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BOOKS

REVIEWS

Controlled Release of Bioactive Materials. Edited by RICHARD BAKER. Academic, 111 Fifth Ave., New York, NY 10003. 1980. 473 pp. 15 × 23 cm. Price \$34.50.

This book constitutes a collection of 27 papers delivered at the sixth International Symposium on Controlled-Release Materials in New Orleans in 1979. The first 12 papers deal with various aspects of controlled drug delivery systems.

In the first paper, Heller and Baker review the theory and practice of controlled drug delivery from biodegradable polymers. The mechanisms of drug release from these polymers are discussed in depth, and several illustrative examples are presented. Applications of biodegradable polymers are discussed further in the ensuing two papers by Pitt *et al.* and Petersen *et al.*

In the fourth paper, Theeuwes and Echenhoff present the applications of osmotic drug delivery systems. The design and experimental performance of two osmotic devices are described. The generic osmotic pump (Alzet) is designed to deliver the contents of 170 μ l at the rate of either 1 μ l/hr over a 1-week period or 0.5 μ l/hr over 2 weeks. The other device is the elementary osmotic pump, which is generally fabricated in the shape of a tablet, with a single-delivery orifice. A paper by Chandrasekaran and Shaw is concerned with controlled, transdermal drug delivery.

Other papers of pharmaceutical interest deal with polymers that include poly(lactic acid) and the hydrogels. Rhine and coworkers present a new approach to achieve zero-order release kinetics from diffusioncontrolled polymer matrix systems. The theoretical basis for these kinetics is presented as is a comparison of kinetics from matrix devices of other geometries.

The second half of the book is concerned essentially with topics not directly related to drug delivery systems. Controlled-release systems containing insecticides, molluscicides, and plant growth regulators are discussed and described. Implantable systems for the delivery of insect growth regulators to livestock are evaluated by Jaffe and coworkers. The basic technology used to design several of these systems is very similar to drug-containing devices.

This book is a collection of high quality research papers, prepared by scientists in widely different fields. As such, the book is highly recommended for both academic and industrial pharmaceutical scientists, chemists, biologists, and chemical engineers who have an interest in controlled-release technology.

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British National Formulary 1981: Number 1. The Pharmaceutical Press, 1 Lambert St., London, SE1 7JN, England. 1981. 387 pp. 12 × 23 cm. Price £3.80

The British National Formulary is designed for use by doctors, pharmacists, and nurses in the National Health Service in the United Kingdom. Unlike earlier editions that were published every 2 or 3 years and contained only those drugs and preparations having the confidence of the Joint Formulary Committee, the 1981 edition is an outgrowth of the Committee's response to requests for a wider coverage of drugs available in the United Kingdom and more detailed guidance in prescribing and dispensing.

This new edition provides more descriptive information to assist the prescriber in selecting the appropriate treatment for a particular patient. A double-column format was followed to accommodate the increased volume of information and to allow the book to "still fit into the doctor's pocket."

The BNF begins with sections on Guidance on Prescribing and Emergency Treatment on Poisoning. The main text consists of classified notes divided into 15 chapters: Gastro-intestinal System; Cardiovascular System; Respiratory System; Central Nervous System; Infections; Endocrine System; Obstetrics and Gynaecology; Malignant Disease and Immunosuppression; Nutrition and Blood; Musculoskeletal and Joint Diseases; Eye; Ear, Nose, and Oropharynx; Skin; Immunological Products and Vaccines; and Anaesthesia. Each chapter begins with appropriate notes for prescribers to facilitate selection of suitable treatment followed by detailed monographs of the relevant drugs and preparations (indications, contraindications, cautions, side-effects, doses, dosage forms, routes of administration, and relative prices). Drugs appear under their pharmacopoeial titles or British Approved Names and are listed alphabetically unless there is a drug of choice, which then is listed first. Preparations are listed immediately following the drug that is their main ingredient.

Appendixes 1-3 contain pertinent information on drug interactions, intravenous additives, and borderline substances. A small formulary section also is included for dispensing those preparations commonly prepared extemporaneously, as are a dental formulary, an index of manufacturers, and an extensive subject index.

The BNF is a pocket book for easy referral, and thus cannot contain all the information necessary for prescribing and dispensing, but should be supplemented by manufacturer's data sheets and specialized texts as needed.

Future editions will be published twice a year to maintain current information on the drugs and preparations.

Staff Review

The Use of Alternatives in Drug Research. Edited by ANDREW N. ROWAN and CARL J. STRATMANN. University Park Press, 233 E. Redwood St., Baltimore, MD 21202. 1980. 190 pp. 15 × 23 cm. Price \$24.50.

The advent of the National Toxicology Program has caused a rethinking of the procedures available for economical toxicological assessment of the thousands of chemicals to which people are exposed and the means whereby such exposure can be limited or prevented. This volume follows the pathway of chemical evaluation by *in vitro* systems designed to reduce, but not eliminate, the use of animals in pharmacological and toxicological research. As the various contributors state, there comes a time when only the whole animal will provide the final answer.

Hansch's contribution points out a logical manner in which modern drug modifications can be carried out *in vitro* utilizing computer techniques that allow rational changes in basic molecules to increase potency and decrease possible side effects, utilizing partition coefficients and binding to receptor sites. Many contributors point out that *in vitro* use of bacteria and cultured cells and tissues can indicate binding sites that cannot be determined by *in vivo* studies. Thus, the techniques that have been used to develop treatments for polio, mumps, and measles now can be used to screen antiviral chemicals to determine their antiviral potency and the maximum concentrations at which no toxic effects are caused to tissue culture cells.

Macrophages can be grown in culture, and *in vitro* studies of cellular immunity can be undertaken prior to whole animal testing. Micropharmacokinetics of various agents can be undertaken with this system. Protozoan diseases now can be studied with culture systems, and the various diseases afflicting humans and animals, such as trypanosomiasis, leishmaniasis, trichomoniasis, and amoebiasis, in either vector or vertebrate forms, can be evaluated for chemical susceptibility.

Pharmacologists have utilized both tissue slices and cell-free systems to study chemical biotransformations, enabling the evaluation of metabolic processes prior to introduction into whole animals, but the conjugation processes are not usually included in such studies and overall excretion may result in damage to such organs as the kidneys. However, tissue perfusion can eliminate this drawback partially. The mechanisms whereby both inorganic and organic chemicals exert their toxic effects on cell membranes and constituents can be studied with such models as amoeba proteus and isolated rat hepatocytes. Immunological preparations have been prepared by *in vitro* methods, but numerous biologicals have caused disease in humans because they contained live viruses; either the viruses were not killed during processing or they were not susceptible to the antiviral agent used. Thus, whole animal testing must be conducted.

By far, the greatest application of *in vitro* tests is the microbiological assessment of mutagenic and possible carcinogenic potentials of chemicals. Such methods are discussed by Rosenkrantz *et al.*, who point out

the various modifications of microbial assays, the activation by S-9 fractions from various tissues, and the pitfalls encountered. However, such tests coupled with various cultured animal and human cell lines greatly assist in showing cell transformations and their possible link to the mutagenic and carcinogenic processes.

Of all *in vivo* tests used for the determination of skin and eye irritation, the Draize test has had the greatest application and has caused the most emotional impact. This eye test does not differentiate intermediate irritants and has a great degree of subjectivity. Recently, a cytotoxicity test was proposed based on the *in vitro* effects of irritants on I-929 mouse embryo cells. The results obtained compare favorably with eye irritation obtained in the Draize test. However, more work must be done to establish it as the method of choice.

In general, this symposium volume should indicate to pharmacologists and toxicologists that *in vitro* procedures should be applied to drug development and chemical evaluation during preliminary research. The succinct nature of the material presented and the extensive bibliography recommend this volume, and it should be in the library of all researchers and students in these fields.

> Reviewed by Thomas J. Haley National Center for Toxicological Research Jefferson, AR 72079

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