Book Reviews

Cannabinoids as Therapeutics. Edited by Raphael Mechoulam. Birkhäuser Verlag, Basel, Switzerland. 2007. x + 272 pp. 16.5 × 24 cm. ISBN 3-7643-7055-6. 136.96 euros.

The endocannabinoid system's ascent into stardom has been documented in a substantial number of reviews and monographs outlining its physiological and biochemical roles and potential opportunities for endocannabinoid-related drug discovery and development. The present volume is edited by Raphael Mechoulam, who made major contributions both in the field of phytocannabinoids in the 1960s with the characterization of Δ^9-THC, the main constituent of cannabis, and in the 1990s with the discovery of the first endocannabinoid, anandamide. Mechoulam has been a worthy champion of the cannabinoid story with a very broad view regarding the possible role of cannabinoids as therapeutics. For this reason, the present volume is a welcome addition to the field. Fourteen chapters explore a variety of what the editor calls "more mundane" topics, including the roles of endocannabinoids in neuroprotection, reproduction, appetite, and cancer. Other topics on "the chemistry less explored linking endocannabinoids with stress, fear, love, satisfaction, despair will have to await further development and additional results from ongoing work".

Chapter 1, which focuses on the origin of cannabis in India and its place in Ayurvedic medicine, is a useful, well-referenced account of cannabis history through its introduction in the West during the 19th century to its current status worldwide. Chapter 2 deals with the chemistry of cannabinoids and includes the key plant phytocannabinoids and numerous cannabinoids and other lipid modulators associated with the endocannabinoid system. This chapter also includes some of the key synthetic ligands used in research laboratories as modulators of CB1 and CB2, the two known cannabinoid receptors, as well as a variety of other compounds representing the ever encompassing space of cannabinergic medicinal chemistry. A special chapter is dedicated to cannabidiol, a natural constituent of cannabis generally regarded as a nonpsychotropic constituent of cannabis but with intriguing pharmacological properties of potential therapeutic value. Each of the following 10 chapters outlines an individual role for cannabinergic compounds in distinct therapeutic areas. These include reproduction, neuroprotection, learning and memory, anxiety, pain, cancer, nausea, osteoprosis, drug abuse, and appetite and obesity. The last topic includes the history of Accomplia, the first modern cannabinoid therapeutic currently being used in Europe.

This concisely written chapter describes the potential therapeutic effects of this CB1 inverse agonist in humans to treat obesity and dyslipidemia. Very recently, a preparation of cannabis products has been developed as an inhalant for use in neuropathic pain and multiple sclerosis. This product, Sativex, is currently approved for use in Canada and is described in great detail in the book's last chapter.

As may be expected in a multiauthored publication, the quality of the individual chapters is variable and a careful reading reveals a small number of errors. The book is nonetheless quite readable and includes a substantial number of references extending to early 2005. Overall, this is a useful contribution to the field, recommended as an introduction for the uninitiated reader and as a reference for cannabis therapeutics.

Alexandros Makriyannis
Center for Drug Discovery
116 Mugar Hall
Northeastern University
Boston, Massachusetts 02115

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Modelling Molecular Structure and Reactivity in Biological Systems. Edited by Kevin J. Naidoo, John Brady, Martin J. Field, Jiali Gao, and Michael Hann. Royal Society of Chemistry Publishing, Cambridge, U.K. 2007. x + 294 pp. 16 × 24 cm. ISBN 0-85404-668-2. £109.95.

This book is based on papers presented at the 7th triennial conference of the World Association of Theoretical and Computational Chemists (WATOC 2005) held in Cape Town, South Africa, in January 2005. As the preface says, half of the 120 invited papers had a special focus on applications in biology, and this review concentrates on those contributions.

The first section, "Molecular Conformation and Electronic Structure of Biomolecules", contains six papers that embrace a wide range of topics from "electroweak quantum chemistry and the dynamics of parity violation in chiral molecules" (Martin Quack) to the structure and mechanism of an ATPase (Brunger and De La Barre). The second and largest section, "Chemical Reactivity in Biological Surroundings", consists of 11 papers that mainly discuss the modeling of enzyme reaction mechanisms although other topics such as prion proteins, membrane modeling, molecular dynamics simulations, and metalloproteinase inhibitors are addressed. The final section, "Toward Drug Discovery", embraces the major "industrial" applications of theoretical chemistry, and this is the use of computational methods in the pharmaceutical industry. This section contains two particularly useful reviews; Hugo Kubinyi describes how the strategies of drug research have evolved, while Mike Hann discusses what computational chemistry can and cannot do.

As always, in a book that is essentially conference proceedings, it is impossible to cover every topic that was addressed at the meeting. This volume, by concentrating on the major theme of applications in biology, has nicely overcome this limitation and forms a very useful source of "state of the art" information about computational modeling of biological systems. I have no hesitation in recommending this book to both academic and industrial researchers in this area.

David J. Livingstone
ChemQuest
Delamere House, 1 Royal Crescent
Sandown, Isle of Wight, PO36 8LZ, U.K.

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The Chemistry of Process Development in Fine Chemical and Pharmaceutical Industry. Second Edition. By C. Someswara Rao. John Wiley and Sons, Ltd., Chichester, West Sussex, U.K., and Asian Books Private Ltd., New Delhi, India. 2006. xi + 1311 pp. 19 × 25 cm. ISBN 0-470-31995-X. $245.00.

This book describes aspects of process chemistry that are of use to those unfamiliar with the science, such as medicinal chemists. Some of the chapters deal with common transformations and provide useful details that can be applied at any scale. This is useful to those who are working in a laboratory environment, as well as those working at plant scale. In some ways, the book documents the uses of various reagents for a transformation, somewhat in the vein of Fieser and Fieser, but with comments as to its use above laboratory scale.

The major problems encountered during scale-up are discussed along with solutions and, in many cases, extensive examples. Solutions to a wide variety of problems can be found within the figures.

The last chapter on safety assessment is written by A. A. Khan and complements the rest of the book highlighting the most important consideration when scaling up reactions.

With a work of this size, it is difficult to provide up to date references for all reactions. However, most references are pre-2003 and in some cases the old company has been cited as performing a reaction rather than the modern day successor. For those new to the industry, this could be very confusing.

The layout of the book and references is not completely intuitive. This could make its use as a reference book difficult. The figures do not always start at the top of a page, even when they span multiple pages, and the accompanying text may be split in midsentence to pick up a number of pages on. The format of the main text and the figures does not allow the reader instantly to see the content change. The use of shading or a completely different font would have been useful. This problem does not occur in all chapters, as some have a footer denoting that the page is a figure. The indices do direct the reader to the main coverage of reagents and reactions, although I did find some useful pieces of information that did not appear in an index. I did not find looking up a reference citation a simple operation, especially if the citation was in a figure. Each figure has a single reference number with different examples being referred to by letters. Going back a number of pages was sometimes required to find the reference number. The references are given by chapter at the back of the book so that in turning to that part of the book at random, one has no idea what chapter number the reference citations found refer to; considerable page turning may be required to find the chapter number and then the reference number and citation one is looking for. The simple incorporation of a page header or footer would have helped navigation through these pages. The reference section also includes some footnotes. The chances are that most readers will miss these useful pieces of information unless they are specifically looking for them.

Experienced readers will be able to put most of the information into context. For example, if dedicated hydrogenation equipment is available, this is preferable to a transfer hydrogenation in most cases. If a hydrogenator is not available, then transfer hydrogenation is safer in multipurpose equipment. There is good discussion on topics that often are not considered by laboratory chemists. Phase transfer catalysis and polymorphism are two examples.

The copy of the book I received had large variations in print quality. Some pages were very light, while others had large amounts of ink that had resulted in blotting and bleeding through to the page on opposite side of the paper, occasionally making reading difficult.

There are a number of typographical errors in the text. Fortunately, the figures have few. The errors seem to be greater in the new material, and some are obvious. In many places the publishers and editors should have seen these typographical mistakes. However, readers just searching for background on a specific topic may be faced with a reference to a Web site that does not work because of a typographical error.

Overall, this book is a good place to start when performing a new transformation at scale. Problems associated with the chemistry, reagent, and solvent are highlighted, and in most cases alternatives or work-arounds are suggested. The safety issues are relevant to chemists working on any scale, while the improvements to cut down side or unwanted reactions should prove to be useful to readers of this journal.

David J. Ager
DSM
PMB 150
9650 Strickland Road, Suite 103
Raleigh, North Carolina 27615

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Handbook of Contemporary Neuropharmacology. *Volumes 1−3. Edited by David R. Sibley, Israel Hanin, Michael Kuhar, and Phil Skolnick. John Wiley & Sons, Inc., Hoboken, NJ. 2007. xx + 2992 pp. 18.5 × 26 cm. ISBN 978-0-471-66053-8. $760.00.*

With about 160 contributing authors, the Handbook of Contemporary Neuropharmacology comprises three volumes and approximately 3000 pages (including a 100-page cumulative index in each volume) of material highly relevant to this very broad and diverse discipline. As noted by the editors, drugs employed to treat neuropsychiatric disorders represent one of the largest groups of therapeutic agents, the demand for such drugs is growing as the population ages, and almost all major pharmaceutical companies have active drug discovery programs in the neurosciences and neuropharmacology. The purpose of this series is to "create a high-level reference work that will be useful to all practitioners of neuropharmacology ranging from graduate students, academicians, and clinicians to industrial scientists working in drug discovery". Were the editors successful in achieving their goal? For the most part, yes.

Volume 1 consists of two parts: Part I, Basic Neuropharmacology; Part II, Mood Disorders. Part I is subdivided into 17 chapters. The first three chapters (∼100 pages) of Part I are devoted to historical perspectives and concepts of synaptic transmission. This is followed by 10 chapters (∼500 pages) on individual neurotransmitters and their receptors and additional chapters (∼140 pages) on voltage gated ion channels, neuropeptides, transporters, and gaseous signaling. Part 2 is made up of five chapters (∼120 pages) on depression and bipolar disorder. Volume 2 is composed of four parts: Part 1, Anxiety and Stress Disorders (six chapters and ∼215 pages); Part II, Schizophrenia and Psychosis (six chapters and ∼200 pages); Part III, Substance Abuse and Addictive Disorders (seven chapters, ∼250 pages); Part IV, Pain (four chapters, ∼70 pages). Volume 3 consists of five parts: Part I, Sleep and Arousal (six chapters, ∼200 pages); Part II, Development and Developmental Disorders (six chapters, ∼150 pages); Part III, Neurodegenerative and Seizure Disorders (seven chapters, ∼250 pages); Part IV, Neuroimmunology (five chapters, ∼150 pages); and Part V, Eating and Metabolic Disorders (four chapters, ∼100 pages). An online version of the series is planned "to maintain its cutting-edge status". Several sample chapters are currently available at http://www.mrw.interscience.wiley.com/emrw/0470101008/home/SampleContent.html.

This three-volume series is a major undertaking, and it represents a most comprehensive treatment of the topic. Because of the breadth and scope of the topics, it seems unfair to be critical in light of what has been accomplished. Indeed, I have already found the series to be quite useful on several occasions. If material is not specifically covered, chances are that appropriate references will be provided. Nevertheless, there are a few minor faults, most of which might be attributed to personal bias on the part of this reviewer. The series contains ample figures, both in black and white and in color. Unfortunately, all the color figures for a given volume are collected together in a central location. Understandable from a cost-savings perspective (I suppose) but still inconvenient and one of my pet peeves. There also are some introductory topics that could have been given more attention. For example, there is very little about the evolution and current understanding of receptor theory, the structural composition of receptors (similarities and differences, homology modeling, site-directed mutagenesis), constitutively active receptors, imaging techniques, generation and application of knockout animals, and various other in vitro and in vivo methods utilized in neuropharmacology. All major neurotransmitter receptors are covered, but there is little (if any) mention of certain receptor types (e.g., adenosine receptors, imidazoline receptors). Although occasionally, some of these topics might be briefly mentioned by a particular chapter author, a general treatment of these concepts and techniques would have been instructive and welcomed as introductory chapters in Part I of Volume 1. Admittedly, some of this information might be found in more fundamental texts, but a current state-of-the-art discussion would have been beneficial here. In fact, Volume 1 might have been best devoted solely to "basic concepts" (indeed, Part II, Mood Disorders, seems out of place in the first volume and might have been moved to one of the other volumes) and served as a stand-alone volume that could be purchased separately. Likewise, although there is some passing discussion of drug discovery and drug development, given that it is mentioned in the Preface, this is mostly reflective of what has come to pass and not of what might come in the future (or techniques being employed in this regard). Also, there is little consideration of the important roles of drug properties (for example, pharmacokinetics, drug metabolism, interaction with hERG) in the drug development process. Certainly, there are far fewer structures of drugs than might please the average medicinal chemist. But here, I must remind myself that this series is likely targeting pharmacologists and clinicians more so than medicinal chemists. Despite these shortcomings, the series deserves a decided "thumbs up".

Entire books could be (and in many instances, already have been) written on subjects covered in individual chapters or sections; those interested in specific topics will undoubtedly purchase these highly focused specialty books. This series, however, does an admirable job of bringing together many aspects of neuropharmacology in one place. There is enough here to keep "experts" happy, and for those of us who have only a cursory interest in certain other topic areas, this series is a good excuse to get better educated. Am I pleased to be in possession of the series? Absolutely. Is it useful? Most assuredly. Should the series be on the desk of those interested in neuropharmacology? Yes. Will it be? Because of its substantial cost, this seems unlikely. On the other hand, I cannot imagine a department or university library being without it. The bottom line is that if it fits your budget or if a copy is available in your library, it would be well worth your while to examine it.

Richard A. Glennon

Department of Medicinal Chemistry
School of Pharmacy
Medical College of Virginia
Virginia Commonwealth University
Richmond, Virginia 23298-0540

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Inhibitors of Cyclin-Dependent Kinases as Anti-Tumor Agents. Edited by Paul J. Smith and Eddy W. Yue. CRC Press, Boca Raton, FL. 2007. xvi + 448 pp. 16.5 × 24 cm. ISBN 0-8493-3774-7. $159.95.

Cyclin-dependent kinases (CDKs) are a family of enzymes involved in regulation of the cell cycle. In principle, compounds that inhibit these enzymes should arrest the cell cycle and might serve to inhibit tumor proliferation. "Inhibitors of Cyclin-Dependent Kinases as Anti-Tumor Agents" is the third volume in CRC's Enzyme Inhibitor Series. In it, Paul Smith and Eddy Yue bring together 18 chapters summarizing efforts to block this family of enzymes.

Editing a multiauthor book is a challenge. Each author has a different perspective on the subject, a different writing style, and even a different way of formatting the references. Smith and Yue have done an admirable job with this volume. There is a clear logic in the arrangement of the chapters. The introductory chapter is well suited to readers who are not familiar with this particular topic. Jargon is kept to a bare minimum. There are two notable features in this book that are not common in multiauthor volumes. First, there are 16 full-color figures in a center section of the book. Second, the book is extensively indexed (40 pages of index!).

The first four chapters summarize the biology of CDKs and the cell cycle. Chapter 6 includes an excellent overview of the CDKs as anticancer targets. For the medicinal chemist, the book has a solid core of nine chapters describing structure−activity relationships of various families of CDK inhibitors. Chapter 17 summarizes the current status of CDK inhibitors that have progressed to clinical trials, with a discussion of their possible use in combination with other chemotherapeutics.

References appear to be quite complete through 2005, with a few 2006 papers included as well. This highly readable volume should serve to get newcomers to the field up to speed quite rapidly.

D. Eric Walters

Department of Biochemistry and Molecular Biology
Rosalind Franklin University of Medicine and Science
North Chicago, Illinois 60064

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