Book Reviews

Cardiovascular Pharmacotherapeutics. Second Edition. Edited by William H. Frishman, Edmund H. Sonnenblick, and Domenic A. Sica. McGraw-Hill Medical Publishing Division, New York. 2003. xxiv + 1072 pp. 22.5 × 29 cm. ISBN 0-07-136981-3. $159.00.

This book consists of five parts. Part I has six introductory chapters. Part II consists of 21 chapters covering a wide variety of drug classes currently in clinical use to treat cardiovascular disorders. Part III addresses new cardiovascular drugs under devlopment. Part IV consists of five chapters, each of which addresses special topics related to carediovascular disease. Part V contains eight appendices.

Part I provides valuable background information on principles of drug kinetics, placebo effects, compliance with drug treatment, FDA process for approving new drugs, economic considerations for cardiovascular drug utilization, and a historical perspective on cardiovascular pharmacology. Some of these chapters were relatively short and might have been better if they were expanded.

Part II represents the major portion of the book. The chapters extensively address a wide variety of drug classes that have a direct or indirect effect on the cardiovascular system. The information provided is in most cases up to date, and the cited references are both abundant and recent. Most of the contributors are physicians or pharmacologists, and the book is aimed mainly at practitioners. Not all of the chapters provided chemical structures of the drugs discussed, and this omission probably makes the book less appealing for medicinal chemists.

Part III addresses several prospective classes of cardiovascular drugs currently under development. These are grouped according to their assumed mechanism of action. This topic of investigational drugs was properly covered and well documented. The chemical structures of the investigational drugs were extensively depicted. Lead references in this section will be useful for chemist researchers working in the area of drug development.

Part IV addresses some important social issues related to cardiovasacular therapy. The selected special topics include use of alternative medicine, drug interactions, pediatric pharmacology, and quality of life aspects associated with therapy. The chapters indicate valuable literature sources.

The appendices included in Part V are well organized and contain generally accurate data. They can be viewed as a handy and quick source of information on cardiovascular drugs and therapeutic indications. In summary, the book represents a valuable source of information on cardiovascular drugs and it reflects an outstanding effort by the authors and editors.

Ahmed S. Mehanna

Department of Pharmaceutical Sciences
Massachusetts College of Pharmacy and Health Sciences
Boston, Massachusetts 02115

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Modern Methods of Drug Discovery. Edited by Alexander Hillisch and Rolf Hilgenfeld. Birkhäuser Verlag, Basel, Switzerland. viii + 292 pp. 17 × 24 cm. ISBN 3-7643-6081-X. 127.00 euro.

It is not an overstatement to say that the shortfall in approved new chemical entities produced by the pharmaceutical industry has reached crisis proportions. In 2002, for the first time, the market share of generic drugs surpassed that of patented prescription medicines in the U.S. In the same year, the number of U.S. new chemical entity approvals, which had hovered in the 20s and 30s, dropped to a 20-year low of 16. Yet, the magnitude of spending on industrial pharmaceutical R&D had tripled during the preceding decade. And the top unmet medical needs—cardiovascular disease, cancer, stroke, chronic respiratory disease, certain infectious diseases, and others—remain as challenges that have been addressed only partially.

In the face of these realities, a bewildering array of novel drug discovery technologies has appeared during the past decade. The genomic revolution, combinatorial chemistry, and the availability of high-speed computers and their associated software, to name only a few of the latest tools, have combined to provide a panoply of new approaches to provide medicinal agents. But of what strategic importance are these techniques to the pharmaceutical industry and how should the medicinal chemist exploit them?

In their attempt to address these issues as the editors of this volume, Hillisch and Hilgenfeld ask the question "Can these methods also improve the economics of drug research, development, and commercialization per se?" Comprising 13 chapters, the book is written by 28 industrial and academic contributors: 12 from Germany, 10 from the U.S., and 6 from the U.K. After an introductory chapter by the editors that includes a discussion of genomics, there are chapters on proteomics and protein 3D structures, bioinformatics, combinatorial chemistry, structure-based library design, computational treatment of molecular diversity, natural products as leads, high-throughput screening, NMR-based screening, 3-D QSAR, physicochemical concepts in drug design, and computer-aided prediction of ADMET.

In the space of a brief review, it is clearly not possible to discuss the content of the individual chapters in any kind of detail, but it may be appropriate to provide some general comments. This volume is an important contribution because it provides a succinct and timely overview of the most important drug discovery methods. It is up-to-date, well written and edited, beautifully printed and produced by the publisher, and has an extensive 14-page index that makes it easy to find topics of interest. Each chapter concludes with a list of mostly recent references including their titles and thus provides easy access to further information. This timely, moderately priced volume is suitable for acquisition by academic and industrial libraries, individual medicinal chemists, and students in advanced courses in medicinal chemistry.

But if there is an answer to the editorial question quoted earlier, it may well be found in the chapter on proteomics. As these authors state, "it is at the protein level that disease processes become manifest and at which most drugs act." And the protein expression profile is now realized to be far larger, more dynamic, and more complex than was believed only recently. Data are presented showing that hundreds of liver proteins are affected by the administration of a single drug, clofibrate, including over a dozen previously unknown proteins that could represent new targets. Thus, the reductionist hope of medicinal chemists from the time of Paul Ehrlich (also ardently embraced in the past decade by business planners)—that drug design would be a fully predictable process if only the nature of the drug/target complex were precisely understood at the atomic level—is unlikely ever to be realized. Instead, the molecular events underlying drug action are so extensive and intertwined that the situation is more akin to global long-range weather prediction or global economic theory, where only partial predictability can be expected.

Manfred E. Wolff

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

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