servation, as stated by Gibaldi and McNamara (3), even though only a change in albumin binding may have occurred. When the apparent drug volume of distribution is large (>50–100 liters), the sum $V_P(1 + R_{E/I}) + \alpha(V_P)(V_E/V_P - R_{E/I})$ in Eq. 17 can be neglected since its largest possible value is 15 liters. The apparent volume of distribution is then:

$$V \cong (V_R)\left(\frac{\alpha}{\alpha_R}\right) \qquad \text{(Eq. 21)}$$

which is also predicted by Eq. 2.

The relationship presented in Eq. 17 should be helpful in analyzing and predicting alterations in the apparent volume of distribution of any drug when there is an alteration in the unbound fraction in plasma, in the unbound fraction outside the extracellular fluids, in the volumes of the extracellular fluids, or in the extravascular to intravascular plasma protein ratio, as occurs, for example, in prolonged bed rest and in severe burns. It will also be useful to identify where the alteration occurs.

(1) J. R. Gillette, *Ann. N.Y. Acad. Sci.*, **281**, 136 (1976).

(2) G. R. Wilkinson and D. G. Shand, *Clin. Pharmacol. Ther.*, **18**, 377 (1975).

(3) M. Gibaldi and P. J. McNamara, *Eur. J. Clin. Pharmacol.*, **13**, 373 (1978).

(4) J. R. Gillette, in "Importance of Fundamental Principles in Drug Evaluation," D. H. Tedeschi and R. E. Tedeschi, Eds., Raven, New York, N.Y., 1968, p. 69.

(5) J. R. Gillette, *Ann. N.Y. Acad. Sci.*, **179**, 43 (1971).

(6) J. R. Gillette and K. S. Pang, *Clin. Pharmacol. Ther.*, **22**, 623 (1977).

(7) A. C. Guyton, "Textbook of Medical Physiology," Saunders, Philadelphia, Pa., 1976, p. 424.

(8) W. J. Jusko and M. Gretch, *Drug Metab. Rev.*, **5**, 43 (1976).

(9) R. L. Williams, T. F. Blaschke, P. J. Meffin, K. L. Melmon, and M. Rowland, *Clin. Pharmacol. Ther.*, **21**, 301 (1977).

Svein Øie ˣ
Thomas N. Tozer
School of Pharmacy
University of California
San Francisco, CA 94143

Received February 2, 1979.
Accepted for publication June 7, 1979.
Supported in part by Grant 1R01 GM 25807-01 from the National Institutes of Health.

BOOKS

REVIEWS

Pharmazeutische Technologie. Edited by HEINZ SUCKER, PETER FUCHS, and PETER SPEISER. George Thieme Verlag, Herdweg 63, Postfach 732, D-7000 Stuttgart 1, West Germany. 1978. 906 pp. 17 × 24 cm. Price DM 235.

Industrial pharmacy as a scientific and technological branch of the profession of pharmacy covers a wide spectrum of operations involving a multidisciplinary body of fundamental knowledge and a diversified technology constrained by a specific set of governmental regulations intended to serve as controls over the laboratory and manufacturing environment as well as the quality of the drug preparation itself. An area of such diversity and complexity remains dynamic, and advances in basic pharmaceutics and pharmaceutical technology have accelerated during the past three decades. These advances have come about as a consequence of the pharmaceutical industry's expanding research and development investment and through the acquisition of scientific knowledge and technology from external sources such as universities and other industries.

An early effort by the Pharmaceutical Institute (ETH) in Zurich to reduce the high level of empiricism in the teaching of pharmacy students through the introduction of "physical pharmacy" principles resulted in the publication of a textbook, "Galenisches Praktikum"[1], in which the authors attempted to relate theoretical concepts to practice by means of explanatory text, laboratory exercises, and pertinent literature references. A decade later, the publication of "The Theory and Practice of Industrial Pharmacy"[2] provided a text much closer to the reality of industrial operations and constraints in the development and production of drug preparations.

The latest textbook that endeavors to portray accurately industrial pharmacy is "Pharmazeutische Technologie," a collaborative effort involving 25 authors, most of whom are associated with Swiss or German pharmaceutical companies and each of whom has been selected as a working specialist in his field. By the judicious decision to organize the material as an applied science based on current theoretical concepts of unit operations, only seven chapters were needed. The book begins with a thorough and excellently organized chapter, which develops the mathematical concepts of practical importance to research and development pharmacists engaged in dosage form design. The statistical section is particularly noteworthy for the manner in which research design and optimization techniques and scale-up theory are presented. Along similar lines, the second chapter reviews the theoretical basis for most of the unit operations involved in pharmaceutical dosage form development and production. Among these are the flow properties of gases and liquids, heat transfer, dissolution, comminution, dispersion, mixing, granulating, compressing, and antimicrobial treatment.

In this period of high interest in biopharmaceutics, since a textbook on technology cannot overlook the biological aspects of pharmaceutical product development, a short third chapter covers pharmacokinetic modeling, methodology, and specific applications to bioavailability, sustained-release formulations, and new delivery systems. The fourth chapter treats the important and often neglected subject of pharmaceutical excipients in accordance with the functional role of the excipient in a dosage form. A series of tables listing most of the commonly used excipients conveniently provides incomplete but useful technical information, including average concentration range. Standards for excipients and other forms of regulatory control are described, but deficiencies in existing standards and variability in controls receive minimal attention.

In covering the key subject of dosage forms, the fifth chapter requires over 40% of the total number of pages in the book. The subdivision of topics is based on physical form, route of administration, and sequence of unit operations. This approach proves to be an effective means of organizing a large mass of technical material which, in general, is representative of the current state of pharmaceutics and process technology. The section on parenteral dosage forms and especially the discussions of production control methods and the organization and technological aspects of parenteral production operations are outstanding.

In the sixth chapter, attention is directed to the protective role of packaging, the types of packaging materials used in pharmaceutical containers, and the various chemical, physical, and microbiological tests used to control their quality. A second section includes a brief review of packaging line operations. The last chapter deals with quality control assurance and begins with a rarely seen section on quality of design as studied during preformulation. This discussion is followed by material covering the subsequent formulation studies, which involve drug release characteristics, bioavailability and tissue tolerance of various dosage

forms, scale-up effects, and in-process controls. The importance of the guidelines for good manufacturing practices as elaborated by the World Health Organization is reviewed in sections dealing with documentation, hygienic requirements, and clean room technology.

The subject matter covered by the text is of such great international interest to pharmaceutical scientists that at least a thousand articles or chapters in books appear annually. Therefore, it is of interest to check the bibliography of over 700 references used by the authors in the preparation of the text. Although the proportion does vary somewhat from chapter to chapter, the overall percentage cited from Swiss or German publications is about 60% of the total. This exceedingly high level may reflect the reading habits of the authors or their language preferences or limitations rather than the true proportion of scientific and technological activity taking place throughout the world.

The emphasis in this German-language book lies squarely in the domain of industrial pharmacy, and it can be highly recommended to pharmaceutical scientists active in the research, development, production, and control departments of the pharmaceutical industry; to teachers of pharmaceutics and pharmaceutical process technology and their graduate students in the universities; and to scientific members of regulatory agencies who wish to gain a valuable perspective of the complex nature of modern drug development and production.

The publisher deserves commendation for the high technical quality of the book itself. Format, typography, figures, and tables are numerous, clear, well-placed, and pertinent to the text. Perhaps that plus inflation explains the price of the book.

[1] "Galenisches Praktikum," K. Münzel, J. Büchi, and O.-E. Schultz, Eds., Wissenschaftliche Verlagsgesellschaft MBH, Stuttgart, West Germany, 1959.

[2] "The Theory and Practice of Industrial Pharmacy", L. Lachman, H. A. Lieberman, and J. L. Kanig, Eds., Lea & Febiger, Philadelphia, Pa., 1970.

Reviewed by Jack Cooper
School of Pharmacy
University of California
San Francisco, CA 94143

Diuretic Agents (ACS Symposium Series 83). Edited by EDWARD J. CRAGOE, Jr. American Chemical Society, Washington, D.C. 1978. IX + 238 pages. 15 × 23 cm. Price $21.50.

This book evolved primarily from an American Chemical Society Symposium on Diuretic Agents in 1977. However, as stated in the preface, since the symposium was brief and a more complete picture of research in this field was desired, four papers were added to the original seven.

The opening chapter (McGigg and Wong) contains an up-to-date review of the role of prostaglandins in renal function. It is followed by a chapter on the structure–activity relationships of the highly potent, high-ceiling aminobenzoic acid diuretics (Tvaermose, Nielsen, and Feit). The third chapter (Lang *et al.*) is on pharmacological effects of tizolemide (HOE 740) as an example of a novel class of sulfonamide compounds.

The fourth chapter (Werner *et al.*) reviews the structure–activity relationships of sulfonamide diuretics. The next two chapters (Bessin *et al.* and Maass *et al.*) are on pharmacology and structure–activity relationships of the newer diuretic uricosuric agent, tienilic acid (Ticrynafen). The seventh chapter (Smith *et al.*) is on 2-aminomethylphenols, a new class of saluretic agent characterized by the experimental compound MK-447. The following chapter (Horstmann *et al.*) reviews a new class of longer acting high-ceiling diuretics (1-aralkyl-2-pyrazolin-5-ones) characterized by muzolimine.

The ninth chapter (Boschman *et al.*) is a discussion of pharmacology and structural requirements of the quincarbates, a unique class of tricyclic diuretics. The following chapter (Saltzinger *et al.*) discusses the novel diuretic etozolin, which has mild choleretic properties. The last chapter (Woltersdorf *et al.*) discusses evolution of some (aryloxy)-acetic acid diuretics after more than a decade of research.

While this book is the result of the 1977 symposium, all chapters are dated as being received in August 1978 and many contain 1977 and a few 1978 references. Therefore, this book is a complete and current review of structure–activity relationships and pharmacology of various classes of diuretic agents. This book includes discussions on experimental agents undergoing testing for possible therapeutic use and would be useful for anyone seeking current information about the newer diuretic agents.

Reviewed by Gary L. Lage
Philadelphia College of
Pharmacy and Science
Philadelphia, PA 19104

NOTICES

Methods of Protein Separation. Vol. 2. Edited by NICHOLAS CATSIMPOOLAS. Plenum, 227 W. 17th St., New York, NY 10011, 1978. 326 pp. 15 × 23 cm. Price $35.00.

Neurotransmitter Systems and their Clinical Disorders. Edited by N. J. LEGG. Academic, 111 Fifth Ave., New York, NY 10003. 1978. 240 pp. 15 × 23 cm.

New Trends and Developments in Vaccines. Edited by A. VOLLER and H. FRIEDMAN. University Park Press, Chamber of Commerce Building, Baltimore, MD 21202. 1978. 323 pp. 15 × 23 cm. Price $29.50.

Pharmacy Technicians' Manual. 2nd Ed. Edited by JANE M. DURGIN, ZACHARY I. HANAN, and CHARLES O. WARD. C. V. Mosby St. Louis, Mo. 1978. 287 pp. 15 × 23 cm. Price $13.95

Psychopharmacology of Affective Disorders. A British Association for Psychopharmacology Monograph. Edited by E. S. PAYKEL and A. COPPEN. Oxford University Press, 200 Madison Ave , New York, NY 10016. 1979. 261 pp. 16 × 24 cm. Price $25.00.

Quality Control of Drugs. Certification Scheme on the Quality of Pharmaceuticals Products Moving in International Commerce. Reprint of the WHO Chronicle, Vol. 31, No. 12. World Health Organization, Geneva, Switzerland. 1977.

Research Design in Clinical Psychology and Psychiatry. 2nd Ed. Revised and enlarged by J. B. CHASSAN. Wiley, One Wiley Drive, Somerset, NJ 08873. 1979. 492 pp. 13 × 21 cm. Price $18.50.

Self-Administration of Abused Substances: Methods for Study. NIDA Research Monograph 20. By NORMAN A. KRASNEGOR. National Institute on Drug Abuse, Division of Research, 5600 Fishers Lane, Rockville, MD 20857. 1978. 246 pp. 15 × 23 cm.

Taxis and Behavior. Elementary Sensory Systems in Biology. Receptors and Recognition. Series B, Vol. 5. Edited by G. L. HAZELBAUER. Wiley, 605 Third Ave., New York, NY 10016, 1978. 341 pp. 15 × 23 cm. Price $45.00.

Topics in Antibiotic Chemistry. Vol. 2. Antibiotics from Marine Organisms, Oligosaccharides, Anthracyclines and their Biological Receptors. By P. G. SAMMES. Wiley, One Wiley Drive, Somerset, NJ 08873. 1979. 283 pp. 15 × 23 cm.

Webster's Medical Office Handbook. By ANNE H. SOUKHANOV and JOHN RHODES HAVERTY. G.& C. Merriam Co., 47 Federal St., Springfield, MA 01101. 1979. 596 pp. 17 × 25 cm. Price $10.95.