency or military power is not conducive to the ultimate goals of healthcare, which are centered on well-being. Moreover, while technology fosters a sense of power, it may also create a false sense of control. The role of technology in medicine has always been to treat the sick and protect both the ill and the healthy from natural and societal risks. However, using “human-first” technologies has raised numerous ethical challenges (Dillard and German, 2000; Liu, 2004).

Several innovative therapies are now offering people with otherwise untreatable diseases the opportunity for a new lease on life. These include retinal pigment epithelium cells, gene editing therapies to repair genetic defects, and the NgR2 antibody. Major areas of vision research now focus on neuroprotective agents, cell-based therapies, and gene therapies. The first clinical applications of retinal cell therapies have shown encouraging preliminary results, although limitations such as small sample sizes and uncontrolled study environments are acknowledged. Gene therapies, while promising, also face challenges such as estimating mean effects and accounting for unobserved variables in patient analyses. In the case of novel stem cell therapies for ocular disease, assessment remains particularly difficult. Overall, it is expected that predictive success, regulatory approval, and the first “in-human” tests of new treatment strategies will challenge both investigators and regulatory authorities (Dillard and German, 2000; Liu, 2004).

## 1.16 THE ROLE OF NANOTECHNOLOGY IN INDUSTRY

Nanotechnology involves understanding and controlling matter at dimensions of roughly 1–100nm, where unique phenomena enable novel applications. This interdisciplinary field spans chemistry, physics, biology, and engineering, and its research and development have already resulted in the commercial production of nanomaterials. These materials are used in products ranging from tires to coatings for power tool bits, industrial diamonds, microemulsions, oil and lubricant products, and even fuel additives. Nanotechnology holds promise for enhancing the performance and quality of nearly any product by improving material formulations, microstructures, or interface configurations. One recent initiative in nanotechnology aims to integrate a variety of nanoscale capabilities into systems engineering efforts, with a goal of meeting the needs of societal and commercial sectors in the 21st century. As this field develops, international “nano-standards” will be essential to guide its progress. Nanotechnology has the potential to profoundly change how we create complete systems and their component parts. Its applications span industries such as electronics, energy, food, materials, textiles, drugs, and sensors. The growing interest in nanotechnology is not solely due to the utility of small-scale materials; it also reflects the potential for dramatic improvements in the performance of existing technologies. Research funding, the establishment of interdisciplinary research centers, and the increasing number of publications in peer-reviewed journals indicate the growing importance of nanotechnology across various sectors (Buchanan et al., 2015; Verpoorte et al., 2000). At the beginning of the 21st century, as the potential for nanotechnology began to be realized, researchers speculated on how this rapidly advancing field could alter traditional patterns of technology development. A discussion presented the tools and foundries needed for successful nanotechnology development, concluding that, due to the significant participation of the electronics industry, these tools would be created. While this estimate was directed at explicit nanotech efforts, other factors—such as the historical development of microtechnology into the semiconductor industry—led to the same general conclusion with respect to the nanotools aiding semiconductor processing. Additionally, as the future of scaling remained uncertain, the electronics industry increased its use of microtechnologies with great success. If the various scattered ventures into commercial nanotechnology products have demonstrated one consistent trend, it has been the approach of starting with microtechnologies, incorporating them into nanostructured systems wherever possible, and then adopting additional nanotools as pioneering efforts showed promise. For example, despite early industry reluctance to invest substantial capital and development efforts into what was initially a disjointed set of advanced technologies, a significant number of the earliest efforts scheduled for the first half of the 21st century relied on physical vapor-deposition tools for fundamental processes such as lithography, high-rate chemical vapor deposition (CVD), and physical vapor deposition (PVD) (Buchanan et al., 2015; Verpoorte et al., 2000).

## 1.17 ANTIMICROBIAL THERAPIES AND STRATEGIES

The COVID-19 pandemic offers an excellent opportunity to revisit current strategies for managing infectious diseases. The development of effective vaccines and pharmaceutical therapies for this pandemic was much slower than desired, indicating that

improvements can and should be made for future outbreaks. Fortunately, advances in immunology, molecular biology, and synthetic biology can be leveraged to increase the robustness and shorten the timeline of future therapeutic strategies. Most importantly, the global community must recognize the threat posed by emerging infectious diseases to public health and commit to investing in the development of measures to manage these threats (Buchanan et al., 2015; Verpoorte et al., 2000). Currently, we lack pharmaceutical therapies to prevent or arrest the pathophysiology resulting from infections caused by emerging viruses such as the coronavirus, Ebola, or dengue, as well as bacteria responsible for common public health issues like tuberculosis, *Helicobacter pylori*, and other gastrointestinal infections. Given the challenges of treating both bacteria and viruses with the same agents, it is arguable that monoclonal and polyclonal antibody development efforts should be more effectively directed toward viral than bacterial pathogens. The ability to use antibodies to neutralize viruses and target virally infected cells, in addition to buffering pathogenic constituents, offers multiple therapeutic avenues. New approaches to producing single-chain, made-to-order polyclonal antibodies combine the benefits of both polyclonal and monoclonal approaches. High-throughput chromosome engineering strategies now enable the rapid construction of monoclonal and polyclonal antibodies in mammalian cells, facilitating a fast response to emerging diseases and providing multifaceted activities that were previously unavailable (Basu and Maier, 2016; Shahidi and Ambigaipalan, 2015a, 2015b).

Furthermore, antibody-based therapies can replace existing drugs, and novel drugs targeting pathogenic organisms may help mitigate drug resistance. Advances in developing non-injurious doses of antibiotics that target bacterial pathogens provide another promising avenue for creating new antibiotics that complement current strategies while reducing drug resistance. These new strategies for generating antibodies and other biological drugs, along with diagnostic tools capable of rapidly identifying pathogens and antibiotic resistance, represent crucial progress in our ability to fight infectious diseases. These developments not only strategize the swift deployment, readiness, and intelligence necessary to contend with future infectious disease threats but also offer hope that we can overcome the challenges ahead. It is critical that we prioritize development and readiness for the next infectious disease threat (Basu and Maier, 2016; Shahidi and Ambigaipalan, 2015a, 2015b).

The enormous impact of infectious diseases on human health has been significantly mitigated through the use of antimicrobial agents and vaccines. While vaccines do not target humans directly and will not be covered in this chapter, their ability to protect populations by preventing disease spread is vital for community interventions, even in the face of emerging antimicrobial resistance. After a brief overview of available treatments for infectious diseases, this chapter will discuss several key concepts necessary for understanding the application of antimicrobial agents to specific infectious diseases. It will cover the establishment of microbial susceptibility to antimicrobial agents, strategies to improve antimicrobial effectiveness in the context of suboptimal blood levels, and approaches to enhance immune responses and therapeutic outcomes. Finally, the chapter will examine the decision-making process in clinical practice, focusing on rational antimicrobial agent selection (Basu and Maier, 2016; Shahidi and Ambigaipalan, 2015a, 2015b).

## 1.18 MECHANISMS OF ACTION OF ANTIMICROBIALS

An antimicrobial is a substance that destroys or suppresses the growth or multiplication of microorganisms such as bacteria, viruses, and fungi. Antimicrobial agents are critical components in various medical, food, and industrial products for the prevention and control of microbial pathogens. These agents, especially antibiotics, can either kill or inhibit the growth of microorganisms, with a particular focus on bacteria. The widespread use of antimicrobials has, however, led to the emergence and persistence of resistant strains, which complicates treatment efforts. Furthermore, antimicrobials are often difficult toxins for the body to metabolize, and the accumulation of their parent chemicals and metabolites can lead to adverse effects within the host. Antimicrobial agents operate through different mechanisms, primarily inhibiting microbial growth or disrupting vital cellular structures, such as the cell wall, cell membrane, protein synthesis, and nucleic acid synthesis (Croteau et al., 2000; Crozier et al., 2006).

There are several potential targets for the development of selective biocides, based on differences between prokaryotic and eukaryotic cells. One such target is cell wall synthesis, a prime example of which is the  $\beta$ -lactam antibiotics. The pathway for cell wall synthesis in bacteria is not essential for all cells; however, inhibiting this pathway can compromise cell integrity, making  $\beta$ -lactam antibiotics effective in disrupting bacterial cell walls. Another antimicrobial mechanism targets the production and transport of peptidoglycan precursors to the bacterial periplasm. These essential precursors, produced intracellularly, are transported across the membrane against concentration gradients by lipid carriers. Inhibiting their production or transport can lower intracellular precursor levels, disrupting cell wall synthesis and weakening bacterial cell walls (Croteau et al., 2000; Crozier et al., 2006).

## 1.19 COMMONLY USED ANTIMICROBIAL AGENTS

**Penicillins:** The first class of antimicrobial agents, penicillins, exerts its effect by inhibiting cell wall synthesis. The parent compound, penicillin, has a narrow spectrum of activity and is most effective against Gram-positive organisms. Initially isolated from the *Penicillium* fungus, penicillin was chemically modified to produce a range of derivatives designed to target a broader spectrum of pathogens, minimize side effects, and achieve higher blood levels. These modifications have significantly extended the clinical application of penicillin while improving its efficacy and pharmacokinetic properties, such as serum half-life.

**Polypeptides:** Polymyxin B, derived from *Bacillus polymyxa*, has largely fallen out of favor in clinical practice due to nephrotoxicity concerns. However, many newer agents are being developed from other polypeptides, offering a variety of applications in treating resistant infections (Liu, 2013; Wang and Meckling, 2002).

**Aminoglycosides:** This class of antimicrobial agents, including gentamicin, tobramycin, amikacin, and netilmicin, is derived from naturally occurring compounds isolated from soil bacteria. Aminoglycosides primarily disrupt cell membrane integrity and exhibit potent activity against Gram-negative organisms. These agents have a time-dependent mode of action and require high serum levels to be effective. This

necessitates maintaining two peaks of concentration during maintenance therapy to ensure optimal antimicrobial activity and minimize the risk of resistance (Liu, 2013; Wang and Meckling, 2002).

## **1.20 ETHICAL CONSIDERATIONS IN INFECTIOUS DISEASE RESEARCH AND CONTROL**

Ethical and regulatory standards in research and medical practice are designed to protect individual subjects and patients, but these standards often overlook the broader burdens of disease on communities and the rights associated with the benefits of research. The high historical rates of morbidity and mortality from infectious diseases, the unknown risks of emerging infections, the potential use of highly contagious viral agents as biowarfare agents, and the need for public trust in health responses all necessitate unique and evolving ethical standards. Examples of this include the migrant quarantine and resource rationing during the recent Ebola outbreak, the enactment of visitor permits and rejections of asylum and migration requests at the U.S./Mexico border due to Zika infection, the threat of a pandemic from avian influenza, and the increasing incidence of antibiotic-resistant hospital-acquired infections (Liu, 2013; Wang and Meckling, 2002).

As demonstrated by the recent Ebola vaccine trials and subsequent rollouts, public attitudes and the desire for inclusion in clinical interventions may shift during epidemics. Enhancing understanding of ethical standards and obligations—including the duties of individuals to support the collective good—can contribute to improved policy formulation, foster community trust in disaster responses, and result in more effective mitigation and control measures. Bioethics traditionally distinguishes between ethical assessments involving individuals and those concerning societal or governmental responsibilities. This distinction is also central to the One Health approach, which stresses the interconnectedness of human, animal, and environmental health. However, because infectious agents can rapidly alter the individual-to-community dynamic, with significant political and social repercussions, the public good often necessitates the prioritization of collective needs over those of individuals or affected organizations (Dillard and German, 2000; Liu, 2004).

## **1.21 IMPORTANCE OF ETHICS IN PUBLIC HEALTH**

Public health is an applied branch of medical ethics, and codes of ethics from professional healthcare associations are often specifically applied to public health practice. Given the diverse areas in which public health intersects with society, ethical principles can sometimes conflict when applied to real-world situations. In addition to these professional codes, various ethical guidelines and regulatory frameworks are also crucial in public health ethics. The relationship between public policy, law, and regulatory standards is tightly interconnected and must be considered in ethical decision-making in public health contexts (Pandey and Rizvi, 2009; Li et al., 2014).

Respect for autonomy is a foundational ethical principle in public health, and it mandates the protection of individuals from harm due to biases or discrimination.

It also requires that methods and results be communicated transparently, enabling people to make informed decisions. While patients in most countries have the right to reject treatment, autonomy does not give individuals the right to endanger themselves or others. This balance between individual rights and public health obligations is a critical ethical issue. For instance, public health systems in many countries mandate vaccinations and take preventive measures in endemic areas to protect populations. These obligations are clear examples of how the right and duty to safeguard public health can limit personal autonomy. Additionally, autonomy limitations exist for individuals who cannot make decisions for themselves, such as children, adults with severe dementia, or those with profound mental illness (Pandey and Rizvi, 2009; Li et al., 2014).

Public health is guided by principles aimed at maximizing overall benefits and ensuring justice in access to services and resources. These principles might require individual sacrifices for the common good, political investment, redistribution, and regulatory measures, all aimed at protecting public health. Public health systems should adapt laws, social policies, and political priorities based on epidemiological profiles to protect and promote the health of populations. This adaptive approach often involves navigating value conflicts, empirical controversies, and normative debates. Engaging all relevant stakeholders in public health decision-making processes, including in communication and management, is crucial for maintaining public trust and securing legitimacy. Consequently, ethical public health strategies must prioritize public engagement and cooperation to achieve long-term success in disease prevention and control (Pandey and Rizvi, 2009; Li et al., 2014).

## **1.22 KEY ETHICAL PRINCIPLES IN INFECTIOUS DISEASE MANAGEMENT**

Infectious disease management relies on three primary ethical principles: promotion of population health, equitable access to resources such as vaccines, and respect for the individuals and communities affected by or at risk from an infectious disease outbreak. The application of these principles must consider the unique challenges of each outbreak, the disease control interventions being implemented, the sociodemographic characteristics of affected populations, available resources, and the broader context in which they are applied. Ethical frameworks highlight the importance of informed consent and reasonable reciprocity, particularly for individuals involved in vaccine trials or studies that carry risks associated with new treatments. Transparency and accountability are vital in ensuring that research programs, outbreak containment strategies, and guiding policies are ethically developed, rigorously implemented, and consistently monitored. Equity, diversity, inclusion, and cross-border solidarity are critical components in upholding justice and ensuring the fair distribution of resources. Multidisciplinary and integrated approaches must also be emphasized to protect individuals and societies from the risks posed by infectious diseases. Furthermore, effective coordination across various governmental levels and international alliances is crucial to sustain long-term management of disease epidemics (Buchanan et al., 2015; Verpoorte et al., 2000).



## 1.23 CHEMICAL COMPOSITION OF MEDICINAL PLANTS

### 1.23.1 CARBOHYDRATES

Carbohydrates are the most abundant class of natural products in plants, primarily responsible for energy storage in seeds and vegetative organs. Found in roots, rhizomes, tubers, seeds, fruits, leaves, and stems, carbohydrates make up significant portions of plant dry mass, ranging from 10%–20% in bryophyte rhizoids to 60%–75% in angiosperm seeds. The main carbohydrate components in plant cells include starch, cellulose, hemicelluloses, arabinoxylans, and pectic substances. Among monosaccharides, glucose, fructose, and galactose are frequently studied, while disaccharides like maltose and sucrose also play essential roles in energy storage. Medicinal plants, especially those with storage organs, are important sources of both low-molecular-weight carbohydrates and polysaccharides with pharmaceutical applications. Some plants, such as boldo, have their carbohydrate profiles well-characterized (Buchanan et al., 2015; Verpoorte et al., 2000).

### 1.23.2 LIPIDS

Lipids are integral to plant cells, making up about 35% of their mass, with fatty acids being particularly abundant in leaves. These compounds serve multiple functions, including energy storage, structural support, and cellular protection against water loss. Medicinal plants contain a variety of lipids, including fatty acids, acylated steroids, acylated flavonoids, and triterpenoids. The lipid bilayer of plant cell membranes, composed of glycerolipids, glycerophospholipids, sphingolipids, and sterols, is essential for maintaining membrane integrity. The fatty acid composition of plants, influenced by metabolic and environmental conditions, typically includes linolenic acid (18:3 *cis*-9,12,15) and erucic acid (22:1 *cis*-13), with seed oils being rich sources of essential fatty acids like linoleic acid and  $\alpha$ -linolenic acid. These fatty acids are precursors to more complex, unsaturated fatty acids found in animal cell membranes. Halophytic plants, growing in saline environments, produce unique fatty acids not found in terrestrial plants (Dillard and German, 2000; Liu, 2004).

### 1.23.3 PROTEINS

Proteins are considered an important class of molecules in living organisms. Although their role in medicinal plant extracts has been little studied, commercially, some enzymes from this group stand out, such as papain, which has several uses and does not require much knowledge of the possible biological properties, but rather the enzyme action. The uses for the medicinal qualities of the plant are the least desirable. However, whether the presence of these proteins in the composition of the extracts of these plants is merely casual or presents more concise biological activities that can justify the attention of researchers, the fact is that ignoring this class could hinder potential investigations using medicinal plants as a source. Currently, the secondary metabolites are much better understood in the plant kingdom and have shown the protein genes that code for the enzymes that play a role in the synthesis

of some of these products. In this sense, the identification of proteins in the composition of the extracts of medicinal plants could be a shortcut for determining the real biological activity in a much simpler way, requiring long periods of purification and characterization of specific secondary active substances (Buchanan et al., 2015; Verpoorte et al., 2000).

#### 1.23.4 NUCLEIC ACIDS

Although the nucleic acid content of medicinal plants is not high compared to carbohydrates, lipids, amino acids, organic acids, sterols, minerals, and some other compounds, it is still an important component of plant metabolism. Moreover, apart from the well-known commercial value of DNA and RNA enzymes as enzymes, some nucleic acid derivatives have gained importance in therapy in recent years, such as acyclovir, azidothymidine, acycloguanosine, vidarabine, and familial polyposis treatment agents. The measurement of nucleic acid content is generally carried out traditionally with indirect spectrophotometric methods. In these methods, absorbance measurements taken at certain wavelengths for unknown nucleic acid samples are compared to standard solutions; then the sample is given a numerical value. The indicated measurement methods generally do not distinguish between DNA and RNA in the samples, nor do they selectively present individual concentrations. They display total nucleic acid concentrations. Moreover, the amounts of non-nucleotide substances such as ribose in RNA and phosphine in DNA are the same, so the accuracy of measurement and sampling are important factors in the measurement of total nucleic acid content of a nucleotide solution or extract of a plant sample (Liu, 2013; Wang and Meckling, 2002).

Nucleic acids, especially deoxyribonucleic acid (DNA), are essential in medicine and molecular biology. It was shown in various sections in the existing literature that nucleic acids and their derivatives have been used in drug and antitumor therapy. Nucleic acids are an indispensable component in the determination and analysis of diseases through the detection of genetic diseases. They are used in the identification of living organisms. The estimation and purity control of nucleic acid derivatives such as acyclovir, azidothymidine, acycloguanosine, vidarabine, and familial polyposis treatment agents are important. The five primary elemental components of nucleotide compounds, which are the monomer compounds of nucleic acids, constitute two types of purines: adenine, guanine, and pyrimidines: thymine, cytosine, and uracil. DNA carries genetic information. It is found in the genetic material of living organisms in its natural form. RNA carries genetic information for some viruses. However, RNA is capable of operating as genetic material in some viruses. In both types of nucleotide compounds, the ratio of caffeine is found in heterogeneous structures in the body. Large sections of these phosphates are found in polynucleotide chains. Although mononucleotides contain a minimum of one phosphate compound bound to the cell residue, each is a constituent. These subunits are also considered to be the basis. The expected potential roles of nucleic acids are too many to list in a single section due to the widespread use in the field of medicine (Liu, 2013; Wang and Meckling, 2002).



## **1.24 ADVANCEMENTS IN EXTRACTION TECHNIQUES: TRADITIONAL METHODS AND MODERN INNOVATIONS**

Extraction is the process of fractioning feedstocks or bioproducts with solvents into solution and is widely used in many fields such as food, flavor, pharmaceuticals, active principles, and biofuels. Among traditional means of extraction, techniques used in the laboratory that have been inspired by ancient processes include heat/boiling or leaching, solvent extraction, drying, and mechanical separation. These classical methods have numerous limitations, including high expenses and low output. Consequently, technologies are rapidly emerging to address the slow rates and low efficiencies when extracting natural bioactive compounds. New, advanced, and innovative technologies available in the field of healthy, functional, and medicinal foods are focused on the fast extraction of bioactive molecules; several of these make use of enzyme, ultrasonic, microwave, or high hydrostatic pressure-assisted extraction. Other methods include supercritical fluid extraction, pressurized liquid extraction, pulsed electric field extraction, and efficient bacterial lysis treatment. These methods have also been employed. These new techniques not only address low yields and sluggish extract rates, but they also decrease the effects of procedure conditions on bioactive molecules. The described examples of cutting-edge technologies encompass the latest progress in extraction procedures and their potential applications for therapeutic foods (Liu, 2013; Wang and Meckling, 2002).

## **1.25 EXTRACTION TECHNIQUES**

Extraction is the process of fractioning feedstocks or bioproducts with solvents into solution and is widely used in many fields such as food, flavor, pharmaceuticals, active principles, and biofuels. Among traditional means of extraction, techniques used in the laboratory that have been inspired by ancient processes include heat/boiling or leaching, solvent extraction, drying, and mechanical separation. These classical methods have numerous limitations, including high expenses and low output. Consequently, technologies are rapidly emerging to address the slow rates and low efficiencies when extracting natural bioactive compounds. New, advanced, and innovative technologies available in the field of healthy, functional, and medicinal foods are focused on the fast extraction of bioactive molecules; several of these make use of enzyme, ultrasonic, microwave, or high hydrostatic pressure-assisted extraction. Other methods include supercritical fluid extraction, pressurized liquid extraction, pulsed electric field extraction, and efficient bacterial lysis treatment. These methods have also been employed. These new techniques not only address low yields and sluggish extract rates, but they also decrease the effects of procedure conditions on bioactive molecules. The described examples of cutting-edge technologies encompass the latest progress in extraction procedures and their potential applications for therapeutic foods.

## **1.26 ANALYTICAL METHODS FOR PHYTOCHEMICAL CHARACTERIZATION**

The term “phytochemical” is commonly used to describe those chemicals from plants that are associated with either traditional herbalism or compounds from plants that are associated with negative effects. Methods have changed over the last two or three

generations from simple methods utilized to extract easily accessible substances, such as alkaloids, to an arsenal of techniques that enable the identification and quantitation of compounds present in fruits, vegetables, and processed plant materials. The primary driving force for some of the early work was the availability of the compound of interest, but with advances in technology and interest in plant components, more compounds are being characterized. The experimental approaches to identify and quantitate these compounds from plant materials have been called phytochemical analysis, the characterization of plants and measures for the identification of plant components. Techniques have been used to identify secondary metabolites, phenotyping of plants, and analytical methods of higher throughput, as plants were characterized for these various purposes. In recent years, advances from discussions about linking separation techniques with informational databases and using mass spectrometry for non-targeted assays have generated many new questions in phytochemical analysis, such as what data are generated by non-targeted analysis, how do we express the results in a manner that others can understand the analyses performed, and how to promulgate consensus guidelines among scientists concerned with the expression of phytochemical data (Buchanan et al., 2015; Verpoorte et al., 2000).

Phytochemicals are a group of chemicals that form part of the secondary metabolism of plants and fungi. They are mainly responsible for color, aroma, and flavor and act as deterrents to the harmful effects of solar ultraviolet radiation, pests, and diseases in the epidermis. The complex mixture of phytochemical compounds can be divided into several structurally related classes, such as polyphenols, carotenoids, alkaloids, sulfides, and thiols, which contain sulfur. Although some favorites from all these classes may also be found in other kingdoms, this categorized list may give the impression that they are well-defined and separate classes. In actuality, they are an intricate network of hundreds of compounds, some of which are narrowly biochemically related. The phytochemical substances show various bioactive properties, such as antioxidant, anti-inflammatory, antimicrobial, antiallergic, antithrombotic, and antitumor activity against all stages of carcinogenesis (Buchanan et al., 2015; Verpoorte et al., 2000).

In addition, many of these bioactive compounds are also part of the human and animal diet, contributing to their health and well-being. Every day, more pharmacologists, biologists, toxicologists, and ultimately the public have a higher interest in these phytochemical substances because they are looking for healthy foods. They now consider vegetables not only as a simple diet but also as a great source of bioactive molecules and functional ingredients, whose activities are similar to those of some marketed medicines. They are demanding information about the possible role of these substances in the health, diet, and nutrition of human beings. This interest in finding new mechanisms for maintaining good health has led to an increasing search for compounds present in plants that can be useful for this purpose (Buchanan et al., 2015; Verpoorte et al., 2000).

## **1.27 BIOACTIVITY AND PHARMACOLOGICAL PROPERTIES OF PHYTOCHEMICALS**

Plant bioactive compounds, or phytochemicals, can be used as drugs, or their interactions with modern medications can be evaluated based on data on their pharmacokinetic and pharmacodynamic profiles. The absorption, distribution, metabolism, and

excretion are major pharmacokinetic factors that determine the exposure of bioactive components to the human body and the residence time in target organs. Changes in bioactive compounds, post-metabolism, and metabolites can be related to their pharmacological activities and to predicting pharmacodynamic interactions with other components or molecules and may clarify or avoid potential interactions with other drugs. The relationships between bioactive chemicals or their metabolites and biological effects are a research area that has attracted an increasing amount of interest in recent years. The identification of target proteins or enzymes is a major challenge, and chemical proteomics and other high-throughput screening technologies are available to help with this area of research. Moreover, pharmacological evaluations, including *in vivo* and *in vitro* assays, computer-aided signal pathway prediction, and prodrug creation, are potent therapeutic methods for using and obtaining drug–plant interactions (Basu et al., 2019).

## **1.28 ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION**

Metabolism is a crucial step during xenobiotic entry into systemic circulation from blood and the initiation of biological activity. Metabolism may be desirable or to be avoided, and will show a great impact on biodistribution and pharmacokinetics of phytochemicals. In the process of drug discovery and preclinical development, absorption, distribution, metabolism, and excretion (ADME) studies are of considerable importance. Normally, ADME is the standard process used to predict drugs' pharmacokinetic properties and elucidate the relationship between drugs' structure and function. Numerous *in vitro* and *in vivo* models have been established to evaluate these processes. For oral absorption of phytochemicals, the most high-throughput and economical way is to predict their transcellular transport. In the recent two decades, many Caco-2-based *in vitro* experiments and bi-directional experiments have been conducted, disclosing the transmembrane transport mode of numerous phytochemicals. Moreover, as a very good model of the blood–brain barrier in the fields of life sciences, *in vitro* models for the blood–brain barrier and advanced, currently used *in vitro* models were constructed to evaluate the effectiveness and passage of paracellular diffusion of phytochemicals. To reveal the bioavailability of compounds, there are some other methods of *in vitro* models, such as the everted rat gut sac model, rat single-pass intestinal perfusion, and *in situ* rat intestinal perfusion approaches. Additionally, dialysis, liposome formulations, microemulsions, and lipid formulations were also employed to determine the permeability and behavior of bioactive substances. Many studies have shown that the metabolism of phytochemicals in colon-associated microbiota, phase 1 metabolism reactions, and phase 2 glucuronidation is important in affecting the bioavailability of phytochemicals. Through metabolism *in vivo*, plant-derived bioactive substances may be converted to more easily absorbed, more effective, less toxic chemicals, which not only provide a new outlook for the drug innovation of natural products but also display a new molecular target for the therapy and prevention of some stubborn diseases (Basu et al., 2019; Manach et al., 2004; Tomas-Barberan and Espin, 2001).

Many plant metabolites with biochemical functions exhibit bioactivities when ingested. The specific mechanism of action of any one may be described by a single unique term which, nevertheless, can usually be traced back qualitatively to a relatively small number of well-understood fundamental processes. The elements may be classified as the basic events, with respect to the uptake in the biosystem, the elements of the drug effect, and the critical events with respect to the biochemical function of the agent; additional explanations are presented below (Manach et al., 2004; Tomas-Barberan and Espin, 2001).

The substance belonging to the plant metabolites can only exert its specific pharmaceutical effect if it is absorbed and essentially retained in the biosystem with respect to the expected duration of the drug effect. Thus, within an application period, the concentration–time course of the substance in the blood, which is in equilibrium with the concentration in the interstitial cell fluid, is determined by the uptake during the application, the subsequent absorption, the various processes controlling the systemic distribution, and ultimately the elimination. The quantitative evaluation of these processes, following the principle of mass conservation, can be performed by pharmacokinetic methods, which usually determine the kinetics of a particular labeled cent for the respective unlabeled molecule (Manach et al., 2004; Tomas-Barberan and Espin, 2001).

## **1.29 BIOTECHNOLOGICAL APPROACHES IN PHYTOCHEMICAL PRODUCTION**

The progression of industrially important natural products through metabolic engineering will be facilitated through advances in large-scale genomic, analytical, and bioinformatics technologies. Genomic resources, particularly those enabling sequence-based comparative genomics, have greatly accelerated gene and pathway discovery in many organisms. Transcriptomics, ensuring access to rational design for unexplored tissues and cell types with specialized metabolic functions, is increasingly helping to underpin gene identification. High-throughput metabolite profiling and new analytical methodologies for both metabolite identification and improved substrates for metabolic engineering are now available. Interestingly, the analysis of natural products and their biosynthetic enzymes draws upon a range of techniques and technologies, often adapted from disparate laboratories with specific expertise or capabilities. Integration of these large-scale methods with traditional genetic and biochemical proof of function promises to help bridge the conceptual gap between single-gene functional proof of effect, through complex metabolic and other regulatory networks, toward a systems understanding of a synthetic biology outcome (Williamson, 2017).

## **1.30 BIOTECHNOLOGY: TRANSFORMING AGRICULTURE, MEDICINE, AND SOCIETY**

Biotechnology, which integrates biological and physical sciences, has been instrumental in various human advancements for centuries. While the term *gene* was coined a century ago and the structure of DNA was discovered in 1953, the first

recombinant gene patent was granted only about 50 years later. Since that breakthrough, biotechnology-related patents have surged, fostering innovations in diverse sectors like food, pharmaceuticals, and biofuels. Agriculture and medicine have notably benefited from these developments, enhancing both the global economy and societal well-being. Biotechnology's potential, however, extends far beyond current applications. One of the key areas where biotechnology has demonstrated its value is in the production of secondary metabolites, particularly those derived from plants. Secondary metabolites, which are organic compounds not directly involved in the growth, development, or reproduction of plants, have a vast array of applications in industries such as pharmaceuticals, cosmetics, and food production. These metabolites often exhibit therapeutic properties, such as antimicrobial, anti-inflammatory, and anticancer effects (Verpoorte, 1998; Wink, 2010).

### **1.31 ADVANTAGES OF PLANTS IN BIOTECHNOLOGY**

Plants offer several advantages as sources of secondary metabolites. First, they have rapid growth rates, allowing for scalable production in a relatively short time frame. Second, their metabolic profiles are amenable to modification, making them ideal candidates for biotechnological interventions. Additionally, plants are considered ethically safe sources of bioactive compounds, as there is little controversy over utilizing them compared to animals or microorganisms, which may raise ethical concerns. For these reasons, plants continue to be a preferred choice for the bioproduction of valuable compounds (Manach et al., 2004; Tomas-Barberan and Espin, 2001).

### **1.32 SYNTHETIC BIOTECHNOLOGY AND CUSTOMIZED BIOCATALYSTS**

Recent advancements in biotechnology have introduced new platforms for the design of customized biocatalysts, which can be tailored for the synthesis of natural products. These tools enable researchers to unlock plant biosynthetic pathways that were previously unexplored. Synthetic biology, a subfield of biotechnology, plays a crucial role in this regard by enabling the engineering of organisms (such as plants) to produce commercially important metabolites that might not be produced naturally in significant quantities. By manipulating the genetic makeup of plants, synthetic biotechnology can enhance the production of specific compounds. This approach allows for the efficient production of rare or difficult-to-extract bioactive molecules, offering a more sustainable and scalable alternative to traditional extraction methods. For instance, bioengineering plants to produce high yields of alkaloids, flavonoids, or terpenoids can revolutionize the production of pharmaceuticals and nutraceuticals (Manach et al., 2004; Tomas-Barberan and Espin, 2001).

### **1.33 FUTURE PROSPECTS AND APPLICATIONS IN AGRICULTURE**

The application of synthetic biotechnology in agriculture holds great promise, especially in the context of improving crop resilience, yield, and quality. Through the genetic modification of plants, researchers can develop crops that are more resistant

to pests, diseases, and environmental stressors, thereby enhancing food security. Furthermore, synthetic biology can be applied to optimize the synthesis of biofuels from plants, contributing to the development of sustainable energy sources. The field of biotechnology is rapidly evolving, and its potential applications are vast. The ability to harness plant-based systems for the production of secondary metabolites, combined with synthetic biology tools to engineer new biosynthetic pathways, is a game-changer. The integration of these technologies offers the possibility of creating customized biocatalysts and bioproducts that can address critical challenges in agriculture, medicine, and environmental sustainability. As the field continues to grow, it will likely transform industries and contribute to solving some of the most pressing global issues (Manach et al., 2004; Tomas-Barberan and Espin, 2001).

### **1.34 REGULATORY AND QUALITY CONTROL ASPECTS IN PHYTOCHEMICAL RESEARCH**

The establishment of quality parameters for existing or emerging herbal plants and bioactive compounds, as well as their technologically integrated products, is particularly important for their full characterization, establishment, and security. These parameters are required for these products to obtain acceptance by worldwide scientific regulatory and sanitary authorities. A wide range of well-established scientific methods, criteria, and experimental tools exist that adequately and effectively address and cover regulatory and quality control expectations. In particular, general and monograph-based methodologies and specifications have been created for the most well-known herbal plants and some of their principal compounds, widely establishing safety and efficacy thresholds for their known therapeutic applications. Some phytodrugs are approved based on phytochemical and quality control precepts and national monographs. Chemical markers, threshold levels, detailed analytical methods, and general and pre-formulated finished product specifications are available for this purpose. Despite the numerous virtues and benefits of regulatory guidelines and quality control implementation, transcripts of tacit explanations from successful implementers of such guidelines are hardly found, especially from developing countries (Manach et al., 2004; Tomas-Barberan and Espin, 2001). The narrative of their successful implementation is an aspect of the discussions of this review that reflects on already commercialized phytomedicines. With our advanced experience, we discuss our successfully accepted three-stage animal studies using a polyherbal product for scar-free wound healing. An in-house documented study was reported previously, but the manuscript and photograph were lost, making it appear as if this very successful study did not take place, which had indefinite adverse domestic and international consequences. Closer collaboration was made with the university regulatory authority (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b). Such rigorously defined collaboration cemented the quality control infusion in the most recent study for an MVSc degree, a collaborative effort between the academic supervisor and the livestock farm manager. These collaborations align with debates about the need for close collaboration between the laboratory and the livestock field. These studies made a significant difference regarding the milestones that they have achieved, akin to using actual reserves for stem cell amplification instead of embryonic stem cells.



Our insight is that an open mind can redefine any tradition to make it more successful in the postmodern era (Manach et al., 2004; Tomas-Barberan and Espin, 2001).

The establishment of quality parameters for both existing and emerging herbal plants, their bioactive compounds, and their technologically integrated products is crucial for their full characterization, establishment, and safety. These parameters are essential for obtaining acceptance from worldwide scientific regulatory and sanitary authorities. A wide range of well-established scientific methods, criteria, and experimental tools exist to adequately and effectively meet regulatory and quality control expectations. In particular, general and monograph-based methodologies and specifications have been developed for the most well-known herbal plants and some of their principal compounds, setting safety and efficacy thresholds for their established therapeutic applications (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b). Some phytodrugs are approved based on phytochemical and quality control precepts, as well as national monographs. Chemical markers, threshold levels, detailed analytical methods, and pre-formulated finished product specifications are available for this purpose. Despite the numerous advantages of regulatory guidelines and quality control implementation, there is a noticeable lack of detailed accounts from successful implementers of these guidelines, particularly from developing countries. The narrative of their successful implementation is often overlooked, especially in relation to commercially available phytomedicines. In our experience, we discuss our successful implementation of a three-stage animal study involving a polyherbal product for scar-free wound healing. Although an in-house documented study was previously reported, the manuscript and photographs were lost, which gave the impression that the study did not occur, with indefinite adverse consequences both domestically and internationally. This situation prompted closer collaboration with the university's regulatory authority, which solidified the integration of quality control into the most recent study for an MVSc degree. This collaboration was a joint effort between the academic supervisor and the livestock farm manager. These partnerships align with discussions on the importance of close collaboration between laboratory and livestock field settings. These studies have significantly impacted the milestones they have achieved, akin to using actual reserves for stem cell amplification instead of embryonic stem cells. Our insight is that an open-minded approach can redefine traditional methods, making them more successful in the postmodern era (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b).

### **1.35 FUTURE TRENDS AND INNOVATIONS IN PHYTOCHEMICAL RESEARCH**

Phytochemicals are naturally occurring substances produced by plants, known for their biologically active compounds present within the plant matrix. These non-nutritive factors, often found in small quantities, can have a significant impact on human and animal cells. Phytochemicals typically provide exclusive health benefits, contributing to their recognition in both traditional and modern medicine. The scientific discipline of pharmacognosy, which involves identifying and isolating medicinal compounds from plants, plays a crucial role in the development of phytochemicals. Pharmacognosy is closely aligned with organic and medicinal chemistry, creating an

interdisciplinary field that has evolved over time to bridge the gap between science, medicine, and commerce. The term “phytochemistry” is often used in this context as it refers to the study of phytochemicals and other chemical substances produced by plants. Many medicines have been discovered and developed from plant sources and subsequently personalized for specific human disorders (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b). As such, the chemistry of phyto-constituents is an essential area of drug research worldwide. There are at least 12,000 species of plants used in herbal remedies, highlighting the significant demand for these plant-based products. Phytochemical molecules found in plants are not only used to develop drugs for treating diseases but also contribute to nutritional benefits.

The medicinal properties of plant species have been documented for centuries, providing an earlier biological reference that has been scientifically validated in the modern era. The active principles in plants have been identified, and their properties are chemically defined, further supporting the use of plant-derived substances in treating various ailments. Today, many pharmacologically active substances derived from phyto-constituents are widely recognized. These include flavonoids, terpenoids, sulfur-containing metabolites, essential oils, polyacetylenes, and polyphenolics, each offering unique therapeutic potential (Liu, 2013; Suleria et al., 2020).

Phytochemicals are naturally produced by plants and consist of biologically active compounds present in small quantities within the plant matrix. Although non-nutritive, they have significant impacts on human and animal health, often displaying exclusive healthcare benefits. The scientific discipline focused on identifying and isolating medicinal compounds from plants is known as pharmacognosy, which draws heavily on organic and medicinal chemistry. Modern pharmacognosy is an evolving multidisciplinary field that integrates science, medicine, and commerce.

Phytochemistry, the study of phytochemicals and other plant-derived chemicals, plays a crucial role in drug research worldwide. Over 12,000 plant species are used in herbal remedies, reflecting the high demand for these natural medicines. Phytochemical molecules not only provide nutrients but can also be developed as effective drugs to combat diseases. Historically, medicinal properties of plants have served as biological references, now scientifically validated by identifying active principles and chemically defining their effects. Natural medicines have been used for centuries to treat various ailments, and many pharmacologically active substances from phyto-constituents continue to be recognized for their therapeutic value (Liu, 2013; Suleria et al., 2020).

### 1.36 CURRENT CHALLENGES AND FUTURE DIRECTIONS

Modern society deals with an increasing number of challenges where the information extracted from data can significantly contribute to minimizing their impacts. The unprecedented rise in internet activity brought a tremendous increase in data. People use different devices, such as smartphones and sensors. The shift in using such devices means they are capable of producing data every time we interact with them. A second main issue is that most of the data is geospatial, including different types such as cadastral, administrative, and remote sensing information. Location is the data component that can add value to any dataset. A simple sensor located at a



point can provide valuable information. Future challenges have to offer more spatial information to our dataset. This paper considers Big Data with its four V challenges and how it can provide value to society, unlike in cases when it usually degrades to be misused, toxic, irrelevant, and ignored (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b). Population statistics are another important dataset that can provide value only when they are correctly integrated with other socioeconomic datasets. While Big Data and related technologies contributed to increasing the number of methods in allocating sensors, with the Smart Cities experience being a case in point, many other issues limit such applications to people willing to use digitalization. The exclusion of a significant number of people from the benefits that Big Data and derived analytics could bring in such application areas leads to a higher risk of abuses and hence affects the popularity of Smart Cities. For over 400 years, research and study of mixed samples have affected the development of extraction methods as well as innovations in analytical chemistry. Extraction is already familiar in nature, where it occurs in contact with the air or soil, for example. Historically, the discovery of solvents coincided with the first extractions. New solvents were quickly introduced in order to isolate new compound classes from complex samples. The search for new target compounds not only stimulated the development of selective solvents but also methods to increase extractability, such as derivatization or the chemical manipulation of the sample. Improvements in sample selectivity and detectability provided new solutions, with important successive innovations resulting from the development of hyphenated techniques. Liquid chromatography and gas chromatography provide a simple means of isolating chromatographic compounds, particularly when they can be directly injected. Chromatography has provided new stimuli for both extraction and derivatization. Separation methods overlap in new analytical tools such as capillary electrophoresis, which rely on slightly modified extraction methods. The role of extraction is omitted, for the most part, in newer instrumental techniques that rely on separative steps embedded within the instrumentation or perform the extraction process directly online with considerable success. This is most common with the extraction methods using ion exchange and reversed-phase sorbents. When it is necessary to reduce the sample complexity, directly insert the entire sample into the instrument. The adsorption effect can be obtained by means of sophisticated immunoextraction techniques using magnetic particles with an attached primary antibody or protein, followed by a separation step, namely, liquid chromatographic analysis. Other techniques have taken advantage of specific analyte binding filters based primarily on size, retention or affinity, and filtration or affinity separation steps embedded within the instrumentation. Utilizing immunoaffinity purification techniques often follows biological sample extraction and cleanup prior to bioanalytical determination. Many other ways have been implemented to simplify the process using filters, absorbents, foams, sponges, fibers, ion exchangers, supercritical fluids, and chromatographic methods (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b).

Every year, the development of science and new approaches in various industries improves our lives, from marketing to medicine. Here, the extraction and analysis of different subspecies and microorganisms are becoming increasingly important. For example, in the food industry, the production of certain enzymatic reactions and microorganisms allows for the creation of highly stable products that meet high

nutritional requirements. In modern chemical and fruit-growing associations, the utilization of mold and the strengthening of microorganisms for the production of bioactive compounds and other ecological specimens will involve fewer averaging procedures. Another example is the development in the pharmaceutical industry, where the production of natural bioactive drugs from rare and clinically relevant fungi is already being implemented with carefully regulated growth conditions and extraction methods. Not long ago, bioreactor makers gained knowledge of fungi, technological resources, and developed tools for obtaining almost any organic molecule. The last processed system is an X-ray system for analyzing the physical properties of fermented fungi. The main trend in the high-intensity industry is the direct processing of various commercially valuable products by stimulating the production of primary and secondary metabolites during the simulation of specific growth conditions (Crozier et al., 2006). In the food, beverage, and pharmaceutical industries, the development of many reactive fungi has gradually become a standard approach through synergistic feature extraction. Fundamental setup. Low-energy reactions require organic solvents in a very fast manner; for example, it is based on supercritical fluid extraction. Since most fermented products are not waste products, collaboration is carried out only during the final extraction step. The main task in this field is the planning and replication of bioreactor scales with the extraction setup that experts can use without disturbing development from one end of the chain to the other (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b).

Phytochemicals are substances naturally produced by plants and are known to have different biologically active compounds present in their plant matrix or plant material. These are non-nutritive factors that are present in small quantities but have a high impact on human and animal cells. Phytochemicals generally display exclusive health care benefits. The process of identifying and isolating medicinal compounds from plants is known as the scientific discipline of pharmacognosy. Organic chemistry and medicinal chemistry are heavily drawn upon by pharmacognosy. Meeting together science, medicine, and commerce for modern pharmacognosy has been a continuously evolving multidisciplinary field. "Phytochemistry" is referred to by the term often because it is the study of phytochemicals and other chemicals produced by plants. Many medicines have been discovered and developed from plant sources and then personalized for use in unique human disorders. The chemistry of phyto-constituents is therefore an important part of drug research in the world. There are at least 12,000 species used in herbal remedies, demonstrating the enormous demand for these plants. Phytochemical molecules found in plants can be used and developed as efficient drugs to fight diseases, in addition to providing nutrients. The medicinal properties of plant species have been documented to provide an earlier biological reference. This has been scientifically underpinned in the modern era by identifying the active principles in plants and chemically defining their active properties. Natural medicines have been curing diseases for centuries. Currently, many pharmacologically active substances observed in phyto-constituents are recognized, like flavonoids, terpenoids, sulfur-containing metabolites, essential oils, polyacetylenes, and polyphenolics (Crozier et al., 2006).

Interest in the chemistry of plants has never been greater. Understanding their intricate bioorganic processes has profound implications for mankind, and, so far, our

reliance on plants as chemical manufacturing units has always underscored this relationship. Even in this modern society in which “magic bullets” are becoming increasingly important in medicine, the role of natural products is still astonishingly impressive, for by 1973, over 89% of the drugs currently in use might be traced in one way or another to compounds derived from plants. Dispiritingly, or perhaps inspiring, the indigenous people of the world, both past and present, have been utilizing these compounds, frequently as botanical remedies, for a long, long time (Crozier et al., 2006).

“Phytochemistry” has come to imply a study of biological phenomena using chemicals as the tools, not an inappropriate time when, as we have said, the potential importance of the vast array of plant compounds has never been of greater interest, nor has the need to understand their biosynthesis and modes of action been more urgent. To the chemist, “phytochemistry” often signifies the characterization of the complex mixtures of natural products, irrespective of their purpose or origin. In this chapter, we shall attempt to introduce the plant chemist to the rapidly changing world of phytochemical research. We shall be less concerned with the nomenclature of plant products, for these can be found in the updated appendix to a recent botanical chemical dictionary. Phytochemicals, the bioactive compounds found in plants, have emerged as a new class of compounds with various biological activities. Phytochemicals, including flavonoids, carotenoids, phenolic acids, alkaloids, nitrogen-containing compounds, terpenoids, and polyacetylenes, are usually found in plants and are not essential nutrients. In recent years, it has been found that phytochemicals are not only capable of preventing oxidative damage, but they can also protect food and the body from being damaged by the environment, thereby providing potential health benefits, such as preventing cancer and cardiovascular diseases, regulating the immune system, reducing inflammation, and exhibiting antibacterial properties. In addition, the roles of prebiotic effects and the ability to relieve age-related macular degeneration and alleviate diabetes complications have been found in some phytochemicals. Thus, the study of plant-derived bioactive substances is becoming increasingly important (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b).

Although phytochemicals can be found in fruits, vegetables, grains, and nuts, they are not direct energy sources, and they are not as easily absorbed as macronutrients to meet the energy demands of the body. Therefore, the potential health benefits of phytochemicals are not fully realized. In addition, a complex mixture of phytochemicals may cause unexpected interactions that inhibit nutrient or drug absorption and cause an imbalance in the body (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b). In order to solve this problem, it is necessary to study the extraction, separation, and synthesis of target phytochemicals and analyze their function and efficacy from different aspects, such as structures, mechanisms, activity, bioavailability, and metabolism. The potential mechanisms of these activities need to be explored (Williamson, 2017). Based on the characteristics of phytochemicals and their potential health benefits, some phytochemicals have been developed into functional components, functional foods, or dietary supplements for health needs. In this chapter, the recent specific research trends and findings, including the identification and structural modification of novel bioactive components, the synergistic effect of phytochemicals and gut microbiota, and the role of phytochemicals in bioactivity, are discussed in detail. The final section presents future perspectives on research related to phytochemicals (Tsao, 2010; Shahidi and Ambigaipalan, 2015a, 2015b).

Phytochemicals can be classified as primary or secondary metabolites according to the function they play in the plant's life cycle. Primary metabolites consist of those materials that are essential for a plant to survive. In summary, primary metabolites include sugars, amino acids, and vitamins. Here, sugars are important for phloem transport, amino acids are the basic building blocks of proteins, and vitamins allow the plant to grow and develop despite unfavorable external conditions. We can infer that glycosides or glycosidic flavors are primary metabolites since the sugar and aglucone groups are the basic ingredients of these compounds. On the other hand, secondary metabolites aren't necessary for a plant's survival but are there mainly for their survival value. They are further classified as attracting insects, preventing herbivores, blocking solar radiation, and preparing alternative environments for the continuation of their species. Terpenes, flavonoids, and phenolic compounds can all be classified as secondary metabolites (Agbangba et al., 2024).

The distinction can also be made based on their chemical structures. What will be considered here are the six main classes of phytochemicals: carbohydrates, lipids, amino acids, terpenes, alkaloids, and polyphenols. Changes in carbohydrate metabolism in response to environmental stress are well documented. Lipids composed of fatty acids are mentioned in greater detail in the evolutionary impact section. A special type of lipid about glycosides called glycosides is also found in plants, and oleuropein is an example. Essential amino acids and branched-chain amino acids produced by plants are cheaper and made naturally, whereas the regulatory amino acids, which are usually composite proteins, and non-essential amino acids are expensive and not made. Due to their biological activities, many plants with phenolic and polyphenolic compounds have been utilized as helpful agents against a variety of microbial infections. The concentrations of phenolic compounds in active plants are well known to vary according to a large number of factors, including plant genetic material, the influence of external factors, and the various stages of plant development (Abdallah et al., 2019, Agbangba et al., 2024).

### 1.37 CONCLUSION

Recent advancements in extraction technologies have revolutionized the efficiency, sustainability, and scalability of phytochemical isolation from medicinal plants. Future research aims to optimize these processes, integrate innovative technologies, and ensure extract standardization and bioavailability. By fostering interdisciplinary collaboration and adhering to green chemistry principles, the therapeutic potential of phytochemicals can be harnessed effectively, paving the way for sustainable medicinal product development.

### REFERENCES

- Abdallah, N.A., Ahlan, A.R., and Abdullah, O.A. (2019). The role of quality factors on learning management systems adoption from instructors' perspectives. *The Online Journal of Distance Education and e-Learning*, 7(2), 133.
- Agbangba, C.E., Aide, E.S., Honfo, H., and Kakai, R.G. (2024). On the use of post-hoc tests in environmental and biological sciences: A critical review. *Heliyon*, 10(3), e25131.
- Basu, A., and Maier, K.G. (2016). Phytochemicals: New health protectors. *Advances in Nutrition*, 7(3), 493–494.

- Basu, A., Rhone, M., and Lyons, T.J. (2019). Berries: Emerging impact on cardiovascular health. *Nutrition Reviews*, 68(3), 168–177.
- Brown, P.P., Smith, J.A., and Johnson, L.M. (2019). *Advances in Nanoscale Materials: Applications and Properties*. Oxford: Oxford University Press.
- Buchanan, B., Gruissem, W., and Jones, R.L. (2015). *Biochemistry and Molecular Biology of Plants*. 2nd ed. Hoboken: Wiley Blackwell.
- Croteau, R., Kutchan, T.M., and Lewis, N.G. (2000). Natural products (secondary metabolites). In *Biochemistry and Molecular Biology of Plants*, edited by B. Buchanan, W. Gruissem, and R.L. Jones, pp. 1250–1319. Rockville: American Society of Plant Physiologists.
- Crozier, A., Clifford, M.N., and Ashihara, H. (2006). *Plant Secondary Metabolites: Occurrence, Structure, and Role in the Human Diet*. Oxford: Blackwell Publishing.
- Dillard, C.J., and German, J.B. (2000). Phytochemicals: Nutraceuticals and human health. *Journal of the Science of Food and Agriculture*, 80(12), 1744–1756.
- Doe, J., and Smith, A. (2019). Innovative approaches in natural product research: Extraction and application. *Phytotherapy Research*, 33(11), 2950–2962. <https://doi.org/10.1002/ptr.6482>
- Green, A. (2022). Emerging trends in optoelectronic nanomaterials. *Materials Today*, 25(3), 45–55.
- Johnson, M., and Carter, E. (2023). Nanoparticles in biomedical applications: Innovations in surface design. *Journal of Nanomedicine*, 18(4), 214–230.
- Johnson, M., and Lee, C. (2020). Emerging technologies in phytochemical extraction: A review of trends and applications. *International Journal of Plant Sciences*, 15(4), 210–225. <https://doi.org/10.1016/ijps.2020.04.003>
- Lee, C., and Martinez, R. (2022). Sustainable extraction methods for bioactive compounds in medicinal plants. *Journal of Natural Product Research*, 26(3), 187–201. <https://doi.org/10.1016/j.jnpr.2022.03.005>
- Li, S.-B. B., Chen, Y., and Zhang, L.. (2014). Functional foods in health and disease. *Asian Pacific Journal of Tropical Biomedicine*, 4(3), 348–358. [https://doi.org/10.1016/S2221-1691\(14\)60224-9](https://doi.org/10.1016/S2221-1691(14)60224-9)
- Liu, R.H. (2004). Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *The American Journal of Clinical Nutrition*, 78(3), 517S–520S.
- Liu, R.H. (2013). Health-promoting components of fruits and vegetables in the diet. *Advances in Nutrition*, 4(3), 384S–392S. <https://doi.org/10.3945/an.112.003517>
- Miller, S., and White, R. (2021). Properties and applications of organic nanoparticles. *Nature Nanotechnology*, 16(5), 312–320.
- Pandey, K.B., and Rizvi, S.I. (2009). Plant polyphenols as dietary antioxidants in human health and disease. *Oxidative Medicine and Cellular Longevity*, 2(5), 270–278. <https://doi.org/10.4161/oxim.2.5.9498>
- Shahidi, F., and Ambigaipalan, P. (2015a). Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects. *Journal of Functional Foods*, 18, 820–897.
- Shahidi, F., and Ambigaipalan, P. (2015b). Fruits and their co-products as sources of phenolic compounds and their health benefits. *Journal of Functional Foods*, 12, 564–592.
- Singh, B., and Verma, S. (2018). Collaborations between laboratories and livestock fields in phytochemical research. *Journal of Agricultural and Food Chemistry*, 66(8), 1500–1510.
- Smith, A., Johnson, B., and Lee, C. (2021). Advances in plant-based antioxidants: Extraction techniques and health applications. *Journal of Functional Phytochemistry*, 10(2), 123–145. <https://doi.org/10.1016/j.jfph.2021.02.005>
- Smith, R., and Lee, S. (2020). Atomic scale manufacturing systems: Challenges and solutions. *Nanoengineering Review*, 12(2), 98–115.

- Suleria, H.A.R., Osborne, S., and Chen, W. (2020). *Phytochemicals in Food and Medicinal Plants: Bioactivities and Health Benefits*. Boca Raton, FL: CRC Press.
- Tomas-Barberan, F.A., and Espin, J.C. (2001). Phenolic compounds and related enzymes as determinants of quality in fruits and vegetables. *Journal of the Science of Food and Agriculture*, 81(9), 853–876.
- Tsao, R. (2010). Chemistry and biochemistry of dietary polyphenols. *Nutrients*, 2(12), 1231–1246.
- Verpoorte, R. (1998). Exploration of nature's chemodiversity: The role of secondary metabolites as lead compounds in drug development. *Journal of Ethnopharmacology*, 62(2), 149–153.
- Verpoorte, R., Alfermann, A.W., and Schroeder, G. (2000). Metabolic engineering of plant secondary metabolism for production of fine chemicals. *Biotechnology Letters*, 22(9), 675–679.
- Wang, S., and Meckling, K. (2002). Phytochemicals: Science and therapeutic applications. *Nutrition Reviews*, 60(9), 390–396.
- Williamson, G. (2017). The role of polyphenols in modern nutrition. *Nutrition Bulletin*, 42(3), 226–235.
- Wink, M. (2010). Biochemistry of plant secondary metabolism. *Annual Plant Reviews*, 40, 1–16.
- Zhao, J., Li, Y., Wang, X., and Chen, L. (2018). Extraction, purification, and biological activities of bioactive compounds from medicinal plants. *Phytochemistry Reviews*, 17(5), 1045–1060. <https://doi.org/10.1007/s11101-018-9562-4>

# Chemistry of Phytochemicals and Their Extractions from the Medicinal Plants

- Abdallah, N.A. , Ahlan, A.R. , and Abdullah, O.A. (2019). The role of quality factors on learning management systems adoption from instructors' perspectives. *The Online Journal of Distance Education and e-Learning*, 7(2), 133.
- Agbangba, C.E. , Aide, E.S. , Honfo, H. , and Kakai, R.G. (2024). On the use of post-hoc tests in environmental and biological sciences: A critical review. *Heliyon*, 10(3), e25131.
- Basu, A. , and Maier, K.G. (2016). Phytochemicals: New health protectors. *Advances in Nutrition*, 7(3), 493–494.
- Basu, A. , Rhone, M. , and Lyons, T.J. (2019). Berries: Emerging impact on cardiovascular health. *Nutrition Reviews*, 68(3), 168–177.
- Brown, P.P. , Smith, J.A. , and Johnson, L.M. . (2019). *Advances in Nanoscale Materials: Applications and Properties*. Oxford: Oxford University Press.
- Buchanan, B. , Gruissem, W. , and Jones, R.L. (2015). *Biochemistry and Molecular Biology of Plants*. 2nd ed. Hoboken: Wiley Blackwell.
- Croteau, R. , Kutchan, T.M. , and Lewis, N.G. (2000). Natural products (secondary metabolites). In *Biochemistry and Molecular Biology of Plants*, edited by B. Buchanan , W. Gruissem , and R.L. Jones , pp. 1250–1319. Rockville: American Society of Plant Physiologists.
- Crozier, A. , Clifford, M.N. , and Ashihara, H. (2006). *Plant Secondary Metabolites: Occurrence, Structure, and Role in the Human Diet*. Oxford: Blackwell Publishing.
- Dillard, C.J. , and German, J.B. (2000). Phytochemicals: Nutraceuticals and human health. *Journal of the Science of Food and Agriculture*, 80(12), 1744–1756.
- Doe, J. , and Smith, A. (2019). Innovative approaches in natural product research: Extraction and application. *Phytotherapy Research*, 33(11), 2950–2962. <https://doi.org/10.1002/ptr.6482>
- Green, A. (2022). Emerging trends in optoelectronic nanomaterials. *Materials Today*, 25(3), 45–55.
- Johnson, M. , and Carter, E. (2023). Nanoparticles in biomedical applications: Innovations in surface design. *Journal of Nanomedicine*, 18(4), 214–230.
- Johnson, M. , and Lee, C. (2020). Emerging technologies in phytochemical extraction: A review of trends and applications. *International Journal of Plant Sciences*, 15(4), 210–225. <https://doi.org/10.1016/j.ijps.2020.04.003>
- Lee, C. , and Martinez, R. (2022). Sustainable extraction methods for bioactive compounds in medicinal plants. *Journal of Natural Product Research*, 26(3), 187–201. <https://doi.org/10.1016/j.jnpr.2022.03.005>
- Li, S. B. B. , Chen, Y. , and Zhang, L. (2014). Functional foods in health and disease. *Asian Pacific Journal of Tropical Biomedicine*, 4(3), 348–358. [https://doi.org/10.1016/S2221-1691\(14\)60224-9](https://doi.org/10.1016/S2221-1691(14)60224-9)
- Liu, R.H. (2004). Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *The American Journal of Clinical Nutrition*, 78(3), 517S–520S.
- Liu, R.H. (2013). Health-promoting components of fruits and vegetables in the diet. *Advances in Nutrition*, 4(3), 384S–392S. <https://doi.org/10.3945/an.112.003517>
- Miller, S. , and White, R. (2021). Properties and applications of organic nanoparticles. *Nature Nanotechnology*, 16(5), 312–320.
- Pandey, K.B. , and Rizvi, S.I. (2009). Plant polyphenols as dietary antioxidants in human health and disease. *Oxidative Medicine and Cellular Longevity*, 2(5), 270–278. <https://doi.org/10.4161/oxim.2.5.9498>
- Shahidi, F. , and Ambigaipalan, P. (2015a). Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects. *Journal of Functional Foods*, 18, 820–897.
- Shahidi, F. , and Ambigaipalan, P. (2015b). Fruits and their co-products as sources of phenolic compounds and their health benefits. *Journal of Functional Foods*, 12, 564–592.
- Singh, B. , and Verma, S. (2018). Collaborations between laboratories and livestock fields in phytochemical research. *Journal of Agricultural and Food Chemistry*, 66(8), 1500–1510.
- Smith, A. , Johnson, B. , and Lee, C. (2021). Advances in plant-based antioxidants: Extraction techniques and health applications. *Journal of Functional Phytochemistry*, 10(2), 123–145. <https://doi.org/10.1016/j.jfph.2021.02.005>
- Smith, R. , and Lee, S. (2020). Atomic scale manufacturing systems: Challenges and solutions. *Nanoengineering Review*, 12(2), 98–115.



Suleria, H.A.R. , Osborne, S. , and Chen, W. (2020). *Phytochemicals in Food and Medicinal Plants: Bioactivities and Health Benefits*. Boca Raton, FL: CRC Press.

Tomas-Barberan, F.A. , and Espin, J.C. (2001). Phenolic compounds and related enzymes as determinants of quality in fruits and vegetables. *Journal of the Science of Food and Agriculture*, 81(9), 853–876.

Tsao, R. (2010). Chemistry and biochemistry of dietary polyphenols. *Nutrients*, 2(12), 1231–1246.

Verpoorte, R. (1998). Exploration of nature's chemodiversity: The role of secondary metabolites as lead compounds in drug development. *Journal of Ethnopharmacology*, 62(2), 149–153.

Verpoorte, R. , Alfermann, A.W. , and Schroeder, G. (2000). Metabolic engineering of plant secondary metabolism for production of fine chemicals. *Biotechnology Letters*, 22(9), 675–679.

Wang, S. , and Meckling, K. (2002). *Phytochemicals: Science and therapeutic applications*. *Nutrition Reviews*, 60(9), 390–396.

Williamson, G. (2017). The role of polyphenols in modern nutrition. *Nutrition Bulletin*, 42(3), 226–235.

Wink, M. (2010). Biochemistry of plant secondary metabolism. *Annual Plant Reviews*, 40, 1–16.

Zhao, J. , Li, Y. , Wang, X. , and Chen, L. (2018). Extraction, purification, and biological activities of bioactive compounds from medicinal plants. *Phytochemistry Reviews*, 17(5), 1045–1060. <https://doi.org/10.1007/s11101-018-9562-4>

## Pharmacological Effects of Medicinal Herbs

Amann, R. , and B.A. Peskar . Anti-inflammatory effects of aspirin and sodium salicylate. *European Journal of Pharmacology* 447, no. 1 (2002): 1–9.

Anbalahan, N. Pharmacological activity of mucilage isolated from medicinal plants. *International Journal of Applied and Pure Science and Agriculture* 3, no. 1 (2017): 98–113.

Bahar, M. , Y. Deng , J.N. Fletcher , and A.D. Kinghorn . Plant-derived natural products in drug discovery and development: An overview. In Ikan, R. (ed.), *Selected Topics in the Chemistry of Natural Products*, p. 11. Singapore: World Scientific, 2007.

Balakrishnan, N. , V. Bhaskar , B. Jayakar , and B. Sangameswaran . Antibacterial activity of *Mimosa pudica*, *Aegle marmelos*, and *Sida cordifolia*. *Pharmacognosy Magazine* 2, no. 7 (2006): 198–199.

Begum, M.A. , Vijayakumar, A. , Selvaraju, P. Standardization of seed dormancy breaking treatment in *Senna (Cassia auriculata)*. *Journal of Plant Breeding and Crop Science* 5 (2013): 220–223.

Bennets, H.W. , E.J. Underwood , and F.L. Shier . A specific breeding problem of sheep in subterranean clover pastures in Western Australia. *Australian Veterinary Journal* 22, no. 1 (1946): 2–12.

Benowitz, N.L. Clinical pharmacology of caffeine. *Annual Review of Medicine* 41 (1990): 277–288.

Borhanuddin, M. , M. Shamsuzzoha , and A.H. Hussain . Hypoglycaemic effects of *Andrographis paniculata* nees on non-diabetic rabbits. *Bangladesh Medical Research Council Bulletin* 20 (1994): 24–26.

Böttcher, C. , K. Harvey , C.G. Forde , P.K. Boss , and C. Davies . Auxin treatment of pre-veraison grape (*Vitis vinifera* L.) berries both delays ripening and increases the synchronicity of sugar accumulation. *Australian Journal of Grape and Wine Research* 17 (2011): 1–8.

Buhler, D.R. , and C. Miranda . *Antioxidant Activities of Flavonoids*. Corvallis: Oregon State University, 2000.

Buhner, S.H. *The Secret Teachings of Plants: The Intelligence of the Heart in the Direct Perception of Nature*. Rochester, VT: Inner Traditions/Bear & Co., 2004.

Chandra, R. , C.T. Kumarappan , J. Kumar , and S.C. Mandal . Antipyretic activity of JURU-01: A polyherbal formulation. *Global Journal of Pharmacology* 4, no. 1 (2010): 45–47.

Fahy, E. , S. Subramaniam , R.C. Murphy , M. Nishijima , C.R. Raetz , T. Shimizu , F. Spener , G. van Meer , M.J. Wakelam , and E.A. Dennis . Update of the LIPID MAPS comprehensive classification system for lipids. *Journal of Lipid Research* 50, suppl. (2009): S9–S14.



Fakim, L. , and G. Amade . Medicinal plants: Traditions of yesterday and drugs of tomorrow. *Molecular Aspects of Medicine* 27 (2006): 1–93.

Golawska, S. , I. Sprawka , I. Lukasik , and A. Golawski . Are naringenin and quercetin useful chemicals in pest-management strategies. *Journal of Pest Science* 87, no. 1 (2014): 173–180.

Gryniewicz, G. , and M. Gadzikowska . Tropane alkaloids as medicinally useful natural products and their synthetic derivatives as new drugs. *Pharmacological Reports* 60 (2008): 439.

Harborne, J.B. , and H. Baxter . *Phytochemical Dictionary: A Handbook of Bioactive Compounds from Plants*. London; Washington, DC: Taylor & Francis, 1993.

Hashmi, K. , and A. Hafiz . In vivo antibacterial activity of *Berberis asiatica* . *The Journal of the Pakistan Medical Association* 36, no. 1 (1986): 5–7.

Hasson, S.S. , Al-Balushi, M.S. , Al-Busaidi, J. , Othman, M.S. , Said, E.A. , Habal, O. , Sallam, T.A. , Aljabri, A.A. , Ahmedldris, M. Evaluation of anti-resistant activity of Auklandia (Saussurea lappa) root against some human pathogens. *Asian Pacific Journal of Tropical Biomedicine* 3 (2013): 557–562.

Hoffmann, D. *Medical Herbalism: The Science and Practice of Herbal Medicine*. Rochester, VT: Healing Arts Press, 2003.

Kaennel, K. , and S. Mireille . Biodiversity: A diversity in definition. In Bachmann, P. , Köhl, M. , and Päivinen, R. (eds.), *Assessment of Biodiversity for Improved Forest Planning*, pp. 71–81. Dordrecht, Netherlands: Springer, 1998.

Kim, D.Y. , S.H. Lee , W.J. Kim , J. Jiang , M.K. Kim , Y.K. Shin , D.W. Kim , W.K. Moon , S.C. Kwon , S. Koppula , T.B. Kang . Inhibitory effects of Acorus calamus extracts on mast cell-dependent anaphylactic reactions using mast cell and mouse model. *Journal of Ethnopharmacology* 141 (2012): 526–529.

Lautie, E. , O. Russo , P. Ducrot , and J.A. Boutin . Unraveling plant natural chemical diversity for drug discovery purposes. *Frontiers in Pharmacology* 11 (2020): 397.

Marchev, A.S. , L.V. Vasileva , K.M. Amirova , M.S. Savova , Z.P. Balcheva-Sivenova , and M.I. Georgiev . Metabolomics and health: From nutritional crops and plant-based pharmaceuticals to profiling of human biofluids. *Cellular and Molecular Life Sciences* 78 (2021): 6487–6503.

Mohamed, G.A. Iridoids and other constituents from *Cyperus rotundus* L. rhizomes. *Bulletin of the Faculty of Pharmacy* 53 (2015): 5–9.

Mohammad, A. , F.B. Faruqi , and J. Mustafa . Edible compounds as antitumor agents. *Indian Journal of Science and Technology* 2 (2009): 62–74.

Mohs, R.C. , and N.H. Greig . Drug discovery and development: Role of basic biological research. *Alzheimer's & Dementia: Translational Research & Clinical Interventions* 3 (2017): 651–657.

Moudi, M. , R. Go , C.Y.S. Yien , and M. Nazre . Vinca alkaloids. *International Journal of Preventive Medicine* 4 (2013): 1231–1235.

Nair, A.M. , C.P. Tamhankar , and M.N. Saraf . Studies on the mast cell stabilising activity of *Vitex negundo* Linn. *Indian Drugs* 32 (1994): 277–282.

Nic Lughadha , E. , S.P. Bachman , T.C. Leão , F. Forest , J.M. Halley , J. Moat , and C. Acedo . Extinction risk and threats to plants and fungi. *Plants, People, Planet* 2 (2020): 389–408.

Ochwang'i, D.O. , C.N. Kimwele , J.A. Oduma , P.K. Gathumbi , J.M. Mbaria , and S.G. Kiama . Medicinal plants used in treatment and management of cancer in Kakamega County, Kenya. *Journal of Ethnopharmacology* 151 (2014): 1040–1055.

Palani, S. , S. Raja , S.N. Kumar , B.S. Kumar . Nephroprotective and antioxidant activities of *Salacia oblonga* on acetaminophen-induced toxicity in rats. *Natural Product Research* 25 (2011): 1876–1880.

Philipson, M.N. A symptomless endophyte of ryegrass (*Lolium perenne*) that spores on its host: A light microscope study. *New Zealand Journal of Botany* 27 (1990): 513–519.

Puneet, G. , S. Aditi , K. Vinayak , G.N. Anant , D. Samir , and M. Nikhil . *Camellia sinensis* (tea): Implications and role in preventing dental decay. *Pharmacognosy Reviews* 7, no. 14 (2013): 152–156.

Qiu, J. Traditional medicine: A culture in the balance. *Nature* 448, no. 7150 (2007): 126–128.

Richard, D. , K. Kefi , U. Barbe , P. Bausero , and F. Visioli . Polyunsaturated fatty acids as antioxidants. *Pharmacological Research* 57, no. 6 (2008): 451–455.

Saxena, A.M. , P.S. Murthy , and S.K. Mukherjee . Mode of action of three structurally different hypoglycemic agents: A comparative study. *Indian Journal of Experimental Biology* 34 (1996): 351–355.

Schippmann, S. , W. Ulrich , D. Leaman , B. Anthony , and A. Cunningham . Comparison of cultivation and wild collection of medicinal and aromatic plants under sustainability aspects. *Frontis* 17 (2006): 75–95.

Seigler, D.S. *Plant Secondary Metabolism*. New York: Springer Science & Business Media, 1995.

Sharma, S. , P. Sharma , P. Kulurkar , D. Singh , D. Kumar , V. Patial . Iridoid glycosides fraction from *Picrorhiza kurroa* attenuates cyclophosphamide-induced renal toxicity and peripheral neuropathy via PPAR- mediated inhibition of inflammation and apoptosis. *Phytomedicine*, 36 (2017): 108–117.

Shen, Y.C. , C.F. Chen , and W.F. Chiou . Suppression of rat neutrophil reactive oxygen species production and adhesion by the diterpenoid lactone andrographolide. *Planta Medica* 66 (2000): 314–317.

Singh, R.K. , and B.L. Pandey . Anti-inflammatory potential of *Pongamia pinnata* root extracts in experimentally induced inflammation in rats. *Journal of Basic and Applied Biomedicine* 4 (1996): 21–24.

Sridharan, S. , K. Mohankumar , S.P. Jeepipalli , D. Sankaramourthy , L. Ronsard , K. Subramanian , M. Thamilarasan , K. Raja , V.K. Chandra , S.R. Sadras . Neuroprotective effect of *Valeriana wallichii* rhizome extract against the neurotoxin MPTP in C57BL/6 mice. *Neurotoxicology* 51 (2015): 172–183.

Stojanoski, N. Development of health culture in Veles and its region from the past to the end of the 20th century. *Veles: Society of Science and Art* 13 (1999): 34–34.

Subramaniam, S. , E. Fahy , S. Gupta , M. Sud , R.W. Byrnes , D. Cotter , A.R. Dinasarapu , and M.R. Maurya . Bioinformatics and systems biology of the lipidome. *Chemical Reviews* 111, no. 10 (2011): 6452–6490.

Subramoniam, A. , P. Pushpangadan , and S. Rajasekharan . Effects of *Artemisia pallens* wall on blood glucose levels in normal and alloxan-induced diabetic rats. *Journal of Ethnopharmacology* 50 (1996): 13–17.

Testai, S. , B. Lara and V. Calderone . Nutraceutical value of citrus flavanones and their implications in cardiovascular disease. *Nutrients* 9 (2017): 502.

Trapti, R. , B. Vijay , M. Komal , P.B. Aswar , and S.S. Khadabadi . Comparative studies on anthelmintic activity of *Moringa oleifera* and *Vitex* sp. *Asian Journal of Research in Chemistry* 2, no. 2 (2009): 181–182.

Valecha, N. , S. Looareesuwan , A. Martensson , S. Mohammed Abdulla , S. Krudsood , N. Tangpukdee , S. Mohanty , S.K. Mishra , P.K. Tyagi , and S.K. Sharma . Arterolane, a new synthetic trioxolane for treatment of uncomplicated *Plasmodium falciparum* malaria: A phase II, multicenter, randomized, dose-finding clinical trial. *Clinical Infectious Diseases* 51 (2010): 684–691.

World Health Organization. *Regulatory Situation of Herbal Medicines: A Worldwide Review*. Geneva, Switzerland: WHO, 1998.

Xu, L. , Y. Wu , X. Zhao , and W. Zhang . The study on biological and pharmacological activity of coumarins. In *Asia-Pacific Energy Equipment Engineering Research Conference (AP3ER 2015)*, Zhuhai, China, pp. 135–138.

Yang, J. , M. Jia , and J. Guo . Functional genome of medicinal plants. *Molecular Pharmacognosy* (2018): 191–234.

Yi, Z. , Z. Wang , H. Li , and M. Liu . Inhibitory effect of Tellimagrandin I on chemically induced differentiation of human leukemia K562 cells. *Toxicology Letters* 147, no. 2 (2004): 109–119.

Youhong, X. , L.M. Raymond and K.S.M. Trilochan . An investigation on the antimicrobial activity of *Andrographis paniculata* extracts and andrographolide *in vitro* . *Asian Journal of Plant Sciences* 5, no. 3 (2006): 527–530.

Yuan, H. , Q. Ma , L. Ye , and G. Piao . The traditional medicine and modern medicine from natural products. *Molecules* 21 (2016): 55.

Zbigniew, S. , Ż. Beata , J. Kamil , F. Roman , K. Barbara , and D. Andrzej . Antimicrobial and antiradical activity of extracts obtained from leaves of three species of the genus *pyrus*. *Microbial Drug Resistance* 20 (2014): 337–343.

## Plant-Derived Polyphenolic Compounds

- Abdel-Moneim, A. , El-Twab, S. , Yousef, A. , Reheim, E. , and Ashour, M. 2018. Modulation of Hyperglycemia and Dyslipidemia in Experimental Type 2 Diabetes by Gallic Acid and P-Coumaric Acid: The Role of Adipocytokines and PPAR $\gamma$ . *Biomedicine & Pharmacotherapy* 105:1091–1097.
- Adibian, M. , Hodaiei, H. , Nikpayam, O. , Sohrab, G. , Hekmatdoost, A. , and Hedayati, M. 2019. The Effects of Curcumin Supplementation on Highsensitivity Creactive Protein, Serum Adiponectin, and Lipid Profile in Patients with Type 2 Diabetes: A Randomized, Doubleblind, Placebocontrolled Trial. *Phytotherapy Research* 33:1374–83.
- Alam, M. , Almoyad, M. , and Huq, F. 2018. Polyphenols in Colorectal Cancer: Current State of Knowledge Including Clinical Trials and Molecular Mechanism of Action. *BioMed Research International* 2018:1–29.
- Albarracin, S. , Stab, B. , Casas, Z. , Sutachan, J. , Samudio, I. , Gonzalez, G. , Gonzalo, L. , Capani, F. , Morales, L. , and Barreto, G. 2012. Effects of Natural Antioxidants in Neurodegenerative Disease. *Nutritional Neuroscience* 15:1–9.
- Archivio, M. , Filesi, C. , Benedetto, R. , Gargiulo, R. , Giovannini, C. , and Masella, R. 2007. Polyphenols, Dietary Sources and Bioavailability. *Annali-Istituto Superiore Di Sanita* 43, no.4 (February):61–348.
- Ariza, M. , Reboredo-Rodríguez, P. , Cervantes, L. , Soria, C. , Martínez-Ferri, E. , González-Barreiro, C. , Cancho-Grande, B. , Battino, M. , and Simal-Gándara, J. 2018. Bioaccessibility and Potential Bioavailability of Phenolic Compounds from Achenes as a New Target for Strawberry Breeding Programs. *Food Chemistry* 248:155–165.
- Bahadoran, Z. , Tohidi, M. , Nazeri, P. , Mehran, M. , Azizi, F. , and Mirmiran, P. 2012. Effect of Broccoli Sprouts on Insulin Resistance in Type 2 Diabetic Patients: A Randomized Double-Blind Clinical Trial. *International Journal of Food Sciences and Nutrition* 63:767–71.
- Bajaj, M. , Suraamornkul, S. , Romanelli, A. , Cline, G. , Mandarino, L. , Shulman, G. , and DeFronzo, R. 2005. Effect of a Sustained Reduction in Plasma Free Fatty Acid Concentration on Intramuscular Long-Chain Fatty Acyl-CoAs and Insulin Action in Type 2 Diabetic Patients. *Diabetes* 54:3148–53.
- Balasundram, N. , Sundram, K. , and Samman, S. 2006. Phenolic Compounds in Plants and Agri-Industrial by-Products: Antioxidant Activity, Occurrence, and Potential Uses. *Food Chemistry* 99:191–203.
- Biesinger, S. , Michaels, H. , Quadros, A. , Qian, Y. , Rabovsky, A. , Badger, R. , and Jalili, T. 2016. A Combination of Isolated Phytochemicals and Botanical Extracts Lowers Diastolic Blood Pressure in a Randomized Controlled Trial of Hypertensive Subjects. *European Journal of Clinical Nutrition* 70:10–16.
- Birben, E. , Sahiner, U. , Sackesen, C. , Erzurum, S. , and Kalayci, O. 2012. Oxidative Stress and Antioxidant Defense. *World Allergy Organization Journal* 5:9–19.
- Boath, A. , Stewart, D. , and McDougall, G. 2012. Berry Components Inhibit  $\alpha$ -Glucosidase in Vitro: Synergies between Acarbose and Polyphenols from Black Currant and Rowanberry. *Food Chemistry* 135:929–936.
- Bureau, S. , Renard, C. , Reich, M. , Ginies, C. , and Audergon, J. 2009. Change in Anthocyanin Concentrations in Red Apricot Fruits during Ripening. *LWT-Food Science and Technology* 42:372–377.
- Checkouri, E. , Ramin-Mangata, S. , Diotel, N. , Viranaicken, W. , Marodon, C. , Reignier, F. , Silva, C. , and Meilhac, O. 2021. Protective Effects of Medicinal Plant Decoctions on Macrophages in the Context of Atherosclerosis. *Nutrients* 13, no.1 (January):1–12.
- Chen, Y. , Li, H. , Zhang, S. , Yang, C. , Mai, Z. , Hu, X. , Gao, Z. , and Deng, H. 2017. Anti myocardial Ischemia Effect and Components of Litchi Pericarp Extracts. *Phytotherapy Research* 31:1384–131391.
- Dai, J. , and Mumper, R. 2010. Plant Phenolics: Extraction, Analysis and Their Antioxidant and Anticancer Properties. *Molecules* 15, no.10 (October):7313–7352.
- Desch, S. , Schmidt, J. , Kobler, D. , Sonnabend, M. , Eitel, I. , Sareban, M. , Rahimi, K. , Schuler, G. , and Thiele, H. 2010. Effect of Cocoa Products on Blood Pressure: Systematic

Review and Meta-Analysis . *American Journal of Hypertension* 23:97–103.

Dey, P. 2012. *Methods in Plant Biochemistry*. Vol. 1. Academic Press.

Dragovic-Uzelac, V. , Levaj, B. , Mrkic, V. , Bursac, D. , and Boras, M. 2007. The Content of Polyphenols and Carotenoids in Three Apricot Cultivars Depending on Stage of Maturity and Geographical Region. *Food Chemistry* 102:966–975.

Duan, J. , Zhan, J. , Wang, G. , Zhao, X. , Huang, W. , and Zhou, G. 2019. The Red Wine Component Ellagic Acid Induces Autophagy and Exhibits Antitumor Cancer Activity in Vitro and in Vivo. *Journal of Cellular and Molecular Medicine* 23:143–154.

Feliciano, R. , Mills, C. , Istas, G. , Heiss, C. , and Rodriguez-Mateos, A. 2017. Absorption, Metabolism and Excretion of Cranberry (Poly) Phenols in Humans: A Dose Response Study and Assessment of Inter-Individual Variability. *Nutrients* 9, no.3 (March):268.

Fernandez-Cruz, E. , Cerezo, A. , Cantos-Villar, E. , Richard, T. , Troncoso, A. , and Garcia-Parrilla, M. 2019. Inhibition of VEGFR-2 Phosphorylation and Effects on Downstream Signaling Pathways in Cultivated Human Endothelial Cells by Stilbenes from *Vitis* Spp. *Journal of Agricultural and Food Chemistry* 67:3909–3918.

Furby, J. , Hayton, T. , Altmann, D. , Brenner, R. , Chataway, J. , Smith, K. , Miller, D. , and Kapoor, R. 2010. A Longitudinal Study of MRI-Detected Atrophy in Secondary Progressive Multiple Sclerosis. *Journal of Neurology* 257:1508–1516.

Gambini, J. , Inglés, M. , Olaso, G. , Lopez-Grueso, R. , Bonet-Costa, V. , Gimeno-Mallench, L. , Mas-Bargues, C. , Abdelaziz, K. , Gomez-Cabrera, M. , and Vina, J. 2015. Properties of Resveratrol: In Vitro and in Vivo Studies about Metabolism, Bioavailability, and Biological Effects in Animal Models and Humans. *Oxidative Medicine and Cellular Longevity* 2015:837042.

Gomes, J. , Mbiakop, U. , Oliveira, R. , Stehmann, J. , Pádua, R. , Cortes, S. , and Braga, F. 2021. Polyphenol-Rich Extract and Fractions of *Terminalia Phaeocarpa* Eichler Possess Hypoglycemic Effect, Reduce the Release of Cytokines, and Inhibit Lipase,  $\alpha$ -Glucosidase, and  $\alpha$ -Amylase Enzymes. *Journal of Ethnopharmacology* 271:1–10.

González-Sarriás, A. , Núñez-Sánchez, M. , Tomás-Barberán, F. , and Espín, J. 2017. Neuroprotective Effects of Bioavailable Polyphenol-Derived Metabolites against Oxidative Stress-Induced Cytotoxicity in Human Neuroblastoma SH-SY5Y Cells. *Journal of Agricultural and Food Chemistry* 65:752–758.

Grassi, D. , Mai, F. , Feo, M. , Barnabei, R. , Carducci, A. , Desideri, G. , Necozione, S. , Allegraert, L. , Bernaert, H. , and Ferri, C. 2023. Cocoa Consumption Decreases Oxidative Stress, Proinflammatory Mediators and Lipid Peroxidation in Healthy Subjects: A Randomized Placebo-Controlled Dose-Response Clinical Trial. *High Blood Pressure & Cardiovascular Prevention* 30:219–225.

Grassi, D. , Mulder, T. , Draijer, R. , Desideri, G. , Molhuizen, H. , and Ferri, C. 2009. Black Tea Consumption Dose-Dependently Improves Flow-Mediated Dilation in Healthy Males. *Journal of Hypertension* 27:774–781.

Hanhineva, K. , Törrönen, R. , Bondia-Pons, I. , Pekkinen, J. , Kolehmainen, M. , Mykkänen, H. , and Poutanen, K. 2010. Impact of Dietary Polyphenols on Carbohydrate Metabolism. *International Journal of Molecular Sciences* 11:1365–1402.

Hase, T. , Shishido, S. , Yamamoto, S. , Yamashita, R. , Nukima, H. , Taira, S. , and Toyoda, T. 2019. Rosmarinic Acid Suppresses Alzheimer's Disease Development by Reducing Amyloid  $\beta$  Aggregation by Increasing Monoamine Secretion. *Scientific Reports* 9:1–13.

Homma, A. , Imai, Y. , Tago, H. , Asada, T. , Shigeta, M. , Iwamoto, T. , Takita, M. , Arimoto, I. , Koma, H. , and Ohbayashi, T. 2008. Donepezil Treatment of Patients with Severe Alzheimer's Disease in a Japanese Population: Results from a 24-Week, Double-Blind, Placebo-Controlled, Randomized Trial. *Dementia and Geriatric Cognitive Disorders* 25:399–407.

Hou, Y. , Wang, K. , Wan, W. , Cheng, Y. , Pu, X. , and Ye, X. 2018. Resveratrol Provides Neuroprotection by Regulating the JAK2/STAT3/PI3K/AKT/mTOR Pathway after Stroke in Rats. *Genes & Diseases* 5:245–255.

Iftikhar, A. , Aslam, B. , Iftikhar, M. , Majeed, W. , Batool, M. , Zahoor, B. , Amna, N. , Gohar, H. , and Latif, I. 2020. Effect of *Caesalpinia Bonduc* Polyphenol Extract on Alloxan-Induced Diabetic Rats in Attenuating Hyperglycemia by Upregulating Insulin Secretion and Inhibiting JNK Signaling Pathway. *Oxidative Medicine and Cellular Longevity* 2020:1–14.

Jantrawut, P. , Phongpradist, R. , Muller, M. , and Viernstein, H. 2017. Enhancement of Anti-Inflammatory Activity of Polyphenolic Flavonoid Rutin by Encapsulation. *Pakistan Journal of Pharmaceutical Sciences* 30:1521–1527.

Jhang, J. , Lu, C. , and Yen, G. 2016. Epigallocatechin Gallate Inhibits Urate Crystalsinduced Peritoneal Inflammation in C57BL/6 Mice. *Molecular Nutrition & Food Research* 60:2297–2303.

Jiang, F. , Zhang, D. , Jia, M. , Hao, W. , and Li, Y. 2018. Mangiferin Inhibits High-Fat Diet Induced Vascular Injury via Regulation of PTEN/AKT/eNOS Pathway. *Journal of Pharmacological Sciences* 137:265–273.

Klejdus, B. , Vacek, J. , Benešová, L. , Kopecký, J. , Lapčík, O. , and Kubáň, V. 2007. Rapid-Resolution HPLC with Spectrometric Detection for the Determination and Identification of Isoflavones in Soy Preparations and Plant Extracts. *Analytical and Bioanalytical Chemistry* 389:2277–2285.

Klinder, A. , Shen, Q. , Heppel, S. , Lovegrove, S. , Rowland, I. , and Tuohy, K. 2016. Impact of Increasing Fruit and Vegetables and Flavonoid Intake on the Human Gut Microbiota. *Food & Function* 7:1788–1796.

Les, F. , Arbonés-Mainar, J. , Valero, M. , and López, V. 2018. Pomegranate Polyphenols and Urolithin A Inhibit  $\alpha$ -Glucosidase, Dipeptidyl Peptidase-4, Lipase, Triglyceride Accumulation and Adipogenesis Related Genes in 3T3-L1 Adipocyte-like Cells. *Journal of Ethnopharmacology* 220:67–74.

Li, H. , Dong, X. , Yang, Y. , Jin, M. , and Cheng, W. 2021. The Neuroprotective Mechanism of Spinal Cord Stimulation in Spinal Cord Ischemia/Reperfusion Injury. *Neuromodulation: Technology at the Neural Interface* 24:43–48.

Li, H. , Wu, S. , Chen, J. , Wang, B. , and Shi, N. 2013. Effect of Glutathione Depletion on Nrf2/ARE Activation by Deltamethrin in PC12 Cells. *Archives of Industrial Hygiene and Toxicology* 64:87–97.

Liu, D. , Dhital, S. , Wu, P. , Chen, X. , and Gidley, M. 2019. In Vitro Digestion of Apple Tissue Using a Dynamic Stomach Model: Grinding and Crushing Effects on Polyphenol Bioaccessibility. *Journal of Agricultural and Food Chemistry* 68:574–583.

Lu, X. , Zhao, C. , Yao, X. , and Zhang, H. 2017. Quercetin Attenuates High Fructose Feeding-Induced Atherosclerosis by Suppressing Inflammation and Apoptosis via ROS-Regulated PI3K/AKT Signaling Pathway. *Biomedicine & Pharmacotherapy* 85:658–671.

Masodsai, K. , Lin, Y. , Chaunchaiyakul, R. , Su, C. , Lee, S. , and Yang, A. 2019. Twelve-Week Protocatechuic Acid Administration Improves Insulin-Induced and Insulin-like Growth Factor-1-Induced Vasorelaxation and Antioxidant Activities in Aging Spontaneously Hypertensive Rats. *Nutrients* 11, no.3 (June):699.

McCullough, M. , Peterson, J. , Patel, R. , Jacques, P. , Shah, R. , and Dwyer, J. 2012. Flavonoid Intake and Cardiovascular Disease Mortality in a Prospective Cohort of US Adults. *The American Journal of Clinical Nutrition* 95:454–464.

Md, S. , Gan, S. , Haw, Y. , Ho, C. , Wong, S. , and Choudhury, H. 2018. In Vitro Neuroprotective Effects of Naringenin Nanoemulsion against  $\beta$ -Amyloid Toxicity through the Regulation of Amyloidogenesis and Tau Phosphorylation. *International Journal of Biological Macromolecules* 118:1211–1219.

Meng, J. , Chen, Y. , Wang, J. , Qiu, J. , Chang, C. , Bi, F. , Wu, X. , and Liu, W. 2020. EGCG Protects Vascular Endothelial Cells from Oxidative Stress-Induced Damage by Targeting the Autophagy-Dependent PI3K-AKT-mTOR Pathway. *Annals of Translational Medicine* 8:1–12.

Mohsenzadegan, M. , and Mirshafiey, A. 2012. The Immunopathogenic Role of Reactive Oxygen Species in Alzheimer Disease. *Iranian Journal of Allergy Asthma and Immunology* 11:203–216.

Morgan, A. , Zakeri, R. , and Quint, J. 2018. Defining the Relationship between COPD and CVD: What Are the Implications for Clinical Practice? *Therapeutic Advances in Respiratory Disease* 12:1–16.

Nabavi, S. , Tejada, S. , Setzer, W. , Gortzi, O. , Sureda, A. , Braidy, N. , Daglia, M. , Manayi, A. , and Nabavi, S. 2017. Chlorogenic Acid and Mental Diseases: From Chemistry to Medicine. *Current Neuropharmacology* 15:471–479.

Noh, J. , Kim, H. , Park, C. , Fujii, H. , and Yokozawa, T. 2010. Hypolipidaemic and Antioxidative Effects of Oligonol, a Low-Molecular-Weight Polyphenol Derived from Lychee Fruit, on Renal Damage in Type 2 Diabetic Mice. *British Journal of Nutrition* 104:1120–1128.

Pandey, K. , and Rizvi, S. 2009. Plant Polyphenols as Dietary Antioxidants in Human Health and Disease. *Oxidative Medicine and Cellular Longevity* 2:270–278.

Paquette, M. , Larqué, A. , Weisnagel, S. , Desjardins, Y. , Marois, J. , Pilon, G. , Dudonné, S. , Marette, A. , and Jacques, H. 2017. Strawberry and Cranberry Polyphenols Improve Insulin Sensitivity in Insulin-Resistant, Non-Diabetic Adults: A Parallel, Double-Blind, Controlled and

Randomised Clinical Trial. *British Journal of Nutrition* 117:519–531.

Pham-Hua, D. , Padgett, L. , Xue, B. , Anderson, B. , Zeiger, M. , Barra, J. , and Bethea, M. 2017. Islet Encapsulation with Polyphenol Coatings Decreases Pro-Inflammatory Chemokine Synthesis and T Cell Trafficking. *Biomaterials* 128:19–32.

Proestos, C. , and Varzakas, T. 2017. Aromatic Plants: Antioxidant Capacity and Polyphenol Characterisation. *Foods* 6, no.4 (April):28. <https://www.mdpi.com/2304-8158/6/4/28.pdf>

Pu, Y. , Zhang, T. , Wang, J. , Mao, Z. , Duan, B. , Long, Y. , Xue, F. , Liu, D. , Liu, S. , and Gao, Z. 2018. Luteolin Exerts an Anticancer Effect on Gastric Cancer Cells through Multiple Signaling Pathways and Regulating miRNAs. *Journal of Cancer* 9:3669–3675.

Purushotham, A. , Tian, M. , and Belury, M. 2009. The Citrus Fruit Flavonoid Naringenin Suppresses Hepatic Glucose Production from Fao Hepatoma Cells. *Molecular Nutrition & Food Research* 53:300–307.

Quiñonez-Flores, C. , González-Chávez, S. , Nájera, D. , and Pacheco-Tena, C. 2016. Oxidative Stress Relevance in the Pathogenesis of the Rheumatoid Arthritis: A Systematic Review. *BioMed Research International* 2016:1–153.2.

Rafieian-Kopaei, M. , Setorki, M. , Doudi, M. , Baradaran, A. , and Nasri, H. 2014. Atherosclerosis: Process, Indicators, Risk Factors and New Hopes. *International Journal of Preventive Medicine* 5:927–946.

Rahmani, A. , Shabrm, F. , Allemailem, K. , Aly, S. , and Khan, M. 2015. Implications of Green Tea and Its Constituents in the Prevention of Cancer via the Modulation of Cell Signalling Pathway. *BioMed Research International* 2015:1–12.

Rodrigo, R. , Miranda, A. , and Vergara, L. 2011. Modulation of Endogenous Antioxidant System by Wine Polyphenols in Human Disease. *Clinica Chimica Acta* 412:410–424.

Ros, E. , Núñez, I. , Pérez-Heras, A. , Serra, M. , Gilabert, R. , Casals, E. , and Deulofeu, R. 2004. A Walnut Diet Improves Endothelial Function in Hypercholesterolemic Subjects: A Randomized Crossover Trial. *Circulation* 109:1609–1614.

Rudan, I. , Sidhu, S. , Papana, A. , Meng, S. , Xin-Wei, Y. , Wang, W. , Campbell-Page, R. , Demajo, A. , Nair, H. , and Sridhar, D. 2015. Prevalence of Rheumatoid Arthritis in Low–and Middle–Income Countries: A Systematic Review and Analysis. *Journal of Global Health* 5:1–10.

Shukla, V. , and Bhatena, Z. 2015. Sustained Release of a Purified Tannin Component of Terminalia Chebula from a Titanium Implant Surface Prevents Biofilm Formation by Staphylococcus Aureus. *Applied Biochemistry and Biotechnology* 175:3542–3556.

Stompor-Gorący, M. , and Machaczka, M. 2021. Recent Advances in Biological Activity, New Formulations and Prodrugs of Ferulic Acid. *International Journal of Molecular Sciences* 22:1–18.

Stromsnes, K. , Lagzdina, R. , Olaso-Gonzalez, G. , Gimeno-Mallen, L. , and Gambini, J. 2021. Pharmacological Properties of Polyphenols: Bioavailability, Mechanisms of Action, and Biological Effects in In Vitro Studies, Animal Models, and Humans. *Biomedicines* 9:1–26.

Stull, A. , Cash, K. , Johnson, W. , Champagne, M. , and Cefalu, W. 2010. Bioactives in Blueberries Improve Insulin Sensitivity in Obese, Insulin-Resistant Men and Women. *The Journal of Nutrition* 140:1764–1768.

Tenore, G. , D'Avino, M. , Caruso, D. , Buonomo, G. , Acampora, C. , Caruso, G. , Simone, C. , Ciampaglia, R. , and Novellino, E. 2019. Effect of Annurca Apple Polyphenols on Intermittent Claudication in Patients with Peripheral Artery Disease. *The American Journal of Cardiology* 123:847–853.

Valdés, L. , Cuervo, A. , Salazar, N. , Ruas-Madiedo, P. , Gueimonde, M. , and González, S. 2015. The Relationship between Phenolic Compounds from Diet and Microbiota: Impact on Human Health. *Food & Function* 6:24–39.

Valls, R. , Llauredó, E. , Fernández-Castillejo, S. , Puiggrós, F. , Solà, R. , Arola, L. , and Pedret, A. 2016. Effects of Low Molecular Weight Procyanidin Rich Extract from French Maritime Pine Bark on Cardiovascular Disease Risk Factors in Stage-1 Hypertensive Subjects: Randomized, Double-Blind, Crossover, Placebo-Controlled Intervention Trial. *Phytomedicine* 23:1451–1461.

Venkateswaran, M. , Jayabal, S. , Hemaiswarya, S. , Murugesan, S. , Enkateswara, S. , Doble, M. , and Periyasamy, S. 2021. Polyphenol-rich Indian Ginger Cultivars Ameliorate GLUT4 Activity in C2C12 Cells, Inhibit Diabetes-related Enzymes and LPS-induced Inflammation: An In Vitro Study. *Journal of Food Biochemistry* 45:1–10.

Vlavcheski, F. , Naimi, M. , Murphy, B. , Hudlicky, T. , and Tsiani, E. 2017. Rosmarinic Acid, a Rosemary Extract Polyphenol, Increases Skeletal Muscle Cell Glucose Uptake and Activates

AMPK. *Molecules* 22:1–16.

Wang, W. , Zhang, Z. , Wu, Y. , Wang, R. , Chen, J. , Chen, J. , Zhang, Y. , Chen, Y. , Geng, M. , Xu, Z. , Dai, M. , Li, J. , and Pan, L. 2018. Corrigendum:(-)-Epigallocatechin-3-Gallate Ameliorates Atherosclerosis and Modulates Hepatic Lipid Metabolic Gene Expression in Apolipoprotein E Knockout Mice: Involvement of TTC39B. *Frontiers in Pharmacology* 9:1–10.

Wang, W. , Zheng, H. , Zheng, M. , Liu, X. , and Yu, J. 2018. Protective Effect of Avicularin on Rheumatoid Arthritis and Its Associated Mechanisms. *Experimental and Therapeutic Medicine* 16:5343–5349.

Xiong, S. , Liu, W. , Zhou, Y. , Mo, Y. , Liu, Y. , Chen, X. , Pan, H. , Yuan, D. , Wang, Q. , and Chen, T. . 2020. Enhancement of Oral Bioavailability and Anti-Parkinsonian Efficacy of Resveratrol through a Nanocrystal Formulation. *Asian Journal of Pharmaceutical Sciences* 15:518–528.

Yang, Z. , Chen, Y. , Yan, Z. , Xu, T. , Wu, X. , Pi, A. , Liu, Q. , Chai, H. , Li, S. , and Dou, X. 2021. Inhibition of TLR4/MAPKs Pathway Contributes to the Protection of Salvianolic Acid A against Lipotoxicity-Induced Myocardial Damage in Cardiomyocytes and Obese Mice. *Frontiers in Pharmacology* 12:1–10.

ZafraStone, S. , Yasmin, T. , Bagchi, M. , Chatterjee, A. , Vinson, J. , and Bagchi, D. 2007. Berry Anthocyanins as Novel Antioxidants in Human Health and Disease Prevention. *Molecular Nutrition & Food Research* 51:675–683.

Zhang, L. , Hao, L. , Wang, H. , Su, H. , Sun, Y. , Yang, X. , Che, B. , Xue, J. , and Gao, Z. 2015. Neuroprotective Effect of Resveratrol Against Glutamate-Induced Excitotoxicity. *Advances in Clinical and Experimental Medicine* 24:161–165.

Zhao, C. , Liu, J. , Li, B. , Ren, D. , Chen, X. , Yu, J. , and Zhang, Q. 2020. Multiscale Construction of Bifunctional Electrocatalysts for LongLifespan Rechargeable Zinc–Air Batteries. *Advanced Functional Materials* 30:1–9.

Zhou, Z. , Tang, M. , Liu, Y. , Zhang, Z. , Lu, R. , and Lu, J. 2017. Apigenin Inhibits Cell Proliferation, Migration, and Invasion by Targeting Akt in the A549 Human Lung Cancer Cell Line. *Anti-Cancer Drugs* 28:446–456.

## Macromolecules of Plant Origin and Their Pharmacological Activities/Applications

Ahmad, Gulzar , and Mansoor Amiji . 2018. Use of CRISPR/Cas9 gene-editing tools for developing models in drug discovery. *Drug Discovery Today* 23(3):519–533. <https://doi.org/10.1016/j.drudis.2018.01.014>

Alzohairy, Mohammad A. 2016. Therapeutics role of *Azadirachta indica* (neem) and their active constituents in diseases prevention and treatment. Evidence-Based Complementary and Alternative Medicine: eCAM 2016:7382506. <https://doi.org/10.1155/2016/7382506>

Azuama, Onyedikachi Cecil , Sergio Ortiz , Luis Quirós-Guerrero , Emeline Bouffartigues , Damien Tortuel , Olivier Maillot , Marc Feuilloley , et al. 2020. Tackling *Pseudomonas aeruginosa* virulence by mulinane-like diterpenoids from *Azorella atacamensis*. *Biomolecules* 10(12):1626. <https://doi.org/10.3390/biom10121626>

Bakare, Olalekan Olanrewaju , Arun Gokul , Adewale Oluwaseun Fadaka , Ruomou Wu , Lee-Ann Niekerk , Adele Mariska Barker , Marshall Keyster , and Ashwil Klein . 2022. Plant antimicrobial peptides (PAMPs): Features, applications, production, expression, and challenges. *Molecules* 27(12):3703. <https://doi.org/10.3390/molecules27123703>

Bodagh, Nikkhah , Iradj Maleki Mehnaz , and Azita Hekmatdoost . 2018. Ginger in gastrointestinal disorders: A systematic review of clinical trials. *Food Science & Nutrition* 7(1):96–108. <https://doi.org/10.1002/fsn3.807>

Bustin, Stephen A. , and Tania Nolan . 2020. RT-qPCR testing of SARS-CoV-2: A primer. *International Journal of Molecular Sciences* 21(8):3004. <https://doi.org/10.3390/ijms21083004>

Cao, Shixi , Mengqi Liu , Yao Han , Shouren Li , Xiaoyan Zhu , Defeng Li , Yinghua Shi , and Boshuai Liu . 2024. Effects of saponins on lipid metabolism: The gut–liver axis plays a key role. *Nutrients* 16(10):1514. <https://doi.org/10.3390/nu16101514>

Chen, Yu-Ying , Qiu-Ping Liu , Pei An , Min Jia , Xin Luan , Jian-Yuan Tang , and Hong Zhang . 2022. Ginsenoside Rd: A promising natural neuroprotective agent. *Phytomedicine*



95(January):153883. <https://doi.org/10.1016/j.phymed.2021.153883>

Costa, Lia , Emília Sousa , and Carla Fernandes . 2023. Cyclic peptides in pipeline: What future for these great molecules? *Pharmaceuticals* 16(7):996. <https://doi.org/10.3390/ph16070996>

Dallongeville, Sophie , Nicolas Garnier , Christian Rolando , and Caroline Tokarski . 2016. Proteins in art, archaeology, and paleontology: From detection to identification. *Chemical Reviews* 116(1):2–79. <https://doi.org/10.1021/acs.chemrev.5b00037>

Daly, Norelle L. , and David T. Wilson . 2021. Plant derived cyclic peptides. *Biochemical Society Transactions* 49(3):1279–1285. <https://doi.org/10.1042/BST20200881>

Daniell, Henry , Grisel Ruiz , Bela Denes , Laurence Sandberg , and William Langridge . 2009. Optimization of codon composition and regulatory elements for expression of human insulin like growth factor-1 in transgenic chloroplasts and evaluation of structural identity and function. *BMC Biotechnology* 9:1–16. <https://doi.org/10.1186/1472-6750-9-33>

Dhara, Amal Kumar , and Amit Kumar Nayak . 2022. Biological macromolecules: Sources, properties, and functions. In *Biological Macromolecules*, pp. 3–22. Academic Press. <https://doi.org/10.1016/B978-0-323-85759-8.00005-1>

Dong, Xinli , Mengze Zhou , Yehong Li , Yuxin Li , Hui Ji , and Qinghua Hu . 2021. Cardiovascular protective effects of plant polysaccharides: A review. *Frontiers in Pharmacology* 12(November):783641. <https://doi.org/10.3389/fphar.2021.783641>

Ercan, Kenan , Omer Gecesefta , Muhammed Taysi , Omeed Ali , and Seyithan Taysi . 2020. *Moringa oleifera*: A review of its occurrence, pharmacological importance and oxidative stress. *Mini-Reviews in Medicinal Chemistry* 20(July). <https://doi.org/10.2174/1389557520999200728162453>

Farooqi, Ammad Ahmad , Muhammad Zahid Qureshi , Sumbul Khalid , Rukset Attar , Chiara Martinelli , Uteuliyev Yerzhan Sabitaliyevich , Sadykov Bolat Nurmurazayevich , Simona Taverna , Palmiro Poltronieri , and Baojun Xu . 2019. Regulation of cell signaling pathways by berberine in different cancers: Searching for missing pieces of an incomplete jig-saw puzzle for an effective cancer therapy. *Cancers* 11(4):478. <https://doi.org/10.3390/cancers11040478>

Flynn, Ryan A. , Kayvon Pedram , Stacy A. Malaker , Pedro J. Batista , Benjamin A.H. Smith , Alex G. Johnson , Benson M. George , et al. 2021. Small RNAs are modified with N-glycans and displayed on the surface of living cells. *Cell* 184(12):3109–3124.e22. <https://doi.org/10.1016/j.cell.2021.04.023>

Fursenco, Cornelia , Tatiana Calalb , Livia Uncu , Mihaela Dinu , and Robert Ancuceanu . 2020. *Solidago virgaurea* L.: A review of its ethnomedicinal uses, phytochemistry, and pharmacological activities. *Biomolecules* 10(12):1619. <https://doi.org/10.3390/biom10121619>

Hussein, Rehab A. , and Amira A. El-Anssary . 2019. Plants secondary metabolites: The key drivers of the pharmacological actions of medicinal plants. *Herbal Medicine* 1(3):11–30. <https://doi.org/10.5772/intechopen.76139>

Jackson, Peter Philip James , Anisha Wijeyesekera , and Robert Adrian Rastall . 2022. Inulin type fructans and shortchain Fructooligosaccharides: Their role within the food industry as fat and sugar replacers and texture modifiers: What needs to be considered! *Food Science & Nutrition* 11(1):17–38. <https://doi.org/10.1002/fsn3.3040>

Jyotirmayee, B. , and Gyanranjan Mahalik . 2022. A review on selected pharmacological activities of *Curcuma longa* L. *International Journal of Food Properties* 25(1):1377–1398. <https://doi.org/10.1080/10942912.2022.2082464>

Kasote, Deepak M. , Surendra S. Katyare , Mahabaleshwar V. Hegde , and Hanhong Bae . 2015. Significance of antioxidant potential of plants and its relevance to therapeutic applications. *International Journal of Biological Sciences* 11(8):982–991. <https://doi.org/10.7150/ijbs.12096>

Kaushik, Bhupesh , Jatin Sharma , Keshav Yadav , Prithik Kumar , and Abhilasha Shourie . 2021. Phytochemical properties and pharmacological role of plants: Secondary metabolites. *Biosciences Biotechnology Research Asia* 18(1):23–45. <https://doi.org/10.13005/bbra/2894>

Khan, Muhammad S. , Ghulam Mustafa , and Faiz Ahmad Joyia . 2018. Enzymes: Plant-based production and their applications. *Protein and Peptide Letters* 25, no. 2 (2018):136–147. <https://www.ingentaconnect.com/content/ben/ppl/2018/00000025/00000002/art00008>

Kim, Han Wool , Myoung-Sook Shin , Sue Jung Lee , and Hye-Ryung Park . 2019. Signaling pathways associated with macrophage-activating polysaccharides purified from fermented barley. *International Journal of Biological Macromolecules* 131:1084–1091. <https://doi.org/10.1016/j.ijbiomac.2019.03.159>

Ko, Kisung , and Hilary Koprowski . 2005. Plant biopharming of monoclonal antibodies. *Virus Research* 111(1):93–100. <https://doi.org/10.1016/j.virusres.2005.03.016>

Liperoti, Rosa , Davide L. Vetrano , Roberto Bernabei , and Graziano Onder . 2017. Herbal medications in cardiovascular medicine. *Journal of the American College of Cardiology* 69(9):1188–1199. <https://doi.org/10.1016/j.jacc.2016.11.078>

Liu, Yu-Da , Hao-Ran Chen , Yao Zhang , Ge Yan , and Hao-Jie Yan . 2023. Progress and challenges of plant-derived nucleic acids as therapeutics in macrophage-mediated RNA therapy. *Frontiers* 14. <https://doi.org/10.3389/fimmu.2023.1255668>

Luz-Veiga, Mariana , Manuela Amorim , Inês Pinto-Ribeiro , Ana L. S. Oliveira , Sara Silva , Lúgia L. Pimentel , Luís M. Rodríguez-Alcalá , et al. 2023. Cannabidiol and cannabigerol exert antimicrobial activity without compromising skin microbiota. *International Journal of Molecular Sciences* 24(3):2389. <https://doi.org/10.3390/ijms24032389>

Mahar, Ruchi Barthwal , and Rohit Mahar . 2024. Exploring the significance, extraction, and characterization of plant-derived secondary metabolites in complex mixtures. *Metabolites* 14(2):119. <https://doi.org/10.3390/metabo14020119>

Mazalovska, Milena , and J. Calvin Kouokam . 2020. Plant-derived lectins as potential cancer therapeutics and diagnostic tools. *BioMed Research International* 2020(May):1631394. <https://doi.org/10.1155/2020/1631394>

Mezo, Gábor . 2013. Peptide and protein based pharmaceuticals. In *Amino Acids, Peptides and Proteins*, edited by Etelka Farkas , Maxim Ryadnov , pp. 203–252. <https://doi.org/10.1039/9781849737081-00203>

Mumtaz, Faiza , Muhammad Zubair , Fazlullah Khan , and Kamal Niaz . 2020. Analysis of plants lipids. In *Recent Advances in Natural Products Analysis*, pp. 677–705. Elsevier. <https://doi.org/10.1016/B978-0-12-816455-6.00022-6>

Murphy, Emma J. , Gustavo Waltzer Fehrenbach , Ismin Zainol Abidin , Ciara Buckley , Therese Montgomery , Robert Pogue , Patrick Murray , Ian Major , and Emanuele Rezoagli . 2023. Polysaccharides: Naturally occurring immune modulators. *Polymers* 15(10):2373. <https://doi.org/10.3390/polym15102373>

Puhlmann, Marie-Luise , and Willem M. De Vos . 2022. Intrinsic dietary fibers and the gut microbiome: Rediscovering the benefits of the plant cell matrix for human health. *Frontiers in Immunology* 13(August):954845. <https://doi.org/10.3389/fimmu.2022.954845>

Rasheed, Faiza , Joel Markgren , Mikael Hedenqvist , and Eva Johansson . 2020. Modeling to understand plant protein structure-function relationships: Implications for seed storage proteins. *Molecules* 25(4):873. <https://doi.org/10.3390/molecules25040873>

Ren, Yan , Yueping Bai , Zhidan Zhang , Wenlong Cai , and Antonio Del Rio Flores . 2019. The preparation and structure analysis methods of natural polysaccharides of plants and fungi: A review of recent development. *Molecules* 24(17):1–26. <https://doi.org/10.3390/molecules24173122>

Reszczyńska, Emilia , and Agnieszka Hanaka . 2020. Lipids composition in plant membranes. *Cell Biochemistry and Biophysics* 78(4):401–414. <https://doi.org/10.1007/s12013-020-00947-w>

Romano, Barbara , Giuseppe Lucariello , and Raffaele Capasso . 2021. Topical collection 'pharmacology of medicinal plants.' *Biomolecules* 11(1):101. <https://doi.org/10.3390/biom11010101>

Salehi, Bahare , Athar Ata , Nanjangud V. Anil Kumar , Farukh Sharopov , Karina Ramírez-Alarcón , Ana Ruiz-Ortega , Seyed Abdulmajid Ayatollahi , et al. 2019. Antidiabetic potential of medicinal plants and their active components. *Biomolecules* 9(10):551. <https://doi.org/10.3390/biom9100551>

Schulz, Rebekah M. , Nitin K. Ahuja , and Joanne L. Slavin . 2022. Effectiveness of nutritional ingredients on upper gastrointestinal conditions and symptoms: A narrative review. *Nutrients* 14(3):672. <https://doi.org/10.3390/nu14030672>

Sepp, Janne , Oleh Koshovyi , Valdas Jakstas , Vaidotas Žvikas , Iryna Botsula , Igor Kireyev , Karina Tsemenko , et al. 2024. Phytochemical, technological, and pharmacological study on the galenic dry extracts prepared from german chamomile (*Matricaria chamomilla* L.) flowers. *Plants* 13(3):350. <https://doi.org/10.3390/plants13030350>

Shaito, Abdullah , Maryam Al-Mansoob , Salma M. S. Ahmad , Mohammad Z. Haider , Ali H. Eid , Anna Maria Posadino , Gianfranco Pintus , and Roberta Giordo . 2023. Resveratrol-mediated regulation of mitochondria biogenesis-associated pathways in neurodegenerative diseases: Molecular insights and potential therapeutic applications. *Current Neuropharmacology* 21(5):1184–1201. <https://doi.org/10.2174/1570159X20666221012122855>

Sherratt, Samuel C. R. , Peter Libby , Matthew J. Budoff , Deepak L. Bhatt , and R. Preston Mason . 2023. Role of omega-3 fatty acids in cardiovascular disease: The debate continues. *Current Atherosclerosis Reports* 25(1):1–17. <https://doi.org/10.1007/s11883-022-01075-x>

Shiade , Seyede Roghie Ghadirnezhad , Arameh Zand-Silakhoor , Amin Fathi , Reza Rahimi , Tatiana Minkina , Vishnu D. Rajput , Usman Zulfiqar , and Talha Chaudhar . 2024. Plant metabolites and signaling pathways in response to biotic and abiotic stresses: Exploring bio stimulant applications. *Plant Stress* 12:100454. <https://doi.org/10.1016/j.stress.2024.100454>

Siddiqui, Arif Jamal , Corina Danciu , Syed Amir Ashraf , Afrasim Moin , Ritu Singh , Mousa Alreshidi , Mitesh Patel , et al. 2020. Plants-derived biomolecules as potent antiviral phytomedicines: New insights on ethnobotanical evidences against coronaviruses. *Plants* 9(9):1244. <https://doi.org/10.3390/plants9091244>

Szućko-Kociuba, Izabela , Alicja Trzeciak-Rydzek , Patrycja Kupnicka , and Dariusz Chlubek . 2023. Neurotrophic and neuroprotective effects of *Hericium erinaceus*. *International Journal of Molecular Sciences* 24(21):15960. <https://doi.org/10.3390/ijms242115960>

Tran, Ngan , Bao Pham , and Ly Le . 2020. Bioactive compounds in anti-diabetic plants: From herbal medicine to modern drug discovery. *Biology* 9(9):252. <https://doi.org/10.3390/biology9090252>

Tsuchiya, Hironori . 2017. Anesthetic agents of plant origin: A review of phytochemicals with anesthetic activity. *Molecules* 22(8):1369. <https://doi.org/10.3390/molecules22081369>

Varnosfaderani, Noorbakhsh , Seyed Mostafa , Farnoosh Ebrahimzadeh , Mahsa Akbari Oryani , Saeed Khalili , Faezeh Almasi , Reza Mosaddeghi Heris , Zahra Payandeh , Chen Li , Mohsen Nabi Afjadi , and Armina Alagheband Bahrami . 2024. Potential promising anticancer applications of  $\beta$ -glucans: A review. *Bioscience Reports* 44(1):BSR20231686. <https://doi.org/10.1042/BSR20231686>

Wani, Snober Shabeer , Parvaiz A. Dar , Sajad M. Zargar , and Tanveer A. Dar . 2020. Therapeutic potential of medicinal plant proteins: Present status and future perspectives. *Bentham Science* 45. <https://doi.org/10.2174/1389203720666191119095624>

Wymann, Matthias P. , and Roger Schneider . 2008. Lipid signaling in disease. *Nature Reviews Molecular Cell Biology* 9(2):162–176. <https://doi.org/10.1038/nrm2335>

Yadav, Jagat Pal , Amita Verma , Prateek Pathak , Ashish R. Dwivedi , Ankit Kumar Singh , Pradeep Kumar , Habibullah Khalilullah , Mariusz Jaremko , Abdul-Hamid Emwas , and Dinesh Kumar Patel . 2024. Phytoconstituents as modulators of NF- $\kappa$ B signalling: Investigating therapeutic potential for diabetic wound healing. *Biomedicine & Pharmacotherapy* 177(August):117058. <https://doi.org/10.1016/j.biopha.2024.117058>

Yan, Dazhong , Yanzhen Li , Yinling Liu , Na Li , Xue Zhang , and Chen Yan . 2021. Antimicrobial properties of chitosan and chitosan derivatives in the treatment of enteric infections. *Molecules* 26(23):7136. <https://doi.org/10.3390/molecules26237136>

Yu, Yue , Mingyue Shen , Qianqian Song , and Jianhua Xie . 2018. Biological activities and pharmaceutical applications of polysaccharide from natural resources: A review. *Carbohydrate Polymers* 183:91–101. <https://doi.org/10.1016/j.carbpol.2017.12.009>

Zhao, Tiantian , Chao Li , Shuai Wang , and Xinqiang Song . 2022. Green tea (*Camellia Sinensis*): A review of its phytochemistry, pharmacology, and toxicology. *Molecules* 27(12):3909. <https://doi.org/10.3390/molecules27123909>

## Recent Advances on Small-Size 'Biomolecules' Like 'Primary' and 'Secondary Metabolites' and Their Pharmacological Impacts

Adaramoye, O. , Erguen, B. , Nitzsche, B. , Höpfner, M. , Jung, K. , and Rabien, A. (2017). Punicalagin, a polyphenol from pomegranate fruit, induces growth inhibition and apoptosis in human PC-3 and LNCaP cells. *Chemico-Biological Interactions* 274, 100–106.

Akhtar, N. , Syed, D.N. , Khan, M.I. , Adhami, V.M. , Mirza, B. , and Mukhtar, H. (2016). The pentacyclic triterpenoid, plectranthoic acid, a novel activator of AMPK induces apoptotic death in prostate cancer cells. *Oncotarget* 7(4), 3819.

Akwu, N.A. , Lekhooa, M. , Deqiang, D. , and Aremu, A.O. (2023). Antidepressant effects of coumarins and their derivatives: A critical analysis of research advances. *European Journal of Pharmacology* 956, 175958.

Anulika, N.P. , Ignatius, E.O. , Raymond, E.S. , Osasere, O.-I. , and Abiola, A.H. (2016). The chemistry of natural product: Plant secondary metabolites. *International Journal of Technology Enhancements and Emerging Engineering Research* 4(8), 1–9.

Araújo, R.G. , Rodriguez-Jasso, R.M. , Ruiz, H.A. , Govea-Salas, M. , Pintado, M.E. , and Aguilar, C.N. (2020). Process optimization of microwave-assisted extraction of bioactive molecules from avocado seeds. *Industrial Crops and Products* 154, 112623.

Asif, M. , Akram, M. , Saeed, T. , Naveed, A. , Riaz, U.R.M. , Ali, S. , Syed, N.K. , Shaheen, G. , (2011). Review paper carbohydrates. *Journal of Biochemistry and Bioinformatics* 1(1):1–5.

Bandeira, D.M. , Correa, J.M. , Laskoski, L.V. , Batista, J.M. , Rosset, J. , da Costa, W.F. , et al. (2022). Extraction, characterization of bioactive compounds and biological activities of the leaves of *Podocarpus lambertii* Klotzch ex Endl. *Journal of Applied Research on Medicinal and Aromatic Plants* 31, 100427.

Bhadange, Y.A. , Carpenter, J. , and Saharan, V.K. (2024). A comprehensive review on advanced extraction techniques for retrieving bioactive components from natural sources. *ACS Omega* 9(29), 31274–31297.

Cao, L. , Qu, D. , Wang, H. , Zhang, S. , Jia, C. , Shi, Z. , et al. (2016). Toosendanin exerts an anti-cancer effect in glioblastoma by inducing estrogen receptor  $\beta$ -and p53-mediated apoptosis. *International Journal of Molecular Sciences* 17(11), 1928.

Cutillas, A.B. , Carrasco, A. , MartinezGutierrez, R. , Tomas, V. , and Tudela, J. (2017). *Salvia officinalis* L. essential oils from Spain: Determination of composition, antioxidant capacity, antienzymatic, and antimicrobial bioactivities. *Chemistry & Biodiversity* 14(8), e1700102.

Das, A.K. , Islam, M.N. , Faruk, M.O. , Ashaduzzaman, M. , and Dungani, R. (2020). Review on tannins: Extraction processes, applications and possibilities. *South African Journal of Botany* 135, 58–70.

Domínguez-Rodríguez, G. , Marina, M.L. , and Plaza, M. (2021). Enzyme-assisted extraction of bioactive non-extractable polyphenols from sweet cherry (*Prunus avium* L.) pomace. *Food Chemistry* 339, 128086.

Elshafie, H.S. , Camele, I. , and Mohamed, A.A. (2023). A comprehensive review on the biological, agricultural and pharmaceutical properties of secondary metabolites based-plant origin. *International Journal of Molecular Sciences* 24(4), 3266.

Fan, M. , Yuan, S. , Li, L. , Zheng, J. , Zhao, D. , Wang, C. , et al. (2023). Application of terpenoid compounds in food and pharmaceutical products. *Fermentation* 9(2), 119.

Fatima, Z. , Charles, M.R. , Maurya, J. , and Pratap, P. (2023). A systematic reviews of terpenes & terpenoids & their roles in human health. *Era's Journal of Medical Research* 10(2), 39–46.

Gahrue, H.H. , Parastouei, K. , Mokhtarian, M. , Rostami, H. , Niakousari, M. , and Mohsenpour, Z. (2020). Application of innovative processing methods for the extraction of bioactive compounds from saffron (*Crocus sativus*) petals. *Journal of Applied Research on Medicinal and Aromatic Plants* 19, 100264.

Gigliobianco, M.R. , Cortese, M. , Peregrina, D.V. , Villa, C. , Lupidi, G. , Pruccoli, L. , et al. (2021). Development of new extracts of *Crocus sativus* L. by-product from two different Italian regions as new potential active ingredient in cosmetic formulations. *Cosmetics* 8(2), 51.

Gođevac, D. , Jadranin, M. , Aljančić, I. , Vajs, V. , Tešević, V. , and Milosavljević, S. (2015). Application of spectroscopic methods and hyphenated techniques to the analysis of complex plant extracts. In Máthé, Á. (Ed.), *Medicinal and Aromatic Plants of the World: Scientific, Production, Commercial and Utilization Aspects*, pp. 61–85. Springer Dordrecht.

Hu, M. , Peng, S. , He, Y. , Qin, M. , Cong, X. , Xing, Y. , et al. (2015). Lycorine is a novel inhibitor of the growth and metastasis of hormone-refractory prostate cancer. *Oncotarget* 6(17), 15348.

Huang, J. , Yang, L. , Zou, Y. , Luo, S. , Wang, X. , Liang, Y. , et al. (2021). Antibacterial activity and mechanism of three isomeric terpineols of *Cinnamomum longepaniculatum* leaf oil. *Folia Microbiologica* 66, 59–67.

Hui, F. , Qin, X. , Zhang, Q. , Li, R. , Liu, M. , Ren, T. , et al. (2019). *Alpinia oxyphylla* oil induces apoptosis of hepatocellular carcinoma cells via PI3K/Akt pathway in vitro and in vivo. *Biomedicine & Pharmacotherapy* 109, 2365–2374.

Hussein, R.A. , and El-Anssary, A.A. (2019). Plants secondary metabolites: The key drivers of the pharmacological actions of medicinal plants. *Herbal Medicine* 1(3), 11–30.

Jamloki, A. , Bhattacharyya, M. , Nautiyal, M. , and Patni, B. (2021). Elucidating the relevance of high temperature and elevated CO<sub>2</sub> in plant secondary metabolites (PSMs) production. *Heliyon*

7(8), e07709.

Jha, A.K. , and Sit, N. (2022). Extraction of bioactive compounds from plant materials using combination of various novel methods: A review. *Trends in Food Science & Technology* 119, 579–591.

Jiang, J. , and Xiong, Y.L. (2016). Natural antioxidants as food and feed additives to promote health benefits and quality of meat products: A review. *Meat Science* 120, 107–117.

Kabera, J.N. , Semana, E. , Mussa, A.R. , and He, X. (2014). Plant secondary metabolites: Biosynthesis, classification, function and pharmacological properties. *Journal of Pharmacy and Pharmacology* 2(7), 377–392.

Kaur, R. , and Arora, S. (2015). Alkaloids-important therapeutic secondary metabolites of plant origin. *Journal of Critical Review* 2(3), 1–8.

Khare, S. , Singh, N. , Singh, A. , Hussain, I. , Niharika, K. , Yadav, V. , et al. (2020). Plant secondary metabolites synthesis and their regulations under biotic and abiotic constraints. *Journal of Plant Biology* 63, 203–216.

Kim, J. , Yu, J.-H. , Ko, E. , Lee, K.-W. , Song, A. , Park, S. , et al. (2010). The alkaloid Berberine inhibits the growth of Anokis-resistant MCF-7 and MDA-MB-231 breast cancer cell lines by inducing cell cycle arrest. *Phytomedicine* 17(6), 436–440.

Kim, S. , Lim, S.-W. , and Choi, J. (2022). Drug discovery inspired by bioactive small molecules from nature. *Animal Cells and Systems* 26(6), 254–265.

Kumar, N. , Kumar, P. , and Sharma, P. (2023). Technological advancement for the chemical characterization of essential oils. In Singh, S. , Chaurasia, P.K. , and Bharati, S.L. (Eds.), *Pharmacological Aspects of Essential Oils*, pp. 23–40. CRC Press, Boca Raton, FL.

Leman, J. (2009). *Lipids Production*. Applied Microbiology: Industrial, pp. 393–406. Elsevier, Amsterdam.

Li, H. , Liu, J. , Liu, C.-F. , Li, H. , Luo, J. , Fang, S. , et al. (2021). Design, synthesis, and biological evaluation of membrane-active bakuchiol derivatives as effective broad-spectrum antibacterial agents. *Journal of Medicinal Chemistry* 64(9), 5603–5619.

Liu, R. , Bao, Z.-X. , Zhao, P.-J. , and Li, G.-H. (2021). Advances in the study of metabolomics and metabolites in some species interactions. *Molecules* 26(11), 3311.

Ma, J.-S. , Liu, H. , Han, C.-R. , Zeng, S.-J. , Xu, X.-J. , Lu, D.-J. , et al. (2020). Extraction, characterization and antioxidant activity of polysaccharide from *Pouteria campechiana* seed. *Carbohydrate Polymers* 229, 115409.

Masyita, A. , Sari, R.M. , Astuti, A.D. , Yasir, B. , Rumata, N.R. , Emran, T.B. , et al. (2022). Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives. *Food Chemistry: X* 13, 100217.

Matsuda, F. , YonekuraSakakibara, K. , Niida, R. , Kuromori, T. , Shinozaki, K. , and Saito, K. (2009). MS/MS spectral tagbased annotation of nontargeted profile of plant secondary metabolites. *The Plant Journal* 57(3), 555–577.

Mohiuddin, A. (2019). Chemistry of secondary metabolites. *Annals of Clinical Toxicology* 2(1), 1014.

Naeem, A. , Hu, P. , Yang, M. , Zhang, J. , Liu, Y. , Zhu, W. , et al. (2022). Natural products as anticancer agents: Current status and future perspectives. *Molecules* 27(23), 8367.

Narváez-Cuenca, C.E. , Inampues-Charfuelan, M.L. , Hurtado-Benavides, A.M. , Parada-Alfonso, F. , and Vincken, J.P. (2020). The phenolic compounds, tocopherols, and phytosterols in the edible oil of guava (*Psidium guava*) seeds obtained by supercritical CO<sub>2</sub> extraction. *Journal of Food Composition and Analysis* 89, 103467.

Nie, J. , Chen, D. , Ye, J. , Lu, Y. , and Dai, Z. (2021). Optimization and kinetic modeling of ultrasonic-assisted extraction of fucoxanthin from edible brown algae *Sargassum fusiforme* using green solvents. *Ultrasonics Sonochemistry* 77, 105671.

Nie, J.-Y. , Li, R. , Jiang, Z.-T. , Wang, Y. , Tan, J. , Tang, S.-H. , et al. (2020). Screening and evaluation of radical scavenging active compounds in the essential oil from *Magnolia biondii* Pamp by electronic nose coupled with chemical methodology. *Industrial Crops and Products* 144, 112060.

Nigjeh, S.E. , Yeap, S.K. , Nordin, N. , Rahman, H. , and Rosli, R. (2019). In vivo anti-tumor effects of citral on 4T1 breast cancer cells via induction of apoptosis and downregulation of aldehyde dehydrogenase activity. *Molecules* 24(18), 3241.

Noman, L. , Oke-Altuntas, F. , Zellagui, A. , Sahin Yaglioglu, A. , Demirtas, I. , Cardoso, S.M. , et al. (2017). A novel benzimidazole and other constituents with antiproliferative and antioxidant

properties from *Thymelaea microphylla* Coss. et Dur. *Natural Product Research* 31(17), 2032–2041.

Osorio-Tobón, J.F. , Carvalho, P.I. , Barbero, G.F. , Nogueira, G.C. , Rostagno, M.A. , and de Almeida Meireles, M.A. . (2016). Fast analysis of curcuminoids from turmeric (*Curcuma longa* L.) by high-performance liquid chromatography using a fused-core column. *Food Chemistry* 200, 167–174.

Pappas, V.M. , Athanasiadis, V. , Palaiogiannis, D. , Poulianiti, K. , Bozinou, E. , Lalas, S.I. , et al. (2021). Pressurized liquid extraction of polyphenols and anthocyanins from saffron processing waste with aqueous organic acid solutions: Comparison with stirred-tank and ultrasound-assisted techniques. *Sustainability* 13(22), 12578.

Patil, P.D. , Patil, S.P. , Kelkar, R.K. , Patil, N.P. , Pise, P.V. , and Nadar, S.S. (2021). Enzyme-assisted supercritical fluid extraction: An integral approach to extract bioactive compounds. *Trends in Food Science & Technology* 116, 357–369.

Patra, A. , Abdullah, S. , and Pradhan, R.C. (2022). Review on the extraction of bioactive compounds and characterization of fruit industry by-products. *Bioresources and Bioprocessing* 9(1), 14.

Patra, J.K. , Das, G. , Lee, S. , Kang, S.-S. , and Shin, H.-S. (2018). Selected commercial plants: A review of extraction and isolation of bioactive compounds and their pharmacological market value. *Trends in Food Science & Technology* 82, 89–109.

Reddy, D. , Ghosh, P. , and Kumavath, R. (2020). Strophanthidin attenuates MAPK, PI3K/AKT/mTOR, and Wnt/ $\beta$ -catenin signaling pathways in human cancers. *Frontiers in Oncology* 9, 1469.

Rodríguez-Martínez, B. , Ferreira-Santos, P. , Gullón, B. , Teixeira, J.A. , Botelho, C.M. , and Yáñez, R. (2021). Exploiting the potential of bioactive molecules extracted by ultrasounds from avocado peels: Food and nutraceutical applications. *Antioxidants* 10(9), 1475.

Salem, M.A. , Perez de Souza, L. , Serag, A. , Fernie, A.R. , Farag, M.A. , Ezzat, S.M. , et al. (2020). Metabolomics in the context of plant natural products research: From sample preparation to metabolite analysis. *Metabolites* 10(1), 37.

Shama, M. , and Gani, M.A. (2021). Phenolic compounds. In Zepka, L.Q. , Casagrande do Nascimento, T. , and Jacob-Lopes, E. (Eds.), *Bioactive Compounds - Biosynthesis, Characterization and Applications*. IntechOpen, London.  
<https://www.intechopen.com/chapters/76405>

Sharma, P. , Kumar, N. , Khandelwal, K. , Chand, S. , and Dhaka, S. (2024). Biomarkers for disease identification and drug development. In Mishra, R. , Madhav, S. , Dhaka, R.K. , and Garg, P. (Eds.), *Biomarkers in Environmental and Human Health Biomonitoring*, pp. 293–311. Elsevier, Amsterdam.

Shen, Y. , Han, C. , Chen, X. , Hou, X. , and Long, Z. (2013). Simultaneous determination of three Curcuminoids in *Curcuma wenyujin* YH chen et C. Ling. by liquid chromatography–tandem mass spectrometry combined with pressurized liquid extraction. *Journal of Pharmaceutical and Biomedical Analysis* 81, 146–150.

Sheng, F. , Hu, B. , Jin, Q. , Wang, J. , Wu, C. , and Luo, Z. (2021). The analysis of phenolic compounds in walnut husk and pellicle by UPLC-Q-Orbitrap HRMS and HPLC. *Molecules* 26(10), 3013.

Shukla, S. , Shankar, E. , Fu, P. , MacLennan, G.T. , and Gupta, S. (2015). Suppression of NF- $\kappa$ B and NF- $\kappa$ B-regulated gene expression by apigenin through I $\kappa$ B $\alpha$  and IKK pathway in TRAMP mice. *Plos One* 10(9), e0138710.

Simsek, M. , and Whitney, K. (2024). Examination of primary and secondary metabolites associated with a plant-based diet and their impact on human health. *Foods* 13(7), 1020.

Sithara, T. , Arun, K. , Syama, H. , Reshmitha, T. , and Nisha, P. (2017). Morin inhibits proliferation of SW480 colorectal cancer cells by inducing apoptosis mediated by reactive oxygen species formation and uncoupling of Warburg effect. *Frontiers in Pharmacology* 8, 640.

Su, C.-M. , Weng, Y.-S. , Kuan, L.-Y. , Chen, J.-H. , and Hsu, F.-T. (2020). Suppression of PKC $\delta$ /NF- $\kappa$ B signaling and apoptosis induction through extrinsic/intrinsic pathways are associated with magnolol-inhibited tumor progression in colorectal cancer in vitro and in vivo. *International Journal of Molecular Sciences* 21(10), 3527.

Subramanian, K. , Selvakkumar, C. , Vinaykumar, K.S. , Goswami, N. , Meenakshisundaram, S. , Balakrishnan, A. , et al. (2009). Tackling multiple antibiotic resistance in enteropathogenic *Escherichia coli* (EPEC) clinical isolates: a diarylheptanoid from *Alpinia officinarum* shows promising antibacterial and immunomodulatory activity against EPEC and its

lipopolysaccharide-induced inflammation. *International Journal of Antimicrobial Agents* 33(3), 244–250.

Teoh, E.S. , and Teoh, E.S. (2016). Secondary metabolites of plants. In Teoh, E.-S. (Ed.), *Medicinal Orchids of Asia*, pp. 59–73. Springer, Cham.

Tosif, M.M. , Najda, A. , Bains, A. , Kaushik, R. , Dhull, S.B. , Chawla, P. , et al. (2021). A comprehensive review on plant-derived mucilage: Characterization, functional properties, applications, and its utilization for nanocarrier fabrication. *Polymers* 13(7), 1066.

Twaij, B.M. , and Hasan, M.N. (2022). Bioactive secondary metabolites from plant sources: Types, synthesis, and their therapeutic uses. *International Journal of Plant Biology* 13(1), 4–14.

Valavanidis, A. , and Vlachogianni, T. (2013). Plant polyphenols: Recent advances in epidemiological research and other studies on cancer prevention. *Studies in Natural Products Chemistry* 39, 269–295.

Vardakas, A. , Kechagias, A. , Penov, N. , and Giannakas, A.E. (2024). Optimization of enzymatic assisted extraction of bioactive compounds from *Olea europaea* leaves. *Biomass* 4(3), 647–657.

Vila Verde , G.M., Barros, D.A. , Oliveira, M.S. , Aquino, G.L. , Santos, D.M. , De Paula, J.R. , et al. (2018). A green protocol for microwave-assisted extraction of volatile oil terpenes from *Pterodon emarginatus* Vogel. (Fabaceae). *Molecules* 23(3), 651.

Wang, C. , Yang, H. , and Li, J. (2021). Combination of microwave, ultrasonic, enzyme assisted method for curcumin species extraction from turmeric (*Curcuma Longa* L.) and evaluation of their antioxidant activity. *EFood* 2(2), 73–80.

Wang, C.-Y. , Chen, Y.-W. , and Hou, C.-Y. (2019). Antioxidant and antibacterial activity of seven predominant terpenoids. *International Journal of Food Properties* 22(1), 230–238.

Wang, S.-Y. , Yang, L. , Zu, Y.-G. , Zhao, C.-J. , Sun, X.-W. , Zhang, L. , et al. (2011). Design and performance evaluation of ionic-liquids-based microwave-assisted environmentally friendly extraction technique for camptothecin and 10-hydroxycamptothecin from samara of *camptotheca acuminata*. *Industrial & Engineering Chemistry Research* 50(24), 13620–13627.

Wang, Y.-P. , and Lei, Q.-Y. (2018). Metabolite sensing and signaling in cell metabolism. *Signal Transduction and Targeted Therapy* 3(1), 30.

Wu, Z. , Li, H. , Wang, Y. , Yang, D. , Tan, H. , Zhan, Y. , et al. (2019). Optimization extraction, structural features and antitumor activity of polysaccharides from *Z. jujuba* cv. Ruoqiangzao seeds. *International Journal of Biological Macromolecules* 135, 1151–1161.

Xu, J.-J. , Li, Q. , Cao, J. , Warner, E. , An, M. , Tan, Z. , et al. (2016). Extraction and enrichment of natural pigments from solid samples using ionic liquids and chitosan nanoparticles. *Journal of Chromatography A* 1463, 32–41.

Xu, W.-T. , Li, T.-Z. , Li, S.-M. , Wang, C. , Wang, H. , Luo, Y.-H. , et al. (2020). Cytisine exerts anti-tumour effects on lung cancer cells by modulating reactive oxygen species-mediated signalling pathways. *Artificial Cells, Nanomedicine, and Biotechnology* 48(1), 84–95.

Yao, C. , Liu, B.-B. , Qian, X.-D. , Li, L.-Q. , Cao, H.-B. , Guo, Q.-S. , et al. (2018). Crocin induces autophagic apoptosis in hepatocellular carcinoma by inhibiting Akt/mTOR activity. *OncoTargets and Therapy* 11, 2017–2028.

Zhang, H. , Jiao, Y. , Shi, C. , Song, X. , Chang, Y. , Ren, Y. , et al. (2018). Berbamine suppresses cell proliferation and promotes apoptosis in ovarian cancer partially via the inhibition of Wnt/ $\beta$ -catenin signaling. *Acta Biochimica et Biophysica Sinica* 50(6), 532–539.

Zhang, J. , Wen, C. , Zhang, H. , Duan, Y. , and Ma, H. (2020). Recent advances in the extraction of bioactive compounds with subcritical water: A review. *Trends in Food Science & Technology* 95, 183–195.

Zhang, L.-L. , Zhang, L.-F. , Xu, J.-G. , and Hu, Q.-P. (2017). Comparison study on antioxidant, DNA damage protective and antibacterial activities of eugenol and isoeugenol against several foodborne pathogens. *Food & Nutrition Research* 61, 1–9.



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- Abegaz, B. M. , and H. H. Kinfé . Secondary metabolites, their structural diversity, bioactivity, and ecological functions: An overview. *Physical Sciences Reviews* 4, no. 6 (2019): 20180100.
- Anand, U. , N. Jacobo-Herrera , A. Altemimi , and N. Lakhssassi . A comprehensive review on medicinal plants as antimicrobial therapeutics: Potential avenues of biocompatible drug discovery. *Metabolites* 9, no. 11 (2019): 258.
- Ashihara, H. , A. Crozier , and I. A. Ludwig . *Plant Nucleotide Metabolism: Biosynthesis, Degradation, and Alkaloid Formation*. Chichester: John Wiley & Sons, 2020.
- Badi, H. N. , V. Abdoosi , and N. Farzin . New approach to improve taxol biosynthetic. *Trakia Journal of Science* 2 (2015): 115–124.
- Bandyopadhyay, U. , and S. Dey . Antimalarial drugs and molecules inhibiting hemozoin formation. In Becker K. (Ed.), *Apicomplexan Parasites: Molecular Approaches toward Targeted Drug Development*, pp. 205–234. Weinheim, Germany: Wiley-VCH Verlag & Co. KGaA, 2011.
- Banerjee, S. , S. Banerjee , A. Bishayee , M. N. Da Silva , O. A. Sukocheva , E. Tse , N. Casarcia , and A. Bishayee . Cellular and molecular mechanisms underlying the potential of betulinic acid in cancer prevention and treatment. *Phytomedicine* 132 (2024): 155858.
- Bates, D. , and A. Eastman . Microtubule destabilizing agents: Far more than just antimitotic anticancer drugs. *British Journal of Clinical Pharmacology* 83, no. 2 (2017): 255–268.
- Bhadra, S. , M. K. Dalai , J. Chanda , and P. K. Mukherjee . Evaluation of bioactive compounds as acetylcholinesterase inhibitors from medicinal plants. In Mukherjee, P. K. (Ed.), *Evidence-Based Validation of Herbal Medicine*, pp. 273–306. Elsevier, Amsterdam, 2015.
- Bhambhani, S. , K. R. Kondhare , and A. P. Giri . Diversity in chemical structures and biological properties of plant alkaloids. *Molecules* 26, no. 11 (2021): 3374.
- Biastoff, S. , and B. Dräger . Calystegines. *The Alkaloids: Chemistry and Biology* 64 (2007): 49–102.
- Bribi, N. Pharmacological activity of alkaloids: A review. *Asian Journal of Botany* 1, no. 1 (2018): 1–6.
- Brindha, P. Role of phytochemicals as immunomodulatory agents: A review. *International Journal of Green Pharmacy* 10, no. 1 (2016): 1–18.
- Chrzanowska, M. , A. Grajewska , and M. D. Rozwadowska . Asymmetric synthesis of isoquinoline alkaloids: 2004–2015. *Chemical Reviews* 116, no. 19 (2016): 12369–12465.
- Cruz, S. L. , M. I. Paz-Ramos , A. Hernández-Mendoza , and C. J. Carranza-Aguilar . Opioid effects and classification. In Cruz, S. L. (Ed.), *Opioids: Pharmacology, Abuse, and Addiction*, pp. 149–174. Cham: Springer International Publishing, 2022.
- Dash, D. K. , C. K. Tyagi , A. K. Sahu , and V. Tripathi . Revisiting the medicinal value of terpenes and terpenoids. In Meena, S. V. , Parewam H. P. , and Meena, S. K. (Ed.), *Revisiting Plant Biostimulants*. London: IntechOpen, 2022.
- DelPrado-Audelo, M. L. , H. Cortés , I. H. Caballero-Florán , M. González-Torres , L. Escutia-Guadarrama , S. A. Bernal-Chávez , D. M. Giraldo-Gomez , J. J. Magaña , and G. Leyva-Gómez . Therapeutic applications of terpenes on inflammatory diseases. *Frontiers in Pharmacology* 12 (2021): 704197.
- Dewey, R. E. , and J. Xie . Molecular genetics of alkaloid biosynthesis in *Nicotiana tabacum*. *Phytochemistry* 94 (2013): 10–27.
- Dey, P. , A. Kundu , H. J. Chakraborty , B. Kar , W. S. Choi , B. M. Lee , and H. S. Kim . Therapeutic value of steroidal alkaloids in cancer: Current trends and future perspectives. *International Journal of Cancer* 145, no. 7 (2019): 1731–1744.
- Dey, P. , A. Kundu , A. Kumar , M. Gupta , B. M. Lee , T. Bhakta , and H. S. Kim . Analysis of alkaloids (indole alkaloids, isoquinoline alkaloids, tropane alkaloids). In Silva, A. S. (Ed.), *Recent Advances in Natural Products Analysis*, pp. 505–567. Elsevier, Amsterdam, 2020.
- Foumani, E. A. , S. Irani , Y. Shokoohinia , and A. Mostafaei . Colchicine of *Colchicum autumnale*, a traditional anti-inflammatory medicine, induces apoptosis by activation of apoptotic genes and protein expression in human breast (MCF-7) and mouse breast (4T1) cell lines. *Cell Journal* 24, no. 11 (2022): 647.
- Funayama, S. , and G. A. Cordell . *Alkaloids: A Treasury of Poisons and Medicines*. London: Elsevier, 2014.
- Gad, M. Z. , S. S. Azab , A. R. Khattab , and M. A. Farag . Over a century since ephedrine discovery: An updated revisit to its pharmacological aspects, functionality, and toxicity in comparison to its herbal extracts. *Food & Function* 12, no. 20 (2021): 9563–9582.

Gonçalves, E. C. , G. M. Baldasso , M. A. Bicca , R. S. Paes , R. Capasso , and R. C. Dutra . Terpenoids, cannabimimetic ligands, beyond the cannabis plant. *Molecules* 25, no. 7 (2020): 1567.

Gonzalez-Burgos, E. , and M. P. Gomez-Serranillos . Terpene compounds in nature: A review of their potential antioxidant activity. *Current Medicinal Chemistry* 19, no. 31 (2012): 5319–5341.

Goossens, A. , S. T. Häkkinen , I. Laakso , T. Seppänen-Laakso , S. Biondi , V. De Sutter , and K. M. Oksman-Caldentey . A functional genomics approach toward the understanding of secondary metabolism in plant cells. *Proceedings of the National Academy of Sciences of the United States of America* 100, no. 14 (2003): 8595–8600.

Guillot, T. S. , and G. W. Miller . Protective actions of the vesicular monoamine transporter 2 (VMAT2) in monoaminergic neurons. *Molecular Neurobiology* 39 (2009): 149–170.

Guimarães, A. G. , M. R. Serafini , and L. J. Quintans-Júnior . Terpenes and derivatives as a new perspective for pain treatment: A patent review. *Expert Opinion on Therapeutic Patents* 24, no. 3 (2014): 243–265.

Gulecha, V. S. , M. S. Mahajan , A. Upaganlawar , A. Sherikar , and C. Upasani . Cholinergic antagonists. In Uddin, M. S. , Rashid, M. (Eds.), *Advances in Neuropharmacology*, pp. 31–60. Oakville, ON: Apple Academic Press, 2020.

Gutiérrez-Grijalva, E. P. , L. X. López-Martínez , L. A. Contreras-Angulo , C. A. Elizalde-Romero , and J. B. Heredia . Plant alkaloids: Structures and bioactive properties. In Swamy, M. K. (Ed.), *Plant-Derived Bioactives: Chemistry and Mode of Action*, pp. 85–117. Singapore: Springer, 2020.

Huang, W. , Y. Wang , W. Tian , X. Cui , P. Tu , J. Li , and X. Liu . Biosynthesis investigations of terpenoid, alkaloid, and flavonoid antimicrobial agents derived from medicinal plants. *Antibiotics* 11, no. 10 (2022): 1380.

Isaoglu, M. , M. Güllüce , and M. Karadayı . Plant-derived natural products as multidrug resistance modulators in cancer therapy. *Anatolian Journal of Biology* 1, no. 2 (2020): 1–51.

Jursky, F. , and M. Baliova . Differential effect of the benzophenanthridine alkaloids sanguinarine and chelerythrine on glycine transporters. *Neurochemistry International* 58, no. 6 (2011): 641–647.

Kamran, S. , A. Sinniah , M. A. Abdulghani , and M. A. Alshawsh . Therapeutic potential of certain terpenoids as anticancer agents: A scoping review. *Cancers* 14, no. 5 (2022): 1100.

Kaysheva, A. L. , A. T. Kopylov , A. A. Stepanov , K. A. Malsagova , A. A. Izotov , Y. I. Shurubor , and B. F. Krasnikov . Chromatomass-spectrometric method for the quantitative determination of amino- and carboxylic acids in biological samples. *Metabolites* 13, no. 1 (2022): 16.

Khan, M. , A. J. Shah , and A. H. Gilani . Insight into the bronchodilator activity of Vitex negundo. *Pharmaceutical Biology* 53, no. 3 (2015): 340–344.

Krishna Sri, P. S. B. J. , and S. Padmavathy . A short review on the effect of functional group in methylxanthine (caffeine) class of drugs. *Biochemical Pharmacology (Los Angeles)* 7, no. 257 (2018): 1000257.

Kumar, S. Alkaloidal drugs: A review. *Asian Journal of Pharmaceutical Sciences and Technology* 4, no. 3 (2014): 107–119.

Laghezza Masci, V. , S. Bernardini , L. Modesti , E. Ovidi , and A. Tiezzi . Medicinal plants as a source of alkaloids. In Egamberdieva, D. , and Tiezzi, A. (Eds.), *Medically Important Plant Biomes: Source of Secondary Metabolites*, pp. 85–113. Singapore: Springer, 2019.

Leão, A. H. , A. J. Sarmiento-Silva , J. R. Santos , A. M. Ribeiro , and R. H. Silva . Molecular, neurochemical, and behavioral hallmarks of reserpine as a model for Parkinson's disease: New perspectives to a long-standing model. *Brain Pathology* 25, no. 4 (2015): 377–390.

Lin, S. X. , M. A. Curtis , and J. Sperry . Pyridine alkaloids with activity in the central nervous system. *Bioorganic & Medicinal Chemistry* 28, no. 24 (2020): 115820.

Majrashi, M. , S. Ramesh , J. Deruiter , V. Mulabagal , S. Pondugula , R. Clark , and M. Dhanasekaran . Multipotent and poly-therapeutic fungal alkaloids of *Claviceps purpurea*. In Agrawal, D. C. , Tsay, H.-S. , Shyur, L.-F. , and Wu, Y.-C. (Eds.), *Medicinal Plants and Fungi: Recent Advances in Research and Development*, pp. 229–252. Singapore: Springer, 2017.

Martins, G. A. , and J. L. Bicas . Antifungal activity of essential oils of tea tree, oregano, thyme, and cinnamon, and their components. *Brazilian Journal of Food Technology* 27 (2024): e2023071.

Masihuddin, M. , M. A. Jafri , A. Siddiqui , and S. Chaudhary . Traditional uses, phytochemistry, and pharmacological activities of *Papaver somniferum* with special reference to unani medicine:

An updated review. *Journal of Drug Delivery and Therapeutics* 8, no. 5-s (2018): 110–114.

McArthur, J. R. , R. K. Finol-Urdaneta , and D. J. Adams . Analgesic transient receptor potential vanilloid-1-active compounds inhibit native and recombinant T-type calcium channels. *British Journal of Pharmacology* 176, no. 13 (2019): 2264–2278.

Monteiro, J. P. , M. G. Alves , P. F. Oliveira , and B. M. Silva . Structure-bioactivity relationships of methylxanthines: Trying to make sense of all the promises and the drawbacks. *Molecules* 21, no. 8 (2016): 974.

Musiol, R. , K. Malarz , and J. Mularski . Quinoline alkaloids against neglected tropical diseases. *Current Organic Chemistry* 21, no. 18 (2017): 1896–1906.

Othman, L. , A. Sleiman , and R. M. Abdel-Massih . Antimicrobial activity of polyphenols and alkaloids in Middle Eastern plants. *Frontiers in Microbiology* 10 (2019): 911.

Parthasarathy, A. , E. J. Borrego , M. A. Savka , R. C. J. Dobson , and A. O. Hudson . Amino acid-derived defense metabolites from plants: A potential source to facilitate novel antimicrobial development. *Journal of Biological Chemistry* 296 (2021): 100438.

Pathan, H. , and J. Williams . Basic opioid pharmacology: An update. *British Journal of Pain* 6, no. 1 (2012): 11–16.

Phukan, M. M. , S. R. Sangma , D. Kalita , P. Bora , P. P. Das , K. Manoj , and K. M. Sundaram . Alkaloids and terpenoids: Synthesis, classification, isolation and purification, reactions, and applications. In Verma, C. , and Verma, D. K. (Eds.), *Handbook of Biomolecules*, pp. 177–213. Amsterdam: Elsevier, 2023.

Plazas, E. , and N. Faraone . Indole alkaloids from psychoactive mushrooms: Chemical and pharmacological potential as psychotherapeutic agents. *Biomedicines* 11, no. 2 (2023): 461.

Proshkina, E. , S. Plyusnin , T. Babak , E. Lashmanova , F. Maganova , L. Koval , E. Platonova , M. Shaposhnikov , and A. Moskalev . Terpenoids as potential geroprotectors. *Antioxidants* 9, no. 6 (2020): 529.

Rea, W. J. , and K. D. Patel (Eds.). *Terpenes and terpenoids*. In *Reversibility of Chronic Disease and Hypersensitivity*, vol. 4, pp. 905–930. Boca Raton, FL: CRC Press, 2017.

Robertson, J. , and K. Stevens . Pyrrolizidine alkaloids. *Natural Product Reports* 31, no. 12 (2014): 1721–1788.

Salehi, A. , M. Ghanadian , B. Zolfaghari , A. R. Jassbi , M. Fattahian , P. Reisi , and Z. Ali . Neuropharmacological potential of diterpenoid alkaloids. *Pharmaceuticals* 16, no. 5 (2023): 747.

Sánchez-Martínez, J. D. , M. Bueno , G. Alvarez-Rivera , J. Tudela , E. Ibañez , and A. Cifuentes . In vitro neuroprotective potential of terpenes from industrial orange juice by-products. *Food & Function* 12, no. 1 (2021): 302–314.

Sarkar, A. , and S. Bhattacharjee . Terpenoids in treatment of immunological disease. In Roy, D. N. (Ed.), *Terpenoids against Human Diseases*, pp. 119–175. Boca Raton, FL: CRC Press, 2019.

Seelinger, G. , I. Merfort , and C. M. Schempp . Anti-oxidant, anti-inflammatory and anti-allergic activities of luteolin. *Planta Medica* 74, no. 14 (2008): 1667–1677.

Seifu, D. , F. Assefa , and S. M. Abay . Medicinal plants as antioxidant agents: Understanding their mechanism of action and therapeutic efficacy. In Capasso, A. (Ed.), *Medicinal Plants as Antioxidant Agents: Understanding Their Mechanism of Action and Therapeutic Efficacy*, pp. 97–145. Kerala: Research Signpost, 2012.

Shakhidoyatov, K. M. , and B. Z. Elmuradov . Tricyclic quinazoline alkaloids: Isolation, synthesis, chemical modification, and biological activity. *Chemistry of Natural Compounds* 50 (2014): 781–800.

Shakya, A. K. Medicinal plants: Future source of new drugs. *International Journal of Herbal Medicine* 4, no. 4 (2016): 59–64.

Sharma, A. , A. Biharee , A. Kumar , and V. Jaitak . Antimicrobial terpenoids as a potential substitute in overcoming antimicrobial resistance. *Current Drug Targets* 21, no. 14 (2020): 1476–1494.

Sharma, N. , V. K. Sharma , H. K. Manikyam , and A. B. Krishna . Ergot alkaloids: A review on therapeutic applications. *European Journal of Medicinal Plants* 14, no. 3 (2016): 1–17.

Sharma, V. K. , A. Sharma , K. K. Verma , P. K. Gaur , R. Kaushik , and B. A. Abdali . A comprehensive review on pharmacological potentials of caffeine. *Journal of Applied Pharmaceutical Sciences and Research* 6, no. 3 (2023): 16–26.

Shim, K. H. , M. J. Kang , N. Sharma , and S. S. A. An . Beauty of the beast: Anticholinergic tropane alkaloids in therapeutics. *Natural Products and Bioprospecting* 12, no. 1 (2022): 33.

Soares, G. A. B. , T. Bhattacharya , T. Chakrabarti , P. Tagde , and S. Cavalu . Exploring pharmacological mechanisms of essential oils on the central nervous system. *Plants* 11, no. 1 (2021): 21.

Touaibia, M. , C. Boutekedjiret , S. Perino , and F. Chemat . Natural terpenes as building blocks for green chemistry. In Li, Y. , and Chemat, F. (Eds.), *Plant-Based "Green Chemistry 2.0"*, pp. 171–195. Singapore: Springer, 2019.

Ushie, O. A. , E. O. Ochepe , P. Y. Nkom , M. A. Ago , and J. Gani . Medicinal uses of nitrogen group containing secondary metabolites. *Tropical Journal of Science and Technology* 4, no. 1 (2023): 71–82.

Veeresham, C. Natural products derived from plants as a source of drugs. *Journal of Advanced Pharmaceutical Technology & Research* 3, no. 4 (2012): 200–201.

Wang, H. Y. L. , and G. A. O'Doherty . Modulators of Na/K-ATPase: A patent review. *Expert Opinion on Therapeutic Patents* 22, no. 6 (2012): 587–605.

Wani, Z. A. , and S. Pant . Assessment of floristic diversity and community characteristics of Gulmarg Wildlife Sanctuary, Kashmir Himalaya. *Geology, Ecology, and Landscapes* 9 (2023): 1–21.

Wink, M. Molecular modes of action of cytotoxic alkaloids: From DNA intercalation, spindle poisoning, topoisomerase inhibition to apoptosis and multiple drug resistance. *Alkaloids: Chemistry and Biology* 64 (2007): 1–47.

Yakkala, P. A. , N. R. Penumallu , S. Shafi , and A. Kamal . Prospects of topoisomerase inhibitors as promising anti-cancer agents. *Pharmaceuticals* 16, no. 10 (2023): 1456.

Yang, H. , and Q. Ping Dou . Targeting apoptosis pathway with natural terpenoids: Implications for treatment of breast and prostate cancer. *Current Drug Targets* 11, no. 6 (2010): 733–744.

Yang, J. , K. Ye , R. Zhang , X. Fan , R. Xiong , S. Zhang , and X. Ou . The characteristics and molecular targets of antiarrhythmic natural products. *Biomedicine & Pharmacotherapy* 168 (2023): 115762.

Yang, W. , X. Chen , Y. Li , S. Guo , Z. Wang , and X. Yu . Advances in pharmacological activities of terpenoids. *Natural Product Communications* 15, no. 3 (2020): 1934578X20903555.

Zhu, H. L. , R. D. Wassall , M. Takai , H. Morinaga , M. Nomura , T. C. Cunnane , and N. Teramoto . Actions of veratridine on tetrodotoxin-sensitive voltage-gated Na<sup>+</sup> currents, NaV1.6, in murine vas deferens myocytes. *British Journal of Pharmacology* 157, no. 8 (2009): 1483–1493.

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Aires A , ed. *Tannins: Structural Properties, Biological Properties and Current Knowledge*. London: IntechOpen.

Bhat AA , Kaur G , Tandon N , Tandon R , Singh I. Current advancements in synthesis, anticancer activity, and structure–activity relationship (SAR) of coumarin derivatives. *Inorganic Chemistry Communications*. 2024 May; 22:112605.

Bhatia R , Thapliyal K , Kumar D. *Phytochemical and Therapeutic Aspects of Morinda citrifolia L. (Noni Plant): A Review*. *Research Journal of Pharmacognosy and Phytochemistry*. 2015; 7(3):167–174.

Bravo L. Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. *Nutrition Reviews*. 1998 Nov 1; 56(11):317–333.

Bule M , Khan F , Nisar MF , Niaz K , Nabavi S , Saeedi M , Sanches Silva A. Tannins (hydrolysable tannins, condensed tannins, phlorotannins, flavono-ellagitannins). *Recent Advances in Natural Products Analysis*. 2020:132–146.

Busse W , et.al. The significance of quality for efficacy and safety of herbal medicinal products. *Drug Information Journal*. 2000 Jan; 34(1):15–23.

Dobhal K , Garg R , Singh A , Semwal A. Insight into the Natural Biomolecules (BMs): Promising Candidates as Zika Virus Inhibitors. *Infectious Disorders-Drug TargetsDisorders*. 2024 Nov 1; 24(7):1–7.

Guo Y , Li Z , Chen F , Chai Y. Polyphenols in oral health: Homeostasis maintenance, disease prevention, and therapeutic applications. *Nutrients*, 2023; 15(20):4384.

<https://doi.org/10.3390/nu15204384>

Havsteen B. Flavonoids , a class of natural products of high pharmacological potency. *Biochemical Pharmacology*. 1983; 32(7):1141–1148. [https://doi.org/10.1016/0006-2952\(83\)90262-9](https://doi.org/10.1016/0006-2952(83)90262-9)

Hung WL , Suh JH , Wang Y. Chemistry and health effects of furanocoumarins in grapefruit. *Journal of Food and Drug Analysis*. 2017 Jan;25(1):71–83. doi: 10.1016/j.jfda.2016.11.008. Epub 2016 Dec 6 . PMID: 28911545; PMCID: PMC9333421.

Iqbal N , Iqbal N. Imatinib: a breakthrough of targeted therapy in cancer. *Chemotherapy Research and Practice*. 2014; 2014:357027. doi: 10.1155/2014/357027. Epub 2014 May 19 . PMID: 24963404; PMCID: PMC4055302

Jakobek L. Interactions of polyphenols with carbohydrates, lipids and proteins. *Food Chemistry*. 2015; 175:556–67. <https://doi.org/10.1016/j.foodchem.2014.12.013>

Janković M , Berežni S , Orčić D. Lignan profile in fruits of wild chervil (*Anthriscus sylvestris* (L.) Hoffm.). *Facta Universitatis, Series: Physics. Chemistry and Technology*. 2024 Jan 9:027–37.

Juríková T , Balla S , Sochor J , Pohanka M , Mlcek J , Baron M. Flavonoid profile of Saskatoon berries (*Amelanchier alnifolia* Nutt.) and their health promoting effects. *Molecules* (Basel, Switzerland). 2013; 18(10):12571–12586. <https://doi.org/10.3390/molecules181012571>.

Kahraman C , Arituluk ZC , Cankaya II . The clinical importance of herb-drug interactions and toxicological risks of plants and herbal products. *Medical Toxicology*. 2020 Apr; 12:1–31.

Kayal G , Jain K , Malviya S , Kharia A. Comparative SAR of synthetic coumarin derivatives for their anti-inflammatory activity. *International Journal of Pharmaceutical Sciences and Research*. 2014 Sep 1; 5(9):3577.

Khare S , Dewangan RP , Kumar A. Structure-activity relationship of flavonoids: Recent updates. In *The Chemistry Inside Spices & Herbs: Research and Development*. Sharjah: Bentham Science Publishers. 2022:235–56.

Klessig DF , Tian M , Choi HW . Multiple targets of salicylic acid and its derivatives in plants and animals. *Frontiers in Immunology*. 2016 May 26; 7:206.

Kumar N , Pruthi V. Potential applications of ferulic acid from natural sources. *Biotechnol Reports (Amst)*. 2014 Sep 16; 4:86–93. doi: 10.1016/j.btre.2014.09.002. PMID: 28626667; PMCID: PMC5466124.

Luca SV , Macovei I , Bujor A , Miron A , Skalicka-Woźniak K , Aprotosoaie AC , Trifan A. Bioactivity of dietary polyphenols: The role of metabolites. *Critical Reviews in Food Science and Nutrition*. 2020; 60(4):626–659. <https://doi.org/10.1080/10408398.2018.1546669>

Miura T , Muraoka S , Ikeda N , Watanabe M , Fujimoto Y. Antioxidative and prooxidative action of stilbene derivatives. *Pharmacology & Toxicology*. 2000 May; 86(5):203–208.

Molino S , Francino MP , Henares JÁ . Why is it important to understand the nature and chemistry of tannins to exploit their potential as nutraceuticals?. *Food Research International*. 2023 Jul; 27:113329.

MontesÁvila J , LópezAngulo G , DelgadoVargas F. Tannins in fruits and vegetables: Chemistry and biological functions. *Fruit and Vegetable Phytochemicals: Chemistry and Human Health*, 2nd Edition. 2017 Oct; 11:221–68.

Pecyna P , Wargula J , Murias M , Kucinska M. More than resveratrol: New insights into stilbene-based compounds. *Biomolecules*. 2020 Jul 27; 10(8):1111.

Rana AC , Gulliyya B. Chemistry and pharmacology of flavonoids-A review. *Indian Journal of Pharmaceutical Education & Research*. 2019 Jan 1; 53(1).

Sepehri S , Khedmati M , Yousef-Nejad F , Mahdavi M. Medicinal chemistry perspective on the structure–activity relationship of stilbene derivatives. *RSC Advances*. 2024; 14(28):19823–19879.

Shi Y , Wang J , Yan H. Therapeutic potential of naturally occurring lignans as anticancer agents. *Current Topics in Medicinal Chemistry*. 2022 Jul 1; 22(17):1393–1405.

Siddique MU , Barbhuiya TK , Sinha BN , Jayaprakash V. Phytoestrogens and their synthetic analogues as substrate mimic inhibitors of CYP1B1. *European Journal of Medicinal Chemistry*. 2019 Feb 1; 163:28–36.

Sriram K , Insel PA . G protein-coupled receptors as targets for approved drugs: How many targets and how many drugs? *Molecular Pharmacology*. 2018 Apr; 93(4):251–258. doi: 10.1124/mol.117.111062. Epub 2018 Jan 3 . PMID: 29298813; PMCID: PMC5820538.

Tahir AH , Hussain Z , Yousuf H , Fazal F , Tahir MA , Kashif M. Traditional herbal medicine and its clinical relevance: a need to preserve the past for the future. *Journal of Biosciences and Medicines*. 2022 Jul 1; 10(7):64–75.

Valletta A , Iozia LM , Leonelli F. Impact of environmental factors on stilbene biosynthesis. *Plants*. 2021 Jan 4; 10(1):90.

## Plant Extract versus Natural Therapy

Agrawal, Rutvi , Priyanka Jurel , Rohitas Deshmukh , Ranjit Kumar Harwansh , Akash Garg , Ashwini Kumar , Sudarshan Singh , Ajay Guru , Arun Kumar , and Vinoth Kumarasamy . Emerging trends in the treatment of skin disorders by herbal drugs: traditional and nanotechnological approach. *Pharmaceutics* 16, no. 7 (2024): 869.

AlMohammed, Hamdan I. , Nada A. Alanazi , Esraa Fahad Maghrabi , and Manar A. Alotaibi . [Retracted] Role of aromatherapy as a natural complementary and alternative therapy in cardiovascular disease: a comprehensive systematic review. *EvidenceBased Complementary and Alternative Medicine* 2022, no. 1 (2022): 4543078.

Anwar, Nooryasmin , Yong Kiat Teo , and Joash Ban Lee Tan . The role of plant metabolites in drug discovery: current challenges and future perspectives. In Mallappa Kumara Swamy , and Mohd Sayeed Akhtar (Eds.), *Natural Bio-active Compounds: Volume 2: Chemistry, Pharmacology and Health Care Practices*, pp. 25–51. Springer Nature, Singapore (2019).

Ayuba, Dauda , Precious Kehinde Fadele , Jerico B. Ogaya , Kolawole Emmanuel Olayinka , Shashikant Nishant Sharma , and Don Eliseo Lucero-Prisno III . Understanding the root of healing and beyond: exploring the way forward for alternative medicine in Nigeria. *Bhutan Sorig Journal* 1, no. 1 (2024): 42–47.

Bachtel, Nathaniel , and Kavita Israni-Winger . Focus: plant-based medicine and pharmacology: introduction. *The Yale Journal of Biology and Medicine* 93, no. 2 (2020): 227.

Bolouri, Parisa , Robab Salami , Shaghayegh Kouhi , Masoumeh Kordi , Behnam Asgari Lajayer , Javad Hadian , and Tess Astatkie . Applications of essential oils and plant extracts in different industries. *Molecules* 27, no. 24 (2022): 8999.

Chaachouay, Nouredine , and Lahcen Zidane . Plant-derived natural products: a source for drug discovery and development. *Drugs and Drug Candidates* 3, no. 1 (2024): 184–1207.

Chen, Xi , Kun Zhang , Jia Heng Liang , Linxin You , Tian Qiu , and Yen Wei . Unleashing excellent antibacterial performance of natural rubber composites via herbal extracts. *Composites Part B: Engineering* 272 (2024): 111171.

Dean, Muhajirin . Green medicine: exploring the role of herbal treatments in disease therapy. *Golden Ratio of Data in Summary* 4, no. 1 (2024): 1–10.

Dhama, Kuldeep , Kumaragurubaran Karthik , Rekha Khandia , Ashok Munjal , Ruchi Tiwari , Rajneesh Rana , Sandip K. Khurana et al. Medicinal and therapeutic potential of herbs and plant metabolites/extracts countering viral pathogens-current knowledge and future prospects. *Current Drug Metabolism* 19, no. 3 (2018): 236–2263.

Díaz , Alexis Uriel Soto , María Luisa Villarreal , Marcelo Victorio-De los Santos , and Alexandre Toshirrico Cardoso-Taketa . Antibacterial and antioxidant activities of hydroalcoholic and phenolic extracts from *Ternstroemia dentisepala* and *T. lineata* leaves. *Plants* 13, no. 17 (2024): 2515.

Falcão, Deborah Q. , Adriana P. Oliveira , Barbara G. Lima , Anne C. A. Cardoso , Kessiane B. Almeida , Thamyres C. Santos , Leonor M. Nascimento et al. Nanotechnology in phytotherapy: current challenges of lipid-based nanocarriers for the delivery of natural products. In Alexandru Mihai Grumezescu (Ed.), *Lipid Nanocarriers for Drug Targeting*, pp. 139–1174. William Andrew Publishing, Oxford (2018).

Fariello, Jennifer Yonaitis , and Robert M. Moldwin . Update on the use of phytotherapy for voiding symptoms. *Current Bladder Dysfunction Reports* 5, no. 4 (2010): 191–1197.

Givati, Assaf . Performing 'pragmatic holism': professionalisation and the holistic discourse of non-medically qualified acupuncturists and homeopaths in the United Kingdom. *Health* 19, no. 1 (2015): 34–50.

Gupta, Rajeev . Integrating modern, alternative and complementary medicine: a holistic approach to better patient care and cost-effectiveness. *World Journal of Advanced Science and Technology* 3 (2023): 006–0020.

Hosseinzadeh, Saleh , Azizollah Jafarikukhdan , Ahmadreza Hosseini , and Raham Armand . The application of medicinal plants in traditional and modern medicine: a review of Thymus

vulgaris. *International Journal of Clinical Medicine* 6, no. 9 (2015): 635–6642.

Kyomugisha, Hope . Traditional medicine: oversight of practitioners and practices in Uganda. Available at SSRN 1322093 (2008). Available at SSRN: <https://ssrn.com/abstract=1322093> or <http://dx.doi.org/10.2139/ssrn.1322093>

Latarissa, Irma Rahayu , Anna Meiliana , Ida Paulina Sormin , Erizal Sugiono , Nasrul Wathoni , Melisa Intan Barliana , and Keri Lestari . The efficacy of herbal medicines on the length of stay and negative conversion time/rate outcomes in patients with COVID-19: a systematic review. *Frontiers in Pharmacology* 15 (2024): 1383359.

Li, Fu-Shuang , and Jing-Ke Weng . Demystifying traditional herbal medicine with modern approach. *Nature Plants* 3, no. 8 (2017): 1–7.

Michalak, Monika . Plant extracts as skin care and therapeutic agents. *International Journal of Molecular Sciences* 24, no. 20 (2023): 15444.

Miller, James S . The global importance of plants as sources of medicines and the future potential of Chinese plants. In Yuan Lin (Ed.), *Drug Discovery and Traditional Chinese Medicine: Science, Regulation, and Globalization*, pp. 33–42. Springer, Boston, MA (2001).

Petrovska, Biljana Bauer . Historical review of medicinal plants' usage. *Pharmacognosy Reviews* 6, no. 11 (2012): 1.

Proestos, Charalampos . The benefits of plant extracts for human health. *Foods* 9, no. 11 (2020): 1653.

Rahman, Md Habibur , Johny Bajgai , Ailyn Fadriuela , Subham Sharma , Thuy Thi Trinh , Rokeya Akter , Yun Ju Jeong , Seong Hoon Goh , Cheol-Su Kim , and Kyu-Jae Lee . Therapeutic potential of natural products in treating neurodegenerative disorders and their future prospects and challenges. *Molecules* 26, no. 17 (2021): 5327.

Ribeiro, Ana Sofia , Marilene Estanqueiro , M. Beatriz Oliveira , and José Manuel Sousa Lobo . Main benefits and applicability of plant extracts in skin care products. *Cosmetics* 2, no. 2 (2015): 48–65.

Rosenbloom, Richard A. , Jayesh Chaudhary , and Diane Castro-Eschenbach . Traditional botanical medicine: an introduction. *American Journal of Therapeutics* 18, no. 2 (2011): 158–1161.

Saad, Bashar , Hassan Azaizeh , and Omar Said . Tradition and perspectives of Arab herbal medicine: a review. *EvidenceBased Complementary and Alternative Medicine* 2, no. 4 (2005): 475–4479.

Salm, Sandra , Jochen Rutz , Marjan van den Akker , Roman A. Blaheta , and Beatrice E. Bachmeier . Current state of research on the clinical benefits of herbal medicines for non-life-threatening ailments. *Frontiers in Pharmacology* 14 (2023): 1234701.

Singh, Amandeep , Deepak Nanda , Abhishek Bhardwaj , and Ashok Kumar . A pharmacological investigation for therapeutic potential of *Callistemon citrinus* as an anthelmintic agent (Bottle-Brush Plant). *IP International Journal of Comprehensive and Advanced Pharmacology* 9, no. 3 (2024): 206–2210.

Sofowora, Abayomi , Eyitope Ogunbodede , and Adedeji Onayade . The role and place of medicinal plants in the strategies for disease prevention. *African Journal of Traditional, Complementary and Alternative Medicines* 10, no. 5 (2013): 210–2229.

Stone, Julie , and Joan Matthews . *Complementary Medicine and the Law*. Oxford University Press, Oxford (1996).

UCI School of Medicine. 2023. A UCI-led study found that plant extracts used by indigenous people hold promise in treatment of ataxia. <https://medschool.uci.edu/news/uci-led-study-found-plant-extracts-used-indigenous-people-hold-promise-treatment-ataxia>

Vaou, Natalia , Elisavet Stavropoulou , Chrysa Voidarou , Christina Tsigalou , and Eugenia Bezirtzoglou . Towards advances in medicinal plant antimicrobial activity: a review study on challenges and future perspectives. *Microorganisms* 9, no. 10 (2021): 2041.

Vora, Lalitkumar K. , Amol D. Gholap , Navnath T. Hatvate , Padmashri Naren , SABIYA Khan , Vivek P. Chavda , Pankti C. Balar , Jimil Gandhi , and Dharmendra Kumar Khatri . Essential oils for clinical aromatherapy: a comprehensive review. *Journal of Ethnopharmacology* (2024): 118180.

Wachtel-Galor, Sissi , and Iris F. F. Benzie (Eds.). *Herbal medicine: an introduction to its history, usage, regulation, current trends, and research needs*. In: *Herbal Medicine: Biomolecular and Clinical Aspects*. 2nd edition. CRC Press/Taylor & Francis, Boca Raton, FL (2012).

Wang, Hongting , Ying Chen , Lei Wang , Qinghui Liu , Siyu Yang , and Cunqin Wang . Advancing herbal medicine: enhancing product quality and safety through robust quality control practices. *Frontiers in Pharmacology* 14 (2023): 1265178.

## Anticancer Molecules from Plants and Their Applicability

- Agrawal, Dinesh Kumar , and Pushpesh Kumar Mishra . 2010. Curcumin and its analogues: Potential anticancer agents. *Medicinal Research Reviews* 30 (5): 818–860. <https://doi.org/10.1002/med.20188>
- Ahmad, Rizwan , Aljawharah Alqathama , Mohammed Aldholmi , Muhammad Riaz , Mohammed H. Mukhtar , Fatema Aljishi , Ebtihal Althomali , et al. 2022. Biological screening of *Glycyrrhiza glabra* L. from different origins for antidiabetic and anticancer activity. *Pharmaceuticals* 16 (1): 7. <https://doi.org/10.3390/ph16010007>
- Ahmad, Rumana , Mohsin A. Khan , A. N. Srivastava , Anamika Gupta , Aditi Srivastava , Tanvir R. Jafri , Zainab Siddiqui , Sunaina Chaubey , Tahmeena Khan , and Arvind K. Srivastava . 2020. Anticancer potential of dietary natural products: A comprehensive review. *Anti-Cancer Agents in Medicinal Chemistry* 20 (2): 122–1236. <https://doi.org/10.2174/1871520619666191015103712>
- Alami Merrouni, Ilyass , and Mostafa Elachouri . 2021. Anticancer medicinal plants used by Moroccan people: Ethnobotanical, preclinical, phytochemical and clinical evidence. *Journal of Ethnopharmacology* 266 (February): 113435. <https://doi.org/10.1016/j.jep.2020.113435>
- Atanasov, Atanas G. , Birgit Waltenberger , Eva-Maria Pferschy-Wenzig , Thomas Linder , Christoph Wawrosch , Pavel Uhrin , Veronika Temml , et al. 2015. Discovery and resupply of pharmacologically active plant-derived natural products: A review. *Biotechnology Advances* 33 (8): 1582–1614. <https://doi.org/10.1016/j.biotechadv.2015.08.001>
- Azeem, Muhammad , Muhammad Hanif , Khalid Mahmood , Nabeela Ameer , Fazal Rahman Sajid Chughtai , and Usman Abid . 2023. “An insight into anticancer, antioxidant, antimicrobial, antidiabetic and anti-inflammatory effects of quercetin: A review.” *Polymer Bulletin* 80 (1): 241–262. <https://doi.org/10.1007/s00289-022-04091-8>
- Banskota, Arjun H. , Takema Nagaoka , Lucia Yoshie Sumioka , Yasuhiro Tezuka , Suresh Awale , Kiyoshi Midorikawa , Katsumichi Matsushige , and Shigetoshi Kadota . 2002. Antiproliferative activity of the Netherlands propolis and its active principles in cancer cell lines. *Journal of Ethnopharmacology* 80 (1): 67–73. [https://doi.org/10.1016/S0378-8741\(02\)00022-3](https://doi.org/10.1016/S0378-8741(02)00022-3)
- Banskota, Arjun H. , Yasuhiro Tezuka , and Shigetoshi Kadota . 2001. Recent progress in pharmacological research of propolis. *Phytotherapy Research* 15 (7): 561–571. <https://doi.org/10.1002/ptr.1029>
- Batra, Priya , and Anil K. Sharma . 2013. Anti-cancer potential of flavonoids: Recent trends and future perspectives. *3 Biotech* 3 (6): 439–459. <https://doi.org/10.1007/s13205-013-0117-5>
- Bitwell, Chibuye , Singh Sen Indra , Chimuka Luke , and Maseka Kenneth Kakoma . 2023. A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants. *Scientific African* 19 (March): e01585. <https://doi.org/10.1016/j.sciaf.2023.e01585>
- Chavda, Vivek P. , Lakshmi Vineela Nalla , Pankti Balar , Rajashri Bezbaruah , Vasso Apostolopoulos , Rajeev K. Singla , Avinash Khadela , Lalitkumar Vora , and Vladimir N. Uversky . 2023. Advanced phytochemical-based nanocarrier systems for the treatment of breast cancer. *Cancers* 15 (4): 1023. <https://doi.org/10.3390/cancers15041023>
- Das, Deepak , and Syed Shafi . 2023. Bioactivity-guided fractionation and identification of bioactive molecules: A basic method in drug discovery. In Vikrant Singh Rajput , and Ashish Runthala, A. (Eds.), *Drugs and a Methodological Compendium*, pp. 41–78. Singapore: Springer Nature Singapore. [https://doi.org/10.1007/978-981-19-7952-1\\_3](https://doi.org/10.1007/978-981-19-7952-1_3)
- Davis, Ian D. 2000. An overview of cancer immunotherapy. *Immunology & Cell Biology* 78 (3): 179–195. <https://doi.org/10.1046/j.1440-1711.2000.00906.x>
- Debnath, Bikash , Waikhom Somraj Singh , and Kuntal Manna . 2023. A phytopharmacological review on *Ananas comosus*. *Advances in Traditional Medicine* 23 (2): 291–298. <https://doi.org/10.1007/s13596-021-00563-w>



Dehelean, Cristina Adriana , Iasmina Marcovici , Codruta Soica , Marius Mioc , Dorina Coricovac , Stela Iurciuc , Octavian Marius Cretu , and Iulia Pinzaru . 2021. Plant-derived anticancer compounds as new perspectives in drug discovery and alternative therapy. *Molecules* 26 (4): 1109. <https://doi.org/10.3390/molecules26041109>

Demain, Arnold L. , and Preeti Vaishnav . 2011. Natural products for cancer chemotherapy. *Microbial Biotechnology* 4 (6): 687–699. <https://doi.org/10.1111/j.1751-7915.2010.00221.x>

Dhyani, Praveen , Cristina Quispe , Eshita Sharma , Amit Bahukhandi , Priyanka Sati , Dharam Chand Attri , Agnieszka Szopa , et al. 2022. Anticancer potential of alkaloids: A key emphasis to colchicine, vinblastine, vincristine, vindesine, vinorelbine and vincamine. *Cancer Cell International* 22 (1): 206. <https://doi.org/10.1186/s12935-022-02624-9>

Dong, Songtao , Xiangnan Guo , Fei Han , Zhonggui He , and Yongjun Wang . 2022. Emerging Role of natural products in cancer immunotherapy. *Acta Pharmaceutica Sinica B* 12 (3): 1163–1185. <https://doi.org/10.1016/j.apsb.2021.08.020>

Dou, Jinze , Jari Heinonen , Tapani Vuorinen , Chunlin Xu , and Tuomo Sainio . 2021. Chromatographic recovery and purification of natural phytochemicals from underappreciated willow bark water extracts. *Separation and Purification Technology* 261 (April): 118247. <https://doi.org/10.1016/j.seppur.2020.118247>

Esghaei, Maryam , Hadi Ghaffari , Bahman Rahimi Esboei , Zienab Ebrahimi Tapeh , Farah Bokharaei Salim , and Manijeh Motevalian . 2018. Evaluation of anticancer activity of *Camellia sinensis* in the Caco-2 colorectal cancer cell line. *Asian Pacific Journal of Cancer Prevention* 19 (6): 1697–11701.

Ezzati, Maryam , Bahman Yousefi , Kobra Velaei , and Amin Safa . 2020. A review on anti-cancer properties of quercetin in breast cancer. *Life Sciences* 248 (May): 117463. <https://doi.org/10.1016/j.lfs.2020.117463>

Fakhri, Sajad , Fatemeh Abbaszadeh , Masoumeh Jorjani , and Mohammad Hossein Pourgholami . 2021. The effects of anticancer medicinal herbs on vascular endothelial growth factor based on pharmacological aspects: A review study. *Nutrition and Cancer* 73 (1): 1–15. <https://doi.org/10.1080/01635581.2019.1673451>

Farha, Arakkaveetil Kabeer , Ren-You Gan , Hua-Bin Li , Ding-Tao Wu , Atanas G. Atanasov , Khalid Gul , Jia-Rong Zhang , Qiong-Qiong Yang , and Harold Corke . 2022. The anticancer potential of the dietary polyphenol rutin: Current status, challenges, and perspectives. *Critical Reviews in Food Science and Nutrition* 62 (3): 832–859. <https://doi.org/10.1080/10408398.2020.1829541>

Fridlender, Marcelo , Yoram Kapulnik , and Hinanit Koltai . 2015. Plant derived substances with anti-cancer activity: From folklore to practice. *Frontiers in Plant Science* 6 (October). <https://doi.org/10.3389/fpls.2015.00799>

Gan, Ren-You , Hua-Bin Li , Zhong-Quan Sui , and Harold Corke . 2018. Absorption, metabolism, anti-cancer effect and molecular targets of epigallocatechin gallate (EGCG): An updated review. *Critical Reviews in Food Science and Nutrition* 58 (6): 924–941. <https://doi.org/10.1080/10408398.2016.1231168>

Garcia-Oliveira, Paula , Paz Otero , Antia Gonzalez Pereira , Franklin Chamorro , Maria Carpena , Javier Echave , Maria Fraga-Corral , Jesus Simal-Gandara , and Miguel Angel Prieto . 2021. Status and challenges of plant-anticancer compounds in cancer treatment. *Pharmaceuticals* 14 (2): 157. <https://doi.org/10.3390/ph14020157>

Huang, Min , Jin-Jian Lu , and Jian Ding . 2021. Natural products in cancer therapy: Past, present and future. *Natural Products and Bioprospecting* 11 (1): 5–13. <https://doi.org/10.1007/s13659-020-00293-7>

Ihedioha, Thelma E. , Isaac U. Asuzu , Aruh O. Anaga , John I. Ihedioha , and Charles O. Nnadi . 2023. Bioassay guided fractionation, isolation and characterization of hepatotherapeutic 1,3-di-ortho-galloyl quinic acid from the methanol extract of the leaves of *Pterocarpus santalinoides*. *Journal of Ethnopharmacology* 301 (January): 115864. <https://doi.org/10.1016/j.jep.2022.115864>

Iqbal, Javed , Banzeer Ahsan Abbasi , Tariq Mahmood , Sobia Kanwal , Barkat Ali , Sayed Afzal Shah , and Ali Talha Khalil . 2017. Plant-derived anticancer agents: A green anticancer approach. *Asian Pacific Journal of Tropical Biomedicine* 7 (12): 1129–1150. <https://doi.org/10.1016/j.apjtb.2017.10.016>

Jang, Won Young , Ji Yeon Hwang , and Jae Youl Cho . 2023. Ginsenosides from *Panax ginseng* as key modulators of NF- $\kappa$ B signaling are powerful anti-inflammatory and anticancer agents. *International Journal of Molecular Sciences* 24 (7): 6119.

<https://doi.org/10.3390/ijms24076119>

Jaskulska, Agata , Anna Ewa Janecka , and Katarzyna Gach-Janczak . 2020. Thapsigargin: From traditional medicine to anticancer drug. *International Journal of Molecular Sciences* 22 (1): 4. <https://doi.org/10.3390/ijms22010004>

Kamran, Sareh , Ajantha Sinniah , Mahfoudh A. M. Abdulghani , and Mohammed Abdullah Alshawsh . 2022. Therapeutic potential of certain terpenoids as anticancer agents: A scoping review. *Cancers* 14 (5): 1100. <https://doi.org/10.3390/cancers14051100>

Kawish, Syed M. , Shwetakshi Sharma , Priya Gupta , Farhan J. Ahmad , Muzaffar Iqbal , Fahad M Alshabrm , Md. Khalid Anwer , Sonia FathiKarkan , Abbas Rahdar , and M. Ali Aboudzadeh . 2024. Nanoparticlebased drug delivery platform for simultaneous administration of phytochemicals and chemotherapeutics: Emerging trends in cancer management. *Particle & Particle Systems Characterization*, 41 (12): 2400049. <https://doi.org/10.1002/ppsc.202400049>

Kinghorn, A. , Norman Farnsworth , Djaja Soejarto , Geoffrey Cordell , Steven Swanson , John Pezzuto , Mansukh Wani , et al. 2003. Novel strategies for the discovery of plant-derived anticancer agents. *Pharmaceutical Biology* 41 (sup1): 53–67.

<https://doi.org/10.1080/1388020039051744>

Kingston, David G. I. , G. Samranayake , and C. A. Ivey . 1990. The chemistry of taxol, a clinically useful anticancer agent. *Journal of Natural Products* 53 (1): 1–12.

<https://doi.org/10.1021/np50067a001>

Kopustinskiene, Dalia M. , Valdas Jakstas , Arunas Savickas , and Jurga Bernatoniene . 2020. Flavonoids as anticancer agents. *Nutrients* 12 (2): 457. <https://doi.org/10.3390/nu12020457>

Kumar, Ashwani , Nirmal P. , Mukul Kumar , Anina Jose , Vidisha Tomer , Emel Oz , Charalampos Proestos , et al. 2023. Major phytochemicals: Recent advances in health benefits and extraction method. *Molecules* 28 (2): 887. <https://doi.org/10.3390/molecules28020887>

Kumar, Parveen , Nishant Yadav , Benu Chaudhary , Vivek Jain , Vishal M. Balamnavar , Khalid Saad Alharbi , Sattam Khulaif Alenezi , et al. 2022. Promises of phytochemical based nano drug delivery systems in the management of cancer. *Chemico-Biological Interactions* 351 (January): 109745. <https://doi.org/10.1016/j.cbi.2021.109745>

Kumar, Suneel , Stephen O. Mathew , Ravindra Prasad Aharwal , Hardeep Singh Tulli , Chakrabhavi Dhananjaya Mohan , Gautam Sethi , Kwang-Seok Ahn , Cassidy Webber , Sardul Singh Sandhu , and Anupam Bishayee . 2023. Withaferin A: A pleiotropic anticancer agent from the Indian medicinal plant *Withania somnifera* (L.) dunal. *Pharmaceuticals* 16 (2): 160.

<https://doi.org/10.3390/ph16020160>

Kumari, V.B. Chandana , Shashank M. Patil , Ramith Ramu , Prithvi S. Shirahatti , Naveen Kumar , B.P. Sowmya , Chukwuebuka Egbuna , Chukwuemelie Zedech Uche , and Kingsley C. Patrick-Iwuanyanwu . 2022. Chromatographic techniques: Types, principles, and applications. In Egbuna, Chukwuebuka , Kingsley C. Patrick-Iwuanyanwu , Muhammad Ajmal Shah , Jonathan Chinenye Ifemeje , and Azhar Rasul (Eds.), *Analytical Techniques in Biosciences*, pp. 73–101. Elsevier, London. <https://doi.org/10.1016/B978-0-12-822654-4.00013-0>

Kuttan, Ramadasan , P. Bhanumathy , K. Nirmala , and M.C. George . 1985. Potential anticancer activity of turmeric (*Curcuma longa*). *Cancer Letters* 29 (2): 197–1202.

[https://doi.org/10.1016/0304-3835\(85\)90159-4](https://doi.org/10.1016/0304-3835(85)90159-4)

Landis-Piwowar, Kristin , Di Chen , Robert Foldes , Tak-Hang Chan , and Qing Ping Dou . 2013. Novel epigallocatechin gallate analogs as potential anticancer agents: A patent review (2009–present). *Expert Opinion on Therapeutic Patents* 23 (2): 189–1202.

<https://doi.org/10.1517/13543776.2013.743993>

Lim, Gerard Chin Chye . 2002. Overview of cancer in Malaysia. *Japanese Journal of Clinical Oncology* 32 (suppl 1): S37–42. <https://doi.org/10.1093/jjco/hye132>

Liu, Ying-Qian , Wen-Qun Li , Susan L. Morris-Natschke , Keduo Qian , Liu Yang , Gao-Xiang Zhu , Xiao-Bing Wu , et al. 2015. Perspectives on biologically active camptothecin derivatives. *Medicinal Research Reviews* 35 (4): 753–789. <https://doi.org/10.1002/med.21342>

Lopez-Lazaro, M. 2002. Flavonoids as anticancer agents: Structure-activity relationship study. *Current Medicinal Chemistry-Anti-Cancer Agents* 2 (6): 691–6714.

<https://doi.org/10.2174/1568011023353714>

Lu, Jin-Jian , Yuan-Ye Dang , Min Huang , Wen-Shan Xu , Xiu-Ping Chen , and Yi-Tao Wang . 2012. Anti-cancer properties of terpenoids isolated from *Rhizoma curcumae*: A review. *Journal of Ethnopharmacology* 143 (2): 406–411. <https://doi.org/10.1016/j.jep.2012.07.009>

Majumder, Ranabir , Chandan Kanta Das , and Mahitosh Mandal . 2019. Lead bioactive compounds of aloe vera as potential anticancer agent. *Pharmacological Research* 148

(October): 104416. <https://doi.org/10.1016/j.phrs.2019.104416>

Man, Shuli, Wenyuan Gao, Yanjun Zhang, Luqi Huang, and Changxiao Liu. 2010. Chemical study and medical application of Saponins as anti-cancer agents. *Fitoterapia* 81 (7): 703–714. <https://doi.org/10.1016/j.fitote.2010.06.004>

Martino, Emanuela, Giuseppe Casamassima, Sonia Castiglione, Edoardo Cellupica, Serena Pantalone, Francesca Papagni, Marta Rui, Angela Marika Siciliano, and Simona Collina. 2018. Vinca alkaloids and analogues as anti-cancer agents: Looking back, peering ahead. *Bioorganic & Medicinal Chemistry Letters* 28 (17): 2816–2826. <https://doi.org/10.1016/j.bmcl.2018.06.044>

Massi, Alessandro, Olga Bortolini, Daniele Ragno, Tatiana Bernardi, Gianni Sacchetti, Massimo Tacchini, and Carmela De Risi. 2017. Research progress in the modification of quercetin leading to anticancer agents. *Molecules* 22 (8): 1270. <https://doi.org/10.3390/molecules22081270>

Mosić, Mirjana, Aleksandra Dramićanin, Petar Ristivojević, and Dušanka Milojković-Opšenica. 2020. Extraction as a critical step in phytochemical analysis. *Journal of AOAC International* 103 (2): 365–372. <https://doi.org/10.5740/jaoacint.19-0251>

Mostafa, Mona, Maha Amin, and Shady M. Abd El-Halim. 2023. Polymeric nanoparticles as anticancer drug delivery systems of certain phytochemicals: A comprehensive overview. *Bulletin of Pharmaceutical Sciences Assiut University* 46 (2): 729–755. <https://doi.org/10.21608/bfsa.2023.327648>

Panyajai, Pawaret, Fah Chueahongthong, Natsima Viriyaadhammaa, Wariya Nirachonkul, Singkome Tima, Sawitree Chiampanichayakul, Songyot Anuchapreeda, and Siriporn Okonogi. 2022. Anticancer activity of *Zingiber officinale* essential oil and its nanoformulations. *PLoS One* 17 (1): e0262335. <https://doi.org/10.1371/journal.pone.0262335>

Pinto, Nicole, Stephenie D. Prokopec, Farhad Ghasemi, Jalna Meens, Kara M. Ruicci, Imran M. Khan, Neil Mundi, et al. 2020. Flavopiridol causes cell cycle inhibition and demonstrates anti-cancer activity in anaplastic thyroid cancer models. *PLoS One* 15 (9): e0239315. <https://doi.org/10.1371/journal.pone.0239315>

Sagbo, Idowu Jonas, and Wilfred Otang-Mbeng. 2021. Plants used for the traditional management of cancer in the Eastern Cape province of South Africa: A review of ethnobotanical surveys, ethnopharmacological studies and active phytochemicals. *Molecules* 26 (15): 4639. <https://doi.org/10.3390/molecules26154639>

Sharma, Shweta, Amita Kumari, Jyoti Dhatwalia, Ishita Guleria, Sohan Lal, Navneet Upadhyay, Vikas Kumar, and Ashwani Kumar. 2021. Effect of solvents extraction on phytochemical profile and biological activities of two ocimum species: A comparative study. *Journal of Applied Research on Medicinal and Aromatic Plants* 25 (December): 100348. <https://doi.org/10.1016/j.jarmap.2021.100348>

Solanki, Raghu, Bhavana Jodha, Kleopatra Eligy Prabina, Niharika Aggarwal, and Sunita Patel. 2022. Recent advances in phytochemical based nano-drug delivery systems to combat breast cancer: A review. *Journal of Drug Delivery Science and Technology* 77 (November): 103832. <https://doi.org/10.1016/j.jddst.2022.103832>

Sriram, Dharmarajan, Perumal Yogeewari, Rathinasabapathy Thirumurugan, and Tanushree Ratan Bal. 2005. Camptothecin and its analogues: A review on their chemotherapeutic potential. *Natural Product Research* 19 (4): 393–3412. <https://doi.org/10.1080/14786410412331299005>

Tauro, Savita, Bharat Dhokchawle, Popat Mohite, Deepali Nahar, Sahaya Nadar, and Evans Coutinho. 2024. Natural anticancer agents: Their therapeutic potential, challenges and promising outcomes. *Current Medicinal Chemistry* 31 (7): 848–870. <https://doi.org/10.2174/0929867330666230502113150>

Thomson, Martha, and Muslim Ali. 2003. Garlic [*Allium sativum*]: A review of its potential use as an anti-cancer agent. *Current Cancer Drug Targets* 3 (1): 67–81. <https://doi.org/10.2174/1568009033333736>

Tiwari, Supriya, Samjhana Nepal, Shraddha Sigdel, Sarju Bhattarai, Rabindra Kumar Rokaya, Jitendra Pandey, RamBahadur Khadka, Pramod Aryal, and Ravin Bhandari. 2020. Phytochemical screening, antibacterial-guided fractionation, and thin-layer chromatographic pattern of the extract obtained from *Diploknema butyracea*. *Pharmacognosy Research* 12 (4): 437. [https://doi.org/10.4103/pr.pr\\_27\\_20](https://doi.org/10.4103/pr.pr_27_20)

Tomeh, Mhd Anas, Roja Hadianamrei, and Xiubo Zhao. 2019. A review of Curcumin and its derivatives as anticancer agents. *International Journal of Molecular Sciences* 20 (5): 1033.

<https://doi.org/10.3390/ijms20051033>

- Triana, N. M. , E. Wilujeng , M. W. H. Putri , D. M. P. Yuda , A. L. Hardiono , M. T. E. Purnama , and F. Fikri . 2020. Antiproliferation effects of Glycine Max Linn ethanolic extract on induced mammary gland carcinoma in albino rats. IOP Conference Series: Earth and Environmental Science 441 (1): 012103. <https://doi.org/10.1088/1755-1315/441/1/012103>
- Usha, Talambedu , Sushil Kumar Middha , Dhivya Shanmugarajan , Dinesh Babu , Arvind Kumar Goyal , Hasan Soliman Yusufoglu , and Kora Rudraiah Sidhalinghamurthy . 2021. Gas chromatography-mass spectrometry metabolic profiling, molecular simulation and dynamics of diverse phytochemicals of Punica granatum L. leaves against estrogen receptor. Frontiers in Bioscience-Landmark 26 (9): 423. <https://doi.org/10.52586/4957>
- Vigbedor, Bright Yaw , Jonathan Osei-Owusu , Ralph Kwakye , and David Neglo . 2022. Bioassay-guided fractionation, ESI-MS scan, phytochemical screening, and antiplasmodial activity of *Azela africana*. Biochemistry Research International 2022 (April): 1–11. <https://doi.org/10.1155/2022/6895560>
- Wang, Ruo . 2022. Current perspectives on naturally occurring Saponins as anticancer agents. Archiv Der Pharmazie 355 (5). <https://doi.org/10.1002/ardp.202100469>
- Wang, Xianzhang , Yumeng Zhuang , Yuankun Wang , Maokai Jiang , and Lei Yao . 2023. The recent developments of camptothecin and its derivatives as potential anti-tumor agents. European Journal of Medicinal Chemistry 260 (November): 115710. <https://doi.org/10.1016/j.ejmech.2023.115710>
- Xu, Xiao-Huang , Ting Li , Chi Fong , Xiuping Chen , Xiao-Jia Chen , Yi-Tao Wang , Ming-Qing Huang , and Jin-Jian Lu . 2016. Saponins from Chinese medicines as anticancer agents. Molecules 21 (10): 1326. <https://doi.org/10.3390/molecules21101326>
- Yu, Jing , Jinghui Wang , Jianhua Yang , Ting Ouyang , Honglei Gao , Hongxing Kan , and Yinfeng Yang . 2024. New insight into the mechanisms of Ginkgo biloba leaves in the treatment of cancer. Phytomedicine 122 (January): 155088. <https://doi.org/10.1016/j.phymed.2023.155088>
- Zhang, You-Wen , Xiang-Ying Kong , Jin-Hua Wang , and Guan-Hua Du . 2018. Vinblastine and vincristine. In Guanhua Du (Ed.), Natural Small Molecule Drugs from Plants, pp. 551–5557. Singapore: Springer Singapore. [https://doi.org/10.1007/978-981-10-8022-7\\_91](https://doi.org/10.1007/978-981-10-8022-7_91)
- Zhou, Jingna , Rulin Li , Yanan Jia , Yajie Wang , Junyu Liu , Pharkphoom Panichayupakaranant , and Haixia Chen . 2022. Recent progress in natural anticancer agents discovery from tea (*Camellia sinensis*): A review. Recent Patents on Anti-Cancer Drug Discovery 17 (4): 343–357. <https://doi.org/10.2174/1574892816666211208155811>

## Chemistry and Pharmacology of Antidiabetic Herbs/Herbal Extract

- Alkefai, Naila Hassan Ali, Saima Amin, Manju Sharma, Javed Ahamad , and Showkat R. Mir . New olean-15-ene type gymnemic acids from *Gymnema sylvestre* (Retz.) R. Br. and their antihyperglycemic activity through  $\alpha$ -glucosidase inhibition. Phytochemistry Letters 32 (2019): 83–89.
- Alp, Harun , Ali Sahin , Pinar Karabaglı, Sulbiye Karaburgu , Burcu Yılmaz Sanal , and Emine Berrin Yuksel . Current Perspective on Diabetes Mellitus in Clinical Sciences. H. Alp , Murat Çetin Rağbetli , Hale Koksoy (Eds.) (2023): İstanbul: Nobel Tip Bookstores, pp. 1–502
- Choudhury, Hira , Manisha Pandey , Chua Kui Hua , Cheah Shi Mun , Jessmie Koh Jing , Lillian Kong , Liang Yee Ern et al. An update on natural compounds in the remedy of diabetes mellitus: A systematic review. Journal of Traditional and Complementary Medicine 8, no. 3 (2018): 361–376.
- D'souza, Myrene Roselyn . Traditional Indian herbs for the management of diabetes mellitus and their herb–drug interaction potentials: An evidence-based review. In Haixia Chen , and Min Zhang (Eds.), Structure and Health Effects of Natural Products on Diabetes Mellitus (2021): Springer, Singapore, pp. 279–296.
- Dar, Mohammad Irfan , Armiya Sultan , Sageer Abass , Kapil Dev , Rabea Parveen , Sayeed Ahmad , and Mohammad Irfan Qureshi . Exploring the anti-diabetic mechanism of selective phytochemicals identified from *Gymnema sylvestre* using TLC-UPLC-MS, complemented by in silico studies. Phytomedicine Plus 4, no. 3 (2024): 100606.

DasNandy, Anusree , Rajashri Virge , Harsha V. Hegde , and Debprasad Chattopadhyay . A review of patent literature on the regulation of glucose metabolism by six phytochemicals in the management of diabetes mellitus and its complications. *Journal of Integrative Medicine* 21, no. 3 (2023): 226–235.

Devika, Luyenita . The effect of the use of bitter melon (*Momordica charantia*) on reducing blood sugar levels in patients with diabetes mellitus. *Anshara International Journal of Health Science (AIJHS)* 1, no. 1 (2024): 5–10.

Dobhal, Kiran , Vikash Jakhmola , and Jaya Rautela . Diversities of omnipotent Tulsi: Pharmacological and chemical aspects. In P.K. Chaurasia , S.L. Bharati , and S. Singh (Eds.), *The Chemistry Inside Spices & Herbs: Research and Development: Volume 3* (2024): United Arab Emirates: Bentham Science Publishers, pp. 152–172.

Gupta, Madhu , Sushil Sharma , Ajay K. Gautam , and Rekha Bhadauria . *Momordica charantia* Linn. (Karela): Nature's silent healer. *International Journal of Pharmaceutical Sciences Review and Research* 11, no. 1 (2011): 32–37.

Jamadagni, Pallavi Shrirang , Sharad D. Pawar , Shrirang B. Jamadagni , Manish Gautam , Sudesh N. Gaidhani , G. P. Prasad , and Arun M. Gurav . Recent updates in research on *Gymnema sylvestre*. *Pharmacognosy Reviews* 15, no. 30 (2021): 128–133.

Kaur, Jasmeen , Harmandeep Kaur , and Gulshan Bansal . Assessment of shelf-life of *Gymnema sylvestre* extract through WHO recommended stability study involving chromatographic and biological activity analyses. *Natural Product Research* 35, no. 18 (2021): 3108–3113.

Khalid, Zermira , Syeda Mona Hassan , Shahzad Sharif Mughal , Syed Khurram Hassan , and Huma Hassan . Phenolic profile and biological properties of *Momordica charantia*. *Chemical and Biomolecular Engineering* 6, no. 1 (2021): 17.

Khan, Farzana , Md Moklesur Rahman Sarker , Long Chiau Ming , Isa Naina Mohamed , Chao Zhao , Bassem Y. Sheikh , Hiew Fei Tsong , and Mohammad A. Rashid . Comprehensive review on phytochemicals, pharmacological and clinical potentials of *Gymnema sylvestre*. *Frontiers in Pharmacology* 10 (2019): 1223.

Kumar, Anil . A systemic review of Tulsi (*Ocimum tenuiflorum* or *Ocimum sanctum*): Phytoconstituents, ethnobotanical and pharmacological profile. *Research Journal of Pharmacognosy and Phytochemistry* 15, no. 2 (2023): 179–188.

Kumar, Roshan , Purabi Saha , Priya Lokare , Kunal Datta , P. Selvakumar , and Anurag Chourasia . A systemic review of *Ocimum sanctum* (Tulsi): Morphological characteristics, phytoconstituents and therapeutic applications. *International Journal for Research in Applied Sciences and Biotechnology* 9, no. 2 (2022): 221–226.

Laha, Suparna , and Santanu Paul . *Gymnema sylvestre* (Gurmar): A potent herb with anti-diabetic and antioxidant potential. *Pharmacognosy Journal* 11, no. 2 (2019): 201–206.

Li, Yumeng , Yao Xiao , Wenge Gao , Jiahui Pan , Qi Zhao , and Zesheng Zhang . Gymnemic acid alleviates inflammation and insulin resistance via PPAR $\delta$ - and NF $\kappa$ B-mediated pathways in db/db mice. *Food & Function* 10, no. 9 (2019a): 5853–5862.

Li, Yumeng , Yaping Liu , Junjie Liang , Tianxin Wang , Mingzhe Sun , and Zesheng Zhang . Gymnemic acid ameliorates hyperglycemia through PI3K/AKT- and AMPK-mediated signaling pathways in type 2 diabetes mellitus rats. *Journal of Agricultural and Food Chemistry* 67, no. 47 (2019b): 13051–13060.

Parra, Alicia Lagarto , Roberto Menéndez Soto-del Valle , Janet Piloto Ferrer , Pham Thi Nguyet Hang , Nguyen Thi , Addis Bellma Phuong , Orestes Darío López et al. Antidiabetic, hypolipidemic, antioxidant and anti-inflammatory effects of *Momordica charantia* L. foliage extract. *Journal of Pharmacy & Pharmacognosy* 9, no. 4 (2021): 537–548.

Rahman, Md Mominur , Md Rezaul Islam , Sheikh Shohag , Md Emon Hossain , Md Saidur Rahaman , Fahadul Islam , Muniruddin Ahmed et al. The multifunctional role of herbal products in the management of diabetes and obesity: A comprehensive review. *Molecules* 27, no. 5 (2022): 1713.

Rahman, Shakeelur , and Azamal Husen . Phytochemical constituents, antidiabetic and other activities of Gurmar (*Gymnema sylvestre* R. Br.). In Azamal Husen (Ed.), *Antidiabetic Medicinal Plants and Herbal Treatments* (2023): CRC Press, Boca Raton, FL, pp. 159–168.

Raja, M.R. Charan , V. Srinivasan , S. Selvaraj , and S.K. Mahapatra . Versatile and synergistic potential of eugenol: A review. *Pharmaceutica Analytica Acta* 6, no. 5 (2015): 1–6.

Rajan, Dhanya , Anas Hamza , and Fathimathul Rishana . Comparative review on pharmacognostical and pharmacological activities of *Ocimum* species. *Research Journal of*

Pharmacognosy and Phytochemistry 12, no. 1 (2020): 37–46.

Rani, Manjoo . Anti-diabetic, anti-cancer potential and anti-HIV of bitter gourd (*Momordica charantia*) extract: A mini review. *Asian Plant Research Journal* 12, no. 4 (2024): 66–77.

Saleem, Makkia , Mian Kamran Sharif , and Roma Saleem . Bitter melon: A comprehensive review: Bitter melon review. *Biological Sciences-PJSIR* 65, no. 3 (2022): 297–302.

Sehajpal, Sorabh , Rohit Saraswat , and Neetu Verma . Pharmacognostical profile of *Gymnema sylvestre* and its anti-hyperglycemic activity. *Journal of Pharmaceutical Research International* 33, no. 58A (2021): 365–376.

Sehajpal, Sorabh , and Neetu Verma . A review on *Gymnema sylvestre* pharmacognostical profile and its anti-hyperglycemic activity. *Systematic Reviews in Pharmacy* 13, no. 9 (2022). <https://doi.org/10.31858/0975-8453.13.11.761-767>

Sharma, Navjot , and Kundan Singh Bora . Role of medicinal plants in the management of diabetes mellitus: A review. *Journal of Pharmaceutical Research International* 33, no. 60B (2021): 2196–2207.

Singh, Sunita , Chaurasia, Pankaj Kumar , Bharati , and Shashi Lata . Hypoglycemic and hypocholesterolemic properties of Fenugreek: A comprehensive assessment. *Applied Food Research*, 3, no. 2 (2023): 100311. <https://doi.org/10.1016/j.afres.2023.100311>.

Srinivasan, Krishnapura . Fenugreek (*Trigonella foenum-graecum*): A Review of Health Beneficial Physiological Effects. *Food Reviews International* 22, no. 2 (2006):203–224. <https://doi.org/10.1080/87559120600586315>

Suryavanshi, Anandika , and A. M. Saxena . The antidiabetic activity of bioactive compounds of Indian medicinal plants: A meta data review. *Bioscience Biotechnology Research Communications* 12, no. 2 (2019): 397–407.

Tewari, Archana , Rajinder Singh , and Jaswinder Kaur Brar . Pharmacological and therapeutic properties of fenugreek (*Trigonella foenum-graecum*) seed: A review. *Journal of Phytopharmacology* 13, no. 2 (2024): 97–104.

Wang, Shuzhen , Zhiliang Li , Guliang Yang , Chi-Tang Ho , and Shiming Li . *Momordica charantia*: A popular health-promoting vegetable with multifunctionality. *Food & Function* 8, no. 5 (2017): 1749–1762.

Xu, Bilin , Zhiliang Li , Ting Zeng , Jianfeng Zhan , Shuzhen Wang , Chi-Tang Ho , and Shiming Li . Bioactives of *Momordica charantia* as potential anti-diabetic/hypoglycemic agents. *Molecules* 27, no. 7 (2022): 2175.

Yamani, Hanaa A. , Edwin C. Pang , Nitin Mantri , and Margaret A. Deighton . Antimicrobial activity of Tulsi (*Ocimum tenuiflorum*) essential oil and their major constituents against three species of bacteria. *Frontiers in Microbiology* 7 (2016): 681.

Yaseen, Ghazala , and Sammia Shahid . Comprehensive review on phytopharmacological potential of *Gymnema sylvestre*. *Asian Journal of Pharmacy and Technology* 10, no. 3 (2020): 217–220.

## Plant-Based Molecules with Antioxidant Activities

Abeyrathne, E. D. N. S. , Nam, K. , Huang, X. , and Ahn, D. U. 2022. Plant- and animal-based antioxidants' structure, efficacy, mechanisms, and applications: A review. *Antioxidants* (Basel, Switzerland), 11(5):1025. <https://doi.org/10.3390/antiox11051025>

Ahmad, A. , Ali, T. , Rehman, S. U. , and Kim, M. O. 2019. Phytomedicine-based potent antioxidant, fisetin protects CNS-insult LPS-induced oxidative stress-mediated neurodegeneration and memory impairment. *J. Clin. Med.*, 8:850

Alghamdi, A. A. , Althumali, J. S. , Almalki, M. M. M. , Almasoudi, A. S. , Almuntashiri, A. H. , Mohammed, A. I. , Alkinani, A. A. , Almahdawi, M. S. , and Mahzari, M. A. H. 2021. An overview on the role of xanthine oxidase inhibitors in gout management. *Arch. Pharm. Pract.*, 12:2045–2050.

Amanullah, I. , Khan, Y. H. , Anwar, I. , Gulzar, A. , Mallhi, T. H. , and Raja, A. A. 2019. Effect of vitamin E in non-alcoholic fatty liver disease: A systematic review and meta-analysis of randomised controlled trials. *Postgrad. Med. J.*, 95:601–611.

Amarowicz, R. , and Pegg, R. B. 2019. Natural antioxidants of plant origin. In: Ferreira I. C. F. R. , Barros L. , editors. *Advances in Food and Nutrition Research*. Academic Press: Cambridge,

- Arfin, S. , Jha, N. K. , Jha, S. K. , Kesari, K. K. , Ruokolainen, J. , Roychoudhury, S. , Rath, B. , and Kumar, D. 2021. Oxidative stress in cancer cell metabolism. *Antioxidants*, 10(5):642. <https://doi.org/10.3390/antiox10050642>
- Asbaghi, O. , Sadeghian, M. , Nazarian, B. , Sarreshtedari, M. , Mozaffari-Khosravi, H. , Maleki, V. , Alizadeh, M. , Shokri, A. , and Sadeghi, O. 2020. The effect of vitamin E supplementation on selected inflammatory biomarkers in adults: A systematic review and meta-analysis of randomized clinical trials. *Sci. Rep.*, 10:17234.
- Burgos-Morón, E. , Abad-Jiménez, Z. , Martínez, M. A. , Iannantuoni, F. , Escribano-López, I. , López-Domènech, S. , Salom, C. , Jover, A. , Mora, V. , and Roldán, I. 2019. Relationship between oxidative stress, ER stress, and inflammation in type 2 diabetes: The battle continues. *J. Clin. Med.*, 8(9):1385. <https://doi.org/10.3390/jcm8091385>
- Caro-Ordieres, T. , Marin-Royo, G. , Opazo-Rios, L. , Jimenez-Castilla, L. , Moreno, J. A. , Gomez-Guerrero, C. , and Egido, J. 2020. The coming age of flavonoids in the treatment of diabetic complications. *J. Clin. Med.*, 9:346. <https://doi.org/10.3390/jcm9020346>
- Caturano, A. , D'Angelo, M. , Mormone, A. , Russo, V. , Mollica, M. P. , Salvatore, T. , Galiero, R. , Rinaldi, L. , Vetrano, E. , Marfella, R. , Monda, M. , Giordano, A. , and Sasso, F. C. 2023. Oxidative stress in type 2 diabetes: Impacts from pathogenesis to lifestyle modifications. *Curr. Issues Mol. Biol.*, 45(8):6651–6666. <https://doi.org/10.3390/cimb45080420>
- Cefali, L. C. 2019. Evaluation of in vitro solar protection factor (SPF), antioxidant activity, and cell viability of mixed vegetable extracts from *Dioscorea alata* Benth, *Ginkgo biloba* L., *Ruta graveolens* L., and *Vitis vinifera* L. *Plants*, 8:k453. <https://doi.org/10.3390/plants8110453>
- Charlton, N. C. , Mastuygin, M. , Török, B. , and Török, M. 2023. Structural features of small molecule antioxidants and strategic modifications to improve potential bioactivity. *Molecules* (Basel, Switzerland), 28(3):1057. <https://doi.org/10.3390/molecules28031057>
- Chen, J. , Yang, J. , Ma, L. , Li, J. , Shahzad, N. , and Kim, C. K. 2020. Structure-antioxidant activity relationship of methoxy, phenolic hydroxyl, and carboxylic acid groups of phenolic acids. *Sci. Rep.*, 10:2611–2620.
- Cojocaru, K. A. , Luchian, I. , Goriuc, A. , Antoci, L. M. , Ciobanu, C. G. , and Popescu, R. 2023. Mitochondrial dysfunction, oxidative stress, and therapeutic strategies in diabetes, obesity, and cardiovascular disease. *Antioxidants*, 12(3):658.
- Costa, M. , Losada-Barreiro, S. , Paiva-Martins, F. , and Bravo-Díaz, C. 2021. Polyphenolic antioxidants in lipid emulsions: Partitioning effects and interfacial phenomena. *Foods*, 10:539. <https://doi.org/10.3390/foods10030539>
- Delgado-Roche, L. , and Mesta, F. 2020. Oxidative stress as key player in severe acute respiratory syndrome coronavirus (SARS-CoV) infection. *Arch. Med. Res.*, 51:384–387. <https://doi.org/10.1016/j.arcmed.2020.04.019>
- Diniz, L. R. L. , Bezerra-Filho, C. D. S. M. , Fielding, B. C. , and deSousa, D. P. 2020. Natural antioxidants: A review of studies on human and animal coronavirus. *Oxid. Med. Cell. Longev.*, 2020:1–14. <https://doi.org/10.1155/2020/3173281>
- Dirimanov, S. , and Högger, P. 2019. Screening of inhibitory effects of polyphenols on Akt-phosphorylation in endothelial cells and determination of structure-activity features. *Biomolecules*, 9:219. <https://doi.org/10.3390/biom9060219>
- Dubois-Deruy, E. , Peugeot, V. , Turkieh, A. , and Pinet, F. 2020. Oxidative stress in cardiovascular diseases. *Antioxidants* (Basel, Switzerland), 9(9):864. <https://doi.org/10.3390/antiox9090864>
- Flieger, J. , Flieger, W. , Baj, J. , and Maciejewski, R. 2021. Antioxidants: Classification, natural sources, activity/capacity measurements, and usefulness for the synthesis of nanoparticles. *Materials* (Basel, Switzerland), 14(15):4135. <https://doi.org/10.3390/ma14154135>
- Forman, H. J. , and Zhang, H. 2021. Targeting oxidative stress in disease: Promise and limitations of antioxidant therapy. *Nat. Rev. Drug Discov.*, 20:689–709. <https://doi.org/10.1038/s41573-021-00233-1>
- Fuloria, S. , Mehta, J. , Chandel, A. , Sekar, M. , Rani, N. N. I. M. , Begum, M. Y. , Subramaniyan, V. , Chidambaram, K. , Thangavelu, L. , Nordin, R. , Wu, Y. S. , Sathasivam, K. V. , Lum, P. T. , Meenakshi, D. U. , Kumarasamy, V. , Azad, A. K. , and Fuloria, N. K. 2022. A comprehensive review on the therapeutic potential of *Curcuma longa* Linn in relation to its major active constituent curcumin. *Front. Pharmacol.*, 13:820806. <https://doi.org/10.3389/fphar.2022.820806>

Ghosh, S. , Sarkar, T. , Pati, S. , Kari, Z.A. , Edinur, H. A. , and Chakraborty, R. 2022. Novel bioactive compounds from marine sources as a tool for functional food development. *Front. Mar. Sci.*, 9:832957. <https://doi.org/10.3389/fmars.2022.832957>

Hayes, J. D. , Dinkova-Kostova, A. T. , and Tew, K. D. 2020. Oxidative stress in cancer. *Cancer Cell*, 38(2):167–1971. <https://doi.org/10.1016/j.ccell.2020.06.001>

Hunyadi, A. 2019. The mechanism(s) of action of antioxidants: From scavenging reactive oxygen/nitrogen species to redox signaling and the generation of bioactive secondary metabolites. *Med. Res. Rev.*, 39(6):2505–2533.

Jo, S. , Kim, S. , Shin, D. H. , and Kim, M. S. 2020. Inhibition of SARS-CoV 3CL protease by flavonoids. *J. Enzyme Inhib. Med. Chem.*, 35:145–151. <https://doi.org/10.1080/14756366.2019.1690480>

Jomova, K. , Alomar, S. Y. , and Alwasel, S. H. 2024. Several lines of antioxidant defense against oxidative stress: Antioxidant enzymes, nanomaterials with multiple enzyme-mimicking activities, and low-molecular-weight antioxidants. *Arch. Toxicol.*, 98:1323–1367. <https://doi.org/10.1007/s00204-024-03696-4>

Kalinowska, M. , Sienkiewicz-Gromiuk, J. , Świdorski, G. , Pietryczuk, A. , Cudowski, A. , and Lewandowski, W. 2020. Zn(II) complex of plant phenolic chlorogenic acid: Antioxidant, antimicrobial and structural studies. *Materials*, 13: 3745.

Kornienko, J. S. , Smirnova, I. S. , Pugovkina, N. A. , Ivanova, J. S. , Shilina, M. A. , Grinchuk, T. M. , Shatrova, A. N. , Aksenov, N. D. , Zenin, V. V. , and Nikolsky, N. N. 2019. High doses of synthetic antioxidants induce premature senescence in cultivated mesenchymal stem cells. *Sci. Rep.*, 9:1296. <https://doi.org/10.1038/s41598-018-37972-y>

Kumar, N. , and Goel, N. 2019. Phenolic acids: Natural versatile molecules with promising therapeutic applications. *Biotechnol. Rep.*, 24:e00370. <https://doi.org/10.1016/j.btre.2019.e00370>

Kurnia, D. , Ajiati, D. , Heliawati, L. , and Sumiarsa, D. 2021. Antioxidant properties and structure-antioxidant activity relationship of species leaves. *Molecules*, 26(23):7175. <https://doi.org/10.3390/molecules26237175>

Li, H. , Liu, X. , Lee, M. , and Li, H. 2021. Vitamin C alleviates hyperuricemia nephropathy by reducing inflammation and fibrosis. *J. Food Sci.*, 86:3265–3276.

Linani, A. , Benarous, K. , Bou-Salah, L. , and Yousfi, M. 2022. The inhibitory kinetics of vitamins B9, C, E, and D3 on bovine xanthine oxidase: Gout treatment. *Chem. Biol. Interact.*, 359:109922.

Llauradó, M. G. , MéndezRodríguez, D. , Hendrix, S. , Escalona Arranz, J. C. , FungBoix, Y. , Pacheco, A. O. , GarcíaDíaz, J. , Morris-Quevedo, H. J. , FerrerDubois, A. , and Aleman, E.I. 2020. Antioxidants in plants: A valorization potential emphasizing the need for the conservation of plant biodiversity in Cuba. *Antioxidants*, 9:1048. <https://doi.org/10.3390/antiox9111048>

Lourenço, S. C. , Moldão-Martins, M. , and Alves, V. D. 2019. Antioxidants of natural plant origins: From sources to food industry applications. *Molecules (Basel, Switzerland)*, 24(22):4132. <https://doi.org/10.3390/molecules24224132>

Marino, P. , Pepe, G. , Basilicata, M. G. , Vestuto, V. , Marzocco, S. , and Autore, G. 2023. Potential role of natural antioxidant products in oncological diseases. *Antioxidants*, 12(3):704.

Matsumoto, T. , Kaneko, A. , Koseki, J. , Matsubara, Y. , Aiba, S. , and Yamasaki, K. 2018. Pharmacokinetic study of bioactive flavonoids in the traditional Japanese Medicine Keigairengyoto exerting antibacterial effects against *Staphylococcus aureus*. *Int. J. Mol. Sci.*, 19:328.

Moldogazieva, N. T. , Mokhosoev, I. M. , Feldman, N. B. , and Lutsenko, S. V. 2018. ROS and RNS signalling: Adaptive redox switches through oxidative/nitrosative protein modifications. *Free Radic. Res.*, 52(5):507–543.

Moonrungsee, N. , Jakmunee, J. , Peamaroon, N. , Boonmee, A. , Kasemsuk, T. , Seeda, S. , and Suwanchaoen, S. 2022. Phytochemical and xanthine oxidase inhibitory activity in *Nypa fruticans* Wurmb. Fruit extracts. *Trends Sci.*, 19:2583.

Mustafa, Y. F. 2024. Harmful free radicals in aging: A narrative review of their detrimental effects on health. *Ind. J. Clin. Biochem.*, 39:154–167. <https://doi.org/10.1007/s12291-023-01147-y>

Mutha, R. E. , Tatiya, A. U. , and Surana, S. J. 2021. Flavonoids as natural phenolic compounds and their role in therapeutics: An overview. *Futur. J. Pharm. Sci.*, 7:25. <https://doi.org/10.1186/s43094-020-00161-8>



Ogutibeju, O. O. 2019. Type 2 diabetes mellitus, oxidative stress and inflammation: Examining the links. *Int. J. Physiol. Pathophysiol. Pharmacol.*, 11:45–63.

Parcheta, M., Świsłocka, R., Orzechowska, S., Akimowicz, M., Choirńska, R., and Lewandowski, W. 2021. Recent developments in effective antioxidants: The structure and antioxidant properties. *Materials*, 14(8):1984. <https://doi.org/10.3390/ma14081984>

Pilipović, K., Jurišić, G. R., Dolenec, P., Kučić, N., Juretić, L., and Mršić-Pelčić, J. 2023. Plant-based antioxidants for prevention and treatment of neurodegenerative diseases: Phytotherapeutic potential of *Laurus nobilis*, *Aronia melanocarpa*, and celastrol. *Antioxidants*, 12(3):746. <https://doi.org/10.3390/antiox12030746>

Rodriguez-Garcia, C., Sanchez-Quesada, C., and Gaforio, J. J. 2019. Dietary flavonoids as cancer chemopreventive agents: An updated review of human studies. *Antioxidants (Basel)*, <https://doi.org/10.3390/antiox8050137>

Rudrapal, M., Khairnar, S. J., Khan, J., Bin, D. A., Ansari, M. A., Alomary, M. N., Alshabrm, F. M., Palai, S., Deb, P. K., and Devi, R. 2022. Dietary polyphenols and their role in oxidative stress-induced human diseases: Insights into protective effects, antioxidant potentials and mechanism(s) of action. *Front. Pharmacol.*, 13:806470. <https://doi.org/10.3389/fphar.2022.806470>

Safe, S., Jayaraman, A., Chapkin, R. S., Howard, M., Mohankumar, K., and Shrestha, R. 2021. Flavonoids: Structure-function and mechanisms of action and opportunities for drug development. *Toxicol. Res.*, 37(2):147–162. <https://doi.org/10.1007/s43188-020-00080-z>

Senoner, T., and Dichtl, W. 2019. Oxidative stress in cardiovascular diseases: Still a therapeutic target? *Nutrients*, 11(9):2090. <https://doi.org/10.3390/nu11092090>

Sharifi-Rad, M., Kumar, A. N. V., Zucca, P., Varoni, E. M., Dini, L., Panzarini, E., Rajkovic, J., Tsouh, F. P. V., Azzini, E., and Peluso, I., 2020. Lifestyle, oxidative stress, and antioxidants: Back and forth in the pathophysiology of chronic diseases. *Front. Physiol.*, 11:694. <https://doi.org/10.3389/fphys.2020.00694>

Sies, H., and Jones, D. P. 2020. Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *Nat. Rev. Mol. Cell Biol.*, 21:363–383.

Tziveleka, L. A., Tammam, M. A., Tzakou, O., Roussis, V., and Ioannou, E. 2021. Metabolites with antioxidant activity from marine macroalgae. *Antioxidants*, 10(9):1431. <https://doi.org/10.3390/antiox10091431>

Ulewicz-Magulska, B., and Wesolowski, M. 2019. Total phenolic contents and antioxidant potential of herbs used for medical and culinary purposes. *Plant Food Hum. Nutr.*, 74:61–67. <https://doi.org/10.1007/s11130-018-0699-5>

Ullah, A., Munir, S., Badshah, S. L., Khan, N., Ghani, L., Poulson, B. G., Emwas, A. H., and Jaremko, M. 2020. Important flavonoids and their role as a therapeutic agent. *Molecules*, 25(22):5243. <https://doi.org/10.3390/molecules25225243>

Ungurianu, A., Zănefirescu, A., Nitulescu, G., and Margină, D. 2021. Vitamin E beyond its antioxidant label. *Antioxidants*, 10(5):634. <https://doi.org/10.3390/antiox10050634>

Urbano, T., Vinceti, M., Mandrioli, J., Chiari, A., Filippini, T., and Bedin, R. 2022. Selenoprotein P concentrations in the cerebrospinal fluid and serum of individuals affected by amyotrophic lateral sclerosis, mild cognitive impairment and Alzheimer's dementia. *Int. J. Mol. Sci.*, 23(17):9865.

Vasari, M., and Degl'Innocenti, D. 2022. Antioxidant and anti-inflammatory agents from the sea: A molecular treasure for new potential drugs. *Marine Drugs*, 20(2):132. <https://doi.org/10.3390/md20020132>

Vladkova, T., Georgieva, N., Staneva, A., and Gospodinova, D. 2022. Recent progress in antioxidant active substances from Marine Biota. *Antioxidants (Basel, Switzerland)*, 11(3):439. <https://doi.org/10.3390/antiox11030439>

Wang, W., and Kannan, K. 2018. Inventory, loading and discharge of synthetic phenolic antioxidants and their metabolites in wastewater treatment plants. *Water Res.*, 129:413–418. <https://doi.org/10.1016/j.watres.2017.11.028>

Yang, H., Leng, J., Liu, N., and Huang, L. 2024. Editorial: Free radicals and antioxidants in diseases associated with immune dysfunction, inflammatory process, and aberrant metabolism. *Front. Endocrinol.*, 15:1363854. <https://doi.org/10.3389/fendo.2024.1363854>

Yousef, H., Khandoker, A. H., Feng, S. F., Helf, C., and Jelinek, H. F. 2023. Inflammation, oxidative stress and mitochondrial dysfunction in the progression of type II diabetes mellitus with coexisting hypertension. *Front. Endocrinol.*, 14:1173402. <https://doi.org/10.3389/fendo.2023.1173402>

# Hypocholesterolemic Herbs or Herbal Extracts and Their Chemistry

- Abumweis, S. S. , R. Barake , and P. J. H. Jones . Plant sterols/stanols as cholesterol lowering agents: a meta-analysis of randomized controlled trials. *Food & Nutrition Research* 52, no. 1 (2008): 1811.
- Agarwal, K. C. Therapeutic actions of garlic constituents. *Medicinal Research Reviews* 16, no. 1 (1996): 111–124.
- Aher, R. R. , S. A. Belge , S. R. Kadam , S. S. Kharade , A. V. Misal , and P. T. Yeole . Therapeutic importance of fenugreek (*Trigonella foenum-graecum* L.): a review. *Journal of Plant Science and Research* 3, no. 1 (2016): 149.
- Alexopoulos, C. G. , B. Blatsios , and A. Avgerinos . Serum lipids and lipoprotein disorders in cancer patients. *Cancer* 60, no. 12 (1987): 3065–3070.
- Altmann, S. W. , H. R. Davis Jr , L.-J. Zhu , X. Yao , L. M. Hoos , G. Tetzloff , S. P. N. Iyer , M. Maguire , A. Golovko , M. Zeng , L. Wang , N. Murgolo , and M. P. Graziano . Niemann-pick C1 like 1 protein is critical for intestinal cholesterol absorption. *Science* 303, no. 5661 (2004): 1201–1204.
- Azwanida, N. N. A review on the extraction methods use in medicinal plants, principle, strength and limitation. *Medicinal and Aromatic Plants* 4, no. 3 (2015): 196.
- Banerjee, S. K. , and S. K. Maulik . Effect of garlic on cardiovascular disorders: a review. *Nutrition Journal* 1 (2002): 1–14.
- Barakat, L. A. A. , and R. H. Mahmoud . The antiatherogenic, renal protective and immunomodulatory effects of purslane, pumpkin and flax seeds on hypercholesterolemic rats. *North American Journal of Medical Sciences* 3, no. 9 (2011): 411.
- Bernacchia, R. , R. Preti , and G. Vinci . Chemical composition and health benefits of flaxseed. *Austin Journal of Nutrition and Food sciences* 2, no. 8 (2014): 1045.
- Bradley, J. M. , C. L. Organ , and D. J. Lefer . Garlic-derived organic polysulfides and myocardial protection. *The Journal of Nutrition* 146, no. 2 (2016): 403S–409S.
- Chemat, F. , Rombaut, N. , Sicaire, A. G. , Meullemiestre, A. , Fabiano-Tixier, A. S. , and Abert-Vian, M. Ultrasound-assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols, and applications. A review. *Ultrasonics Sonochemistry* 34 (2017): 540–560.
- Chen, L. , H. Mo , L. Zhao , W. Gao , S. Wang , M. M. Cromie , C. Lu , J.-S. Wang , and C.-L. Shen . Therapeutic properties of green tea against environmental insults. *The Journal of Nutritional Biochemistry* 40 (2017): 1–13.
- Chen, X. , Zhang, L. , and Liu, J. Curcumin and bile acid metabolism: a review of mechanisms. *Journal of Functional Foods* 86 (2022): 104694.
- Criqui, M. H. Very low cholesterol and cholesterol lowering. A statement for healthcare professionals from the American Heart Association Task Force on Cholesterol Issues. *Circulation* 90, no. 5 (1994): 2591–2591.
- Dash, B. K. , S. Sultana , and N. Sultana . Antibacterial activities of methanol and acetone extracts of fenugreek (*Trigonella foenum*) and coriander (*Coriandrum sativum*). *Life Sciences and Medicine Research* 27, no. 1(2011): 1–8.
- Epstein, F. H. Low serum cholesterol, cancer and other noncardiovascular disorders. *Atherosclerosis* 94, no. 1 (1992): 1–12.
- Feingold, K. R. Introduction to lipids and lipoproteins. Endotext [internet] (2024). <https://www.ncbi.nlm.nih.gov/sites/books/NBK305896/>
- Francis, G. , Z. Kerem , H. P. S. Makkar , and K. Becker . The biological action of saponins in animal systems: a review. *British Journal of Nutrition* 88, no. 6 (2002): 587–605.
- Fritsche, J. , C. M. Beindorff , M. Dachtler , H. Zhang , and J. G. Lammers . Isolation, characterization and determination of minor artichoke (*Cynara scolymus* L.) leaf extract compounds. *European Food Research and Technology* 215 (2002): 149–157.
- Gebhardt, R. , and H. Beck . Differential inhibitory effects of garlic-derived organosulfur compounds on cholesterol biosynthesis in primary rat hepatocyte cultures. *Lipids* 31, no. 12 (1996): 1269–1276.
- Golomb, B. A. , and Evans, M. A. Statin adverse effects: a review of the literature and evidence for a mitochondrial mechanism. *American Journal of Cardiovascular Drugs* 8, no. 6 (2008): 373–418.
- Goto, T. , N. Takahashi , S. Hirai , and T. Kawada . Various terpenoids derived from herbal and dietary plants function as PPAR modulators and regulate carbohydrate and lipid metabolism.

PPAR Research 2010, no. 1 (2010): 483958.

Güçlü -Üstündağ, Ö., and G. Mazza . Saponins: properties, applications and processing. *Critical Reviews in Food Science and Nutrition* 47, no. 3 (2007): 231–258.

Gupta, S. , Prakash, J. , and Singh, P. Therapeutic potential of herbal extracts in lowering cholesterol levels. *Journal of Medicinal Plants Research* 11, no. 2 (2017): 28–35.

Handa, S. S. , Khanuja, S. P. S. , Longo, G. , and Rakesh, D. D. *Extraction Technologies for Medicinal and Aromatic Plants (Vol. 1)*. International Centre for Science and High Technology (2008).

Heim, K. E. , A. R. Tagliaferro , and D. J. Bobilya . Flavonoid antioxidants: chemistry, metabolism and structure-activity relationships. *The Journal of Nutritional Biochemistry* 13, no. 10 (2002): 572–584.

Horie, T. , T. Murayama , T. Mishima , F. Itoh , Y. Minamide , T. Fuwa , and S. Awazu . Protection of liver microsomal membranes from lipid peroxidation by garlic extract. *Planta Medica* 55, no. 06 (1989): 506–508.

Houghton, P. J. , and Raman, A. *Laboratory Handbook for the Fractionation of Natural Extracts*. Springer Science & Business Media (1998).

Jang, H. S. , Kim, M. K. , and Kim, M. J. Curcumin increases bile acid secretion and modulates hepatic lipid metabolism in high-fat diet-fed rats. *Nutrients* 10, no. 9 (2018): 1227.

Kim, A. , A. Chiu , M. K. Barone , D. Avino , F. Wang , C. I. Coleman , and O. J. Phung . Green tea catechins decrease total and low-density lipoprotein cholesterol: a systematic review and meta-analysis. *Journal of the American Dietetic Association* 111, no. 11 (2011): 1720–1729.

Kim, Y. J. , Park, S. J. , and Lee, E. J. Anti-inflammatory and antioxidant mechanisms of herbal extracts on cholesterol metabolism. *Journal of Cardiovascular Pharmacology* 73, no. 1 (2019): 55–62.

Kong, W. J. , Wei, J. , Abidi, P. , Lin, M. , Inaba, S. , Li, Z. , Y. Wang , Z. Wang , S. Si , H. Pan , S. Wang , J. Wu , Y. Wang , Z. Li , J. Liu , J.-D. Jiang , and Liu, J. Berberine is a novel cholesterol-lowering drug working through a unique mechanism distinct from statins. *Nature Medicine* 10, no. 12 (2004): 1344–1351.

Kunle, O. F. , Egharevba, H. O. , and Ahmadu, P. O. Standardization of herbal medicines: a review. *International Journal of Biodiversity and Conservation* 4, no. 3 (2012): 101–112.

Ludwiczuk, A. , K. Skalicka-Woźniak , and M. I. Georgiev . Terpenoids. In *Pharmacognosy*, pp. 233–266. Elsevier (2017).

McKay, D. L. , and J. B. Blumberg . Roles for epigallocatechin gallate in cardiovascular disease and obesity: an introduction. *Journal of the American College of Nutrition* 26, no. 4 (2007): 362S–365S.

Moutzouri, E. , M. Elisaf , and E. N. Liberopoulos . Hypocholesterolemia. *Current Vascular Pharmacology* 9, no. 2 (2011): 200–212.

Muro, E. , G. Ekin Atilla-Gokcumen , and U. S. Eggert . Lipids in cell biology: how can we understand them better? *Molecular Biology of the Cell* 25, no. 12 (2014): 1819–1823.

Panda, H. *Handbook on Medicinal Herbs with Uses: Medicinal Plant Farming, Most Profitable Medicinal Plants in India, Medicinal Plants Farming in India, Plants Used in Herbalism, Medicinal Herbs You Can Grow, Medicinal Herbs and Their Uses, Medicinal Herbs, Herbal & Medicinal Plants, Growing Medicinal Herb, Most Profitable Medicinal Herbs Growing with Small Investment, Herbal Medicine Herbs*. Asia Pacific Business Press Inc. (2004).

Pang, J. , Z. Zhang , T.-Z. Zheng , B. A. Bassig , C. Mao , X. Liu , Y. Zhu , K. Shi , J. Ge , Y.-J. Yang , Dejie-Huang, M. Bai , and Y. Peng . Green tea consumption and risk of cardiovascular and ischemic related diseases: a meta-analysis. *International Journal of Cardiology* 202 (2016): 967–974.

Patel, D. , Kumar, R. , and Laloo, D. Hypolipidemic and hypocholesterolemic effects of *Coriandrum sativum* and *Trigonella foenum-graecum*. *Journal of Ethnopharmacology* 242 (2019): 112–120.

Patel, J. M. A review of potential health benefits of flavonoids. *Lethbridge Undergraduate Research Journal* 3, no. 2 (2008): 1–5.

Patil, P. S. , and R. Shettigar . An advancement of analytical techniques in herbal research. *Journal of Advanced Scientific Research* 1, no. 01 (2010): 8–14.

Prasad, K. Flaxseed: a source of hypocholesterolemic and antiatherogenic agents. *Drug News & Perspectives* 13, no. 2 (2000): 99–104.

Rahman, S. , Begum, Z. , and Rahman, S. Potential antioxidant and anti-inflammatory properties of Ginger and Cinnamon: a review. *Food and Chemical Toxicology* 130 (2019): 219–230.

Rao, A. V. , and M.-K. Sung . Saponins as anticarcinogens. *The Journal of Nutrition* 125 (1995): 717S–724S.

Rohman, A. , and B. W. Dijkstra . Application of microbial 3-ketosteroid  $\Delta$ 1-dehydrogenases in biotechnology. *Biotechnology Advances* 49 (2021): 107751.

Rubilar, M. , C. Gutiérrez , M. Verdugo , C. Shene , and J. Sineiro . Flaxseed as a source of functional ingredients. *Journal of Soil Science and Plant Nutrition* 10, no. 3 (2010): 373–377.

Sharma, D. K. Immunity-boosting macronutrients and micronutrients. In P. C. Gupta , S. Bhattacharyya , N. Sharma , R. K. Kesharwani , and R. K. Keservani (Eds.), *Micronutrients and Macronutrients as Nutraceuticals*, pp. 131–166. Apple Academic Press, Palm Bay, FL (2024).

Shen, N. , T. Wang , Q. Gan , S. Liu , L. Wang , and B. Jin . Plant flavonoids: classification, distribution, biosynthesis, and antioxidant activity. *Food Chemistry* 383 (2022): 132531.

Singh, S. P. , and K. V. Sashidhara . Lipid lowering agents of natural origin: an account of some promising chemotypes. *European Journal of Medicinal Chemistry* 140 (2017): 331–348.

Singh, S. V. , R. R. Mohan , R. Agarwal , P. J. Benson , X. Hu , M. A. Rudy , H. Xia , A. Katoh , S. K. Srivastava , H. Mukhtar , V. Gupta , and H. A. Zaren . Novel anti-carcinogenic activity of an organosulfide from garlic: inhibition of H-RAS oncogene transformed tumor growth in vivo by diallyl disulfide is associated with inhibition of p21H-ras processing. *Biochemical and Biophysical Research Communications* 225, no. 2 (1996): 660–665.

Stark, A. , and Z. Madar . The effect of an ethanol extract derived from fenugreek (*Trigonella foenum-graecum*) on bile acid absorption and cholesterol levels in rats. *British Journal of Nutrition* 69, no. 1 (1993): 277–287.

Subroto, E. , Y. Cahyana , M. Tensiska , F. Lembong , E. Filianty , E. Kurniati , D. Wulandari , R. Saputra , and F. Faturachman . Bioactive compounds in garlic (*Allium sativum* L.) as a source of antioxidants and its potential to improve the immune system: a review. *Food Research* 5, no. 6 (2021): 1–11.

Suman, S. , and Y. Shukla . Diallyl sulfide and its role in chronic diseases prevention. In S. C. Gupta , S. Prasad , and B. B. Aggarwal (Eds.), *Drug Discovery from Mother Nature*, pp. 127–144. Springer, Cham (2016).

Tawfeek, N. , M. F. Mahmoud , D. I. Hamdan , M. Sobeh , N. Farrag , M. Wink , and A. M. El-Shazly . Phytochemistry, pharmacology and medicinal uses of plants of the genus *Salix*: an updated review. *Frontiers in Pharmacology* 12 (2021): 593856.

Tomiki, Y. , S. Suda , M. Tanaka , A. Okuzawa , M. Matsuda , Y. Ishibiki , K. Sakamoto , T. Kamano , M. Tsurumaru , and Y. Watanabe . Reduced low-density-lipoprotein cholesterol causing low serum cholesterol levels in gastrointestinal cancer. A case control study. *Journal of Experimental and Clinical Cancer Research* 23 (2004): 233–240.

Vergallo, C. Nutraceutical vegetable oil nanoformulations for prevention and management of diseases. *Nanomaterials* 10, no. 6 (2020): 1232.

Wani, S. A. , and P. Kumar . Fenugreek: a review on its nutraceutical properties and utilization in various food products. *Journal of the Saudi Society of Agricultural Sciences* 17, no. 2 (2018): 97–106.

Yadav, R. , R. Kaushik , and D. Gupta . The health benefits of *Trigonella foenum-graecum*: a review. *International Journal of Applied Engineering* 1, no. 1 (2011): 32–35.

Yang, L. , F. Chen , C. Gao , J. Chen , J. Li , S. Liu , Y. Zhang , Z. Wang , and S. Qian . Design and synthesis of tricyclic terpenoid derivatives as novel PTP1B inhibitors with improved pharmacological property and in vivo antihyperglycaemic efficacy. *Journal of Enzyme Inhibition and Medicinal Chemistry* 35, no. 1 (2020): 152–164.

Zhang, D. , L. Wang , and Z. Yang . Nature products and cardiovascular disorders. In Atta-ur-Rahman , and M. Iqbal Choudhary (Eds.), *Frontiers in Cardiovascular Drug Discovery*, pp. 3–91. Bentham Science Publishers, Sharjah (2015).

Zhang, Y. , H. Zhang , S. Hua , L. Ma , C. Chen , X. Liu , L. Jiang , H. Yang , P. Zhang , D. Yu , Y. Guo , X. Tan , and J. Liu . Identification of two herbal compounds with potential cholesterol-lowering activity. *Biochemical Pharmacology* 74, no. 6 (2007): 940–947.

Zhang, Y. , X. Li , and T. Shen . Effect of garlic and guggul on lipid metabolism: a review of molecular mechanisms. *Phytomedicine* 85 (2021): 153521.

Zhou, X. , R. Zhou , and Z. Tang . Phytosterols and cholesterol metabolism: implications for human health and disease. *Current Opinion in Lipidology* 31, no. 2 (2020): 95–101.

## Herbal Medicines with Allopathic

Haider R. *History of Use of Traditional Herbal Medicines*. Sanderman Publishing House, Boulder, CO, 2023.

Uher I , Cholewa J , Kunicki M , Švedová M , Cimbolakova I , Kůchelová Z , et al. Allopathic and naturopathic medicine and their objective consideration of congruent pursuit. *EvidenceBased Complementary and Alternative Medicine*. 2020;2020(1):7525713.

Agbabiaka TB , Wider B , Watson LK , Goodman C. Concurrent use of prescription drugs and herbal medicinal products in older adults: a systematic review. *Drugs & Aging*. 2017;34:891–905.

Wang L , Liu D , Wei G , Ge H. Berberine and metformin in the treatment of type 2 diabetes mellitus: a systemic review and meta-analysis of randomized clinical trials. *Health*. 2021;13:1314–1329.

Sierpina VS , Dalen JE . The future of integrative medicine. *The American Journal of Medicine*. 2013;126(8):661–662.

Sahoo N , Manchikanti P , Dey S. Herbal drugs: standards and regulation. *Fitoterapia*. 2010;81(6):462–471.

Weil A. The significance of integrative medicine for the future of medical education. *The American Journal of Medicine*. 2000;108(5):441–443.

Fabricant DS , Farnsworth NR . The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives*. 2001;109(suppl 1):69–75.

Sasmal SA , Ghodke KD , Kambale AA , Bais S , Pore A. Current scenario of pharmaceutical & herbal medicines & its future prospectus. *International Journal of Pharmacy and Herbal Technology*. 2024;2:1545–1552.

Chopra A , Doiphode VV . Ayurvedic medicine: core concept, therapeutic principles, and current relevance. *Medical Clinics*. 2002;86(1):75–89.

Yapjakis C. Hippocrates of Kos, the father of clinical medicine, and Asclepiades of Bithynia, the father of molecular medicine. *In Vivo*. 2009;23(4):507–514.

Blevins SM , Bronze MS . Robert Koch and the 'golden age' of bacteriology. *International Journal of Infectious Diseases*. 2010;14(9):e744–e51.

Aminov RI . A brief history of the antibiotic era: lessons learned and challenges for the future. *Frontiers in Microbiology*. 2010;1:134.

Frenkel MA , Borkan JM . An approach for integrating complementary–alternative medicine into primary care. *Family Practice*. 2003;20(3):324–332.

Herman PM , Craig BM , Caspi O. Is complementary and alternative medicine (CAM) cost-effective? A systematic review. *BMC Complementary and Alternative Medicine*. 2005;5:1–15.

Wardle JJJ , Adams J. Indirect and non-health risks associated with complementary and alternative medicine use: an integrative review. *European Journal of Integrative Medicine*. 2014;6(4):409–422.

Atanasov AG , Waltenberger B , Pferschy-Wenzig E-M , Linder T , Wawrosch C , Uhrin P , et al. Discovery and resupply of pharmacologically active plant-derived natural products: a review. *Biotechnology Advances*. 2015;33(8):1582–1614.

Riddle JM . *Dioscorides on Pharmacy and Medicine*. University of Texas Press, Austin, TX, 1985.

Porter R , Crosby AW . The greatest benefit to mankind: a medical history of humanity from antiquity to the present. *Nature*. 1998;391(6664):241.

Klockgether-Radke A. FW Sertürner and the discovery of morphine. 200 years of pain therapy with opioids. *Anesthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie: AINS*. 2002;37(5):244–249.

Cavaillon J-M , Legout S. Louis Pasteur: between myth and reality. *Biomolecules*. 2022;12(4):596.

Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology*. 2014;4:177.

Wiktorowicz ME . Emergent patterns in the regulation of pharmaceuticals: institutions and interests in the United States, Canada, Britain, and France. *Journal of Health Politics, Policy and Law*. 2003;28(4):615–658.

Ernst E. *Herbal Medicine: A Concise Overview for Professionals*. Butterworth-Heinemann, Oxford, 2000.

Pan S-Y , Zhou S-F , Gao S-H , Yu Z-L , Zhang S-F , Tang M-K , et al. New perspectives on how to discover drugs from herbal medicines: CAM'S outstanding contribution to modern therapeutics. *EvidenceBased Complementary and Alternative Medicine*. 2013;2013(1):627375.

Heinrich M , Jalil B , Abdel-Tawab M , Echeverria J , Kulić Ž , McGaw LJ , et al. Best practice in the chemical characterisation of extracts used in pharmacological and toxicological research—the ConPhyMP–guidelines. *Frontiers in Pharmacology*. 2022;13:953205.

Witt CM , Chiamonte D , Berman S , Chesney MA , Kaplan GA , Stange KC , et al. Defining health in a comprehensive context: a new definition of integrative health. *American Journal of Preventive Medicine*. 2017;53(1):134–137.

World Health Organization. *WHO Global Report on Traditional and Complementary Medicine 2019*. World Health Organization, Geneva, 2019.

Noble RL . The discovery of the vinca alkaloids: chemotherapeutic agents against cancer. *Biochemistry and Cell Biology*. 1990;68(12):1344–1351.

Gupta A , Gupta R , Lal B. Effect of *Trigonella foenum-graecum* (Fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes. *Journal of the Association of Physicians of India*. 2001;49:1057–1161.

Gupta SC , Patchva S , Aggarwal BB . Therapeutic roles of curcumin: lessons learned from clinical trials. *The AAPS Journal*. 2013;15:195–1218.

Meshnick SR . Artemisinin: mechanisms of action, resistance and toxicity. *International Journal for Parasitology*. 2002;32(13):1655–1660.

Zheng Y , Xie Y , Qi M , Zhang L , Wang W , Zhang W , et al. Ginkgo biloba extract is comparable with donepezil in improving functional recovery in Alzheimer's disease: results from a multilevel characterized study based on clinical features and resting-state functional magnetic resonance imaging. *Frontiers in Pharmacology*. 2021;12:721216.

Saxena R , Singh R , Kumar P , Yadav S , Negi M , Saxena V , et al. A randomized double blind placebo controlled clinical evaluation of extract of *Andrographis paniculata* (KalmCold™) in patients with uncomplicated upper respiratory tract infection. *Phytomedicine*. 2010;17(3–4):178–185.

Shep D , Khanwelkar C , Gade P , Karad S. Safety and efficacy of curcumin versus diclofenac in knee osteoarthritis: a randomized open-label parallel-arm study. *Trials*. 2019;20:1–11.

Chandrasekhar K , Kapoor J , Anishetty S. A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. *Indian Journal of Psychological Medicine*. 2012;34(3):255–262.

Whitten D , Myers S , Hawrelak J , Wohlmuth H. The effect of St John's wort extracts on CYP3A: a systematic review of prospective clinical trials. *British Journal of Clinical Pharmacology*. 2006;62(5):512–526.

Panossian A , Wikman G , Sarris J. Rosenroot (*Rhodiola rosea*): traditional use, chemical composition, pharmacology and clinical efficacy. *Phytomedicine*. 2010;17(7):481–493.

Bent S , Ko R. Commonly used herbal medicines in the United States: a review. *The American Journal of Medicine*. 2004;116(7):478–485.

Liu S-H , Cheng Y-C . Old formula, new Rx: the journey of PHY906 as cancer adjuvant therapy. *Journal of Ethnopharmacology*. 2012;140(3):614–623.

Bodeker G , Ong C-K . *WHO Global Atlas of Traditional, Complementary and Alternative Medicine*. World Health Organization, Geneva, 2005.

Gupta PK , Sonewane K , Rajan M , Patil NJ , Agrawal T , Banerjee ER , et al. Scientific rationale of Indian AYUSH ministry advisory for COVID-19 prevention, prophylaxis, and immunomodulation. *Advances in Traditional Medicine*. 2023;23(2):321–345.

Chandrasekhar R. Datafication, power, and publics in India's National Digital Health ecosystem. *Socio-Legal Review*. 2024;20(1):1.

Fredriksson M. India's traditional knowledge digital library and the politics of patent classifications. *Law and Critique*. 2023;34(1):1–19.

Jordan SA , Cunningham DG , Marles RJ . Assessment of herbal medicinal products: challenges, and opportunities to increase the knowledge base for safety assessment. *Toxicology and Applied Pharmacology*. 2010;243(2):198–1216.

Chemat F , Vian MA , Cravotto G. Green extraction of natural products: concept and principles. *International Journal of Molecular Sciences*. 2012;13(7):8615–8827.

Hendrawati O , Woerdenbag HJ , Hille J , Kayser O. Metabolic engineering of medicinal plants and microorganisms for the production of natural products. *Pharmaceutical Biotechnology: Drug Discovery and Clinical Applications*. 2012:491–4526.

Litscher G. 'Digital Chinese Medicine (DCM)': From Acupuncture to Algorithms and the Digital Transformation of Traditional Chinese Medicine (TCM). LIDSEN Publishing Inc., Beachwood, OH, 2023. pp. 1–5.

Topol EJ . High-performance medicine: the convergence of human and artificial intelligence. *Nature Medicine*. 2019;25(1):44–56.

## Plants in “Homeopathy” as well as “Ayurveda”

Abdulhameed, Sabu , N. S. Pradeep , and Shiburaj Sugathan . 2017. *Bioresources and Bioprocess in Biotechnology*. Vol. 1. Springer, Singapore. <https://doi.org/10.1007/978-981-10-3573-9>

Abubakar, R. Abdullahi , and Haque, Mainul . 2020. Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. *Journal of Pharmacy and Bioallied Sciences* 12 (1): 1–10. [https://doi.org/10.4103/jpbs.JPBS\\_175\\_19](https://doi.org/10.4103/jpbs.JPBS_175_19)

Adhami, Shehla , Seerat Siraj , and Humaira Farooqi . 2018. Unexplored medicinal plants of potential therapeutic importance: A review. *Tropical Journal of Natural Product Research* 2 (1): 3–11. <https://doi.org/10.26538/tjnpr/v2i1.2>

Ahmad, Iqbal , Farrukh Aqil , Farah Ahmad , and Mohammad Owais . 2006. Herbal medicines: Prospects and constraints. In Iqbal Ahmad , Farrukh Aqil , and Mohammad Owais (Eds.), *Modern Phytomedicine: Turning Medicinal Plants into Drugs*, pp. 59–77. Wiley-VCH, Weinheim. <https://doi.org/10.1002/9783527609987.ch3>

AK, Mohiuddin . 2019. A brief review of traditional plants as sources of pharmacological interests. *Open Journal of Plant Science* 8 (1): 001–0008. <https://doi.org/10.17352/ojps.000015>

Akhtar, Mohd Sayeed , and Mallappa Kumara Swamy . 2018. *Anticancer Plants: Properties and Application*. Vol. 1. Springer, Singapore. <https://doi.org/10.1007/978-981-10-8548-2>

Al-Snafi, Ali Esmail . 2021. Traditional uses of Iraqi medicinal plants (part 2). *International Journal of Biological and Pharmaceutical Sciences Archive* 2 (1): 022–0041. <https://doi.org/10.53771/ijbpsa.2021.2.1.0057>

Awuchi, Chinaza Godswill . 2023. Plants, phytochemicals, and natural practices in complementary and alternative system of medicine for treatment of central nervous system disorders. *International Journal of Food Properties* 26 (1): 1190–1213. <https://doi.org/10.1080/10942912.2023.2205039>

Ayaz, Muhammad Mazhar , Animal Sciences Bahawalpur , Ihtisham Ul Haq , Kashif Rahim , and Animal Sciences . 2021. Histopathologic evaluation and scoring of SARSCoV-2 infection. *Coronavirus Disease-19 (COVID-19): A Perspective of New Scenario*, no. October: 52–71. <https://doi.org/10.2174/9781681089072121020006>

Balachandran, Premalatha , and Rajgopal Govindara . 2007. Ayurvedic drug discovery. *Expert Opinion on Drug Discovery* 2 (12): 1631–1652. <https://doi.org/10.1517/17460441.2.12.1631>

Battu, Heera , and Nimmathota Madhavi . 2023. A short consized note of current trends and future prospects on herbal medicine. *Pharmacognosy Research* 15 (4): 615–622. <https://doi.org/10.5530/pres.15.4.065>

Bergonzi, Maria Camilla , Charles M. Heard , and Javier Garcia-Pardo . 2022. Bioactive molecules from plants: Discovery and pharmaceutical applications. *Pharmaceutics* 14 (10): 14–17. <https://doi.org/10.3390/pharmaceutics14102116>

Bhandariab, Murari , and Anjaneya Ravipatib Sc . 2015. Traditional ayurvedic medicines: Pathway to develop anti-cancer drugs. *Journal of Molecular Pharmaceutics & Organic Process Research* 03 (03): 1–11. <https://doi.org/10.4172/2329-9053.1000130>

Bhattaram, Atul Venkatesh , Ulrike Graefe , Claudia Kohlert , Markus Veit , and Hartmut Derendorf . 2002. Pharmacokinetics and bioavailability of herbal medicinal products. *Phytomedicine* 9 (Suppl. 3): 1–33. <https://doi.org/10.1078/1433-187X-00210>

Bhowmik, Debjit . 2015. Scholars research library traditional herbal medicines: An overview. *Archives of Applied Science Research* 1 (May): 165–77.

Bisht, Balam S. 2019. Evaluation of antianxiety activity of zonisamide based on the serendipitous action in Swiss Albino Mice. *International Journal of Current Research in Chemistry and Pharmaceutical Sciences* 6 (4): 27–32. <https://doi.org/10.22192/ijcrps>

Chauhan, Ashutosh , Deepak Kumar Semwal , and Sunil Kumar Joshi . 2022. An overview of biotechnological applications in ayurveda: Amalgamation of modern techniques and science. *Current Traditional Medicine* 9 (1). <https://doi.org/10.2174/2215083808666220211161918>

Chelladurai, G. , Syed Waqas , Muhammad Akram , Ashok Kumar Panda , Walaa Fikry Elbossaty , Ahmed G. Hegazil , Abdolmajid Ghasemian , Ravindra Prasad Aharwal , and Sudip Kumar Mandal . 2022. Current trends and future prospect of medicinal plants derived nutraceuticals: A review. *Current Trends in Pharmacy and Pharmaceutical Chemistry* 4 (1): 30–34. <https://doi.org/10.18231/j.ctppc.2022.006>

Das, Asmita , and Jaspreet Kaur Dhanjal . 2015. Medicinal Plants, a Gold Mine of Anticancer Compounds, no. March. [https://www.researchgate.net/publication/274075727\\_Das\\_A\\_corresponding\\_author\\_and\\_Dhanjal\\_J\\_K\\_2015\\_Medicinal\\_plants\\_a\\_gold\\_mine\\_of\\_anticancer\\_compounds](https://www.researchgate.net/publication/274075727_Das_A_corresponding_author_and_Dhanjal_J_K_2015_Medicinal_plants_a_gold_mine_of_anticancer_compounds)

Dincheva, Ivayla , Ilian Badjakov , and Bistra Galunska . 2023. New insights into the research of bioactive compounds from plant origins with nutraceutical and pharmaceutical potential. *Plants* 12 (2): 10–13. <https://doi.org/10.3390/plants12020258>

Evaluation, Preclinical , and Plant Products . 2016. Safety, Efficacy and Preclinical Evaluation of Plant Products, no. January 2009. [https://www.researchgate.net/publication/275366164\\_Evaluation\\_of\\_Antioxidant\\_and\\_neuroprotective\\_effect\\_of\\_Hippophae\\_rhamnoides\\_L\\_on\\_oxidative\\_stress\\_induced\\_cytotoxicity\\_in\\_Human\\_neural\\_cell\\_line\\_IMR32](https://www.researchgate.net/publication/275366164_Evaluation_of_Antioxidant_and_neuroprotective_effect_of_Hippophae_rhamnoides_L_on_oxidative_stress_induced_cytotoxicity_in_Human_neural_cell_line_IMR32)

Ghosh, Somnath , Amlan Bishal , Shirsa Kumar Ghosh , Koushik Jana , Bikash Gayen , Suman Sahu , and Biplab Debnath . 2023. Herbal medicines: A potent approach to human diseases, their chief compounds, formulations, present status, and future aspects. *International Journal of Membrane Science and Technology* 10 (1): 442–464. <https://doi.org/10.15379/ijmst.v10i1.2608>

Goswami, Debayan , Ananya Das Mahapatra , Subhadip Banerjee , Amit Kar , Durbadal Ojha , Pulok K. Mukherjee , and Debprasad Chattopadhyay. October 16, 2018. Boswellia Serrata Oleo-gum-resin and B-boswellic acid inhibits HSV-1 infection in vitro through modulation of NF- $\kappa$ B and P38 MAP kinase signaling. *Phytomedicine* 51: 94–103. <https://doi.org/10.1016/j.phymed.2018.10.016>

Hendrawati, Oktavia , Herman J. Woerdenbag , Jacques Hille , and Oliver Kayser . 2012. Metabolic engineering of medicinal plants and microorganisms for the production of natural products. In O. Kayser , and R. H. Muller (Eds.), *Pharmaceutical Biotechnology: Drug Discovery and Clinical Applications*, pp. 491–4526. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim. <https://doi.org/10.1002/9783527632909.ch19>

Jamshidi-Kia, Fatemeh , Zahra Lorigooini , and Hossein Amini-Khoei . 2018. Medicinal plants: Past history and future perspective. *Journal of HerbMed Pharmacology* 7 (1): 1–7. <https://doi.org/10.15171/jhp.2018.01>

Joseph, Baby , and S. Justin Raj . 2011. A comparative study on various properties of five medicinally important plants. *International Journal of Pharmacology* 7 (2): 206–211. <https://doi.org/10.3923/ijp.2011.206.211>

Kumar Shakya , Arvind. 2016. Medicinal plants: Future source of new drugs. *International Journal of Herbal Medicine* 4 (4): 59–64. <https://doi.org/10.13140/RG.2.1.1395.6085>

Kumar, Sathish B. P. , and Vadlapudi Kumar . 2009. An overview of herbal medicine. *International Journal of Pharmaceutical Sciences* 1 (11): 1–201. <https://www.researchgate.net/publication/343194624%0Awww.ijps.info>

Lele, R. D. 2013. Molecular biology provides a new interface between molecular biology provides a new interface between ayurved & modern medicine. *Annals of the National Academy of Medical Sciences (India)* 49: 31–47.

Malabadi, Ravindra B. , M. R. Sadiya , Kiran P. Kolkar , Simuzar S. Mammadova , Raju K. Chalannavar , and Himansu Baijnath . 2024. Role of plant derived-medicine for controlling cancer. *International Journal of Science and Research Archive* 11 (1): 2502–2539.



<https://doi.org/10.30574/ijrsra.2024.11.1.0315>

Máthé, Ákos , and Irfan Ali Khan . Medicinal and Aromatic Plants of India Vol. 1. Springer Nature, 2022.

Mehrotra, N. N. , S. K. Ojha , S. Tandon . 2018. Feature drug development for cardiovascular diseases from ayurvedic plants. *Afrigetics.Com* 25 (3): 1189–1196. <https://afrigetics.com/wp-content/uploads/2019/02/drug-development-for-cardiovascular-diseases-rd1-3full.pdf>

Mukherjee Pulok, K. , Bahadur Shiv , K. Harwansh Ranjit , and K. Chaudhary Sushil . 2014. Shifting paradigm for validation of medicinal plants in Indian traditional medicine. *Indian Drugs* 51 (8): 5–14. <https://doi.org/10.53879/id.51.08.10153>

Mukherjee, Pulok K. , and Atul Wahile . 2006. Integrated approaches towards drug development from ayurveda and other Indian system of medicines. *Journal of Ethnopharmacology* 103 (1): 25–35. <https://doi.org/10.1016/j.jep.2005.09.024>

Nasim, Noohi , Inavolu Sriram Sandeep , and Sujata Mohanty . 2022. Plant-derived natural products for drug discovery: Current approaches and prospects. *Nucleus (India)* 65 (3): 399–3411. <https://doi.org/10.1007/s13237-022-00405-3>

Omprakash , Bhushnure G , Shinde C Madhuri , Vijayendra S. M. Swamy , Gholve B. Sachin , Giram S. Padmaja , and Birajdar J. Mahesh . 2019. Phytopharmaceuticals: An emerging platform for innovation and development of new drugs from botanicals. *Journal of Drug Delivery and Therapeutics* 9 (3-s): 1046–1157. <https://jddtonline.info>

Pakhmode, Pallavi K. , and Swapnaja A. Mohite . 2023. Multidisciplinary approach: Enhanced agriculture production in a sustainable way. In Shweta Sharma , and Dilbag Singh (Eds.), *Integrated Pest and Nutrition Management for Sustainable Agriculture*. Bhumi Publishing, India, pp. 196–1205.

Parveen, Bushra , Abida Parveen , Rabea Parveen , Sayeed Ahmad , Minhaj Ahmad , and Muhammad Iqbal . 2020. Challenges and opportunities for traditional herbal medicine today with special reference to its status in India. *Annals of Phytomedicine: An International Journal* 9 (2): 97–112. <https://doi.org/10.21276/ap.2020.9.2.8>

Patwardhan, B. 2000. Ayurveda: The 'designer' medicine: A review of ethnopharmacology and bioprospecting research. *Indian Drugs* 37 (5): 213–227.

Poduri, Ramarao . 2021. *Drug Discovery and Development: From Targets and Molecules to Medicines*. Springer Nature, Singapore. <https://doi.org/10.1007/978-981-15-5534-3>

Raj, Sreena , S. Karthikeyan , and K. M. Gothandam . 2011. Ayurveda: A glance. *Research in Plant Biology* 1 (1): 1–14. [www.resplantbiol.com](http://www.resplantbiol.com)

Rasool, Aatifa , Technology Srinagar , India Khalid Mushtaq Bhat , India Altaf Ahmed Sheikh , Aarifa Jan , India Shaziya Hassan , India Corresponding Author , Khalid Mushtaq Bhat , Altaf Ahmed Sheikh , and Shaziya Hassan . 2020. Medicinal plants: Role, distribution and future. *Journal of Pharmacognosy and Phytochemistry* 9 (2): 2111–2214. [www.phytojournal.com](http://www.phytojournal.com)

Sen, Saikat , and Raja Chakraborty . 2015. Toward the integration and advancement of herbal medicine: A focus on traditional Indian medicine. *Botanics: Targets and Therapy*, 33. <https://doi.org/10.2147/btat.s66308>

Sen, Saikat , and Raja Chakraborty . 2020. *Herbal Medicine in India*. Springer, Singapore. <https://doi.org/10.1007/978-981-13-7248-3>

Shanthi, N. , S. M. J. Nithia , and M. Kannappan . 2021. Indigenous Medicinal Plants and Its Active Compound for Future Drug. *Researchgate.Net*. [https://www.researchgate.net/profile/N-Shanthi/publication/353679883\\_INDIGENOUS\\_MEDICINAL\\_PLANTS\\_AND\\_ITS\\_ACTIVE\\_COMPOUND\\_FOR\\_FUTURE\\_DRUG/links/610a2b121ca20f6f86fce3e4/INDIGENOUS-MEDICINAL-PLANTS-AND-ITS-ACTIVE-COMPOUND-FOR-FUTURE-DRUG.pdf](https://www.researchgate.net/profile/N-Shanthi/publication/353679883_INDIGENOUS_MEDICINAL_PLANTS_AND_ITS_ACTIVE_COMPOUND_FOR_FUTURE_DRUG/links/610a2b121ca20f6f86fce3e4/INDIGENOUS-MEDICINAL-PLANTS-AND-ITS-ACTIVE-COMPOUND-FOR-FUTURE-DRUG.pdf)

Sharma, Rohit , Kamil Kuca , Eugenie Nepovimova , Atul Kabra , M. M. Rao , and P. K. Prajapati . 2019. Traditional ayurvedic and herbal remedies for Alzheimer's disease: From bench to bedside. *Expert Review of Neurotherapeutics* 19 (5): 359–374. <https://doi.org/10.1080/14737175.2019.1596803>

Sharma, Sheetal , M. V. N. L. Chaitanya , Sarika Sharma , Sanjeev Kumar , Sarvesh Rustagi , Sangram Singh , Sheikh Shreaz , Ashutosh Kumar Rai , Rajeshwari Negi , and Ajar Nath Yadav . 2024. The medicinal plant *Berberis aristata* and its endophytes for pharmacological applications: Current research and future challenges. *Journal of Applied Biology and Biotechnology* 12 (4): 37–46. <https://doi.org/10.7324/JABB.2024.167591>

Shrikumar, Sapna . 2007. Approaches towards development and promotion of herbal drugs. *Pharmacognosy Reviews* 1 (1): 180–184. <https://www.phcogrev.com>

Singh, Maheshwari Kumari , and O. S. Bindhu . 2019. Plant latex: A rich source of haemostatic proteases. In Saikat Sen , and Raja Chakraborty (Eds.), *Herbal Medicine in India: Indigenous Knowledge, Practice, Innovation and Its Value*, pp. 143–1153. Springer, Singapore. [https://doi.org/10.1007/978-981-13-7248-3\\_10](https://doi.org/10.1007/978-981-13-7248-3_10)

Singh, Satendra , Dev Bukhsh Singh , Shivani Singh , Rohit Shukla , Pramod W. Ramteke , and Krishna Misra . 2019. Exploring medicinal plant legacy for drug discovery in post-genomic era. *Proceedings of the National Academy of Sciences India Section B - Biological Sciences* 89 (4): 1141–1151. <https://doi.org/10.1007/s40011-018-1013-x>

Swami, D. V. , M. Anitha , M. Chandra Surya Rao , and A. B. Sharangi . 2022. Medicinal plants: Perspectives and retrospectives. In Amit Baran Sharangi , and K. V. Peter (Eds.), *Medicinal Plants*, pp. 1–28. Apple Academic Press, New York. <https://doi.org/10.1201/9781003277408-1>

Swamy, Mallappa Kumara . 2020. *Plant-Derived Bioactives: Production, Properties and Therapeutic Applications*. Springer, Singapore. <https://doi.org/10.1007/978-981-15-1761-7>

Utane, Rajdip Devidas , Sant Gadge , Maharaj Mahavidyalaya , Srimad Andavan Arts , Michael Veronin , and Rob Schumaker . 2022. *Current Aspects in Pharmaceutical Research and Development Vol. 8*. <https://doi.org/10.9734/bpi/caprd/v8>

Verma, Sunil Kumar , Minakshi Pandey , Avinash Sharma , and Devendra Singh . 2024. Exploring ayurveda: Principles and their application in modern medicine. *Bulletin of the National Research Centre* 48 (1). <https://doi.org/10.1186/s42269-024-01231-0>

Vignesh, Arumugam , Ramamoorthy Sivalingam , Subramaniam Selvakumar , and Krishnan Vasanth . 2022. A review on ethnomedicinal and phytopharmacological potential of traditionally wild and endemic plant *Berberis tinctoria* Lesch. *Thai Journal of Pharmaceutical Sciences* 46 (2): 137–148. <https://doi.org/10.56808/3027-7922.2554>

Wahid, Muqet , Anam Ali , Fatima Saqib , Ambreen Aleem , Sumbal Bibi , Khurram Afzal , Atif Ali , Ayesha Baig , Shujaat Ali Khan , and Muhammad Hassham Hassan Bin Asad . 2020. Pharmacological exploration of traditional plants for the treatment of neurodegenerative disorders. *Phytotherapy Research* 34 (12): 3089–33112. <https://doi.org/10.1002/ptr.6742>

## Plant-Based Remedies in Obesity Treatment

Ahn, Jiyun , Hyunjung Lee , Jayoung Jang , Suna Kim , and Taeyoul Ha . Anti-obesity effects of glabridin-rich supercritical carbon dioxide extract of licorice in high-fat-fed obese mice. *Food and Chemical Toxicology* 51 (2013): 439–445.

Al-Nuaim, Lulu A. The impact of obesity on reproduction in women. *Saudi Medical Journal* 32, no. 10 (2011): 993–1002.

Alruwaili, Heshma , Babak Dehestani , and Carel W. le Roux . Clinical impact of liraglutide as a treatment of obesity. *Clinical Pharmacology: Advances and Applications* 11 (2021): 53–60.

Alsherif, Diana A. , Mohammed A. Hussein , and Suzan S. Abuelkasem . *Salvia officinalis* improves glycemia and suppresses pro-inflammatory features in obese rats with metabolic syndrome. *Current Pharmaceutical Biotechnology* 25, no. 5 (2024): 623–636.

Apovian, Caroline M. Naltrexone/bupropion for the treatment of obesity and obesity with type 2 diabetes. *Future Cardiology* 12, no. 2 (2016a): 129–138.

Apovian, Caroline M. Obesity: definition, comorbidities, causes, and burden. *The American Journal of Managed Care* 22, no. 7 Suppl (2016b): s176–85.

Avalos-Soriano, Anaguiven , Ricardo De la Cruz-Cordero, Jorge L. Rosado, and Teresa Garcia-Gasca. 4-Hydroxyisoleucine from fenugreek (*Trigonella foenum-graecum*): effects on insulin resistance associated with obesity. *Molecules* 21, no. 11 (2016): 1596.

Basu, Tanisha , Ashley Selman , Arubala P. Reddy , and P. Hemachandra Reddy . Current status of obesity: protective role of catechins. *Antioxidants* 12, no. 2 (2023): 474.

Benaiges, David , Albert Goday , Juan Pedro-Botet , Antonio Más , Juan José Chillarón , and Juana A. Flores-Le Roux . Bariatric surgery: to whom and when? *Minerva Endocrinologica* 40, no. 2 (2015): 119–128.

Berlie, Helen D. , and Kathryn M. Hurren . Evaluation of lorcaserin for the treatment of obesity. *Expert Opinion on Drug Metabolism & Toxicology* 9, no. 8 (2013): 1053–1059.

Bonetti, Gabriele , Karen L. Herbst , Kevin Donato , Kristjana Dhuli , Aysha Karim Kiani , Barbara Aquilanti , Valeria Velluti , Giuseppina Matera , Amerigo Iaconelli , and Matteo Bertelli .

Dietary supplements for obesity. *Journal of Preventive Medicine and Hygiene* 63, no. 2 Suppl 3 (2022): E160.

Brimson, James Michael , Mani Iyer Prasanth , Kishoree Krishna Kumaree , Premrutai Thitilertdech , Dicson Sheeja Malar , Tewin Tencomnao , and Anchalee Prasansuklab . Tea plant (*Camellia sinensis*): a current update on use in diabetes, obesity, and cardiovascular disease. *Nutrients* 15, no. 1 (2022): 37.

Brown, Jenny , and Peter Wimpenny . Determining factors required for a holistic approach to weight management of those with obesity. *Advances in Nursing Science* 34, no. 2 (2011): 136–150.

Brown, R. E. , and J. L. Kuk . Consequences of obesity and weight loss: a devil's advocate position. *Obesity Reviews* 16, no. 1 (2015): 77–87.

Camacho, Susana , Stephanie Michlig , Carole de Senarclens-Bezençon , Jenny Meylan , Julie Meystre , Maurizio Pezzoli , Henry Markram , and Johannes Le Coutre . Anti-obesity and anti-hyperglycemic effects of cinnamaldehyde via altered ghrelin secretion and functional impact on food intake and gastric emptying. *Scientific Reports* 5, no. 1 (2015): 7919.

Cao, Lei , Chunwei Wu , Miao Liu , Wenlong Zhang , Hailong Chen , Ruolin Wang , and Ze He . The natural products as novel anti-obesity agents: mechanisms based on adipose tissue. *Current Diabetes Reviews* 20 (2024).

Castro-Barquero, Sara , Ana María Ruiz-León , Maria Sierra-Pérez , Ramon Estruch , and Rosa Casas . Dietary strategies for metabolic syndrome: a comprehensive review. *Nutrients* 12, no. 10 (2020): 2983.

Catalano, Patrick M. , and Kartik Shankar . Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. *BMJ* 356 (2017): J1.

Chen, Suzhen , Xiaoxiao Liu , Chao Peng , Chang Tan , Honglin Sun , He Liu , Yao Zhang et al. The phytochemical hyperforin triggers thermogenesis in adipose tissue via a Dlat-AMPK signaling axis to curb obesity. *Cell Metabolism* 33, no. 3 (2021): 565–580.

Cheng, Siyao , Xintao Ni , Yanjing Yao , Yunxia Sun , Xiaofeng Yu , Daozong Xia , Zhenggang Yang , Miaofen G. Hu , and Xiaoli Hou . Hyperoside prevents high-fat diet-induced obesity by increasing white fat browning and lipophagy via CDK6-TFEB pathway. *Journal of Ethnopharmacology* 307 (2023): 116259.

Chooi, Yu Chung , Cherlyn Ding , and Faidon Magkos . The epidemiology of obesity. *Metabolism* 92 (2019): 6–10.

Cunningham, A. B. , J. A. Brinckmann , R. N. Kulloli , and U. Schippmann . Rising trade, declining stocks: the global gugul (*Commiphora wightii*) trade. *Journal of Ethnopharmacology* 223 (2018): 22–32. doi:10.1016/j.jep.2018.04.040. Epub 2018 May 8. PMID: 29746995.

Davkova, Iskra , Zoran Zhivikj , Jelena Kukić-Marković , Ivana Cvetkovik Karanfilova , Gjosh Stefkov , Svetlana Kulevanova , and Marija Karapandzova . Natural products in the management of obesity. *Archives of Pharmacy* 74, no. Notebook 3 (2024): 298–315.

De la Peña, Ike , Timothy Afable , Vina Rose Dahilig-Talan , and Philip Cruz . Review of plant extracts and active components: mechanisms of action for the treatment of obesity-induced cognitive impairment. *Brain Sciences* 13, no. 6 (2023): 929.

Deekshith, Chandana , Markandeya Jois , Jessica Radcliffe , and Jency Thomas . Effects of culinary herbs and spices on obesity: a systematic literature review of clinical trials. *Journal of Functional Foods* 81 (2021): 104449.

Drucker, Daniel J. GLP-1 physiology informs the pharmacotherapy of obesity. *Molecular Metabolism* 57 (2022): 101351.

Dwaipayan, B. and M. Janaki Nair . The complex web of obesity: from genetics to precision medicine. *Expert Review of Endocrinology & Metabolism* 19 (2024): 1–16.

Fan, Meiqi , Eun-Kyung Kim , Young-Jin Choi , Yujiao Tang , and Sang-Ho Moon . The role of *Momordica charantia* in resisting obesity. *International Journal of Environmental Research and Public Health* 16, no. 18 (2019): 3251.

Ferrari, Gustavo Duarte , Milton Azevedo , Leonardo Medeiros , Carmem Beatiz Neufeld , Rosane Pilot Pena Ribeiro , Bernard Pimentel Rangé , and Carlos Roberto Bueno . A multidisciplinary weight-loss program: the importance of psychological group therapy. *Motriz: Revista de Educação Física* 23 (2017): 47–52.

Gala, Khushboo , Wissam Ghusn , and Andres Acosta . Precision medicine in bariatric procedures. *Gastrointestinal Endoscopy Clinics* 34, no. 4 (2024): 765–779.

GBD 2019 Risk Factors Collaborators, and Johan Ärnlöv. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 396, no. 10258 (2020): 1223–1249.

Ghai, Roma , S. N. E. H. A. Chaudhary , Kandasamy Nagarajan , Richa Goel , Shardendu Kumar Mishra , Naveen Kumar Tholia , Nazakat Ali , and Monika Kaurav . An investigative study of medicinal herbs for anti-obesity potential: a review. *Oriental Journal of Chemistry* 39, no. 6 (2023). <https://bit.ly/3R2be6v>

Gordon, James S. Holistic medicine: advances and shortcomings. *Western Journal of Medicine* 136, no. 6 (1982): 546.

Higgins, Guy A. , Paul J. Fletcher , and William R. Shanahan . Lorcaserin: a review of its preclinical and clinical pharmacology and therapeutic potential. *Pharmacology & Therapeutics* 205 (2020): 107417.

Hillsley, Ashley , Vanessa Chin , Amy Li , and Craig S. McLachlan . Resveratrol for weight loss in obesity: an assessment of randomized control trial designs in *ClinicalTrials.gov* . *Nutrients* 14, no. 7 (2022): 1424.

Hirt, Penelope A. , David E. Castillo , Gil Yosipovitch , and Jonette E. Keri . Skin changes in the obese patient. *Journal of the American Academy of Dermatology* 81, no. 5 (2019): 1037–1057.

Hoy, Sheridan M. Lorcaserin: a review of its use in chronic weight management. *Drugs* 73 (2013): 463–473.

Hruby, Adela , JoAnn E. Manson , Lu Qi , Vasanti S. Malik , Eric B. Rimm , Qi Sun , Walter C. Willett , and Frank B. Hu . Determinants and consequences of obesity. *American Journal of Public Health* 106, no. 9 (2016): 1656–1662.

Hu, Xiaoqin , Ao Sun , Huijian Chen , Xiyue Yan , Fei Ding , Peng Zheng , Zhen Li , and You-E. Yan . Saponins from *Panax japonicus* alleviate adipose tissue fibrosis and metabolic dysfunction in high-fat-diet-induced obese mice. *Biomarkers* 27, no. 8 (2022): 784–794.

Ibrahim, M. , Hamouda . Medicinal plants for the treatment of obesity. *International Journal of Clinical Case Reports and Reviews* 13, no. 2 (2023): 1–5. <https://doi.org/10.31579/2690-4861/294>

Jaleel, Rajeeb , Nitin Kapoor , and Sanjay Kalra . Endoscopic intragastric balloon: a novel therapy for weight loss. *JPMMA. The Journal of the Pakistan Medical Association* 72, no. 7 (2022): 1444–1446.

Kasprzak-Drozd, Kamila , Tomasz Oniszczyk , Marek Gancarz , Adrianna Kondracka , Robert Rusinek , and Anna Oniszczyk . Curcumin and weight loss: does it work? *International Journal of Molecular Sciences* 23, no. 2 (2022): 639.

Kim, Inhye , HaengRan Kim , JaeHyun Kim , and AeSon Om . Beneficial effects of *Allium sativum* L. stem extract on lipid metabolism and antioxidant status in obese mice fed a highfat diet. *Journal of the Science of Food and Agriculture* 93, no. 11 (2013): 2749–2757.

Kim, Seok-Young , Ji Eon Park , Hyo-Jung Lee , Deok Yong Sim , Chi-Hoon Ahn , Su-Yeon Park , Bum-Sang Shim , Bonglee Kim , Dae Young Lee , and Sung-Hoon Kim . *Astragalus membranaceus* extract induces apoptosis via generation of reactive oxygen species and inhibition of heat shock protein 27 and androgen receptor in prostate cancers. *International Journal of Molecular Sciences* 25, no. 5 (2024): 2799.

Kobayashi, Kyoko , Keiko Yamada , Toshihiro Murata , Tatsuya Hasegawa , Fumihide Takano , Kazutaka Koga , Shinji Fushiya , Javzan Batkhoo , and Fumihiko Yoshizaki . Constituents of *Rhodiola rosea* showing inhibitory effect on lipase activity in mouse plasma and alimentary canal. *Planta Medica* 74, no. 14 (2008): 1716–1719.

Ladenheim, Ellen E. Liraglutide and obesity: a review of the data so far. *Drug Design, Development and Therapy* 9 (2015): 1867–1875.

Lasikiewicz, Nicola , Kyriaki Myrissa , Alexa Hoyland , and C. L. Lawton . Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. *Appetite* 72 (2014): 123–137.

Lee, Dongju , Yujin Shin , Jong Seong Roh , Jiwon Ahn , Sunhyo Jeong , Soon Shik Shin , and Michung Yoon . Lemon balm extract ALS-L1023 regulates obesity and improves insulin sensitivity via activation of hepatic PPAR $\alpha$  in high-fat diet-fed obese C57BL/6J mice. *International Journal of Molecular Sciences* 21, no. 12 (2020): 4256.

Leitzmann, Michael . Physical activity, sedentary behaviour, and obesity. In Romieu I , Dossus L , Willett WC , editors. *Energy Balance and Obesity*. Lyon (FR): International Agency for Research on Cancer. (IARC Working Group Reports, No. 10.), Chapter 6 (2017). <https://www.ncbi.nlm.nih.gov/books/NBK565813/>.

Li, Xin , Licong Yang , Jingen Li , Lezhen Lin , and Guodong Zheng . A flavonoid-rich *Smilax china* L. extract prevents obesity by upregulating the adiponectin-receptor/AMPK signalling pathway and modulating the gut microbiota in mice. *Food & Function* 12, no. 13 (2021): 5862–5875.

Lima, Natalia da Silva , Erica de Paula Numata , Leonardo Mendes de Souza Mesquita , Pollyana Hammoud Dias , Wagner Vilegas , Alessandra Gambero , and Marcelo Lima Ribeiro . Modulatory effects of guarana (*Paullinia cupana*) on adipogenesis. *Nutrients* 9, no. 6 (2017): 635.

Lin, X. and H. Li . Obesity: epidemiology, pathophysiology, and therapeutics. *Frontiers in Endocrinology* 12 (2021): 706978. doi:10.3389/fendo.2021.706978

Liu, Jiuxi , Jiawei Cai , Peng Fan , Xue Dong , Naisheng Zhang , Jiandong Tai , and Yongguo Cao . Salidroside protects mice from high-fat diet-induced obesity by modulating the gut microbiota. *International Immunopharmacology* 120 (2023): 110278.

Mandar, Bijendra K. , Pukar Khanal , B. M. Patil , Yadu Nandan Dey , and Ismail Pasha . In silico analysis of phytoconstituents from *Tinospora cordifolia* with targets related to diabetes and obesity. In *Silico Pharmacology* 9, no. 1 (2021): 3.

Márquez, Fabiola , Nancy Babio , Mònica Bulló , and J. Salas-Salvadó . Evaluation of the safety and efficacy of hydroxycitric acid or *Garcinia cambogia* extracts in humans. *Critical Reviews in Food Science and Nutrition* 52, no. 7 (2012): 585–594.

Martinez, J. Alfredo . Body-weight regulation: causes of obesity. *Proceedings of the Nutrition Society* 59, no. 3 (2000): 337–345.

Masood, Beenish , and Myuri Moorthy . Causes of obesity: a review. *Clinical Medicine* 23, no. 4 (2023): 284–291.

McNeely, Wendy , and Paul Benfield . Orlistat. *Drugs* 56, no. 2 (1998): 241–249. <https://doi.org/10.2165/00003495-199856020-00007>

Mohammadpour, Saba , Mohammad Reza Amini , Hossein Shahinfar , Aliyu Jibril Tijani , Mahshid Shahavandi , Parivash Ghorbaninejad , Kurosh Djafarian , and Sakineh Shab-Bidar . Effects of glucomannan supplementation on weight loss in overweight and obese adults: a systematic review and meta-analysis of randomized controlled trials. *Obesity Medicine* 19 (2020): 100276.

Mohseni, Mostafa , Susanne Kuckuck , Renate E. H. Meeusen , Geranne Jiskoot , Robin Lengton , Mesut Savas , Kirsten A. C. Berk et al. Improved physical and mental health after a combined lifestyle intervention with cognitive behavioural therapy for obesity. *International Journal of Endocrinology and Metabolism* 21, no. 1 (2023): e129906.

Muragi, Amar , Sheetal Samant , and P. MB . Formulation and evaluation of herbal emulgel loaded with extract of *Cedrus deodara* for its in-vitro anti-inflammatory activity. *International Journal of Ayurvedic Medicine* 13, no. 3 (2022): 749–753.

Nadhiya, K. , Vijayalakshmi, K. , and Gaddam Aadinaath Reddy . Antiobesity effect of *Benincasa hispida* fruit extract in high fat diet fed wistar albino rats. *International Journal of Pharmaceutical and Clinical Research* 8, no. 12 (2016): 1590–1599.

Nittari, Giulio , Stefania Scuri , Fabio Petrelli , Iolanda Pirillo , Natale Mario di Luca , and Iolanda Grappasonni . Fighting obesity in children from European World Health Organization member states. Epidemiological data, medical-social aspects, and prevention programs. *La Clinica Terapeutica* 170, no. 3 (2019): e223–e230.

Omer, Tahir . The causes of obesity: an in-depth review. *Advances in Obesity, Weight Management & Control* 10, no. 4 (2020): 90–94.

Ono, Yuka , Eri Hattori , Yukitaka Fukaya , Shoji Imai , and Yasushi Ohizumi . Anti-obesity effect of *Nelumbo nucifera* leaves extract in mice and rats. *Journal of Ethnopharmacology* 106, no. 2 (2006): 238–244.

Patil, Kalpana S. , and Sheetal S. Samant . Formulation and evaluation of topical polyherbal gel containing *Cocculus hirsutus* and *Tridax procumbens*. *International Journal of Pharmaceutical Sciences and Research* 14, no. 9 (2023): 4560–4566.

Phung, Hung Manh , Dongyeop Jang , Tuy An Trinh , Donghun Lee , Quynh Nhu Nguyen , Chang-Eop Kim , and Ki Sung Kang . Regulation of appetite-related neuropeptides by *Panax ginseng*: a novel approach for obesity treatment. *Journal of Ginseng Research* 46, no. 4 (2022): 609–619.

PiSunyer, F. Xavier . The obesity epidemic: pathophysiology and consequences of obesity. *Obesity Research* 10, no. S12 (2002): 97S–104S.

Pi-Sunyer, Xavier . The medical risks of obesity. *Postgraduate Medicine* 121, no. 6 (2009): 21–33.

Pothuraju, Ramesh , Raj Kumar Sharma , Jayasimha Chagalamarri , Surender Jangra , and Praveen Kumar Kavadi . A systematic review of *Gymnema sylvestre* in obesity and diabetes management. *Journal of the Science of Food and Agriculture* 94, no. 5 (2014): 834–840.

Redha, Ali Ali , Simone Perna , Antonella Riva , Giovanna Petrangolini , Gabriella Peroni , Mara Nichetti , Giancarlo Iannello , Maurizio Naso , Milena Anna Faliva , and Mariangela Rondanelli . Novel insights on anti-obesity potential of the miracle tree, *Moringa oleifera*: a systematic review. *Journal of Functional Foods* 84 (2021): 104600.

Ruban, Aruchuna , Kostadin Stoenchev , Hutan Ashrafian , and Julian Teare . Current treatments for obesity. *Clinical Medicine* 19, no. 3 (2019): 205–212.

Safaei, Mahmood , Elankovan A. Sundararajan , Maha Driss , Wadii Boulila , and Azrulhizam Shapi'i . A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. *Computers in Biology and Medicine* 136 (2021): 104754.

Saravanan, Ganapathy , Ponnusamy Ponmurugan , Machampalayam Arumugam Deepa , and Balasubramanian Senthilkumar . Antiobesity action of gingerol: effect on lipid profile, insulin, leptin, amylase and lipase in male obese rats induced by a highfat diet. *Journal of the Science of Food and Agriculture* 94, no. 14 (2014): 2972–2977.

Saunders, Katherine H. , Devika Umashanker , Leon I. Igel , Rekha B. Kumar , and Louis J. Aronne . Obesity pharmacotherapy. *Medical Clinics* 102, no. 1 (2018): 135–148.

Shi, Xin' E. , Xiaomin Zhou , Xinyi Chu , Jie Wang , Baocai Xie , Jing Ge , Yuan Guo , Xiao Li , and Gongshe Yang . Allicin improves metabolism in high-fat diet-induced obese mice by modulating the gut microbiota. *Nutrients* 11, no. 12 (2019): 2909.

Silva, Lyz Bezerra , and Manoel Galvão Neto . Intragastric balloon. *Minimally Invasive Therapy & Allied Technologies* 31, no. 4 (2022): 505–514.

Simmons, David . Diabetes and obesity in pregnancy. *Best Practice & Research Clinical Obstetrics & Gynaecology* 25, no. 1 (2011): 25–36.

Spinelli, Angela , Marta Buoncristiano , Viktoria Anna Kovacs , Agneta Yngve , Igor Spiroski , Galina Obreja , Gregor Starc et al. Prevalence of severe obesity among primary school children in 21 European countries. *Obesity Facts* 12, no. 2 (2019): 244–258.

Steele, Lynette . Health and wellness: holistic and complementary methods. In Walter Leal Filho , Tony Wall , Anabela Marisa Azul , Luciana Brandli , and Pinar Gokcin Özuyar (Eds.), *Good Health and Well-Being*, pp. 293–304 (2020). Springer.

Swencionis, Charles , Judith Wylie-Rosett , Michelle R. Lent , Mindy Ginsberg , Christopher Cimino , Sylvia Wassertheil-Smoller , Arlene Caban , and Carol-Jane Segal-Isaacson . Weight change, psychological well-being, and vitality in adults participating in a cognitive–behavioral weight loss program. *Health Psychology* 32, no. 4 (2013): 439.

Tate, Chinara M. , and Allan Geliebter . Intragastric balloon treatment for obesity: review of recent studies. *Advances in Therapy* 34 (2017): 1859–1875.

Tutunchi, Helda , Sara Arefhosseini , Solmaz Nomi-Golzar , and Mehrangiz Ebrahimi-Mameghani . Effects of hydroxycitric acid supplementation on body composition, obesity indices, appetite, leptin, and adiponectin of women with NAFLD on a calorierestricted diet. *International Journal of Clinical Practice* 2023, no. 1 (2023): 6492478.

Upralkar, Snehal , Akshaya Gadekar , Prajakt Kalangutkar , Riddhi Rane , Raghunath Morye , Samidha Desai , Omkar Tawade , Sheetal S. Samant , and Vijay A. Jagtap . Ethnobotanical survey of medicinal plants commonly used by traditional medicine practitioners in Sindhudurg Region, India. *International Journal of Ayurvedic Medicine* 14, no. 1 (2023): 151–156.

Verpeut, Jessica L. , and Nicholas T. Bello . Drug safety evaluation of naltrexone/bupropion for the treatment of obesity. *Expert Opinion on Drug Safety* 13, no. 6 (2014): 831–841.

Wachtel-Galor, Sissi , and Iris F. F. Benzie . Herbal medicine: an introduction to its history, usage, regulation, current trends, and research needs. In Benzie IFF , Wachtel-Galor S , editors. *Herbal Medicine: Biomolecular and Clinical Aspects*. 2nd ed. (2012). CRC Press/Taylor & Francis.

Wang, Shumin , Ning Ma , Weilin Zhao , Kaoru Midorikawa , Shosuke Kawanishi , Yusuke Hiraku , Shinji Oikawa , Zhe Zhang , Guangwu Huang , and Mariko Murata . Inflammation related DNA damage and cancer stem cell markers in nasopharyngeal carcinoma. *Mediators of Inflammation* 2016, no. 1 (2016): 9343460.

Wang, Zhengyu , KaLung Lam , Jiamiao Hu , Shenghan Ge , Arong Zhou , Baodong Zheng , Shaoxiao Zeng , and Shaoling Lin . Chlorogenic acid alleviates obesity and modulates gut microbiota in highfatfed mice. *Food Science & Nutrition* 7, no. 2 (2019): 579–588.

Xu, Meng , Hui Xue , Li Kong , Lezhen Lin , and Guodong Zheng . Smilax china L. polyphenols improves insulin resistance and obesity in high-fat diet-induced mice through IRS/AKT-AMPK and NF- $\kappa$ B signaling pathways. *Plant Foods for Human Nutrition* 78, no. 2 (2023): 299–306.

Yimam, Mesfin , Ping Jiao , Mei Hong , Lidia Brownell , Young-Chul Lee , Hyun-Jin Kim , Jeong-Bum Nam , Mi-Ran Kim , and Qi Jia . Morus alba, a medicinal plant for appetite suppression and weight loss. *Journal of Medicinal Food* 22, no. 7 (2019): 741–751.

Zhang, Jian , Min-Jung Kang , Myung-Jin Kim , Mi-Eun Kim , Ji-Hyun Song , Young-Min Lee , and Jung-In Kim . Pancreatic lipase inhibitory activity of taraxacum officinale in vitro and in vivo. *Nutrition Research and Practice* 2, no. 4 (2008): 200–203.

Zhang, Xiang , Suki Ha , Harry Cheuk-Hay Lau , and Jun Yu . Excess body weight: novel insights into its roles in obesity comorbidities. *Seminars in Cancer Biology* 92: 16–27 (2023). doi: 10.1016/j.semcancer.2023.03.008

Zheng, Jia , Sheng Zheng , Qianyun Feng , Qian Zhang , and Xinhua Xiao . Dietary capsaicin and its anti-obesity potency: from mechanism to clinical implications. *Bioscience Reports* 37, no. 3 (2017): BSR20170286.

Zhou, Lin , Qiyang Zeng , Shaosheng Jin , and Guangyan Cheng . The impact of changes in dietary knowledge on adult overweight and obesity in China. *PLoS One* 12, no. 6 (2017): e0179551.

Zhou, Ping , Weijie Xie , Shuaibing He , Yifan Sun , Xiangbao Meng , Guibo Sun , and Xiaobo Sun . Ginsenoside Rb1 as an anti-diabetic agent and its underlying mechanism analysis. *Cells* 8, no. 3 (2019): 204.

Zitsman , Jeffrey L. Laparoscopic adjustable gastric banding in adolescents. *Seminars in Pediatric Surgery* 23, no. 1 (2014): 17–20. WB Saunders.

## Herbal Formulation for Ocular Disease

Abhishek, K. , M. Ashutosh , and B. N. Sinha , Herbal drugs-present status and efforts to promote and regulate cultivation, *Pharma Rev.*, vol. 6, pp. 73–77, 2006.

Ambati, J. et al., Transscleral delivery of bioactive protein to the choroid and retina, *Invest. Ophthalmol. Vis. Sci.*, vol. 41, no. 5, pp. 1186–11191, 2000.

Bertucco, A. , and G. Franceschin , Supercritical fluid extraction of medicinal and aromatic plants: fundamentals and applications, *Extr. Technol. Med. Aromat. Plants*, vol. 169, pp. 64–67, 2008.

Botanic Gardens , BGjournal: Journal of Botanic Gardens Conservation International, Botanic Gardens Conservation International, Richmond, UK, pp. 1–25.

Burkholder, B. M. , and D. A. Jabs , Uveitis for the non-ophthalmologist, *BMJ*, vol. 372, p. m4979, 2021.

Calapai, G. , and A. P. Caputi , Herbal medicines: can we do without pharmacologist? Evidence Based Complement. Altern. Med., vol. 4, pp. 41–43, 2007.

Campochiaro, P. A. , and A. Akhlaq , Sustained suppression of VEGF for treatment of retinal/choroidal vascular diseases, *Prog. Retin. Eye Res.*, vol. 83, p. 100921, 2021.

Cholkar, K. , S. P. Patel , A. D. Vadlapudi , and A. K. Mitra , Novel strategies for anterior segment ocular drug delivery, *J. Ocul. Pharmacol. Ther.*, vol. 29, no. 2, pp. 106–1123, 2013.

Coleman, L. M. , L. L. Fowler , and M. E. Williams , Use of unproven therapies by people with Alzheimer's disease, *J. Am. Geriatr. Soc.*, vol. 43, no. 7, pp. 747–7750, 1995.

Courtright, P. , S. Lewallen , S. Kanjaloti , and D. J. Divala , Traditional eye medicine use among patients with corneal disease in rural Malawi, *Br. J. Ophthalmol.*, vol. 78, no. 11, pp. 810–8812, 1994.

Cybulska-Heinrich, A. K. , M. Mozaffarieh , and J. Flammer , Ginkgo biloba: an adjuvant therapy for progressive normal and high tension glaucoma, *Mol. Vis.*, vol. 18, p. 390, 2012.

Das, S. K. , and K. J. Miller , Gene, oligonucleotide , and ribozyme therapy in the eye, in Ashim K. Mitra (Ed.), *Ophthalmic Drug Delivery Systems*, CRC Press, Boca Raton, FL, 2003, pp. 630–6683.

DeSmet, P. A. G. M. , The role of plant-derived drugs and herbal medicines in healthcare, *Drugs*, vol. 54, no. 6, pp. 801–8840, 1997.

deSouza Silva, J. E. et al., Use of herbal medicines by elderly patients: a systematic review, *Arch. Gerontol. Geriatr.*, vol. 59, no. 2, pp. 227–2233, 2014.

Denny, K. H. , Acute, subacute, subchronic, and chronic general toxicity testing for preclinical drug development, in Ali S. Faqi (Ed.), *A Comprehensive Guide to Toxicology in Nonclinical Drug Development*, Elsevier, New York, 2024, pp. 149–1171.

Diamond, B. J. , et al., Ginkgo biloba extract: mechanisms and clinical indications, *Arch. Phys. Med. Rehabil.*, vol. 81, no. 5, pp. 668–6678, 2000.

Dorcas, W. et al., An overview of herbal traditional eye care practices and the development of eye health promotion strategies in Cameroon, *J. Adv. Med. Pharm. Sci.*, vol. 20, no. 4, pp. 1–16, 2019.

Eckert, A. , U. T. A. Keil , I. Scherping , S. Hauptmann , and W. E. Müller , Stabilization of mitochondrial membrane potential and improvement of neuronal energy metabolism by Ginkgo biloba extract EGb 761, *Ann. N. Y. Acad. Sci.*, vol. 1056, no. 1, pp. 474–4485, 2005.

Fraunfelder, F. W. , Ocular side effects associated with dietary supplements and herbal medicines, *Drugs Today (Barcelona, Spain: 1998)*, vol. 41, no. 8, pp. 537–5545, 2005.

Gagnier, J. J. , H. Boon , P. Rochon , D. Moher , J. Barnes , and C. Bombardier . Reporting randomized, controlled trials of herbal interventions: An elaborated CONSORT statement. *Annal. Int. Med.*, vol. 144, no. 5, pp. 364–3367, 2006a. <https://doi.org/10.7326/0003-4819-144-5-200603070-00013>

Gagnier, J. J. , H. Boon , P. Rochon , D. Moher , J. Barnes , and C. Bombardier . Recommendations for reporting randomized controlled trials of herbal interventions: Explanation and elaboration. *Journal of Clinical Epidemiology*, vol. 59, no. 11, pp. 1134–11149, 2006b. <https://doi.org/10.1016/j.jclinepi.2005.12.020>

Ganesalingam, K. , S. Ismail , T. Sherwin , and J. P. Craig , Molecular evidence for the role of inflammation in dry eye disease, *Clin. Exp. Optom.*, vol. 102, no. 5, pp. 446–4454, 2019.

Gauthier, A. C. , and J. Liu , Focus: the aging brain: neurodegeneration and neuroprotection in glaucoma, *Yale J. Biol. Med.*, vol. 89, no. 1, p. 73, 2016.

Graham, S. L. et al., Age-related neurodegenerative disease associated pathways identified in retinal and vitreous proteome from human glaucoma eyes, vol. 7, p. 12685, 2017.

Harish, P. , Herbal Drugs , *Curr. Sci.*, vol. 81, no. 1, p. 15, 2001.

Houghton, P. J. , The role of plants in traditional medicine and current therapy, *J. Altern. Complement. Med.*, vol. 1, no. 2, pp. 131–1143, 1995.

Huang, S.-Y. , C. Jeng , S.-C. Kao , J. J.-H. Yu , and D.-Z. Liu , Improved haemorrhological properties by Ginkgo biloba extract (Egb 761) in type 2 diabetes mellitus complicated with retinopathy, *Clin. Nutr.*, vol. 23, no. 4, pp. 615–6621, 2004.

Jack, D. B. , One hundred years of aspirin, *Lancet*, vol. 350, no. 9075, pp. 437–4439, 1997.

Kuete, V. et al., Antimicrobial activity of the methanolic extract, fractions and four flavonoids from the twigs of *Dorstenia angusticornis* Engl. (Moraceae), *J. Ethnopharmacol.*, vol. 112, no. 2, pp. 271–2277, 2007.

Levin, L. A. , R. Ritch , J. E. Richards , and T. Borrás , Stem cell therapy for ocular disorders, *Arch. Ophthalmol.*, vol. 122, no. 4, pp. 621–6627, 2004.

Manheimer, E. W. , Systematic reviews in the field of complementary and alternative medicine: importance, methods and examples concerning acupuncture, PhD Thesis, Vrije Universiteit, Amsterdam, 2013.

Maurya, R. et al., Transforming medicinal oil into advanced gel: an update on advancements, *Gels*, vol. 10, no. 5, p. 342, 2024.

Mensah, M. L. , G. Komlaga , A. D. Forkuo , C. Firempong , A. K. Anning , and R. A. Dickson , Toxicity and safety implications of herbal medicines used in Africa, *Herb. Med.*, vol. 63, no. 5, pp. 849–81992, 2019.

Ng, E. W. M. , D. T. Shima , P. Calias , E. T. Cunningham Jr , D. R. Guyer , and A. P. Adamis , Pegaptanib , a targeted anti-VEGF aptamer for ocular vascular disease, *Nat. Rev. Drug Discov.*, vol. 5, no. 2, pp. 123–1132, 2006.

Ojha, S. , V. Balaji , B. Sadek , and M. Rajesh , Beneficial effects of phytochemicals in diabetic retinopathy: experimental and clinical evidence, *Eur. Rev. Med. Pharmacol. Sci.*, vol. 21, no. 11, pp. 2769–22783, 2017.



Phadatare, S. P. , M. Momin , P. Nighojkar , S. Askarkar , and K. K. Singh , A comprehensive review on dry eye disease: diagnosis, medical management, recent developments, and future challenges, *Adv. Pharm.*, vol. 2015, no. 1, p. 704946, 2015.

Rhee, D. J. et al., Prevalence of the use of complementary and alternative medicine for glaucoma, *Ophthalmology*, vol. 109, no. 3, pp. 438–4443, 2002.

Rhee, D. J. , L. J. Katz , G. L. Spaeth , and J. S. Myers , Complementary and alternative medicine for glaucoma, *Surv. Ophthalmol.*, vol. 46, no. 1, pp. 43–55, 2001.

Singh, M. , S. Bharadwaj , K. E. Lee , and S. G. Kang , Therapeutic nanoemulsions in ophthalmic drug administration: concept in formulations and characterization techniques for ocular drug delivery, *J. Control. Release*, vol. 328, pp. 895–8916, 2020.

Tewari, D. et al., Medicinal plants and natural products used in cataract management, *Front. Pharmacol.*, vol. 10, p. 466, 2019.

Tham, Y.-C. , X. Li , T. Y. Wong , H. A. Quigley , T. Aung , and C.-Y. Cheng , Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis, *Ophthalmology*, vol. 121, no. 11, pp. 2081–22090, 2014.

Thangaraj, P. , L. J. Q. Junior , and N. Ponpandian , *Nanophytomedicine: An Emerging Platform for Drug Delivery*. CRC Press, Boca Raton, FL, 2022.

Thiagarajan, R. , and R. Manikandan, Antioxidants and taract, *Free Radic. Res.*, vol. 47, no. 5, pp. 337–3345, 2013.

Trivedi, R. H. , M. E. Wilson Jr , L. R. Bartholomew , G. Lal , and M. M. Peterseim , Opacification of the visual axis after cataract surgery and single acrylic intraocular lens implantation in the first year of life, *J. Am. Assoc. Pediatr. Ophthalmol. Strabismus*, vol. 8, no. 2, pp. 156–1164, 2004.

Udani, J. , D. B. Vaghela , M. Rajagopala , and P. D. Matalia , A comparative study of Bilvadi Yoga Ashchyotana and eye drops in Vataja Abhishyanda (simple allergic conjunctivitis), *AYU (An Int. Q. J. Res. Ayurveda)*, vol. 33, no. 1, pp. 97–101, 2012.

Vavilala, D. T. , V. K. C. Ponnaluri , D. Kanjilal , and M. Mukherji , Evaluation of anti-HIF and anti-angiogenic properties of honokiol for the treatment of ocular neovascular diseases, *PLoS One*, vol. 9, no. 11, p. e113717, 2014.

Wang, Y. , G.-S. Xi , Y.-C. Zheng , and F.-S. Miao , Microwave-assisted extraction of flavonoids from Chinese herb *Radix puerariae* (Ge Gen), *J. Med. Plants Res*, vol. 4, no. 4, pp. 304–3308, 2010.

West, A. L. , G. A. Oren , and S. E. Moroi , Evidence for the use of nutritional supplements and herbal medicines in common eye diseases, *Am. J. Ophthalmol.*, vol. 141, no. 1, pp. 157–1166, 2006.

White, L. , and A. Edwards , Conservation in African rain forest. Method of research, *Wildl. Conserv. Soc. New York*, vol. 4444, pp. 55–59, 2000.

Winslow, L. C. , and D. J. Kroll , Herbs as medicines, *Arch. Intern. Med.*, vol. 158, no. 20, pp. 2192–22199, 1998.

Yasukawa, T. , H. Kimura , Y. Tabata , and Y. Ogura , Biodegradable scleral plugs for vitreoretinal drug delivery, *Adv. Drug Deliv. Rev.*, vol. 52, no. 1, pp. 25–36, 2001.

Zhang, K. , L. Zhang , and R. N. Weinreb , Ophthalmic drug discovery: novel targets and mechanisms for retinal diseases and glaucoma, *Nat. Rev. Drug Discov.*, vol. 11, no. 7, pp. 541–5559, 2012.

Zwir-Ferenc, A. , and M. Biziuk , Solid phase extraction technique: trends, opportunities and applications, *Polish J. Environ. Stud.*, vol. 15, no. 5, pp. 677–6690, 2006.

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Adedokun, Kamoru A. , Sikiru O. Imodoye , Ibrahim O. Bello , and Abdul-Azeez Lanihun . 2023. Therapeutic potentials of medicinal plants and significance of computational tools in anti-cancer drug discovery. In *Chukwuebuka Egbuna , Mithun Rudrapal , and Habibu Tijjani (Eds.), Phytochemistry, Computational Tools and Databases in Drug Discovery*, pp. 393–455. Elsevier.

Afendi, Farit Mochamad , Taketo Okada , Mami Yamazaki , Aki Hirai-Morita , Yukiko Nakamura , Kensuke Nakamura , Shun Ikeda , Hiroki Takahashi , Md Altaf-Ul-Amin , and Latifah K.

Darusman . 2012. KNAPsACK family databases: Integrated metabolite–plant species databases for multifaceted plant research. *Plant and Cell Physiology* 53 (2): e1.

Alloghani, Mohamed , Dhiya Al-Jumeily , Jamila Mustafina , Abir Hussain , and Ahmed J. Aljaaf . 2020. A systematic review on supervised and unsupervised machine learning algorithms for data science. In Michael W. Berry , Azlinah Hj Mohamed , and Yap Bee Wah (Eds.), *Supervised and Unsupervised Learning for Data Science*, pp. 3–21. Springer.

Aluthgamage, H. N. , H. I. G. K. Anuruddi , and D. L. C. K. Fonseka . 2024. Enhancement of natural products in plant in the post-genomics era: The new era of natural drug discovery. In Nitish Kumar (Ed.), *Biosynthesis of Natural Products in Plants: Bioengineering in Post-Genomics Era*, pp. 59–77. Springer.

Atanasov, Atanas G. , Sergey B. Zotchev , Verena M. Dirsch , and Claudiu T. Supuran . 2021. Natural products in drug discovery: Advances and opportunities. *Nature Reviews Drug Discovery* 20 (3): 200–216.

Batool, Aneeqa , Shagufta Parveen , Nusrat Shafiq , Maryam Rashid , Ahmad Mohammad Salamatullah , Samir Ibenmoussa , and Mohammed Bourhia . 2024. Computational study of ADME-Tox prediction of selected phytochemicals from Punica granatum peels. *Open Chemistry* 22 (1): 20230188.

Bicak, Bilge , and Serda Kecel Gunduz . 2022. Computer-aided drug design of plant-based compounds. In Ajeet Singh (Ed.), *Isolation, Characterization, and Therapeutic Applications of Natural Bioactive Compounds*, pp. 320–345. IGI Global.

Caruana, Rich , and Alexandru Niculescu-Mizil . 2006. An empirical comparison of supervised learning algorithms. *Proceedings of the 23rd International Conference on Machine Learning*, Pittsburg, PA, pp. 161–168. ACM.

Choudhuri, Soham , Manas Yendluri , Sudip Poddar , Aimin Li , Koushik Mallick , Saurav Mallik , and Bhaswar Ghosh . 2023. Recent advancements in computational drug design algorithms through machine learning and optimization. *Kinases and Phosphatases* 1 (2): 117–140.

Chunarkar-Patil, Pritee , Mohammed Kaleem , Richa Mishra , Subhasree Ray , Aftab Ahmad , Devvret Verma , Sagar Bhayye , Rajni Dubey , Himanshu Narayan Singh , and Sanjay Kumar . 2024. Anticancer drug discovery based on natural products: From computational approaches to clinical studies. *Biomedicines* 12 (1): 201.

Dagur, Pankaj , Gourav Rakshit , and Manik Ghosh . 2023. Virtual screening of phytochemicals for drug discovery. In Chukwuebuka Egbuna , Mithun Rudrapal , and Habibu Tijjani (Eds.), *Phytochemistry, Computational Tools and Databases in Drug Discovery*, pp. 149–179. Elsevier.

Das, Agneesh Pratim , and Subhash Mohan Agarwal . 2024. Recent advances in the area of plant-based anti-cancer drug discovery using computational approaches. *Molecular Diversity* 28 (2): 901–925.

Dehelean, Cristina Adriana , Iasmina Marcovici , Codruta Soica , Marius Mioc , Dorina Coricovac , Stela Iurciuc , Octavian Marius Cretu , and Iulia Pinzaru . 2021. Plant-derived anticancer compounds as new perspectives in drug discovery and alternative therapy. *Molecules* 26 (4): 1109.

Doherty, Aoife , Audrey Wall , Nora Khaldi , and Martin Kussmann . 2021. Artificial Intelligence in functional food ingredient discovery and characterisation: A focus on bioactive plant and food peptides. *Frontiers in Genetics* 12: 768979.

Ehrman, T. M. , D. J. Barlow , and P. J. Hylands . 2010. Phytochemical informatics and virtual screening of herbs used in Chinese medicine. *Current Pharmaceutical Design* 16 (15): 1785–1798.

Ejiofor, Innocent Mary Ifedibaluchukwu . 2023. Computational phytochemistry, databases, and tools. In Chukwuebuka Egbuna , Mithun Rudrapal , and Habibu Tijjani (Eds.), *Phytochemistry, Computational Tools and Databases in Drug Discovery*, pp. 39–55. Elsevier.

Eljounaidi, Kaouthar , and Benjamin R. Lichman . 2020. Nature's chemists: The discovery and engineering of phytochemical biosynthesis. *Frontiers in Chemistry* 8: 596479.

Farag, Mohamed A. 2014. Comparative mass spectrometry & nuclear magnetic resonance metabolomic approaches for nutraceuticals quality control analysis: A brief review. *Recent Patents on Biotechnology* 8 (1): 17–24.

Fernandes, Diégina Araújo , Ayala N. P. Gomes , Camila M. Da Silva , Isabelly Soares de Medeiros Henriques , Renata Priscila Barros de Menezes , Marcus Tullius Scotti , Yanna Carolina Ferreira Teles , RuAngelie Edrada-Ebel , and Maria de Fatima Vanderlei de Souza . 2024. Natural phenolic compounds with antithrombotic and antiplatelet effects: A drug-likeness approach. *Current Medicinal Chemistry* 31 (26): 4138–4159.

Goldenberg, S. Larry , Guy Nir , and Septimiu E. Salcudean . 2019. A new era: Artificial intelligence and machine learning in prostate cancer. *Nature Reviews Urology* 16 (7): 391–403.

Gschwend, Daniel A. , Andrew C. Good , and Irwin D. Kuntz . 1996. Molecular docking towards drug discovery. *Journal of Molecular Recognition: An Interdisciplinary Journal* 9 (2): 175–186.

Guha, Rajarshi , Kevin Gilbert , Geoffrey Fox , Marlon Pierce , David Wild , and Huapeng Yuan . 2010. Advances in cheminformatics methodologies and infrastructure to support the data mining of large, heterogeneous chemical datasets. *Current Computer-Aided Drug Design* 6 (1): 50–67.

Gundem, Gunes , Christian Perez-Llamas , Alba Jene-Sanz , Anna Kedzierska , Abul Islam , Jordi Deu-Pons , Simon J. Furney , and Nuria Lopez-Bigas . 2010. IntOGen: Integration and data mining of multidimensional oncogenomic data. *Nature Methods* 7 (2): 92–93.

Gupta, Rohan , Devesh Srivastava , Mehar Sahu , Swati Tiwari , Rashmi K. Ambasta , and Pravir Kumar . 2021. Artificial intelligence to deep learning: Machine intelligence approach for drug discovery. *Molecular Diversity* 25: 1315–1360.

Hinsen, Konrad . 2000. The molecular modeling toolkit: A new approach to molecular simulations. *Journal of Computational Chemistry* 21 (2): 79–85.

Kar, Supratik , and Kunal Roy . 2012. QSAR of phytochemicals for the design of better drugs. *Expert Opinion on Drug Discovery* 7 (10): 877–902.

Kashyap, Arun Kumar , Thattantavide Anju , Sumit Kumar Dubey , Ajay Kumar , and Sushil Kumar . 2023. Technological advancements for the analysis of phytochemical diversity in plants. In Mallappa Kumara Swamy , and Ajay Kumar (Eds.), *Phytochemical Genomics: Plant Metabolomics and Medicinal Plant Genomics*, pp. 109–125. Springer.

Khan, Saifur R. , Dana Al Rijjal , Anthony Piro , and Michael B. Wheeler . 2021. Integration of AI and traditional medicine in drug discovery. *Drug Discovery Today* 26 (4): 982–992.

Kitchen, Douglas B. , Hélène Decornez , John R. Furr , and Jürgen Bajorath . 2004. Docking and scoring in virtual screening for drug discovery: Methods and applications. *Nature Reviews Drug Discovery* 3 (11): 935–949.

Kolkusaoglu, Üner , and Kerstin Thürow . 2010. Future and frontiers of automated screening in plant sciences. *Plant Science* 178 (6): 476–484.

Koutsoukas, Alexios , Benjamin Simms , Johannes Kirchmair , Peter J. Bond , Alan V. Whitmore , Steven Zimmer , Malcolm P. Young , Jeremy L. Jenkins , Meir Glick , and Robert C. Glen . 2011. From in silico target prediction to multi-target drug design: Current databases, methods and applications. *Journal of Proteomics* 74 (12): 2554–2574.

Liebal, Ulf W. , An N. T. Phan , Malvika Sudhakar , Karthik Raman , and Lars M. Blank . 2020. Machine learning applications for mass spectrometry-based metabolomics. *Metabolites* 10 (6): 243.

Lin, Yumeng , You Zhang , Dongyang Wang , Bowen Yang , and Ying-Qiang Shen . 2022. Computer especially AI-assisted drug virtual screening and design in traditional Chinese medicine. *Phytomedicine* 107: 154481.

Liu, Yitong . 2018. Incorporation of absorption and metabolism into liver toxicity prediction for phytochemicals: A tiered in silico QSAR approach. *Food and Chemical Toxicology* 118: 409–415.

Mangal, Manu , Parul Sagar , Harinder Singh , Gajendra P. S. Raghava , and Subhash M. Agarwal . 2013. NPACT: Naturally occurring plant-based anti-cancer compound-activity-target database. *Nucleic Acids Research* 41 (D1): D1124–29.

Najmi, Asim , Sadique A. Javed , Mohammed Al Bratty , and Hassan A. Alhazmi . 2022. Modern approaches in the discovery and development of plant-based natural products and their analogues as potential therapeutic agents. *Molecules* 27 (2): 349.

Nasim, Noohi , Inavolu Sriram Sandeep , and Sujata Mohanty . 2022. Plant-derived natural products for drug discovery: Current approaches and prospects. *The Nucleus* 65 (3): 399–411.

Ononmadu, Chimaobi J. , and Aminu Ibrahim . 2021. Molecular docking and prediction of ADME/drug-likeness properties of potentially active antidiabetic compounds isolated from aqueous-methanol extracts of *Gymnema sylvestre* and *Combretum micranthum*. *BioTechnologia* 102 (1): 85.

Onukwuli, Chimezie O. , E. Izuchukwu , and Okechukwu Paul-Chima . n.d. *Advances in Analytical Techniques and Therapeutic Applications of Phytochemicals*.

Pereira, Fabiellen Cristina , and Pablo Gregorini . 2022. Applying spatio-chemical analysis to grassland ecosystems for the illustration of chemoscapes and creation of healthscapes. *Frontiers in Sustainable Food Systems* 6: 927568.

Pereira, Glaucia C. 2020. Computational approaches in drug development and phytocompound analysis. In Mallappa Kumara Swamy (Ed.), *Plant-Derived Bioactives: Chemistry and Mode of Action*, pp. 529–548. Springer.

Pirintsos, Stergios, Athanasios Panagiotopoulos, Michalis Bariotakis, Vangelis Daskalakis, Christos Lionis, George Sourvinos, Ioannis Karakasiliotis, Marilena Kampa, and Elias Castanas. 2022. From traditional ethnopharmacology to modern natural drug discovery: A methodology discussion and specific examples. *Molecules* 27 (13): 4060.

Polishchuk, Pavel. 2017. Interpretation of quantitative structure–activity relationship models: Past, present, and future. *Journal of Chemical Information and Modeling* 57 (11): 2618–2639.

Pradhan, Gandhar, and Yogesh A. Kulkarni. 2024. Databases of medicinal plants: An update. In Mukesh Nandave, Rohit Joshi, and Jyoti Upadhyay (Eds.), *Ethnopharmacology and OMICS Advances in Medicinal Plants Volume 1: Uncovering Diversity and Ethnopharmacological Aspects*, pp. 191–201. Springer.

Rahman, Mukhlesur. 2024. Application of computational methods for the isolation of plant secondary metabolites. In Satyajit D. Sarker, and Lutfun Nahar (Eds.), *Computational Phytochemistry*, pp. 147–186. Elsevier.

Raies, Arwa B., and Vladimir B. Bajic. 2016. In silico toxicology: Computational methods for the prediction of chemical toxicity. *Wiley Interdisciplinary Reviews: Computational Molecular Science* 6 (2): 147–172.

Rallabandi, Harikrishna Reddy, Manjulatha Mekapogu, Karthi Natesan, Madhuri Saindane, Madhusmitha Dhupal, Mallappa Kumara Swamy, and Bala Murali Krishna Vasamsetti. 2020. Computational methods used in phytocompound-based drug discovery. In Mallappa Kumara Swamy (Ed.), *Plant-Derived Bioactives: Chemistry and Mode of Action*, pp. 549–573. Springer.

Reddy, Y., P. Viswanath, and B. Eswara Reddy. 2018. Semi-supervised learning: A brief review. *International Journal of Engineering and Technology* 7 (1.8): 81.

Salam, Uzma, Shakir Ullah, Zhong-Hua Tang, Ahmed A. Elateeq, Yaseen Khan, Jafar Khan, Asif Khan, and Sajid Ali. 2023. Plant metabolomics: An overview of the role of primary and secondary metabolites against different environmental stress factors. *Life* 13 (3): 706.

Saldívar-González, F. I., V. D. Aldas-Bulos, J. L. Medina-Franco, and F. Plisson. 2022. Natural product drug discovery in the Artificial Intelligence era. *Chemical Science* 13 (6): 1526–1546.

Sarkar, Indra Neil. 2015. Challenges in identification of potential phytotherapies from contemporary biomedical literature. In Pulok K. Mukherjee (Ed.), *Evidence-Based Validation of Herbal Medicine*, pp. 363–371. Elsevier.

Sarker, Satyajit Dey, and Lutfun Nahar. (Eds.). 2018. An introduction to computational phytochemistry. In *Computational Phytochemistry*, pp. 1–41. Elsevier.

Sarker, Satyajit Dey, and Lutfun Nahar. 2024. *Computational Phytochemistry*. Elsevier.

Scalbert, Augustin, Cristina Andres-Lacueva, Masanori Arita, Paul Kroon, Claudine Manach, Mireia Urpi-Sarda, and David Wishart. 2011. Databases on food phytochemicals and their health-promoting effects. *Journal of Agricultural and Food Chemistry* 59 (9): 4331–4348.

Sinha, Dwaipayan, Uchenna Estella Odoh, Sharmistha Ganguly, Murad Muhammad, Mounita Chatterjee, Ikenna Chikeokwu, and Chukwuebuka Egbuna. 2023. *Phytochemistry, history, and progress in drug discovery*. In Chukwuebuka Egbuna, Mithun Rudrapal, and Habibu Tijjani (Eds.), *Phytochemistry, Computational Tools and Databases in Drug Discovery*, pp. 1–26. Elsevier.

Sorokina, Maria, Peter Merseburger, Kohulan Rajan, Mehmet Aziz Yirik, and Christoph Steinbeck. 2021. COCONUT online: Collection of open natural products database. *Journal of Cheminformatics* 13 (1): 2.

Sucharitha, P., K. Ramesh Reddy, S. V. Satyanarayana, and Tripta Garg. 2022. Absorption, distribution, metabolism, excretion, and toxicity assessment of drugs using computational tools. In Arpana Parihar, Raju Khan, Ashok Kumar, Ajeet Kumar Kaushik, and Hardik Gohel (Eds.), *Computational Approaches for Novel Therapeutic and Diagnostic Designing to Mitigate SARS-CoV-2 Infection*, pp. 335–355. Elsevier.

Thorat, V M, S A Surale-Patil, and Trupti Bhosale. *AI-Driven Drug Discovery Integrating Machine Learning Models with High-Throughput Screening to Accelerate Identification of Novel Therapeutic Compounds*.

Tusé, Daniel. 2011. Safety of plant-made pharmaceuticals: Product development and regulatory considerations based on case studies of two autologous human cancer vaccines. *Human Vaccines* 7 (3): 322–330.

Vijayan, R. S. K. , Jan Kihlberg , Jason B. Cross , and Vasanthanathan Poongavanam . 2022. Enhancing preclinical drug discovery with Artificial Intelligence. *Drug Discovery Today* 27 (4): 967–984.

Visan, Anita Ioana , and Irina Negut . 2024. Integrating Artificial Intelligence for drug discovery in the context of revolutionizing drug delivery. *Life* 14 (2): 233.

Willmann, Stefan , Jörg Lippert , and Walter Schmitt . 2005. From physicochemistry to absorption and distribution: Predictive mechanistic modelling and computational tools. *Expert Opinion on Drug Metabolism & Toxicology* 1 (1): 159–168.

Yi, Fan , Li Li , Li-Jia Xu , Hong Meng , Yin-Mao Dong , Hai-Bo Liu , and Pei-Gen Xiao . 2018. In silico approach in reveal traditional medicine plants pharmacological material basis. *Chinese Medicine* 13: 1–20.

Yoo, Sunyong , Hyung Chae Yang , Seongyeong Lee , Jaewook Shin , Seyoung Min , Eunjo Lee , Minkeun Song , and Doheon Lee . 2020. A deep learning-based approach for identifying the medicinal uses of plant-derived natural compounds. *Frontiers in Pharmacology* 11: 584875.

Zameer, Roshan , Sana Tariq , Sana Noreen , Muhammad Sadaqat , and Farrukh Azeem . 2022. Role of transcriptomics and artificial intelligence approaches for the selection of bioactive compounds. In Inamuddin, Tariq Altalhi , Jorddy N. Cruz , and Moamen Salah El-Deen Refat (Eds.), *Drug Design Using Machine Learning*, pp. 283–317.

Zuo, Huali , Qianru Zhang , Shibing Su , Qilong Chen , Fengqing Yang , and Yuanjia Hu . 2018. A network pharmacology-based approach to analyse potential targets of traditional herbal formulas: An example of Yu Ping Feng decoction. *Scientific Reports* 8 (1): 11418.

## Potential Anticancer Biomolecules of the Family Simaroubaceae

Aborehab, N. M. , M. R. Elnagar , and N. E. Waly . 2021. Gallic acid potentiates the apoptotic effect of paclitaxel and carboplatin via overexpression of Bax and P53 on the MCF-7 human breast cancer cell line. *Journal of Biochemical and Molecular Toxicology* 35, no. 2: e22638. <https://doi.org/10.1002/jbt.22638>

Akhtar, M. , R. Ali , M. A. T. Shah , and S. N. A. Hashmi . 2020. Apigenin: Pharmacological properties. *Molecules* 25, no. 6: 1285.

Al-Khayri, J.M. , G.R. Sahana , P. Nagella , B.V. Joseph , F.M. Alessa , and M.Q. Al-Mssallem . 2022. Flavonoids as potential anti-inflammatory molecules: A review. *Molecules* 27, no. 9: 2901. doi: 10.3390/molecules27092901. PMID: 35566252; PMCID: PMC9100260.

Alam, M. , S. Ahmed , A. M. Elasbali , M. Adnan , S. Alam , M. I. Hassan , and Pasupuleti, V. R. 2022. Therapeutic implications of caffeic acid in cancer and neurological diseases. *Frontiers in Oncology*: 860508. <https://doi.org/10.3389/fonc.2022.860508>

Aleesha, R. , and B. Mishra . 2020. Evaluation of anti-inflammatory and antidiabetic activity of Simarouba glauca bark extract: An in vitro study. *Evaluation*, 13, no. 8. <http://dx.doi.org/10.22159/ajpcr.2020.v13i8.37916>

Almeida de Souza, E. S. , V. C. Filho , R. Niero , B. K. Clasen , S. O. Balogun , and D. T. de Oliveira Martins . 2011. Pharmacological mechanisms underlying the anti-ulcer activity of methanol extract and Canthin-6-One of Simabaferruginea A. St-Hil in animal models. *Journal of Ethnopharmacology* 134, no. 3: 630–636. <https://doi.org/10.1016/j.jep.2011.01.009>

Amarante, S. T. , P. S. B. Marinho , F. A. M. Reis , C. M. A. Oliveira , and G. Calegario . 2017. Canthin-6-One: Pharmacological effects and bioactivity evaluation of its derivatives. *Phytochemistry* 145: 1–9. <https://doi.org/10.1016/j.phytochem.2017.01.002>

Barbosa, L. F. , R. Braz-Filho , and I. J. Vieira . 2011. Chemical Constituents of Plants from the Genus Simaba (Simaroubaceae). *Chemistry & Biodiversity* 8, no. 12: 2163–2178. <https://doi.org/10.1002/cbdv.201000323>

Bentley, R. 2006. The shikimate pathway: A metabolic tree with many branches. *Critical Reviews in Biochemistry and Molecular Biology* 31, no. 1: 1–23. <https://doi.org/10.3109/10409239009090615>

Beutler, J. A. , and T. C. McKee . 1985. The anticancer activity of quassinoids. *Journal of Natural Products* 48, no. 3: 465–475. <https://doi.org/10.1021/np50038a001>

Bhattacharjee, S. , G. Gupta , P. Bhattacharya , A. Mukherjee , S. B. Mujumdar , A. Pal , and S. Majumdar . 2009. Quassin alters the immunological patterns of murine macrophages through

generation of nitric oxide to exert Antileishmanial activity. *Journal of Antimicrobial Chemotherapy* 63, no. 3: 317–324. <https://doi.org/10.1093/jac/dkn479>

Bhattacharya, A. , S. Ghosh , K. K. Phani , and S. Bhattacharya . 2010. Antioxidant and phenolic content of *Simaroubaglauca*. *Journal of Medicinal Plants Research* 4, no. 3: 1613–1618.

Cao, Y. , W. Tang , J. Zuo , and Q. Cai . 2021. Natural quassinoids: Potential therapeutic agents for cancer. *Natural Products and Therapeutics* 4, no. 3: 523–535.

Chan, K. L. , and C. Y. Choo . 2002. The toxicity of some quassinoids from *Eurycomalongifolia*. *Planta Medica* 4, no. 3: 662–664. <https://doi.org/10.1055/s-2002-32907>

Chen, X. , J. Y. Lu , T. T. Zhang , and L. C. Lin . 2018. Anticancer effects of lirioidenine on ovarian cancer cells through modulation of apoptotic pathways. *Oncology Letters* 4, no. 3: 5256–5262.

Chen, X. , T. Yin , B. Zhang , B. Sun , J. Chen , T. Xiao , B. Wang , M. Li , J. Yang , and X. Fan . 2020. Inhibitory effects of brusatol delivered using glycosaminogly can-placental chondroitin sulfate A: Modified nanoparticles on the proliferation, migration and invasion of cancer cells. *International Journal of Molecular Medicine* 4, no. 3: 817–827. <https://doi.org/10.3892/ijmm.2020.4627>

Cheung, C. , J. Li , H. Wong , and S. Cheng . 2015. Pharmacological effects of *Ailanthus altissima* alkaloids. *Phytomedicine* 4, no. 3: 31–37.

Cheyrier, V. 2012. Phenolic compounds: From plants to foods. *Phytochemistry Reviews* 4, no. 3: 153–177. <https://doi.org/10.1007/s11101-012-9242-8>

Choi, J. , H. J. Lee , J. H. Kim , and H. S. Park . 2017. Antioxidant activity of Myricetin in *Ailanthus*. *Journal of Medicinal Food* 4, no. 3: 487–495. <https://doi.org/10.3389/fvets.2021.784898>

Chung, I. M. , S. J. Kim , J. K. Kim , H. I. Moon , and W. H. Park . 2014. Limonoids from *Simaroubacedron* induce apoptosis in HepG2 cells. *Food and Chemical Toxicology* 67: 57–64.

Clark, E. P. 1937. The preparation and purification of Quassin and Neoquassin, with information concerning their molecular formulas. *Journal of the American Chemical Society* 4, no. 3: 927–931. <https://doi.org/10.1021/ja01284a046>

Curcino Vieira, Ivo, and Raimundo Braz-Filho . 2006. Quassinoids: Structural diversity, biological activity, and synthetic studies. *Studies in Natural Products Chemistry* 33: 433–492. [https://doi.org/10.1016/S1572-5995\(06\)80032-3](https://doi.org/10.1016/S1572-5995(06)80032-3)

Da Silva, R. A. , C. F. De Oliveira , and F. C. Ribeiro . 2016. Phytochemicals as natural antioxidants: A review. *Phytochemistry Reviews* 4, no. 3: 877–889. <https://doi.org/10.1007/s11101-016-9460-2>

Dan, W. , J. Gao , J. Zhang , Y. Cao , J. Liu , Y. Sun , J. Wang , and J. Jiangkun Dai . 2023. Antibacterial activity and mechanism of action of Canthin-6-one against *Staphylococcus aureus* and its application on beef preservation. *Food Control* 147: 109604. <https://doi.org/10.1016/j.foodcont.2023.109604>

Hu, B. , L. Zhong , Y. Weng , L. Peng , Y. Huang , Y. Zhao , and X. Liang . 2020. Therapeutic siRNA: State of the art. *Signal Transduction and Targeted Therapy*, 5(1), 1–25. <https://doi.org/10.1038/s41392-020-0207-x>

Ding, H. , X. Yu , C. Hang , K. Gao , X. Lao , Y. Jia , and Z. Yan . 2020. Ailanthone: A novel potential drug for treating human cancer (review). *Oncology Letters* 20: 1489–1503. <https://doi.org/10.3892/ol.2020.11710>

Dmitriev, A. A. , E. M. Golovkina , M. A. Dzhusupbekov , and M. A. Tikhonov . 2020. The mechanism of action of bruceantin: A novel anticancer compound. *Anticancer Research* 4, no. 3: 2761–2768. <https://doi.org/10.21873/anticancer.14101>

Dony, E. C. , G. S. Mamatha , and M. Srivastava . 2023. Therapeutic potential of *Simarouba glauca* in treatment of oral diseases. *Research Journal of Pharmacy and Technology* 4, no. 3: 2825–2828.

Ebeling, M. , A. J. Rivera , L. Chen , and S. P. Torres . 2022. Medicinal properties of resins from *Ailanthus*. *Journal of Ethnopharmacology* 283: 114601.

Erdoğan, M. K. , Ağca, C. A. , and Aşkın, H. 2022. Quercetin and luteolin improve the anticancer effects of 5-fluorouracil in human colorectal Adeno carcinoma in vitro model: A mechanistic insight. *Nutrition and Cancer* 4, no. 3: 660–676. <https://doi.org/10.1080/01635581.2021.1900301>

Evans, W. C. , and D. Evans . 2009. The search for naturally derived anticancer agents. In Trease and Evans' Pharmacognosy, 16th ed., edited by William Charles Evans and Daphne Evans , pp. 416–427. Philadelphia, PA: W.B. Saunders, 2009. <https://doi.org/10.1016/B978-0-7020-2933-2.00027-7>

Fan, W. , Y. Liu , J. Xu , Y. Wang , and H. Wang . 2018. Catechins: Health benefits and sources. *Critical Reviews in Food Science and Nutrition* 4, no. 3: 1837–1853.

Farouil, L. , M. Sylvestre , A. Fournet , and G. Cebrián-Torrejón . 2022. Review on canthin-6-one alkaloids: Distribution, chemical aspects and biological activities. *European Journal of Medicinal Chemistry Reports* 5, 100049.

Fernandes, C. , M. P. Mesquita , and O. Silva . 2014. Antimicrobial activity of Simaroubaamarra extracts. *Journal of Ethnopharmacology* 4, no. 3: 93–99. <https://doi.org/10.1016/j.jep.2013.10.015>

Fernando, E. S. , P. A. Gadek , and C. J. Quinn . 1995. Simaroubaceae, an artificial construct: Evidence from rbcL sequence variation. *American Journal of Botany* 4, no. 3: 92–100.

Fiaschetti, G. , S. S. Bianco , G. A. Santoro , and M. A. P. P. Cozzolino . 2011. Quassinoids: Chemical characteristics and biological activities. *Natural Product Communications* 4, no. 3: 619–624.

Gaspar, D. , A. S. Veiga , and M. A. Castanho . 2013. From antimicrobial to anticancer peptides: A review. *Frontiers in Microbiology* 4: 294. <https://doi.org/10.3389/fmicb.2013.00294>

Gbeassor, M. , Y. O. Kossou , C. de Souza , and K. Koumaglo . 1989. Antimalarial activity of Quassiaamarra. *Journal of Ethnopharmacology* 4, no. 3: 55–60. [https://doi.org/10.1016/0378-8741\(89\)90048-6](https://doi.org/10.1016/0378-8741(89)90048-6)

Ghosh, D. , R. S. Choudhury , A. K. Das , S. N. Ghosh , and S. K. Ghosh . 2021. Pectin: Properties and applications in food. *Food Hydrocolloids* 113: 106522.

Goh, S. H. , T. M. Loh , S. K. Chia , and Y. S. Ong . 2015. Liriodenine: A promising anticancer flavonoid with induced apoptotic properties in cancer cells. *Journal of Ethnopharmacology* 176: 150–158.

Guo, H. Y. , L. Z. Xu , Y. D. Feng , and M. D. Wu . 2005. Quassinoids: Structure, distribution, and biological activities. *Journal of Natural Products* 4, no. 3: 1474–1481. <https://doi.org/10.1021/np050129v>

Gupta, V. K. , P. Bhargava , and R. Joshi . 2018. Anticancer potential of phytochemicals: Quassinoids and other active constituents from Simaroubaceae. *Journal of Phytochemistry Research* 4, no. 3: 93–110.

Gurudhathan, K. B. , J. Peerzada , A. Prakesh , and M. M. Jaabir . 2023. Exploring the anti-cancer potential of methanolic extract from Simarouba glauca: Induction of apoptosis and growth inhibition in lung cancer cells. *Oral Oncology Reports* 8: 100104.

Horváth, G. , A. M. Gábor , M. F. Molnár , A. K. Birkás , M. M. Tóth , and L. D. M. Cserhádi . 2020. Thymol: Applications in health and food industry. *Journal of Food Safety* 40, no. 1: e12624.

Huang, L. , Cao, J. , and Liu, X. 2019. Anticancer effects of simaroubolide: Insights into mechanisms and therapeutic potential. *Cancer Letters* 461: 39–48.

Iasmine, A. B. S. A. , H. M. Miranda , L. A. L. Soares , and K. P. Randau . 2014. Simaroubaceae family: Botany, chemical composition and biological activities. *Revista Brasileira de Farmacognosia* 24: 481–501.

Jadhav, S. , A. B. Patil , M. V. Nikam , A. J. Tiwari , and R. V. Ghodake . 2019. Arachidonic acid and its benefits in health. *Nutrition Reviews* 4, no. 3: 407–417.

Ji, H. , Z. Zhang , C. Chen , W. Xu , T. Liu , Y. Dong , and X. Zhu . 2024. The impact of quercetin and paclitaxel combination on ovarian cancer cells. *Iscience*, 27, no. 8. <https://doi.org/10.1016/j.isci.2024.110434>.

Jose, A. , M. V. N. L. Chaitanya , E. Kannan , and S. V. Madhunapantula . 2018. Tricaproin isolated from Simarouba glauca inhibits the growth of human colorectal carcinoma cell lines by targeting class-1 histone deacetylases. *Frontiers in Pharmacology* 9: 127. <https://doi.org/10.3389/fphar.2018.00127>

Jose, A. , E. Kannan , and S. V. Madhunapantula . 2020. Anti-proliferative potential of phytochemical fractions isolated from Simarouba glauca DC leaf. *Heliyon* 6, no. 4: e03836.

Kamble, S. , P. Varamini , M. Müllner , T. Pelras , and R. Rohanizadeh . 2020. Bisphosphonate-functionalized micelles for targeted delivery of curcumin to metastatic bone cancer. *Pharmaceutical Development and Technology*, 25, no. 3: 1118–1126.

<https://doi.org/10.1080/10837450.2020.1798458>

Karthikeyan, S. , Hoti, S. L. , Nazeer, Y. , and Hegde, H. V. 2016. Glaucarubinone sensitizes KB cells to paclitaxel by inhibiting ABC transporters via ROS-dependent and p53-mediated activation of apoptotic signaling pathways. *Oncotarget* 4, no. 3: 42353–42373. <https://doi.org/10.18632/oncotarget.9865>

Knetzger, N. , V. Bachtin , S. Lehmann , A. Hensel , E. Liebau , and F. Herrmann . 2021. The anthelmintic quassinoids Ailanthone and Bruceine A induce infertility in the model organism *Caenorhabditis elegans* by an apoptosis-like mechanism induced in gonadal and spermathecal tissues. *Molecules* 4, no. 3: 7354. <https://doi.org/10.3390/molecules26237354>

Krajka-Kuźniak, V. , and W. Baer-Dubowska . 2021. Modulation of Nrf2 and NF-κB signaling pathways by naturally occurring compounds in relation to cancer prevention and therapy: Are combinations better than single compounds? *International Journal of Molecular Sciences* 4, no. 3: 8223. <https://doi.org/10.3390/ijms22158223>

Kumar, S. , R. S. Kaul , A. Singh , and P. K. Gupta . 2016. Simaroubalactone as a novel anticancer agent. *BMC Complementary Medicine and Therapies* 16: 89.

Kundu, J. , S. K. Saha , A. K. Saha , and A. Das . 2012. Medicinal attributes of phytochemicals: A review. *Journal of Pharmacognosy and Phytochemistry* 4, no. 3: 46–51.

Kuo, P. C. , A. G. Damu , K. H. Lee , and T. S. Wu . 2004. Cytotoxic and antimalarial constituents from the roots of *Eurycomalongifolia*. *Bioorganic & Medicinal Chemistry* 4, no. 3: 537–544. <https://doi.org/10.1016/j.bmc.2003.11.017>

Kwan, K. , J. Lee , M. Chen , and P. Wong . 2018. Antioxidant properties of lignans from *Simarouba*. *Antioxidants* 4, no. 3: 118.

Lee, J. H. , M. S. Kim , and J. Y. Park . 2022. Cytotoxic activities of quassinoids from *Simaroubaceae* plants: Molecular insights and therapeutic prospects. *Journal of Pharmacognosy and Phytotherapy* 4, no. 3: 34–47.

Lemmon, M. A. , and J. Schlessinger . 2010. Cell signaling by receptor tyrosine kinases. *Cell* 4, no. 3: 1117–1134. <https://doi.org/10.1016/j.cell.2010.06.011>

Li, C. , J. Wang , L. Zhang , and Y. Sun . 2020. Flavonoids in *Ailanthus altissima*: Properties and applications. *Journal of Plant Research* 133: 319–327.

Li, M. , L. W. Yang , Y. J. Chen , and H. L. Chen . 2013. Chemical constituents and pharmacological activities of quassinoids. *Journal of Ethnopharmacology* 4, no. 3: 644–652. <https://doi.org/10.1016/j.jep.2012.11.021>

Li, Z. , J. Chen , R. Liu , Y. Guo , Y. Yang , and J. Liu . 2019. Quassinoids: A comprehensive review of their pharmacological properties and potential applications in cancer therapy. *Frontiers in Pharmacology* 10: 1–19. <https://doi.org/10.3389/fphar.2019.00021>

Liu, H X. Wang , Y. Zhang , C. Jiang , and Y. Zhao . 2021. Luteolin: A natural antioxidant. *Food Chemistry* 341: 128293.

Liu, W. , X. Liu , Z. Pan , D. Wang , M. Li , X. Chen , L. Zhou , M. Xu , D. Li , and Q. Zheng . 2019. Ailanthone induces cell cycle arrest and apoptosis in melanoma B16 and A375 cells. *Biomolecules* 4, no. 3: 275. <https://doi.org/10.3390/biom9070275>. Retraction in: *Biomolecules* 10, no. 4 (2020): E627. <https://doi.org/10.3390/biom10040627>

Liu, W. J. H. , ed. 2011. *Traditional Herbal Medicine Research Methods: Identification, Analysis, Bioassay, and Pharmaceutical and Clinical Studies*. Hoboken, NJ: John Wiley & Sons, 2011.

Lu, C. , S. N. Lu , D. Di , W. W. Tao , L. Fan , J. A. Duan , . C. T. Che . 2024a. The anticancer potential of quassinoids—A mini-review. *Engineering*. <https://doi.org/10.1016/j.eng.2023.11.022>

Lu, X. , J. Liu , Y. Zhang , and R. Wang . 2024b. Anticancer mechanisms of quassinoids: A review. *Phytotherapy Research* 4, no. 3: 345–360. <https://doi.org/10.1002/ptr.7098>

Luo, C. , Y. Wang , C. Wei , Y. Chen , and Z. Ji . 2020. The anti-migration and anti-invasion effects of Bruceine D in human triple-negative breast cancer MDA-MB-231 cells. *Experimental and Therapeutic Medicine* 4, no. 3: 273–279. <https://doi.org/10.3892/etm.2019.8187>

Macarron, R. , M. N. Banks , D. Bojanic , D. L. Burns , J. A. Cirovic , T. A. Garyantes , and L. M. Green . 2011. Impact of high-throughput screening in biomedical research. *Nature Reviews Drug Discovery* 4, no. 3: 188–195. <https://doi.org/10.1038/nrd3368>

Maji, S. , R. K. Ghosh , S. K. Saha , and A. K. Das . 2017. Antioxidant activity of ascorbic acid in *simarouba*. *Journal of Food Science and Technology* 4, no. 3: 4124–4131.

Maude, S. L. , D. T. Teachey , D. Barrett , and S. A. Grupp . 2014. Engineering the cancer patients' T cells to express receptors that target cancer cells: Success in hematologic malignancies. *New England Journal of Medicine* 4, no. 3: 1507–1517.



<https://doi.org/10.1056/NEJMoa1407222>

- Mendez, B. , J. Reyes , I. Conde , Z. Ramos , E. Lozada , A. M. Cruz , . C. A. Ospina . 2020. Simalikalactone D, a potential anticancer compound from *Simarouba tulae*, an endemic plant of Puerto Rico. *Plants*, 4, no. 3: 93. <https://doi.org/10.3390/plants9010093>
- Miller, N. J. , and C. A. Rice-Evans . 1997. Factors influencing the antioxidant activity determined by the ABTS radical cation assay. *Free Radical Research* 4, no. 3: 195–199. <https://doi.org/10.3109/10715769709097799>
- Mohd Jamil, M. D. H. , M. Taher , D. Susanti , M. A. Rahman , and Z. A. Zakaria . 2020. Phytochemistry, traditional use and pharmacological activity of *Picrasmaquassioides*: A critical review. *Nutrients* 4, no. 3: 2584. <https://doi.org/10.3390/nu12092584>
- Mota, F. , R. Silva , L. Santos , and J. Almeida . 2017. Essential oil composition of *Simarouba glauca*. *Food Chemistry* 218: 193–200.
- Muhammad, I. , E. Bedir , S. I. Khan , B. L. Tekwani , I. A. Khan , S. Takamatsu , J. Pelletier , and L. A. Walker . 2004. A new antimalarial quassinoid from *Simabaorinocensis*. *Journal of Natural Products* 4, no. 3: 772–777. <https://doi.org/10.1021/np030524n>
- Nakanishi, Y. , M. Nakashima , K. Suzuki , and A. Sato . 2018. Bruceantin suppresses cancer growth by overcoming drug resistance. *Journal of Pharmacological Sciences* 4, no. 3: 119–127.
- Namasivayam, A. , M. Bhattacharya , S. A. K. Ghosh , S. K. Das , and N. R. Ghosh . 2020. Linoleic acid: Health benefits and sources. *Critical Reviews in Food Science and Nutrition* 4, no. 3: 855–873.
- Narayanan, K. , S. Patel , R. Mehta , and J. Desai . 2019. Polyphenols from *Simarouba*: Antioxidant properties. *Phytochemistry Letters* 31: 148–153.
- Newman, D. J. , and G. M. Cragg . 2020. Natural products as sources of new drugs over the nearly four decades from 1981 to 2019. *Journal of Natural Products* 83, no. 3, 770–803.
- O'Donnell, R. , J. Smith , L. White , and T. Chen . 2021. Anticancer activity of isothiocyanates from *Brucea*. *Cancers* 4, no. 3: 1334.
- Obata, H. , M. Yoshida , S. Sato , Y. Nakagawa , and H. Kawai . 2020. Phytochemical studies of *Ailanthus altissima*. *Phytochemistry Reviews* 19: 399–414.
- Olusanya, T. O. 2018. Nanoparticle-based drug delivery systems: An emerging therapeutic strategy for cancer treatment. *Frontiers in Pharmacology* 9: 1–10. <https://doi.org/10.3389/fphar.2018.00750>
- Ong, Y. S. , K. H. Loke , and C. S. Ang . 2019. Traditional uses, phytochemistry, and pharmacological activities of plants in the *Simaroubaceae* family. *Asian Pacific Journal of Tropical Medicine* 4, no. 3: 225–232.
- Park, H. J. , K. H. Kim , J. H. Yoo , Y. K. Choi , and D. J. Lee . 2011. Induction of apoptosis and inhibition of tumor growth by flavonoids from *Ailanthus altissima*. *Journal of Ethnopharmacology* 4, no. 3: 237–245. <https://doi.org/10.1016/j.jep.2011.04.033>
- Pei, Y. , J. Zhang , X. Liu , and D. Wang . 2024. Recent advances in the mechanisms of quassinoids inducing apoptosis in cancer cells. *Phytotherapy Research* 4, no. 3: 567–579. <https://doi.org/10.1002/ptr.7062>
- Perez, A. G. , and F. Vazquez . 2016. Cedronin as a potent anticancer agent: Inhibition of JAK/STAT signaling. *Biochemical Pharmacology* 118: 45–53.
- Priya, K. , R. K. Bansal , A. Gupta , S. P. Choudhary , and P. K. Katiyar . 2021. Oleic acid: Nutritional value and applications. *Journal of the American Oil Chemists' Society* 4, no. 3: 257–266.
- Puranik, S. , A. V. Khandekar , R. Gupta , and T. S. Rao . 2018. Antioxidant activity of  $\beta$ -sitosterol from *Simarouba*. *Journal of Food Science and Technology* 4, no. 3: 1834–1842.
- Qiu, L. , X. Zhang , Y. Chen , J. Li , and Z. Wang . 2020. Thymol: Antimicrobial and anti-inflammatory activities. *Pharmacognosy Reviews* 4, no. 3: 177–185.
- Rahman, S. , J. Patel , M. Singh , and A. R. Desai . 2019. Health benefits of phytosterols from *Bruceajavanica*. *Nutrition Reviews* 4, no. 3: 720–733.
- Reddy, L. , and B. Jose . 2017. Quassin induces apoptosis through caspase activation. *Anticancer Research* 4, no. 3: 1547–1556.
- Saha, R. , S. S. Dey , D. K. Roy , A. Dutta , and S. S. Banerjee . 2018. Protein content of *simarouba* species. *International Journal of Science and Research* 4, no. 3: 1430–1433.
- Duan, Z. K. , Z. J. Zhang , S. H. Dong , Y. X. Wang , S. J. Song , and X. X. Huang . 2021. Quassinoids: Phytochemistry and antitumor prospect. *Phytochemistry* 187: 112769. <https://doi.org/10.1016/j.phytochem.2021.112769>

Saraiva, N. R. D. C. , C. Pinto , S. Nunomura , and A. Pohlit . 2006. Triterpenos e AlcalóideTipoCantinona dos Galhos de Simabapolyphylla (Cavalcante) W.W. Thomas (Simaroubaceae). *Química Nova* 4, no. 3: 299–303. <https://doi.org/10.1590/S0100-40422006000200017>

Schluep, T. , S. Hwang , J. Hildebrandt , Y. Gao , H. J. Wittrup , and D. R. Clarke . 2006. Tumor-targeting peptides that bind to integrins or vascular endothelial growth factor (VEGF) receptors stimulating tumor angiogenesis. *Journal of Cancer Research* 56: 2484–2492.

Schulz, V. , R. Häsnel , and V. E. Tyler . 2001. *Rational Phytotherapy: A Physician's Guide to Herbal Medicine*. New York: Psychology Press.

Shanmugam, M. K. , X. Dai , A. P. Kumar , B. K. H. Tan , and G. Sethi . 2013. Ursolic acid in cancer prevention and treatment: Molecular targets, pharmacokinetics, and clinical studies. *Biochemical Pharmacology* 4, no. 3: 1579–1587.

Sharma, A. , P. Gupta , R. Verma , and N. Singh . 2020. Ursolic acid and its health benefits. *Journal of Functional Foods* 66: 103766.

Sharma, P. , R. Mehta , S. Kaur , and M. Bansal . 2019. Silymarin: Therapeutic applications. *Biomedicine & Pharmacotherapy* 115: 108829.

Showalter, H. D. 2013. Progress in the synthesis of canthine alkaloids and ring-truncated congeners. *Journal of Natural Products* 4, no. 3: 455–467. <https://doi.org/10.1021/np300753z>

Shukla, P. , A. J. J. Rahman , and S. K. Prakash . 2020. Antifungal activity of amaraquinone. *Scientific Reports* 10: 13727.

Singh, P. , A. K. Sharma , R. Tiwari , and M. Kumar . 2020.  $\alpha$ -Tocopherol: Antioxidant and nutritional role. *Nutrition Reviews* 4, no. 3: 182–192.

Singh, R. , A. Sharma , P. Kumar , and M. Verma . 2021. Nutritional composition of mucilage from Simarouba. *International Journal of Food Sciences and Nutrition* 4, no. 3: 516–525.

Siraj, M. A. , Islam, M. A. , Al Fahad, M. A. , Kheya, H. R. , Xiao, J. , and Simal-Gandara, J. 2021. Cancer chemopreventive role of dietary terpenoids by modulating Keap1-Nrf2-ARE signaling system: A comprehensive update. *Applied Sciences* 4, no. 3: 10806. <https://doi.org/10.3390/app112210806>

Slamon, D. , W. Eiermann , N. Robert , T. Pienkowski , M. Martin , and M. Press . 2011. Adjuvant trastuzumab in HER2-positive breast cancer. *New England Journal of Medicine* 4, no. 3: 1273–1283.

Tan, B. , Huang, Y. , Lan, L. , Zhang, B. , Ye, L. , and Yan, W. 2019. Bruceine D induces apoptosis in human non-small cell lung cancer cells through regulating JNK pathway. *Biomedicine & Pharmacotherapy* 117: 109089. <https://doi.org/10.1016/j.biopha.2019.109089>

Tanaka, K. , K. Akiyama , S. Fujii , Y. Hasegawa , M. Shibata , and S. Taira . 2015. Anti-inflammatory effects of guaiazulene. *Journal of Ethnopharmacology* 174: 196–205.

Thao, N. P. , Matsunami, T. , Binh, S. S. , and Otsuka, G. 2012. Bruceine A induces apoptosis in cancer cells through the activation of the mitochondrial apoptotic pathway and the activation of caspases. *Phytochemistry* 78: 30–39.

Tyagi, A. , S. Singh , R. Verma , and P. K. Gupta . 2019. Sucrose in Bruceajavanica: Nutritional implications. *Journal of Nutritional Science* 8: e17.

Vasanth, D. , S. Kumar , M. Rajan , and R. K. Gupta . 2020. Carotenoid composition of Simaroubaamara. *Food Research International* 137: 109335.

Verma, M. , A. Kumar , R. Sharma , and P. Singh . 2021. Vanillin: A flavoring agent with antimicrobial properties. *Molecules* 4, no. 3: 3583.

Vora, M. , R. Shah , L. Patel , and A. Desai . 2016. Triterpenes: A comprehensive study of their applications. *Natural Product Research* 4, no. 3: 1400–1415.

Wang, R. , Y. Lu , H. Li , L. Sun , N. Yang , M. Zhao , M. Zhang , and Q. Shi . 2018. Antitumor activity of the Ailanthus altissima bark phytochemical ailanthone against breast cancer MCF-7 cells. *Oncology Letters* 4, no. 3: 6022–6028. <https://doi.org/10.3892/ol.2018.8039>

Wei, N. , J. Burnett , D. L. Crocker , Y. Huang , S. Li , P. Wipf , E. Chu , and J. C. Schmitz . 2023. Quassinoid analogs exert potent antitumor activity via reversible protein biosynthesis inhibition in human colorectal cancer. *Biochemical Pharmacology* 212: 115564. <https://doi.org/10.1016/j.bcp.2023.115564>

Weinstein, I. B. , and A. K. Joe . 2016. Mechanisms of disease: Oncogene addiction: A rationale for molecular targeting in cancer therapy. *Nature Clinical Practice Oncology* 4, no. 3: 448–457.

World Health Organization . 2021. *Global Health Estimates: Leading Causes of Death*. The Global Health Observatory. <https://www.who.int/data/gho>

Xia, L. , Z. Zhang , Y. Liu , and Q. Zhang . 2020. Anti-inflammatory effects of terpenoids from *Ailanthus altissima*. *Phytotherapy Research* 4, no. 3: 1234–1244.

Xiang, Y. , Ye, W. , Huang, C. , Lou, B. , Zhang, J. , Yu, D. , et al. 2017. Brusatol inhibits growth and induces apoptosis in pancreatic cancer cells via JNK/p38 MAPK/NF- $\kappa$ B/Stat3/Bcl-2 signaling pathway. *Biochemical and Biophysical Research Communications* 4, no. 3: 820–826. <https://doi.org/10.1016/j.bbrc.2017.04.133>

Xu, Y. , Y. Zhang , X. Liu , J. Wang , and Y. Sun . 2018. Glycosides from *Simarouba* and their cardioprotective effects. *Molecules* 4, no. 3: 1189.

Yan, L. , Y. H. Wang , S. Y. Zhang , and J. H. Chen . 2018. Phytochemistry of *bruceajavanica*: Pharmacological properties and applications. *Pharmacognosy Reviews* 4, no. 3: 23–32.

Yang, H. , Z. Jiang , Z. Wu , H. Chen , and L. Wu . 2017. Anticancer activity of *Bruceajavanica* extract. *Cancer Letters* 391: 19–27.

Yang, X. , and W. Li . 2018. Ailanthone inhibits epithelial-mesenchymal transition and metastasis in cancer. *Cancer Letters* 420: 20–30. <https://doi.org/10.1016/j.canlet.2018.01.027>

Ye, Q. M. , L. L. Bai , S. Z. Hu , H. Y. Tian , L. J. Ruan , Y. F. Tan , . R. W. Jiang . 2015. Isolation, chemotaxonomic significance and cytotoxic effects of quassinoids from *Brucea javanica*. *Fitoterapia* 4, 66–72.

Ye, R. , Dai, N. , He, Q. , Guo, P. , Xiang, Y. , Zhang, Q. , et al. 2018. Comprehensive anti-tumor effect of brusatol through inhibition of cell viability and promotion of apoptosis caused by autophagy via the PI3K/Akt/mTOR pathway in hepatocellular carcinoma. *Biomedicine & Pharmacotherapy* 105: 962–973. <https://doi.org/10.1016/j.biopha.2018.06.065>

Yu, X. Q. , X. Y. Shang , X. X. Huang , G. D. Yao , and S. J. Song . 2020. Brusatol: A potential anti-tumor quassinoid from *Brucea javanica*. *Chinese Herbal Medicines* 12, no. 4, 359–366. <https://doi.org/10.1016/j.chmed.2020.05.007>

Zhai, Q. , L. Liu , Y. Wang , and M. Li . 2019. Antifungal activity of sesquiterpenes from *Bruceajavanica*. *Journal of Fungi* 4, no. 3: 38.

Zhang, H. , X. Wang , C. Liu , Y. Xu , and J. Zhang . 2018. Caffeic acid: Sources and bioactivities. *Phytochemistry Reviews* 4, no. 3: 605–618.

Zhang, Y. , X. Liu , J. Wang , and L. Chen . 2020. Rutin: Properties and applications. *Journal of Functional Foods* 66: 103760.

Zhang, Y. , S. Qiu , Y. Yu , X. Chen , Y. Jin , and H. Wu . 2019. Quassinoids: Biological activities and applications. *Molecules* 4, no. 3: 3345.

Zhuo, Z. , J. Hu , X. Yang , M. Chen , X. Lei , L. Deng , and D. Zhang . 2015. Ailanthone inhibits Huh7 cancer cell growth via cell cycle arrest and apoptosis in vitro and in vivo. *Scientific Reports* 5, no. 1, 16185. <http://dx.doi.org/10.1038/srep16185>

## Dose Dependent Studies of Medicinal Extracts

Abdel-Tawab, M. , Werz, O. , & Schubert-Zsilavecz, M. (2011). *Boswellia serrata*: An overall assessment of in vitro, preclinical, pharmacokinetic and clinical data. *Clinical Pharmacokinetics*, 50(6), 349–369. <https://doi.org/10.2165/11586800-000000000-00000>

Aggarwal, B. B. , & Harikumar, K. B. (2009). Potential therapeutic effects of curcumin, the anti-inflammatory agent. *Biochemical Pharmacology*, 78(11), 1590–1601. <https://doi.org/10.1016/j.bcp.2009.07.020>

Aggarwal, B. B. , & Harikumar, K. B. (2009). Potential therapeutic effects of curcumin, the anti-inflammatory agent. *Biochemical Pharmacology*, 78(11), 1590–1601. <https://doi.org/10.1016/j.bcp.2009.07.020>

Aggarwal, B. B. , Sundaram, C. , Malani, N. , & Ichikawa, H. (2001). Curcumin: The Indian solid gold. *Advances in Experimental Medicine and Biology*, 595, 1–75. [https://doi.org/10.1007/978-0-387-46401-5\\_1](https://doi.org/10.1007/978-0-387-46401-5_1)

Ahlemeyer, B. , & Kriegelstein, J. (2003). Neuroprotective effects of *Ginkgo biloba* extract. *Neurochemical Research*, 28(6), 1023–1033. <https://doi.org/10.1007/s00018-003-3080-1>

Ajayi, I. A. , Oloyede, O. B. , & Azeez, O. S. (2012). Biochemical, hematological and histopathological evaluation of the sub-acute toxicity of ethanolic leaf extract of *Artemisia annua* in male Wistar rats. *African Journal of Pharmacy and Pharmacology*, 6(6), 417–423. <https://doi.org/10.5897/AJPP12.074>

Al-Malki, A. L. , & El Rabey, H. A. (2015). The anti-diabetic effect of low doses of *Moringa oleifera* Lam. seeds on streptozotocin-induced diabetes and diabetic nephropathy in male rats. *BioMed Research International*, 2015, 381040. <https://doi.org/10.1155/2015/381040>

Almeida, L. , VazdaSilva, M. , Falcão, A. , Soares, E. , Costa, R. , Loureiro, A. I. , Fernandes Lopes, C. , Rocha, J. , Nunes, T. , Wright, L. , & SoaresdaSilva, P. (2009). Pharmacokinetic and safety profile of transresveratrol in a rising multiple dose study in healthy volunteers. *Molecular Nutrition & Food Research*, 53(S1), Portico. <https://doi.org/10.1002/mnfr.200800177>

Ammon, H. P. T. , Safayhi, H. , Mack, T. , & Sabieraj, J. (1993). Mechanism of antiinflammatory actions of curcumin and boswellic acids. *Journal of Ethnopharmacology*, 38(2–3), 105–112. [https://doi.org/10.1016/0378-8741\(93\)90005-p](https://doi.org/10.1016/0378-8741(93)90005-p)

Athar, M. , Back, J. H. , Tang, X. , Kim, K. H. , Kopelovich, L. , Bickers, D. R. , & Kim, A. L. (2009). Resveratrol: A review of preclinical studies for human cancer prevention. *Toxicology and Applied Pharmacology*, 240(2), 151–162. <https://doi.org/10.1016/j.taap.2009.06.025>

Athar, M. , Back, J. H. , Tang, X. , Kim, K. H. , Kopelovich, L. , Bickers, D. R. , & Kim, A. L. (2009). Resveratrol: A review of preclinical studies for human cancer prevention. *Toxicology and Applied Pharmacology*, 240(2), 151–162. <https://doi.org/10.1016/j.taap.2009.06.025>

Baki, M. A. , Khan, A. , Al-Bari, M. A. A. , Mosaddik, A. , Sadik, G. , & Mondal, K. (2007). Sub-acute toxicological studies of Pongamol isolated from *Pongamia pinnata*. *Research Journal of Medical Sciences*, 2(2), 53–57.

Devi, P. R. , Adilaxmamma, K. , Rao, G. S. , Srilatha, C.H. , & Raj, M. A. (2012). Safety Evaluation of Alcoholic Extract of *Boswellia ovalifoliolata* Stem-bark in Rats. *Toxicology International*, 19(2), 115–120. <https://doi.org/10.4103/0971-6580.97198>

Bauer, R. , Tittel, G. , & Wagner, H. (2020). Standardization of herbal medicines: A review of requirements and approaches. *Phytotherapy Research*, 34(3), 473–485. <https://doi.org/10.1002/ptr.6600>

Bent, S. , Padula, A. , Moore, D. , Patterson, M. , & Mehling, W. (2006). Valerian for sleep: A systematic review and meta-analysis. *The American Journal of Medicine*, 119(12), 1005–1012. <https://doi.org/10.1016/j.amjmed.2006.02.026>

Biswas, K. , Chattopadhyay, I. , Banerjee, R. K. , & Bandyopadhyay, U. (2002). Biological activities and medicinal properties of neem (*Azadirachta indica*). *Current Science*, 82(11), 1336–1345.

Boots, A. W. , Haenen, G. R. M. M. , & Bast, A. (2008). Health effects of quercetin: From antioxidant to nutraceutical. *European Journal of Pharmacology*, 585(2–3), 325–337. <https://doi.org/10.1016/j.ejphar.2008.03.008>

Borgert, C. J. , Fuentes, C. , & Burgoon, L. D. (2021). Principles of dose-setting in toxicology studies: The importance of kinetics for ensuring human safety. *Archives of Toxicology*, 95(12), 3651–3664. <https://doi.org/10.1007/s00204-021-03155-4>

Borra, S. K. , Bharath Kumar, V. , & Biswas, S. (2019). Resveratrol: A boon for treating Alzheimer's disease? *Biomedicine & Pharmacotherapy*, 109, 2076–2085. <https://doi.org/10.1016/j.biopha.2018.11.127>

Boudreau, M. D. , & Beland, F. A. (2006). An evaluation of the biological and toxicological properties of *Aloe barbadensis* (Miller), *Aloe vera*. *Journal of Environmental Science and Health, Part C*, 24(1), 103–154. doi: 10.1080/10590500600614303.

Briguglio, G. , Costa, C. , Pollicino, M. , Giambò, F. , Catania, S. , & Fenga, C. (2020). Polyphenols in cancer prevention: New insights (Review). *International Journal of Functional Nutrition*, 1(2). <https://doi.org/10.3892/ijfn.2020.9>

Brown, R. P. , Gerbarg, P. L. , & Ramazanov, Z. (2002). *Rhodiola rosea*. A phytomedicinal overview. *HerbalGram*, 56, 40–52.

Bülbül, E. Ö. , & Okur, N. Ü. (2025). Difficulties in using natural herbal substances and their current use in some pharmaceutical dosage forms. *Current Pharmaceutical Design*, 31(28), e13816128346715. doi: 10.2174/0113816128346715250120074519.

Calderon, S. N. , Eiden, C. , & De Waele, J. (2019). Opioid receptor pharmacology and signaling in pain management. *Nature Reviews Drug Discovery*, 18(11), 762–772. <https://doi.org/10.1038/s41573-019-0005-8>

Chaachouay, N. , & Zidane, L. (2024). Plant-derived natural products: A source for drug discovery and development. *Drugs and Drug Candidates*, 3(1), 184–207. <https://doi.org/10.3390/ddc3010011>

Chan, P.-C. , Xia, Q. , & Fu, P. P. (2007). Ginkgo biloba leave extract: Biological, medicinal, and toxicological effects. *Journal of Environmental Science and Health, Part C*, 25(3), 211–244.

<https://doi.org/10.1080/10590500701569414>

- Chandran, B. , & Goel, A. (2012). A randomized, pilot study to assess the efficacy and safety of curcumin in patients with active rheumatoid arthritis. *Phytotherapy Research*, 26(11), 1719–1725. <https://doi.org/10.1002/ptr.4639>
- Chen, H. , Gao, W. , & Li, Y. (2021). Integration of bioinformatics in medicinal plant research: Enhancing predictive modeling for toxicity and efficacy. *Phytochemistry*, 186, 112740. <https://doi.org/10.1016/j.phytochem.2021.112740>
- Chen, S. , Li, S. , Li, W. , & Zhang, Y. (2018). Pharmacokinetics of ginsenosides in rat plasma by UPLC-Q-TOF-MS. *Journal of Pharmaceutical and Biomedical Analysis*, 148, 49–56. <https://doi.org/10.1016/j.jpba.2017.09.027>
- Chow, H. S. , Cai, Y. , Hakim, I. A. , Crowell, J. A. , Shahi, F. , Brooks, C. A. , ... & Alberts, D. S. (2003). Pharmacokinetics and safety of green tea polyphenols after multiple-dose administration of epigallocatechin gallate and Polyphenon E in healthy individuals. *Clinical Cancer Research*, 9(9), 3312–3319.
- Chow, H. H. , Hakim, I. A. , & Alberts, D. S. (2001). Pharmacokinetics and safety of green tea polyphenols after multiple-dose administration of epigallocatechin gallate and polyphenon E in healthy individuals. *Cancer Epidemiology and Prevention Biomarkers*, 10(1), 53–58.
- Claridge, T. D. W. (2016). *High-Resolution NMR Techniques in Organic Chemistry* (3rd ed.). Elsevier.
- Cohen, M. M. (2014). Tulsi-*Ocimum sanctum*: A herb for all reasons. *Journal of Ayurveda and Integrative Medicine*, 5(4), 251–259. <https://doi.org/10.4103/0975-9476.146554>
- Cos, P. , Vlietinck, A. J. , Berghe, D. V. , & Maes, L. (2006). Anti-infective potential of natural products: How to develop a stronger in vitro 'proof-of-concept'. *Journal of Ethnopharmacology*, 106(3), 290–302.
- Cragg, G. M. , & Newman, D. J. (2013). Natural products: A continuing source of novel drug leads. *Biochimica et Biophysica Acta*, 1830(6), 3670–3695. <https://doi.org/10.1016/j.bbagen.2013.02.008>
- D'Andrea, G. (2015). Quercetin: A flavonol with multifaceted therapeutic applications? *Fitoterapia*, 106, 256–271. <https://doi.org/10.1016/j.fitote.2015.09.018>
- D'Souza, D. C. , Braley, G. , Blaine, S. K. , & Vendetti, M. (2019). Dose-related effects of cannabis extract in pain and anxiety management. *Journal of Clinical Psychology*, 67(5), 392–399. <https://doi.org/10.1002/jclp.22338>
- de Hoffmann, E. , & Stroobant, V. (2013). *Mass Spectrometry: Principles and Applications* (3rd ed.). John Wiley & Sons.
- de Villiers, A. , Arendt, J. , & Stander, M. (2016). High-performance liquid chromatography for the analysis of bioactive compounds in medicinal plant extracts. *Journal of Chromatography A*, 1446, 21–30. <https://doi.org/10.1016/j.chroma.2016.03.024>
- Devinsky, O. , Cilio, M. R. , Cross, H. , FernandezRuiz, J. , French, J. , Hill, C. , ... & Friedman, D. (2014). Cannabidiol: Pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders. *Epilepsia*, 55(6), 791–802. <https://doi.org/10.1111/epi.12631>
- Devinsky, O. , et al. (2014). Cannabidiol: Pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders. *Epilepsia*, 55(6), 791–802. <https://doi.org/10.1111/epi.12631>
- Dhawan, K. , Dhawan, S. , & Sharma, A. (2004). Passiflora: A review update. *Journal of Ethnopharmacology*, 94(1), 1–23. <https://doi.org/10.1016/j.jep.2004.02.023>
- Dias, D. A. , Urban, S. , & Roessner, U. (2012). A historical overview of natural products in drug discovery. *Metabolites*, 2(2), 303–336. <https://doi.org/10.3390/metabo2020303>
- Dilmurodovich, A. D. (2025). Pharmacological effects of the ashwagandha extract on the marquee nervous system. *American Journal of Social Science*, 3(3), 43–58.
- Fahey, J. W. , Holtzclaw, W. D. , Wehage, S. L. , Wade, K. L. , Stephenson, K. K. , & Talalay, P. (2015). Sulforaphane bioavailability from glucoraphanin-rich broccoli: Control by active endogenous myrosinase. *PloS One*, 7(11), e51222.
- Flora, K. , Hahn, M. , Rosen, H. , & Benner, K. (1998). Milk thistle (*Silybum marianum*) for the therapy of liver disease. *American Journal of Gastroenterology*, 93(2), 139–143. <https://doi.org/10.1111/j.1572-0241.1998.00139.x>
- Fotsing Yannick Stéphane, F. F. Y. , Fongang, Bankeu Kezetas Jean Jules, B. K. J. , Gaber El-Saber Bathia, G. E.-S. , Iftikhar Ali, I. , and & Lenta Ndjakou Bruno, L. N. (2022). 'Extraction of bioactive compounds from medicinal plants and herbs'. In *Natural Medicinal Plants*.

IntechOpen. <https://doi.org/doi:10.5772/intechopen.98602>.

Fulda, S. , & Debatin, K. M. (2006). Resveratrol modulation of apoptosis pathways in cancer cells. *Cancer Letters*, 238(2), 157–164. <https://doi.org/10.1016/j.canlet.2005.06.041>

Ganzer, M. , & Sturm, S. (2018). Recent advances on HPLC/MS in medicinal plant analysis—An update covering 2011–2016. *Journal of Pharmaceutical and Biomedical Analysis*, 147, 211–233. <https://doi.org/10.1016/j.jpba.2017.07.038>

Garcia-Alonso, M. , Ros, G. , & Periago, M. J. (2017). Development and validation of an HPLC method for quantification of resveratrol in red wine extracts. *Food Chemistry*, 237, 636–642. <https://doi.org/10.1016/j.foodchem.2017.05.059>

Gastpar, M. , Singer, A. , & Zeller, K. (2021). Standardized *Hypericum perforatum* extract for the treatment of mild to moderate depression: Reproducibility of results across studies. *Journal of Psychiatric Research*, 138, 291–298. <https://doi.org/10.1016/j.jpsychires.2021.03.041>

Gerbeth, K. , Hüsche, J. , Fricker, G. , Werz, O. , Schubert-Zsilavecz, M. , & Abdel-Tawab, M. (2013) Boswellic acids: Novel leukotriene synthesis inhibitors and biphasic regulators of the eicosanoid network. *Phytomedicine*, 20(4), 348–356. <https://doi.org/10.1016/j.phymed.2012.10.017>

Goel, A. , Kunnumakkara, A. B. , & Aggarwal, B. B. (2008). Curcumin as “Curecumin”: From kitchen to clinic. *Biochemical Pharmacology*, 75(4), 787–809. <https://doi.org/10.1016/j.bcp.2007.08.016>

Grover, V. , & Singh, P. (2021). Neuropharmacology of *Bacopa monnieri*: Therapeutic versus toxic effects at varying doses. *Neuropharmacology*, 188, 108556. <https://doi.org/10.1016/j.neuropharm.2021.108556>

Grundmann, O. , Wang, J. , McGregor, G. P. , & Butterweck, V. (2008) Anxiolytic activity of *Passiflora incarnata* in laboratory rats. *Journal of Ethnopharmacology*, 115(2), 433–436. <https://doi.org/10.1016/j.jep.2007.10.015>

Grzanna, R. , Lindmark, L. , & Frondoza, C. G. (2005). Ginger—: An herbal medicinal product with broad anti-inflammatory actions. *Journal of Medicinal Food*, 8(2), 125–132. <https://doi.org/10.1089/jmf.2005.8.125>

Hampson, A. J. , Grimaldi, M. , Lolic, M. , Wink, D. , Rosenthal, R. , & Axelrod, J. (1998). Neuroprotective antioxidants from marijuana. *Proceedings of the National Academy of Sciences*, 95(14), 8268–8273.

Han, J. , Lawson, L. , Han, G. , & Han, P. (1995). A spectrophotometric method for quantitative determination of allicin and total garlic thiosulfates. *Analytical Biochemistry*, 225(1), 157–160. <https://doi.org/10.1006/abio.1995.1124>

Hema Nagadurga, Divvela . 2020. ‘Bioavailability and bioequivalence studies’. *Pharmaceutical Formulation Design - Recent Practices*. IntechOpen. doi:10.5772/intechopen.85145.

Houghton, P. J. (1999). The scientific basis for the reputed activity of valerian. *Journal of Pharmacy and Pharmacology*, 51(5), 505–512. <https://doi.org/10.1211/0022357991772772>

Huntley, A. L. , & Ernst, E. (2005). The safety of Echinacea: A systematic review of controlled clinical trials. *Drug Safety*, 28(5), 387–400. <https://doi.org/10.2165/00002018-200528050-00002>

Iffland, K. , & Grotenhermen, F. (2017). An update on safety and side effects of cannabidiol: A review of clinical data and relevant animal studies. *Cannabis and Cannabinoid Research*, 2(1), 139–154. <https://doi.org/10.1089/can.2016.0034>

Ioannidis, J. P. (2019). Why most published research findings are false. *PLoS Medicine*, 2(8), e124. <https://doi.org/10.1371/journal.pmed.0020124>

Isbrucker, R. A. , & Burdock, G. A. (2006). Risk and safety assessment on the consumption of licorice root (*Glycyrrhiza* sp.), its extract, and powder as a food ingredient, with emphasis on the pharmacology and toxicology of glycyrrhizin. *Regulatory Toxicology and Pharmacology*, 46(3), 167–192. <https://doi.org/10.1016/j.yrtph.2006.06.002>

Isbrucker, R. A. , Edwards, J. A. , Wolz, E. , Davidovich, A. , & Bausch, J. (2006). Safety studies on epigallocatechin gallate (EGCG) preparations. Part 2: Dermal, acute and short-term toxicity studies. *Food and Chemical Toxicology*, 44(5), 636–650. <https://doi.org/10.1016/j.fct.2005.11.003>

Ishida, T. , & Inoue, T. (2012). Effect of glycyrrhizin on pharmacokinetics of methotrexate in rats. *European Journal of Pharmaceutical Sciences*, 45(3), 328–332.

Jayaprakasha, G. K. , Nagana Gowda, G. A. , Marquez, S. , & Patil, B. S. (2013). Rapid separation and quantitation of curcuminoids combining pseudo two-dimensional liquid flash chromatography and NMR spectroscopy. *Journal of Chromatography. B, Analytical*

Technologies in the Biomedical and Life Sciences, 937, 25–32.

<https://doi.org/10.1016/j.jchromb.2013.08.011>

Johnson, J. J. , Nihal, M. , & Mukhtar, H. (2011). Synergistic effects of piperine and resveratrol in neuroprotection and anti-inflammation. *Journal of Pharmacology and Experimental Therapeutics*, 338(1), 119–127. <https://doi.org/10.1124/jpet.110.170654>

Kakkar, S. , Yadav, S. K. , Yadav, D. , Kumar, A. , Kaur, H. , Kumar, D. , & Kumar, V. (2025). Glycyrrhiza glabra-based food and herbal products. In *Liquorice* (pp. 191–216). CRC Press.

Kapoor, L. , Singh, A. , & Pandey, B. (2019). Dose-dependent toxicology in *Withania somnifera*: Preclinical findings. *Pharmacological Reports*, 71(4), 606–613.

<https://doi.org/10.1016/j.pharep.2019.03.006>

Kaschel, R. (2011). No effects of Ginkgo biloba special extract EGb 761 on neuropsychological functioning of healthy volunteers. *Human Psychopharmacology: Clinical and Experimental*, 26(7), 442–449. <https://doi.org/10.1002/hup.1217>

Kensler, T. W. , Wakabayashi, N. , & Biswal, S. (2013). Cell survival responses to environmental stresses via the Keap1-Nrf2-ARE pathway. *Annual Review of Pharmacology and Toxicology*, 47, 89–116. <https://doi.org/10.1146/annurev.pharmtox.46.120604.141046>

Kim, H. J. , Son, T. H. , & Kang, S. H. (2020). Panax ginseng: Hepatotoxicity and its clinical implications. *Traditional and Integrative Medicine*, 15(1), 54–62.

<https://doi.org/10.1016/j.tim.2019.10.002>

Kim, J. G. , Bak, S.-B. , Kim, G.-D. , Choi, H.-S. , Kwon, D.-A. , Kim, H.-Y. , Son, D.-W. , Jeong, J.-H. , Lee, B.-W. , An, H.-J. , & Lee, H. S. (2024). Evaluation of acute, repeated dose 28-day and 13-week oral toxicity and genotoxicity of a standardized fraction (HemoHIM) from *Angelica gigas*, *Cnidium officinale*, and *Paeonia lactiflora*. *Toxicological Research*, 41(1), 13–26.

<https://doi.org/10.1007/s43188-024-00252-1>

Kim, J. H. , Mai, X. , Kim, K. Y. , Sim, M. , Lee, S. , Seo, H. , Lee, G. , Kim, D. J. , & Kim, K. H. (2019). A sensitive and rapid LC-MS/MS method for determination of berberine in human plasma. *Mass Spectrometry Letters*, 10(2), 56–60. <https://doi.org/10.5478/MSL.2019.10.2.56>

Kim, H. K. (2013). Pharmacokinetics of ginsenoside Rb1 and its metabolite compound K after oral administration of Korean Red Ginseng extract. *Journal of Ginseng Research*, 37(4), 451–456. <https://doi.org/10.5142/jgr.2013.37.451>

Kimmatkar, N. , Thawani, V. , Hingorani, L. , & Khiyani, R. (2003). Efficacy and tolerability of *Boswellia serrata* extract in treatment of osteoarthritis of knee--a randomized double blind placebo controlled trial. *Phytomedicine: International Journal of Phytotherapy and Phytopharmacology*, 10(1), 3–7. <https://doi.org/10.1078/094471103321648593>

Kocaadam, B. , & Şanlıer, N. (2017). Curcumin, an active component of turmeric (*Curcuma longa*), and its effects on health. *Critical Reviews in Food Science and Nutrition*, 57(13), 2889–2895. <https://doi.org/10.1080/10408398.2015.1077195>

Krüger, P. , Schäpperle, A. , Hemmler, R. , Zimmermann, D. , Werz, O. , Schubert-Zsilavecz, M. , & Steinhilber, D. (2008). Boswellic acids from *Boswellia serrata* inhibit topoisomerase I and II and induce apoptosis in pancreatic cancer cells. *BMC Cancer*, 8, 264.

Lafka, T. I. , Lazou, A. E. , Sinanoglou, V. J. , & Lazos, E. S. (2007). Phenolic and antioxidant composition of olive oil mill wastes. *Food Chemistry*, 104(1), 179–186.

<https://doi.org/10.1016/j.foodchem.2006.11.063>

Lambert, J. D. , & Elias, R. J. (2010a). The antioxidant and pro-oxidant activities of green tea polyphenols: A mechanistic perspective. *Food and Function*, 1(3), 177–180.

<https://doi.org/10.1039/c0fo00110b>

Lambert, J. D. , & Elias, R. J. (2010b). The antioxidant and pro-oxidant activities of green tea polyphenols: A role in cancer prevention. *Archives of Biochemistry and Biophysics*, 501(1), 65–72. <https://doi.org/10.1016/j.abb.2010.06.013>

Langmead, L. , Makins, R. J. , & Rampton, D. S. (2004). Anti-inflammatory effects of aloe vera gel in human colorectal mucosa in vitro. *Alimentary Pharmacology & Therapeutics*, 19(5), 521–527. <https://doi.org/10.1111/j.1365-2036.2004.01878.x>

Lawson, L. D. , & Wang, Z. J. (1992). Allicin and allicin-derived garlic compounds increase breath acetone through allyl methyl sulfide: Use in measuring allicin bioavailability. *Journal of Agricultural and Food Chemistry*, 40(12), 2418–2424. <https://doi.org/10.1021/jf00024a007>

Li, W. , Cheng, S. , & Chen, J. (2021). Analysis of chemical composition and standardization of medicinal plant extracts using advanced techniques. *Journal of Chromatography A*, 1636, 461712. <https://doi.org/10.1016/j.chroma.2020.461712>

Li, Y. , Li, W. , & Zhang, W. (2017). Characterization of catechins in green tea using MS/MS. *Food Chemistry*, 225, 230–238. <https://doi.org/10.1016/j.foodchem.2017.01.002>

Liang, J. , Xu, J. , & Cheng, X. (2019). Optimizing traditional methods in modern practice: An analysis of ginger preparation and bioactivity. *Phytotherapy Research*, 33(10), 2696–2704. <https://doi.org/10.1002/ptr.6481>

Liang, Y. Z. , Xie, P. , & Chan, K. (2016). Quality control of herbal medicines. *Journal of Chromatography B*, 812(1–2), 53–70. <https://doi.org/10.1016/j.jchromb.2004.09.028>

Liu, X. , Li, Y. , Ma, Q. , Wang, Y. , & Song, A. L. (2019). Withaferin-A inhibits growth of drug-resistant breast carcinoma by inducing apoptosis and autophagy, endogenous reactive oxygen species (ROS) production, and inhibition of cell migration and nuclear factor kappa B (Nf- $\kappa$ B)/mammalian target of rapamycin (m-TOR) signalling pathway. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*, 25, 6855–6863. <https://doi.org/10.12659/MSM.916931> (Retraction published Med Sci Monit. 2021 Mar 25 ;27:e932348. doi: 10.12659/MSM.932348.)

Li-Weber, M. (2009). New insights into the mechanism of action of baicalin in cancer prevention and therapy. *Cancer Letters*, 281(2), 133–139. <https://doi.org/10.1016/j.canlet.2008.10.032>

Mahdi, J. G. , Mahdi, A. J. , & Mahdi, A. J. (2006). Pharmacological uses of salicin: From the ancient willow to aspirin. *Saudi Medical Journal*, 27(12), 1791–1800.

Mandal, V. , Mohan, Y. , & Hemalatha, S. (2007). Microwave assisted extraction—: An innovative and promising extraction tool for medicinal plant research. *Pharmacognosy Reviews*, 1(1), 7–18.

March, R. E. , & Brodbelt, J. S. (2008). Quadrupole ion trap mass spectrometry: Theory, simulation, recent advances, and applications. *Mass Spectrometry Reviews*, 27(5), 491–558.

Mathur, S. , Goyal, G. , & Yadav, S. (2011). Role of withanolides in inducing apoptosis in cancer cells: An in vitro study on *Withania somnifera*. *Journal of Ethnopharmacology*, 134(2), 367–372. <https://doi.org/10.1016/j.jep.2011.01.015>

McGhie, T. K. , & Walton, M. C. (2007). The bioavailability and absorption of anthocyanins: Towards a better understanding. *Journal of Food Science*, 72(9), R107–R114. <https://doi.org/10.1111/j.1750-3841.2007.00552.x>

McKay, D. L. , & Blumberg, J. B. (2006). A review of the bioactivity and potential health benefits of chamomile tea (*Matricaria recutita* L.). *Phytotherapy Research*, 20(7), 519–530. <https://doi.org/10.1002/ptr.1900>

Melnyk, J. P. , Marcone, M. F. , & Jones, P. J. (2020). Serotonin syndrome from St. John's Wort overdose. *Phytotherapy Research*, 34(6), 1182–1190. <https://doi.org/10.1002/ptr.6634>

Mix, J. A. , & Crews, W. D., Jr (2000). An examination of the efficacy of Ginkgo biloba extract EGb761 on the neuropsychologic functioning of cognitively intact older adults. *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, 6(3), 219–229. <https://doi.org/10.1089/acm.2000.6.219>

Molyneux, P. (2004). The use of the stable free radical diphenylpicrylhydrazyl (DPPH) for estimating antioxidant activity. *Songklanakarin Journal of Science and Technology*, 26(2), 211–219.

Mukherjee, P. K. , Harwansh, R. K. , & Bahadur, S. (2019). The challenges in developing medicinal plant products and standardized extracts. *Journal of Traditional and Complementary Medicine*, 9(4), 349–357. <https://doi.org/10.1016/j.jtcme.2019.06.001>

Müller, W. E. , Singer, A. , Wonnemann, M. , Hafner, U. , Rolli, M. , & Schäfer, C. (1998). Hyperforin represents the neurotransmitter reuptake inhibiting constituent of hypericum extract. *Pharmacopsychiatry*, 31 Suppl 1, 16–21. <https://doi.org/10.1055/s-2007-979341>

Nagadurga, D. H. (2020). Bioavailability and bioequivalence studies. In *Pharmaceutical Formulation Design: Recent Practices*. IntechOpen. <https://doi.org/10.5772/intechopen.85145>

Naresh, K. S. , Ansari, S. J. , Biswas, A. , Dandamudi, U. , Mogurampelly, S. , & Chaudhari, S. R. (2025). Investigating curcuminoid encapsulation in  $\beta$ -cyclodextrin: Insights from NMR spectroscopy and MD simulations. *Food Hydrocolloids*, 162, 110958.

Niessen, W. M. A. (2006). *Liquid Chromatography-Mass Spectrometry*, (Third 3rd Editioned.). CRC Press.

Nováková, L. , Solich, P. , Solichová, D. , & Solich, P. Hajslová, J. (2006). Applications of ultra performance liquid chromatography in pharmaceutical analysis. *Journal of Chromatography A*, 1130(1), 2–30.



Nutt, D. J. , King, L. A. , & Nichols, D. E. (2020). Psychoactive effects of Cannabis sativa in medical contexts: Ethical challenges and clinical guidelines. *Neuropharmacology*, 177, 108240. <https://doi.org/10.1016/j.neuropharm.2020.108240>

Nyiredy, S. (2004). Progress in forced-flow planar chromatography. *Journal of Chromatography A*, 1000(1–2), 985–999.

Obolentseva, G. , Litvinenko, V. , & Litvinenko, Y. (2018). Chronic toxicity evaluation of Glycyrrhiza glabra extracts. *Toxicology Reports*, 8, 189–194. <https://doi.org/10.1016/j.toxrep.2018.10.010>

OECD . (2019). OECD Guidelines for the Testing of Chemicals, Section 4. Test No. 423: Acute Oral Toxicity - Acute Toxic Class Method. OECD Publishing. <https://doi.org/10.1787/9789264071001-en>

Olaniyan, M. F. , & Olagunju, J. A. (2022). Acute toxicity study of neem (Azadirachta indica) leaf aqueous extract in chickens. *African Scientist*, 23(3), 1099–1110. <https://publications.africanscientistjournal.org/sites/default/files/2022-12/1099-4144-1-PB.pdf>

Onakpoya, I. J. , Hung, S. K. , Perry, R. , Wider, B. , & Ernst, E. (2011). The use of Garcinia extract (hydroxycitric acid) as a weight loss supplement: A systematic review and meta-analysis of randomized clinical trials. *Journal of Obesity*, 2011, 509038. <https://doi.org/10.1155/2011/509038>

Panossian, A. , Wikman, G. , Kaur, P. , & Asea, A. (2009). Adaptogens exert a stress-protective effect by modulation of expression of molecular chaperones. *Phytomedicine: International Journal of Phytotherapy and Phytopharmacology*, 16(6–7), 617–622. <https://doi.org/10.1016/j.phymed.2008.12.003>

Patel, K. R. , Scott, E. , & Brown, V. A. (2011). Resveratrol and its analogues: Promising anticancer agents. *Annals of the New York Academy of Sciences*, 1215(1), 150–160. <https://doi.org/10.1111/j.1749-6632.2010.05843.x>

Pathak, R. , & Sharma, D. (2019). Assessment of hepatotoxicity in chronic use of Curcuma longa extract in rats. *Journal of Traditional and Complementary Medicine*, 9(4), 309–316. <https://doi.org/10.1016/j.jtcme.2019.06.001>

Pertwee, R. G. (2008). The diverse CB1 and CB2 receptor pharmacology of three plant cannabinoids:  $\Delta^9$ -tetrahydrocannabinol, cannabidiol and  $\Delta^9$ -tetrahydrocannabivarin. *British Journal of Pharmacology*, 153(2), 199–215. <https://doi.org/10.1038/sj.bjp.0707442>

Pitt, J. J. (2009). Principles and applications of mass spectrometry in clinical biochemistry. *Clinical Biochemist Reviews*, 30(1), 19–34.

Prakash, P. , & Gupta, N. (2005). Therapeutic uses of Ocimum sanctum Linn (tulsi) with a note on eugenol and its pharmacological actions: A short review. *Indian Journal of Physiology and Pharmacology*, 49(2), 125–131.

Ramautar, R. , Somsen, G. W. , & de Jong, G. J. (2017). CE-MS for metabolomics: Developments and applications in the field of herbal analysis. *Electrophoresis*, 38(12), 1606–1624. <https://doi.org/10.1002/elps.201700077>

Rasool, M. , & Varalakshmi, P. (2006). Immunomodulatory role of Withania somnifera against inflammatory changes. *Phytotherapy Research*, 20(5), 348–354. <https://doi.org/10.1002/ptr.1860>

Rizvi, S. A. A. , Einstein, G. P. , Tulp, O. L. , Sainvil, F. , & Branly, R. (2022). "Introduction to traditional medicine and their role in prevention and treatment of emerging and re-emerging diseases." *Biomolecules*, 12 (10): 1442. <https://doi.org/10.3390/biom12101442>.

Russo, E. , & Scicchitano, F. (2014). Hypericum perforatum: Pharmacological effects and clinical evidence. *Fitoterapia*, 94, 124–130. <https://doi.org/10.1016/j.fitote.2014.02.011>

Ryu, B. , Jiang, H. , & Lee, S. H. (2016). Enhanced bioavailability and pharmacokinetics of ginseng-derived saponins through oral absorption. *Journal of Ginseng Research*, 40(3), 261–268. <https://doi.org/10.1016/j.jgr.2015.10.001>

Santos, D. , Félix, L. , Luzio, A. , Parra, S. , Bellas, J. , & Monteiro, S. M. (2021). Single and combined acute and subchronic toxic effects of microplastics and copper in zebrafish (Danio rerio) early life stages. *Chemosphere*, 277, 130262.

Sap, A. , & Yaman, M. (2022). Optimization and validation of HPLC-DAD method for the quantification of curcuminoids in turmeric (Curcuma Longa L.). *Pakistan Journal of Analytical & Environmental Chemistry*, 23(1), 93.

Sertkaya, A. , Neumann, P. , & Weaver, J. (2021). Ethical issues in high-dose toxicity testing of herbal medicines. *Ethics in Science and Environmental Politics*, 21, 101–109. <https://doi.org/10.3354/esep00206>

Shankar, T. N. , Shantha, N. V. , Ramesh, H. P. , Murthy, I. A. , & Murthy, V. S. (1980). Toxicity studies on turmeric (*Curcuma longa*): Acute toxicity studies in rats, guinea pigs & monkeys. *Indian Journal of Experimental Biology*, 18(1), 73–75.

Shao, L. , Liu, K. , Huang, F. , Guo, X. , Wang, M. , & Liu, B. (2013). Opposite effects of quercetin, luteolin, and epigallocatechin gallate on insulin sensitivity under normal and inflammatory conditions in mice. *Inflammation*, 36(1), 1–14. <https://doi.org/10.1007/s10753-012-9522-0>

Shara, M. , & Stohs, S. J. (2015). Efficacy and safety of white willow bark (*Salix alba*) extracts. *Phytotherapy Research*, 29(8), 1112–1116. <https://doi.org/10.1002/ptr.5359>

Sharma, A. , & Lee, H. J. (2020). Ginsenoside compound K: Insights into recent studies on pharmacokinetics and health-promoting activities. *Biomolecules*, 10(7), 1028. <https://doi.org/10.3390/biom10071028>

Sharma, J. N. , Srivastava, K. C. , & Gan, E. K. (1996). Suppressive effects of eugenol and ginger oil on arthritic rats. *Pharmacology*, 55(3), 199–206. <https://doi.org/10.1159/000139456>

Sharma, R. A. , Steward, W. P. , & Gescher, A. J. (2007). Pharmacokinetics and pharmacodynamics of curcumin. *Advances in Experimental Medicine and Biology*, 595, 453–470. [https://doi.org/10.1007/978-0-387-46401-5\\_20](https://doi.org/10.1007/978-0-387-46401-5_20)

Shi, L. , Qiu, Z. , & Li, Y. (2021). Pharmacogenomics and the impact of CYP450 polymorphisms on *Hypericum perforatum* efficacy. *Clinical and Translational Science*, 14(4), 1710–1720. <https://doi.org/10.1111/cts.12937>

Shoba, G. , Joy, D. , & Joseph, T. (1998). Enhanced bioavailability of curcumin with piperine: Evidence from human clinical studies. *Planta Medica*, 64(4), 353–356. <https://doi.org/10.1055/s-2006-957450>

Simmler, C. , Kulakowski, D. , Lankin, D. C. , McAlpine, J. B. , Chen, S.-N. , & Pauli, G. F. (2016). Holistic Analysis Enhances the Description of Metabolic Complexity in Dietary Natural Products. *Advances in Nutrition*, 7(1), 179–189. <https://doi.org/10.3945/an.115.009365>

Singh, A. , Bajpai, M. , Yadav, S. , & Kumar, V. (2018a). Dose-dependent effects of medicinal plants and phytoconstituents in therapeutics and toxicology. *Journal of Pharmacology & Pharmacotherapeutics*, 9(2), 79–85. [https://doi.org/10.4103/jpp.JPP\\_15\\_18](https://doi.org/10.4103/jpp.JPP_15_18)

Singh, N. , Bhalla, M. , Jager, P. D. , & Gilca, M. (2018b). An overview on Ashwagandha: A rasayana (rejuvenator) of ayurveda. *African Journal of Traditional, Complementary and Alternative Medicines*, 14(3), 33–42. <https://doi.org/10.4314/ajtcam.v14i3.5>

Sparkman, O. D. , Penton, Z. , & Kitson, F. G. (2011). *Gas Chromatography and Mass Spectrometry: A Practical Guide* (2nd ed.). Academic Press.

Srinivasan, K. (2007). Black pepper and its pungent principle-piperine: A review of diverse physiological effects. *Critical Reviews in Food Science and Nutrition*, 47(8), 735–748. <https://doi.org/10.1080/10408390601062054>

Srivastava, J. K. , Shankar, E. , & Gupta, S. (2010). Chamomile: A herbal medicine of the past with bright future. *Molecular Medicine Reports*, 3(6), 895–901. doi: 10.3892/mmr.2010.377.

Sterk, V. , Buchele, B. , Simmet, T. , & Schneider, B. (2004). LC/MS/MS assay for boswellic acids in human plasma and pharmacokinetics of oral 11-keto-beta-boswellic acid in healthy humans. *Journal of Pharmaceutical and Biomedical Analysis*, 36(5), 1013–1022. <https://doi.org/10.1016/j.jpba.2004.07.006>

Stuart, B. H. (2004). *Infrared Spectroscopy: Fundamentals and Applications*. John Wiley & Sons.

Subapriya, R. , & Nagini, S. (2005). Medicinal properties of neem leaves: A review. *Current Medicinal Chemistry - Anti-Cancer Agents*, 5(2), 149–156. <https://doi.org/10.2174/1568011053174828>

Sukardiman, S. , Mutiah, R. , & Handayani, R. (2024). Potential and mechanisms of indigenous Indonesian medicinal plants in treating sexual dysfunction: A systematic review and pharmacological network overview. <https://doi.org/10.2139/ssrn.4974500>

Sumiyoshi, H. , Kanezawa, A. , Masamoto, K. , Harada, H. , Nakagami, S. , Yokota, A. , Nishikawa, M. , & Nakagawa, S. (1984). Histological analysis showed mild kidney damage, indicating potential nephrotoxicity at high doses. *The Journal of Toxicological Sciences*, 9(1), 61–75. <https://doi.org/10.2131/jts.9.61>

Tan, X. S. , Ma, J. Y. , & Feng, R. (2013). Biliary excretion and enterohepatic circulation of berberine and its derivatives in rat. *Xenobiotica*, 43(11), 1046–1052. <https://doi.org/10.3109/00498254.2013.787394>

Tang, J. , Zhang, M. , & Gao, Y. (2019). Medicinal plants and phytochemicals with immunomodulatory effects. *Journal of Ethnopharmacology*, 245, 112161. <https://doi.org/10.1016/j.jep.2019.112161>

Tariq, L. , Bhat, B. A. , Hamdani, S. S. , & Mir, R. A. (2021). Phytochemistry, pharmacology and toxicity of medicinal plants. In *Medicinal and Aromatic Plants: Healthcare and Industrial Applications* (pp. 217–240). Cham: Springer International Publishing.

Telange, D. R. , Deshmukh, V. S. , Gangane, P. S. , More, S. M. , & Warokar, A. S. (2025). Development and optimization of double-loaded phytosomal soft nanoparticles for enhancing the biopharmaceutical and synergistic hepatoprotective performance of silymarin and curcuminoids. *BioNanoScience*, 15(3), 1–34.

Tiwari, R. , Siddiqui, M.H. , Mahmood, T. , et al. (2020). An exploratory analysis on the toxicity & safety profile of Polyherbal combination of curcumin, quercetin and rutin. *Clinical Phytoscience* 6, 82. <https://doi.org/10.1186/s40816-020-00228-2>

Tsai, T. H. , & Liu, S. C. (2002). Pharmacokinetics and liver distribution of baicalin and baicalein in rats. *Journal of Pharmacy and Pharmacology*, 54(10), 1273–1278.

Vaou, N. , E. Stavropoulou , C. C. Voidarou , Z. Tsakris , G. Rozos , C. Tsigalou , and E. Bezirtzoglou . 2022. "Interactions between medical plant-derived bioactive compounds: Focus on antimicrobial combination effects." *Antibiotics* (Basel, Switzerland), 11(8): 1014. <https://doi.org/10.3390/antibiotics11081014>.

Wagner, H. , & Bladt, S. (1996). *Plant Drug Analysis: A Thin Layer Chromatography Atlas* (2nd ed.). Springer.

Wahab, S. , Annadurai, S. , Abullais, S. S. , Das, G. , Ahmad, W. , Ahmad, M. F. , Kandasamy, G. , Vasudevan, R. , Ali, M. S. , & Amir, M. (2021). *Glycyrrhiza glabra* (Licorice): A Comprehensive review on its phytochemistry, biological activities, clinical evidence and toxicology. *Plants* (Basel, Switzerland), 10(12), 2751. <https://doi.org/10.3390/plants10122751>

Wang, H. , Y. Chen , Y., L. Wang , L., Q. Liu , Q., S. Yang , S., and & C. Wang , C. (2023). "Advancing herbal medicine: Enhancing product quality and safety through robust quality control practices." *Frontiers in Pharmacology*, 14:, 1265178. <https://doi.org/10.3389/fphar.2023.1265178>.

Wang, Q. , Xu, Y. , & Wang, J. (2019). Integrating traditional medicine into modern pharmacological research: The role of TCMD and Ayurveda Pharmacopoeia. *Journal of Ethnopharmacology*, 239, 111916. <https://doi.org/10.1016/j.jep.2019.111916>

Wang, Y. , Mou, C. , Hu, Y. , He, Z. , Cho, J. Y. , & Kim, J. H. (2025). In vivo metabolism, pharmacokinetics, and pharmacological activities of ginsenosides from ginseng. *Journal of Ginseng Research*, May 15.

Wellington, K. , & Jarvis, B. (2001). Silymarin: A review of its clinical properties in the management of hepatic disorders. *BioDrugs*, 15(7), 465–489. <https://doi.org/10.2165/00063030-200115070-00005>

Wenzel, E. , & Somoza, V. (2005). Resveratrol bioavailability and metabolism. *Molecular Nutrition & Food Research*, 49(5), 472–481. <https://doi.org/10.1002/mnfr.200500010>

Wilsey, B. , Marcotte, T. , Deutsch, R. , Gouaux, B. , & Sakai, S. (2013). Low-dose vaporized cannabis significantly improves neuropathic pain. *The Journal of Pain*, 14(2), 136–148. <https://doi.org/10.1016/j.jpain.2012.10.009>

Wurglics, M. , & Schubert-Zsilavecz, M. (2006). *Hypericum perforatum*: A "modern" herbal antidepressant. *Deutsche Apotheker Zeitung*, 146, 3718–3722.

Yang, Z. , Zhang, H. , & Ma, Y. (2020). High-resolution mass spectrometry in analyzing bioactive components of medicinal plant extracts. *Journal of Chromatography B*, 1154, 122291. <https://doi.org/10.1016/j.jchromb.2020.122291>

Yuan, H. , Ma, Q. , Ye, L. , & Piao, G. (2016). The traditional medicine and modern medicine from natural products. *Molecules*, 21(5), 559. <https://doi.org/10.3390/molecules21050559>

Zhang, X. , Zhao, L. , & Li, J. (2018a). Personalized approaches in herbal medicine: Tailoring dose and formulation based on pharmacogenomics. *Journal of Ethnopharmacology*, 213, 98–106. <https://doi.org/10.1016/j.jep.2017.11.043>

Zhang, Y. , Liang, Z. , Bi, Y. , Wu, S. , & Wang, H. (2018b). The herbal medicine and its development based on modern approaches. *Current Pharmaceutical Design*, 24(35), 4176–4181. <https://doi.org/10.2174/1381612825666190211144757>

Zhang, Y. , Talalay, P. , Cho, C. G. , & Posner, G. H. (1992). A major inducer of anticarcinogenic protective enzymes from broccoli: Isolation and elucidation of structure. *Proceedings of the National Academy of Sciences of the United States of America*, 89(6),

2399–2403. <https://doi.org/10.1073/pnas.89.6.2399>

Zhou, Y. , Lu, Y. , & Luo, Q. (2019). UPLC-MS profiling of phenolic compounds in *Camellia sinensis*: Implications for antioxidant and anti-inflammatory activity. *Food Chemistry*, 277, 604–612. <https://doi.org/10.1016/j.foodchem.2018.11.043>

## Naturally Derived Antimicrobial Agents in Food Packaging Material

Alam, F. , Mohammadin, K. , Shafique, Z. , Amjad, S.T. , Asad, M.H.H.B. (2022) *Citrus flavonoids* as potential therapeutic agents: A review. *Phytother. Res.* 36:1417–1441.

Alonso, P. , Fernández-Pastor, S. , Guerrero, A. (2024) Application of cinnamon essential oil in active food packaging: A review. *Appl. Sci.* 14:6554.

Aloui, H. , Khwaldia, K. (2016) Natural antimicrobial edible coatings for microbial safety and food quality enhancement. *Compr. Rev. Food Sci. Food Saf.* 15:1080–1103.

Amani, F. , Rezaei, A. , Akbari, H. , Dima, C. , Jafari, S.M. (2022) Active packaging films made by complex coacervation of tragacanth gum and gelatin loaded with curcumin, characterization and antioxidant activity. *Foods* 11:3168.

Andevári, G.T. , Rezaei, M. (2011) Effect of gelatin coating incorporated with cinnamon oil on the quality of fresh rainbow trout in cold storage. *Int. J. Food Sci. Technol.* 46:2305–2311.

Andrade, M. , Ribeiro-Santos, R. , Bonito, M. , Saraiva, M. , Sanches-Silva, A. (2018) Characterization of rosemary and thyme extracts for incorporation into a whey protein based film. *LWT* 92:497–508.

Arvanitoyannis, I.S. , Stratakis, A.C. (2012) Application of modified atmosphere packaging and active/smart technologies to red meat and poultry: A review. *Food Bioprocess Technol.* 5:1423–1446.

Bartmanska, A. , Walecka-Zacharska, E. , Tronina, T. , Poplonski, J. , Sordon, S. , Brzezowska, E. , Bania, J. , Huszcza, E. (2018) Antimicrobial properties of spent hops extracts, flavonoids isolated therefrom, and their derivatives. *Molecules* 23:2059.

Batpho, K. , Boonsupthip, W. , Rachtanapun, C. (2017) Antimicrobial activity of collagen casing impregnated with nisin against foodborne microorganisms associated with ready-to-eat sausage. *Food Control* 73:1342–1352.

Betts, T.J. (2001) Chemical characterisation of the different types of volatile oil constituents by various solute retention ratios with the use of conventional and novel commercial gas chromatographic stationary phases. *J. Chromatogr. A* 936:33–46.

Beuchat, L.R. (2002) Control of foodborne pathogens and spoilage microorganisms by naturally occurring antimicrobials, in Wilson C.L. , Droby S. (Eds.), *Microbial Food Contamination*, Boca Raton, FL, CRC Press, pp. 149–169.

Bi, J. , Tian, C. , Zhang, G.L. , Hao, H. , Hou, H.M. (2021) Novel procyanidins-loaded chitosan-graft-polyvinyl alcohol film with sustained antibacterial activity for food packaging. *Food Chem.* 15:130534.

Bolumar, T. , LaPeña, D. , Skibsted, L. , Orlén, V. (2016) Rosemary and oxygen scavenger in active packaging for prevention of high-pressure induced lipid oxidation in pork patties. *Food Packag. Shelf Life* 7:26–33.

Bora, H. , Kamle, M. , Mahato, D.K. , Tiwari, P. , Kumar, P. (2020) Citrus essential oils (CEOs) and their applications in food: An overview. *Plants* 9:357.

Burt, S. (2004) Essential oils: Their antibacterial properties and potential applications in foods: A review. *Int. J. Food Microbiol.* 94:223–253.

Burt, S. , Reinders, R. (2003) Antibacterial activity of selected plant essential oils against *Escherichia coli* O157: H7. *Lett. Appl. Microbiol.* 36:162–167.

Byun, Y. , Ward, A. , Whiteside, S. (2012) Formation and characterization of shellac-hydroxypropyl methylcellulose composite films. *Food Hydrocoll.* 27:364–370.

Carina, D. , Sharma, S. , Jaiswal, A.K. , Jaiswal, S. (2021) Seaweeds polysaccharides in active food packaging: A review of recent progress. *Trends Food Sci. Technol.* 110:559–572.

Cassidy, A. , Mukamal, K.J. , Liu, L. , Franz, M. , Eliassen, A.H. , Rimm, E.B. (2013) High anthocyanin intake is associated with a reduced risk of myocardial infarction in young and middle-aged women. *Circulation* 127:188–196.

Chaves, F. , Pavan, I. , da Silva, L. , de Freitas, L. , Rostagno, M. , Antunes, A. , Simabuco, F. (2020) Pomegranate juice and peel extracts are able to inhibit proliferation, migration and colony formation of prostate cancer cell lines and modulate the Akt/mTOR/S6K SIGNALING Pathway. *Plant Foods Human Nutr.* 75:54–62.

Chen, C. , Liu, C.H. , Cai, J. , Zhang, W. , Qi, W.L. , Wang, Z. , Yang, Y. (2018) Broadspectrum antimicrobial activity, chemical composition and mechanism of action of garlic (*Allium sativum*) extracts. *Food Control* 86:117–125.

Chen, H. , Hoover, D.G. (2003) Bacteriocins and their food applications. *Compr. Rev. Food Sci. F.* 2:82–100.

Cheng, G. , Dai, M. , Ahmed, S. , Hao, H. , Wang, X. , Yuan, Z. (2016) Antimicrobial drugs in fighting against antimicrobial resistance. *Front. Microbiol.* 7:470.

Cho, J.M. , Howard, L.R. , Prior, R.L. , Clark, J.R. (2004) Flavonoid glycosides and antioxidant capacity of various blackberry, blueberry and red grape genotypes determined by high-performance liquid chromatography/mass spectrometry. *J. Sci. Food Agric.* 84:1771–1782.

Chowdhury, A.K. , Ahsan, M. , Islam, S.N. , Ahmed, Z.U. (1991) Efficacy of aqueous extract of garlic & allicin in experimental shigellosis in rabbits. *Indian J. Med. Res.* 93:33–36.

Cooksey, K. (2005) Effectiveness of antimicrobial food packaging materials. *Food Addit. Contam.* 22:980–987.

Cowan, M.M. (1999) Plant products as antimicrobial agents. *Clin. Microbiol. Rev.* 12, 564–582.

Cressy, H.K. , Jerrett, A.R. , Osborne, C.M. , Bremer, P.J. (2003) A novel method for the reduction of numbers of *Listeria monocytogenes* cells by freezing in combination with an essential oil in bacteriological media'. *J. Food Prot.* 66:390–395.

Da Silva Sabo, S. , Vitolo, M. , González, J.M.D. , de Souza Oliveira, R.P. (2014) Overview of *Lactobacillus plantarum* as a promising bacteriocin producer among lactic acid bacteria. *Food Res. Int.* 64:527–536.

Dai, C. , Lin, J. , Li, H. , Shen, Z. , Wang, Y. , Velkov, T. , Shen, J. (2022) The natural product curcumin as an antibacterial agent: Current achievements and problems. *Antioxidants* 11:459.

Delaquis, P. , Mazza, G. (1995) Antimicrobial properties of isothiocyanates in food preservation. *Food Technol.* 49:73.

Dias, M.V. , Soares, N.D.F.F. , Borges, S.V. , De Sousa, M.M. , Nunes, C.A. , De Oliveira, I.R. , Medeiros, E.A. (2013) Use of allyl isothiocyanate and carbon nanotubes in an antimicrobial film to package shredded, cooked chicken meat. *Food Chem.* 141:3160–3166.

Fakraoui, O. , Atanase, L. , Salhi, S. , Royaud, I. , Arous, M. , Ayadi, Z. (2024) Investigation of lemon peel extract as a natural additive in polyvinyl alcohol/chitosan blend for advanced bioactive food packaging. *J. Polym. Sci.* <https://doi.org/10.1002/pol.20240268>

Feng, Y. , Lin, J. , He, G. , Liang, L. , Liu, Q. , Yan, J. , Yao, Q. (2022) Compositions and biological activities of pomegranate peel polyphenols extracted by different solvents. *Molecules* 27:47–96.

Ferysiuk, K. , Wojciak, K.M. (2020) Reduction of nitrite in meat products through the application of various plant-based ingredients. *Antioxidants* 9:711.

Filho, J.G. , Egea, M.B. (2022) Edible bioactive film with curcumin: A potential “functional” packaging? *Int. J. Mol. Sci.* 23:5638.

Fimland, G. , Johnsen, L. , Dalhus, B. , Nissen-Meyer, J. (2005) Pediocin-like antimicrobial peptides (class IIa bacteriocins) and their immunity proteins: Biosynthesis, structure, and mode of action. *J. Pept. Sci. Off. Publ. Eur. Pept. Soc.* 11:688–696.

Fiore, A. , Park, S. , Volpe, S. , Torrieri, E. , Masi, P. (2021) Active packaging based on PLA and chitosan-caseinate enriched rosemary essential oil coating for fresh minced chicken breast application. *Food Packag. Shelf Life* 29:100708.

Florentini, C. , Duserm Garrido, G. , Bassani, A. , Cortimiglia, C. , Zaccone, M. , Montalbano, L. , Martinez-Nogues, V. , Cocconcelli, P.S. , Spigno, G. (2021) Citrus peel extracts for industrial-scale production of bio-based active food packaging. *Foods* 23:30.

Gao, H.X. , He, Z. , Sun, Q. , He, Q. , Zeng, W.C. (2019) A functional polysaccharide film forming by pectin, chitosan, and tea polyphenols. *Carbohydr. Polym.* 215:1–7.

Ghosh, S. , Roy, S. , Naskar, J. , Kole, R.K. (2023) Plant-mediated synthesis of mono and bimetallic (Au-Ag) nanoparticles: Future prospects for food quality and safety. *J. Nanomater.* 2023:2781667.

Giannakas, A.E. , Baikousi, M. , Karabagias, V.K. , Karageorgou, I. , Iordanidis, G. , Emmanouil-Konstantinos, C. , Leontiou, A. , Karydis-Messinis, A. , Zafeiropoulos, N.E. ,

Kehayias, G. (2021) Low-density polyethylene-based novel active packaging film for food shelf-life extension via thyme-oil control release from SBA-15 nanocarrier. *Nanomaterials* 14:423.

Grzebeniarz, W. , Biswas, D. , Roy, S. , Jamróz, E. (2023) Advances in biopolymer-based multi-layer film preparations and food packaging applications. *Food Packag. Shelf Life* 35:101033.

Gu, L. , Kelm, M.A. , Hammerstone, J.F. , Beecher, G. , Cunningham, D. , Vannozzi, S. , Prior, R.L. (2004) Concentrations of proanthocyanidins in common foods and estimations of normal consumption. *J. Nutr.* 134:613–617.

Hao, Y. , Zhang, M. , Wang, L. , Tao, N. , Li, L. , Zhu, W. , Xu, C. , Wang, Y. (2022) Mechanism of antimicrobials immobilized on packaging film inhibiting food borne pathogens. *LWT* 169:114037.

Haro-Gonzalez, J.N. , Castillo-Herrera, G.A. , Martínez-Velazquez, M. , EspinosaAndrews, H. (2021) Clove essential oil (*Syzygium aromaticum* L. Myrtaceae): Extraction, chemical composition, food applications, and essential bioactivity for human health. *Molecules* 26:6387.

Hassan, R.A. , Heng, L.Y. , Tan, L.L. (2019) Novel DNA biosensor for direct determination of carrageenan. *Sci. Rep.* 9:6379.

Huang, J. , Hu, Z. , Hu, L. , Li, G. , Yao, Q. , Hu, Y. (2021) Pectin-based active packaging: A critical review on preparation, physical properties and novel application in food preservation. *Trends Food Sci. Technol.* 118:167–178.

Hussain, Y. , Alam, W. , Ullah, H. , Dacrema, M. , Daglia, M. , Khan, H. , Arciola, C.R. (2022) Antimicrobial potential of curcumin: Therapeutic potential and challenges to clinical applications. *Antibiotics* 11:322.

Iheaturu, N.C. , Nwakaudu, A.A. , Nwakaudu, M.S. , Owuamanam, C.I. (2018) The use of natural antioxidant active polymer packaging for food preservation: A review. *Futo J. Ser.* 4:94–112.

Jancikova, S. , Dordevic, D. , Jamroz, E. , Behalova, H. , Tremlova, B. (2020) Chemical and physical characteristics of edible films, based on  $\kappa$ - and  $\iota$ -carrageenans with the addition of lapacho tea extract. *Foods* 9:357.

Joerger, M.C. , Klaenhammer, T.R. (1986) Characterization and purification of helveticin J and evidence for a chromosomally determined bacteriocin produced by *Lactobacillus helveticus* 481. *J. Bacteriol.* 167:439–446.

Kahya, N. , Kestir, S.M. , Öztürk, S. , Yolaç, A. , Torlak, E. , Kalaycıoğlu, Z. , Akın-Evingür, G. , Erim, F.B. (2022) Antioxidant and antimicrobial chitosan films enriched with aqueous sage and rosemary extracts as food coating materials: Characterization of the films and detection of rosmarinic acid release. *Int. J. Biol. Macromol.* 30:470–480.

Khan, N.G. , Correia, J. , Adiga, D. , Rai, P.S. , Dsouza, H.S. , Chakrabarty, S. , Kabekkodu, S.P. (2021) comprehensive review on the carcinogenic potential of bisphenol A: Clues and evidence. *Environ. Sci. Pollut. Res.* 28:19643–19663.

Kim, H.W. , Jeong, J.Y. , Seol, K.H. , Seong, P.N. , Ham, J.S. (2016) Effects of edible films containing procyanidin on the preservation of pork meat during chilled storage. *Korean J. Food Sci. Anim. Resour.* 36:230–236.

Knez Hrncic, M. , Spaninger, E. , Kosir, I.J. , Knez, Z. , Bren, U. (2019) Hop compounds: Extraction techniques, chemical analyses, antioxidative, antimicrobial, and anticarcinogenic effects. *Nutrients* 11:257.

Koontz, J.L. , Moffitt, R.D. , Marcy, J.E. , O'Keefe, S.F. , Duncan, S.E. , Long, T.E. (2010) Controlled release of  $\alpha$ -tocopherol, quercetin, and their cyclodextrin inclusion complexes from linear low-density polyethylene (LLDPE) films into a coconut oil model food system. *Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess.* 27:1598–1607.

Lambert, R.J.W. , Skandamis, P.N. , Coote, P.J. , Nychas, G.J.E. (2001) A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. *J. Appl. Microbiol.* 9:453–462.

Leonida, M.D. , Belbekhouche, S. , Benzecry, A. , Peddineni, M. , Suria, A. , Carbonnier, B. (2018) Antibacterial hop extracts encapsulated in nanochitosan matrices. *Int. J. Biol. Macromol.* 120:1335–1343.

Lim, G. , Jang, S. , Kim, J. , Kim, H. , Song, K. (2010) Use of a gelatin film containing grapefruit seed extract in the packaging of strawberries. *Food Sci. Preserv.* 17:196–201.

Liu, B. , Wang, X. , Wang, Y. , Chen, X. , Jin, X. , Luo, X. (2023) Review of compounds and activities from mangrove *Sonneratia* genus and their endophytes. *J. Holist. Integr. Pharm.* 4:218–227.

Liu, Y. , Zhang, X. , Li, C. , Qin, Y. , Xiao, L. , Liu, J. (2020) Comparison of the structural, physical and functional properties of kappa-carrageenan films incorporated with pomegranate flesh and peel extracts. *Int. J. Biol. Macromol.* 147:1076–1088.

Lucera, A. , Costa, C. , Conte, A. , Del Nobile, M.A. (2012) Food applications of natural antimicrobial compounds. *Front. Microbiol.* 3:287.

Maruthupandy, M. , Seo, J. (2019) Allyl isothiocyanate encapsulated halloysite covered with polyacrylate as a potential antibacterial agent against food spoilage bacteria. *Mater. Sci. Eng. C Mater. Biol. Appl.* 105:110016.

Masuda, S. , Hara-Kudo, Y. , Kumagai, S. (1998) Reduction of *E. coli* O157: H7 populations in soy sauce, a fermented seasoning. *J. Food Prot.* 61:657–661.

Meade, E. , Slaterry, M.A. , Garvey, M. (2020) Bacteriocins, potent antimicrobial peptides and the fight against multi drug resistant species: Resistance is futile? *Antibiotics* 9:32.

Mokoena, M.P. , Omatola, C.A. , Olaniran, A.O. (2021) Applications of lactic acid bacteria and their bacteriocins against food spoilage microorganisms and foodborne pathogens. *Molecules* 26:7055.

Mulla, M. , Ahmed, J. , Al-Attar, H. , Castro-Aguirre, E. , Arfat, Y.A. , Auras, R. (2017) Antimicrobial efficacy of clove essential oil infused into chemically modified LLDPE film for chicken meat packaging. *Food Control* 73:663–671.

Mulla, M. , Ahmed, J. , Vahora, A. , Pathania, S. , Rashed, M. (2024) Characterization of biopolymers based antibacterial films enriched with thyme essential oil and their application for milk cake preservation. *Front. Food Sci. Technol.* 4. <https://doi.org/10.3389/frfst.2024.1356582>

Müller-Auffermann, K. , Grijalva, F. , Jacob, F. , Hutzler, M. (2015) Nisin and its usage in breweries: A review and discussion. *J. Inst. Brew.* 121:309–319.

Muppalla, S.R. , Kanatt, S.R. , Chawla, S. , Sharma, A. (2014) Carboxymethyl cellulose–polyvinyl alcohol films with clove oil for active packaging of ground chicken meat. *Food Packag. Shelf Life.* 2:51–58.

Murgia, M. , Pani, S.M. , Sanna, A. , Marras, L. , Manis, C. , Banchiero, A. , Coroneo, V. (2024) Antimicrobial activity of grapefruit seed extract on edible mushrooms contaminations: Efficacy in preventing *Pseudomonas* spp. in *Pleurotus eryngii* . *Foods* 13:1161.

Muxika, A. , Etxabide, A. , Uranga, J. , Guerrero, P. , de la Caba, K. (2017) Chitosan as a bioactive polymer: Processing, properties and applications. *Int. J. Biol. Macromol.* 105:1358–1368.

Nguyen, T. , Dao, U. , Bui, Q. , Bach, G. , Thuc, C. , Thuc, H. (2020) Enhanced antimicrobial activities and physiochemical properties of edible film based on chitosan incorporated with *Sonneratia caseolaris* (L.) Engl. leaf extract. *Prog. Org. Coat.* 140:105487.

Nishie, M. , Nagao, J.-I. , Sonomoto, K. (2012) Antibacterial peptides “bacteriocins”: An overview of their diverse characteristics and applications. *Biocontrol Sci.* 17:1–16.

Núñez, L. , D'Aquino, M. (2012) Microbicide activity of clove essential oil (*Eugenia caryophyllata* ). *Braz. J. Microbiol.* 43:1255–1260.

Núñez, N. , Vidal-Casanella, O. , Sentellas, S. , Saurina, J. , Núñez, O. (2020) Characterization, classification and authentication of turmeric and curry samples by targeted LC-HRMS polyphenolic and curcuminoid profiling and chemometrics. *Molecules* 25:2942.

Nya, E.J. , Dawood, Z. , Austin, B. (2010) The garlic component, allicin, prevents disease caused by *Aeromonas hydrophila* in rainbow trout, *Oncorhynchus mykiss* (Walbaum). *J. Fish Dis.* 33:293–300.

Ocak, B. (2020) Properties and characterization of thyme essential oil incorporated collagen hydrolysate films extracted from hide fleshing wastes for active packaging. *Environ. Sci. Pollut. Res.* 27:29019–29030.

Ojeda-Sana, A.M. , van Baren, C.M. , Elechosa, M.A. , Juárez, M.A. , Moreno, S. (2013) New insights into antibacterial and antioxidant activities of rosemary essential oils and their main components. *Food Control* 31:189–195.

Otoni, C.G. , Espitia, P.J.P. , Avena-Bustillos, R.J. , McHugh, T.H. (2016) Trends in antimicrobial food packaging systems: Emitting sachets and absorbent pads. *Food Res. Int.* 83:60–73.

Ouattara, B. , Simard, R.E. , Holley, R.A. , Piette, G.J. , Bégin, A. (1997) Antibacterial activity of selected fatty acids and essential oils against six meat spoilage organisms. *Int. J. Food Microbiol.* 22:37.

Perez, R.H. , Zendo, T. , Sonomoto, K. (2022) Multiple bacteriocin production in lactic acid bacteria. *J. Biosci. Bioeng.* 134(4):277–287.

Petkoska, A.T. , Daniloski, D. , D'Cunha, N.M. , Naumovski, N. , Broach, A.T. (2021) Edible packaging: Sustainable solutions and novel trends in food packaging. *Food Res. Int.* 140:109981.

Rajakumar, T. , Pugalendhi, P. (2023) Allyl isothiocyanate regulates oxidative stress, inflammation, cell proliferation, cell cycle arrest, apoptosis, angiogenesis, invasion and metastasis via interaction with multiple cell signaling pathways. *Histochem. Cell Biol.* 161:211–221.

Reis, D. , Jones, T. (2017) Aromatherapy: Using essential oils as a supportive therapy. *Clin. J. Oncol. Nurs.* 21:16–19.

Riahi, Z. , Priyadarshi, R. , Rhim, J. , Bagheri, R. (2021) Gelatin-based functional films integrated with grapefruit seed extract and TiO<sub>2</sub> for active food packaging applications. *Food Hydrocol.* 112:106314.

Ribeiro-Santos, R. , Carvalho-Costa, D. , Cavaleiro, C. , Costa, H.S. , Albuquerque, T.G. , Castilho, M.C. , Ramos, F. , Melo, N.R. , Sanches-Silva, A. (2015) A novel insight on an ancient aromatic plant: The rosemary (*Rosmarinus officinalis* L.). *Trends Food Sci. Technol.* 45:355–368.

Rivlin, R.S. (2001) Historical perspective on the use of garlic. *J. Nutr.* 131:951S–954S.

Roy, S. , Priyadarshi, R. , Ezati, P. , Rhim, J.W. (2022) Curcumin and its uses in active and smart food packaging applications: A comprehensive review. *Food Chem.* 1(375):131885.

Roy, S. , Zhang, W. , Biswas, D. , Ramakrishnan, R. , Rhim, J.W. (2023a) Grapefruit seed extract-added functional films and coating for active packaging applications: A review. *Molecules* 11:730.

Roy, S. , Priyadarshi, R. , Łopusiewicz, L. , Biswas, D. , Chandel, V. , Rhim, J.-W. (2023b) Recent progress in pectin extraction, characterization, and pectin-based films for active food packaging applications: A review. *Int. J. Biol. Macromol.* 239:124248.

Schmitz, C. , Auza, L.G.A. , Koberidze, D. , Rasche, S. , Fischer, R. , Bortesi, B. (2019) Conversion of chitin to defined chitosan oligomers: Current status and future prospects. *Mar. Drugs* 17:452.

Sharma, K. , Mahato, N. , Lee, Y.R. (2019) Extraction, characterization and biological activity of Citrus flavonoids. *Rev. Chem. Eng.* 35:265–284.

Sihombing, N. , Elma, M. , Thala'ah, R. , Simatupang, F. , Pradana, E. , Rahma, A. (2022) Garlic essential oil as an edible film antibacterial agent derived from Nagara sweet potato starch applied for packaging of Indonesian Traditional Food: Dodol. *IOP Conf. Ser. Earth Environ. Sci.* 999:012026.

Sikkema, J. , Debont, J.A.M. , Poolman, B. (1995) Mechanisms of membrane toxicity of hydrocarbons. *Microbiol. Rev.* 59:201–222.

Silva, M. , de Lima, A. , Silva, M. , Caetano, V. , de Andrade, M. , da Silva, R. , Filho, L. , Silva, I. , Vinhas, G. (2024) Clove essential oil and eugenol: A review of their significance and uses. *Food Biosci.* 62:105112.

Silva, S. , Costa, E.M. , Veiga, M. , Morais, R.M. , Calhau, C. , Pintado, M. (2020) Health promoting properties of blueberries: A review. *Crit. Rev. Food Sci. Nutr.* 60:181–200.

Silvestri, J.D.F. , Paroul, N. , Czyewski, E. , Lerin, L. , Rotava, I. , Cansian, R.L. , Mossi, A. , Toniazio, G. , Oliveira, D. , Treichel, H. (2010) Perfil da composição química e atividades antibacteriana e antioxidante do oleoessencial do cravo-da-índia (*Eugenia caryophyllata* Thunb.). *Revista Ceres* 57:589–594.

Simpson, W.J. , Smith, A.R. (1992) Factors affecting antibacterial activity of hop compounds and their derivatives. *J. Appl. Bacteriol.* 72:327–334.

Sung, S.Y. , Sin, L.T. , Tee, T.T. , Bee, S.T. , Rahmat, A.R. , Rahman, W.A.W.A. , Tan, A.C. , Vikhraman, M. (2013) Antimicrobial agents for food packaging applications. *Trends Food Sci. Technol.* 33:110–123.

Tafesh, A. , Najami, N. , Jadoun, J. , Halahlih, F. , Riepl, H. , Azaizeh, H. (2011) Synergistic antibacterial effects of polyphenolic compounds from olive mill wastewater. *Evid. Based Complement. Alternat. Med.* 9:431021.

Tan, C. , Han, F. , Zhang, S. , Li, P. , Shang, N. (2021) Novel bio-based materials and applications in antimicrobial food packaging: Recent advances and future trends. *Int. J. Mol. Sci.* 22:9663.



Tarar, A. , Peng, S. , Cheema, S. , Peng, C.A. (2022) Anticancer activity, mechanism, and delivery of allyl isothiocyanate. *Bioengineering* (Basel) 9:470.

Tas, B. , Sehiti, E. , Tas, C. , Unal, S. , Cebecia, F. , Menciloglu, Y. , Unal, H. (2019) Carvacrol loaded halloysite coatings for antimicrobial food packaging applications. *Food Packag. Shelf Life* 20:100300.

Thangaleela, S. , Sivamaruthi, B.S. , Kesika, P. , Bharathi, M. , Kunaviktikul, W. , Klunklin, A. , Chanthapoon, C. , Chaiyasut, C. (2022) Essential oils, phytoncides, aromachology, and aromatherapy: A review. *Appl. Sci.* 12:4495.

Theivendran, S. , Hettiarachchy, N.S. , Johnson, M.G. (2006) Inhibition of *Listeria monocytogenes* by Nisin combined with grape seed extract or green tea extract in soy protein film coated on Turkey Frankfurters. *J. Food Sci.* 71:39–44.

Tian, B. , Wang, J. , Liu, Q. , Liu, Y. , Chen, D. (2021a) Formation chitosan-based hydrogel film containing silicon for hops  $\beta$ -acids release as potential food packaging material. *Int. J. Biol. Macromol.* 30:288–298.

Tian, B. , Xu, D. , Cheng, J. , Liu, Y. (2021b) Chitosan-silica with hops  $\beta$ -acids added films as prospective food packaging materials: Preparation, characterization, and properties. *Carbohydr. Polym.* 15:118457.

Tie, S. , Zhang, Q. , Zhao, Y. , Wu, Y. , Liu, D. , Zhao, L. , Gu, S. (2024) Design and preparation of novel antioxidant and antibacterial films containing procyanidins and phycocyanin for food packaging. *RSC Adv.* 4:7572–7581.

Tirillini, B. (2000) Grapefruit: The last decade acquisitions. *Fitoterapia* 71:29–S37.

Ultee, A. , Bennik, M.H.J. , Moezelaar, R. (2002) The phenolic hydroxyl group of carvacrol is essential for action against the food-borne pathogen *Bacillus cereus*. *Appl. Environ. Microbiol.* 68:1561–1568.

Xu, D. , Chen, T. , Liu, Y. (2020) The physical properties, antioxidant and antimicrobial activity of chitosan–gelatin edible films incorporated with the extract from hop plant. *Polym. Bull.* 78:3607–3624.

Yadav, D. , Borpatra Gohain, M. , Karki, S. , Ingole, P.G. (2022) A novel approach for the development of low-cost polymeric thin-film nanocomposite membranes for the biomacromolecule separation. *ACS Omega* 7:47967–47985.

Yang, C. , Lu, J. , Xu, M. , Shi, X. , Song, Z. , Chen, T. (2022) Evaluation of chitosan coatings enriched with turmeric and green tea extracts on postharvest preservation of strawberries. *LWT* 163:113551.

Yang, G. , Yue, J. , Gong, X. , Qian, B. , Wang, H. , Deng, Y. , Zhao, Y. (2014) Blueberry leaf extracts incorporated chitosan coatings for preserving postharvest quality of fresh blueberries. *Postharvest Biol. Technol.* 92:46–53.

Yemis, G.P. , Candogan, K. (2017) Antibacterial activity of soy edible coatings incorporated with thyme and oregano essential oils on beef against pathogenic bacteria. *Food Sci. Biotechnol.* 26:1113–1121.

Yildirim, S. , Rocker, B. , Pettersen, M.K. , Nilsen-Nygaard, J. , Ayhan, Z. , Rutkaite, R. , Radusin, T. , Suminska, P. , Marcos, B. , Coma, V. (2018) Active packaging applications for food. *Compr. Rev. Food Sci. Food Saf.* 17(1):165–199.

Younes, I. , Rinaudo, M. (2015) Chitin and chitosan preparation from marine sources. Structure, properties and applications. *Mar. Drugs* 13:1133–1174.

Yun, D. , Wang, Z. , Li, C. , Chen, D. , Liu, J. (2023) Antioxidant and antimicrobial packaging films developed based on the peel powder of different citrus fruits: A comparative study. *Food Biosci.* 51:102319.

Wang, Y. , Chung, S.-J. , Song, W.O. , Chun, O.K. (2014) Estimation of daily proanthocyanidin intake and major food sources in the U.S. diet. *J. Nutr.* 141:447–452.

Wani, N.R. , Rather, R.A. , Farooq, A. , Padder, S.A. , Baba, T.R. , Sharma, S. , Mubarak, N.M. , Khan, A.H. , Singh, P. , Ara, S. (2024) New insights in food security and environmental sustainability through waste food management. *Environ. Sci. Pollut. Res. Int.* 31(12):17835–17857.

Winther, M. , Nielsen, P.V. (2019) Active packaging of cheese with allyl isothiocyanate, an alternative to modified atmosphere packaging. *J. Food Prot.* 69:2430–2435.

Zhong, Y. , Godwin, P. , Jin, Y. , Xiao, H. (2020) Biodegradable polymers and green-based antimicrobial packaging materials: A mini-review. *Adv. Ind. Eng. Polym. Res.* 3:27–35.

Zielinska, A. (2019) Comparative analysis of circular economy implementation in Poland and other European Union countries. J. Int. Stud. 12:337–347.

## Herbal Remedies for Ulcers

- Alam, S , Asad, M , Asdaq SMB , Prasad VS , Antiulcer activity of methanolic extract of *Momordica charantia* L. in rats, Journal of Ethnopharmacology, 123, 2009, 464–469.
- Amandeep K , Robin S , Ramica S , Sunil K , Peptic ulcer: A review on etiology and pathogenesis, International Research Journal of Pharmacy, 3, 2012, 34–38.
- Bello H , Mohammed Z , Katsayal UA , Anti-ulcer activity of ethanol root extracts of *Cassia sieberiana* D.C. in albino rats, European Journal of Medicinal Plants, 11, 2016, 1–9.
- Bharathi T , Shrishra SN , Siddaiah M , Evaluation of antiulcer activity of ethanolic extract of *Terminalia pallida* leaves in experimental rats, Journal of Global Trends in Pharmaceutical Sciences, 6, 2015, 2794–2797.
- Bhoumik D , Masresha B , Mallik A , Antiulcer properties of herbal drugs: A review, International Journal of Biomedical Research, 8, 2017, 116–124.
- Boligon AA , de Freitas RB , de Brum TF , Waczuk EP , Klimaczewski CV , de Ávila DS , Athayde ML , de Freitas Bauermann L , Antiulcerogenic activity of *Scutia buxifolia* on gastric ulcers induced by ethanol in rats. Acta Pharmaceutica Sinica B, 4, 2014, 358–367.
- Bongu S , Vijayakumar S , Animal models in experimental gastric ulcer screening: A review, International Journal of Pharmacological Screening Methods, 2, 2012, 82–87.
- Cuevas VM , Calzado YR , Guerra YP , Yera AO , Despaigne SJ , Ferreiro RM , Quintana DC , Effects of grape seed extract, vitamin C, and vitamin E on ethanol-and aspirin-induced ulcers. Advances in Pharmacological Sciences, 2011, 2011, 1–6.
- Da Silva LM , Boeing T , Somensi LB , Cury BJ , Steimbach VMB , Silveria AC , Neiro R , Filho VC , Santin JR , de Andrade SF , Evidence of gastric ulcer healing activity of *Maytenus robusta* Reissek: In vitro and in vivo studies, Journal of Ethnopharmacology, 175, 2015, 75–85.
- Da Silva MFGF , Agostinho SMM , de Paula JR , Neto JO , Gamboa IC , Filho ER , Fernandes JB , Vieira PC , Chemistry of *Toona ciliata* and *Cedrela odorata* graft (Meliaceae): Chemosystematic and ecological significance, Pure and Applied Chemistry, 71, 1999, 1083–1087.
- Deshpande SS , Shah GB , Parmar NS , Antiulcer activity of *Tephrosia purpurea* in rats. Indian Journal of Pharmacology, 35, 2003, 168–172.
- Dharmani P , Kuchibhotla VK , Maurya R , Srivastava S , Sharma S , Palit G , Evaluation of anti-ulcerogenic and ulcer-healing properties of *Ocimum sanctum* Linn, Journal of Ethnopharmacology, 93, 2004, 197–206.
- Đorđević S , Petrović S , Dobrić S , Milenković M , Vučićević D , Žižić S , Kukić J , Antimicrobial, anti-inflammatory, anti-ulcer and antioxidant activities of *Carlina acanthifolia* root essential oil, Journal of Ethnopharmacology, 109, 2007, 458–463.
- Esteves I , Souza IR , Rodrigues M , Cardoso LG , Santos LS , Sertie JAA , Perazzo FF , Lima LM , Schneedorf JM , Bastos JK , Carvalho JCT , Gastric antiulcer and anti-inflammatory activities of the essential oil from *Casearia sylvestris* Sw, Journal of Ethnopharmacology, 101, 2005, 191–196.
- Hamed S , Arian AA , Farzaei MH , Gastroprotective effect of aqueous stem bark extract of *Ziziphus jujuba* L. against HCl/ethanol-induced gastric mucosal injury in rats, Journal of Traditional Chinese Medicine, 35, 2015, 666–670.
- Inaparthi VK , Patibandla NB , Prasad K , Nagaraju B , Prasanthi B , Srinivas B , Evaluation of anti ulcer and in-vitro antioxidant activities of aqueous and methanolic extracts of *Neolamarckia cadamba* leaves and bark in wistar albino rats, International Journal of Pharmaceutical Sciences and Research, 5, 2014, 1852–1858.
- Iqbal SF , Parray SA , Wadud A , Jahan N , Concept of gastric ulcer (qarhemedah) in unani system of medicine: A review, International Journal of Industrial Pharmacy and Bio Sciences, 1, 2012, 133–143.
- Jamal A , Siddiqui A , Tajuddin , Jafri MA , A review on gastric ulcer remedies used in unani system of medicine, Natural Product Radiance, 5, 2006, 153–158.

Kumar S , Singh SK , In vivo studies on aqueous extract of gum resin obtained from *Commiphora wightii* for the treatment of peptic ulcer, World Journal of Pharmacy and Pharmaceutical Sciences, 5, 2016, 1857–1863.

Lemos M , Santin JR , Júnior LCK , Niero R , Andrade De FS , Gastroprotective activity of hydroalcoholic extract obtained from the leaves of *Brassica oleracea* var. *acephala* DC in different animal models, Journal of Ethnopharmacology, 138, 2011, 503–507.

Liu XM , Zakaria MNM , Islam MW , Radhakrishnan R , Ismail A , Chen HB , Chan K , Al-Attas A , Anti-inflammatory and anti-ulcer activity of *Calligonum comosum* in rats, Fitoterapia, 72, 2001, 487–491.

Malairajan P , Gopalakrishnan G , Narasimhan S , Veni KJ , Evalution of anti-ulcer activity of *Polyalthia longifolia* (Sonn.) Thwaites in experimental animals, Indian Journal of Pharmacology, 40, 2008, 126–128.

Malairajan P , Gopalakrishnan G , Narasimhan S , Veni KJ , Kavimani S , Anti-ulcer activity of crude alcoholic extract of *Toona ciliata* Roemer (heart wood), Journal of Ethnopharmacology, 110, 2007, 348–351.

Mehta D , Ulcer-review on types, anti-ulcer drugs, anti-ulcer medicinal plants, anti-ulcer drug market, diagnostics and current global clinical trials status, Invention and Rapid Pharmacy Practice, 2016, 2016, 1–8.

Mohan H , Textbook of Pathology. 7th Ed., Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, 2015, pp. 533–537.

Niero R , de Andrade SF , Filho CV , A review of the ethnopharmacology, phytochemistry and pharmacology of plants of the *Maytenus* Genus , Current Pharmaceutical Design, 17, 2011, 1851–1871.

Pandian RS , Anuradha, CV , Viswanathan P , Gastroprotective effect of fenugreek seeds ( *Trigonella foenum graecum*) on experimental gastric ulcer in rats. Journal of Ethnopharmacology, 81, 2002, 393–397.

Pattanayak P , Behera P , Das D , Panda S , Ocimum sanctum Linn . A reservoir plant for therapeutic applications: An overview, Pharmacognosy Reviews, 4, 2010, 95–105.

Raju D , Ilango K , Chitra V , Ashish K , Evaluation of anti-ulcer activity of methanolic extract of *Terminalia chebula* fruits in experimental rats, Journal of Pharmaceutical Sciences and Research, 1, 2009, 101–107.

Ramasubramaniraja R , Babu MN , Peptic ulcer and phytochemistry: An overview, Journal of Pharmacy Research, 4, 2011, 156–160.

Rao CV , Ojha SK , Radhakrishnan K , Govindarajan R , Rastogi S , Mehrotra S , Pushpangadan P , Antiulcer activity of *Utleria salicifolia* rhizome extract, Journal of Ethnopharmacology, 91, 2004, 243–249.

Ravisankar P , Koushik OS , Reddy AA , Kumar UE , Anvith PS , Pragna P , A detailed analysis on acidity and ulcers in esophagus, gastric and duodenal ulcers and management, IOSR Journal of Dental and Medical Sciences, 15, 2016, 94–114.

Roy S , Clinical study of peptic ulcer disease, Asian Journal of Biomedical and Pharmaceutical Sciences, 6, 2016, 41–43.

Sabiu S , Garuba T , Sunmonu T , Ajani E , Sulyman A , Nurain I , Balogun A , Indomethacin-induced gastric ulceration in rats: Protective roles of Spondias mombin and Ficus exasperate. Toxicology Reports, 2, 2015, 261–267.

Thabrew MI , Arawwawala LDAM , An overview of in vivo and in vitro models that can be used for evaluating anti-gastric ulcer potential of medicinal plants, Austin Biology, 1, 2016, 1–9.

Thomas S , Femeesh M , Nafia K , Siyad M , Shrikumar S , Pharmacological review of anti ulcer screening, World Journal of Pharmacy and Pharmaceutical Sciences, 6, 2017, 1369–1387.

Umashanker M , Shruti S , Traditional Indian herbal medicine used as antipyretic, antiulcer, antidiabetic and anticancer: A review, International Journal of Research in Pharmacy and Chemistry, 1, 2011, 1152–1159.

## Case Studies on Herbal Extracts and Their Pharmaceutically Active Molecules

- Afqir, Hajar , Saadia Belmalha , Ayoub Farihi , Amine Elbouzidi , Mohamed Bouhrim , Amal Elrherabi , Abdellatif Boutagayout , Asmae Oubihi , and Mohammed Ouhsine . Comparative analysis of phenolic and flavonoid content, antioxidant, antibacterial activities, and functional groups of chemicals from *Hypericum perforatum* L., and *Papaver rhoeas* L. flower extracts. *Ecological Engineering & Environmental Technology* 25 (2024): 88–101.
- Ahuja, Akash , Ji Hye Kim , Jong-Hoon Kim , Young-Su Yi , and Jae Youl Cho . Functional role of ginseng-derived compounds in cancer. *Journal of Ginseng Research* 42, no. 3 (2018): 248–254.
- Akash, Muhammad Sajid Hamid , and Kanwal Rehman . *Essentials of Pharmaceutical Analysis*. Singapore: Springer, 2020. pp. 167–174.
- Alam, Md Ashraf , Raton Kumar Bishwas , Sabrina Mostofa , Debasish Sarkar , and Shirin Akter Jahan . X-ray crystallography derived diffraction properties of cuprite crystal as revealed by transmission electron microscopy. *Physics Open* 20 (2024): 100228.
- Althobaiti, Saed A. , Daklallah A. Almalki , Safa H. Qahl , Layaly Elsigar , Lobna M. A. Gurafi , Zeinab Kanani , and Omaira Nasir . Effect of *Artemisia annua* on kidney in gentamicin-induced nephrotoxicity in mice through regulation of the COX-2, NF- $\kappa$ B pathway. *Journal of King Saud University-Science* 35, no. 7 (2023): 102813.
- Ameer, Kashif , Hafiz Muhammad Shahbaz , and JoongHo Kwon . Green extraction methods for polyphenols from plant matrices and their byproducts: a review. *Comprehensive Reviews in Food Science and Food Safety* 16, no. 2 (2017): 295–315.
- Bagheri, Reza , Amir Rashidlamir , DamoonAshtaryLarky, Alexei Wong , MeysamAlipour , Mohamad S. Motevalli , AmelChebbi, Ismail Laher , and Hassane Zouhal . Does green tea extract enhance the antiinflammatory effects of exercise on fat loss? *British Journal of Clinical Pharmacology* 86, no. 4 (2020): 753–762.
- Barroso, Rosmeire Aparecida , Ricardo Navarro , Carla Roberta Tim , Lucas de Paula Ramos , Luciane Dias de Oliveira , Ângela Toshie Araki , Karina Gonzales Camara Fernandes , Daniela Macedo , and Livia Assis . Antimicrobial photodynamic therapy against *Propionibacterium acnes* biofilms using hypericin (*Hypericum perforatum*) photosensitizer: in vitro study. *Lasers in Medical Science* 36 (2021): 1235–1240.
- Binns, S. E. , J. Hudson , S. Merali , and J. T. Arnason . Antiviral activity of characterized extracts from *Echinacea* spp. (*Heliantheae*: *Asteraceae*) against herpes simplex virus (HSV-I). *Planta Medica* 68, no. 09 (2002): 780–783. <https://doi.org/10.1055/s-2002-34397>
- Britannica . The Editors of Encyclopaedia. "Ginseng". *Encyclopedia Britannica*, 27 Sep. 2024, <https://www.britannica.com/plant/ginseng>. Accessed 1 October 2024 .
- Canbay, Hale Seçilmiş . Effectiveness of liquidliquid extraction, solid phase extraction, and headspace technique for determination of some volatile watersoluble compounds of rose aromatic water. *International Journal of Analytical Chemistry* 2017, no. 1 (2017): 4870671.
- Chaachouay, Nouredine , and Lahcen Zidane . Plant-derived natural products: a source for drug discovery and development. *Drugs and Drug Candidates* 3, no. 1 (2024): 184–207.
- Chan, Lok Yung , Hoi Hin Kwok , Renee Wan Yi Chan , Malik Joseph Sriyal Peiris , Nai Ki Mak , Ricky Ngok Shun Wong , Michael Chi Wai Chan , and Patrick Ying Kit Yue . Dual functions of ginsenosides in protecting human endothelial cells against influenza H9N2-induced inflammation and apoptosis. *Journal of Ethnopharmacology* 137, no. 3 (2011): 1542–1546.
- Chu, Yang , Hongbo Wang , Jing Chen , and Yue Hou . New sesquiterpene and polymethoxy-flavonoids from *Artemisia annua* L. *Pharmacognosy Magazine* 10, no. 39 (2014): 213.
- de Faveri Favero, Fabricio , Rogério Grando , Fabiana R. Nonato , Ilza M. O. Sousa , Núbia C. A. Queiroz , Giovanna B. Longato , Rafael R. T. Zafred , João E. Carvalho , Humberto M. Spindola , and Mary A. Foglio . *Artemisia annua* L.: evidence of sesquiterpene lactones' fraction antinociceptive activity. *BMC Complementary and Alternative Medicine* 14 (2014): 1–11.
- de Faveri Favero, Fabrício , Rosanna Tarkany Basting , Ailane Souza de Freitas , Luan da Silva Dias Rabelo , Fabiana Regina Nonato , Rafael Rosolen Teixeira Zafred , Ilza Maria de Oliveira Sousa et al. Artemisinin and deoxyartemisinin isolated from *Artemisia annua* L. promote distinct antinociceptive and anti-inflammatory effects in an animal model. *Biomedicine & Pharmacotherapy* 178 (2024): 117299.
- El -Askary, Hesham Ibrahim , Sarah S. Mohamed , H. M. A. El-Gohari , Mohamed Ezzat , Shahira Mohammed , and M. R. Meselhy . Quinic acid derivatives from *Artemisia annua* L.

leaves; biological activities and seasonal variation. *South African Journal of Botany* 128 (2020): 200–208. <https://doi.org/10.1016/j.sajb.2019.11.008>

Gargouri, Brahim , Johanna Carstensen , Harsharan S. Bhatia , Michael Huell , Gunnar PH Dietz , and Bernd L. Fiebich . Anti-neuroinflammatory effects of Ginkgo biloba extract EGb761 in LPS-activated primary microglial cells. *Phytomedicine* 44 (2018): 45–55.

Günay, Nahide Ekici , Sabahattin Muhtaroglu , and Abdulkadir Bedirli . Administration of Ginkgo biloba extract (EGb761) alone and in combination with FK506 promotes liver regeneration in a rat model of partial hepatectomy. *Balkan Medical Journal* 35, no. 2 (2018): 174–180.

Haruna, Abdurrahshid , and Sharhabil Musa Yahaya . Recent advances in the chemistry of bioactive compounds from plants and soil microbes: a review. *Chemistry Africa* 4, no. 2 (2021): 231–248.

Jibhkate, Yogeshri J. , Abhijit P. Awachat , R. T. Lohiya , Milind J. Umekar , Atul T. Hemke , and Krishna R. Gupta . Extraction: an important tool in the pharmaceutical field. *International Journal of Science and Research Archive* 10, no. 1 (2023): 555–568.

Kadhim, Sura Mohammed , Mustafa Taha Mohammed , and Sura Mohsin Abbood . Biochemical studies of Ginkgo biloba extract on oxidative stress-induced myocardial injuries. *Drug Invention Today* 14, no. 6 (2020): 817–820.

Khalaf, Abdelazeem Ali , Shaymaa Hussein , Adel FathyTohamy , Sherif Marouf , Hanan Dawood Yassa , Amr Reda Zaki , and Anupam Bishayee . Protective effect of Echinacea purpurea (Immulant) against cisplatin-induced immunotoxicity in rats. *DARU Journal of Pharmaceutical Sciences* 27 (2019): 233–241.

Kim, Dong-Hyun . Gut microbiota-mediated pharmacokinetics of ginseng saponins. *Journal of Ginseng Research* 42, no. 3 (2018): 255–263.

Lang, Sophia J. , Michael Schmiech , Susanne Hafner , Christian Paetz , Carmen Steinborn , Roman Huber , Menna El Gaafary et al. Antitumor activity of an Artemisia annua herbal preparation and identification of active ingredients. *Phytomedicine* 62 (2019): 152962.

Li, Jing , Chao Zhang , Muxin Gong , and Manyuan Wang . Combination of artemisininbased natural compounds from Artemisia annua L. for the treatment of malaria: pharmacodynamic and pharmacokinetic studies. *Phytotherapy Research* 32, no. 7 (2018): 1415–1420.

Liu, Qiu , Zhiquan Jin , Zhiliang Xu , Hao Yang , Liang Li , Guiping Li , Fang Li et al. Antioxidant effects of ginkgolides and bilobalide against cerebral ischemia injury by activating the Akt/Nrf2 pathway in vitro and in vivo. *Cell Stress and Chaperones* 24, no. 2 (2019): 441–452.

Liu, Rui , Nadia L. Caram-Salas , Wei Li , Lili Wang , John Thor Arnason , and Cory Steven Harris . Interactions of Echinacea spp. root extracts and alkylamides with the endocannabinoid system and peripheral inflammatory pain. *Frontiers in Pharmacology* 12 (2021): 651292.

Lu, Guanyu , Zhuoting Liu , Xu Wang , and Chunling Wang . Recent advances in Panax ginseng CA Meyer as a herb for anti-fatigue: an effects and mechanisms review. *Foods* 10, no. 5 (2021): 1030.

Messaili, Souhila , Cyril Colas , Laëtitia Fougère , and Emilie Destandau . Combination of molecular network and centrifugal partition chromatography fractionation for targeting and identifying Artemisia annua L. antioxidant compounds. *Journal of Chromatography A* 1615 (2020): 460785.

Mirmalek, Seyed Abbas , Mohammad Amin Azizi , Ehsan Jangholi , Soheila Yadollah-Damavandi , Mohammad Amin Javidi , Yekta Parsa , Tina Parsa , Seyed Alireza Salimi-Tabatabaee , Hossein Ghasemzadeh Kolagar , and Reza Alizadeh-Navaei . Cytotoxic and apoptogenic effect of hypericin, the bioactive component of Hypericum perforatum on the MCF-7 human breast cancer cell line. *Cancer Cell International* 16 (2015): 1–9.

Miroshina, Tatyana , and Valeriy Poznyakovskiy . Echinacea purpurea as a medicinal plant: characteristics, use as a biologically active component of feed additives and specialized foods. *E3S Web of Conferences* 380 (2023): 01005. EDP Sciences.

Mishra, Jai Narayan , and Navneet Kumar Verma . An overview on Panax ginseng. *International Journal of Pharma and Chemical Research* 3, no. 3 (2017): 516–522.

Mohamed, Fakry F. , Darisuren Anhlán , Michael Schöfbänker , André Schreiber , Nica Classen , Andreas Hensel , Georg Hempel et al. Hypericum perforatum and its ingredients hypericin and pseudohypericin demonstrate an antiviral activity against SARS-CoV-2. *Pharmaceuticals* 15, no. 5 (2022): 530.

Nair, Manoj S. , Yaoxing Huang , David A. Fidock , Stephen J. Polyak , Jessica Wagoner , M. J. Towler , and P. J. Weathers . Artemisia annua L. extracts inhibit the in vitro replication of SARS-CoV-2 and two of its variants. *Journal of Ethnopharmacology* 274 (2021): 114016.

Sharma, Neha , Shailesh Deshpande , Nitika Ganjoo , and Amandeep Aman . Botanical description, phytochemistry, traditional uses, and pharmacology of green tea (*Camellia Sinensis*): an updated review. *International Journal of Biology, Pharmacy and Allied Sciences* 11, no. 2 (2022): 76–88 ISSN: 2277–4998.

Nobakht, Seyedeh Zahra , Maryam Akaberi , Amir Hooshang Mohammadpour , Ali Tafazoli Moghadam , and Seyed Ahmad Emami . *Hypericum perforatum*: traditional uses, clinical trials, and drug interactions. *Iranian Journal of Basic Medical Sciences* 25, no. 9 (2022): 1045.

Pagidipati, Neha Jadeja , and Thomas A. Gaziano . Estimating deaths from cardiovascular disease: a review of global methodologies of mortality measurement. *Circulation* 127, no. 6 (2013): 749–756.

Park, EunHye , Jung Yum , Keun Bon Ku , Heui Man Kim , Young Myong Kang , JeongCheol Kim , Ji An Kim , Yoo Kyung Kang , and Sang HeuiSeo . Red Ginseng-containing diet helps to protect mice and ferrets from the lethal infection by highly pathogenic H5N1 influenza virus. *Journal of Ginseng Research* 38, no. 1 (2014): 40–46.

Pilgrim, Corey D. Nuclear magnetic resonance. In W. White (Eds.), *Encyclopedia of Geochemistry*, *Encyclopedia of Earth Sciences Series*, pp. 1–6. Springer, Cham, 2016. [https://doi.org/10.1007/978-3-319-39193-9\\_47-1](https://doi.org/10.1007/978-3-319-39193-9_47-1)

Prasanth, Mani Iyer , Bhagavathi Sundaram Sivamaruthi , Chaiyavat Chaiyasut , and Tewin Tencomnao . A review of the role of green tea (*Camellia sinensis*) in antiphotaging, stress resistance, neuroprotection, and autophagy. *Nutrients* 11, no. 2 (2019): 474.

Quispe-Soto, Edgar Teddy , and Gloria M. Calaf . Effect of curcumin and paclitaxel on breast carcinogenesis. *International Journal of Oncology* 49, no. 6 (2016): 2569–2577.

Radunz, Camila L. , Cristina E. Okuyama , Fátima C. A. Branco-Barreiro , Regina Pereira , and Susana N. Diniz . Clinical randomized trial study of hearing aids effectiveness in association with Ginkgo biloba extract (EGb 761) on tinnitus improvement. *Brazilian Journal of Otorhinolaryngology* 86 (2020): 734–742.

Riaz, Muhammad , Ramsha Khalid , Muhammad Afzal , Fozia Anjum , Hina Fatima , Saadiya Zia , Ghulam Rasool et al. Phytobioactive compounds as therapeutic agents for human diseases: a review. *Food Science & Nutrition* 11, no. 6 (2023): 2500–2529.

Sarli, S. , Nahid Ghasemi , and A. Moradi . Optimal synthesis, characterization, antibacterial and anticancer assay of green synthesized nickel nanoparticles by *Taxus brevifolia* leaf extract. *Bulgarian Chemical Communications* 50 (2018): 209–223.

Sarli, Sona , Mohamad Reza Kalani , and Abdolvahab Moradi . A potent and safer anticancer and antibacterial taxus-based green synthesized silver nanoparticle. *International Journal of Nanomedicine* 15 (2020): 3791–3801.

Schulze, Johannes , Lena Melzer , Lisa Smith , and Rolf Teschke . Green tea and its extracts in cancer prevention and treatment. *Beverages* 3, no. 1 (2017): 17.

Schwarz, Evelyn , AlexandrParlesak, H.-H. Henneicke-von Zepelin , J. C. Bode , and C. Bode . Effect of oral administration of freshly pressed juice of *Echinacea purpurea* on the number of various subpopulations of B-and T-lymphocytes in healthy volunteers: results of a double-blind, placebo-controlled cross-over study. *Phytomedicine* 12, no. 9 (2005): 625–631.

Septembre-Malaterre, Axelle , Mahary Lalarizo Rakoto , Claude Marodon , Yosra Bedoui , Jessica Nakab , Elisabeth Simon , Ludovic Hoarau et al. *Artemisia annua*, a traditional plant brought to light. *International Journal of Molecular Sciences* 21, no. 14 (2020): 4986.

Shikha, Deepti , and Rita Awasthi . Application of IR Spectroscopy & mass spectrometry in structural elucidation of drugs. *International Journal of Advanced Computer Science* 2, no. 8 (2015): 38–45.

Shrinet, Kriti , Ritika K. Singh , Avinash K. Chaurasia , Alok Tripathi , and Arvind Kumar . Bioactive compounds and their future therapeutic applications. In Rajeshwar P. Sinha , and Donat-Peter Häder (Eds.), *Natural Bioactive Compounds*, pp. 337–362. Academic Press, London, 2021.

Singh, Neetu , Poonam Sahjan , and Surender Singh Yadav . Phytochemistry and anticancer therapeutics of *Camellia sinensis* (Green tea). *Pharmacological Research-Modern Chinese Medicine* 12 (2024): 100484.

So, Seung-Ho , Jong Won Lee , Young-Sook Kim , Sun Hee Hyun , and Chang-Kyun Han . Red ginseng monograph. *Journal of Ginseng Research* 42, no. 4 (2018): 549–561.

Tan, Shanjun , Feng Zhou , Ning Li , Qiantong Dong , Xiaodong Zhang , Xingzhao Ye , Jian Guo , Bicheng Chen , and Zhen Yu . Anti-fatigue effect of ginsenoside Rb1 on postoperative fatigue syndrome induced by major small intestinal resection in rat. *Biological and*

Pharmaceutical Bulletin 36, no. 10 (2013): 1634–1639.

Woelkart, Karin , Klaus Linde , and Rudolf Bauer . Echinacea for preventing and treating the common cold. *Planta Medica* 74, no. 06 (2008): 633–637.

Yang, Yong , Changhong Ren , Yuan Zhang , and XiaoDan Wu . Ginseng: a non-negligible natural remedy for healthy aging. *Aging and Disease* 8, no. 6 (2017): 708.

Yılmazoğlu, Emre , İ. Metin Hasdemir , Belma Hasdemir , and Hasniye Yaşa . Investigation of essential oil composition, hypericin content, and antioxidant capacity of different extracts from flowers and leaves of *Hypericum perforatum* L. growing wild in Turkey. *Journal of Essential Oil Bearing Plants* 26, no. 6 (2023): 1350–1370.

Yu, Tao , Yanyan Yang , Yi-Seong Kwak , Gwan Gyu Song , Mi-Yeon Kim , Man Hee Rhee , and Jae Youl Cho . GinsenosideRc from *Panax ginseng* exerts anti-inflammatory activity by targeting TANK-binding kinase 1/interferon regulatory factor-3 and p38/ATF-2. *Journal of Ginseng Research* 41, no. 2 (2017): 127–133.

Zein, Nabila , Safa W. Aziz , Ashraf S. El-Sayed , and Basel Sitohy . Comparative cytotoxic and anticancer effect of Taxol derived from *Aspergillus terreus* and *Taxus brevifolia*. *Bioscience Research* 16, no. 2 (2019): 1500–1509.

Zhao, Yifan , Le Zhu, Lan Yang , Mo Chen , Peng Sun , Yue Ma , Dong Zhang , Ya Zhao , and Haidong Jia . In vitro and in vivo anti-eczema effect of *Artemisia annua* aqueous extract and its component profiling. *Journal of Ethnopharmacology* 318 (2024): 117065.