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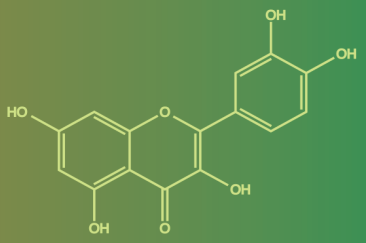

ANTIOXIDANT NUTRACEUTICALS

PREVENTIVE AND HEALTHCARE APPLICATIONS

Edited by
Chuanhai Cao • Sarvadaman Pathak
Kiran Patil

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Antioxidant Nutraceuticals

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We dedicate this book to all the ancient and modern scientific wisdom, the physicians, and scientists who pioneered all aspects of medicine, the pharmacists who prescribe and the patients who benefit. Advancement in science is not possible without students with inquisitive minds, who strive to become the best providers.

We express our gratitude to Adryan Perez and Richard Nguyen for their hard work to make this book a success. We sincerely thank all our contributing authors as without them there is no book, and our families, as without their support we would not be editors.

Sincerely
Sarvadaman Pathak,
Kiran Patil, and Chuanhai Cao

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Foreword

Promotion of longevity, vitality, strength, mental health and wellness in general, are all rooted in food.

Charaka Samhita 1.25.350

Charaka (2000 BCE), the father of Ayurveda, the science of life, has propounded the wisdom that food sustains life, augments health and wellness, and prevention of disease. Hippocrates (460 BCE), the father of modern medicine, had echoed the same insight into food in his oft-quoted teaching, *Let food be thy medicine and medicine be thy food*. This wisdom of yore has developed the concept of a new class of food supplements termed *nutraceuticals*, which bridged together foods and drugs.

To start with the understanding of nutraceuticals, they are categories of food, which not only provide necessary nutrition but also act to prevent diseases and promote strength and vitality. Nutraceuticals over the course of the past two decades have grown exponentially and have currently reached the US$200 billion mark. It is further expected to reach the approximately US$300 billion mark in the next 10 years. With this stupendous growth, the precise definition of nutraceuticals has become fuzzy and now includes multiple categories of food comprising a wide variety of classifications that includes food additives that provide medical or health benefits; products isolated or purified from food; medicines that are not associated with food; isolates that provide concentrated nutrients in the form of pills, tablets or other forms; commodities derived from foods in the form of medicines with demonstrated physiological benefits; and a range of products that have properties of health promotion, including the concept of enhanced performance. With commercial growth of this range of food supplements, regulatory processes have

also developed with a good deal of variations across countries and even within a country as applied to particular types of nutritional supplements. This has led to efforts to redefine nutraceuticals and classify them on pharmaceutical, physiological, and therapeutic grounds. Some of the classes are already well-recognized, such as antioxidants, probiotics, phytopharmaceuticals, energy foods, and so on. Defining these classes with scientific precision and using this research as guidelines for regulatory purposes will serve to address the present chaotic stage of the vast ocean of nutraceuticals that are emerging.

This book, *Antioxidant Nutraceuticals: Preventive and Healthcare Applications,* usefully bridges present gaps in the literature on this subject. The content by experienced authors portrays a wide view of the topic in a total of 19 chapters. The authors discuss diverse topics ranging from historical perspectives and traditional systems to antioxidant nutraceuticals in the prevention and treatment of acute diseases. The chapter on current status of market and future trends illustrates the background of the topic. This book addresses many clinical specialties like cancer, dementia, diabetes, preeclampsia, heart diseases, depression, inflammatory diseases, skin care, ocular diseases, and lung diseases. A chapter on pharmacology and pharmacokinetics provides an in-depth analysis of possible mechanisms of natural antioxidants. The topic also covers pharmaceutics approach through probiotic applications as health drinks for disease prevention.

An important chapter of this book, "Antioxidant Nutraceuticals: Historical Perspective and Applications in Various Traditional Systems Worldwide," is particularly noteworthy. Ayurveda, in particular, is known across the world for its fundamental contributions on concepts of health and personalized therapeutic approaches. The theory of Ayurveda and Yoga suggests that nutrition is not only for nourishment of the body but also to nourish mind and spirit. Charaka Samhita, Sushruta Samhita, and many other classics are resources for discovery of new nutraceuticals and health supplements. Ayurveda has described properties of fruits, spices, herbs, animal products, minerals, and medicated recipes for specific diseases. An effort to integrate such research with modern medical practices is the need of the hour.

The methodology for research investigating nutraceuticals has posed a challenge on the background of nutritional genomics that decodes variations of nutritional effects. We know that reactive oxygen species (ROS) play a major role in the pathogenesis of several diseases. There is lack of clarity in the role of ROS in origin and progression of many diseases. Another challenge is antioxidant paradox that several clinical trials have reported. Antioxidant supplements have demonstrated little or no preventative, or therapeutic effect in large doses. There is a need to revisit traditional knowledge and practices and support them with current

advances of biology and medicine. Ongoing and prospective research worldwide on this important subject can only enhance the future editions of this book.

Dr. Patil, Dr. Pathak, and Dr. Cao have to be commended in coordinating this effort to produce this publication, which addresses a felt need of defining application of antioxidants in wide-ranging clinical conditions.

This book makes useful reading not only for stimulating research on this important subject for scientists but also provides useful guidance for practitioners of medicine and medical students.

Dr. Gururaj Mutalik
Former Director of the World Health Organization
at the United Nations

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Series Preface

In biology, both in plant and animals, abiotic components or abiotic factors are nonliving chemical and physical parts of the environment that affect living organisms and the functioning of ecosystems. Abiotic factors and the phenomena associated with them underpin all biological systems. *Abiotic stress* is defined as the negative impact of nonliving factors on the living organisms in a specific environment. Various abiotic stress processes lead to the overproduction of reactive oxygen species abbreviated as ROS. These are highly reactive species causing damage to proteins, lipids, carbohydrates, and other biological systems leading to low—severe toxicity. These also damage the tissues and cells resulting in a large number of diseases and disorders.

Many natural cellular processes in our bodies lead to formation of free radicals that are also part of the ROS. If these highly reactive substances aren't neutralized, they can cause damage in our bodies, which can lead to inflammation. A consistently high state of inflammation is considered to be a precursor to many common conditions in older adults, such as cardiovascular diseases, neurodegenerative diseases, and various types of cancer.

Our bodies do have a mechanism to create antioxidants to balance this damage due to free radicals or ROS. Antioxidants bind to free radicals and suppress their damage. However, since we are exposed to additional free radicals from pollution, cigarette smoke, pesticides, radiation, and some processed foods, we need to also take, in addition, antioxidants to neutralize the free radicals.

In recent years, increasing attention has been given to understand the abiotic stress processes and how the nature is dealing with such processes. This led to looking at various natural components, which

have exhibited protective effects that have been ascribed often as antioxidant effects. Traditionally, reactive oxygen intermediates (ROIs) were considered to be toxic by-products of aerobic metabolism, which were disposed of using antioxidants. However, in recent years, it has become apparent that plants actively produce ROIs as signaling molecules to control processes such as programmed cell death, abiotic stress responses, pathogen defense, and systemic signaling.

Recent technological advances in understanding these processes including microarray studies and the development of mutants with altered ROI-scavenging mechanisms provide new insights into how the steady-state level of ROIs is controlled in cells. These raise several intriguing questions about the relationships between ROI signaling, ROI stress, and the production and scavenging of ROIs in the different cellular compartments; several researchers are dedicating their time and efforts in this area and many of them are focusing significantly on natural antioxidants.

New insights from genetic analyses of ROS detoxifying and signaling mutants are shedding light on the complexity and roles that ROS plays in plants. Considering recent ROS-induced genome-wide expression analyses, the possible functions and mechanisms for ROS sensing and signaling in plants are comparable to those in animals.

A variety of antioxidant compounds derived from natural products (Nutraceuticals) have demonstrated neuroprotective activity in either *in vitro* or *in vivo* models of neuronal cell death or neurodegeneration, respectively.

The World Health Organization reported that cardiovascular disease (CVD) is the leading cause of death globally, resulting in 17.5 million deaths in 2012. Antioxidants may benefit many health factors that lead to CVD, including blood pressure, cholesterol, and circulation.

Arthritis and diabetes, two significant concerns for the aging population, involve inflammatory processes that generate extra free radicals. The antioxidant nutraceuticals have been shown to improve joint health by reducing inflammation caused by free radicals and may also help to reduce blood sugar among diabetics.

The antioxidant nutraceuticals market is growing significantly. The 2014 data reported 14.8 million for vitamin A, 331 million for vitamin C, green tea supplements over 60 million, and so on, and it is growing day-by-day.

The scope of the CRC series on *Nutraceuticals: Basic Research/Clinical Applications* aims at bringing out a range of books edited by distinguished scientists and researchers who have significant experience in

scientific pursuit and critical analysis. This series will address various aspects of the nutraceutical products, including the historical perspective, traditional knowledge base, analytical evaluations, green food to processing, and applications. This series will be very useful to not only the researchers and academicians but also as valuable reference books for personnel in the nutraceuticals and food industries.

The purpose of the inclusion of this particular book titled *Antioxidant Nutraceuticals: Preventive and Healthcare Applications* in the series is to cover the recent trends in this area, which is significantly enhanced with the advent of understanding about the ROS and related preventive processes as mentioned earlier. This series has successfully included several titles in the area of nutraceuticals and functional foods, including *Handbook of Metallonutraceuticals*, *Marine Nutraceuticals, Nutraceuticals and Human Health: Review of Human Evidence, Herbal Bioactives for Food Fortification*, *Handbook of Nutraceuticals Volume I: Ingredients, Formulations, and Applications, Handbook of Nutraceuticals Volume II, Scale-Up, Processing, and Automation*, and *Nanotechnology and Nutraceuticals: Production to Consumption*.

The forthcoming titles in the series include *Seaweed Bioactives*: *Health Benefits and Potential Applications, Nutrigenomics and Nutraceuticals: Recent Developments and Market Trends,* and *Food By-Product Based Functional Food Powders*.

Antioxidant Nutraceuticals: Preventive and Healthcare Applications is edited by three scientists: Dr. Chuanhai Cao, PhD, Dr. Sarvadaman Pathak, MD, and Dr. Kiran Patil, MD. Some of the top-ranking scientists in this field have contributed to this book and I am sure this book will be very useful to the academicians and industry people equally.

This series has proven to be a very good resource to the academicians, industrial scientists, and students in the area of nutraceuticals basic research and clinical applications. We request scientists and academicians working in this field to contribute to this series.

Yashwant Pathak
College of Pharmacy, University of South Florida Health

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Preface

The term antioxidant refers to a substance that inhibits oxidation, especially to counteract the deterioration of stored food products. The term nutraceutical refers to a food-based substance with potential health benefits. Nutraceuticals cover a broad spectrum of substances, including antioxidants. Antioxidant nutraceuticals have been used widely in ancient medical systems for preventive and curative ailments. In today's modern medical system, nutraceuticals are considered beneficial but have unsubstantiated claims with regard to specific ailments, thus further research needs to be conducted in this area. It is also important to determine if nutraceuticals are necessary in western populations with adequate nourishment from food.

This book further explores the antioxidant properties and benefits of nutraceuticals and expert authors and scientists have contributed chapters based on their research. This book covers historical aspect and development, current and future market trends, prostate cancer, general cancer prevention, Alzheimer's disease and dementia, Parkinson's disease, general well-being, obstetric applications, and ophthalmic applications, among others. It also covers research, both epidemiological and scientific, based on each organ system, as well as novel delivery approaches for enhanced absorption for antioxidant nutraceuticals.

This book will be a good resource for students, clinicians, researchers, public health officials, and the general public, who are all interested in the area of nutraceuticals and their application in human health and disease.

Sarvadaman Pathak

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Editors

Chuanhai Cao is an experienced and independent neuroimmunologist, vaccinologist, and a dedicated nutraceutical researcher with a tenure-track assistant professor position in the Department of Pharmaceutical Sciences at the College of Pharmacy, University of South Florida (USF), Tampa, Florida. Dr. Cao has been working with the clinical core of the Florida Alzheimer's Research Center (FADRC, NIH funded center) for more than 8 years and has combined his contemporary immunology and vaccine skills with molecular biology to search for novel biomarkers and therapies for neurodegenerative diseases. He believes that most diseases occur due to changes in the immune system, and that targeting the immune system is a promising solution to diseases.

Sarvadaman Pathak went to the University of Houston for undergraduate studies with a concentration in biochemistry and premedicine. Following that, he pursued a doctor of medicine degree from Avalon University School of Medicine, Youngstown, Ohio, summa cum laude. He was educated partially in Belize and Mexico with all clinical experience in Chicago, Illinois. After graduating from medical school with honors, he focused on research and worked at the University of South Florida, Tampa, Florida. In 2013, he completed a 1-year clinical fellowship in traditional Chinese medicine, including Chinese herbalism, with a focus on eastern–western integrative medicine at the Dalian Medical University in Dalian, Liaoning province in Mainland China. In 2017, he completed a master's level program and graduated from the Harvard Medical School, Boston, Massachusetts, with a focus on clinical trials and drug development. Currently, he works as a clinical research

director in a hospital and outpatient setting. Sarvadaman has traveled to over 35 countries and has had a fascination with traditional medicines of the world since his childhood.

Kiran Patil was trained in both the United States and India and has a lot of interest in the Ayurvedic system of medicine, which has been practiced for more than 3000 years in India. He is currently working as a neurologist in Pittsburg, Pennsylvania, with more than 15 years of experience in research and medical practice.

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