DRUG METABOLISM
Drug Metabolism
Current Concepts

Edited by

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Springer
Dedication

To the memory of my parents

To my beloved husband and son, for their continuous support, understanding and encouragement.

Corina Ionescu
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PREFACE

This book is intended to serve a wide audience, including students of chemistry, pharmacy, pharmacology, medicine, biochemistry and related fields, as well as health professionals and medicinal chemists. Our aim in preparing it has been threefold: to introduce essential concepts in drug metabolism (drug biotransformation), to illustrate the wide-ranging medical implications of such biological processes and to provide the reader with a perspective on current research in this area. The general intention is to demonstrate that the metabolism of a drug is a primary concern throughout its lifetime, from its inception (chemical design and optimisation) to its final clinical use, and that for any given drug, the multiple factors influencing its metabolism necessitate on-going studies of its biotransformation.

In the first chapter, the principles underlying drug absorption, distribution, metabolism and elimination are described, with drug metabolism highlighted within the context of these fundamental processes. Chapters 2 and 3 deal with the chemistry of drug biotransformation, describing both Phase I (‘asynthetic’) and Phase II (‘synthetic’) biotransformations and the enzymes that mediate them. Further details of the structural features, mechanisms of action in biotransformation, and regulation of enzymes appear in Chapter 4. Enzyme induction and inhibition, with special reference to the cytochrome P450 system, are examined in Chapter 5. This is followed, in Chapter 6, by a discussion of the influence of sex, age, hormonal status and disease state on drug biotransformation. An introduction to the relatively new discipline of pharmacogenetics, probing the effects of gene variability on drug biotransformation, is the subject of Chapter 7. This includes commentary on the implications of pharmacogenetics for the future dispensing of medicines. Chapter 8 treats two special topics that have significant clinical implications, namely drug-drug interactions and adverse reactions. Included in this chapter is an extensive tabulation of drug-drug interactions and their biological consequences. Finally, Chapter 9 attempts to demonstrate how considerations based on a sound understanding of the principles of drug metabolism (described in the earlier chapters) are incorporated into the drug design process in order to maximise the therapeutic efficacy of candidate drugs. This is of paramount interest to the medicinal chemist whose aim is to design safe and effective drugs with predictable and controllable metabolism.

The text is supported extensively by pertinent examples to illustrate the principles discussed and a special effort has been made to include frequent literature references to recent studies and reviews in order to justify the term ‘current’ in the title of this work.

Corina Ionescu                                      Mino Caira
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