

## REVIEWS

**Assay of Drugs and Other Trace Compounds in Biological Fluids. Methodological Developments in Biochemistry. Vol. 5.** Edited by ERIC REID. North-Holland, 52 Vanderbilt Ave., New York, NY 10017. 1976. 254 pp. 17 × 25 cm. Price \$24.95.

This book consists of the proceedings of a "Techniques Forum" held in September 1975 at the University of Surrey, Guildford, United Kingdom. It is divided into four sections. The first section deals with advances in instrumental techniques and includes GLC-mass spectrometry, polarography, luminescence, quantitative TLC, and high-performance liquid chromatography. The second section deals with general analytical strategy and discusses chromatographic approaches, affinity methods, and ion-pair solvent extraction.

The third section deals with sample preparation and discusses logical approaches one can follow for different biological samples. The fourth section describes methodology for 16 different compounds extracted from biological fluids using the analytical instrumentation and techniques described in the preceding sections.

The first three sections of the book are written in such a general fashion that an experienced researcher may gain some useful knowledge, although a novice may not. The fourth section, however, which comprises most of the book, presents some very useful approaches to the assay of a variety of drugs from biological fluids. This section should definitely help both the novice and experienced researcher concerned with method development.

The ever increasing need to monitor drugs in biological fluids with enhanced sensitivity and specificity makes this book a very practical reference work for the analytical chemist.

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**Drug Disposition and Pharmacokinetics, 2nd Ed.** By STEPHEN H. CURRY. Blackwell Scientific Publications, 85 Marylebone High Street, London W1, England. 1977. 275 pp. 15 × 23 cm. Price \$18.00. Distributed by Lippincott, East Washington Square, Philadelphia, PA 19105.

The book is primarily a teaching text directed to the undergraduate student. The text covers a wide range of subjects, ranging from the chemical properties of drugs to pharmacological relationships, and does not attempt to treat any one topic in depth.

This edition has similar content and format to the first edition. The only significant changes are the separation of the topic of drug-protein binding into a new chapter, expansion of the chapter on quantitative pharmacological relationships, and inclusion of a small section on non-linear pharmacokinetics in Chapter 7. Other minor revisions have been made in other parts of the text to include more recent material.

The opening chapter deals with the chemical properties of drugs. Chapters 2-5 are concerned principally with qualitative aspects of drug absorption, distribution, metabolism, and excretion. A brief treatment of drug bioavailability is followed by sections on basic pharmacokinetics and the kinetics associated with urinary drug excretion. The pharmacokinetics chapter deals with the kinetics of the one- and two-compartment models, nonlinear kinetics, and multiple dosing. Some numerical examples are given, but no worked problems.

A chapter on drug interactions precedes an expanded discussion on relationships between drug levels and pharmacological effects. Topics include plasma level-effect relationships of chemotherapeutic agents, chlorpromazine, anticonvulsants, tricyclic antidepressants, and  $\beta$ -blocking agents. Dosage adjustment of antibiotics in patients with renal failure is included as an appendix. Although addressed to antibiotics in particular, the arguments presented there apply equally to all drugs whose effect is related to circulating levels and whose elimination is dependent wholly or partially on kidney function. The very brief treatment afforded this subject is probably justified in view of its extensive coverage by other authors.

In the reviewer's opinion, the book is a useful undergraduate teaching aid for students in pharmacy, pharmacology, medicine, and other related health disciplines and provides sufficient references for further indepth reading in specific subject areas.

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**Medicinal Chemistry V. Proceedings of the 5th International Symposium on Medicinal Chemistry. Paris, July 19-22, 1976.**

Edited by J. MATHIEU. Elsevier Scientific, 52 Vanderbilt Ave., New York, NY 10017. 1977. 456 pp. 17 × 25 cm. Price \$52.95.

This volume presents the proceedings of the Fifth International Symposium on Medicinal Chemistry, Paris, July 19-22, 1976. Four types of articles are included: main lectures on fundamental subjects by academicians, brief applied lectures by pharmaceutical industrial researchers, round-table discussion of strategy in drug research directed by Professor E. J. Ariens of Nijmegen, and some miscellaneous topics. The program of the symposium also included poster sessions organized by Professor C. G. Wermuth of Strasbourg.

The main subjects range from the fields of peptides, prodrugs, the central nervous system, cardiovascular agents, and immunology to the fields of organic synthesis, the Hansch approach to drug design, and prevention of aging.

Hypothalamic regulatory hormones and their synthetic analogs are concisely discussed with emphasis on the latest developments in research on synthetic studies and structure-activity relationships. This review was authored by numerous collaborators headed by Nobel Laureate A. V. Schally.

The section on peptides also contains reviews on the identity and mode of action of hypothalamic hypophysiotropic hormones, diverse roles of hypothalamic regulatory peptides, synthetic methodology of bioactive peptides, approaches of peptide chemistry to insulin, and synthesis in the field of 1-34 human parathyroid hormone fragments.

The section on prodrugs begins with A. J. Glazko's presentation of his personal experiences in this area over the last 25 years. This presentation reviews studies of factors affecting metabolic disposition of chloramphenicol and some of its derivatives, 4,4-diacetyldiaminodiphenylsulfone (DADDS), adenine arabinoside, adenosine monophosphate, and prophenytoin. The second review of this section is on modulation of distribution of efficacy of prodrugs. This discussion is a very interesting review of the conception and synthesis of prodrugs on the basis of metabolic pathways and structure-activity correlation using Hansch's approach.

The third article is on long-chain esters of pipotiazine as long-acting psychotropic prodrugs; these prodrugs are supposed to assure a beneficial continuity in drug distribution at the target level with smaller doses administered by injection than those required by the oral route to achieve the same therapeutic effect. The subsequent review summarizes  $k_{cat}$  inhibitors as a new class of enzyme proinhibitors. Finally, this section concludes with an article titled Pro-drugs, Protective Groups and the Medicinal Chemist summarizing that it is possible to design prodrugs on a rational basis.

The section dealing with the central nervous system is in itself a major contribution to the literature of medicinal chemistry and pharmacology. The key article is on brain neurotransmitters and drug receptors and it contains valuable discussions of principles of methodology, the dopamine receptor, antischizophrenic agents, prediction of extrapyramidal and autonomic side effects, and a two-state model of the dopamine receptor. Thereafter, neural inhibition as a tool for research of anticonvulsants is the theme for the discussion of  $\gamma$ -aminobutyric acid, taurine, and glycine. The third paper of this section summarizes recent approaches in psychochemotherapy, including the biochemical classification of antidepressants and stereochemical classifications.

The next presentation is on the effects of neuroleptics on dopamine metabolism in the nigrostriatal, mesolimbic, and mesocortical dopaminergic systems. Piracetam is characterized as a nootropic agent in the following article. It is noted that this drug does not fit any of the

classical categories of psychotropic agents but has a positive effect on brain integrative mechanism without affecting limbic and reticular excitability; hence, it is assumed that functional telencephalic selectivity is involved, and on this basis piracetam is characterized as a "nootropic" agent because it affects noetic functions.

The topics on the central nervous system conclude with a discussion of a novel series of annelated benzodiazepines. Noticing that the imine function is not the principal site of metabolism of the benzodiazepines, it was rationalized that appropriate annelations might render the imine function more susceptible to metabolism and inactivation. Some of the compounds reported herein show interesting pharmacological properties.

Cardiovascular agents are reviewed from various standpoints: inhibitors of the renin-angiotensin system, new prospects in coronary theory,  $\beta$ -adrenergic antagonists, and central sites of action in the development of antihypertensive drugs.

The contribution of immunology to medicinal chemistry is the theme of the discussion of natural and synthetic immunostimulants related to the mycobacterial cell wall, immunopharmacology and immunotherapy of residual disease in cancer patients, and the biochemistry of thymic hormones.

Gerontology is surveyed in three articles. First, the pharmaceutical research aspects include illustrations of how biological aging can be studied experimentally and discussion of pharmaceutical aspects of aging based on age-associated deficiencies. Second, molecular and cellular mechanisms of aging of intercellular matrix are outlined. The third paper is organized on the basis of four categories: evidence that free radicals are involved in pathological processes occurring upon exposure to high oxidative stress, evidence that free radicals are involved in normal and abnormal cellular processes under conditions of normal oxidative stress, reactions of radicals expected to proceed *in vivo*, and speculation about the role of radical reactions in human aging and carcinogenesis.

The synthetic methodology included in this volume is another significant contribution to medicinal chemistry; *i.e.*, it emphasizes silyl enol ethers, the transformation of carboxylic acids to heterocycles, and new methods applied to the synthesis of natural products.

The round-table discussion of strategy in drug research is the final section. This discussion proved to be very fruitful because it included, among other topics: a manual method for applying the Hansch approach to drug design, correlation studies with antimycotics and fungicides of the azole group, and a strategy for the design of potent hormones. This section effectively concluded the symposium and provides an excellent finale to an excellent volume.

This reviewer recommends this book to every medicinal chemist and pharmacologist. The coverage of the topics noted is adequate and can serve as the basis for further research of the current literature.

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**Analytical Profiles of Drug Substances, Vol. 6.** Edited by KLAUS FLOREY *et al.* Academic, 111 Fifth Ave., New York, NY 10003. 1977. 16 x 23.5 cm. ix + 600 pp. Price \$27.50.

This book is the sixth (although erroneously referred to in the Preface as the fifth) in a series of monograph compilations under the sponsorship of the Pharmaceutical Analysis and Control Section of the APhA Academy of Pharmaceutical Sciences. The objective of this series is to provide, in a single source, information about drug substances not ordinarily included in the official compendia and which may not always be readily retrievable from the literature. The official compendia generally contain tests and specifications for drugs and drug products related to identity, purity, quality, and strength plus other information of greater value to the practitioner than to the pharmaceutical scientist.

In this series, each drug profile presents useful data in the following categories: description, physical properties, synthesis or method of manufacture, stability and degradation, metabolism and pharmacokinetics, analytical methods, and literature references. Included under physical properties are spectral data, melting characteristics, solubility data, crystal properties, and solution characteristics. Analytical methods are thoroughly reviewed and encompass colorimetry, spectrophotometry, fluorometry, titrimetry, chromatography, polarography, coulometry, and also microbiological methods where applicable. Identification tests and

elemental analyses are also included. Of particular significance are analytical methods applicable to the drug substance and its metabolites in body fluids.

As noted for the previous volumes, each drug profile is well organized and is presented in a systematic and uniform manner. Each profile is introduced by a table of contents. It would be helpful if each entry of the table of contents were page referenced. This table is followed in orderly sequence by each category covered for that particular drug. The monograph is concluded by a listing of quoted references which, in most cases, is extensive and comprehensive. As is true with the previous volumes of this series, this one is printed clearly and is replete with tables, figures, and graphical presentations. Space is used economically and to maximum advantage.

Volume 6 contains 17 drug profiles which brings to a total of 114 the number of drugs for which profiles are now available. An excellent format has been developed for the presentation of the "vital statistics" on drugs, and hopefully a pattern has been established for a continuous flow of monographs for drug substances currently in the marketplace, drugs in the process of development, and drugs yet to be discovered. Pharmaceutical scientists are reminded of the Editor's standing invitation for the contribution of monographs of drugs in which they have an interest. The continued success of this series will depend on such participation.

"Analytical Profiles" serves well as a companion volume to the official compendia and is an essential addition to the library of those engaged in pharmaceutical research.

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## NOTICES

*Findings of Drug Abuse Research. Vols. 1 and 2. NIDA Research Monograph 1.* National Institute on Drug Abuse, 11400 Rockville Pike, Rockville, MD 20852. 1975. 20 x 27 cm. Price \$7.00, Vol. 1; \$5.05, Vol. 2. Available from Superintendent of Documents, U.S. Government of Printing Office, Washington, DC 20402.

*The Epidemiology of Drug Abuse: Current Issues. NIDA Research Monograph 10.* Edited by LOUISE G. RICHARDS and LOUISE B. BLEVENS. National Institute on Drug Abuse, 11400 Rockville Pike, Rockville, MD 20852. 1977. 259 pp. 15 x 24 cm. Price \$2.60.

*Cholesterol.* By JOHN R. SABINE. Dekker, 270 Madison Ave., New York, NY 10016. 1977. 489 pp. 15 x 23 cm. Price \$25.00.

*Immunology Of The Gut. Ciba Foundation Symposium 46 (new series).* Elsevier North-Holland, 52 Vanderbilt Ave., New York, NY 10017. 1977. 376 pp. 7 x 25 cm.

*Antifungal Compounds. Vol. 1.* Edited by MALCOLM R. SIEGEL and HUGH D. SISLER. Dekker, 270 Madison Ave., New York, NY 10016. 1977. 600 pp. 15 x 23 cm. Price \$55.00.

*Environmental Cancer. Advances in Modern Toxicology Vol. 3.* Edited by H. F. KRAYBILL and MYRON A. MEHLMAN. Wiley, 605 Third Ave., New York, NY 10016. 1977. 388 pp. 15 x 23 cm. Price \$24.50.

*Immunology: A Programmed Text.* By J. WAYNE STREILEIN and JOHN D. HUGHES. Little Brown, 34 Beacon St., Boston, MA 02106. 1977. 337 pp. 21 x 28 cm.

*Rational Management of Diabetes.* By HABEEB BACCHUS. University Park Press, Chamber of Commerce Bldg., Baltimore, MD 21202. 1977. 221 pp. 15 x 23 cm. Price \$16.50.

*The Fetus and Birth. Ciba Foundation Symposium 47 (new series).* Elsevier Scientific, 52 Vanderbilt Ave., New York, NY 10017. 1977. 481 pp. 17 x 25 cm.

*Psychopharmacology: A Biochemical and Behavioral Approach.* By LEWIS S. SEIDEN and LINDA A. DYKSTRA. Van Nostrand Reinhold, 450 W. 33rd St., New York, NY 10001. 1977. 451 pp. 15 x 23 cm. Price \$19.95.

*Reagents for Organic Synthesis. Vol. 6.* By MARY FIESER and LOUIS F. FIESER. Wiley, 605 Third Ave., New York, NY 10016. 1977. 765 pp. 15 x 23 cm. Price \$29.50.

*An Introduction to Clay Colloid Chemistry. 2nd Ed.* By H. van OLPHEN. Wiley, 605 Third Ave., New York, NY 10016. 1977. 318 pp. 15 x 23 cm. Price \$21.50.