drive receptor-mediated siderophore uptake. These chapters also provide a more limited description of iron uptake pathways that do not involve siderophores, such as uptake of heme and ferric citrate.

A second major grouping of six chapters, representing about 30% of the book, focuses on the proteins involved in mammalian iron transport and storage: ferritin, transferrin, and the transferrin receptor. There are three very complementary chapters on ferritin. One chapter by Harrison et al. focuses heavily on crystallographic studies of the protein structure, while a second chapter by Chasteen puts more emphasis on iron binding and oxidation. Both of these chapters include some discussion of bacterioferritin. The third chapter by Powell is devoted exclusively to mineralization and iron core formation, with an interesting discussion of the edge effects associated with the very small iron cores. There are also chapters on transferrin and the transferrin receptor and on the iron responsive element on mRNA's and the genetic control of iron uptake. The final chapter in this group by Crichton and Ward covers the broad topic of iron homeostasis and serves as a nice summary of much of the material covered in the other chapters in this group.

This book also attempts to cover iron transport and storage in plants. Thus there are chapters on the role of both microbial and plant siderophores in plant iron uptake and on plant ferritin. However, the coverage of iron metabolism in plants is not that extensive and somewhat fragmented. Other than a general discussion of the role of proteins and siderophores in limiting the iron available to pathogenic organisms and one chapter on clinical iron chelators, there is not much coverage of clinical issues.

Wesley R. Harris

Department of Chemistry
University of Missouri−St. Louis
8001 Natural Bridge Road
St. Louis, Missouri 63121

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Progress in Medicinal Chemistry. Volume 35. Edited by G. P. Ellis, D. K. Luscombe, and A. W. Oxford. Elsevier Science B.V., Amsterdam, The Netherlands. 1998. vii + 270 pp. 14.5 × 21 cm. ISBN 0-444-82909-1. $198.50.

This book is the latest volume in this well-established medicinal chemistry review series. Chapters in this volume include: Modern View of Vitamin D_3 and its Medicinal Uses by M. J. Beckman and H. F. DeLuca (56 pages, 410 references), Neurokinin Receptor Antagonists by C. J. Swain (24 pages, 75 references), Opioid Receptor Antagonists by H. Schmidhammer (49 pages, 207 references), Mechanisms of Bacterial Resistance to Antibiotics and Biocides by A. D. Russell (64 pages, 326 references), and Towards Cannabinoid Drugs - Revisited by R. Mechoulam, L. Hanus, and E. Fride (44 pages, 202 references). The first three chapters cite references up to and including 1996, the last two, 1998. The volume contains a 6-page subject index.

The chapter on vitamin D_3 includes a detailed description of its biosynthesis, metabolism, and current understanding of mechanism of action, followed by a discussion of the therapeutic uses of vitamin D_3 and its analogues. In the last section of the chapter, the authors discuss the potential of vitamin D_3 analogues in the treatment of cancer and immune-related diseases.

The next chapter reveals the therapeutic potential and structural diversity of the many high-affinity neurokinin (NK) receptor antagonists. The authors classify the antagonists as NK_1, NK_2, or NK_3 receptor-selective or as dual NK_1/NK_2 receptor-selective. In the body of the text, useful comparative quantitative receptor affinity and pharmacological data are presented.

The chapter on opioid receptor antagonists begins with a description of receptor antagonism and universal opioid receptor antagonists. The remainder is divided into three sections: μ-opioid, κ-opioid, and δ-opioid receptor-selective antagonists. In each of the three sections, opioid antagonists are classified as peptide or non-peptide and, within these subheadings, as competitive or irreversible/long-acting. Binding affinity and receptor selectivity data are presented in 11 tables. Concise descriptions of the synthesis of the opioid antagonists are presented throughout the text.

The chapter on antibiotic resistance begins with some definitions and in turn discusses the mechanisms of intrinsic resistance, mechanisms of acquired resistance, pathogenic-resistant Gram-positive bacteria, mechanisms of multidrug resistance in Gram-negative bacteria, linked antibiotic-biocide resistance, and overcoming bacterial resistance. The use of drug combinations as a strategy to overcome bacterial drug resistance is only briefly mentioned, and the stereochemistry for some of the structures is not indicated. Despite these minor flaws, this chapter presents some well-organized information on this important topic.

The chapter on cannabinoid drugs describes cannabinoid receptors and the SAR of both the classical cannabinoids and the endogenous ligands, anandamide and 2-arachidonoyl glycerol. This is followed by a discussion of the medicinal properties of the cannabinoids which includes a discussion of the recently discovered oleamide and its potential in the treatment of sleep disorders. An interesting perspective is also provided on the ongoing debate over "medical marijuana."

The quality of the volume is very good. This book will likely be quite useful not only to those familiar with the topics presented but also to those who wish to learn more about these subjects.

Jonathan L. Vennerstrom

College of Pharmacy
University of Nebraska Medical Center
Omaha, Nebraska 68198-6025

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Integration of Pharmaceutical Discovery and Development: Case Histories. Edited by Ronald T. Borchardt, Roger M. Freidinger, Tomi K. Sawyer, and Philip L. Smith. Plenum Press, New York. 1998. xxix + 607 pp. 16 × 23 cm. ISBN 0-306-45743-1. $125.00.

In the past few years, an almost bewildering array of novel drug discovery technologies has appeared. The genomic revolution, combinatorial chemistry, and the availability of high-speed computers and associated software, to name only a few of the latest tools, have combined to provide a panoply of new approaches for drug discovery. But the importance of factors other than ligand−target affinity is sometimes seriously underestimated in drug discovery. Of equal, if not greater, importance to potency are issues of absorption, distribution, metabolism, and excretion (ADME). These questions are normally faced during the *development* phase of the R&D process. But as more is understood about these processes, the possibility of specifically maximizing drug activity through rational structural changes designed to enhance absorption and distribution to the site of action, while favorably influencing metabolism and excretion, is increasingly feasible. Thus, a closer integration of discovery and development in pharmaceutical R&D is clearly desirable, and this timely and important book takes an excellent approach to exploring the implications of this challenge.

Written almost exclusively by industrial scientists from "big-pharma", the volume comprises 25 case histories that describe, with varying degrees of success, both the discovery and the development issues encountered in bringing agents from discovery to market. Experiences with renin inhibitors, angiotensin II antagonists, thrombin inhibitors, and endothelin receptor antagonists comprise the first five chapters in the book. These reports are followed by case histories that consider LHRH agonists and antagonists, as well as somatostatin agonists. The discussions of the development of agonist drugs are of special interest inasmuch as the medicinal chemical theories underlying agonist design are still almost nonexistent. Further lessons are drawn from antiviral projects, prodrug development, and the development of topically active carbonic anhydrase inhibitors for the treatment of glaucoma.

The importance of the search for orally active drugs is considered again and again in these case histories. Important factors for enhancing this property were found to be aqueous solubility and relatively low molecular weight to minimize biliary excretion. The use of Caco-2 cells to study intestinal absorption is discussed in several places.

Pharmaceutical development in an era of cost containment brings on a new set of challenges for new products. One important factor is the price of production, considered in discussions of large-scale synthesis. Another is the choice of medical indication, examined by Doherty and Uprichard in their interesting discourse on endothelin antagonists. The development of new antihypertensive agents had little appeal, given the availability of cheap but effective generic diuretics and ACE inhbitors that cost the patient only $0.10−0.20/day. Additionally, the expense of lengthy clinical studies to determine outcomes of antihypertensive therapy mandated an examination of other indications for clinical studies of endothelin antagonists.

There is a wealth of interesting and important information for the medicinal chemist in this reasonably priced, well-produced book. A welcome addition would have been a chapter that classifies and summarizes the issues and answers discussed in the individual chapters.

Manfred E. Wolff
Intellepharm, Inc.
1304 Morningside Drive
Laguna Beach, California 92651-2809

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