Neuroprotective Natural Products
Clinical Aspects and Mode of Action
Neuroprotective Natural Products

Clinical Aspects and Mode of Action

Edited by Goutam Brahmachari
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Dedication

Dr. Arnold L. Demain (Drew University, USA).
Preface

“Neuroprotective Natural Products: Clinical Aspects and Mode of Action” is an endeavor to offer an account of the recent cutting-edge research advances in the field of bioactive natural products with neuroprotective potential against various neurological diseases and disorders, particularly focusing on their clinical aspects and mode of action, and also to underline how natural product research continues to make significant contributions in the domain of discovery and development of new medicinal entities. This book consists of a total of 13 chapters contributed by eminent researchers from several countries in response to my personal invitation. I am most grateful to the contributors for their generous and timely response in spite of their busy and tight schedules with academics, research, and other responsibilities.

The term neuroprotection refers to strategies able to defend the nervous system against neuronal injury and/or death when exposed to trauma and surgery and that developed due to both acute and chronic neurodegenerative disorders. Among central nervous system (CNS) disorders, neurodegenerative disorders affect majority of population worldwide and are a major health problem in the twenty-first century. Neurodegenerative disorders such as Parkinson’s disease (PD), Alzheimer’s disease (AD), Huntington’s disease (HD), and amyotrophic lateral sclerosis (ALS) are currently incurable pathologies with huge social and economic impacts closely related to the increasing of life expectancy in modern times. In the course of time, a number of neurotransmitters and signaling molecules have been identified, which have been considered as therapeutic targets against these devastating disorders, and conventional and newer molecules have been tried against these targets. Still the progress is too limited. Neuroprotection is, thus, an important part of care for all types of neurological disorders. Treatment of neurological disorders should not be merely symptomatic, but an effort should be made to prevent the progression of the underlying disease and to develop therapies for regeneration.

The history of neuroprotection dates back to ancient Greek physicians who used hypothermia as treatment of head injury. Neuroprotection has been used in medical practice for more than the past half century. The earliest agents were barbiturates and nonpharmacological approaches such as hypothermia and hyperbaric oxygen. Neuroprotection has now been placed on a firm scientific basis due to an improved understanding of the molecular basis of neurological diseases. The concept of neuroprotection has found increased acceptance in
neurology during the past decade and is linked initially to the role of free radicals in the etiology of neurological disorders, particularly stroke and degenerative neurological symptoms. Considerable work has been performed to elucidate the pathomechanism of various neurological disorders; consequently, a number of neurotoxic phenomena have been identified.

Nature stands as an inexhaustible source of novel chemotypes and pharmacophores; natural products present in the plant and animal kingdoms offer a huge diversity of chemical structures, which are the result of biosynthetic processes that have been modulated over the millennia through genetic efforts. Natural products continue to provide useful drugs in their own right and also provide templates for the development of other useful compounds. A major advantage of natural products approach to drug delivery is that it is capable of providing complex molecules that are not accessible by other routes. Many of such bioactive molecules are found to play a vital role in maintaining the brain’s chemical balance by influencing the function of receptors for the major inhibitory neurotransmitters. In traditional medicinal practice, several plants have been reported to treat cognitive disorders. Plant secondary metabolites include an array of bioactive constituents from both medicinal and food plants that are able to improve human health. The exposure to these phytochemicals, including phenylpropanoids, isoprenoids, and alkaloids, through proper dietary habits may promote health benefits, protecting against chronic degenerative disorders. Recently, it has been suggested that drug discovery should not always be limited to the discovery of a single molecule, and the current belief is that rationally designed polyherbal formulation could also be investigated as an alternative in multitargeted therapeutics and prophylaxis. Development of standardized, safe, and effective herbal formulation with proven scientific evidence can also provide an economical alternative in several disease areas.

It is regarded that herbal medicine may represent a valuable resource in prevention rather than in therapy of some CNS diseases, in association with a healthy lifestyle including beneficial dietary habits and moderate physical activities. Nutritional therapy is a healing system using functional foods and nutraceuticals as therapeutics. This complementary therapy is based on the assumption that food not only is a source of nutrients and energy but also can provide health benefits. In particular, the reported health-promoting effects of plant foods and beverages can be ascribed to the numerous bioactive chemicals present in plant tissues and, consequently, occurring in foods. Consumed as part of a normal diet, plant foods are thus a source of nutrients and energy. It may additionally provide health benefits beyond basic nutritional functions by virtue of their dietary therapeutics. Thus, neuroprevention appears to be an important target and strategy in overcoming neurodegenerative disorders! Prevention coupled with curing therapy for various neurodegenerative diseases is of demanding importance in modern medicinal chemistry.

This book, which comprises 13 chapters written by active researchers and leading experts working in the field of neuroprotective natural products, brings together an overview of current discoveries and trends in this remarkable field. Chapter 1 presents an overview of the book and summarizes the contents of other chapters so as to offer glimpses of the subject matter covered to the readers.
before they go in for a detailed study. Chapters 2–13 are devoted to exploring the ongoing chemical, biological, and pharmacological advances in naturally occurring neuroprotective agents with a focus on their clinical aspects and mode of action. This timely volume encourages interdisciplinary work among chemists, biologists, pharmacologists, botanists, and agronomists with an interest in bioactive natural products. It is also an outstanding source of information with regard to the industrial application of natural products for medicinal purposes. The broad interdisciplinary approach dealt with in this book would surely make the work much more interesting for scientists deeply engaged in the research and/or use of neuroprotective natural products.

Representation of facts and their discussions in each chapter are exhaustive, authoritative, and deeply informative; hence, the book would serve as a key reference for recent developments in the frontier research on neuroprotective natural products at the interface of chemistry and biology and would also be of much utility to scientists working in this area. I would like to express my sincere thanks once again to all the contributors for their excellent reviews on the chemistry, biology, and pharmacology of these medicinally promising agents. It is their participation that makes my effort to organize such a book possible. Their masterly accounts will surely provide the readers with a strong awareness of current cutting-edge research approaches being followed in some of the promising fields of biologically active natural products.

Finally, I would like to express my deep sense of appreciation to all of the editorial and publishing staff–members associated with Wiley-VCH, Weinheim, Germany, for their keen interest in publishing the work and also for their all-round help so as to ensure that the highest standards of publication are maintained in bringing out this book.

Goutam Brahmachari
Visva-Bharati University, Chemistry Department, Santiniketan, India
November 2016
Editor Biography

Professor (Dr) Goutam Brahmachari currently holds the position of full professor of chemistry at the Department of Chemistry, Visva-Bharati University, Santiniketan, India. He was born at Barala in the district of Murshidabad (West Bengal, India) in 1969. He received B.Sc. (Honours) in Chemistry and M.Sc. with specialization in organic chemistry from Visva-Bharati University, India, in 1990 and 1992, respectively. Thereafter, he received his Ph.D. in organic chemistry in 1997 from the same university. In 1998, he joined his alma mater as an assistant professor. He became an associate professor in 2008 and was promoted to full professor in 2011. At present, he is responsible for teaching courses in organic chemistry, natural products chemistry, and physical methods in organic chemistry. Several students received their Ph.D. degree under the supervision of Prof. Brahmachari during this period, and couples of research fellows are presently working with him in the fields of both natural products and synthetic organic chemistry. Prof. Brahmachari’s research is supported by several funding organizations including SERB-DST (New Delhi), CSIR (New Delhi), DBT (New Delhi), and UGC (New Delhi). He is a 2015 and 2016 Who’s Who in the World listee and also a recipient of the 2015 Academic Brilliance Award (Excellence in Research). He is the series editor of the book series Natural Product Drug Discovery.

Prof. Brahmachari’s research interests include (i) isolation, structural determination, and/or detailed NMR study of new natural products from medicinal plants; (ii) synthetic organic chemistry with special emphasis on green chemistry; (iii) semisynthetic studies with natural products; and (iv) evaluation of biological activities and pharmacological potential of natural and synthetic compounds. With more than eighteen years of teaching experience, he has also produced so far nearly 160 publications including original research papers, review articles, and invited book chapters in edited books in the field of natural products and organic synthesis from internationally reputed presses. Prof. Brahmachari has authored/edited a number of textbooks and reference books, including Organic Name Reactions: A Unified Approach (Narosa Publishing House, New Delhi; copublished by Alpha Science International, Oxford, 2006), Chemistry of Natural Products: Recent Trends & Developments (Research Signpost, 2006), Organic Chemistry Through Solved Problems (Narosa Publishing House, New Delhi; copublished by Alpha Science International, Oxford, 2007), Natural Products: Chemistry, Biochemistry and Pharmacology (Narosa Publishing House, New Delhi; copublished by Alpha Science International, Oxford, 2009),
Editor Biography


Prof. Brahmachari serves as a member of the Indian Association for the Cultivation of Science (IACS) and Indian Science Congress Association (ISCA), Kolkata, and as an editor-in-chief of Signpost Open Access Journal of Organic and Biomolecular Chemistry. He also serves as an editorial advisory board member for several international journals. He is regularly consulted as a referee by leading international journals including Elsevier, Royal Society of Chemistry, American Chemical Society, Wiley, Taylor & Francis, Springer, Bentham Science, Indian Chemical Society, Indian Journal of Chemistry (Sec. B), Korean Chemical Society, Pakistan Chemical Society, Brazilian Chemical Society, Bulgarian Academy of Sciences, and so on and also by various financial commissions.

Goutam Brahmachari enjoys songs of Rabindranath Tagore and finds interests in literature as well!
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Neuroprotective Natural Products: Clinical Aspects and Modes of Action – An Overview

Goutam Brahmachari

Visva-Bharati (a Central University), Department of Chemistry, Laboratory of Natural Products and Organic Synthesis, Santiniketan, West Bengal 731 235, India

1.1 Introduction

The book titled *Neuroprotective Natural Products: Clinical Aspects and Modes of Action* is an endeavor to the present cutting-edge research in the neuroprotective natural products and helps the reader understand how natural product research continues to make significant contributions in the discovery and development of new medicinal entities. The reference is meant for phytochemists, synthetic chemists, combinatorial chemists, biologists, pharmacologists, clinicians, as well as other practitioners and advanced students in related fields. This book, comprising 12 technical chapters, highlights the clinical aspects and modes of action of potential neuroprotective natural products with an intention to unravel their pharmaceutical applicability in modern drug discovery processes in the field of neurodegenerative diseases.

This introductory chapter presents an overview of the book and summarizes the contents and subject matter of each chapter so as to offer certain glimpses of the coverage of discussion to the readers before they go for detailed study.

1.2 An Overview of the Book

This book contains a total of 12 technical chapters – Chapters 2–13; this section summarizes the contents and subject matter of each of these chapters.

1.2.1 Chapter 2

In Chapter 2, Volsko and Dutta have offered an overview on the general modes of action of neuroprotective agents in several neurodegenerative disorders as studied in various animal models. The results suggest that administration of such therapeutic candidates postpones disease progression and increases survival rate. Neuroprotective agents act through certain key pathways associated with
development, maturation, and repair in abnormal pathological environments during neurodegenerative diseases, thereby resulting in the reduction of cellular distress and slowing disease development in the nervous system. Specific trophic factors, polypeptides, and heterodimers activate or block the receptors during pathogenesis to slow disease progression. Natural neuroprotective agents that are effective in humans and suppress symptoms and delay disease progression are regarded as promising lead candidates in the drug discovery process in treating neurodegenerative diseases. Modifying treatments based on neuropathology of each such disease is essential, and this chapter boosts the ongoing research in this remarkable field.

1.2.2 Chapter 3

Sil and his group have furnished a thorough discussion on the beneficial effects of different classes of naturally occurring antioxidant compounds against various neurological disorders in Chapter 3. Oxidative stress (elevation of intracellular reactive oxygen species level) is a major cause in the development and progression of neurological diseases such as neurodegenerative diseases, movement disorders, and so on. The brain in particular is prone to this oxidative stress phenomenon, and impairment in memory and cognition are hallmarks of progressive neurodegenerative diseases. Therefore, targeting these diseases with antioxidants may be expected to be a fruitful solution. Antioxidant molecules combat oxidative stress by neutralizing excessively produced free radicals and inhibiting them from initiating the signaling cascades and chain reactions that result in various diseases and premature aging. Several natural compounds with antioxidant property have been found to be greatly effective in treating these diseases as they effectively scavenged free radicals and inhibited their generation. This chapter covers the sources of such antioxidants and the general mechanism by which they play a protective role in different cognitive and movement-related neurological disorders. This illuminating review on natural antioxidants would obviously enrich the readers and would motivate them in undertaking in-depth further research.

1.2.3 Chapter 4

Chapter 4 is dedicated to natural neuroprotectives for the management of Parkinson’s disease (PD) by Ali and his group. PD is regarded as the second most general neurodegenerative disorder that involves a decreased nigrostriatal availability of dopamine, resulting in motor impairment including bradykinesia, rigidity, and tremor. Currently, the exact cause of this devastating disease is unclear with no single factor accountable for neurodegeneration. It shows that several factors may contribute to its development, such as formation of reactive oxygen species (ROS), protein misfolding, and neuroinflammation. The deficiency of dopamine occurs due to loss of dopaminergic neurons and degradation of dopamine. It has been evidenced that oxidative stress is critically involved in the pathogenesis of PD, and thus antioxidants may find beneficial role in treating the disease. This chapter deals with the literature covering the use of various natural antioxidative neuroprotective agents including naringenin, curcumin,