Now we wish to report the first[1] isolation and characterization of a shark anticancer constituent. The hammerhead shark, *Sphyrna lewini*[2], was found to produce two new antineoplastic agents designated sphyrnastatin 1 and sphyrnastatin 2. These anticancer components were isolated from the blood (and other body fluids), the fins (and other muscle tissue), and the liver.

In a typical isolation sequence, the water extract of blood and body fluids was first chromatographed on macroreticular resin[3]. The aqueous fraction (20 → 13.5 g) was next subjected to gel[4] permeation chromatography (10 × 100-cm column). Following elution with 3.25 liters of water, the PS inhibitory fraction (0.6 g from 5.0 g) was finally purified by chromatographic separation[5] (5 × 69-cm column and elution with a mixture of 0.05 *M* tromethamine and 0.1 *M* potassium chloride). The two highest molecular weight fractions (0.076 and 0.34 g) represented the antineoplastic components.

Sphyrnastatins 1 and 2, isolated by this procedure, were glycoproteins [~22 and 26% carbohydrate, respectively (6)] with apparent molecular weights (7) of at least 40×10^6. Amino acid analyses indicated a minimum protein segment of 274 amino acid units for sphyrnastatin 1 and 380 amino acid units for sphyrnastatin 2. Upon preliminary biological evaluation, the sphyrnastatins produced a 30–40% (at 11–13 mg/kg) life extension in mice inoculated with the PS leukemia. More extensive antineoplastic evaluation of sphyrnastatins 1 and 2 in the National Cancer Institute's exploratory screening systems is in progress. Presently, we are attempting to isolate other shark and marine vertebrate anticancer constituents.

Perhaps the sphyrnastatins and other high molecular weight antineoplastic substances (4) act by stimulating the immune system to more effective action against invading neoplastic disease. If this hypothesis is valid, then immunotherapy approaches to cancer treatment with, for example, BCG might better be considered as just another facet of cancer chemotherapy.

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[1] More broadly, this report represents the first isolation and characterization of a marine vertebrate antineoplastic agent.
[2] Specimens of *S. lewini* were collected off the coast of Florida from 1971 to 1974, and we thank Dr. C. Swift for the taxonomic identification. Except for inclusion in a recent study of elasmobranch hemoglobins, no prior assessment of *S. lewini* constituents has been made. See Ref. 5.
[3] XAD-2.
[4] G-50 Sephadex.
[5] Sepharose 2B.

BOOKS

REVIEWS

Drug Metabolism: Chemical and Biochemical Aspects. By BERNARD TESTA and PETER JENNER. Dekker, 270 Madison Ave., New York, NY 10016, 1976. xii + 500 pp. 18.5 × 26 cm. Price $47.50.

This is the fourth volume in the new "Drug and Pharmaceutical Sciences" series of textbooks and monographs edited by James Swarbrick. As stated by the editor, the purpose of the series is "to enable the pharmacist, and others in the health sciences field, to stay abreast of the changing trends, advances and innovations associated with drugs and the body of knowledge that has come to be known as the pharmaceutical sciences." According to the authors, the purpose of this volume is "to create a fundamental awareness of the basis of drug metabolic processes to those entering the subject or to those who have worked at higher levels of *in vivo* organization." Both purposes have been admirably met with this volume.

As promised in the title, the authors treat both the chemical and biochemical aspects of drug metabolism. The book is divided into these two major sections, with 60% of the text devoted to chemical considerations.

The five chapters devoted to chemical aspects include the major chapter of the book, phase I (biotransformation of chemical groupings) reactions, and a somewhat shorter chapter, phase II (conjugation) reactions. Together, these two chapters account for nearly one-half the total text. Having detailed the specific chemical reactions of drug metabolism, these chapters are brought together and placed in perspective in the third chapter of this section by presenting schematic views of the metabolism of 15 selected drugs. This is followed by a chapter concerning the stereochemical aspects of drug metabolism, a topic recently reviewed in some depth by the authors. The final chapter of this section deals with the influence of physiochemical factors on drug metabolism. This very short chapter (five pages) perhaps should have been expanded or eliminated.

The biochemical aspects of drug metabolism, primarily at the enzymatic level, are presented in four chapters of approximately equal length. The first describes the basic biochemical nature of the drug-metabolizing enzyme systems responsible for phase I and phase II reactions. The effects

of inducers and inhibitors of these enzymatic systems and the mechanisms of actions involved are treated in the next chapter. The third chapter of this section deals with the physiological factors influencing drug metabolism, including species, strain, sex, and age. The final chapter of the section, and the book, is devoted to a comparison of the biochemical aspects of extrahepatic drug metabolism.

This book deals with "drug metabolism" in the sense of biotransformation, not in the sense of the overall fate, of drugs. Commendably, it has not been diluted with pharmacokinetics, methodology, or extensive physiology. The authors selected, organized and wrote the material in such a manner that the text is entirely readable and instructive, yet valuable for reference. The many references are grouped so that pertinent ones usually are no more than five pages, and never more than 20 pages, away. The subject and author indexes should be useful. This book fills a need in the field for a definitive text relating the chemical and biochemical aspects of drug metabolism.

This reviewer highly recommends the book to anyone engaged in drug metabolism activities; it should be particularly valuable to those entering the field and to those whose experience has been primarily with *in vivo* systems. Unfortunately, its rather high price may prevent many from having a personal copy.

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Clinical Chemistry. Principles and Procedures. 4th Ed. By JOSEPH S. ANNINO and ROGER W. GIESE. Little, Brown, 34 Beacon St., Boston, MA 02106, 1976. 412 pp. 16 × 24 cm. Price $15.00.

The fourth edition of this book reflects the rapid growth in the field of clinical chemistry. Part I, which details fundamental information on basic analytical techniques, includes chapters on automation, separation techniques, and radioimmunoassay for the first time. In addition, quality control and spectrophotometry have been expanded and a section on atomic absorption has been added to the chapter dealing with emission spectrophotometry. The overall treatment in Part I is very basic and quite brief; however, most of the important techniques are appropriately referenced.

The majority of this book (Part II) is devoted to descriptions of analytical methods for most of the tests performed in a modern clinical chemistry laboratory. The authors attempted to limit the material presented to one or two established methods for each test, and specific automated procedures are omitted entirely. In addition to the experimental details, most chapters contain a brief discussion of the principle of the method as well as limitations and clinical significance of the results. A concise survey of other current methods with references is also included. One notable weakness is the expanded section on drugs and poisons. It is still quite short and details procedures that are useful in toxicology but not sensitive enough for therapeutic monitoring.

This book is generally well written and appears to be most useful as an inexpensive, concise reference source for the nonclinical chemist who requires access to the principles and details of a variety of clinical chemistry procedures.

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Pharmacokinetics of Psychoactive Drugs: Blood Levels and Clinical Response. Edited by LOUIS A. GOTTSCHALK and SIDNEY MERLIS. Wiley, 605 Third Ave., New York, NY 10016, 1976. 255 pp. 16 × 23.5 cm. Price $20.00.

At the annual meeting of the American College of Neuropsychopharmacology held in December 1974 in Puerto Rico, a series of papers was presented at the first study group dealing with pharmacokinetics and clinical response. This book represents an organized compilation of those papers.

The book contains 16 chapters divided into two main sections: Methodological Problems and Approaches (six chapters, 114 pp) and Pharmacological–Clinical Response (10 chapters, 136 pp). A major contribution of the book is the emphasis on the critical evaluation of measurement techniques, analytical as well as behavioral. Particularly noteworthy are Chapters 4 and 6. Chapter 4 includes a limited quality control study (five laboratories) of the determination of chlorpromazine and three metabolites, and Chapter 6 involves comparisons of three types of psychological measurement procedures. The second section of the book illustrates well the challenges of establishing relationships between blood level and clinical response with predictive capabilities.

The references at the end of each chapter are generally adequate. Since the book is the result of contributions at a scientific meeting, the reader should expect a certain amount of discontinuity in content and style. However, the book illustrates the state of the art in this highly interdisciplinary field of research and represents the first attempt to draw attention to several problem areas.

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Alicyclic Chemistry. Vol. 4. Edited by W. PARKER *et al.* The Chemical Society, Burlington House, London W1V OBN, England, 1976. 511 pp. 14 × 22 cm. Price $75.75.

The present volume is organized identically to Volume 2 [reviewed in *J. Pharm. Sci.*, **64**, 2032 (1975)], which dealt with the literature of alicyclic chemistry published during 1972. Four large chapters cover three- and four-membered rings, five- and six-membered rings (and related fused systems), medium- and large-ring compounds, and bridged carbocyclics. Each chapter is extensively subdivided and deals with ring characteristics of the systems, methods of synthesis, and reactions. The format is the same as in the earlier volumes. The general comments made by this reviewer about Volume 2 are equally applicable here.

As in all areas of chemistry (all science), the sheer quantity of information available each year continues to grow exponentially. For example, the number of publications dealing with three- and four-membered rings alone increased by 35% in 1974 over the previous year.

Each chapter in this book is prepared by different authors (reporters), with W. Parker serving as the senior reporter for this and previous volumes. Finally, I think it is fair to state that the price of this volume (obtainable through the American Chemical Society) is simply exorbitant. The price in England is considerably less (£27.50). This price differential is hard to understand.

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Drug Treatment. Principles and Practice of Clinical Pharmacology and Therapeutics. Edited by GRAEME S. AVERY. Publishing Sciences Group, 162 Great Neck Rd., Acton, MA 01720, 1976. 1048 pp. 18.5 × 27 cm. Price $25.00.

This text is composed of 28 chapters authored by 53 contributors from around the world. It is arranged in three sections: clinical pharmacology, therapeutics, and a section of five appendixes containing mostly tables of data on physiochemical and pharmacokinetic properties of drugs, adverse reactions to drugs, drug interactions, selection of systemic antibacterial agents, and a guide to dosage in renal failure.

Each chapter begins with a synopsis of important principles which itemizes generalities that should be understood and retained as residual information even after the smaller nitty-gritty facts in each chapter fade from one's mind.

The specific aim of the book is to aid the clinician in selecting a drug