Book Reviews

Neurochemical Mechanisms of Opiates and Endorphins, Advances in Biochemical Psychopharmacology. Volume 20. Edited by H. L. Loh and D. H. Ross. Raven Press, New York. 1979. 16 × 24 cm. xi + 563 pp. $39.00.

The basis of the mechanism of action, tolerance development, and physical dependence to the opiate drugs has been the subject of active investigation in recent years. While much of the early investigations on the narcotics centered around pharmacologic and behavioral observations, the advent of opiate receptor binding techniques and the discovery of neuroactive endogenous opioid peptides have produced a major new area for opiate research. These studies, together with the identification of opiate receptors, have provided an immense amount of new literature. Thus, the need arose for a concise body of available information about this new molecular approach to narcotic research. This volume successfully provides a comprehensive review of the current state of our understanding of neurochemical mechanisms for opiate and endorphin actions.

The work of 39 authors is represented in the book's 21 chapters. Topics in this volume cover areas such as opiate–endorphin–receptor interactions, including a thorough discussion of the stereochemical anatomy of morphinomimetics. The chemistry and neurobiology of the endogenous opiate peptides are reviewed in four other chapters. The role of messenger systems, such as the cyclic nucleotides and calcium, in opiate actions is well summarized. Five chapters concentrate on the interaction of the opiates with neurotransmitters and the use of operant techniques to study the neuropsychopharmacology of the opiates. The effects of opiates on macromolecule biosynthesis and membrane function are also reviewed. Introductory and concluding chapters review the history of narcotic research and likely future directions for new investigations. Most chapters are subdivided into clear sections with a useful summary at the end. The editors were mostly effective in managing to have each of the authors review all the pertinent literature relevant to the topic rather than just concentrating on data produced in their own laboratories. Thus, this book should prove useful to neurochemists and other neuroscientists who may be expanding their interests within the field of narcotic research as well as in peripheral areas.

Northeastern University **Jeffrey B. Blumberg**

Bleomycin: Current Status and New Developments. Edited by S. K. Carter, S. T. Crooke, and H. Umezawa. Academic Press, New York. 1978. xiii + 365 pp. 15.5 × 23.5 cm. $25.00.

As the title indicates, this volume is concerned with bleomycin, a chemotherapeutic agent having clinically useful activity in the treatment of certain human malignancies. The volume is based on the proceedings of a symposium held in Oakland, Calif., in Oct 1977 and includes 30 papers as individual chapters. The first three chapters, one by each of the editors, give an overview of bleomycin, its biochemical characteristics, and current role in cancer chemotherapy. There are a few additional early chapters dealing with "molecular" aspects of bleomycin, such as its mechanism of action and metabolism, but the emphasis of the book is in the area of clinical and preclinical investigations and it does provide a comprehensive survey of research at this level.

Chapters 24 and 25 deal with the question of pulmonary toxicity of bleomycin, an issue of central importance given that this effect limits the clinical utility of the bleomycins at present and probably holds the key to the development of bleomycins with improved anticancer activity. Following these chapters there is a discussion by Dr. Umezawa (the discoverer of bleomycin) of the search for new bleomycins and then three chapters dealing with the development of second- and third-generation bleomycins. In the final chapter, Dr. Crooke discusses future directions in bleomycin research.

The book is appropriate for use by experienced investigators in this and related fields. It is well organized, contains pertinent literature references, and gives the reader a good overview of preclinical and clinical studies. It is probably worth noting that, while the present text provides much less comprehensive coverage of structural and mechanistic studies of bleomycin, another text, that emphasizes this aspect of bleomycin studies, will soon appear.

University of Virginia **Sidney M. Hecht**

Carbon-13 NMR Shift Assignments of Amines and Alkaloids. By Maurice Shamma and David M. Hindenlang. Plenum Press, New York. 1979. xi + 303 pp. 15.5 × 23.5 cm. $29.50.

The advertised purpose of this book was to gather illustrative but not necessarily exhaustive carbon-13 nuclear magnetic resonance data available on natural and synthetic alkaloids in a single volume. Appreciative researchers will undoubtedly agree that the authors have succeeded. The literature has been surveyed through 1977 and the spectral assignments of representative compounds are grouped into chapters of alkaloid families. The preponderance of isoquinoline and indole alkaloid citations testify to the intensity of research in these areas. Each chapter of compounds proceeds in increasing degree of structural complexity to assist the correlation of ^{13}C NMR spectral changes with variation in molecular structure. Chemical-shift data for each alkaloid are clearly presented as easily read numbers superimposed on handsomely drawn structures with no more than three figures to a page. References collected at the end of the volume allow the reader to explore in depth the chemical-shift assignment rationale. An attempt has been made by the authors to critically review the data given and point out possible instances of assignment ambiguity. Indexed at the end of the volume by common or systematic nomenclature, 687 representative alkaloids with chemical-shift assignments are presented in this way.

New England Nuclear **Crist N. Filer**

Glutamic Acid: Advances in Biochemistry and Physiology. Monographs of the Mario Negri Institute for Pharmacological Research. Edited by L. J. Filer, Jr., S. Garattini, M. R. Kare, W. A. Reynolds, and R. Wurtman. Raven Press, New York. 1979. xiv + 400 pp. 16 × 24 cm. $28.00.

This book should be considered together with two related books, "Kainic Acid as a Tool in Neurobiology" (edited by McGeer, Olney, and McGeer, Raven Press, New York, 1978) and "Amino Acids as Chemical Neurotransmitters" (edited by Fonnum). Each is a multiauthor compendium; there is noticeable overlap of authors, and sometimes chapters, between the three books. Of the three, "Kainic Acid as a Tool in Neurobiology" is the most coherent. It also focuses upon structure–activity analysis and mechanisms of toxicity in a manner familiar to pharmacologists and medicinal chemists. Kainic acid is a useful tool for experimental neuroscience, but it cannot be accurately described as a general toxin for neuronal cell bodies, and it is not certain that it acts via glutamate receptors or glutamate release. Recent work with a variety of excitotoxic amino acids suggests the existence of several different receptors for excitotoxins. Whether this points to the existence of several different excitotoxic "endogenous ligands" is unclear at present.

"Glutamic Acid: Advances in Biochemistry and Physiology" is a rambling book which touches on at least five different themes: glutamate and taste physiology, whole body studies of glutamate metabolism, the role of glutamate in the mammalian CNS, glutamate neurotoxicity, and research with humans about glutamate disposition and possible toxicity. I was disappointed in the taste studies and also felt that most of the section on glutamate as a neurotransmitter was superficial and out of date. The short chapter by Johnston pointing to different types of excitotoxin receptors is useful. The chapter by Watkins in "Kainic Acid as a Tool in Neurobiology" gives a nice review of excitant amino acids

from the pharmacological and chemical viewpoint but does not do justice to the biology of excitatory neurotransmission. The same is true of Cotman and Hamberger's chapter in "Amino Acids as Chemical Neurotransmitters". Studies of glutamate metabolism show clearly that glutamate in water or saline evokes much greater increases in plasma glutamate than glutamate given with food. Indeed, as Wurtman points out, glutamate with food has never been shown to produce a CNS lesion in any experimental animal. It is difficult to defend food additives, but I agree that glutamate is acceptable as a food additive. Although the available data suggest that even premature infants handle glutamate-rich casein hydrolysates well, I would be a bit more cautious about parenteral infusions rich in dicarboxylic amino acids, since both the liver and the gut, two regulatory organs, are bypassed during parenteral feeding. It is not certain that even peripheral infusions of glutamate produce brain lesions in primates. Further, it seems that the incidence of the so-called Chinese restaurant syndrome (CRS, which seems not of CNS origin) has been inflated by suggestive questionnaires. Also, the frequent association of nonspecific symptoms with many foods has not been sufficiently appreciated. In Kerr's study, the food most often reported to cause trouble was pizza. It has been shown that MSG, orally or intravenously, can reproduce symptoms of CRS in susceptible persons, but it is likely that other substances can also do so, and the high incidence of symptoms after control feedings should be noticed.

There may well be a small group of humans who are intolerant of glutamate taken with food and have symptoms beyond those of CRS, just as some humans must restrict their intake of sugar, phenylalanine, galactose, or protein. However, at the present time, legal restrictions on the dietary use of dicarboxylic acid amino acids seem to be unnecessary. It is still unclear why newborns are more susceptible to glutamate neurotoxicity. Note that newborns are *insensitive* to direct striatal injections of kainic acid. Taking a broad look at CNS neurotransmitters, it seems that they fall into two distinct groups: fast acting, fast binding "ionotropic transmitters" (which directly change membrane conductance) such as GABA, acetylcholine at "nicotinic synapses", glycine, and the excitatory transmitter(s) contrasted to slow binding, slow acting "indirect transmitters" (which have no effect on membrane conductance) such as the monoamines, acetylcholine at "muscarinic synapses", opioid peptides, substance P, etc. It is interesting that in vitro membrane binding studies seem to accurately classify the two types of transmitters and that so very little is known about excitatory neurotransmission in the CNS. Of these three state of the art books, "Kainic Acid as a Tool" will be most useful to pharmacologists and medicinal chemists. A good book on CNS excitatory transmission is yet to come, and it probably will not be a multiauthor compendium.

The Childrens Hospital Medical Center **S. Robert Snodgrass**

Dielectric and Electronic Properties of Biological Materials. By Ronald Pethig. Wiley, Somerset, N.J. 1979. xiv + 376 pp. 15 × 25 cm. $37.50.

This book would be a worthy addition to the bookshelf of any pharmaceutical scientist, if only for the chapter on water in biological systems. The author has a clear and fluent style which makes reading the book rather pleasant.

Of particular note is the very large selection of references after each chapter, including many from as late as 1977. The author has the knack of extracting important concepts of the several referenced papers and of presenting these concepts woven together as a concise overview of work in a particular area. The review of dielectric theory is presented in just this manner, including fundamental equations as required but still keeping mathematical manipulations at a minimum.

Pharmaceutical scientists involved in "active site–drug" interactions would be well advised to review Chapters 5 through 7 on biological membranes and tissues. For instance, techniques of dielectric dispersion now permit the observation of water tightly bound to the protein matrix, and it is possible to differentiate between such bound "ice-like" water and bulk solvent. The amount of bound water and the effect it may have on drug interactions with some active site are of importance to pharmaceutical science.

The last chapters of the book consider electronic properties of biological polymers. After some introduction to the quantum mechanical concepts, the author applies these quantum mechanical results to electronic effects, such as semiconductivity, photoconductivity, and charge transfer in proteins and nucleic acids. In concluding remarks, the author looks forward to increased understanding of such properties in biological polymers forming the basis of a more complete understanding of life processes themselves.

There is very little to criticize in this book. An apparent contradiction on the effect of relative humidity on the helical form of DNA is found on page 137, which may be corrected by inserting "disordered state" instead of "B helix" in line 18. This reviewer would have liked a chapter on instrumentation requirements for the measurement of dielectric properties of biological polymers, in particular when reference is frequently made to measurements on polymers in the dry state as well as in solution.

Overall, the book is highly recommended to the pharmaceutical scientist and certainly to the library of any college of pharmacy.

Virginia Commonwealth University **Alfred J. Richard**

Pharmaceutical Manufacturing Encyclopedia. Edited by Marshall Sitting. Noyes Data Corp., Park Ridge, N.J. 1979. xviii + 702 pp. 16 × 24 cm. $72.00.

This book gives details for the manufacture of 673 major pharmaceuticals, the required information having been obtained from the appropriate patent literature. The emphasis in this book is on the process for drug preparation or manufacture. It is arranged alphabetically by generic name of the drug and indexed by trade name to provide easy access. It is also indexed by chemical raw materials as a guide to those selling to the pharmaceutical industry as well as an information source for researchers. This volume, in combination with the "Merck-Index" and Remington's "Pharmaceutical Science", will provide additional information on the specific material, its properties, and therapeutic use. The chemist who is interested in routes of synthesis is referred to Lednicer and Mitscher's "The Organic Chemistry of Drug Synthesis" for more information on routes to these products and to products having similar structures. This volume will provide an invaluable resource for chemists active in pharmaceutical research and manufacture for many years to come. It's purchase is recommended.

Staff

Books of Interest

Aging. Volume 9. Neuropsychiatric Side Effects of Drugs in the Elderly. By Alvin J. Levenson. Raven Press, New York. 1979. xi + 240 pp. 16 × 24 cm. $20.00.

Chemistry and Chemical Engineering in the People's Republic of China. By John D. Baldeschweiler. American Chemical Society, Washington, D.C. 1979. xix + 266 pp. 16 × 23.5 cm. $15.00 (hardback), $9.50 (paperback).

The International Challenge of Drug Abuse. NIDA Research Monograph. No. 19. By Robert C. Petersen. Department of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, Washington, D.C. 1978. xiii + 349 pp. 14.5 × 23 cm. $5.25.

Environmental Aspects of *N*-Nitroso Compounds. Proceedings of a Working Conference at the New England Center for Continuing Education, University of New Hampshire, Durham, NH, Aug 22–24, 1977. By E. A. Walker, M. Castegnaro, L. Griciute, and R. E. Lyle. World Health Organization, Geneva. 1978. xxiv + 566 pp. 18 × 24 cm. $50.00.

Principles of Organic Synthesis. Second Edition. By R. O. C. Norman. Halsted Press (Wiley), New York. 1978. xiii + 800 pp. 15.5 × 23 cm. $18.50.

Tuberculosis Case-Finding and Chemotherapy (Questions and Answers). By K. Toman. World Health Organization, Geneva. 1979. xii + 239 pp. 16 × 24 cm. Swiss francs 32.00.