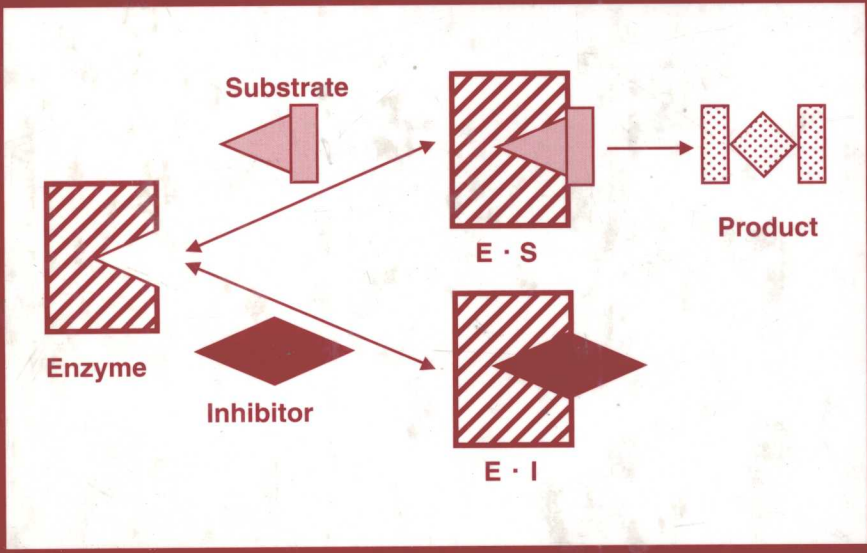
DRUGS AND THE PHARMACEUTICAL SCIENCES VOLUME 116

Drug—Drug Interactions



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Drug—Drug Interactions

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Preface

Our knowledge of the various human drug metabolizing enzyme systems continues to grow. In recent years, this expansion in knowledge has been fueled by significant advances in molecular biology, the increased availability of human tissue, and the development of reliable model systems and sensitive assay methods for studying drug metabolism in vitro. In fact, in vitro methodology has become increasingly ''standardized'' and has been widely accepted by academic institutions, the pharmaceutical industry and regulatory agencies. However, while in vitro approaches can be used to screen large numbers of compounds preclinically, it is recognized that accurate forecasting of drug–drug interaction is predicated on sound knowledge of in vivo pharmacokinetics and the availability of validated in vitro–in vivo correlations.

Towards this end, the purpose of *Drug–Drug Interactions* is to relate pharmacokinetic concepts to the Michaelis–Menten kinetics describing in vitro enzyme-catalyzed biotransformation reactions. With kinetics as a foundation, the topic of drug–drug interactions is presented in terms of the various in vitro models, representative enzyme systems (e.g., cytochromes P450 and UDP-glucuronosyltransferases), and approaches (e.g., kinetics-based in vitro–in vivo correlations, computer-aided molecular modeling studies and informational databases). Although the subject matter focuses on metabolism-based drug–drug interactions resulting from inhibition and induction of drug-metabolizing enzymes, it is acknowledged that drug–drug interactions can occur via other mechanisms (e.g., competition for drug transporters and binding sites on plasma proteins, or pharmacodynamic drug–drug interactions).

An additional objective of this book is to present the subject of drug–drug interactions from preclinical, clinical, toxicological, regulatory, and marketing

perspectives. Therefore, it is hoped that *Drug–Drug Interactions* will be useful to students and seasoned scientists in the fields of molecular biology, pharmacokinetics, enzymology, toxicology, drug metabolism, pharmacology, clinical pharmacology, medicine, and medicinal chemistry. The subject matter will also appeal to those involved in the marketing of drugs. In the end, the book will have achieved its purpose if it serves merely to provoke constructive debate among individuals within these various disciplines.

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