

De Regis for the PD₅₀ results and Mrs. V. Z. Rossomano for the bioautographic assays.

References and Notes

- (1) G. A. Hardcastle, D. A. Johnson, C. A. Panetta, A. I. Scott, and S. A. Sutherland, *J. Org. Chem.*, **31**, 897 (1966).
- (2) R. D. G. Cooper, P. V. Demarco, J. C. Cheng, and N. D. Jones, *J. Am. Chem. Soc.*, **91**, 1408 (1969); R. D. G. Cooper, P. V. Demarco, and D. O. Spry, *ibid.*, **91**, 1528 (1969).
- (3) D. H. Barton, F. Comer, and P. G. Sommes, *J. Am. Chem. Soc.*, **91**, 1529 (1969).
- (4) J. M. Essery, K. Dadabo, W. J. Gottstein, A. Hallstrand, and L. C. Cheney, *J. Org. Chem.*, **30**, 4388 (1965).
- (5) E. Gaddal, P. Morch, and L. Tybring, *Tetrahedron Lett.*, 381 (1962).
- (6) R. D. G. Cooper, P. V. Demarco, and D. O. Spry, *J. Am. Chem. Soc.*, **91**, 1408 (1969).
- (7) D. O. Spry, *J. Org. Chem.*, **37**, 793 (1972).
- (8) Thin-layer bioautograms were run using a 95% acetone–5% acetic acid system on Analtech silica-gel plates. A 10- μ L solution with a concentration of 1 mg/mL in 0.1 M, pH 7, phosphate buffer was spotted on the plate. The plates were developed and neutralized of 10% ammonia vapors and overlaid on pH 6 *Bacillus subtilis* agar with reference to known concentrations of hetacillin as a control.
- (9) Phenoxymethylpenicillin (*R*)-sulfoxide has been reported to have five times greater gram-positive antibacterial activity than the corresponding (*S*)-sulfoxide: "Cephalosporins and Penicillins: Chemistry and Biology", E. H. Flynn, Ed., Academic Press, New York, N.Y., 1972, p 540.

Book Reviews

Venoms: Chemistry and Molecular Biology. By Anthony T. Tu. Wiley, New York, N.Y. 1977. x + 560 pp. 18 × 25 cm. \$34.50.

It takes but a cursory examination of this volume to recognize that the title does not do justice to the breadth of material contained therein. While our all too limited knowledge of the chemistry and molecular biology of venoms is thoroughly reviewed, there is also a great deal of information about the biological effects of the various venoms at the subcellular, cellular, tissue, and organ levels. In preparing this volume, the author has reviewed the rather extensive literature on venoms from many disciplines.

Most of this book is devoted to snake venoms, where the literature is most abundant; however, arachnid and insect venoms are also covered, and there is a brief discussion of Gila monster venoms. The book is organized into four sections, the first presenting a discussion of nonprotein components of snake venoms. This is preceded by a very brief, but helpful introduction to snakes, their occurrence, their classification, and the general properties of their venoms. Eight chapters devoted to snake venom enzymes and one chapter on enzyme inhibitors comprise the second section of the book. The third section, which occupies almost 60% of the book, is devoted largely to the properties and actions of nonenzymatic proteins found in snake venoms. This section has five chapters devoted to the five families of venomous snakes, eleven chapters dealing with the pharmacological and pathological effects of snake venoms and some of their purified constituents, and a chapter which summarizes attempts at chemical detoxification of snake venoms. There are several chapters in section three which are of particular interest to the medicinal chemist. These present extensive discussions of the chemistry and actions of the neurotoxic, cardiotoxic, and cytotoxic components of snake venoms; and also the effects of venom components on the blood clotting system, the immune system, and nerve growth. Surprisingly, however, one of the few clinical uses of snake venoms, the use of cobra neurotoxin as an analgesic, is not mentioned. The fourth section, some 75 pages, is devoted to venoms from creatures other than snakes. Most of this section is divided between scorpion venoms, spider venoms, and the venoms of bees, hornets, and wasps.

The author has succeeded in providing a broad overview of venoms by incorporating into this volume information abstracted from a very large body of literature. At times, however, it is difficult not to lose sight of the larger picture. There is a tendency to incorporate too much detail and too many examples without adequate discussion. In some instances, detailed factual material is presented which, when read out of the context of the original literature, is confusing or misleading. In some places, the text is so punctuated by examples and references that reading becomes quite tedious. The chapters of greatest interest to medicinal chemists are, fortunately, among the better written ones, thus

making for easy as well as interesting reading.

This volume can provide the medicinal chemist with a very good overview of a fascinating class of pharmacologically active natural products. As a reference book on venoms, its value is more limited but it does provide a useful guide to the literature on venoms.

Virginia Commonwealth
University

Graham C. Windridge

Analysis of Drugs and Metabolites by Gas Chromatography–Mass Spectrometry. Volume 1. By Benjamin J. Gudzinowicz and Michael J. Gudzinowicz. Marcel Dekker, New York, N.Y. 1977. vii + 223 pp. 15 × 22.5 cm. \$23.75.

This is the first in a series of volumes (five are already in publication and others are in preparation) devoted to the GC–MS analysis of drugs and metabolites. In the particular case of volume 1, however, the title is misleading, as the use of mass spectrometry is hardly mentioned. The book is divided into two chapters with 145 and 253 literature references, respectively, and including both author and subject indexes. Chapter 1 is subdivided into three sections: (1) respiratory and blood gases; (2) volatile anesthetics; and (3) a collection of miscellaneous volatile compounds which includes sterilizing agents, organic solvents, and riot-control aerosol irritants. Much of the information presented is a historical review of the development of GC methods (equipment, columns, and detectors) for analyzing these highly volatile substances. The literature cited ranges from work published in the late 1950's to 1974 publications. Representative gas chromatograms, diagrams of specialized equipment, and tables of data (retention times, quantitative determinations, etc.) supplement the discussion. In addition to GC information, the authors present a review of sample preparation and injection techniques. Examples of applications of the GC data to problems in cardiopulmonary research and in anesthesiology are also included.

Chapter 2 is divided into a section on the analysis of ethyl alcohol and a section on the analysis of volatile constituents in human breath, fluids, and tissues. The first section begins with a description of the biochemistry and pharmacology of ethanol, followed by a lengthy discussion of methods for analyzing ethanol in various specimens (blood, urine, tissue, and breath). GC techniques and sampling methods are reviewed. While the focus is on ethanol, analytical data on drugs and other compounds are also presented. Although the authors review metabolic profile analysis in the second section of chapter 2, the treatment is very sketchy. They devote insufficient space to the analysis of volatile metabolites (which is consistent with the subject matter of volume 1), while including a discussion of the analysis of nonvolatile metabolites such as organic acids and steroids (which is an inappropriate inclusion).

In summary, this volume is a valuable review of the evolution of gas chromatographic techniques for analyzing highly volatile compounds from the early days of GC through 1974.

University of Colorado

John A. Thompson

Drug Fate and Metabolism. Volume 1. Edited by Edward R. Garrett and Jean L. Hirtz. Marcel Dekker, New York, N.Y. 1977. xv + 313 pp. 15.5 × 23 cm. \$35.00.

This volume is the first of a new series, "Drug Fate and Metabolism", dealing with various methods and techniques used in the study of drug metabolism and pharmacokinetics in living organisms. Leading authorities in their fields have been chosen to author the eight chapters which make up this volume. Chapter titles (authors) are 1, Autoradiography (Waddell, Marlowe); 2, Autoradiography in Cytopharmacology (Roth, Diab, Watanabe, Dinerstein); 3, Electrophoresis (Conway); 4, Ion-Pair Extraction and Chromatography (Schill, Modin, Borg, Persson); 5, Protein Binding (Chignell); 6, Atomic Absorption Spectroscopy (Harth, Haines, Bondy); 7, Spin Immunoassay (Montgomery, Holtzman, Leute); 8, Animal Care and Use (Ward, Elsea).

Each chapter is well written and well documented. It includes a discussion of the background and theory of every method or technique, its uses, limitations, pitfalls, and future potential. Minimal theoretical treatment of a method is included whenever necessary for proper evaluation of the results presented. Numerous examples from the literature are included to demonstrate the practical application of each method in drug metabolism and pharmacokinetic studies. Many chapters contain figures and tables from the available literature on appropriate topics. Each chapter has a selected, adequate, and updated bibliography. Thus, this series may serve as a source of material and provide a background for those interested in using any of these techniques. A subject index and an author index are included which contribute to the usefulness of this volume.

In summary, this volume and future volumes in this series might provide a useful reference on methods and techniques for any research scientist investigating the fate of drugs in living organisms.

Northeastern University

Simon H. Kuttub

Foreign Compound Metabolism in Mammals. Volume 4. Specialist Periodical Reports. Edited by D. E. Hathway. The Chemical Society, Burlington House, London. 1977. 14 × 22 cm. xii + 411 pp. \$55.00.

This volume of the Specialist Periodical Reports series reviews literature published during 1974–1975. The book is divided into four chapters which present comprehensive coverage of appropriate literature in a factual dialogue, replete with structural representation. In the first chapter, Drug Kinetics, by P. G. Welling, several reviews of drug absorption, bioavailability, and drug distribution and elimination are cited in the introduction. This section is followed by specific coverage of various drugs arranged by pharmacological class. In part I of the second chapter, Biotransformations I: Drugs, Food Additives and Contaminants; Carcinogens; and Toxins, by D. E. Hathway, the rapid growth in the field of drug metabolism is reflected by a list of 13 new books, pertinent to the discipline, published during this period. Specific reviews are presented for immunosuppressants, diagnostic agents, radiation protection agents, anti-infective agents, cancer-chemotherapeutic agents, anesthetics, oral contraceptives, and for drugs acting on the following systems: alimentary, cardiovascular, central nervous system, endocrine, genito-urinary, metabolic-nutritional, and respiratory system. Literature for food additives and contaminants, carcinogens, and toxins is also reviewed. Highlights of this section include elucidation of the metabolic pathways for the interrelated benzodiazepines, several carcinogenic mechanisms, biotransformations of lipid-soluble vitamins, and the implications of sweetening agents in nutrition. In part II to this chapter, agricultural and industrial chemicals and miscellaneous organics are reviewed by C. T. Bedford. Chapter 3, Mechanisms of Biotransformation, by D. H. Hutson, is divided into four sections covering oxidation, reduction, hy-

drolysis, and conjugation. Oxidative mechanisms receive the most attention with considerable discussion of the various reactions catalyzed by microsomal monooxygenases, characteristics of the monooxygenase electron-transport chain, and inhibition and induction mechanisms. Chapter 4, by J. D. Baty, appropriately concludes the volume by reviewing Species, Strain, and Sex Differences in Metabolism.

Although the factual style of the presentations does not lend itself to exciting reading, such style is dictated by the sheer magnitude of the review effort (tabulation reveals a total of 2172 references), and the job at hand must be regarded as having been admirably accomplished by each of the authors. Similarly, lack of background development for the various topics and the aforementioned style preclude the use of this book as a readily readable text, and the volume would seem most appropriate as a library reference rather than as a personal copy. In this regard, its compound and author indexes are an asset.

Arnar-Stone Laboratories

Paul W. Erhardt

Nutrition and the Brain. Volumes 1 and 2. Edited by R. J. Wurtman and J. J. Wurtman. Raven Press, New York, N.Y. 1977. Volume 1: 16 × 24 cm, xi + 324 pp, \$25.00. Volume 2: 16 × 24 cm, vii + 313 pp, \$25.00.

These first two volumes and later ones to come are intended to be multidisciplinary in approach and therefore useful to brain scientists, nutritionists, and others with interest in one or both of these areas. Mostly the chapters (by different authors) are clearly written and are interesting even to the nonexpert. The Wurtmans are able to show their creativity though their only writing in these volumes consists of brief prefaces. Their main contribution is in assembling a diverse group of essays to give the reader a different perspective and overall view of nutrition and the brain than he is likely to have had before.

Volume 1 includes chapters on the natural diet of humans and other primates, cerebral nutrition and energy metabolism, and others on the availability of amino acids, folic acid, choline, and B vitamins to the brain. Volume 2 deals with control of feeding behavior and with the effects of undernutrition on brain morphology and biochemistry and on behavior.

Most chapters are thoroughly referenced (one has 827 references) with reasonably up-to-date citations. Inevitably some small errors have crept into the books, but I detected no major ones. Chemists may notice a wrong formula for a Schiff base and a five-bonded carbon. Indexes for multiauthor works are difficult to prepare, and the indexes in these two volumes are commendable despite some deficiencies (for instance, the listings under tryptophan in the index to Volume 2 are incomplete).

The volumes are not written with pharmacological or medicinal emphasis. Medicinal chemists interested in anorexic drugs would profit by reading the chapters on control of feeding behavior and on natural diet. Though there is only limited direct discussion of pharmacological control of appetite or of obesity, nutritional considerations important to these areas are discussed in depth. Some additional sections might interest medicinal chemists who work on CNS drugs, e.g., nutritional influences on the synthesis of brain transmitters. Since all of us eat and have brains, much of the volumes have general interest.

I am impressed with these volumes but suggest that few medicinal chemists will want to add them to their personal libraries.

Eli Lilly and Company

Ray W. Fuller

Cardiovascular Pharmacology. Edited by Michael J. Antonaccio. Raven Press, New York, N.Y. 1977. ix + 534 pp. 16 × 24 cm. \$22.50.

"Cardiovascular Pharmacology" has been written with the intent of serving as a basic text for graduate students in the biological sciences. Certainly there has been a need for such a text in the past, and several have been published recently.

The amount of research taking place in the broadly defined area of cardiovascular pharmacology is overwhelming. It is truly ambitious to attempt to evaluate, simplify, and integrate the

resultant data into a textbook format. The standard reference texts of pharmacology (e.g., Goodman and Gilman's) have heretofore been utilized in the absence of a single specific cardiovascular text. The question then arises: Does this volume offer sufficient advantages over analogous portions of available multitopic texts?

The text assumes little prior knowledge and begins with introductory physiology as related to the regulation of circulatory function (cardiac and autonomic nervous system). Chapters dealing with pharmacology include Renal, Renin-Angiotensin, Prostaglandins, Hypertension, Antiarrhythmic agents, Inotropic agents, Shock therapy, Platelet function, and Antianginal agents. Of the eleven chapters, no more than two are authored by the same person. This latter situation detracts from the intent of this text to achieve a logical and unified presentation. In fact, the sequence of chapters does not appear to move logically one to the next, but each rather stands upon itself. References are uniformly adequate and average 15% of chapter length. Figures (including drug structures, anatomical representations, and data) are appropriate in number.

In my opinion, there is some variability in the quality of chapters. The chapter on hypertension contains a well-integrated description of etiology and pathology, but the pharmacology, which should have been the focus of the chapter, was given less thorough treatment—several paragraphs per drug. The chapter on central neurochemical mechanisms is also excellent in describing the physiologic control of cardiovascular function, but the centrally active pharmacologic agents are reviewed in a subsequent chapter rather lightly and distant from the physiology discussion. On the other hand, the chapter on antianginals is excellent.

The strong point of this text is its inclusion of extensive physiology data. However, this is offset by the spotty depth of drug information. Another weakness is the absence of dosage considerations or pharmacokinetic data for the various agents. Overall, this text contains much more cardiovascular information than standard pharmacology compendia; however, it probably contains less pharmacology information per se.

Recognizing the difficulty of preparing a broad cardiovascular text, one should perhaps not expect perfection, especially in the initial edition. Revision and reorganization could vastly improve this text.

Northeastern University

Richard C. Deth

Cholesterol. By John R. Sabine. Marcel Dekker, New York and Basel. 1977. 22.7 × 15.2 cm. xii + 489 pp. \$25.00.

In his preface to this volume, the author states that he intends to discuss (1) the role of cholesterol in mammalian systems; (2) its biosynthesis, uptake, elimination, and the factors which regulate them; and (3) the evidence which implicates cholesterol in the genesis of atherosclerosis, cancer, and cholelithiasis.

In view of the enormous importance of these problems for all of us, this orientation is perfectly legitimate, and the topics mentioned appear to be treated well and comprehensively. It seems regrettable, though, that the title of the book does not more clearly indicate its content and that it creates the impression of giving a wider coverage than it actually provides. "Cholesterol", without further qualifications, would seem to suggest a monograph which discusses *all* significant aspects of the topic. As it is, the book brings rather little on the chemistry of cholesterol; the account of the elucidation of its structure—a fascinating story if there ever was one, although of course not a recent development—gets little more than 1 page; the equally impressive biosynthesis does better but is, again, rather sketchy in the

treatment of the intermediates after lanosterol. The role of cholesterol as a parent substance of the steroid hormones would likewise have deserved a more detailed coverage.

In contrast, the discussion of the physiological, pathological, and nutritional aspects is thorough and interesting. The merit of a volume presenting the essential findings contained in the enormous and diffuse literature requires no further comment. In many places, the author points out the gaps in the existing knowledge. The book should thus be of value for research workers in the fields of physiology, pathology, and adjacent areas of biochemistry and to medicinal chemists engaged in research on drugs influencing the biosynthesis of cholesterol.

The volume includes an impressive bibliography of 1556 titles and also that useful device which, like so many others, is rapidly becoming extinct: an author index. Less essential are the cartoons which occupy about one-third of the first page of each of the 14 chapters. A bit of humor has its place in science, but the connection of these drawings with either the contents of the volume or with humor or wit seems too remote to justify the expenditure of valuable space and newsprint. Apart from this criticism, however, and the earlier ones about the discrepancy between title and contents, I think that the book should be valuable to research workers concerned with role, function, uptake, and elimination of cholesterol.

National Institutes of Health

Ulrich Weiss

Topics in Bioelectrochemistry and Bioenergetics. Volume

1. Edited by G. Milazzo. Wiley, New York, N.Y. 1977. 15.5 × 23.5 cm. ix + 378 pp. \$41.00.

This, the first in a series of volumes concerning the use of electrochemical techniques in studying biochemical problems, was initiated by Professor G. Milazzo, who has been instrumental in organizing interdisciplinary meetings and the first journal in this area. This first volume does not provide much insight into the overall approach of the series. It contains five major chapters, which are general in nature and cover a wide range of topics, including membrane electrochemistry and electrochemical thermodynamics of metabolism, as well as several on more applied polarography and electrochemical studies. The individual articles are well written, although some are quite lengthy and detailed and, I would suspect, tell more about the electrochemistry of some biochemical systems than biologists care to know.

One can probably best evaluate this initial volume of the series by asking two questions: (1) how does it serve specialists in this interdisciplinary field and (2) would it serve as an introduction to would-be new workers in the area? With regard to the first question, although a limited area is covered, it is an excellent reference source. I doubt, on the other hand, that any new workers will find it of much value because of the (necessarily) limited selection of topics. Certainly it would seem to have little to offer medicinal chemists with the exception of the chapter on bioenergetics of metabolism. The individual chapters are certainly specifically useful to researchers in various subdisciplines of biochemistry. However, I would suggest this book is much more of a library reference volume. At the price of \$41.00 for the single volume, it is hard to justify buying it on an individual purchase basis. While one probably can make that statement about almost any scientific book these days (it would seem that publishing costs are somehow bioenergetically coupled with petroleum prices), these particular volumes do not appear to be something one would refer to each and every day—rather, a library source would be quite sufficient.

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