

The Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease

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Volume 595

THE MOLECULAR TARGETS AND THERAPEUTIC USES OF CURCUMIN IN HEALTH AND DISEASE

Edited by Bharat B. Aggarwal, Young-Joon Surh and Shishir Shishodia

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Young-Joon Surh
Shishir Shishodia
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The Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease

With 77 Illustrations

 Springer

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Dedicated to our gurus and parents whose guidance continues to inspire us!

*Sarve bhavantu sukhinah sarve santu niramayah
Sarve bhadrani pasyantu ma kascid duhkhabhag bhavet*

“May all be happy; may all be healthy;
may all enjoy prosperity; may none suffer.”

PREFACE

The subject of this monograph, curcumin, which gives the yellow color to turmeric, best known as *Haridra* in Sanskrit (means dear to Hari or Lord Krishna). Turmeric is known by several synonyms related to its appearance or use, including *Pita* (yellow, leading to the name *Peethamber dhari* for Lord Krishna based on wearing only yellow clothes), *Gauri* (brilliant), *Kanchani* (looks like gold), *Nisha* (beautiful as a full moon night), *Krimighni* (antibacterial and antihelmenthic), *Mahaghni* (antidiabetic), and *Yoshit priya* (gynecological disorders). In Hindi, turmeric is known as *Haldi*, in Japanese as *Ukon* or *Gajyutsu*, and in Korean as *Ulgeum* or *Gangwhang*.

Turmeric is mentioned in the writings of the Italian explorer Marco Polo, who was introduced to it during his voyage to China and India around 1290 AD. Although he gets credit for bringing Far East spices to Europe, turmeric was actually introduced in Europe in the 13th century AD by Arab traders. The Portuguese explorer Vasco de Gama visited the Indian subcontinent during the 15th century and brought turmeric and other spices of the Orient to the West. It was only during the rule of the British in India that turmeric was combined with various other spices and renamed “curry powder,” as it is called in the West.

Turmeric became of special importance to man with the discovery that when added to various food preparations, its dried and powdered rhizome preserved their freshness and nutritive value and improved the palatability and presentation of food. The brilliant yellow color of turmeric, which persists even at very high dilutions, found its way to commercial use as a coloring agent for various items, including cotton, silk, paper, wood, foodstuffs, and cosmetics. In Ayurveda (science of long life), turmeric has been used internally as a stomachic, tonic, and blood purifier and topically in the prevention and treatment of skin diseases. Turmeric concoctions have been traditionally used for the treatment of flatulence, dyspepsia, liver disorder, jaundice, urinary tract diseases, cold, chronic otorrhea, parasitic skin infection, bruises, sprain, wound, infected wound, and inflammation.

We are currently living in an era when 80% of the world’s population cannot afford modern medicine. Even for those 20% who can, much of modern medicine is ineffective and has numerous side effects. It is a good time to revive the medicinal use of the ancient medicine curcumin. In this volume we bring together the contribution of modern science to one of the most ancient spices known to mankind. Curcumin’s beneficial role in health and disease and its molecular targets are the focus of this monograph. This volume is directed at clinicians and scientists working in the areas of experimental and molecular therapeutics, molecular medicine, translational cancer research, Ayurveda, herbal medicine, naturopathy, and biomedical sciences in general and, most importantly, to the end users of curcumin. We hope that this book will “add spice to everybody’s life.”

We would like to thank all of the contributors for their valuable contributions to this work. We would also like to thank those who have contributed significantly to curcumin research but could not, because of limitations on space, be invited to contribute.

Bharat B. Aggarwal, Ph.D.

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Shishir Shishodia, Ph.D.

FOREWORD

It is indeed a matter of pride and privilege to write the Foreword; to this scholarly contribution on curcumin—the major constituent of turmeric. The volume has been successful in seamlessly connecting the traditional knowledge available on turmeric to the findings of systematic modern research on turmeric and, based on this effort, building the possibilities of developing novel drugs to treat diverse diseases. Turmeric (*Curcuma longa*)—a widely cultivated tropical plant—has been used since ancient times as a spice, as a beauty care agent, and as a traditional medicine.

The rhizome of turmeric is highly aromatic and antiseptic. The medicinal properties of turmeric have been expounded in Ayurvedic and traditional Chinese medicine (TCM) texts. Turmeric is traditionally known as a stomachic, blood purifier and is useful for the common cold, leprosy, intermittent fevers, afflictions of the liver, indolent ulcer, pyogenic (forming pus) afflictions, wound-healing, and inflammation.

In recent years, the medicinal properties of turmeric have increasingly been recognized. It is being researched systematically even in the Western world. I remember fighting the “turmeric battle” on the wrong patent on the wound-healing properties of turmeric that was given by the US Patent Office almost a decade ago.

As per the US National Library of Medicine, 256 research papers were published last year on curcumin. The researchers have found in curcumin a near-perfect starting material for drug discovery. Thus, a variety of curcumin analogues have been prepared and evaluated biologically. Curcumin exhibits a wide range of activities [e.g., antibacterial, anti-inflammatory, hypolipidemic, hepatoprotective, lipoxigenase (LOX), cyclooxygenase (COX), protease inhibitory effects, in addition to being effective as an active oxygen scavenger and lipid peroxidase (a class of oxidoreductase enzymes) inhibitor]. Curcumin and the curcuminoids also lower cholesterol, reduce platelet aggregation, inhibit the proliferation of cancer cells, and improve digestion by increasing the flow of bile from the gallbladder. The desirable preventive or putative therapeutic properties of curcumin have been considered to be associated with its antioxidant and anti-inflammatory properties.

Curcumin has been found to modulate the activity of several key transcription factors and, in turn, the cellular expression profiles. The effect of curcumin has been examined on most of the targets discovered within the last three decades. Curcumin modulates several different transcription factors, cytokines, growth factors, kinases and other enzymes. The research results have been elaborately covered in this book and explanations provided would add to knowledge pool.

The National Institutes of Health has four clinical trials in progress on curcumin treatment, namely for pancreatic cancer, multiple myeloma, Alzheimer's disease, and colorectal cancer. Curcumin has been found to possess potential

chemopreventive activities. It shows cytotoxic potential against tumor cells both *in vitro* and *in vivo*. Thus, curcumin fits well in the effort of chemoprevention by edible phytochemicals, which is now considered to be an inexpensive, readily applicable, and accessible approach to cancer management. The optimization of intervention trials of diet-derived putative chemopreventive agents is currently under development in normal populations as well as in high-risk groups. Curcumin is also a good immunomodulator. These biological activities warrant further studies of curcumin in the treatment and prevention of human neoplasia.

Curcumin has enormous potential as an antiangiogenic drug. It has been elaborately explained in the chapter discussing this. The property has been attributed to curcumin's ability to downregulate certain transcription factors and proangiogenic factors. Curcumin also has the necessary characteristics of a neuroprotective drug. The activity has been proven in a variety of disease models. Thus, it has great potential for the prevention of multiple neurological conditions for which current therapeutics are less than optimal. The chapter entitled "Neuroprotective Effects of Curcumin" embodies the research carried out on the subject and the existing necessity for further efforts. The curcumin-mediated regulation of COX and LOX enzymes for obtaining their beneficial effects in preventing diverse inflammatory diseases has been dwelt upon in another chapter. Interestingly, curcumin has an edge over conventional nonsteroidal anti-inflammatory drugs and selective COX-2 inhibitors. This might pave the way for path-breaking research in the domain.

This volume in fact covers the length and breadth of research undertaken on curcumin and research results thus far obtained. The diversity ranges from molecular targets, cell growth regulation, antioxidant and anti-inflammatory properties, chemosensitivity, radio protection, and radio sensitivity to immunomodulation, anticancer effects, cardioprotective effects, nephroprotective to hepatoprotective effects, protection from acute and chronic lung diseases to pharmacokinetics and pharmacodynamics and clinical studies undertaken with curcumin. The canvas thus covered is indeed brilliant.

As research advances, it poses newer challenges as well. Several questions in the light of the new drug development effort thus remain to be answered in order to put curcumin in a higher orbit. These pertain to the solubility and stability of curcumin, its optimum dose, pharmacokinetics, mechanism of action of curcumin for a given disease, bioavailability profile, and intricacies of prevention and cure of an identified disease. Further research is thus necessary on these aspects. There is also a need to find out whether other components of turmeric than curcumin have beneficial effects, either alone or in combination with curcumin.

I am happy to see that the contributions in this book have proven beyond doubt that curcumin—an ingredient of the traditional Indian spice turmeric—has enormous potential against a variety of malignant and nonmalignant diseases. I am confident that the state-of-the-art on curcumin research so nicely compiled and analyzed throughout this volume would provide an insight and learning not only to professionals in the field but also to budding researchers. I hope that they would be inspired to answer the unanswered questions on curcumin based on new research

endeavors. I congratulate the editors of the volume and the contributors of the various chapters for creating this unique and scholarly marvel.

R.A. Mashelkar, FRS
Director General
Council of Scientific & Industrial Research, New Delhi, India
October 19, 2006

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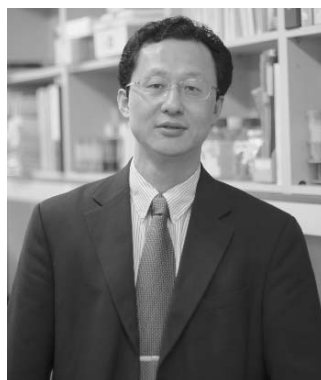
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He is currently a member of the editorial boards of more than 10 international journals, including *Carcinogenesis*, *Molecular Carcinogenesis*, *Cancer Letters*, *Mutation Research*, *Food and Chemical Toxicology*, and *Biofactors*. He is also

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