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Edited by Mohammad Fahad Ullah
and Aamir Ahmad

Nutraceuticals and Natural Product Derivatives

Disease Prevention & Drug Discovery



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Nutraceuticals and Natural Product Derivatives: Disease Prevention & Drug Discovery

Edited by

*Mohammad Fahad Ullah
Aamir Ahmad*

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Editor Biographies

Mohammad Fahad Ullah, PhD, is an Assistant Professor of Biochemistry in the Department of Medical Laboratory Technology (FAMS) and a research scientist at Prince Fahd Research Chair, University of Tabuk, Tabuk, Saudi Arabia. He received his academic degrees along with a gold medal in MSc (biochemistry) from Aligarh Muslim University, Aligarh, India. Furthermore, he worked as a research associate at the Experimental Oncology Laboratory, Department of Biomedical & Diagnostic Sciences, University of Tennessee, Knoxville, TN, USA. His research interests include assessing novel plant- or diet-derived bioactive compounds for their mechanism of action and translational potential against chronic diseases, including cancer and diabetes. He is an active member of the American Association for Cancer Research (AACR, USA) and the Royal Society of Chemistry (UK), and a member of the editorial/reviewer board of a number of scientific journals. Dr. Ullah has more than eight years of experience in teaching biochemistry to the students of health sciences. His academic works include close to 50 publications in reputed journals and two books entitled *Critical Dietary Factors in Cancer Chemoprevention* (Springer, Switzerland) and *Illustrated Notes on Biomolecules* (Partridge, Singapore).

Aamir Ahmad, PhD, is an Assistant Professor of Oncologic Sciences at University of South Alabama's Mitchell Cancer Institute, Mobile, AL, USA. He received his academic degrees from Aligarh Muslim University, Aligarh, India, and received university gold medals for the highest marks in his department as well as all the faculties combined. He completed postdoctoral training at the National Cancer Institute, National Institutes of Health, Bethesda, MD, USA. His research interests include understanding the mechanisms of cancer drug resistance and metastasis in different cancers, with emphasis on the roles of microRNAs, noncoding RNAs, epigenetics, exosomes, and cancer stem cells. He has authored more than 140 scientific research or review articles, authored more than 20 book chapters, and edited or coedited 6 books. He is the Founding Editor-in-Chief of the journal *Non-coding RNA Research* and serves as a Section Editor for the journal *PLoS ONE*. He is also the Editor-in-Chief of the Elsevier Cancer Metastasis series.

List of Contributors

Faisal M. Abu-Duhier

Laboratory of Phytomedicine
and Therapeutics
Prince Fahd Research Chair
Department of Medical Laboratory
Technology
Faculty of Applied Medical Sciences
University of Tabuk
Tabuk, Saudi Arabia

Zeliha S. Akdemir

Department of Pharmacognosy
Faculty of Pharmacy
Hacettepe University
Ankara, Turkey

Amparo Alegría

Nutrition and Food Science Area
Faculty of Pharmacy
University of Valencia
Burjassot, Valencia, Spain

Aliye Aras

Department of Botany
Faculty of Science
Istanbul University
Istanbul, Turkey

Muhammad Arif

Faculty of Pharmacy
Integral University
Lucknow, Uttar Pradesh, India

Reyes Barberá

Nutrition and Food Science Area
Faculty of Pharmacy
University of Valencia
Burjassot, Valencia, Spain

Showket Hussain Bhat

Laboratory of Phytomedicine
and Therapeutics
Prince Fahd Research Chair
Department of Medical Laboratory
Technology
Faculty of Applied Medical Sciences
University of Tabuk
Tabuk, Saudi Arabia

Adelar Bracht

Post Graduate Program of Food
Science
Universidade Estadual de Maringá
Maringá, Paraná, Brazil

Lindsay Brown

School of Health and Wellbeing *and*
Functional Foods Research Group
Institute for Agriculture and the
Environment
University of Southern Queensland
Toowoomba, Queensland, Australia

Antonio Cilla

Nutrition and Food Science Area
Faculty of Pharmacy
University of Valencia
Burjassot, Valencia, Spain

Rúbia Carvalho Gomes Corrêa

Post Graduate Program of Food
Science
Universidade Estadual de Maringá
Maringá, Paraná, Brazil

Vanesa Gesser Correa

Post Graduate Program of Food
Science
Universidade Estadual de Maringá
Maringá, Paraná, Brazil

Abhijit Dey

Department of Life Sciences
Presidency University
Kolkata, India

Ammad Ahmad Farooqi

Institute of Biomedical and Genetic
Engineering
Islamabad, Pakistan

Mohd Farhan

Department of Biochemistry
Faculty of Life Sciences
Aligarh Muslim University
Aligarh, Uttar Pradesh, India

Geetika Garg

Department of Biochemistry
University of Allahabad
Allahabad, Uttar Pradesh, India

S.M. Hadi

Department of Biochemistry
Faculty of Life Sciences
Aligarh Muslim University
Aligarh, Uttar Pradesh, India

Syed Misbah Hasan

Faculty of Pharmacy
Integral University
Lucknow, Uttar Pradesh, India

Carla Iacobini

Dipartimento di Medicina Clinica
Molecolare
Università "La Sapienza"
Roma, Italy

Fyaz M.D. Ismail

Pharmacy and Biomolecular Sciences
Faculty of Science
Liverpool John Moores University
Liverpool, UK

Oliver John

School of Health and Wellbeing and
Functional Foods Research Group
Institute for Agriculture and the
Environment
University of Southern Queensland
Toowoomba, Queensland, Australia

Cigdem Kahraman

Department of Pharmacognosy
Faculty of Pharmacy
Hacettepe University
Ankara, Turkey

Eloá Angélica Koehnlein

Department of Nutrition
Federal University of Southern
Border
Campus Realeza-PR
Realeza, Paraná, Brazil

Gabriel López-García

Nutrition and Food Science Area
Faculty of Pharmacy
University of Valencia
Burjassot, Valencia, Spain

Jingyi Ma

Department of Clinical
Pharmacology
Aerospace Center Hospital
Beijing, China

Sudatta Maity

Department of Life Sciences
Presidency University
Kolkata, India

Stefano Menini

Dipartimento di Medicina Clinica
Molecolare
Università “La Sapienza”
Roma, Italy

Syed Mudassar

Department of Clinical Biochemistry
Sher-I-Kashmir Institute of Medical
Sciences (SKIMS)
Srinagar, Jammu and Kashmir, India

Samapika Nandy

Department of Life Sciences
Presidency University
Kolkata, India

Sunil K. Panchal

Functional Foods Research Group
Institute for Agriculture and
the Environment
University of Southern Queensland
Toowoomba, Queensland, Australia

Rosane Marina Peralta

Post Graduate Program of Food
Science
Universidade Estadual de Maringá
Maringá, Paraná, Brazil

Carlo Pesce

Dipartimento di Neuroscienze,
riabilitazione, oftalmologia,
genetica e scienze materno-infantili
(DINOEMI)
Università di Genova
Genova, Italy

Muhammad Zahid Qureshi

Department of Chemistry
Government College University
Lahore, Pakistan

Syed Ibrahim Rizvi

Department of Biochemistry
University of Allahabad
Allahabad, Uttar Pradesh, India

Mirna Azalea Romero

Laboratorio de Investigación Clínica
Unidad Académica de Medicina
Universidad Autónoma de Guerrero
Acapulco, Guerrero, México

Aaliya Shah

Department of Clinical Biochemistry
Sher-I-Kashmir Institute of Medical
Sciences (SKIMS)
Srinagar, Jammu and Kashmir, India

Uzma Shamim

Department of Biochemistry
Faculty of Life Sciences
Aligarh Muslim University
Aligarh, Uttar Pradesh, India

Abhishek Kumar Singh

Department of Biochemistry
University of Allahabad
Allahabad, Uttar Pradesh, India

Sandeep Singh

Department of Biochemistry
University of Allahabad
Allahabad, Uttar Pradesh, India

I. Irem Tatli

Department of Pharmaceutical
Botany
Faculty of Pharmacy
Hacettepe University
Ankara, Turkey

Mohammad Fahad Ullah

Laboratory of Phytomedicine and
Therapeutics
Prince Fahd Research Chair
Department of Medical Laboratory
Technology
Faculty of Applied Medical Sciences
University of Tabuk
Tabuk, Saudi Arabia

Shazia Usmani

Faculty of Pharmacy
Integral University
Lucknow, Uttar Pradesh, India

Tatiane Francielli Vieira

Post Graduate Program of Food
Science
Universidade Estadual de Maringá
Maringá, Paraná, Brazil

Lara Hanna Wakim

Faculty of Agricultural and Food
Sciences
Holy Spirit University of Kaslik
Jounieh, Mount Lebanon, Lebanon

Xuelin Zhou

Department of Pharmacy
302 Military Hospital of China
Beijing, China

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.

When 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 phytoosterols, 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

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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Dr. Jan Frederik Stevens, Professor
Linus Pauling Institute & College of Pharmacy,
Oregon State University, Corvallis, Oregon, USA

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

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 pro- and 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

