Book Reviews

Antiepileptic Drugs: Quantitative Analysis and Interpretation. Edited by C. E. Pippenger, J. K. Penry, and H. Kutt. Raven Press, New York, N.Y. 1978. xv + 367 pp. 16 × 24 cm. $29.50.

This book provides a survey of analytical techniques for estimating anticonvulsant drugs and their metabolites in serum or plasma (19 chapters) and discusses the clinical significance of such determinations (9 chapters).

The range of methods available for antiepileptic drug analysis has become confusingly diverse. Spectrophotometric methods have been superseded by chromatographic procedures, including thin-layer, gas–liquid, and high-pressure liquid chromatography utilizing increasingly sophisticated detector systems from flame-ionization to electron capture, nitrogen–phosphorus and mass spectrometric detectors. Immunoassay procedures include radioimmunoassay (with a liquid scintillation counter as readout) or an enzyme multiplied immunochemical technique (with a spectrophotometric readout).

The chapters on analytical methods described the theoretical basis of each technique, its practical application, and its particular advantages and disadvantages (an appendix gives some methodology in a lab-manual format but is far from comprehensive). It is clear that at this stage there is no one optimal procedure. The data provided here will help those setting up or supervising clinical chemistry services to choose the techniques most appropriate to their particular resources and requirements.

In the chapters concerned with clinical applications, most of the data are familiar from earlier publications. Considered as a review, there are numerous omissions; e.g., drug interactions are inadequately discussed.

The accurate measurement of anticonvulsant drug concentrations in plasma can lead to a marked improvement in the control of seizures in patients with epilepsy. The information in this volume will help clinical chemists and neurologists to improve the accuracy and usefulness of such determinations.

Institute of Psychiatry **B. S. Meldrum**

Advances in Drug Research. Volume 11. Edited by Alma B. Simmonds. Academic Press, New York, N.Y. 1977. 240 pp. 15.5 × 23.5 cm. $27.00.

Volume 11 of this series contains five reviews, the first of which cover "Miscellaneous Antirheumatic Drugs and their Possible Modes of Action", by P. Bresloff. The agents discussed are gold compounds, chloroquine, and D-penicillamine with regard to their immunological behavior and effects on cartilage, collagen, enzymes, and proteins. The author presents a brief but concise description of the disease process and the current hypothesis on the mechanism of action of these drugs.

The next chapter entitled "Significance of Melanocyte Stimulating Hormone (MSH)", by A. J. Thody, focuses on the role that MSH plays, the physiological aspects of the hormone, its occurrence, and its secretory mechanism. The review further summarizes the functionality of MSH in mammals, such as its influence on cardiovascular action, various endocrine glands, and the CNS. However, as the author points out, the significance of MSH in man is unknown, except for its possible effect on brain function and adaptive behavior. With references covering the last 25 years, this review will be of interest to investigators in the field of hormonal activity.

The following chapter entitled the "Pineal Gland", by K. M. Shaw, is somewhat related to the previous review on MSH, because of its role on hormonal homeostasis. The author describes the biochemistry, physiology, and pathological consequences of this gland. Since melatonin is the active principle in the pineal gland, the clinical use of this indole in Parkinsonism and epilepsy was reviewed. The general conclusion that this endocrine gland may be the long sought "biological clock" underscores the need for additional study, particularly in the regulatory control of hormones in man.

The chapter entitled "Potential Therapeutic Agents Derived from the Cannabinoid Nucleus", by H. G. Pars, R. K. Razdan, and J. F. Howes, could not have been written by more informed investigators in this field. Although this review of the cannabinoids was sought by the series editors about 10 years ago, its appearance at this time is appropriate because this fascinating class of compounds has reached a turning point if not an end point. The chapter summarizes the pharmacological activities of the carbocyclic cannabinoids (both natural and synthetic) and the heterocyclic analogues appearing in the literature in the last 15 years. The remarkable range of activities of these compounds such as pyschotomimetic, ataxia, analgesia, anticonvulsants, hypnotic, etc. apparently do not despair the authors. However, in the opinion of this reviewer, the principal drawback with the cannabinoids after extensive clinical trials is the lack of biospecificity. The review is very extensive and well organized and together with the next chapter on benzothiophene derivatives represent the highlights of this volume in terms of overall general interest.

The final chapter entitled "Biologically Active Benzo(*b*)-thiophene Derivatives. II." by T. R. Bosin and E. E. Campaigne is a continuing review of the recent literature on these compounds begun by Dr. Campaigne in 1970. The chapter is divided into biochemical, physiological, toxicological, and pharmacological activities. The pharmacological review includes antifertility, antiinflammatory, cardiovascular, diurectic, chemotherapeutic, CNS, and pesticidal agents. In most cases, biological data are compared with those of the corresponding tryptophans, indoles, and benzofurans. Investigators active in this field will find the chapter useful as a reference source.

New England Nuclear **Felix E. Granchelli**

Encyclopedia of the Alkaloids. Volume 3. By John S. Glasby. Plenum Press, New York and London. 1977. 519 pp. 16 × 23.5 cm. $49.50.

The third volume of this encyclopedia includes a number of older alkaloids unlisted in the previous volumes, a number of new compounds which have been recorded in the recent literature, and a rather large contribution to the list of known plant bases resulting from earlier work of several Russian investigators in their studies of the Soviet flora. Many of the structures have not been established, but the listing of botanical origin and physical properties, when known, constitutes a valuable reference to these compounds other than the abstract journals.

A welcome addition is a molecular formula index to the compounds listed in this and the previous volumes. Where indicated, the formulas have been corrected on the basis of new data. Addenda and corrigenda are not listed separately but indicated by an asterisk preceding the entry in the body of the text itself. The compilation would have considerable added usefulness were future volumes, if such are planned, to include some type of index to the taxa from which the alkaloids have been isolated.

Northeastern University **Robert F. Raffauf**

Advances in Drug Research. Volume 12. Edited by N. J. Harper and A. B. Simmonds. Academic Press, New York, N.Y. 1978. 356 pp. 15.2 × 22.9 cm. $33.50.

This volume of the series contains five chapters, beginning with a chapter by M. S. Amer on "Cyclic Nucleotides as Targets for Drug Design", followed by reviews on "Cyclic Nucleotides and the Heart" by W. G. Nayler, "Integrated Control of Trematode

Diseases" by N. O. Crossland, "Chemical and Biological Studies on Indomethacin, Sulindac and Their Analogs" by T.-Y. Shen and C. A. Winter, and "Bromocriptine" by D. Parkes.

The chapter by Amer is an updating of an article on the same subject appearing in *Annual Reports in Medicinal Chemistry*, Volume 9, 1974. The present review expands considerably the original version. Cyclic nucleotides are conviently classified according to their site of action, with emphasis given to those areas where the author feels there exists a reasonable probability for developing an agent for the selective regulation of cyclic nucleotide levels.

Nayler's chapter, the shortest (12 pp) in the book, discusses a rather narrow area concerning cyclic nucleotides and their effect on heart muscle function. The author points out that the desirability of elevating cyclic AMP levels in heart muscle is offset by the fact that raised cyclic AMP levels also mobilize free fatty acids which are themselves arrhythmogenic.

Crossland gives an overview of two parasitic diseases, fascioliasis and schistosomiasis. A mathematical treatment of the biological problem will be of interest only to the specialist in large-scale control of parasitic disease. Various control methods and the epidemiology of the diseases are discussed, but chemotherapy is only a very minor part of this section. This chapter will reach the wrong audience by appearing in this volume. Readers interested in specific drugs, their chemical structures, or directions for future drug research in this area will have to look elsewhere.

The review by Shen and Winter is a masterful account of the major effort at the Merck Sharp and Dohme Research Laboratories aimed at developing new antiinflammatory agents. In a 156 page article, the authors present detailed accounts of the discovery of indomethacin and sulindac from a historical perspective, from the early 1960's to the present. This chapter has value not just as a review of the chemistry, biology, metabolism, mechanism of action, and clinical studies of these two agents but also because the reader gains insight into the drug discovery process. Their rationale for studying indoles and an explanation of the early chemical leads proceeds to a description of the structure–activity relationships developed in this series. Their test systems are described, and the important contribution of the carrageenan rat paw edema model to the success of the project is carefully pointed out. It is rare to find an article where the major participants trace the historical development of a new drug and include the setbacks as well as the successes. Both the novice and experienced medicinal researcher will profit from reading the case histories described in this chapter.

The chapter on bromocriptine by Parkes is a comprehensive up-to-date review of the subject. It covers a broad range of subjects from the multiplicity of dopamine receptors to a complete review of clinical studies of bromocriptine in Parkinson's disease and acromegaly. Certain sections, such as the detailed physiological effects of prolactin and growth hormone, may appeal only to specialists, but overall the chapter is an excellent review of the subject.

In summary, the reviews in this volume cover several areas of importance to those involved in drug research. The book should be of value to those specializing in the particular areas and should be made available in all institutional libraries serving scientists involved in medicinal research. The relatively high price may limit acquisition for personal use to those researchers working in the specific fields reviewed in the book.

Pfizer Central Research **Joseph G. Lombardino**

Advances in Chromatography. Volume 16. Edited by J. C. Giddings, E. Grushka, J. Cazes, and P. R. Brown. Marcel Dekker, New York, N.Y. 1978. xvi + 290 pp. 15.5 × 23.5 cm. $28.75.

This latest volume in the series comprises eight "Chapters", which are self-contained review articles. In general, the reviews in this series have been well written and authoritative. Those included in volume 16 are "Analysis of Benzo(*a*)pyrene Metabolism by High-Pressure Liquid Chromatography", by J. K. Selkirk (36 pp, 59 references); "High-Performance Liquid Chromatography of the Steroid Hormones", by F. A. Fitzpatrick (36 pp, 40 references); "Numerical Taxonomy in Chromatography", by D. L. Massart and H. L. O. De Clercq (36 pp, 31 references); "Chromatography of Oligosaccharides and Related Compounds on Ion-Exchange Resins", by O. Samuelson (36 pp, 64 references); "Applications and Theory of Finite Concentration Frontal Chromatography", by J. F. Parcher (23 pp, 76 references); "The Liquid-Chromatographic Resolution of Enantiomers", by I. S. Krull (35 pp, 138 references); "The Use of High-Pressure Liquid Chromatography in Research on Purine Nucleoside Analogs", by W. Plunkett (37 pp, 40 references); and "The Determination of Di- and Polyamines by High-Pressure Liquid and Gas Chromatography", by M. M. Abdel-Monem (19 pp, 74 references). Author and subject indexes and contents of the preceding volumes are provided.

There is much in this volume which will provide stimulating reading for the medicinal chemist. This reviewer found the articles by Fitzpatrick and Krull especially interesting and useful. The volume reflects the general adoption of LC methods as a means to cope with what Fitzpatrick infers is a goal of enterprising organic chemists: "to perplex the analytical chemist" with continually decreasing drug quantities in pharmaceuticals and ever more miniscule amounts in biological fluids through increasing potency of the compounds synthesized.

Warner-Lambert Research **Lester Chafetz**

Cell Surface Carbohydrate Chemistry. Edited by Robert E. Harmon. Academic Press, New York, N.Y. 1978. xv + 359 pp. 16 × 23.5 cm. $19.50

This text is a record of the Cell Surface Carbohydrate Chemistry Symposium held in conjunction with the American Chemical Society Centennial Meeting in San Francisco, September, 1976. The 17 contributed articles have as their main theme the characterization of cell-surface glycoconjugates of normal and abnormal cells and the roles these glycoconjugates play in cell recognition and communication, neoplastic transformation, immunogenicity, membrane transport, and other recognition processes. In addition, one of the articles deals with the structural basis for saccharide recognition by the lectin concanavalin A, and three other articles deal with the effects of various synthetic carbohydrate analogues on the membrane transport of monosaccharides and nucleosides and on the biosynthesis of glycoproteins.

The various articles are well documented and provide an in-depth view of selected research areas in this burgeoning field.

University of Minnesota **Gary R. Gray**

GLC and HPLC Determination of Therapeutic Agents. Part 1. Edited by K. Tsuji and W. Morozowich. Marcel Dekker, New York and Basel. 1978. xiv + 415 pp. 25 × 18 cm. $37.50.

This book constitutes part 1 of a three-volume series devoted to a review of chromatographic techniques—GC and HPLC—as applied to the analysis of therapeutic agents. Part 1 deals largely with many of the fundamental aspects of GC and HPLC and ancillary techniques. Parts 2 and 3, according to the table of contents, will concern themselves with the specific aspects of analysis of individual classes of therapeutic agents, such as steroids, vitamins, prostaglandins, etc. One's initial reaction to the contents of Part 1 might be that another review of the fundamentals of GC and HPLC could well be totally redundant; after all, numerous, thorough texts and/or monographs on this subject have appeared in the recent literature. Nevertheless, the editors and the authors of the individual chapters have done a most creditable job in putting together a brief and yet comprehensive summary of the up-to-date technology in this area. More significantly, the various chapters form a cohesive unit leading to Parts 2 and 3.

In this initial volume, after a discussion of the essential aspects of the chromatographic theory, much of the remainder is taken up with a consideration of many of the practical aspects of chromatographic analysis, which makes for a very worthwhile contribution. Noteworthy are the chapters on the column selection process and chemical derivatization techniques in GC and HPLC. The literature citations are numerous and should be of great help

to the reader. Particularly significant is the inclusion of a chapter on sample handling and preparation for chromatographic analysis. While somewhat general in nature, this chapter fills a serious gap as it has been frequently overlooked in previous publications of this type. Additional chapters cover the subjects of the mass spectrometer as a GC and HPLC detector, quality control in GC and HPLC, preparative HPLC, and computer interfacing methods. In summary, this is a well-prepared publication which should be valuable to most researchers and analytical chemists working in chromatography. Judging from the quality of Part 1, one should look forward to examining Parts 2 and 3 in this three-volume series.

Northeastern University **Paul Vouros**

Bacterial Transport. Volume 4. Microbiology Series. Edited by Barry P. Rosen. Marcel Dekker, New York, N.Y. 1978. xi + 684 pp. 16 × 23 cm. Swiss Francs 150.00

"Bacterial Transport" presents a comprehensive description and analysis of current knowledge of active transport through the membrane of bacteria. The book begins with a historical analysis of the field, followed by a general description of the methodology used, and then, one-by-one, specific categories of transport systems are covered. The final chapter looks at the molecular mechanisms of transport with emphasis on the bioenergetics of membrane processes. The comprehensive coverage provided makes this the only book to cover bacterial transport phenomena in this much depth and breadth together.

Each contributor was encouraged to summarize briefly his or her area of interest and then provide an intensive look at specific points. Contributors were also encouraged to offer opinion and speculation wherever possible.

"Bacterial Transport" is directed toward students and researchers in biochemistry and microbiology. This book is elementary enough for recommended reading in graduate courses on membrane biochemistry and yet sophisticated and complete enough to be a valuable reference to scientists and investigators of bacterial transport system.

Staff Review

Disposition of Toxic Drugs and Chemicals in Man. Volume 1. Centrally Acting Drugs. Edited by Randall C. Baselt. Biomedical Publications, Canton, Conn. 1978. 306 pp. 16 × 23.5 cm. $22.50.

This first of a two-volume work presents in a single, convenient source the current essential information on the disposition of the chemicals and drugs most frequently encountered in episodes of human poisoning. The data included for each of 129 licit and ilicit drugs affecting the central nervous system relate to the body fluid concentrations of substances in normal or therapeutic situations, concentrations in fluids and tissues of toxicity, and the known metabolic fate of these substances in man. Brief mention is also made of specific analytical procedures which are applicable to the determination of each substance and its active metabolites in biological specimens.

This volume will be of particular interest and use to toxicologists, pharmacologists, and clinical chemists who have need either to conduct an analytical search for these materials in specimens of human origin or interpret analytical data resulting from such a search.

Staff Review

Inflammation and Antiinflammatories. By Edoardo Arrigoni-Martelli. Spectrum Publications, New York, N.Y. 1977. 343 pp. 15 × 23 cm. $30.00.

This book provides a broad view of antiarthritic research from a discussion of possible mediators and modulators of inflammation (first third of book) to agents in use and under clinical study (last third). In between are chapters on the experimental evaluation of antiinflammatories and immunoregulators and on the toxicity, possible mechanisms of action, and clinical evaluation of antiinflammatory agents. Some of the better portions of this book are the discussions in areas of the author's research interests on the clinical use, possible mechanisms of action, and toxicity of penicillamine, gold compounds, and immunoregulants. There are numerous helpful charts and figures showing biological data, though many are not labeled as to source. Presumably they are from the author's laboratory.

An error rate of over 20% in the structural formulas (at least 18) is inexcusable and sad to see. The errors range from carelessly missing double bonds and miscounted hydrogens to more serious errors, including a missing chlorine in bucloxic acid, incorrect ring sizes in colchicine and benzydamine, and loss of a hydroxyl group on metabolism of serotonin (both in structure and as named). Xanthine is consistently misspelled without the h.

There is an unfortunate time delay between the writing and publication of this work, with few references beyond 1974 in the first portion (but some references into 1976 in the last third). Thus, the explosive development in the area of PG endoperoxides, thromboxanes, and prostacyclins beginning in 1975 is missed (cf. *Annual Reports in Medicinal Chemistry*, 1977). Inevitably, alternative clinical candidates have come to the fore; diflunisal (in place of flufenisal) and auranofin (instead of SKF 36914) are not included. There could have been a better integration of some topics. It is several chapters past the one on prostaglandins that the potent inhibition of their synthesis by nonsteroidal antiinflammatory agents is mentioned (under Possible Mechanisms of Action...). The relation of cyclic nucleotide levels to the promotion and inhibition of lysosomal enzyme release, covered in the chapter on cyclic nucleotides, is not mentioned in the preceding chapter on the lysosomal enzymes.

With the qualifications indicated, this book does serve as an introduction to the field and a compilation of much information, but the active researcher will more likely want to rely on the more current excellent reviews in recent *Annual Reports in Medicinal Chemistry* and the faster appearing reports of frequent symposia noted therein.

Riker Laboratories **Robert A. Scherrer**