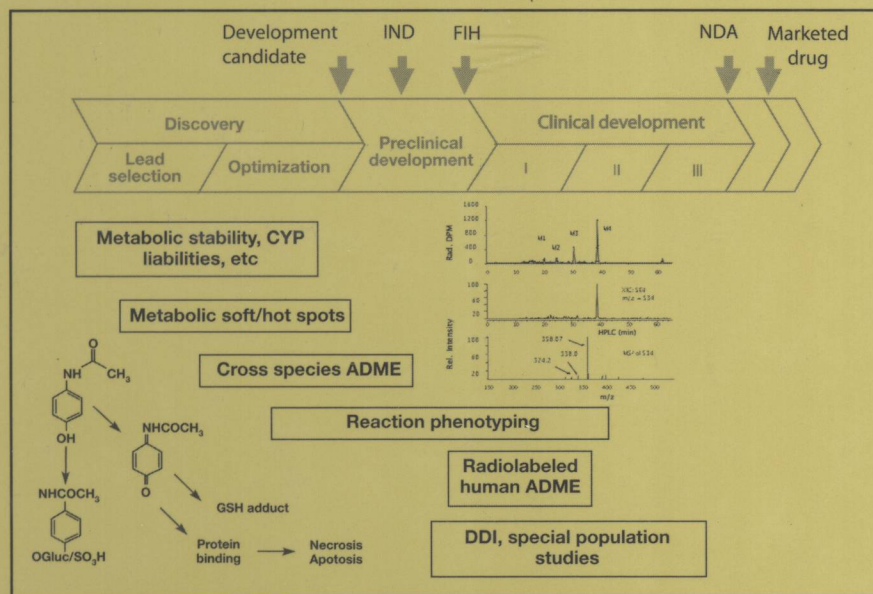


DRUG METABOLISM IN DRUG DESIGN AND DEVELOPMENT



Edited by
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DRUG METABOLISM IN DRUG DESIGN AND DEVELOPMENT

Basic Concepts and Practice

EDITED BY

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IN DRUG DESIGN
AND DEVELOPMENT**



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PREFACE

Information on the metabolism and disposition of candidate drugs has become a critical part of all aspects of the drug discovery and development process. This comprehensive involvement of drug metabolism information has been brought about by a desire for quality design at an early stage, sometimes referred to as designing good “developability” characteristics, and then to work proactively with clinical and safety organizations to impact the design of the various development programs. This desire is driven by the need to reduce attrition rates as a means to effectively lower the cost of drug development.

Drug metabolism information in the early stages of discovery can help guide medicinal chemistry efforts toward optimization of preclinical safety and efficacy properties. This approach can be made even more effective with the active involvement of other disciplines such as pharmaceutics and toxicology. Candidates can be optimized by examining a variety of parameters beyond potency and efficacy. During the development stages drug metabolism information can help guide drug–drug interaction and special population clinical studies. Metabolism information is also critical for designing toxicology studies to that ensure the safety of metabolites is adequately tested and can also be a key part of addressing whether toxicology found in animals is likely to translate to humans.

Drug metabolism, as practiced in the pharmaceutical industry, is a multidisciplinary field that requires knowledge of analytical technologies, expertise in mechanistic and kinetic enzymology, organic reaction mechanism, pharmacokinetic analysis, animal physiology, basic chemical toxicology, preclinical pharmacology, and molecular biology. Scientists entering the field from academia often receive coursework in many of the above areas, but have usually focused the bulk of their research efforts on only one of above mentioned fields. It often requires a number of years of practice for a new scientist to gain a comprehensive understanding of all the disciplines necessary to apply drug metabolism knowledge effectively to the drug discovery and development processes.

This book offers background information as well as practical descriptions of what happens during the drug design and development process. Emphasis will be

placed on issues such as what data are needed, what experiments and analytical methods are typically employed, and how to interpret and apply data. The chapters of this book will highlight facts, detailed experimental designs, applications, and limitations of techniques.

The book was not intended to be a collection of individual reviews, rather a coherent integration of all relevant background information as well as detail of the experimental strategies and processes necessary for drug metabolism research during drug design and development. Authors aimed at providing a balanced, comprehensive perspective on their subject matter and were encouraged to include a full range of experimental approaches. The book contains four parts that should serve to integrate the entire process: Part I, Basic Concepts of Drug Metabolism; Part II, Role of Drug Metabolism in Pharmaceutical Industry; Part III, Analytical Techniques in Drug Metabolism; Part IV, Common Experimental Approaches and Protocols. This structure should provide a valuable resource to researchers seeking to broaden their knowledge of drug metabolism science as practiced in the modern pharmaceutical industry.

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