



Molecules and Medicine

By E. J. Corey, Barbara Czakó and László Kürti. John Wiley & Sons, Hoboken 2007. 272 pp., softcover € 39.90.—ISBN 978-0-470-22749-7

Molecules and Medicine describes the discovery of small-molecule medicines across the full range of therapeutic areas, focusing on the chemical structures and features of each drug. The scientific development and mechanism of action of different classes of drugs are described from the molecular level perspective, highlighting the importance of understanding the chemistry associated with these highly successful medicines. The authors provide proper biological and medical context to convey a full appreciation of the development of these drugs.

This book consists of concise, highly informative, one-page descriptions of individual drugs, each of which is selected to be representative of that class (e.g., beta-blockers, HIV protease inhibitors). The medicines are generally grouped together in chapters according to therapeutic area (e.g., cardiovascular, infectious disease). An important supplement to this arrangement is the incorporation of biological and pharmacological overviews of the area under discussion. The format of these overviews is consistent with the succinct and focused nature of this monograph, and they provide enough background information to put the molecules of interest in proper context. The overall concise and modular design of the book makes it possible to read it in installments, and therefore it is likely to serve as a valuable reference source. It includes a useful glossary and an index.

The entry for each molecule contains the following information: generic and trade names, three structural representations (traditional structural formula, ball-and-stick model, and a space-filling model), year of discovery, year of introduction, drug category, main uses, and related drugs in that category. In general, this format is maintained consistently throughout the monograph and provides a useful synopsis of the key information. However, the drug category entries could be made more precise by including a differentiation between drug *category* and drug *mechanism*. For example, the entry for atorvastatin lists the drug category as “statin”, which could be nicely complemented by an entry “HMG-CoA reductase inhibitor” under the heading *mechanism*.

Before embarking on the descriptions of the representative molecules for each drug class, the authors present a tutorial on the bonding principles that govern the structures of the organic molecules that comprise these medicines (Part I). Additionally, a brief overview of protein structure is given to provide context for the molecular interactions between the proteinaceous drug targets and the small molecule medicines with which they interact. These sections provide a concise fundamental guide that will serve as a useful refresher for the reader who has been exposed to the topics previously; however, readers without some form of scientific training might find this structural primer intimidating.

Part II is the largest chapter, and focuses on inflammatory, cardiovascular, and metabolic diseases. This section begins with acetylsalicylic acid, and includes a historical perspective. Where appropriate, such historical viewpoints are provided throughout the book, and are an enrichment to the scientific information. Also contained within this chapter is an overview of the inflammation process, focusing on the biosynthetic pathways that convert arachidonic acid to the prostaglandins and leukotrienes; notably, the enzymes that catalyze these transformations, as well as the receptors for the resultant products, are the drug targets of the small molecules discussed (e.g., the COX-2 inhibitor celecoxib for osteoarthritis, and the

CysLT antagonist montelukast for asthma).

The subsection of Part II that deals with antidiabetic and cholesterol-lowering agents is complemented by an overview of metabolic syndrome. The incorporation of the DPP-4 inhibitor sitagliptin for the treatment of Type 2 diabetes illustrates the fact that even the most recent small-molecule medicines are captured within this monograph. Despite the tremendous impact on human health, as well the interesting chemical structures that are critical for potency, only a single one-page entry is allotted to the drug class of statins as cholesterol-lowering agents (i.e., atorvastatin). Representative examples of cardiovascular drugs, such as beta-blockers, ACE and renin inhibitors, angiotensin receptor antagonists, and calcium channel antagonists round off Part II.

The next chapter (Part III) describes medicines that treat multiple therapeutic areas, including reproductive medicine, osteoporosis, glaucoma, and anti-ulcer agents. A crisp account of the processes that govern bone formation and resorption is well-placed to precede the discussion on therapeutics for osteoporosis. The intriguing molecular mechanism of action of the proton pump inhibitors (e.g., omeprazole) is given due attention to highlight the importance of understanding the chemistry that underlies these medicines.

Part IV deals with immunosuppressive agents and drugs to treat infectious diseases. These two seemingly disparate areas are unified by a survey of the immune system, which is considerably more detailed and complex in comparison to the other biological area overviews. The outstanding two-page entry for amoxicillin begins the discussion of antibiotics with a historical perspective on the β -lactam substructure and its importance to drug discovery. This section ends with an important discussion of the mechanisms that lead to drug resistance, which provides a nice bridge to the following section on antiviral agents. These entries on antivirals incorporate much of the detailed mechanistic and structural information generated over the course of the last two decades, as well as showing how this data has been used to develop highly effective

medicines. For example, the importance of the transition-state mimetic as a critical pharmacophore in the development of potent HIV protease inhibitors is well documented in the entry for lopinavir.

Therapeutics for the treatment of malignant disease are covered in Part V, and the authors outline the major small-molecule advances. The impact that natural products have made on the field of oncology medicines is illustrated by several pertinent examples (e.g., vinblastine, paclitaxel).

The final chapter (Part VI) is concerned with the development of drugs that act on the nervous system. Pain (analgesia) treatments are grouped together, including thorough coverage of the opiate (morphine) and barbiturate (sodium thiopental) drug classes. This is then followed by the last pharmacological overview, which covers neurotransmitters and neurotransmission. This chapter then breaks from format by describing several different drug classes grouped together for CNS disorders (instead of the previous format of one molecule per drug class). For example, there is a general section on antidepressants, in which examples of MAO inhibitors, tricyclics, and SSRIs are all grouped together. As acknowledged by the authors, this is a consequence of the relative dearth of treatments for neurodegenerative and psychiatric diseases.

The authors intend this monograph to be of interest to a broad readership, from the active practitioner of life sciences and medicine to the educated and interested lay person. It is the authors' desire that this book will enhance public understanding of medical science, and specifically of pharmaceutical research. Another significant objective of this work is to stimulate the interest of students of the life sciences to consider a career in the health and medical fields, so that the momentum of advances outlined herein can be sustained indefinitely. Finally, this book acknowledges the tremendous difficulty associated with the discovery of novel drugs, and is intended to pay tribute to the creativity, talent, and effort of the teams of scientists and physicians that have produced these medicines.

Overall, *Molecules and Medicine* accomplishes the objective of astutely, yet concisely, describing the discovery of small-molecule medicines, while focusing on the essential chemical features of each drug. This monograph could serve as a superb guidebook for a university course on medicinal chemistry as applied to the pharmaceutical industry. Additionally, this book should be utilized by all scientists, especially medicinal chemists, who are embarking on careers in drug discovery, and in that respect *Molecules and Medicine* fills a significant void and should be of tremendous value.

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