1. Record Nr. UNINA9910143982103321

Titolo	Drug-drug interactions in pharmaceutical development [[electronic resource] /] / edited by Albert P. Li
Pubbl/distr/stampa	Hoboken, N.J., : Wiley-interscience, c2008
ISBN	1-282-02206-7 9786612022067 0-470-18792-1 0-470-18791-3
Descrizione fisica	1 online resource (261 p.)
Collana	Wiley series in drug discovery and development
Altri autori (Persone)	LiA. P
Disciplina	615.7045 615/.7045
Soggetti	Drug interactions Drug development
Lingua di pubblicazione	Inglese
Formato	Materiale a stampa
Livello bibliografico	Monografia
Note generali	Description based upon print version of record.
Nota di bibliografia	Includes bibliographical references and index.
Nota di contenuto	DRUG-DRUG INTERACTIONS IN PHARMACEUTICAL DEVELOPMENT; CONTENTS; Preface; Contributors; 1 In Vitro Evaluation of Metabolic Drug-Drug Interactions: Concepts and Practice; 1.1 Introduction; 1.2 Mechanisms of Adverse Drug-Drug Interactions; 1.2.1 Pharmacological Interactions; 1.2.2 Pharmacokinetic Interactions; 1.3 Drug Metabolism; 1.3.1 Phase I Oxidation; 1.3.2 Phase II Conjugation; 1.4 CYP Isoforms; 1.5 Human In Vitro Experimental Systems for Drug Metabolism; 1.5.1 Hepatocytes; 1.5.2 Liver Postmitochondrial Supernatant (PMS); 1.5.3 Human Liver Microsomes; 1.5.4 Recombinant P450 Isoforms (rCYP) 1.5.5 Cytosol1.6 Mechanisms of Metabolic Drug-Drug Interactions; 1.7 Mechanism-Based Approach for Evaluation of Drug-Drug Interaction Potential; 1.7.1 Metabolic Phenotyping; 1.7.2 Evaluation of Inhibitory Potential for Drug-Metabolizing Enzymes; 1.7.3 Induction Potential for Drug-Metabolizing Enzymes; 1.8 Experimental Approaches for In Vitro Evaluation of Drug-Drug Interaction Potential; 1.8.1 Study 1: Metabolic Phenotyping 1-Metabolite Identification; 1.8.2 Study 2: Metabolic Phenotyping 2-Identification of Major Metabolic Pathways 1.8.3 Study 3: Metabolic Phenotyping 3-Identification of P450 Isoform

Pathways (P450 Phenotyping)1.8.4 Study 4: CYP Inhibitory Potential; 1.8.5 Study 5: Enzyme Induction Potential; 1.8.6 Study 6: In Vitro Empirical Drug-Drug Interactions; 1.9 Data Interpretation; 1.9.1 Pathway Evaluation; 1.9.2 P450 Inhibition; 1.9.3 P450 Induction; 1.10 Conclusion; References; 2 In Vitro Approaches to Anticipating Clinical Drug Interactions; 2.1 In Vitro Systems for Human CYP450 Metabolism; 2.1.1 Incubation Buffer (pH and Ionic Strength); 2.1.2 MgCl(2) and Cytochrome b(5); 2.1.3 Nonspecific Binding
2.1.4 Organic Solvents and Excipients2.2 Analysis of Data from In Vitro Systems; 2.2.1 Linear Transformation of Michaelis-Menten Equation (Lineweaver-Burk and Eadie-Hofstee); 2.2.2 Nonlinear Regression Analysis of Hyperbolic Kinetic Data; 2.2.3 Consideration of Non-Michaelis-Menten Kinetics; 2.3 Use of In Vitro Kinetic Data to Predict In Vivo Clearance; 2.3.1 Calculation of In Vitro (Predicted) Hepatic Clearance; 2.3.2 Comparison of In Vitro (Predicted) with In Vivo Hepatic Clearance; 2.4 Use of In Vitro Kinetic Data to Predict Drug-Drug Interactions
2.4.1 Choice of Probe Substrates for Inhibition Studies2.4.2 Determining the Mechanism of CYP450 Inhibition; 2.4.3 Prediction of In Vivo Drug-Drug Inhibition Interactions from In Vitro Data; 2.5 Consideration of Non-CYP Enzymatic Systems; 2.5.1 Flavin-Containing Monooxygenase (FMO); 2.5.2 UDP-glucuronosyltransferase (UGT); 2.5.3 Sulfotransferase (SULT); 2.5.4 N-Acetyltransferase (NAT); 2.5.5 Methyltransferase; 2.5.6 Epoxidase Hydrolase; 2.5.7 Aldehyde Oxidase and Dehydrogenase; 2.5.8 Glutathione-S-transferase (GST); 2.6 Summary; 2.7 Acknowledgments; References
3 Inhibition of Drug-Metabolizing Enzymes and Drug-Drug Interactions in Drug Discovery and Development

Sommario/riassunto

Drug-Drug Interactions in Pharmaceutical Development comprehensively reviews the relevant science, industrial practice, and regulatory agency positions on drug-drug interactions. It focuses on the evaluation of potential drug-drug interactions, allowing researchers to address risk factors before a drug is put to market. The book covers both clinical and nonclinical aspects for understanding drug-drug interactions as well as in vitro and in vivo studies for use in studying interactions at the drug discovery stage.