

fully to other contamination problems and other areas of interest.

- (1) D. V. Herbst, *J. Pharm. Sci.*, **66**, 1646 (1977).
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BOOKS

REVIEWS

Drug Design, Vol. VIII. Edited by E. J. ARIENS. Academic, 111 Fifth Ave., New York, NY 10003. 1979. 420 pp. 15 × 23 cm. \$42.00.

This book is the eighth member of a continuing set, which collectively comprises Volume 11 of the series of monographs entitled "Medicinal Chemistry." Dr. Ariens has produced another valuable book. As stated in the preface of this volume, the term "drug" is to be interpreted in the widest sense. Indeed, this volume includes such diverse agents as synthetic sweeteners, ionophores, and potential environmental pollutants.

In the first chapter, Martin discusses "Advances in the Methodology of Quantitative Drug Design." This chapter is a systematic survey of the approaches available for finding the substituent group giving optimum activity from a lead compound either by batch or stepwise selection of new derivatives. The parameters for describing electronic, steric, and, particularly, lipophilic effects of substituents are considered. Considerable attention is devoted to theoretical models for the distribution of drugs into different compartments depending on their physicochemical properties. Finally, the information that can be obtained by regression and discriminate analyses is discussed. The most valuable aspect of the chapter probably is the many caveats concerning the limitations and pitfalls of quantitative structure-activity relationship methods.

In the second chapter, Kirschner and Kowalski deal with the "Application of Pattern Recognition to Drug Design." The first portion covers the general methodology of pattern recognition, and the second portion covers applications to drugs. Although development of this powerful mathematical tool has been initiated, much more work is needed.

In Chapter 3, the design of drug delivery systems that will release a constant amount of drug over a long period is discussed by Chandrasekaran, Theeuwes, and Yum. This chapter primarily describes the features and theory behind three currently available systems; OROS Theophyllin for oral use, a transdermal scopolamine system, and the Alzet osmotic minipump. Chapter 4 is an excellent discussion of the use of receptor binding data for the design of steroid hormones by Raynaud, Ojasoo, Bouton, and Philibert. The general techniques of receptor isolation and displacement of bound, radiolabeled ligands for various hormonal activities are presented. Then, the specific structure-activity relationships for receptor binding of estrogens, progestins, androgens, and mineralocorticoid and glucocorticoid hormones are considered. The relationship between receptor binding and *in vivo* activity is discussed last.

The fifth chapter, authored by Crosby, DuBois, and Wingard, covers synthetic sweeteners. There is an interesting discussion of the theory of taste and the known structure-activity relationships for sweet substances; however, too much basic material on molecular interactions, Hansch treatment, *etc.*, is included that is covered elsewhere in the series and detracts from this chapter. Chapter 6, "Prospective Assessment of Environmental Effects of Chemicals," by Hueck-van der Plas and Hueck is concerned with the test systems that can be used to predict the environmental impact of chemicals. This chapter probably will be of more interest to researchers dealing with agricultural chemicals rather than to those concerned with drugs for human use.

The final chapter is fascinating; it describes the "Design of Selective Ion Binding Macrocyclic Compounds and Their Biological Applications" and was authored by Izatt, Lamb, Eatough, Christensen, and Rytting.

The factors affecting the selective-ion complexation by crown ethers and derivatives are discussed in detail.

This volume generally is well written and free from typographical errors. Every medicinal chemist should find something of interest.

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Foreign Compound Metabolism in Mammals, Vol. 5. A Review of the Literature Published During 1976 and 1977. Senior Reporter, D. E. HATHWAY. The Chemical Society, Burlington House, London W1V 0BN, England. 1979. 567 pp. 13 × 22 cm. Price \$70.00. (Available from the American Chemical Society, 1155 16th St., N.W., Washington, DC 20036.)

This volume is an organized condensation of almost 3000 major metabolism-pharmacokinetics papers published in 1976 and 1977. The first half of the volume consists of five subject-oriented chapters, which are followed by eight product-oriented chapters.

Chapter 1, Drug Kinetics by P. G. Wellington, is the longest chapter (86 pages) and has the highest density of references (758 total references for a mean of 8.6 references/page). This chapter has 20 well-selected sections and deals with prostaglandins, ethanol, inorganic ions, and diagnostic agents in addition to a wide variety of drug classes. Chapter 2, Enzymic Mechanisms of Oxidation, Reduction, and Hydrolysis by P. Bentley and F. Oesch, interestingly covers the assigned terrain. Many readers will appreciate the subsection on epoxide hydratase for its inclusion of topics such as control and induction and occurrence in extrahepatic tissues.

P. C. Hirom and P. Millburn cover Enzymic Mechanisms of Conjugation (Chapter 3) in a fairly lively fashion. They briefly discuss new conjugation reactions and amino acid conjugations, and they animate their treatment of "the usual suspects" by reporting the tissue distribution of the enzymes responsible for conjugations with glucuronic acid, sulfate, and glutathione. In Chapter 4, J. D. Baty deals selectively and well with Species, Strain, and Sex Differences in Metabolism. Beside discussing comparative catabolic and conjugation reactions, Baty focuses on comparative differences in biliary excretion. The final subject-oriented chapter, Mechanisms of Chemical Carcinogenesis by D. E. Hathway, has this reviewer's enthusiastic endorsement for its interesting, valuable, and topical content. Its 54 pages utilize 358 well-chosen references that are integrated superbly.

The first product-oriented chapter has a more pharmacological orientation than do the others. This chapter, the Effect of Drugs on the Central Nervous System by B. E. Leonard, integrates mechanisms of action with biotransformations. C. Rhodes divides his report on Cardiovascular Drugs into sections dealing with thrombosis, hypertension, and cardiac disorders and summarizes some particularly interesting interspecies differences in biotransformation pathways of numerous drugs. L. G. Dring and P. Millburn address the metabolism of Sympathomimetic Amines and Bronchodilators and underscore many differences between *in vivo* and *in vitro* biotransformation routes.

The short chapter on Anti-Infective Agents by P. Johnson and J. D. Coombes deals with the biotransformation of some unusual structures while covering antiparasitics, antibiotics, antimycotic agents, antidiarrheals, antitubercular drugs, antivirals, and sulfonamides. Interesting interspecies and *in vivo-in vitro* comparisons pervade the coverage of Prostaglandins and Steroids by G. R. Bourne and D. E. Hathway. In the chapter on Food Constituents, D. E. Hathway objectively evaluates the saccharin and cyclamate problems under the heading of sweetening agents and deals with single-cell proteins, flour, vitamins, urethane and diethyl dicarbonate, food colorants, flavoring principles, and natural constituents.

C. T. Bedford reviews Agricultural Chemicals in sections on animal health products, rodenticides, insecticides, herbicides, and fungicides. This chapter is enlivened by descriptions of an anticoagulant with selective toxicity for vampire bats, an anthelmintic that is degraded to benzene, and an unusual example of *N*-dearylation. C. T. Bedford also contributed the final chapter, Industrial Chemicals and Miscellaneous Organic Compounds, which contains sections on aliphatic compounds, aromatic compounds, heteroaromatic compounds, and organometallic and inorganic compounds. Like the previous chapter, this chapter summarizes the biotransformation of many important environmental contaminants. Some of the more interesting reactions involve the formation of a metabolite of 4-dimethylaminophenol, which contains three glutathione residues attached to a single aromatic ring, and the formation of phosgene and carbon monoxide as metabolites.

The few typographical errors in this book are readily understood, as are the misspellings of the names of some prominent scientists in the author index. The compound index lists only substrates, not metabolites. More unfortunate is the absence of a comprehensive subject index that would enable readers to use the volume cross-sectionally; for example, to collect valuable information on studies performed in the wide variety of species covered in the volume (including humans, subhuman primates, sheep, cattle, lambs, pigs, tree shrews, and insects) or on reaction types or sites of biotransformation.

Overall, this volume is recommended highly as an organized source of metabolism-pharmacokinetics literature on important xenobiotics of many kinds. One of its major achievements is that it demonstrates the richness of opportunities for valuable future investigations.

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Quality Control in the Pharmaceutical Industry, Vol. 3. Edited by M. S. COOPER. Academic, 111 Fifth Ave., New York, NY 10003. 1979. 292 pp. 15.5 × 22.5 cm. Price \$29.50.

Volume 3 of this series consists of six chapters covering the interpretation of current good manufacturing practice regulations, the auditing function in the total control of quality, filtrative sterilization with porous membranes, bioavailability standards for pharmaceutical products, quality control of poliomyelitis vaccines, and quality control of ophthalmic products.

The chapter by A. S. Arambulo on "Interpretation of Current Good Manufacturing Practice Regulations" exceeds 100 pages and presents an excellent comprehensive review. The concept and parts of the regulations are discussed and illustrated by examples. This chapter should be of special interest to graduate students and recent graduates who are joining the pharmaceutical industry and to management personnel who have not been trained as physical or biological scientists.

The chapter on "Auditing Function in the Total Control of Quality" by A. J. Schmitz, Jr., reviews the quality control of the product and the quality control of operations and control techniques. Auditing includes managerial review of quality assurance to a firm to procure, produce, distribute, and control all phases of the function of a firm including facilities, personnel, standards, and the auditing method.

The chapter on "Filtrative Sterilization with Porous Membranes" by T. H. Meltzer and R. C. Lukaszewicz is concerned with the technology of porous membranes. It does not discuss sterility testing, but it does discuss pore properties, manufacture, filter rating, retentivity, and types of filters used. Prefilters and filter construction, design, preparation for use, and usage are discussed.

The chapter on "Bioavailability Standards for Pharmaceutical Products" by R. V. Smith and G. J. Yakatan is the shortest chapter. It

presents elemental remarks on bioequivalency and gives an overview of analytical methods and their selection in bioavailability studies.

The chapter on "Quality Control of Poliomyelitis Vaccines" is by P. B. Stone. A review is given of tissue culture and animal testing of inactivated polio vaccine and the testing of live polio vaccine for adventitious agents, mycoplasma, and identity.

The chapter on "Quality Control of Ophthalmic Products" by J. D. Mullins and T. C. Fleming presents an elemental review of the anatomy of the eye, absorption, ophthalmic dosages, formulation, and processing.

This volume presents useful information for those seeking an overview of quality control in the specific areas covered; however, pharmaceutical scientists currently involved in quality assurance may find the treatment too cursory.

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Handbook of Analytical Derivatization Reactions. By DANIEL R. KNAPP. Wiley, One Wiley Drive, Somerset, NJ 08873. 1979. 741 pp. 15 × 23 cm. Price \$34.95.

This book presents a collection of analytical derivatization methods for gas chromatographic, liquid chromatographic, and mass spectral analysis. The reactions involve only the covalent derivatives of organic compounds formed prior to analysis. Part I briefly discusses the uses of analytical derivatization, the types of derivatives formed, and a typical apparatus employed in such reactions.

Part II features 15 sections concerning the derivatization of particular compound types. Among the classes considered are steroids, prostaglandins, and drugs. An overview of derivatization for the sample type is given along with specific derivatization methods. For each major compound type, the derivatization reactions are organized further into subsections of the compound type and within each subsection according to the type of derivative formed. Each method description includes structural formulas for the reaction, experimental directions, and references to the original literature. Sections on derivatives for substituent location by mass spectrometry and derivatives for chromatographic separation of optical isomers also are included.

Part III contains author and general subject indexes along with appendixes listing the composition of brand name reagents and U.S. and foreign suppliers of reagents and apparatuses used for analytical derivatization. An index of the derivatives and reagents discussed in Part II also is included.

This book should serve both as a self-contained methodology reference and as an introduction to the literature on analytical derivatization.

Staff Review

Pharmacognosy, 11th ed. By G. E. TREASE and W. C. EVANS. Cassell and Collier Macmillan Publishers Ltd., 35 Red Lion Square, London WC1R 49G, England. 1978. 784 pp. 16 × 23 cm. Price \$32.50.

This is the 11th edition of a longstanding series of revisions that trace their origin to the original work in 1934. The latest revision reflects the increasing awareness and knowledge of the active constituents of natural, particularly vegetable, drugs. The book has been partially rearranged from the 10th edition with lengthy revisions in the parts dealing with drug sources, including production and quality control and the consideration of the various classes of drugs of biological origin.

The book is composed of eight parts with a total of 41 chapters, including an index. It is liberally filled with numerous structural formulas, pictures (none in color), tables, and illustrations. Part 1 (Chapters 1-3) deals with drug classification, the literature of pharmacognosy, and plant nomenclature and taxonomy. Part 2 (Chapters 4-7) covers plant morphology, anatomy, histology, and cellular content. Part 3 (Chapters 8-12) discusses the botanical and chemical characteristics of the more important orders and families of both nonflowering and flowering plants with references taken from Volumes 74-84 of *Chemical Abstracts*. Part 4 (Chapters 13-18) includes a discussion of the sources of crude drugs, drug production, quality control, drug deterioration, and plant growth regu-