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Book Review

Metabolism, Pharmacokinetics and Toxicity of Functional Groups. Edited by Dennis A. Smith. Royal Society of Chemistry Publishing, Cambridge, U.K. 2010. xiv +530 pp. 16 × 24 cm. ISBN 978-1-84973-016-7. $173.76.

Given the many books that have already appeared on the subject of absorption, distribution, metabolism, excretion, and toxicology (ADMET) in drug discovery, I was initially skeptical that there could be room for yet another one, but I was wrong. This volume is directed almost exclusively at the practicing medicinal chemist and uniquely arranges the topic of drug metabolism and pharmacokinetics in specific chapters, each devoted to a single functional group or isostere. Within each chapter various drugs that contain the same functional group are discussed and the influence of that particular group on the drug's ADMET is explained.

The book is edited by Dennis Allen Smith of Pfizer in the U.K., and even though all of the authors are also in some way associated with Pfizer, the diverse drugs they cover are from every imaginable source in the pharmaceutical industry. The book includes 11 large chapters, each with well-developed subsections. After a preface by Smith, the first chapter reviews the current financial hurdles facing the pharmaceutical industry and the daunting challenges of quickly bringing a candidate drug successfully to market. It also explores the concepts of chemical space and the many and often complex reasons for compound attrition. Chapter 2 is a rather thorough review of ADMET concepts for the medicinal chemist, covering drug delivery, tissue distribution, and the main anatomical routes of drug metabolism and final clearance. The remaining chapters sequentially address the ADMET influence of different functional groups on drugs with numerous examples. These groups include carboxylic acids, amines, sulfonamides, aromatic and heteroaromatic rings, peptides, alcohols, and phenols. Deviating slightly from this pattern is Chapter 9, which specifically discusses enzyme inhibitors. The interesting final chapter is forward-looking and poses several challenges. First, the authors argue for the existence of a "genome gap" and point out that researchers "have only scratched the surface of druggable and disease-modifying proteins" revealed by the human genome project. Of special interest to the medicinal chemist reader is also their observation of a "chemistry gap" with the urgent need for new synthetic tools and methodology to assemble increasingly complex target molecules. Each of the chapters includes numerous pertinent references to the original literature, with some citations as recent as 2009. The book concludes with a comprehensive subject index.

The book is easily read and contains many useful illustrations, tables, and scores of chemical structures. The authors have done a complete job of clearly explaining such a complex field to a specific audience. For that reason this timely volume will be valuable to experienced medicinal chemists as both an introduction to ADMET and a valuable reference work.

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