Book Reviews

Prodrugs. Topical and Ocular Drug Delivery. Edited by Kenneth B. Sloan. Marcel Dekker, New York and Basel, 1992, 313 pp.

The book represents a complete overview with minimal overlap among various chapters. The editor has done a remarkable job in putting together the fundamental physicochemical properties of prodrugs and their dermal and ocular transport characteristics. The chapter authors demonstrate considerable expertise in their respective areas. The primary focus relates to the application of bioreversible modification of active drugs for enhanced dermal, transdermal, and ocular permeation. The volume contains seven chapters, beginning with the mechanisms of dermal and transdermal absorption and continuing with the practical aspects of prodrug development and applications.

Chapter 1 opens the book with a brief overview of the mechanisms of topical, dermal and transdermal drug delivery. A brief discussion of the routes of transdermal mass transfer is followed by a discussion of the physicochemical variables that are relevant to stratum corneum permeability, including lipophilicity, molecular weight and volume, and solubilities in vehicle and membrane biophase.

An exhaustive review of the prodrug approaches that have been utilized in an attempt to optimize dermal and transdermal topical delivery of compounds is presented in Chapter 2. The functional groups amenable to prodrug derivatization are examined. The author organizes the remainder of the chapter into various functional groups and further divides this into the promoieties that have been used with these functional groups. Numerous experimental results are given for each functional group/promoiety discussed. The interested reader would be forced to sift through dozens of review articles to acquire the information organized in this chapter.

Chapters 3 through 5 describe different mathematical and empirical models of transdermal flux useful in optimizing topical delivery. Chapter 3 explores the modeling of drug flux taking into consideration the effect of molecular size, lipophilicity, and solubility. The thermodynamic contribution of functional groups to the permeability of compounds is also explored. This chapter offers experimental support for the models developed and concludes by detailing the experiments utilized to optimize the topical dermal delivery of various nonsteroidal antiinflammant drugs using the prodrug approach. Chapter four compares the utility and predictive value of four models used to describe the transdermal flux of a compound. The experimentally determined flux of 50 compounds are compared to the flux values obtained from the predictive models. A method for utilization of these models to optimize the dermal and transdermal flux of a compound concludes this chapter. Chapter 5 deals with the use of solution theory, theoretically derived solute and solvent activity coefficients, and calculated vehicle/membrane partition coefficients to yield theoretical permeability coefficients for partitioning-driven processes. The author addresses membrane permeability in general, then follows this with discussions on dermal delivery, transdermal delivery, and the use of prodrug modifications. The method of calculating permeability coefficients from theoretically derived activity coefficients in this manner and the extrapolation of these permeability coefficients to multiple vehicles are then discussed.

Chapter 6 provides an interesting caveat to the use of prodrugs in the dermal and transdermal delivery of drugs. Rather than taking an overly enthusiastic stance on the utility of prodrugs, the author examines the success of actual cases of drug absorption enhancement involving the use of prodrugs. While in many cases the permeability coefficient of a compound is increased, the flux and, hence, absorption are only marginally affected. This chapter provides many practical examples and discusses the failure of prodrug approach in greatly increasing the net flux of a compound. The variables influencing the transdermal flux of a compound, solubility, oil/water partition coefficient, and enzymatic hydrolysis are discussed. The chapter details some of the factors that must be overcome if prodrug technology is to be successful as theoretically suggested.

The volume concludes with a chapter on topical ocular drug delivery. The constraints and barriers unique to ocular drug delivery are outlined. The authors present the formulation, physicochemical, and physiologic considerations of corneal drug absorption. The prodrug approaches that have been used to date to enhance corneal absorption are reviewed. Other methodologies commonly used to optimize the ocular delivery of drugs are also discussed.

The stated goal of this work is to organize the abundance of literature available on prodrugs into one concise, well-referenced volume. The book presents the theoretical and practical aspects of prodrug derivatization to enhance topically administered drugs. This work is complete enough to be a valuable reference to researchers involved with prodrugs as well as anyone interested in topical drug delivery. To this end, the book fulfills its stated objectives.

Ashim K. Mitra
Department of Industrial and Physical Pharmacy
School of Pharmacy and Pharmacal Sciences
Purdue University
West Lafayette, Indiana 47907-1336

Protein Folding. Edited by Thomas E. Creighton. W. H. Freeman, New York, 1992, xv + 547 pp., ISBN 0-7167-7027-x, $59.95 (hardback).

Our knowledge of how and why polypeptides fold into specific shapes has progressed a very long way from the early studies by Anfinsen on the denaturation and renaturation of RNase A. The book in hand is an excellent summary of the current state of knowledge in protein folding from the point of view of biophysical chemists.

The book is a collection of chapters on individual topics in protein folding, each chapter written by one or two experts in that area. A masterly introductory chapter by Rich-

0724-8741/93/1200-1812$07.00/0