1. Record Nr. UNINA9910830456403321 Drug metabolism in drug design and development [[electronic resource] Titolo 1: basic concepts and practice //edited by Donglu Zhang, Mingshe Zhu, W. Griffith Humphreys Hoboken, N.J., : Wiley-Interscience, c2008 Pubbl/distr/stampa **ISBN** 1-281-09423-4 9786611094232 0-470-19169-4 0-470-19168-6 Descrizione fisica 1 online resource (633 p.) Altri autori (Persone) ZhangDonglu ZhuMingshe HumphreysW. Griffith Disciplina 615.7 615/.7 Soggetti Drugs - Metabolism Drugs - Design Drug development Lingua di pubblicazione Inglese **Formato** Materiale a stampa Livello bibliografico Monografia Description based upon print version of record. Note generali Nota di bibliografia Includes bibliographical references and index. DRUG METABOLISM IN DRUG DESIGN AND DEVELOPMENT; CONTENTS; Nota di contenuto Preface; Contributors; PART I BASIC CONCEPTS OF DRUG METABOLISM; 1 Overview: Drug Metabolism in the Modern Pharmaceutical Industry; 1.1 Introduction; 1.2 Technology; 1.3 Breadth of Science; 1.3.1 Chemistry; 1.3.2 Enzymology and Molecular Biology; 1.4 Impact of Drug Metabolism on Efficacy and Safety; 1.4.1 Efficacy; 1.4.2 Safety; 1.5 Regulatory Impact and IP Position; 1.6 Summary; References; 2 Oxidative, Reductive, and Hydrolytic Metabolism of Drugs; 2.1 Introduction; 2.2 Nomenclature and Terminology 2.3 General Features of the Enzymes2.4 Fractional Contributions of Different Enzymes; 2.5 Oxidation Enzymes; 2.5.1 Cytochrome P450 (P450, CYP); 2.5.2 Flavin-Containing Monooxygenase (FMO); 2.5.3 Monoamine Oxidase (MAO); 2.5.4 Aldehyde Oxidase and Xanthine Dehydrogenase; 2.5.5 Peroxidases; 2.5.6 Alcohol Dehydrogenases

(ADH); 2.5.7 Aldehyde Dehydrogenases (ALDH); 2.6 Reduction; 2.6.1 P450, ADH; 2.6.2 NADPH-P450 Reductase; 2.6.3 Aldo-Keto Reductases (AKR); 2.6.4 Quinone Reductase (NQO); 2.6.5 Glutathione Peroxidase (GPX); 2.7 Hydrolysis; 2.7.1 Epoxide Hydrolase; 2.7.2 Esterases and Amidases 2.8 SummaryReferences; 3 Conjugative Metabolism of Drugs; 3.1 UDP-Glucuronosyltransferases; 3.1.1 Location Within the Cell; 3.1.2 Endogenous Substrates; 3.1.3 Enzyme Multiplicity; 3.1.4 Inducibility;

Enzyme Selective Substrates and Inhibitors; 3.1.8 Drug-Drug Interactions and Glucuronidation; 3.1.9 Summary; 3.2 Cytosolic Sulfotransferases; 3.2.1 Cellular Location and Tissue Expression; 3.2.2 The SULT Superfamily of Cytosolic Enzymes; 3.2.3 Inducibility; 3.2.4 SULT Pharmacogenetics

3.1.5 Pharmacogenetics: 3.1.6 Experimental Considerations: 3.1.7

3.2.5 Analytical Detection of Sulfonated Metabolites 3.2.6 SULT Inhibitors (Pacifici and Coughtrie, 2005); 3.2.7 Drug-Drug Interactions and Sulfonation; 3.2.8 Summary; 3.3 Glutathione-S-Transferases; 3.3.1 General Overview; 3.3.2 Classification of the GST Enzymes; 3.3.3 Localization and Expression; 3.3.4 Reactions Catalyzed by GSTs; 3.3.5 Regulation of GSTs; 3.3.6 GST Alpha Class; 3.3.7 GST Mu Class; 3.3.8 GST Pi Class; 3.3.9 GST Theta Class; 3.3.10 GST Zeta Class; 3.3.11 Incubation Conditions and Analytical Methods; 3.3.12 Glutathione Conjugate Metabolism (Mercapturic Acid Pathway)

References4 Enzyme Kinetics; 4.1 Introduction; 4.2 Enzyme Catalysis; 4.3 Michaelis-Menten Kinetics; 4.3.1 Meanings of K(m), V(max) and Their Clinical Relevance; 4.4 Graphical Kinetic Plots; 4.5 Atypical Kinetics-Allosteric Effects; 4.5.1 Overview of Atypical Kinetic Phenomena; 4.5.2 Homotropic Cooperativity; 4.5.3 Heterotropic Cooperativity; 4.6 Graphical Analysis of Atypical Kinetic Data; 4.7 Enzyme Inhibition Kinetics; 4.7.1 Overview; 4.7.2 Competitive Inhibition; 4.7.3 Mixed Inhibition; 4.7.4 Noncompetitive Inhibition; 4.7.5 Uncompetitive Inhibition

4.7.6 Summary of Effects of Various Inhibition Types of Kinetic Parameters

Sommario/riassunto

The essentials of drug metabolism vital to developing new therapeutic entitiesInformation on the metabolism and disposition of candidate drugs is a critical part of all aspects of the drug discovery and development process. Drug metabolism, as practiced in the pharmaceutical industry today, is a complex, multidisciplinary field that requires knowledge of sophisticated analytical technologies and expertise in mechanistic and kinetic enzymology, organic reaction mechanism, pharmacokinetic analysis, animal physiology, basic chemical toxicology, preclinical pharmacology, and molecular biol