

In the two subjects, more than 50% of the administered dose was excreted mainly as intact drug in the 0-48-hr. period. Both the N_1 - and N_3 -oxides were found in the urine of man in approximately equal quantities, totaling 4.7 and 2.6% of the dose administered in Subjects 1 and 2, respectively. The urines from two dogs receiving tablets containing a total of 1000 mg. sulfamethoxazole and 200 mg. trimethoprim (16 mg. trimethoprim/kg. body weight) were analyzed for trimethoprim and its N -oxide metabolites (Table II). In the two dogs, 19.0 and 29.1% of the dose were excreted as intact drug. A significant amount of the N_3 -oxide was excreted by both dogs in the 0-48-hr. period, while only a trace amount of the N_1 -oxide was excreted. The urines of four rats receiving 28 mg. (140 mg./kg. body weight) and 10 mg. (50 mg./kg. body weight) trimethoprim i.p. in 5% gum arabic were analyzed for trimethoprim and its N -oxide metabolites. Between 5 and 12% of the dose was excreted as intact drug at both dose levels. Only the N_1 -oxide metabolite was found in the 0-48-hr. rat urine, totaling between 0.6 and 2.7% of the administered dose (Table III).

Schwartz *et al.* (2) studied the metabolism of trimethoprim in man, dog, and rat and found that each species excreted the N_1 -oxide as a urinary metabolite; this finding was confirmed in the present study. Meshi

and Sato (3) detailed the metabolism of trimethoprim in the rat and reported levels of an N -oxide, but they were unable to determine the point of attachment of the oxygen to either nitrogen of the pyrimidine ring. Additional information on the N -oxidation of trimethoprim is presented in this study. Although limited numbers of subjects and animals of each species were studied, the results suggest that the human converts trimethoprim to the N_1 -oxide and N_3 -oxide with equal facility, whereas N_3 -oxide formation is favored by the dog and N_1 -oxide formation is favored by the rat.

(1) M. A. Brooks, J. A. F. de Silva, and L. D'Arconte, *Anal. Chem.*, **45**, 263(1973).

(2) D. E. Schwartz, E. Vetter, and C. Englert, *Arzneim.-Forsch.*, **20**, 1867(1970).

(3) T. Meshi and Y. Sato, *Chem. Pharm. Bull.*, **20**, 2079(1972).

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BOOKS

REVIEWS

Basic and Clinical Pharmacology of Digitalis. (Proceedings of a Symposium sponsored by the Ohio State University College of Medicine, the American Heart Association, and the Central Ohio Heart Chapter). Edited by B. H. MARKS and A. M. WEISSLER. Charles C Thomas, Springfield, IL 62703, 1972. 328 pp. 14.5 × 23 cm. Price \$21.00.

The editors successfully present the work of distinguished scientists and clinicians who bring together the most recent advances in basic and clinical aspects of digitalis. In most instances, each of the 16 chapters presents a clear, readable, and succinct picture of the most important facets of digitalis glycosides. The materials throughout the book are well documented with adequate and current references (through 1971).

The application of basic pharmacological concepts to the clinical use of digitalis is the major theme of this book. The last five chapters of Part Two are particularly good and very useful for clinicians. In some instances, different views have been expressed by the authors on the same topic, but this is understandable, since all of these topics can be approached from a different point of view. Inclusion of chemical structures of various digitalis glycosides would have been helpful in following the discussions on the absorption and metabolic transformations of digitalis presented in chapters 2 and 12. However, this is a minor inconvenience since structural information is readily accessible from several reference books.

These authoritative presentations on basic and clinical aspects of digitalis glycosides deserve the careful scrutiny of pharmaceutical and medicinal chemists, practicing cardiologists, and internists, as well as academic and research specialists in cardiovascular physi-

ology and pharmacology and all others who may be obliquely interested with digitalis.

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Amino-Acids, Peptides, and Proteins, Volume 4. Senior Reporter, G. T. YOUNG. The Chemical Society, Burlington House, London, W1V 0BN, England, 1973. 498 pp. 13 × 21.5 cm. Price £9.00.

This volume is the fourth in the series of the literature review in the field of amino acids, peptides, and proteins. The selection of the reviewers by the Chemical Society is highly commendable. Under the able leadership of Dr. Young, these specialists have done a wonderful job and have provided an indispensable service by critically reviewing the wealth of the literature during the year 1971. The present volume is divided into five chapters. The first four chapters are devoted to the detailed survey of the literature on Amino-Acids, Structural Investigations of Peptides and Proteins, and Peptide Synthesis and Peptides with structural features not typical of proteins. The fifth chapter, a short one, concerns the revision of the I.U.P.A.C.-I.U.B. recommendations for the nomenclature of amino acids, peptides, and proteins. The second chapter is, by far, the most comprehensive and provides detailed survey of the litera-

ture concerning the primary structure and chemical modification of proteins and enzymes. The literature related to the use of X-rays for the studies of protein structure and the analytical tools employed in the elucidation of conformation and interaction of peptides and proteins is extremely well documented. The other chapters, likewise, have received the proper treatment.

The subject index has been abolished in this volume. However, this hardly reflects on the ease with which the proper subject reference can be located. This has been achieved by providing a detailed table of contents. This volume is a must for the desk of the scientist working in the areas of amino acids, peptides, and proteins.

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Chemical and Biological Aspects of Drug Dependence. Edited by S. J. MULE and Henry BRILL, M.D. CRC Press, 18901 Cranwood Pkwy., Cleveland, OH 44128, 1972. 561 pp. 18 × 26.5 cm.

The purpose of this publication is to provide, in one reference source, the basic knowledge and background information that currently define the chemical and biological basis of drug dependence. To obtain a better understanding of drug dependence and drug abuse, the characteristics of drug dependence of various pharmacological classes of drugs are described. Theories related to tolerance development and physical dependence are then discussed. Finally, the biochemical mechanisms associated with biological strata, e.g., enzymes, proteins, and hormones, are explained in relationship to drug dependence. Twenty-five separately authored discussions are divided into five sections covering significance and characteristics of drug dependence, criteria for their evaluation, chemical aspects, physiological and pharmacological aspects, and biochemical aspects.

Staff Review ■

Modern Analytical Methods. By D. BETTERIDGE and H. E. HALLAM. The Chemical Society, Burlington House, London W1V 0BN, England, 1972. 220 pp. 14 × 21.5 cm. Price £2.00.

The objective of this publication is to acquaint teachers with the most important methods of modern analysis. To aid in understanding the analytical methods, modern methods of testing complex equilibria are also included. Although the discussion of individual techniques is condensed, an attempt has been made to include the fundamental theory necessary to understand the method or technique being discussed.

Staff Review ■

Handbook of Commercial Scientific Instruments, Volume 1: Atomic Absorption. By CLAUDE VEILLON. Marcel Dekker, Inc., 95 Madison Ave., New York, NY 10016, 1972. 174 pp. 15 × 23 cm. Price \$11.75.

Commercially available instruments, by type, will be detailed in this new multivolume series. In volume 1, the instrumentation available for atomic absorption spectroscopy is covered. Specifications, descriptions, schematic drawings, photographs, approximate prices, and accessories are given in separate discussions for each manufacturer, and in summary tables given at the end of the book for quick comparisons.

The information is essentially that provided by the manufacturer. The volume authors are engaged in research in the area covered by their respective books and are familiar with the available instrumentation. The authors do not represent any instrument manufacturer.

This volume begins with a general discussion of atomic absorption spectroscopy requirements and instruments, followed by sections on each manufacturer and his instruments. A summary section focusing on cost considerations and tables comparing the discussed instruments complete the book.

This book and, presumably the rest of the series, bring together information available but from many diverse sources. The book should be useful in preliminary considerations of equipment acquisitions.

Staff Review ■

NOTICES

Medicaments Organiques de Synthèse, Chimie et Pharmacologie, Volume V. Edited by Leon VELLUZ. Masson et C^o, 120 Boulevard Saint-Germain, Paris VI^e, France. 270 pp. 15 × 21.5 cm. Price Fr. 165. (French)

Molecular Mechanisms of Antibiotic Action on Protein Biosynthesis and Membranes, Proceedings of a Symposium held at the University of Granada (Spain), June 1-4, 1971. Edited by E. MUNOZ, F. GARCIA-FERRANDIZ, and D. VAZQUEZ. American Elsevier, 52 Vanderbilt Ave., New York, NY 10017, 1973. 804 pp. 16 × 24 cm. Price \$27.50.

Carbohydrate Chemistry, Volume V, A Specialist Periodical Report. Senior Reporter, J. S. BRIMACOMBE. The Chemical Society, Burlington House, London, W1V 0BN, England, 1972. 434 pp. 13 × 21.5 cm. Price £8.00.

Philosophy of Medicine and Science: Problems and Perspectives. Compiled by Department of Philosophy of Medicine and Science, Institute of History of Medicine and Medical Research, New Delhi 62, India. 289 pp. 16 × 24 cm.

Developmental Physiology and Aging. By P. S. TIMIRAS. Macmillan, 866 Third Ave., New York, NY 10022, 1972. 692 pp. 17.5 × 25 cm. Price \$19.95.

Glucagon: Molecular Physiology, Clinical and Therapeutic Implications. Edited by PIERRE J. LEFEBVRE and ROGER H. UNGER. Pergamon Press, Inc., Maxwell House, Fairview Park, Elmsford, NY 10523, 1972. 370 pp. 17 × 25 cm. Price \$37.50.