

Edited by Mohammad Fahad Ullah and Aamir Ahmad

# Nutraceuticals and Natural Product Derivatives

**Disease Prevention & Drug Discovery** 



Nutraceuticals and Natural Product Derivatives

# Nutraceuticals and Natural Product Derivatives: Disease Prevention & Drug Discovery

Edited by

Mohammad Fahad Ullah Aamir Ahmad

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# Foreword



This book contains a collection of review articles highlighting the potential and demonstrated health-promoting effects of foods, natural products in foods, and their derivatives. While the research community has established that a diet rich in fruits and vegetables helps maintain health, large gaps in our knowledge still exist regarding the biological effects of

individual food components. We know even less about the effects of their metabolites and derivatives. In the past, the focus has been primarily on the antioxidant effects of components naturally present in plant-derived foods. In recent years, it has become increasingly clear that food components (in common with pharmaceuticals) can interact with molecular targets to regulate cell signaling, such as inflammation, and metabolism. While beneficial to the host to fight off infections, inflammation can be detrimental to human health when it persists chronically. Many basic science and clinical researchers are interested in mitigating chronic inflammation and dysregulated metabolism by dietary means, with the goal to prevent the early stages of a pathological condition from progressing into disease. Other investigators focus their research on developing naturally occurring chemicals as drugs to treat disease. The reader will find excellent examples, in 14 chapters, of either approach in this book.

In Chapter 1, researchers from the Universities of Genoa and Rome, Italy, discuss nutraceuticals and phytochemicals used in folk medicine for management of diabetes and metabolic syndrome. As a specific example, researchers from the University of Southern Queensland, Australia, review in Chapter 3 the broad-spectrum effects of active principles in *Garcinia* fruit for mitigating metabolic syndrome. Diabetes and metabolic syndrome are also the focus of Chapter 8, specifically how phenolic acids, catechins, and methylxanthines from yerba mate can influence dysregulated metabolism in these abnormal physiological conditions.

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Whey protein-derived sulfur-containing amino acids and a cellular antioxidant, glutathione, are the topic of Chapter 2, in which researchers from the University of Allahabad, India, make a case that intake of sulfur-containing proteins might offer protection against metabolic and neurodegenerative diseases. In Chapter 9, pharmaceutical scientists from the University of Hacettepe, Ankara, Turkey, review the redox properties of secondary metabolites from *Verbascum, Scrophularia*, and *Buddleja* species and how they may retard or halt the initiation and progression of neurodegenerative diseases. Alzheimer's disease, with its various pathologies and potential targets for treatment with plant secondary metabolites, is discussed in the following Chapter 10, contributed by researchers from Presidency University, India.

Angiogenesis, or the formation of new blood vessels, has long been recognized as a target for therapies aimed against tumorigenesis and metastasis. In Chapter 4, Beijing hospital researchers summarize the effects of naturally occurring polyphenols, alkaloids, and terpenoids in cell culture and animal models of angiogenesis.

In Chapter 5, investigators from the University of Tabuk, Saudi Arabia, argue that nature's enormous chemical diversity offers endless opportunities for discovery and development of natural products that can prevent, ameliorate, or treat cancer, diabetes, and neurodegenerative diseases. Honeybees take nature's chemical diversity home to their beehives in the form of honey, propolis, pollen, and wax. In Chapter 6, an international group of researchers describes the pharmacological effects of honey and propolis on the regulation of protein networks in cancer cells. In Chapter 7, researchers from the University of Valencia review the antiproliferative and apoptotic effects of phytosterols, an understudied group of natural products, in cultured breast, prostate, and colon cancer cells. The cancer-related properties of green tea polyphenols, specifically those of the catechin type, are discussed in Chapter 12. The authors of this chapter propose that the cancer-related properties of these flavanols can be attributed to a copper-dependent pro-oxidant effect, resulting in death of the cancer cell. In Chapter 14, researchers from SKIMS (Sher-i-Kashmir Institute of Medical Sciences), Srinagar, India, outline the studies that relate the benefits of fruits and vegetables in hepatopathological conditions.

In Chapter 11, Shazia Usmani from Integral University, India, discusses the use and formulation of metals in Ayurvedic medicine from a therapeutic and toxicological perspective. Extending the significance of natural products to the realm of infectious diseases, in Chapter 13, Fyaz Ismail from Liverpool John Moores University, UK, describes several natural and semisynthetic drug candidates for malarial infections, focusing on different geographical regions worldwide.

The collection of chapters spans a wide range of highly complementary topics with minimal overlap. This book will be a useful resource for researchers

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interested in herbal medicine and pharmacognosy at all career stages. I congratulate the editors, Drs. Ullah and Ahmad, for recruiting a group of diverse contributors, all experts in their chosen subjects, from all over the world.

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# Preface

The burden of chronic diseases in the human population has increased exponentially ever since the beginning of recorded history. Despite advancements in modern diagnostic and therapeutic paradigms, the projected global rates of incidence of these diseases, including cancer, diabetes, and neurodegenerative disorders, and the associated mortality for future decades display many challenges and poor outcomes. Rejuvenated interest in the natural product pharmacology in the last two decades has been partially based on the fact that some of the most effective drugs in clinical practice are derivatives of natural products. It is known that over the centuries, human civilizations have acquired sophisticated knowledge of disease cures from sources derived from their environment, and this perhaps represents natural product-based traditional and complementary medicine worldwide. The advent of synthetic chemistry and combinatorial approaches has indeed revolutionized the drug development premises. However, this has also impeded interest in the natural products that have in the past served as an enormous repository of bioactive compounds. The huge diversity in chemical structures of natural products provides inexhaustible potential as leads in drug discovery. This book, Nutraceuticals and Natural Product Derivatives: Disease Prevention and Drug Discovery, is an attempt to archive a few such ideas in the scientific and public domains. We commend John Wiley & Sons for providing the platform for this endeavor and entrusting us with the task of managing, compiling, and editing the current volume that we present before the audience.

Precisely, the volume contains an expert commentary that is followed by 14 chapters, each focusing on the significance of natural products in disease prevention. The expert commentary provides an excellent presentation of the concept that is important to understanding the relevance of natural products. Chapter 1, "Natural Food Sources for the Control of Glycemia and the Prevention of Diabetic Complications," deals with the vast literature that has appeared in the last decade on specific food nutrients with purported beneficial effects to prevent type 2 diabetes and its microvascular and macrovascular complications. Chapter 2, "Anti-Aging Effect of Sulfur-Containing Amino

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Acids and Nutraceuticals," focuses on proteins rich in L-cysteine as redox modulators during age-associated diseases and the possibility of future strategies employing sulfur-containing amino acids in intervention to treat multiple metabolic and neuronal diseases. Chapter 3, "Garcinia Fruits: Their Potential to Combat Metabolic Syndrome," discusses the potential of the bioactive compounds found in Garcinia species as therapeutic candidates for metabolic syndrome. Chapter 4, "Pro-Angiogenic and Anti-Angiogenic Effects of Small Molecules from Natural Products," describes recent research findings on proand anti-angiogenic effects of small molecules from nutraceuticals and natural products by modulating key factors in cell proliferation, migration, invasion, and assembly. Chapter 5, "Nutraceuticals and Natural Product Derivatives in the Premises of Disease Prevention," presents an overview of the therapeutic significance of natural products in chronic diseases, including cancer, diabetes, gout, and neurodegenerative disorders. Chapter 6, "Honey and Propolis-Mediated Regulation of Protein Networks in Cancer Cells," summarizes most recent evidence related to anticancer activities of honey and propolis and how these amazingly effective products modulate different proteins in cancer cells to inhibit or prevent cancer. Chapter 7, "Antiproliferative Effects and Mechanism of Action of Phytosterols Derived from Bioactive Plant Extracts," reviews the activity of plant extracts containing phytosterols, or isolated phytosterols obtained from plant extracts, upon breast, prostate, and colon cancer. Chapter 8, "Yerba Mate (Ilex paraguariensis A. St. Hil.): A Promising Adjuvant in the Treatment of Diabetes, Obesity, and Metabolic Syndrome," reports on the beneficial actions of yerba mate, known to be rich in phenolic acids and used in different kinds of beverages, as an adjuvant in the treatment of diabetes, obesity, and metabolic syndrome. Chapter 9, "Role of Natural Antioxidants from Selected Plants Belonging to the Scrophulariaceae and Buddlejaceae Families in the Prevention and Treatment of Neurodegenerative Diseases," describes Verbascum, Scrophularia, and Buddleja species used in traditional medicines and relates their significance in oxidative stress and neurodegenerative disorders. Chapter 10, "Recent Trends in Drug Discovery against Alzheimer's Disease: Use of Natural Products and Nutraceuticals from Botanicals," discusses the underlying mechanism of disease onset along with therapeutic effects of different phytochemicals and traditional herbal formulations in both crude and synergistic forms. Chapter 11, "Therapeutic Potential of Metallo-Herbal Nanoceuticals: Current Status and Future Perspectives," describes the metallo-herbal formulations of ancient Indian Ayurvedic medicine and their implications in alternative therapies. Chapter 12, "Green Tea Polyphenols: A Putative Mechanism for Cytotoxic Action against Cancer Cells," discusses a copper-dependent pro-oxidant mechanism of action of green tea polyphenols that accounts for their observed chemopreventive properties. Chapter 13, "Nature's Armamentarium against Malaria: Antimalarials

and Their Semisynthetic Derivatives," focuses on the putative sources of new drugs or prototypes from plant sources with antiplasmodial activity. Chapter 14, "Nutraceutical-Based Pharmacological Intervention in the Management of Liver Diseases," describes dietary natural products as key elements for prevention and treatment of liver diseases.

We express our gratitude to all the authors for valuable contributions from around the globe. It is indeed their willingness to share their onerous experiences that has facilitated this piece of scientific literature. We appreciate the support of Ms. Mindy Okura-Marszycki (Senior Acquisitions Editor) for working out the procedural framework of our book proposal. Fortunately, we had Ms. Kshitija Iyer and Mr. Antony Sami (Project Editors), Priya Subbrayal (Production editor), who were instrumental in ensuring the required basics of attractive and meaningful academic production. We are indeed honored to have Professor Fred Stevens introducing the substance of the book in the foreword.

Lastly, we wish that the audience will like the content of this book and that this book will, as desired, serve as a promising literature for inspiring researchers who intend to explore the vast armamentarium of natural products for disease prevention and drug discovery.

> Mohammad Fahad Ullah, Saudi Arabia Aamir Ahmad, USA