

Book Reviews

Human Medicinal Agents from Plants. ACS Symposium Series 534. Edited by A. Douglas Kinghorn and Manuel F. Balandrin. American Chemical Society, Washington DC. 1993. xii + 356 pp. 15.5 × 23.5 cm. ISBN 0-8412-2705-5. \$89.95.

Periodically, new generations of medicinal chemists are treated to reviews of the history of human's use of plants as sources of drugs, the need for and the problems attendant upon the discovery of new ones, and the progress achieved through recent efforts in that direction. This volume, based on a symposium sponsored by the American Chemical Society at its San Francisco Meeting in April 1992, is one of these. It begins with the familiar recitation of the historical drugs still used in current medical practice and proceeds through 21 other chapters to review the progress in the discovery of additional examples that has taken place over the past 25 years.

Chapter 2 on tropical forest diversity contains a couple of surprises: The less potent non-cocaine alkaloids of *Erythroxylon* are used to flavor Coca-Cola (Is this true?); the ethnobotanical approach to the discovery of new medicinal plants is very recent. Using even the conservative definition of ethnobotany as applicable only to preliterate societies, it was certainly practiced over 50 years ago by government, academic, and industrial groups in the search for new medicinals, and by the explorers of the 19th century, if not by Orellana himself at the time of the Conquest, to mention but a few examples.

The contrasting philosophies of western Europe and the United States with respect to the use of herbal remedies (Chapter 3) raises a number of interesting questions which might warrant a symposium in their own right. Perhaps if scientists would talk more directly to the public instead of to each other, consumer awareness might indeed bring phytomedicinals out from "under the counter".

Chapters 4 and 5 deal respectively with biological diversity and the resurgence of British industrial interest in natural products while Chapter 6 highlights progress in the production of compounds by manipulation of cell culture techniques. Chapter 8 is a guide to the collection of plants—nothing new, but certainly instructive to the laboratory chemists and pharmacologists who may have had no experience with the problems to be faced at the front end of a plant discovery program.

At least 10 chapters (7-16) deal with recent work done at, or under the aegis of, the National Institutes of Health in their programs directed toward a treatment or cure of cancer, AIDS, and HIV-related diseases. In addition to the recent approval of taxol for use in ovarian cancer, a few synthetic compounds derived from natural models are expected to be approved in the reasonably near future.

Good news is reported from the antimalarial front in Chapter 17: Artemesinin, a sesquiterpene lactone from *Artemisia annua*, and several of its derivatives show considerable promise as schizontocides with little or no mammalian toxicity. A comprehensive review of earlier brief reviews is promised.

Larvicidal and molluscicidal compounds (Chapter 18), while not direct human medicinal agents, act against some

of the vectors of human disease and could play an important role in the control of schistosomiasis and malaria.

The secondary metabolites of algae are reviewed in Chapter 19, the activation of protein kinase receptors by phorbol esters in Chapter 20 and the constituents of garlic and their relationship to cardiovascular disease in Chapter 21 which supplies the scientific background for recent emphasis of the subject in the popular press. The final chapter describes potentially useful analogs of forskolin, a diterpenoid activator of adenylate cyclase, and of rohitukine analogs as anti-inflammatories.

There are indices of subject, author and author affiliation. As with all books prepared from camera-ready copy, final appearance might have been improved through the use of a uniform type style and size for the manuscripts, but in view of the amount of material presented, the reader may be inclined to overlook this.

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Receptors: Model Systems and Specific Receptors, Methods in Neurosciences, Vol. 11. Edited by P. Michael Conn. Academic Press, Inc., San Diego, CA. 1993. xv + 440 pp. 20 × 23 cm. ISBN 0-12-185272. \$59.95.

Volume 11 continues the tradition of the "Methods" series by focusing on examples of techniques for studying receptors and drug-receptor interactions while attempting to remain broad enough to be applicable to systems not specifically explored. Each of the 24 chapters begins with an introduction describing the receptor in question and proceeds to more or less detailed protocols describing procedures to examine receptor properties or function. Information is not limited to *in vitro* binding, and the range of material covered includes *in situ* hybridization, autoradiography, solubilization and purification of proteins, tissue bath methods, computational modeling and *in vivo* approaches. In so far as presenting a broad overview of procedures to study receptors, Volume 11 is largely successful.

Although it is put forth that, (Receptors) "will prove invaluable not only to the experienced researcher but to the student as well", some caution must be exercised with this generality. For example, "the wide latitude in nomenclature and usage (given contributors)" makes the volume confusing at times when identical systems are discussed in different chapters. At some points, protocols have been reduced to a series of one-line sentences and assume the reader is knowledgeable of terminology and abbreviations. While some contributions are delightful in attention to the underlying concepts of receptor theory, others seem to ignore basic fundamentals (inclusion of inverted U- or nonsaturating Scatchards). Chapters which

attempt to couple computational modeling with molecular biology are notable for their lack of discussion of the limitations of point mutations (much less deletion of entire amino acid sequences) on defining ligand binding site configuration. It seems to be taken for granted that alterations in protein sequence, should these lead to loss of binding or function, automatically describe the necessary functionalities defining the ligand binding site.

At the practical level, Volume 11 consists of 24 chapters written by 62 experienced academic, government, or industry investigators. Each averages 18 pages and is highly focused, allowing each contribution to be read individually. Citations per chapter (range 14–186) are current (but are given in short format without titles). There is no delineation of chapters according to subject matter making the individual works appear as random contributions.

Overall, to read this volume of "Methods" was variously exciting or disappointing. To the experienced scientist interested in specific topics (and who could recognize obvious flaws), the book would be a useful reference. If the object is to educate students in the fundamentals of receptor practice or theory, Limbird or Kinaken would probably be a superior investment.

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Marine Biotechnology. Volume 1. Pharmaceutical and Bioactive Natural Products. Edited by David H. Attaway and Oskar R. Zaborsky. Plenum Press, New York. 1993. xix + 500 pp. 15.5 × 23 cm. ISBN 0-306-44174-8. \$89.50.

This is the first volume of a series that will explore basic knowledge, applied research and development, and commercial and institutional issues that relate to marine biotechnology. In it are examined chemical and biological properties of some natural marine products that are useful or potentially useful in the pharmaceutical and chemical industries. Following introductory chapters that consider the biomedical potential of marine natural products and their structure, isolation, and mode of action are ones that deal with the pharmacology of novel marine metabolites, eicosanoids from marine algae, clinical applications of marine proteins and macroalgal polysaccharides, and antitumor, cytotoxic, antiviral, and antiparasitic agents from marine sources. The final four chapters are directed to dinoflagellates and marine microorganisms as sources of bioactive materials, production of vitamins by chlorophyte *Dunaliella*, and the significant role of university scientists in the discovery of bioactive marine natural products.

This book effectively demonstrates the rich array of chemistry and chemicals in the marine world that have no terrestrial counterparts. It seems likely that by better understanding the ocean's biological materials and processes much information of value for technological development will be derived. Marine products, described in this volume, may be expected to provide novel "leads" for

both organic and medicinal chemical research. Pharmacologists and chemists will find this volume a rich source of novel approaches to the understanding of complex cellular events and potential therapeutic agents.

Staff

The Search For Antiviral Drugs. Case Histories From Concept to Clinic. Edited by Julian Adams and Vincent Merluzii. Birkhauser, Boston, MA. 1993. xii + 240 pp. 16 × 23 cm. ISBN 0-8176-3606-4. \$75.00.

This book provides several case histories of how initial "concepts" for therapeutic agents were reduced to practice and the resulting compounds taken to the clinic. The first chapter gives a historical perspective of the development of 5-iodo-2'-deoxyuridine (IUDR), the first marketed antiviral agent. The following seven chapters discuss the development of compounds which became clinical candidates, namely, AZT, three non-nucleoside reverse transcriptase (RT) inhibitors, the first HIV protease inhibitor to the clinic (Ro 31-8959), the Roche TAT inhibitor, and Piradovir, the broad spectrum inhibitor of rhinoviruses. These seven cases all highlight the importance of management commitment and the essential need to form interdisciplinary teams at an early stage. Formation of these teams early allows progress to be made in a parallel rather than in a linear manner. One of the strengths of this book is that it allows the reader to understand the aspects of research and development which can speed up important projects.

The three chapters on non-nucleoside RT inhibitors, since they deal with similar topics, are a little repetitive. They do show, however, how different approaches can be used toward the same end point. Especially interesting is how the three groups focused on different issues (enzyme target, development of resistance, etc.). These three chapters, along with the chapters on Piradovir and the TAT inhibitor, underscore the importance of compound repositories to companies in modern drug research. The chapter on Piradovir describes the only recent non-HIV example in the book which has reached the clinic. It provides an interesting juxtaposition to the other AIDS case histories. The discussion on how the Janssen group broadened the spectrum of their lead compounds and developed their theory of two sets of antiviral binding sites has little of the "thrill of the chase" about it. This chapter also illustrates the important lesson that one can do very good science and make all the correct decisions, but still not take a drug to market. The final two chapters illustrate promising new approaches to the discovery of inhibitors of herpes simplex virus and rhinovirus which are still in the preclinical stages.

Overall, the book meets its goal. I found the book enjoyable and easy to read. All chapters are well written and use good diagrams to illustrate their points. The literature references are timely and provide useful sources for further reading. The key word index is a little short

to be very useful. Individuals with an interest in antiviral chemotherapy will find this good reading.

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Biological Barriers to Protein Delivery. Edited by Kenneth L. Audus and Thomas J. Raub. Plenum Press, New York. 1993. 495 pp. 15.5 × 23 cm. ISBN 0-306-44368-6. \$85.00.

Many of the recent major advances in biology have been in the field of biotechnology, the products of which are proteins and peptides. However, utilizing these materials as therapeutic agents requires their delivery into the body. This has proven to be a difficult task, and this book summarizes both the challenges and opportunities in the delivery of proteins across biological barriers.

The book is divided into five parts, organized by the type of barrier involved. Cellular barriers include the paracellular pathway, ectopeptidases, endosomal and lysosomal hydrolases, and uptake and cytoplasmic access. Epithelial barriers discussed are intestinal transepithelial transport, intraoral absorption, nasal and respiratory epithelia, dermal absorption, and rectal and vaginal absorption. The vascular barrier section discusses the vascular endothelial barrier and transcytosis through the blood-brain barrier. The fourth part of this book addresses elimination barriers, with chapters on renal uptake and disposal of proteins and peptides, mechanisms for the hepatic clearance and implications for elimination rates, bioavailability, and cell-specific drug delivery to the liver, and the role of the immune system. The final section on tissue barriers contains chapters on extravasation and interstitial transport in tumors and on diffusion, bulk flow, and volume transmission within the brain.

Each of the 16 chapters is well referenced, and the book contains an excellent index. It will serve as an excellent introduction to those new to the field, as well as a useful reference work for those who continually deal with the problems inherent in the delivery of proteins across biological barriers.

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Small Peptides. Chemistry, Biology and Clinical Studies. Pharmaco Chemistry Library Volume 19. By A. S. Dutta. Elsevier Science Publishers B. V., Amsterdam. 1993. xvi + 616 pp. 17 × 24 cm. ISBN 0-444-88655-9. Dfl. 450.00.

The past decade has witnessed an exponential growth of peptide-related research. Peptide and non-peptide agonists and antagonists of neuropeptides have been rationally designed, studied, and developed. In addition, a number of small peptide and non-peptide inhibitors of a variety of important enzymes have been designed in a rational fashion to, in some instances, afford useful therapeutic agents. This book details many aspects of

peptide research. The first eight chapters summarize the results of research on the neuropeptides angiotensin II, bombesin/gastrin-releasing peptide, bradykinin, cholecystokinin, CCK/gastrin, enkephalin, luteinizing hormone-releasing hormone (LHRH), somatostatin, and tachykinins. In these chapters approaches that have led to receptor classification and the discovery of potent agonists and antagonists are highlighted. The next three chapters summarize important research on inhibitors of the enzymes renin, HIV protease, and metallopeptidases [angiotensin converting enzyme (ACE), enkephalinase, and atriopeptidase]. Detailed pharmacology and clinical data are presented for inhibitors that are marketed or are nearing market. The final chapter highlights approaches to the useful delivery of peptides as drugs. The book is thoroughly referenced with the inclusion of a number of citations to reviews. An excellent subject index is also included.

This is a timely, clearly-written book which will be of interest to all scientists concerned with drug discovery and peptide research. The many structures and detailed presentations of structure-activity relationship information enhance the value of this book to medicinal chemists.

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Books of Interest

Bioactive Natural Products. Detection, Isolation, and Structural Determination. By Steven M. Colegate and Russel J. Molyneux. CRC Press, Inc., Boca Raton, FL. 1993. 528 pp. 18 × 26 cm. ISBN 0-8493-4372-0. \$125.00.

Nitrate Therapy and Nitrate Tolerance. Current Concepts and Controversies. Edited by Dz. E. Reza-kovic and J. S. Alpert. S. Karger AG, Basel, Switzerland. 1993. x + 548 pp. 17 × 24 cm. ISBN 3-8055-5669-1. \$232.00.

Parkinson's Disease. Symposium Review 1992. Edited by Merton Sandler. John Libbey & Company Limited, London. 1993. xi + 65 pp. 17 × 24 cm. ISBN 0-86196-404-7. U.S. \$24.00.

Biological Applications of Photochemical Switches. Edited by Harry Morrison. John Wiley & Sons, Inc., New York. 1993. ix + 316 pp. 16 × 24 cm. ISBN 0-471-57293-4. \$59.95.

Multinational Pharmaceutical Companies: Principles and Practices. Second Edition. By Bert Spilker. Raven Press, New York. 1993. xli + 803 pp. 22 × 28 cm. ISBN 0-7817-0100-7. \$115.00.

Practical Organic Mass Spectrometry. Second Edition. A Guide for Chemical and Biochemical Analysis. By J. R. Chapman. John Wiley & Sons, Inc., New York. 1993. xiii + 330 pp. 15 × 23 cm. ISBN 0-471-92753-8. \$54.95.

Water Channels. (Molecular Biology Intelligence Unit). By Alan S. Verkman. R. G. Landes Company, Austin, TX. 1993. 117 pp. 18.5 × 26.5 cm. ISBN 1-57059-017-6. \$89.95.

Calcium-Dependent Potassium Channels. (Molecular Biology Intelligence Unit). By Robert D. Hinrichsen. R. G. Landes Company, Austin, TX. 1993. 148 pp. 18.5 × 26.5 cm. ISBN 1-57059-011-7. \$89.95.

Opioid Peptides in Substance Abuse. By Jozsef I. Szekely. CRC Press, Inc., Boca Raton, FL. 1994. 277 pp. 16 × 24 cm. ISBN 0-8493-7937-7. \$99.95.

The Development of Iron Chelators for Clinical Use. Edited by Raymond J. Bergeron and Gary M. Brittenham. CRC Press Inc., Boca Raton, FL. 1994. xiii + 416 pp. 16 × 24 cm. ISBN 0-8493-8679-9. \$129.95.

Desmopressin in Bleeding Disorders. Series A: Life Sciences. Volume 242. Edited by G. Mariani, P.

M. Mannucci, and M. Cattaneo. Plenum Publishing Corporation, New York. 1993. x + 361 pp. 17 × 25 cm. ISBN 0-306-44414-3. \$105.00.

Cyclophane Chemistry: Synthesis, Structures, and Reactions. By Fritz Vogtle. John Wiley & Sons, Inc., New York. 1993. vii + 501 pp. 15.5 × 23 cm. ISBN 0-471-93199-3. \$123.95.

Planning Pharmaceutical Clinical Trials. Basic Statistical Principles. By William M. Wooding. John Wiley & Sons, Inc., New York. 1993. xx + 539 pp. 16 × 24 cm. ISBN 0-471-62244-3. \$69.95.