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## BOOKS

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### REVIEWS

**Current Concepts in the Pharmaceutical Sciences: Dosage Form Design and Bioavailability.** Edited by JAMES SWARBRICK. Lea & Febiger, Philadelphia, PA 19106, 1973. xi + 230 pp. 18 × 26 cm. Price \$19.50.

The first volume in this series [reviewed in *J. Pharm. Sci.*, **61**, 319(1972)] dealt with several general aspects of biopharmaceutics and pharmacokinetics and partly laid the groundwork for this second volume. The contributors orient their chapters toward assessing bioavailability, showing the significance of variable bioavailability, and indicating ways in which such variability might be overcome.

The first of the six chapters of the book is by S. A. Kaplan who provides a useful review of biopharmaceutics in the preformulation stages of dosage form development. It begins with a brief consideration of how the physicochemical properties of the drug and *in vitro* tests such as dissolution and permeability measurements provide useful input into planning a dosage form. Protocol design, execution of bioavailability studies, pharmacokinetic methods of data analysis, and demonstration of bioavailability problems are the major topics covered.

W. H. Barr takes a unique systems analysis approach to examine the variables that are interspersed between the dosage form and the ultimate clinical effects of the drug. Physiological, pathological, and pharmacokinetic functions including bioavailability are expressed as linear or nonlinear gains which relate the system input and output. A large number of clinically relevant bioavailability problems are provided in this systematic approach to clarification of the role of bioavailability as a primary variable in a sequence of pharmacokinetic and pharmacological factors which ultimately determine both the clinical effects and the risks of drug usage in diverse patient populations.

The third chapter is a useful survey of the effect of formulation additives on drug bioavailability from oral solutions and suspensions by S. L. Hem. Factors that can alter the dissolution and bioavailability of drugs are considered such as type of vehicle and buffer system and presence of sugars, surface-active agents, chelating agents, viscosity-inducing agents, dyes, adsorbents, and crystal growth inhibitors.

W. G. Gorman and G. D. Hall provide a comprehensive treatment of drug absorption from inhalation aerosols. They initially review the normal and pathological anatomy and physiology of the respiratory system. Much of the chapter is concerned with the physicochemical factors of importance in aerosol biopharmaceutics with respect to the formulation of particles and their deposition in various parts of the respiratory system. The final section deals with the complexities and limitations of current mathematical models for inhalation and lung clearance of drugs and drug particles.

Statistical considerations in the design and interpretation of bioavailability trials are crucial topics which have previously lacked clarification by someone with expertise in both pharmacokinetics and biostatistics. W. J. Westlake furnishes an excellent chapter which should provide rational statistical guide-

lines for all scientists who perform bioavailability studies. The major performance characteristics of a drug formulation are identified as the bioavailability, the blood concentration *versus* time pattern (a multivariate characteristic), and particular univariate properties (*e.g.*, peak blood level). The use of statistics in the design and analysis of bioavailability studies to compare such parameters is lucidly presented and a detailed set of analyzed data nicely demonstrates the statistical methodology.

M. Rowland authors the sixth chapter which is a quantitative examination of the influence of various physiological factors on drug bioavailability from oral dosage forms. Events prior to hepatic distribution, including GI biotransformation and local blood flow, and the influence of hepatic elimination, including use of clearance concepts and the role of hepatic extraction of drugs, are reviewed. A number of linear and nonlinear pharmacokinetic relationships are provided along with data simulations which complement examples from the literature describing most physiological factors affecting bioavailability.

All chapters of the book are amply illustrated, currently documented, and the approach to many of the topics is often innovative. The present clinical, governmental, and industrial activities in seeking optimal bioavailability of drug products, make it a useful and timely publication. The editor and authors have succeeded in providing both an extensive review of the area as well as basic methodology for recognizing and avoiding bioavailability problems with new products.

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**Aliphatic, Alicyclic, and Saturated Heterocyclic Chemistry,** Specialist Periodical Reports, Volume 1 (in three parts). **Part I: Aliphatic Chemistry.** vii + 213 pp. **Part II: Three- and Four-Membered Rings (Carbocyclic and Saturated Heterocyclic).** ix + 517 pp. **Part III: Five- and Six-Membered Rings; Medium Sized Rings; Bridged and Caged Systems (Carbocyclic and Saturated Heterocyclic).** xi + 567 pp. Senior Reporter, W. PARKER. The Chemical Society, Burlington House, London, W1V 0BN, England, 1973. 14.5 × 22 cm. Price £20.00 (all three parts).

This volume, the first of the Specialist Periodical Reports of the Chemical Society published under this title, surveys the literature published during the 2-year period of 1970-1971. Subsequent Reports on the areas included in the three Parts of this volume are to be published annually. Part I consists of three chapters. Chapter 1 by R. S. Atkinson deals with acetylenes, allenes, and alkenes. Chapter 2 by E. W. Colvin reviews aliphatic compounds

with other functional groups (alkanes, carboxylic acids, esters, amides, nitriles, aldehydes and ketones, amines, alkyl halides, alcohols, and sulfur compounds). It is the stated intention of the publisher to devote the third chapter of aliphatic chemistry to a "class of related natural products." In this volume, the third chapter of Part I, by F. D. Gunstone, reports various facets, from physical properties to biological reactions, of the literature on fatty acids and related compounds. Part II also consists of three chapters: Chapter 1 by H. Maskill reviews developments in the chemistry of three- and four-membered carbocyclic rings; Chapter 2 by D. R. Boyd and B. J. Walker summarizes progress on three-membered heterocyclic rings; and Chapter 3 by the same authors similarly treats four-membered heterocyclic rings. The basic format is similar for each chapter of Parts I and II: first, syntheses of each class of compounds are surveyed and, then, reactions of each class are subdivided by reaction type and are reviewed. However, physical properties, theoretical and structural considerations, mechanistic interpretations, and published reviews of the various topics are either covered in separate sections or are interwoven with the chemistry in the sections dealing with reactions.

Part III is comprised of six chapters devoted to the following areas: (1) five- and six-membered, saturated (and partially saturated) heterocyclic rings by F. G. Riddell; (2) conformational analysis of five- and six-membered saturated heterocyclic rings also by F. G. Riddell; (3) five- and six-membered carbocyclic rings by D. G. Morris; (4) medium- and large-ring carbocyclic and saturated-heterocyclic rings by M. S. Baird; (5) bridged carbocyclic rings by J. M. Mellor; and (6) bridged, saturated heterocyclic rings also by J. M. Mellor. Both syntheses and reactions of the numerous types of structures are again summarized; but, as one should expect from the nature of the subject matter, conformational analysis, structural properties and theory, physical properties, and mechanistic aspects are prominent, if not dominant, in Part III.

All three parts of this volume contain a wealth of information organized systematically and presented, generally, in concise form. The various chapters are not mere recitals of what was published during the 2-year period; rather, the basic substance of the significant literature is presented for the reader. In general, coverage of the significant, but not the routine, literature is comprehensive, particularly in those chapters dealing with the various carbocyclic and bridged-ring systems and three-membered heterocycles. The liberal use of structural formulas and equations is an invaluable aid to the reader or rapid scanner.

The areas included in Part I obviously constitute part of general or basic organic chemistry; most of the other areas are equally fundamental because of their importance to structural theory and reaction mechanisms. Because of the nature of the material covered by this Specialist Report, most organic chemists, as well as the specialist interested in a particular area, will profit by reading or by browsing through the parts of this volume. Those inter-

ested in the more specialized areas of Parts II and III are provided with the opportunity to review, and to gain an overall view of, recent significant developments in their areas of interest. For others, the great value of this volume derives from the fact that it brings together in one place recent progress in syntheses and reactions and in many of the fundamental concepts of organic chemistry. For research, development, or teaching, this Report and subsequent annual volumes, if they maintain the quality of Volume 1, should be a valuable reference source for many years.

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## NOTICES

*Angewandte Biopharmazie.* By W. A. RITSCHER. Wissenschaftliche Verlagsgesellschaft MBH, Stuttgart, Germany, 1973. 17 × 24 cm. Price DM 138 (German).

*Microsomes and Drug Oxidations.* Edited by R. W. ESTABROOK, J. R. GILLETTE, and K. C. LEIBMAN. Williams & Wilkins, Baltimore, MD 21202, 1972. 486 pp. 17.5 × 26 cm. Price \$30.00.

*Pharmakokinetik.* By E. GLADTKE and H. M. von HUTTINGBERG. Springer-Verlag, Berlin, Germany, 1973. 13.5 × 20.5 cm. Price \$7.00 (German).

*Heroin and Behaviour.* By GARY B. STIMSON. Halsted Press, 605 Third Ave., New York, NY 10016, 1973. 14 × 22 cm. Price \$11.50.

*Principles of Immunology.* Edited by N. R. ROSE, F. MILGROM, and C. J. van OSS. Macmillan, 866 Third Ave., New York, NY 10022, 1973. 16 × 24 cm. Price \$14.95.

*Locomotion of Tissue Cells,* Ciba Foundation Symposium 14. Associated Scientific Publishers, P.O. Box 1270, Amsterdam, The Netherlands, 1973. 17 × 24 cm.

*Haemopoietic Stem Cells,* Ciba Foundation Symposium 13. Associated Scientific Publishers, P.O. Box 1270, Amsterdam, The Netherlands, 1973. 17 × 24 cm.

*Medical Management of Primary Hypertension.* By L. B. PAGE and J. J. SIDD. Little, Brown, 34 Beacon St., Boston MA 02106, 1973. 103 pp. 14 × 21 cm. Price \$9.50.

*Synthetic Methods of Organic Chemistry.* Edited by W. THEILHEIMER. S. Karger, Basel, Switzerland, 1973. 585 pp. 15.5 × 23 cm. Price \$27.70.