on the chest from a surface area of 50 cm^2 was significantly ($p < 0.002$) greater (36.4 ± 4.3%) than the absorption from the smaller surface area. Therefore, differences in these anatomical sites did not affect absorption, but increasing the size of the skin surface area did increase absorption.

The anatomical site of application has been shown to affect the percutaneous absorption of compounds in humans (4, 5) and the rhesus monkey (7). Site dependence for absorption of nitroglycerin has been reported in the rat (8) and humans (9). In the human study, the topical dose and the surface area were not controlled, but both of these parameters affect absorption (2).

Two points should be stressed. First, the topical dose and the surface area must be controlled in percutaneous absorption studies. Second, future studies may show that nitroglycerin absorption can vary with some anatomical sites. However, there also will be anatomical sites where absorption is similar. Therefore, a patient may have the convenience of choosing a preferred site.

(1) R. C. Wester and H. I. Maibach, *Toxicol. Appl. Pharmacol.*, **32**, 394 (1975).
(2) R. C. Wester and H. I. Maibach, *J. Invest. Dermatol.*, **67**, 518 (1976).
(3) D. L. Karsh, R. E. Umbach, L. S. Cohen, and R. A. Langou, *Am. Heart J.*, **96**, 587 (1978).
(4) H. I. Maibach, R. J. Feldmann, T. H. Milby, and W. F. Serat, *Arch. Environ. Health*, **23**, 208 (1971).
(5) R. J. Feldmann and H. I. Maibach, *J. Invest. Dermatol.*, **48**, 181 (1967).
(6) S. T. Horhota and H. Fung, *J. Pharm. Sci.*, **68**, 608 (1979).
(7) R. C. Wester, P. K. Noonan, and H. I. Maibach, *J. Soc. Cosmet. Chem.*, **30**, 297 (1979).
(8) S. T. Horhota and H. Fung, *J. Pharm. Sci.*, **67**, 1345 (1978).
(9) M. S. Hansen, *Am. J. Cardiol.*, **42**, 1061 (1978).

Patrick K. Noonan
Ronald C. Wester ˣ
Department of Drug Metabolism
G. D. Searle and Co.
Skokie, IL 60076

Received September 14, 1979.
Accepted for publication December 21, 1979.

BOOKS

REVIEWS

GLC and HPLC Determination of Therapeutic Agents, Parts I–III. (Chromatographic Science Series, Vol. 9).

Part I edited by K. TSUJI and W. MOROZOWICH.

Parts II and III edited by K. TSUJI.

Dekker, 270 Madison Ave., New York, NY 10016.

Part I: 1978, 415 pp., 18 × 26 cm, Price $37.50.

Part II: 1978, 432 pp., 18 × 26 cm, Price $45.00.

Part III: 1979, 528 pp., 18 × 26 cm, Price $45.00.

Part I has chapters entitled: Theory and Instrumentation, Column Selection in GLC, Column Selection in HPLC, Derivatization Techniques in Gas–Liquid Chromatography, Derivatization Techniques in HPLC, The Mass Spectrometer as a Detector for Gas–Liquid Chromatography, Isolation of Samples Prior to Chromatography, Preparative HPLC: Small Scale and Trace Collection, Preparative HPLC: Milligram Quantities, Quality Control in GLC, Automation and Quality Control in HPLC, Computer Interfacing, and Data Processing. Much new material as well as an exhaustive critical review of the literature is included. The writing has an immediacy and authority which are most welcome, indicating that the authors are directly involved with the techniques they describe. The volume is recommended to all in the field who wish to update their knowledge of the theory and practice of GLC and HPLC. It is particularly recommended to graduate students and would make an excellent course text except for one problem: an index is available only in Part III. Use of the index is made more annoying since the three parts are successively paginated so that the index does not immediately indicate the volume to open.

Part II is devoted to therapeutic drug monitoring with GLC and HPLC. It contains chapters 14–24, which give scientific methods and detailed directions for individual drugs. In addition to the literature review, there are author-preferred-and-tested methods for each drug. The drug classes covered are: narcotic analgesics, narcotic antagonists and related drugs, central nervous system (CNS) depressants, cocaine and phenylethylamines, hallucinogens, cannabis preparations, barbiturates, anticonvulsants, salicylates, aniline derivatives, pyrazolones, synthetic opiate-like drugs of low potency and low addictive potential, analgesic combinations, nonbarbiturate hypnotics, glutethimide, methaqualone, anorexigenics, antipsychotics, antianxiety agents, antidepressives, stimulants, antihypertensives, pulmonary and vasoactive drugs, antimicrobials, antimycotics, antiparasitics, adrenocorticosteroids, androgens, estrogens, and antifertility steroids. In addition, there are chapters on preservatives and on the determination of residues in gaseous sterilants.

The editor has been extremely careless in Part II, allowing the same material about the same drug to appear in two different chapters. For example, Fig. 9 of Chapter 14, showing GLC analysis of opium alkaloids, is reproduced as Fig. 15 of Chapter 16. The duplicated information involves the narcotic analgesics, barbiturates, amphetamine, papaverine, and, perhaps, others.

Part III continues with the drugs used in metabolic diseases, those that affect endocrine functions and nutritional agents. Drug classes included are: nonsteroidal anti-inflammatories, prostaglandins, cardiac glycosides, antiarrhythmics, vasodilators, oral anticoagulants (there are no methods for heparin in this collection), antidiabetics, diuretics, lipid- and cholesterol-lowering agents, thyroid agents, X-ray contrast agents, nucleosides and nucleotides, alkaloids, antihistamines and antitussives, water-soluble vitamins, fat-soluble vitamins, amino acids and peptides, sugar and sugar alcohols, and saccharin. The last chapter deals with serum lipid and fatty acid analysis.

The methods reported in Parts II and III include sample preparation (including separation from clinical samples or drug formulations and derivatization) as well as the determinations. Most chapters contain a summary table of the drugs included in it, choosing between GLC and HPLC as the method of choice and giving the chromatographic conditions.

It is an amusing coincidence that while this review was being prepared, the August issue of "Chromatography Newsletter" was received, which was devoted entirely (15 pages) to drug analysis, thus showing again that reviews, no matter how well done, can only supplement and not substitute for current periodicals.

These three volumes are an indispensible reference to all scientists who use or intend to use GLC and HPLC, particularly drug analysts, forensic scientists, clinical chemists, and biochemists. Good use of the collection will be made by "anyone concerned with the potency, purity, stability,

pharmacokinetics and mechanisms of actions of drugs. . . ."

The type is clear and readable. The books have glossy paper covered boards, are easy to open, and lie flat, as are typical of Marcel Dekker volumes.

Despite the nuisances and repetitiveness noted, the set is highly recommended.

Reviewed by Murray M. Tuckerman
School of Pharmacy
Temple University
Philadelphia, PA 19140

The Chemistry of Antitumor Antibiotics, Vol. 1. By WILLIAM A. REMERS. Wiley–Interscience, One Wiley Drive, Somerset, NJ 08873. 1979. 289 pp. 15 × 22.5 cm.

A lack of fundamental knowledge concerning many aspects of the biological sciences still restricts most oncologists to dealing with the treatment rather than the causes of cancer. Nevertheless, encouraging results have been attained with many drugs in the treatment of certain neoplastic diseases such as acute lymphocytic leukemia, Burkitt's lymphoma, choriocarcinoma, Hodgkin's disease, squamous cell cancer, and Wilm's tumor, Many of these remissions were achieved by the use of antitumor antibiotics.

Antibiotics are unique in their extreme diversity of chemical structures and in the fact that the "rational approach" followed so enthusiastically in the design of other classes of antineoplastic agents has played only a minor role in the discovery of their striking effects. As a result, information gained by assessing the antitumor activity of these antibiotics may be more objective than studies of more conventional drug classes. There can be little doubt that the information will contribute significantly to the future design of better antineoplastic agents and will provide a guide to the proper selection of agents for use in combination chemotherapy.

Since the discovery in 1952 that actinomycin D (dactinomycin) shows activity against experimental tumors, antibiotics have gained firm ground as a unique class of agents for the management of cancer. As a result, numerous studies on this subject mushroomed, and publications were scattered in every possible chemical, biological, pharmacological, and medical journal. Although some reviews and chapters were published occasionally on certain antitumor antibiotics, this book is the first of its type in which pertinent information in this area has been assembled in a comprehensive yet precise and clear manner. Dr. Remers' effort should be appreciated by investigators working in this field. His achievement is particularly admired by those who have tried to compile similar information, even on a smaller scale.

Volume 1 of this book is divided into five chapters: the actinomycins, the anthracyclines, the aureolic acid group, the bleomycins and phleomycins, and the mitomycins and porfiromycins. At least one member of each of these categories has recognition in cancer chemotherapy [*e.g.*, actinomycin D, adriamycin (doxorubicin), mithramycin, bleomycin B_2, and mitomycin C, respectively]. Each chapter has a concise, general introduction and is divided further into specific discussions including the discovery, isolation, and characterization, structural elucidation, possible mode of action, chemical synthesis and biosynthesis, and structure–activity relationships. Three of these five chapters also include the chemical transformations among related antibiotics.

Since many antibiotics discussed in this book tend to form chelates or complexes with certain metal ions, the author has emphasized repeatedly a significant point which, if not noticed, would cause confusion and misinterpretation by other investigators. This point is that physical properties such as optical rotation often are influenced by traces of metals and other impurities that are difficult to separate or remove from the pure compound. This case is especially true with antibiotics of the aureolic acid group in which samples with the same chemical structure were assigned as different antibiotics based on the observed discrepancy in specific rotation values.

This reviewer agrees with the author's comment that in a field where anticancer activity is the primary goal of synthesis and structural modification, it is surprising that not enough data have been published on the inhibition of experimental tumors. Judging from the many elegant total or partial syntheses recorded in this book, I cannot help but wonder whether the lengthy ones under the name of an alternate synthesis or a novel approach are of value to other investigators. Indeed, the aim of a chemical synthesis is to identify the structural assignment, to devise a practical method for more plentiful procurement of a specific antibiotic, or to facilitate analog synthesis. With the current limited funding in research, perhaps now is the best time for every dedicated investigator to reassess the true value and implication of his or her own work.

The order of tetracyclic rings in the anthracycline antibiotics (Chapter 2) given in this book was from the aromatic ring (ring A) toward the alicyclic ring (ring D) in which the glycoside is attached. However, on p. 88 and p. 102, ring A was designated as the alicyclic ring. In the literature, the conflicting order of rings A → D or D ← A has been assigned and has aroused unnecessary confusion. Since the original Italian investigators [Arcamone *et al.*, *Gazz. Chim. Ital.*, **100**, 949 (1970)] designated the alicyclic ring on the aglycone portion as ring A, perhaps such assignment should be honored rather than the general order of assignment in this book. The author also may wish to change the cell line of He La to HeLa in forthcoming books.

This reviewer also would like to add one piece of interesting information concerning the phleomycin antibiotics. Although it is known that the low therapeutic indexes of phleomycins hamper their use as antibacterial or antitumor agents, the addition of certain thioethers of purine or related heterocyclic compounds as potentiators ("amplifiers") permits the use of phleomycins at much lower levels, thereby raising their therapeutic indexes to potentially useful levels [Grigg *et al.*, *J. Bacteriol.*, **107**, 599 (1971); and Brown *et al.*, *Austr. J. Chem.*, **31**, 397 (1978) and the references cited therein].

All in all, this is a well-written and valuable book. Readers can follow easily the historical development of important antibiotics and recognize the work that has been accomplished as well as areas that still need to be studied. This book should be of interest to chemists, biochemists, toxicologists, pharmacologists, and clinicians who are interested in research.

Reviewed by C. C. Cheng
Mid-America Cancer Center
University of Kansas Medical Center
Kansas City, KS 66103

The Alkaloids: The Fundamental Chemistry—A Biogenetic Approach. (Studies in Organic Chemistry Series, Vol. 7). By D. R. DALTON. 270 Madison Ave., New York, NY 10016. 1979. x + 789 pp. 18 × 26 cm. Price $49.50 (A special price of $29.50 is available in the United States and Canada on orders of five or more copies).

The alkaloids represent the largest and most diverse group of plant-derived natural products, with well over 10,000 known members of the class involving 300 different ring systems. In view of their importance, including their significance in pharmacy and medicine, it is surprising that few textbooks on alkaloids have appeared in recent years. Thus, apart from reviews in "The Alkaloids" series, the Chemical Society Specialist Periodical Reports of the same name, and specialized reviews such as the one by Shamma and Moniot on isoquinoline alkaloids, no comprehensive general treatment of the alkaloids has appeared since that edited by Pelletier almost a decade ago. The publication of the book that is the subject of this review is thus a timely event and one that will be welcomed by all researchers involved in the alkaloid field.

The book is an outgrowth of a course taught by the author at Temple University, and this is the origin of its greatest strength and its greatest weakness. The strength of the book is that it provides for the first time, in one place, a unified account of the biosynthesis and chemistry of the alkaloids. It is organized along biosynthetic lines rather than along the traditional lines of previous works. Thus, instead of chapters on subjects such as the ipecac (ipecacuanha) alkaloids or the cinchona alkaloids, there are chapters on alkaloids derived from ornithine, lysine, nicotinic acid, tyrosine, and tryptophan and on alkaloids derived by introduction of nitrogen into a terpenoid skeleton. Although the traditional classification, largely by plant of origin, does group alkaloids of similar type, our present understanding of alkaloid biosynthesis makes the approach adopted in this book logical and desirable. Furthermore, the discussion of the biosynthesis and the chemistry of each alkaloid is integrated within each chapter rather than having the biosynthesis discussed in a separate chapter. This feature allows the reader to appreciate the synthetic approaches to the alkaloids more readily, particularly those that are modeled on an actual or presumed biosynthetic pathway.

The major weakness of the book as a standard reference on the alka-