One microliter of the aqueous methanolic solution was then injected into a gas chromatograph[1] equipped with a flame-ionization detector. A 1.8-m glass column[2] (2 mm i.d.) was packed with 3% OV-17 on 100–120-mesh Gas Chrom Q[3]. The following conditions were used: injector temperature, 260°; column temperature, 210°; detector temperature, 250°; nitrogen flow, 35 ml/min; hydrogen flow, 50 ml/min; and compressed air (19–23% O_2 and 77–81% N_2) flow, 300 ml/min. The retention times for phenytoin and the internal standard were 4.1 and 5.8 min, respectively. With 0.5 *M* trimethylanilinium hydroxide in place of tetramethylammonium hydroxide (0.1 *M*)–trimethylanilinium hydroxide (0.01 *M*) and identical column conditions, the interfering peak had a retention time of 5.6 min.

Peak height ratios were used to prepare standard curves in the 1–20-μg/ml range. The lower limit of sensitivity was 0.5 μg/ml, and repeated injections showed assay reproducibility in the ±0.5-μg/ml range.

With the described procedure, a clean chromatogram that was easily quantitated was obtained. The phenytoin peak at the higher sensitivity settings, *i.e.*, low concentration range, did elute on the solvent front tailing. However, if analysis time is not critical, the column temperature can be lowered slightly, resulting in a slightly longer retention time but a better chromatogram for quantitation purposes.

Use of the mixed methylating agents apparently provides sufficient methylating and alkalizing properties while minimizing peak interferences resulting from high concentrations of trimethylanilinium hydroxide and the relatively poor methylating capability of tetramethylammonium hydroxide.

[1] Varian Aerograph model 2100, Walnut Creek, Calif.
[2] Supelcoport, Supelco, Inc., Supelco Park, Bellefonte, Pa.
[3] Applied Sciences Laboratories, State College, Pa.

(1) J. MacGee, *Anal. Chem.*, **42**, 421 (1970).
(2) R. H. Hammer, B. J. Wilder, R. R. Streiff, and A. Meyersdorf, *J. Pharm. Sci.*, **60**, 327 (1971).
(3) H. J. Kupferberg, *Clin. Chim. Acta*, **29**, 283 (1970).
(4) A. Estes and P. A. Dumont, *J. Chromatogr.*, **82**, 307 (1973).
(5) M. A. Evenson, P. Jones, and B. Darcey, *Clin. Chem.*, **16**, 107 (1970).
(6) K. K. Midha, I. J. McGilveray, and D. L. Wilson, *J. Pharm. Sci.*, **65**, 1240 (1976).
(7) M. Orme, O. Borgå, C. E. Cook, and F. Sjöquist, *Clin. Chem.*, **22**, 246 (1976).
(8) E. Brochmann-Hanssen and T. O. Oke, *J. Pharm. Sci.*, **58**, 370 (1969).

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BOOKS

REVIEWS

Textbook of Organic Medicinal and Pharmaceutical Chemistry. 7th ed. Edited by CHARLES O. WILSON, OLE GISVOLD, and ROBERT F. DOERGE. Lippincott, East Washington Square, Philadelphia, PA 19105, 1977. 1085 pp. 18 × 26 cm. Price $33.00.

The seventh edition of this book represents a continued effort of the editors to provide a useful undergraduate pharmacy textbook. The book includes a discussion of all products described in USP XIX, NF XIV, and "Accepted Dental Remedies," as well as other important pharmaceuticals. The introductory material of a few chapters has been completely rewritten, but the overall format remains essentially unchanged.

Three major changes in style represent a departure from the older editions and will considerably improve the practical application of the textbook. One outstanding feature is the extensive use of tables to focus attention upon groups of therapeutic agents in common use (a combination of chemical and pharmacologic classification). The information provided by the tables includes the official title of the drug, proprietary name(s), official dosage forms, usual dose and route of administration, and usual dose range. For the appropriate drugs, the usual pediatric dose is given in terms of body weight and body surface.

A second outstanding feature of this edition is the addition of appendixes. Material relative to pharmaceutic aids and necessities has been extracted from the several chapters of the older editions and placed in one appendix. The title of another appendix, Amine Salts, is misleading, because it actually provides the USAN designations, chemical names, and structural formulas of the anions of the more common organic acids used to form salts with amines. A third appendix provides a referenced list of pKa values of several drugs and reference compounds. A fourth appendix provides an alphabetical list of official titles of chemical entities in the USP and NF. For each title, the Chemical Abstracts Service Index Name and Registry Number, IUPAC name, empirical formula, and molecular weight are given.

A third change from the previous editions is deletion of the material previously discussed in Chapters 4–8, thus reducing the number of chapters to 24. Much of the deleted material has been placed in other appropriate chapters and in an appendix.

All chapters now include literature citations and a selected reading list.

The titles of the remaining 24 chapters are the same as those of the sixth edition. But seven of the chapters were contributed by different authors, thus giving a different slant to the introductory material in each. In the seventh edition, the new authors are Robert F. Doerge, Sulfonamides and Sulfones with Antibacterial Action (Chapter 6) and Adrenergic Agents (Chapter 12); H. Wayne Schultz, Surfactants and Chelating Agents (Chapter 7); Arnold R. Martin, Antibiotics (Chapter 9); Dwight S. Fullerton, Steroids and Therapeutically Related Compounds; and Jaime N. Delgado, Carbohydrates (Chapter 21) and Amino Acids, Proteins, Enzymes, and Hormones with Protein-like Structure (Chapter 22).

The purchaser should be aware of several printing errors that appear in Chapter 20. If the Errata list mailed to schools of pharmacy in January

is not available, a copy can probably be obtained by writing one of the editors. The errors were corrected in the second printing.

A rapid reading revealed surprisingly few misspelled words and only a few errors in the other chapters. Most errors are minor and do not significantly detract from the usefulness of the material.

Errors in structural formulas include carbenicillin indanyl sodium, p. 289; cephalothin sodium, p. 292; cephapirin sodium, cephamycin, and cefoxitin, p. 294; anhydrotetracycline, p. 308; oleandomycin, p. 317; lincomycin, p. 320; nystatin, p. 330; carbachol intermediate, p. 469; and neostigmine, p. 472.

Other minor errors were also noted. On p. 306, a "2" should be replaced by a "3" to read, ". . . protonation of the enol group on carbon atom 3 . . . ." In the "Mechanism of Hydrolysis of AChE," p. 467, a positive charge was omitted and the orientation of a water molecule is misleading. On p. 477, the acid proton is incorrectly placed on pilocarpine hydrochloride. The structural formula number (I) was omitted on p. 555. In the third line on p. 560 "R" should replace "S," which refers to the absolute configuration of bisquaternary species. Since rotoxamine is the levorotatory isomer of carbinoxamine, the following statement should be deleted from pp. 652 and 654: "In compounds that exhibit optical isomerism the dextrorotatory isomer possesses most of the antihistaminic activity." Finally, on p. 665, the acid proton is incorrectly placed on antazoline hydrochloride.

A footnote in the chapter on Analgesic Agents explains that the popular term "analgesic" is used in preference to the etymologically correct term "analgetic." Perhaps it would be appropriate to explain a similar relationship in the usage of the terms "antitubercular" and "antituberculous" either on p. 144 or 331.

In the reviewer's opinion, the seventh edition is an improvement of an already good textbook. It should be well received in the classroom and is highly recommended as a textbook for courses in undergraduate medicinal and pharmaceutical chemistry.

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Assessing Drug Reactions—Adverse and Beneficial, Vol. 7: Philosophy and Technology of Drug Assessment. Edited by FRANK N. ALLAN. Interdisciplinary Communication Associates, Smithsonian Institute, Washington, DC, 1976. 158 pp. 15 × 23 cm.

This book contains the report of the seventh conference in a series on the Philosophy and Technology of Drug Assessment. This conference dealt with the basic problem of defining, detecting, reporting, and assessing adverse drug reactions. The conference was conducted by the Interdisciplinary Communications Program of the Smithsonian Institution.

The topics discussed in the book include terminology and definition of adverse drug reactions, risk–benefit analysis of adverse drug reactions, and various approaches that can be used in collecting data about adverse drug reactions. The book is written in a narrative style and includes edited statements of conference participants.

The book indicates that there was a lack of agreement among the conference participants regarding the magnitude of the problem, how to assess that magnitude, or who needed the most increased understanding. However, there was a consensus agreement that a national adverse drug reaction monitoring system is needed and that the system should be part of a larger system that includes data collection of the patient's whole response to drug therapy.

The book provides an informative insight into the controversy surrounding the collection and evaluation of adverse drug reaction data. The personal experiences of some conference participants are very enlightening and enable the reader to obtain a better grasp of the problems associated with collecting and evaluating adverse drug reaction data.

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AMA Drug Evaluations, 3rd Ed. Prepared by the AMA Department of Drugs in cooperation with the American Society for Clinical Pharmacology and Therapeutics. Publishing Sciences Group, 545 Great Rd., Littleton, MA 01460, 1977. 1327 pp. 18 × 26 cm. Price $29.50.

The third edition of this valuable reference source has been completely reorganized, updated, and expanded. The book is divided into 19 sections based on therapeutic category. Each section contains more specific chapters, which begin with a brief introduction and include detailed evaluations for individual drugs and compounds.

The book gives information on dosage, contraindications, and adverse reactions and includes structural formulas for most single-entity drugs. It also lists generic and proprietary names and available dosage forms and sizes. Included are evaluations of over 1300 drugs, information on investigational agents, and extensive listings for normal values of clinical laboratory tests. Also, there is information on drug interactions, labeling, and use of drugs during pregnancy.

This book is essential for those who prescribe, dispense, or administer drugs or who require information on applied therapeutics.

Staff review

Organic Chemistry of Drug Synthesis. By DANIEL LEDNICER and LESTER A. MITSCHER. Wiley, 605 Third Ave., New York, NY 10016, 1977. 471 pp. 16 × 23 cm. Price $22.50.

This book is an attempt to present to synthetic organic and medicinal chemists the synthetic routes used to prepare a great majority of organic compounds used as drugs. The book focuses on compounds that are either used in the clinic or have undergone clinical trial, concentrating on those assigned generic names by the USAN Council. There are 22 chapters, each of which is organized by structural rather than pharmacological classes. The pharmacology involved in the various disease states discussed and the mode of action in selected drug classes are written in terms useful to the chemist with a rudimentary knowledge of biology. A glossary of commonly used pharmacological terms is included.

The book is filled with errors of all types, which the reviewer found to be extremely irritating. In at least three places, the authors refer to substituted ureas as carbamates (structure 10, p. 7). No chapter was error free. Frequently compounds were given wrong numbers in the discussion section. Structure 61 (p. 36) is a piperidyl derivative, not a pyrrolidino derivative as listed. Structure 30 (p. 150) is referred to twice (p. 151) as an allylic halide when it is not one. Alkylation reactions using *N*-(2-chloroethyl)diethylamine are common throughout the book. Only twice is an aziridinium salt mentioned as an intermediate (methadone, p. 79, and promethazine, p. 373). It is quite possible that aziridinium salts play important roles in all such alkylations, not just the two unsymmetrical cases listed by the authors.

The only three groups of compounds with recent references are the benzodiazepines, prostaglandins, and cephalosporins. Only at the end of the chapter on steroids do the authors indicate that drug research in this area has not stopped. This statement can surely be made about all of the other areas covered in the book and should not have been limited to the steroids alone. No mention was made of any drugs for neoplastic diseases, which is certainly another shortcoming of the book.

Short statements related to medicinal chemistry appear throughout the book (rigid analogs, pp. 355 and 387; the role of aromatic rings, pp. 40 and 108; and receptor, p. 218). The statements are often vague, and it would have been helpful if the authors had included an introductory chapter covering the major aspects of medicinal chemistry.

Organic chemists with no background in drugs should find this a useful introduction to the subject. This book provides only a superficial coverage of the subjects included and cannot be recommended as either an introductory text or as a reference source for anyone actively engaged in drug research.

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