Traditional Medicines in Drug Discovery and Development

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Edited by
Varughese George
and Thadiyan Parambil Ijinu

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Top right: *Rauvolfia serpentina* (L.) Benth. ex Kurz and serpentine
Bottom left: *Withania somnifera* (L.) Dunal and withanolide A
Bottom right: *Piper nigrum* L. and piperine

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Prof. Dr. Varughese George (Ph.D., FNSE, FABMS, FNABS, FRSC) is a distinguished academician and researcher in natural product chemistry. He served as an Academic Advisor and Member of the Board of Governors at Mar Dioscorus College of Pharmacy, Thiruvananthapuram, India. His career spans roles as Director at the Amity Institute of Phytochemistry and Phytomedicine (2008-2021), Head and Chief Scientist at the KSCSTE-Jawaharlal Nehru Tropical Botanic Garden and Research Institute (1992-2008), and Senior Scientist at the CSIR-Indian Institute of Integrative Medicine (1970-1992). Dr. George's consultancy with Proctor and Gamble contributed to a herbal cough syrup, and he co-invented *Jeevani* (a stamina booster) and *Sisairosp* (an anti-psoriatic drug). He holds an impressive record, with 350+ research papers, 60 book chapters, 9 books, and 35 patents. He has guided many students and held visiting scientist positions at esteemed institutions worldwide and served as the General Secretary of the National Society of Ethnopharmacology, India (1986-2023). His research focus encompasses natural product chemistry, ethnomedicine, and herbal product development.

Dr. Thadiyan Parambil Ijinu (Ph.D., MRSB, MRSC, FNSE, FLS) is an ethnopharmacologist and an entrepreneur leading Naturæ Scientific, a startup at Kerala University Business Innovation and Incubation Centre in Thiruvananthapuram, India. He holds a doctoral degree in biotechnology from the KSCSTE-Jawaharlal Nehru Tropical Botanic Garden and Research Institute (University of Kerala), where he studied the ethnopharmacological properties of plants in the Western Ghats. He is a recipient of the Young Scientist Fellowship instituted by the Department of Science and Technology, Govt. of India for postdoctoral research. Between 2008 and 2014, Dr. Ijinu and colleagues documented 6,008 instances of traditional knowledge about medicinal and food plants throughout Kerala state, India, and created a valuable database useful for developing scientifically validated products and benefit-sharing models to support sustainability and welfare of the society. He actively engaged in projects promoting the well-being of vulnerable populations, including initiatives in rural nutrition and maternal health. His extensive research output includes 26 journal papers, 56 book chapters, 2 authored books, 14 popular articles, and 2 patents filed. He prepared digitised monographs of 10 economically valuable medicinal plants for the National Medicinal Plant Board, Govt. of India. His areas of interest include ethnopharmacology and applied natural-product-based discoveries and innovations.

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FOREWORD

Medicinal plants have been the basis of traditional medicines since antiquity. In the contemporary era, they have played a central role as sources of new medicines and nutraceuticals. With tens of thousands of plants on earth, an enormous wealth of chemical constituents is within reach. Theoretically each phytochemical is capable of locking a particular disease mechanism. Despite popularization of modern synthetic medicines, natural products, and their derivatives still represent over 50% of all the drugs in clinical use.

> "*As an organic chemist, I have been truly captivated from the enormous chemical diversity present in biodiversity".*

I was excited when I received an invitation from distinguished Prof. Dr. Varughese George to write a Foreword for his book entitled, *"Traditional Medicines in Drug Discovery and Development".* His kind invitation was in line with my lifelong commitment to promote bioorganic, natural products, and medicinal chemistry for human welfare. In all those years, I tried to highlight the significance of plant-based medicines as better, sustainable, inclusive, and safe alternatives of chemical drugs. I am delighted that Prof. George and his team are contributing in this field through their original research, and through raising awareness. Prof. George is known to me since the past three decades. I am a silent admirer of his vision and contributions in the field of phytochemistry and phytomedicine. He has a vast experience in medicinal plant research, and has made significant contributions in this field.

Based on traditional knowledge and practices, diverse methods of treatments were successfully adopted in different communities and countries. In context of successful practices of traditional medicine, there is a need of developing applications of modern scientific methods for not only validating the safety and efficacy of pharmacopeial medicines, but also to investigate traditionally used plants for their bioactive constituents. Plants produce a diverse array of secondary metabolites and are great sources of drug candidates. There are numerous unmet medical needs such as infections, cancers, cardiovascular abnormalities, diabetes, gastrointestinal disorders, skin diseases, neurodegenerative, tropical diseases, etc. Medicinal plants and associated ethnomedical knowledge can form the basis of innovative

and novel therapies. However, drug discovery from traditional medicines is not without challenges. Inherent inconsistency in plant chemistry makes it challenging to produce standardized and consistent products. Complex multicomponent traditional remedies are difficult to be standardized by currently available hyphenated methods. Complex chemical constituents often work in synergy and it is often difficult to identify "one single compound" responsible of activity. Similarly yield of bioactive compound from plants is insufficient to conduct preclinical, toxicological, and clinical trials and often needs the help of synthetic chemistry. However, despite all challenges, drug discovery from medicinal plants is truly rewarding. Modern scientific methods enable us to overcome many of these obstacles. I am glad how well these contemporary challenges are highlighted and addressed in this book, which will give readers a broader overview of modern scientific methods, capable of overcoming such obstacles.

Within the foregoing context it needs to be emphasized that while much scientific literature is available, there is a serious dearth of focused literature which addresses the enduring question of *how traditional medicines can be transformed into evidence-based therapies and modern drugs?* The presented book is an excellent effort to fill this void. The contents of the book sufficiently cover the whole spectrum of medicinal plant-related topics in easy-to-understand language, but without losing the scholarly finesse. I am confident that *"Traditional Medicines in Drug Discovery and Development"*, will receive a wide appreciation, both from novice, as well as professional readers.

Prof. Dr. M. Iqbal Choudhary
Mustafa (pbuh) Prize Laureate, H. I., S. I., T. I.
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PREFACE

Traditional medicine is one of the pillars on which modern medicine is built. Pain, disease, and pestilence accompanied humanity right from the beginning. Unlike other life forms, humanity alone is endowed with the capability of rational thinking, and they are naturally empowered with the ability to meet all sources of challenges with their power of reasoning, observation, and inference. Having lived close to nature, our early ancestors attempted to find remedies for their afflictions in their immediate neighbourhood. Through trial and error, they slowly discovered the healing power of plants, plant products, fauna, and minerals. Gradually they developed the healing art, and as the civilisation advanced, they started developing sound explanations for the causative factors of diseases and the principles of the healing art. They developed methods to prevent the occurrence of diseases. They discovered the prophylactic, promotive and curative properties of plants, animal products and minerals through experiments and observations.

Until the introduction of Western medicine in the 19th century, the only available therapeutics were of natural origin. Initially, Western medicine also depended on TM to develop different therapeutic agents. Today more than 25% of prescription drugs in Western medicine are of natural origin, mostly developed from traditional medicines. Additionally, another 20% of prescription drugs in Western medicine are derivatives or synthetic modifications of naturally occurring bioactive molecules. Thus, traditional medicines have contributed substantially to the development of modern drugs.

Drug discovery and development have recently shifted from focusing on single active components and specific targets to a "multi-component" "multitarget" approach. This shift reflects a deeper understanding of traditional medicines like Ayurveda and traditional Chinese medicine (TCM), which have long been recognised as the intricate interactions between multiple components in traditional medicines and their effects on various targets in the body. These traditional medicine systems prioritise holistic healthcare, aiming to restore balance and harmony within the body. They acknowledge that therapeutic effects are not solely attributed to a single component acting on a single target but result from the synergistic interactions of multiple components on multiple targets.

The book "*Traditional Medicines in Drug Discovery and Development*" is a collection of scholarly articles from India and abroad by eminent scientists, academicians, scholars, and researchers. The chapters cover various topics, from the scientific validation of traditional knowledge to exploring leads for modern drug development.

Chapter 1, "Role of Traditional Knowledge and Medicines in Healthcare" by M. D. Nair, sets the foundation for the book by discussing the importance of traditional knowledge systems and their integration into modern healthcare. It explores the cultural and historical context of traditional medicines and highlights their relevance in addressing the modern healthcare needs of diverse populations.

Chapter 2, "Scientific Validation of Traditional Knowledge: Development of Herbal Drugs and Exploration of Leads for Modern Drug Discovery" by Ijinu et al., delves into the scientific validation of traditional knowledge. It explores the methods and approaches used to develop herbal drugs based on traditional medicine principles, focusing on identifying and exploring leads for modern drug discovery.

Chapter 3, "Ayugenomics in Drug Discovery and Development" by Kalpana Joshi and Siddhesh Solanke, explores the emerging field of Ayugenomics, which combines traditional Ayurvedic principles with genomics and modern drug discovery approaches. It highlights the potential of reverse pharmacology in identifying novel drug targets and developing effective therapies.

Chapter 4, "Phylogenomics in Plant-based Drug Discovery" by Mehar Hasan Asif and K. Narayanan Nair, discusses the application of phylogenomics in plant-based drug discovery. It explores how using genomic techniques helps select plant species for drug discovery and development.

Chapter 5, "Medicinal *Goniothalamus* Species as Source of Bioactive Secondary Metabolites" by Nur Vicky Bihud et al., focuses on the medicinal properties of the *Goniothalamus* genus. It highlights the bioactive secondary metabolites present in these species and their potential applications in drug discovery.

Chapter 6, "Traditional Medicines of India and Thailand: A Rich Source of Phytochemicals with Promising Antiviral Properties against Coronaviruses" by Charu Gupta et al., explores the potential of traditional medicines from

India and Thailand in the context of viral diseases, with a particular focus on their antiviral properties against coronaviruses.

Chapter 7, "Species from the Genus *Rosa*-Sources of Natural Medicines for Skin Related Problems" by Gaweł-Bęben and Antosiewicz-Klimczak, delves into the therapeutic potential of species from the *Rosa* genus for skin-related problems. It discusses the bioactive constituents present in these plants and their potential applications in skincare.

Chapter 8, "Therapeutic Potential of Swertisin: A Flavone-C-Glycoside from Natural Plant Sources" by Abhishek Gour et al., focuses on the therapeutic potential of swertisin. It explores the pharmacological properties and potential applications of swertisin in drug development.

Chapter 9, "Phytochemicals as Potential Lead Molecules in Cancer Drug Research and Development" by Rayginia et al., highlights the role of phytochemicals in cancer drug research and development. It explores the diverse range of bioactive compounds present in plants and their potential as lead molecules for anticancer drug discovery.

Chapter 10, "Potential Bioactive Compounds from Indian Medicinal Plants as Antidiabetic Agents" by Km Swati and Pamita Bhandari, focuses on the potential of bioactive compounds derived from Indian medicinal plants. It explores the mechanisms of action of these compounds and their therapeutic potential in managing diabetes.

Chapter 11, "Medicinal Mushroom Bioactives: Potential Sources for Cardioprotective Drug Discovery and Development" by Ajith et al., explores the medicinal properties of molecules derived from medicinal mushrooms. It highlights their potential applications in cardioprotective drug development and discusses their mechanisms of action.

Chapter 12, "Chemistry and Therapeutic Potential of Plant-based Fatty Acids" by Priya Rani and Rameshkumar, delves into the chemistry and therapeutic potential of plant-based fatty acids. It explores their diverse applications in drug discovery and development, ranging from cardiovascular health to inflammation.

Chapter 13, "Exploring the Potential of *Rasayana* Herbs in Ayurvedic Medicine for Developing Phytopharmaceuticals" by Krishnakumar and Ijinu, focuses on *Rasayana* herbs in Ayurvedic medicine and their potential for developing phytopharmaceuticals. It explores the concept of rejuvenation and highlights the medicinal properties of these herbs.

Chapter 14, "Essential Oils and their Constituents in Skin Care and Cosmetics" by Rajani et al., discusses the therapeutic potential of essential oils and their constituents in skincare and cosmetics. It explores their antimicrobial, antioxidant, and anti-inflammatory properties.

Chapter 15, "Chemotaxonomy-guided Effective Herbal Product Development: A Sustainable Model for AYUSH Industries" by Mridul Kant Chaudhary et al., explores the chemotaxonomy-guided approach to herbal product development. It discusses how this approach can facilitate the standardisation and quality control of plant-based drugs in the AYUSH industries.

Chapter 16, "Observations on the Zingiberaceae Members Used in Traditional Medicines" by Mathew Dan and V. P. Thomas, focuses on the taxonomy of the Zingiberaceae family members used in traditional medicines. It provides valuable insights into the classification, identification, ethnomedicinal uses and essential oil components of these plant species.

Chapter 17, "Toxicology in Plant-based Drug Research and Development" by Sakthivel Jafni et al., delves into the importance of toxicology studies in plant-based drug research and development. It explores the various standard approaches and methodologies used to assess the safety and toxicity of natural products.

Chapter 18, "Sustainable Greener Approaches for Extraction and Separation of Bioactive Natural Products" by Zeena Pillai et al., highlights the importance of sustainable and environmentally friendly approaches for extracting and separating bioactive natural products. It explores innovative techniques and methods that minimise environmental impact.

Chapter 19, "Phytosome-mediated Targeted Delivery of Herbal Drugs and Isolated Molecules" by Zeena Pillai et al., explores the phytosome-mediated targeted delivery of herbal drugs and isolated molecules. It discusses the formulation and delivery strategies that enhance the bioavailability and efficacy of plant-based therapeutics.

Finally, **Chapter 20**, "Regulatory Aspects in Quality Control and Standardization of Plant-based Drugs" by Govindarajan Raghavan et al., discusses the regulatory aspects and challenges involved in the quality control and standardisation of plant-based drugs. It highlights the importance of ensuring safety, efficacy, and consistency in herbal medicinal products.