Book Reviews

Annual Review of Pharmacology and Toxicology. Volume 38. Edited by Arthur K. Cho. Annual Reviews, Palo Alto, CA. 1998. vi + 581 pp. 16 × 23 cm. ISBN 0-8243-0438-1. $60.00.

As is characteristic of the series, this volume presents short reviews on a wide range of topics, covering a variety of neurotransmitter receptors and transporters, metabolic enzymes, and other drug targets, with the focus ranging from molecular to clinical.

Several chapters address the cytochrome P450 (CYP) drug-metabolizing enzymes, either as part of an evaluation of the predictive value of in vitro toxicologic or metabolic models (Davila et al., Ito et al.) or as the role of a specific isoform in drug interactions (Thummel and Wilkinson). In addition to oxidation by CYP, other biotransformation mechanisms are discussed, including hydrolytic ester cleavage (Satoh and Hosokawa), glutathione conjugation (Monks and Lau; Anders and Dekant), and transport across renal, hepatic, and intestinal epithelia (Zhang et al.).

Another focus is signal transduction, with discussion of the role of environmental toxins on the major transduction pathways (L. G. Costa), signal transduction by a variety of neurotransmitters and hormones (Felder and Glass; E. Costa; Miller), role of the cyclooxygenases in linking cytokines and growth factors to their biological responses (Vane et al.), and role of receptor kinases and arrestins in modulating adrenergic receptor activation (Krupnick and Benovic). Several of these chapters also cover the characterization and subclassification of receptors for cannabinoids (Felder and Glass), catecholamines (Krupnick and Benovic; Rohrer and Kobilka), GABA (E. Costa; Miller), adenosine (Miller), and acetylcholine and glutamic acid (Miller).

Clinical chapters include reviews of the role of endogenous and environmental estrogens in the induction of breast cancer (Safe), the postulated utility of growth hormone for treatment of age-related loss in bone density and lean body mass (Marcus and Hoffman), the neuronal toxicities associated with HIV infection (Lipton), and the pharmacological utility of sesquiterpene lactones derived from Mexican Asteraceae (Heinrich et al.).

The individual chapters are generally well-written and comprehensive, considering their limited length. The bibliographies are extensive, with several hundred references in some cases. References up to 1997 are included, as well as some interesting unpublished information, such as the cardiovascular and central nervous system effects of α_2-adrenoceptor agonists in mice where specific α_2-adrenoceptor subtypes have been disrupted (Rohrer and Kobilka).

This series of volumes continues to be useful, offering an overview of topics both related and unrelated to a particular area of expertise. Even the unrelated group can often be helpful, by providing insight into new techniques, drug targets, and therapeutic protocols which can have broad application.

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JM980535R

10.1021/jm980535r

Mass Spectrometry of Biological Materials. Second Edition, Revised and Expanded. Edited by B. S. Larsen and C. N. McEwen. Marcel Dekker, Inc., New York, NY. 1998. xiii + 469 pp. 15.5 x 23 cm. ISBN 0-8247-0157-7. $195.00.

This volume arises in response to extensive growth in biological mass spectrometry in two interrelated areas over the last 10 years: new ionization methods and instrumentation, and in the integration of mass spectrometry into biological protocols, which has been particularly notable in the field of protein chemistry. The book deals with methods based on electrospray ionization and matrix-assisted laser desorption ionization (MALDI), both of which have opened numerous new doors in structural and analytical chemistry. Although listed as a second edition, the book is essentially new, particularly from the standpoint of topics covered. The editors' stated intent was to create an instructional volume rather than a series of reviews, a goal that has been very largely achieved. No pretense has been made (nor would it be practical) to include all areas implied by the book title, but the topics covered are all of current importance and interest.

An introductory chapter on contemporary instrumentation and ionization methods provides a welcome and practical starting point for readers not well-versed in these topics. It is followed by 16 chapters written by experts in their respective fields, emphasizing methods under recent development with examples of applications from their laboratories. Each chapter is self-contained and is grouped somewhat loosely into aspects of instrumentation (Chapters 2 and 3), target compound isolation or concentration from complex mixtures (Chapters 4−6), indentification or characterization of proteins and related compounds (Chapters 7−12), measurement of noncovalent interactions and of hydrogen−deuterium exchange in studies of tertiary structure (Chapters 13 and 14), oligonucleotides and DNA (Chapters 15 and 16), and uses of mass spectral data for the screening of protein databases (Chapter 17).

Three excellent chapters stand out in providing insightful treatment of topics that are otherwise poorly covered in the literature: discussions of the roles of contemporary mass spectrometry in industrial drug discovery; a highly readable account of strategies for glycoprotein analysis; and the use of bioinformatics in protein analysis. Several chapters are similar to coverage by the same authors elsewhere in the literature but

offer the advantage of concise descriptions, with practical experimental details. These include techniques for the characterization of histocompatibility antigens and studies of noncovalent interactions in the gas phase as a mimic of solution-phase properties.

The literature covered appears to extend into early 1997. The provision of a subindex at the start of each chapter is particularly helpful, as is the inclusion of article titles in each set of references. The book is well-suited for those wishing to gain an introductory through intermediate understanding of selected topics in the applications of mass spectrometry. It would be particularly recommended to graduate or postdoctoral students, but consideration must be given to the high price of the volume.

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JM9805844

10.1021/jm9805844

The Antidepressant Era. By David Healy. Harvard University Press, Cambridge, MA. 1998. x + 317 pp. 16 x 24.5 cm. ISBN 0674039572. $39.95.

Who discovered chlorpromazine? Charpentier, who synthesized it in 1950? Courvoisier, who reported distinctive effects on animal behavior and neurophysiology? Laborit, who first noticed distinctive psychotropic effects in man? Or Delay and Denicker, who clearly outlined what has now become its accepted use in psychiatry and without whose endorsement and prestige Rhône-Poulene might never have developed it further as an antipsychotic? There have been bitter disputes over this issue, as a result of which no Nobel Prize was ever awarded for what has been the single most important breakthrough in psychiatric treatment.

Similarly, the question of who discovered imipramine can be asked. Many suggest that it was a collaborative effort. In 1954, a series of 42 tricyclic compounds (iminodibenzyl analogues) were synthesized and reported by Schindler and Haefliger (*Helv. Chim. Acta* **1954**, *37*, 4) working at Geigy Pharmaceuticals in Basel, Switzerland. One of these compounds, G-22355 (which was the iminodibenzyl closest in structure to chlorpromazine), was selected for clinical trial and distributed to a wide range of clinicians for evaluation. This group included some psychiatrists, among whom was Ronald Kuhn at the Münsterlingen Hospital in Switzerland on Lake Konstanz. Kuhn, who is now credited by many as the "discoverer" of the antidepressant effects of imipramine (G-22355), made his discovery as a result of careful observations on depressed patients from 1955 to 1956. In February 1957, Kuhn sent a report to Geigy endorsing the drug as a potential antidepressant, and in August of that year, he published his findings in a Swiss medical journal and presented his research at the World Conference of Psychiatry, which was held in Zurich in September. Interestingly however, Kuhn was not invited to participate at the First International Congress of Neuropsychopharmacology (CINP) held in Rome in 1958, even though there were presentations on imipramine. He was also not invited to the second and third CINP meetings.

Multiple independent discovery happens often enough in science, and the discovery of the antidepressants is no exception. Nathan Kline is generally credited with the discovery of the antidepressant effect of iproniazid. Kline, in contrast to Kuhn, was flamboyant and cosmopolitan, ready to adopt new ideas, and had considerable political savvy. Kline, at the time of his involvement with iproniazid in 1954, was an Assistant Clinical Professor of Psychiatry at Columbia University and director of the research facility at Rockland State Hospital in New York. He published the initial account of the clinical effects of iproniazid in the *Congressional Record* of 1956. However, where no one was honored for the discovery of chlorpromazine or imipramine, Kline was awarded the Lasker Prize in 1957 for his role in demonstrating the antidepressant effects of reserpine. Subsequently, Kline was awarded a second Lasker Prize in 1964 for his contributions to psychiatry.

In this book, Healy, himself a psychiatrist, having previously published two volumes of interviews with leading psychopharmacologists, presents a fascinating story of considerable historical scholarship and amusing and interesting anecdotes. I rarely bring "technical books" with me on my vacation, but having started to read *The Antidepressant Era* before leaving, I was compelled to finish reading this story of the discovery of the antidepressants during my vacation. The complex story that Healy tells in this book not only details the discovery of the antidepressants, the emergence of the idea of depressive disease, and the evolvement of psychopharmacology but also details the origins of the pharmaceutical industry and the pressures for the regulation of drug companies. Of particular interest are Healy's observations into the current efforts expended in the marketing of antidepressants. He emphasizes that pharmaceutical companies are as much in the business of selling psychotropic diagnoses as of selling psychotropic drugs.

There are two minor aspects of this book which I feel compelled to point out. A section at the end of the book lists a series of notes and references cited in the text. Many of these references are incomplete and difficult to locate. The second minor annoyance is that the structures shown for the antidepressants on pages 50, 51, 75, and 200 were carelessly drawn and in most cases are incorrect.

This book will be of interest not only to chemists, pharmacologists, and clinicians in the pharmaceutical industry and in academia but to all those interested in the history of science and the politics of scientific discovery. The book makes fascinating reading and is highly recommended.

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JM980585W

10.1021/jm980585w

The Chemistry, Biology, and Medical Applications of Hyaluronan and Its Derivatives. Edited by T. C. Laurent. Portland Press, London, U.K. 1998. xvi + 341 pp. 17 × 25 cm. ISBN 1-85578-119-0. $127.50.

This book compiles the proceedings of work presented at the International Conference on Hyaluronan at the Wenner−Gren Center in Stockholm, Sweden. It is composed of 34 chapters written by 61 authors who are the world's experts on hyaluronan. Throughout the book the important contributions of Dr. Endre Balasz in discovering and elucidating the chemistry and biology of hyaluronan are extensively highlighted. The contributed chapters are grouped into subsections that focus on physicochemical properties, biosynthesis, protein binding, hyaluronan receptors, cellular interactions, medical applications, and hyaluronan as a clinical marker. Each subsection contains 4-6 well-written contributions which provide background and current data concerning on-going research on hyaluronan. The subsection on hyaluronan−protein interactions is notable for its comprehensive review of the numerous proteins that bind hyaluronan. However, it is the in-depth coverage of basic research in combination with the biomedical applications dealt with in this book that provides the reader with a firm grasp of the state-of-the-art in hyaluronan research.

This book would complement the library of any laboratory involved in research in extracellular matrixes, biomaterials, advanced drug delivery systems, and glycobiochemistry. I highly recommend it, both to newcomers and to experienced researchers in these fields of study.

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JM980609Z

10.1021/jm980609z

The Alkaloids. Volume 51. Chemistry and Biology. Edited by Geoffrey A. Cordell. Academic Press, San Diego, CA. 1998. x + 439 pp. 15.5 × 23.5 cm. ISBN 0-12-469551-5. $135.

The Alkaloids is a familiar series, dating to 1950. The editor describes this latest addition as being in a traditional motif covering isolation, structure elucidation, and synthetic studies on four groups: aspidospermine, *Cephalotaxus*, ipecac, and Amaryllidaceae alkaloids. To summarize the editor further, a significant theme in all chapters is the substantial number of new alkaloids and the emphasis on enantioselective synthesis.

The chapter on aspidospermine alkaloids, by J. E. Saxton, is the longest. This field was last reviewed in this series 20 years ago. The isolations of some 240 alkaloids in the 1977−1996 period are listed in an 18-page tabulation, not all of them being new structures. The literature on *Cephalotaxus* alkaloids is updated from 1984, when they were last covered in this series. As well as the traditional sections, there is also a section on pharmacological and clinical studies. Cephalotaxine esters such as homoharringtonine are undergoing trials as antileukemic agents. This section also reviews the unnatural esters synthesized in China for leukemia trials. The ipecac alkaloids, reviewed by T. Fujii and M. Ohba, comprise the shortest section. The area is updated from 1983, with particular emphasis on biosynthetic and pharmacological studies. Amaryllis alkaloids were last covered in Volume 30 (1987). This area is updated by O. Hoshino, each subgroup of alkaloids being discussed in terms of isolation, structure elucidation, synthetic studies, and biological activity.

The book is copiously illustrated, with structural drawings comprising almost half of the book. The tables occupy another 8%, and of course, each chapter is fully referenced. As with the other volumes in this series, this book takes its place as standard reference material for the selected groups of alkaloids.

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JM980610Y

10.1021/jm980610y