Book Reviews

Analog-Based Drug Discovery. Edited by Janos Fischer and C. Robin Ganellin. Wiley/VCH Verlag GmbH, Weinheim, Germany. 2006. xxi + 575 pp. 17.5 × 42.5 cm. ISBN 3527312579. $180.00.

The demand for effective pharmaceuticals to address unmet medical needs is as great as it ever has been, but with ever-increasing requirements for safety, efficacy, and economy, the difficulties are even greater. Whether new to the field or experienced, drug designers—medicinal chemists—must improve the quality of their designed analogues if they are to shorten the long odds of success. This book modestly states an aim to "describe selected analogue classes in a more detailed manner", but it is actually much more. It is an excellent tutorial on the most important precepts of drug design, and the breadth and generality of the principles described will aid all medicinal chemists. It also serves very well as a reference book, with chapters generously appended with citations.

The editors are eminently qualified medicinal chemists and inventors of successful drugs, as are the authors of the individual chapters. The book shows an adroit hand in the editing; the texts of diverse chapters are consistently crisply written, and they are generously populated with figures that illustrate the topics discussed, with clear examples.

Part 1 teaches general principles. Chapter 1 classifies approaches to the design of drug structures, for example, how and why to modulate electronic or lipophilic properties or to make positional isomers. Also illustrated is the SOSA approach that the chapter author has advocated, wherein known drugs can be used as cores and be extensively modified to produce new structures. Chapter 2 illuminates a topic often discussed ("drug-likeness") with reference to structural determinants of molecular and physicochemical properties. The concept of privileged structures is ably and clearly described in Chapter 3 and is illustrated by reference to the broad target categories (GPCRs, kinases, etc.).

Part 2 of the book moves beyond the general tutorial of Part 1, with an impressive set of case histories—many of them written by the inventors or developers of key drugs in the class—that specifically illustrate how general principles were used to design well-known drugs. The discovery of antiulcer H_2 antagonists is described in Chapter 1 by the inventor of cimetidine. The fascinating story of the proton pump inhibitor esomeprazole is the topic of Chapter 2, and the story of pantoprazole is in Chapter 3.

The discovery, optimization, and profiles of cardiovascular classes is told in Chapter 4 (HMG-CoA reductase), in Chapter 5 (angiotensin antagonists), in Chapter 6 (ACE inhibitors), in Chapter 7 (lacidipine and calcium channel antagonists), in Chapter 8 (β -adrenergic receptor blockers), in Chapter 9 (the ultra-short acting β-blocker esmolol), and in Chapter 10 (organic nitrates). Extensive histories of the discovery and development of CNS agents are addressed in Chapter 11 (opioids), Chapter 12 (anticholinergic stigmines), and in Chapter 13 (clozapine and analogues). Additional drugs covered are the quinolinone antibiotics and moxifloxacin (Chapter 14), bisphosphonates (Chapter 15), cisplatin and oncolytic analogues (Chapter 16), drosperienone (Chapter 17), histamine H_1 receptor antagonists (Chapter 18), and corticosteroids (Chapter 19). A treasure of knowledge is to be found in most of these chapters. They are not eclectic reports directed only to devotees of the particular target, but instead they are written in an accessible style meant to allow chemists across a wide range of backgrounds to learn from the experiences of expert teams.

Part 3 of the book is unique: it contains extensive tables of all of the principle therapeutic drug categories, with drug structures, launch dates, and lead patent numbers and molecular weights. This affords the reader the convenience of scanning structures of known drugs and the appreciation of how these drugs illustrate the druglikeness principles discussed in Part 1 of the book.

This book is eminently capable of educating both newcomers and experienced practitioners to the fields of medicinal chemistry and pharmacology, and it is highly recommended as an addition to the personal collection of the practicing drug designer and as a reference volume for institutional use as well.

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