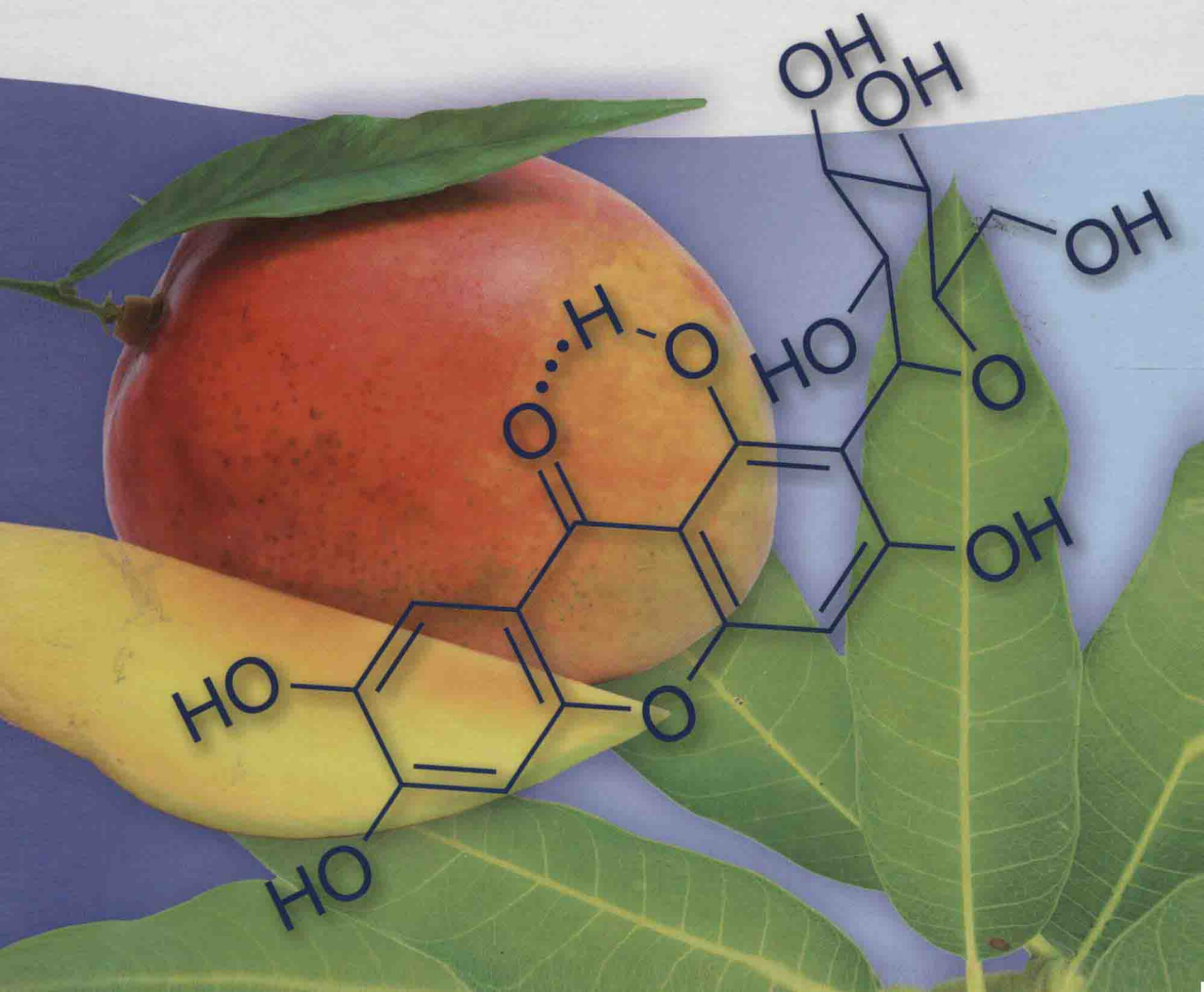


WILEY-VCH

Edited by Goutam Brahmachari

Bioactive Natural Products

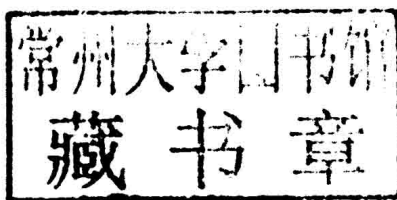
Chemistry and Biology



Edited by
Goutam Brahmachari

Bioactive Natural Products

Chemistry and Biology



WILEY-VCH
Verlag GmbH & Co. KGaA

The Editor

Prof. Dr. Goutam Brahmachari
Visva-Bharati University
Department of Chemistry
Santiniketan 732 235
India

All books published by **Wiley-VCH** are carefully produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at <<http://dnb.d-nb.de>>.

© 2015 Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Print ISBN: 978-3-527-33794-1

ePDF ISBN: 978-3-527-68441-0

ePub ISBN: 978-3-527-68442-7

Mobi ISBN: 978-3-527-68443-4

oBook ISBN: 978-3-527-68440-3

Typesetting Laserwords Private Limited, Chennai, India

Printing and Binding Markono Print Media Pte Ltd, Singapore

Printed on acid-free paper

Edited by
Goutam Brahmachari

Bioactive Natural Products

Related Titles

Brahmachari, G.

Handbook of Pharmaceutical Natural Products

2010

Print ISBN: 978-3-527-32148-3

Hanessian, S. (ed.)

Natural Products in Medicinal Chemistry

2014

Print ISBN: 978-3-527-33218-2 (Also available in a variety of electronic formats)

Kim, S. (ed.)

Marine Microbiology Bioactive Compounds and Biotechnological Applications

2013

Print ISBN: 978-3-527-33327-1 (Also available in a variety of electronic formats)

Osbourn, A., Goss, R.J., Carter, G.T.

Natural Products Discourse, Diversity, and Design

2014

Print ISBN: 978-1-118-29806-0 (Also available in a variety of electronic formats)

Civjan, N. (ed.)

Natural Products in Chemical Biology

2012

Print ISBN: 978-1-118-10117-9 (Also available in a variety of electronic formats)

Tang, W., Eisenbrand, G.

Handbook of Chinese Medicinal Plants Chemistry, Pharmacology, Toxicology

2011

Print ISBN: 978-3-527-32226-8

All those who are working globally with bioactive natural products for the cause of human welfare

Foreword

Bioactive Natural Products: Chemistry and Biology edited by Professor (Dr.) Goutam Brahmachari and published by Wiley-VCH is a timely, highly significant, and useful book for readers engaged in chemical, biological, pharmacological, and medicinal study as well as research in these emerging areas.

Natural product science was one among the very few key areas of research in ancient times. Despite substantial progress in many other areas, research on natural product chemistry remains in the fuzzy region between chemical and biological research with undefined boundaries. It is argued that natural product chemistry is not a separate subject any longer: it is a hybrid discipline. In reality, the success in natural product research and its applications has opened up many other subdomains in science that are widely accepted in the academic world as well as in the modern chemical and pharmaceutical industries. For example, owing to the availability of many bioactive natural products, synthetic organic chemistry, computational chemistry, medicinal chemistry, biochemistry, and analytical chemistry as well as molecular biology, pharmacognosy, biotechnology, and clinical science have all become major areas of scientific research in recent decades. It has been extensively demonstrated that the search for natural products, or products obtained from natural sources through synthesis, is directed toward identifying new molecules for diseases and investigating their mechanisms of action and their specific targets of interaction (for example, DNA, RNA, proteins, and enzymes).

Natural products are classified on the basis of their origins, biological functions, and structures. Plants are a vast source of many natural drugs. A number of drugs are also synthesized from natural products through different chemical reactions. The most important of these natural products are terpenoids, alkaloids, steroids, phenolic compounds, vitamins, carbocyclics and heterocyclic aromatic compounds, proteins, and carbohydrates. Bacteria and fungi are microorganisms that are also extremely useful in the search for and identification of organic molecules that have the potential to serve as drugs and highly active compounds. Many different drugs other than antibiotics have been isolated for medicinal

use from microorganisms. Marine sources are relatively unexplored for the identification of bioactive compounds. However, there is considerable interest now in the isolation of novel molecules from various marine sources and the possibilities here are endless. The ocean is a huge source for natural biological and chemical products. In their search for natural products in the ocean's fish, snails, algae, sponges, reefs, bacteria, and microorganisms, it would appear that the journey of chemists and biologists to explore unknown, diverse, structurally unique, and potentially useful amazing naturally occurring molecules has only just begun. In addition to these sources, animals, venoms, and toxins are also screened for bioactive organic natural compounds.

Most of the natural products are found in combination with many other active or nonactive components. The first objective of research in natural product chemistry is to isolate, purify, determine the structure and structural alteration, and test these molecules as entities that can be used in medicine to enhance the quality of animal and human life. This is achieved through total or partial synthesis of bioactive natural products. In fact, the combined and tireless efforts of chemists and other scientists including clinicians have solved numerous complex medical problems through research on natural products. The second objective of research in this area is to study the mechanisms of action of natural products that may find use as drugs or lead molecules by identification of biochemical pathways using modern methods including genomic and proteomic analyses. The biodiversity of nature is available to us. Clearly, nature remains the most valuable source of chemical and biological investigation of molecules with novel stereochemistry. Therefore, new natural products and established bioactive natural products will remain a key for our well-being.

This book, edited by Professor Brahmachari, has a depth of knowledge and information. I believe expert scientists, researchers, and students will use this book for a tremendous learning and research experience. The quality and timeliness of this book in a market of competitive research will stimulate the present and future generations of scientists who are interested in improving the quality of human life through working on natural products and derivatives stemming from them. The book contains a wealth of features that include information on a diverse number of bioactive natural products presented by prominent authors with many pertinent references. This will help even persons without sufficient knowledge in natural products to undertake research in the area in the future.

The editor has a long history of publishing many books that have received tremendous scientific attention. The dedication of the editor in the selection of the authors, subject matter, and organization of the chapters proves his experience and scholarly activity in this particular area. He has chosen numerous contributors who are active in this specific field. Each chapter is presented in a highly elegant and precise manner. Scientists working on natural product chemistry will find this a handy resource book that will help them with their work. The enduring work of many scientists on biologically active natural products in

the isolation, detection, and structure elucidation along with biological study as described in the content of every chapter will prove to be very useful for the current and future generations of scientists.

I strongly recommend this state-of-the-art book on the chemistry and biology of bioactive natural products to students and researchers who are engaged in natural product research as well as synthesis and biological evaluation of novel molecules for different types of medical disorders and for those who are pursuing their activities to improve the quality of our lives.

Bimal K. Banik
The University of Texas-Pan American
Edinburg, USA

Preface

This single volume entitled *Bioactive Natural Products: Chemistry and Biology* is an endeavor to focus the recent cutting-edge research advances in the field of bioactive natural products, very particularly operating at the interface of chemistry and biology, 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 17 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.

Natural products usually refer to chemical substances produced by a living organism or found in nature that have distinctive biological and pharmacological effects; they encompass a wide variety of chemical compound classes, including alkaloids, antibiotics, terpenoids, flavonoids, xanthonoids, phenolics, carbohydrates, lipids, proteins and amino acids, and nucleic acids. The huge diversity in chemical structures of natural products is an outcome of biosynthetic processes that have been modulated over the millennia through genetic effects. Such chemical entities have played a crucial role in modern drug development and still constitute a prolific source of novel lead compounds, or pharmacophores, for ongoing drug discovery programs. Most significantly, natural products operate at the interface of chemistry and biology. Hence, search for bioactive molecules from nature (plants, animals, microflora) continues to play an important role in fashioning new medicinal agents. With the advent of modern techniques, very particularly the rapid improvements in spectroscopic as well as accompanying advances in high-throughput screening techniques, it has become possible to have an enormous repository of bioactive natural compounds, thus opening up exciting new opportunities in the field of new drug development to the pharmaceutical industry.

Medicinal chemistry of such bioactive compounds encompasses a vast area that includes their isolation and characterization from natural sources; structure modification for optimization of their activity and other physical properties;

and also total and semisynthesis for a thorough scrutiny of structure–activity relationships. It has been well documented that natural products played a significant role in modern drug development, especially for antibacterial and antitumor agents; however, their uses in the treatment of other epidemics such as AIDS and cardiovascular, cancerous, neurodegradative, infective, and metabolic diseases have also been extensively explored. The need for leads to solve such health problems threatening the world population makes all natural sources important for the search of novel molecules, diversified and unique structural architectures of which inspired scientists to pursue new chemical entities with completely different structures from known drugs. Researchers around the globe are deeply engaged in exploring the detailed chemistry, pharmacology, and biology of such potent and naturally occurring efficacious bioactive compounds. Current research trends in the field suggest an optimistic future for natural products in drug discovery; however, novel strategies and innovative approaches in addition to the introduction of more sophisticated technical requirements are still needed today for the development of natural products into new drugs.

This book, which comprises a variety of 17 chapters written by active researchers and leading experts working in the field of chemistry of biologically active 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 the 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 through 17 are devoted to exploring the ongoing chemical, biological, and pharmacological advances in naturally occurring organic compounds and describe their biosynthesis, semisynthesis, total synthesis, chemical transformations, structure–activity relationships, nucleic acid and protein-binding aspects, biodiversity, and bioproduction, including mechanism of action, high-throughput drug screening, and drug design.

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 bioactive natural products. It will serve as a valuable resource for researchers in their own fields not only to predict promising leads for developing pharmaceuticals to treat various ailments and disease manifestations but also to motivate young scientists to the dynamic field of bioactive natural products research.

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 bioactive 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 the excellent reviews on the chemistry, biology, and pharmacology of bioactive natural products. 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.

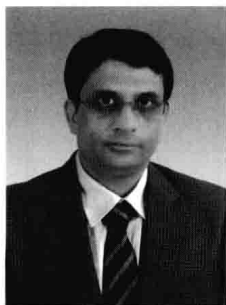
I would like to express my sincere thanks and deep sense of gratitude to Professor Bimal K. Banik, Department of Chemistry, The University of Texas-Pan American, United States, for his keen interest in the manuscript and for writing foreword to the book.

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 the book.

October 2014

Goutam Brahmachari
Visva-Bharati University
Chemistry Department
Santiniketan, India

About the Editor



Professor (Dr.) Goutam Brahmachari was born at Barala in the district of Murshidabad (West Bengal), India, on April 14, 1969. He received his high school degree in scientific studies in 1986 at Barala R. D. Sen High School under the West Bengal Council of Higher secondary Education (WBCHSE). Then he moved to Visva-Bharati (a central University founded by Rabindranath Tagore at Santiniketan, West Bengal, India) to study chemistry at the undergraduate level. After graduating from this University in 1990, Prof. Brahmachari completed his masters in 1992 with specialization in organic chemistry and thereafter received his Ph.D. degree in 1997 in chemistry from the same University. He was appointed as assistant professor of organic chemistry at Visva-Bharati University, Department of Chemistry, in 1998, then became associate professor in 2008. In 2011, he became full professor of organic chemistry in the same faculty. At present, he is responsible for teaching courses in organic chemistry, natural products chemistry, and physical methods in organic chemistry. Several students have received their Ph.D. degree under the supervision of Prof. Brahmachari during this period, and a couple of research fellows are presently working with him both in the fields of natural products and synthetic organic chemistry. He serves as a member of the Indian Association for the Cultivation of Science (IACS) and Indian Science Congress Association (ISCA), Kolkata. He also serves as an Editor-in-Chief, *Signpost Open Access Journal of Organic and Biomolecular Chemistry*, and as editorial board member of several journals.

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 16 years of teaching experience, he has produced so far nearly 120 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 text and reference books that include *Organic Name Reactions: A Unified Approach* (Narosa Publishing House, New Delhi; Co-published 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; Co-published by Alpha Science International, Oxford, 2007), *Natural Products: Chemistry, Biochemistry and Pharmacology* (Narosa Publishing House, New Delhi; Co-published by Alpha Science International, Oxford, 2009), *Handbook of Pharmaceutical Natural Products – 2 volume-set* (Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2010), *Bioactive Natural Products: Opportunities & Challenges in Medicinal Chemistry* (World Scientific Publishing Co. Pte. Ltd., Singapore, 2011), *Chemistry and Pharmacology of Naturally Occurring Bioactive Compounds* (CRC Press, Taylor & Francis group, USA, 2013), and *Natural Bioactive Molecules: Impacts & Prospects* (Narosa Publishing House, New Delhi; Co-published by Alpha Science International, Oxford, 2014), *Green Synthetic Approaches for Biologically Relevant Heterocycles* (Elsevier Inc., USA, 2014).

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, Korean Chemical Society, Brazilian Chemical Society, Bulgarian Academy of Sciences and so on, and also various financial commissions.

Goutam Brahmachari enjoys songs of Rabindranath Tagore, and finds interests in Literature as well!