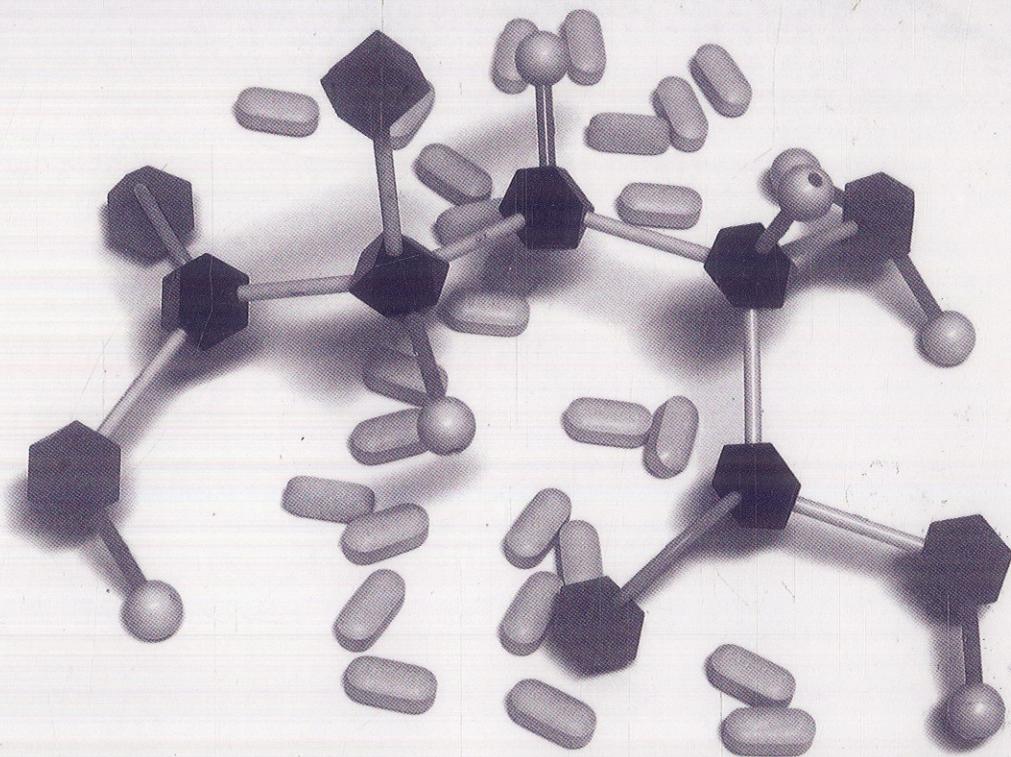


# CHEMISTRY AND MOLECULAR ASPECTS OF DRUG DESIGN AND ACTION



CRC Press  
Taylor & Francis Group

E. A. Rekka  
P. N. Kourounakis

---

# Contents

Editors.....	ix
Contributors .....	xi
Rational Drug Design Based Mainly on the Pathobiochemistry of the Disease.....	xv
<i>E. A. Rekka, A. P. Kourounakis, and P. N. Kourounakis</i>	

## PART I

### **CHEMICAL, BIOCHEMICAL, AND BIOLOGICAL ASPECTS OF PATHOPHYSIOLOGICAL CONDITIONS**

<b>Chapter 1</b> Inflammatory Mechanisms in Alzheimer's Disease and Other Neurodegenerative Disorders .....	3
<i>Joseph Rogers, Thomas Beach, Rena Li, Zhe Liang, Lih-Fen Lue, Alexander Roher, Marwan Sabbagh, Yong Shen, Ronald Strohmeyer, and Douglas Walker</i>	
<b>Chapter 2</b> Treatment Development Strategies for Alzheimer's Disease.....	13
<i>Ernst Wulfert</i>	
<b>Chapter 3</b> Lipoprotein-Associated Phospholipase A <sub>2</sub> as A New Prognostic Factor for Coronary Artery Disease.....	35
<i>Alexandros D. Tselepis</i>	
<b>Chapter 4</b> New Molecular Targets for the Prevention and Treatment of Gastrointestinal Ulcers and Inflammation .....	43
<i>Sandor Szabo, Ganna Tolstanova, Lajos Nagy, Longchuan Chen, Tetyana Khomenko, Xiaoming Deng, and Zsuzsanna Sandor</i>	
<b>Chapter 5</b> Stress Activates Corticotropin Releasing Factor Signaling Pathways: Implication in Functional Bowel Disorders .....	75
<i>Yvette Taché</i>	

**PART II****CLASSICAL MEDICINAL CHEMISTRY**

<b>Chapter 6</b>	Design, Synthesis, and Pharmacological Evaluation of High-Affinity and Selectivity Sigma-1 and Sigma-2 Receptor Ligands.....	93
	<i>Jacques H. Poupaert</i>	
<b>Chapter 7</b>	Synthesis of Biologically Active Taxoids.....	101
	<i>K. C. Nicolaou and R. K. Guy</i>	
<b>Chapter 8</b>	From the Molecular Pharmacology to the Medicinal Chemistry of Cannabinoids.....	109
	<i>Didier M. Lambert</i>	
<b>Chapter 9</b>	An Appraisal of Fomocaines: Current Situation and Outlook.....	123
	<i>Herbert Oelschläger and Andreas Seeling</i>	
<b>Chapter 10</b>	Ligands for the GABA Recognition Site at the GABA <sub>A</sub> Receptor: Structure–Activity Studies .....	139
	<i>Bente Frølund, Uffe Kristiansen, Povl Krogsgaard-Larsen, and Tommy Lilje fors</i>	
<b>Chapter 11</b>	Strategies for Development of New Lead Structures for Inhibition of Acetylcholinesterase .....	149
	<i>Petra Kapkova, Vildan Alptuzun, Eberhard Heller, Eva Kugelmann, Gerd Folkers, and Ulrike Holzgrabe</i>	

**PART III****DRUG DESIGN, CHEMICAL AND MOLECULAR ASPECTS OF DRUG ACTION**

<b>Chapter 12</b>	Discovery of Potent and Selective Inhibitors of Human Aldosterone Synthase (CYP11B2): A New Target for the Treatment of Congestive Heart Failure and Myocardial Fibrosis—A Review .....	165
	<i>R. W. Hartmann, U. Müller-Vieira, S. Ulmschneider, and M. Voets</i>	

<b>Chapter 13</b>	Thiocarboxanilides: A New Class of Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs) with Great Potential for the Treatment of Human Immunodeficiency Virus Type 1 (HIV-1) Infections.....	177
	<i>E. De Clercq, A. Karlsson, and J. Balzarini</i>	
<b>Chapter 14</b>	Histamine H <sub>3</sub> -Receptor Agonists and Antagonists: Chemical, Pharmacological, and Clinical Aspects .....	199
	<i>Holger Stark and Walter Schunack</i>	
<b>Chapter 15</b>	Anti-Inflammatory Actions of Flavonoids and Structural Requirements for New Design .....	215
	<i>Theocharis C. Theocharides</i>	
<b>Chapter 16</b>	Molecular Mechanisms of H <sub>2</sub> O <sub>2</sub> -Induced DNA Damage: The Action of Desferrioxamine .....	227
	<i>M. Tenopoulou, P.-T Doulias, and D. Galaris</i>	
<b>Chapter 17</b>	LNA (Locked Nucleic Acid) and Functionalized LNA: Toward Efficient Gene Targeting .....	239
	<i>Jesper Wengel</i>	

## PART IV

### **DRUG – XENOBIOTIC METABOLISM**

<b>Chapter 18</b>	The Effect of Diet on Drug Metabolism .....	247
	<i>K.J. Netter</i>	
<b>Chapter 19</b>	Cytochromes P450 in the Metabolism and Bioactivation of Chemicals.....	253
	<i>Costas Ioannides</i>	
<b>Chapter 20</b>	<i>In Vitro</i> Methods to Measure Drug Metabolism and Drug Interactions in Drug Discovery and Development.....	273
	<i>O. Pelkonen, M. Turpeinen, J. Uusitalo, P. Taavitsainen, and H. Raunio</i>	

**PART V****PHYSICAL ORGANIC AND THEORETICAL  
MEDICINAL CHEMISTRY**

<b>Chapter 21</b> How to Probe the Sites of Action of Drug Molecules.....	289
<i>A. Makriyannis and F. Bitter</i>	
<b>Chapter 22</b> Physicochemical Profiling in Early Drug Discovery: New Challenges at the Age of High-Throughput Screen and Combinatorial Chemistry.....	303
<i>Bernard Faller</i>	
<b>Chapter 23</b> Drug-Membrane Interaction and Its Importance for Drug Efficacy .....	313
<i>J.K Seydel, E.A. Coats, K. Visser, and M. Wiese</i>	
<b>Chapter 24</b> The Fight Against AIDS: New Avenues for Inhibiting Reverse Transcriptase (RT), an Old Target.....	325
<i>Maurizio Botta, Lucilla Angeli, Marco Radi, and Giovanni Maga</i>	
<b>Index.....</b>	347