

Contents

Contributing Authors	ix
Foreword	xvii
Preface	xix
Acknowledgments	xxi

Section I: Prediction of Drug Interactions From *In Vitro* Studies: Basic Principles

1 Metabolically-Based Drug–Drug Interactions: Principles and Mechanisms	3
<i>Kenneth E. Thummel, Kent L Kunze, and Danny D. Shen</i>	
2 From <i>In Vitro</i> to <i>In Vivo</i> : An Academic Perspective	21
<i>René H. Levy and William F. Trager</i>	
3 Industrial Viewpoint: Application of <i>In Vitro</i> Drug Metabolism in Various Phases of Drug Development	29
<i>Barbara J. Ring and Steven A. Wrighton</i>	
4 Regulatory Viewpoint: Prediction of Drug Interactions from <i>In Vitro</i> Studies	41
<i>Jerry M. Collins</i>	

Section II: Enzymes and Transporters

5 Cytochromes P450: Historical Overview	51
<i>John B. Schenkman</i>	
6 CYP1A	61
<i>John O. Miners and Ross A. McKinnon</i>	
7 CYP2C	75
<i>Allan E. Rettie, Dennis R. Koop, and Robert L. Haining</i>	
8 CYP2D6	87
<i>Ulrich M. Zanger and Michel Eichelbaum</i>	
9 CYP2E1	95
<i>Judy Raucy and Susan P. Carpenter</i>	
10 CYP3A	115
<i>Steven A. Wrighton and Kenneth E. Thummel</i>	
11 P-Glycoprotein	135
<i>Jeffrey A. Silverman</i>	

12	Other CYP: 2A6, 2B6, 4A	145
	<i>Michael P. Pritchard and C. Roland Wolf</i>	
13	UDP-Glucuronosyltransferases	161
	<i>Thomas R. Tephly and Mitchell D. Green</i>	
14	Glutathione S-Transferases	175
	<i>David L. Eaton and Theo K. Bammler</i>	
15	Sulfotransferases and Methyltransferases	191
	<i>Richard M. Weinshilboum and Rebecca B. Raftogianis</i>	
16	Epoxide Hydrolases	205
	<i>Curtis J. Omiecinski</i>	

Section III: Drugs As Substrates of Metabolic Enzymes
Treatment of CNS Diseases

17	Anticonvulsants	217
	<i>Gary G. Mather and René H. Levy</i>	
18	Antidepressants	233
	<i>Kan Chiba and Kaoru Kobayashi</i>	
19	Antipsychotics	245
	<i>C. Lindsay DeVane and John S. Markowitz</i>	
20	Sedative-Hypnotic and Anxiolytic Agents	259
	<i>David J. Greenblatt and Lisa L. von Molke</i>	
21	Volatile, Intravenous, and Local Anesthetics	271
	<i>Evan D. Kharasch and Andra E. Ibrahim</i>	
22	Opioid Analgesics	297
	<i>Evan D. Kharasch</i>	
23	Agents for the Treatment of Migraine, Parkinson's, and Alzheimer's Diseases	321
	<i>Tina M. deVries and S. Thomas Forge</i>	

Treatment of Cardiovascular Diseases

24	Calcium Channel Blockers	333
	<i>David R. Jones and Stephen D. Hall</i>	
25	β -Adrenoreceptor Antagonists	347
	<i>Martin S. Lennard</i>	
26	Angiotensin II Antagonists, ACE Inhibitors, and Diuretics	359
	<i>Michael Goldberg</i>	
27	Cholesterol-Lowering Agents and Cardiac Glycosides	379
	<i>Yves Horsmans</i>	
28	Antiarrhythmics	391
	<i>Martin F. Fromm and Michel Eichelbaum</i>	
29	Oral Anticoagulants	403
	<i>William F. Trager</i>	

Treatment of Microbial Diseases

30	Oral Antifungals	415
	<i>David J. Edwards</i>	
31	Antivirals	421
	<i>Jashvant D. Unadkat and Yi Wang</i>	

Treatment of Inflammation

32	H ₁ -Receptor Antagonists	435
	<i>Danny D. Shen, Soraya Madani, Christopher Banfield, and Robert P. Clement</i>	
33	Analgesics—Antipyretics	447
	<i>Sidney D. Nelson</i>	
34	Nonsteroidal Antiinflammatory Drugs	457
	<i>Timothy S. Tracy</i>	
35	Methylxanthines	469
	<i>Donald J. Birkett and John O. Miners</i>	

Treatment of Other Diseases

36	H ₂ -Antagonists, Proton-Pump Inhibitors, and Antiemetics	483
	<i>Ronald M. Laethem and Cosette J. Serabjit-Singh</i>	
37	Immunosuppressive Agents	499
	<i>Mary F. Hebert</i>	
38	Estrogens and Progestins	511
	<i>Maurice G. Emery</i>	
39	Hypoglycemic Agents	529
	<i>William R. Brian</i>	
40	Antineoplastic Agents	545
	<i>James B. Mangold and Volker Fischer</i>	

Section IV: Drugs as Inhibitors of Metabolic Enzymes**Treatment of CNS Diseases**

41	Anticonvulsants	557
	<i>René H. Levy, Gary G. Mather, and Gail D. Anderson</i>	
42	Antidepressants	563
	<i>Mujeeb U. Shad and Sheldon H. Preskorn</i>	
43	Neuroleptics and Antipsychotics	579
	<i>Michael Murray</i>	

Treatment of Cardiovascular Diseases

44	Calcium Channel Blockers	591
	<i>Dagmar Busse and Michel Eichelbaum</i>	

45	Antiarrhythmics	603
	<i>Kim Brøsen</i>	
Treatment of Microbial Diseases		
46	Antimicrobials and Antiparasitics	615
	<i>Ronald E. Polk</i>	
47	Antifungals	623
	<i>Janne T. Backman, Kari T. Kivistö, Jun-Sheng Wang, and Pertti J. Neuvonen</i>	
48	Protease Inhibitors	647
	<i>Jashvant D. Unadkat and Yi Wang</i>	
Treatment of Other Diseases		
49	H₂-Receptor Antagonists	653
	<i>Mary F. Paine</i>	
50	Inhibitors in the Diet: Grapefruit Juice–Drug Interactions	661
	<i>David G. Bailey, J. Malcolm O. Arnold, and J. David Spence</i>	
Section V: Drugs as Inducers of Metabolic Enzymes		
51	Phenobarbital, Phenytoin, and Carbamazepine	673
	<i>Susan M. Abdel-Rahman and J. Steven Leeder</i>	
52	Rifampin, Dexamethasone, and Omeprazole	691
	<i>Graham R. Jang and Patrick J.P. Maurel</i>	
53	Isoniazid and Ethanol	707
	<i>John T. Slattery</i>	
Section VI: Clinical Considerations		
54	Clinical and Pharmacoeconomic Significance of Metabolic Drug Interactions	715
	<i>Philip D. Hansten</i>	
55	Pharmacist Management of Drug Interactions	723
	<i>Philip D. Hansten</i>	
56	Interactions in the Elderly	729
	<i>Robert E. Vestal and Barry J. Cusack</i>	
Section VII: Appendix		
Other Drugs		745
	<i>Kenneth E. Thummel and René H. Levy</i>	
Drug Interaction Index		749
General Index		765