



Richter Ltd

ANALOGUE-BASED DRUG DISCOVERY IUPAC project

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IUPAC

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Introduction (J. Fischer and C. R. Ganellin)

Main Directions of Medicinal Chemistry:

1. Analogue-based drug discovery (ABDD)
method: using existing drugs as lead compounds
existing drugs: natural products or synthetic drugs
2. Ligand-based drug discovery (LBDD)
method: screening using a target without knowing its structure
3. Structure-based drug discovery (SBDD)
method: drug design knowing the target structure

Analogue types

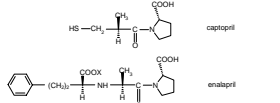
- a.) structural and pharmacological analogues
- b.) structural analogues
- c.) pharmacological analogues

Structural and Pharmacological Analogues

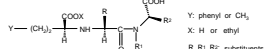
Drugs which have similar chemical structures and whose pharmacological activity is similar.

Special class of direct analogues with identical pharmacophores

Examples: captopril and enalapril



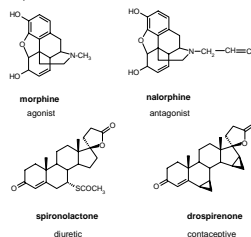
direct analogues of enalapril: general structure



Structural Analogues

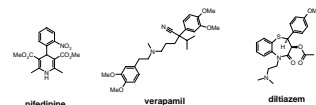
Drugs which have a similar chemical structure but whose pharmacological activity is quite different.

Examples:

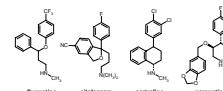


Pharmacological Analogues

Examples: L class voltage gated calcium channel blockers:



selective serotonin reuptake inhibitors:



Part I General Aspects of Analogue-Based Drug Discovery

Chapter 1

Analogs as Means of Discovering New Drugs (C. G. Wernuth)

Traditional methods (homologues, vinylogues, isomers, positional isomers, optical isomers, ring transformations, and twin-drugs)
SOSA approach (Selective Optimization of Side Activities)

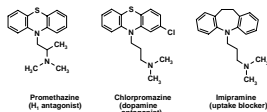
Chapter 2

Drug Likeness and Analogue-Based Drug Discovery (J. Proudfoot)

Rule of five and ABDD (examples)

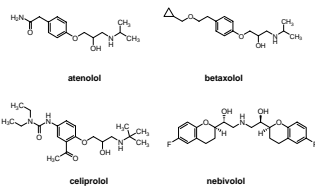
Chapter 3

Privileged Structures and Analogue-Based Drug Discovery (H. Kubinyi)



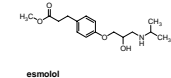
Chapter 8

Selective Beta-Adrenergic Receptor Blocking Agents (P.W. Erhardt and L. Matos)



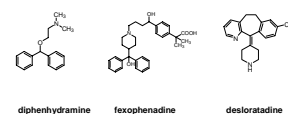
Chapter 9

Case Study of Esmolol (P.W. Erhardt)



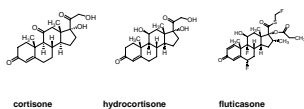
Chapter 18

Histamine H₁ Blockers: from Relative Failures to Blockbusters within the Series of Analogues (H. Timmerman)



Chapter 19

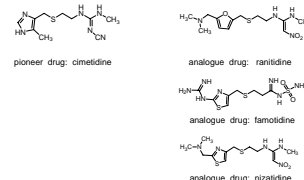
Corticosteroids: from Natural Products to Useful Analogues (Z. Táta, S. Mahó and C. Sánta)



Part II Selected Examples from the ABDD

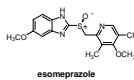
Chapter 1

Development of Anti-ulcer H₂-receptor Histamine Antagonists (C. R. Ganellin)



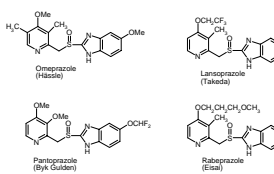
Chapter 2

Case History Omeprazole-Esomeprazole (P. Lindberg and E. Carlsson)



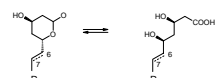
Chapter 3

Case History of Pantoprazole (J. Serrn-Billinger and E. Sturm)



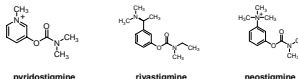
Chapter 4

Optimizing the Clinical Pharmacological Properties of the HMG-CoA Reductase Inhibitors (S. Kerpel-Fronius and J. Fischer)



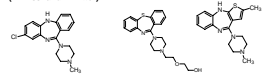
Chapter 12

Stigmines (Z. Tashma)



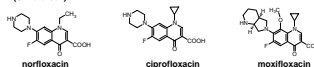
Chapter 13

Structural Analogues of Clozapine (B. Kiss and I. Bitter)



Chapter 14

Quinolone Antibiotics. The Development of Moxifloxacin (U. Petersen)



Part III

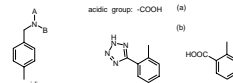
Tables of Selected Analogue Classes (E. M. Alapi and J. Fischer)

A. Alimentary Tract and Metabolism

A02BA	H ₂ -receptor antagonists
Cimidine	MW: 252.35 P: US 3,950,333 (1971, Smith Kline & French Lab.) L: 1977 (Smith Kline & French Lab.) S:
Ranitidine	MW: 314.42 P: DE 2,734,070 (1976, Allen & Hanburys Ltd.) L: 1981 (Glaxo, GSK) S: HCl, bismuth citrate
Roxatidine	MW: 348.44 P: EP 245,110 (1979, Teikoku Hormone) L: 1986 (Teikoku Hormone) S: HCl, acetate
Famotidine	MW: 337.45 P: DE 2,951,675 (1979, Yamanouchi) L: 1985 (Yamanouchi) S:

Chapter 5

Optimizing Antihypertensive Therapy by Angiotensin Receptor Blockers (C. Farang and J. Fischer)



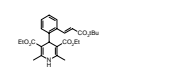
Chapter 6

Optimizing Antihypertensive Therapy by Angiotensin-Converting Enzyme Inhibitors (S. Alföldi and J. Fischer)

pioneer drug: captopril
direct analogues: enalapril and its analogues (s. introduction)

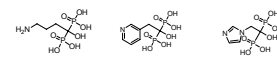
Chapter 7

Case Study of Lacidipine in the Research of New Calcium Antagonists (G. Gavraghi)



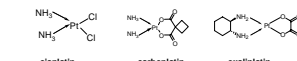
Chapter 15

The Development of Bisphosphonates as Drugs (E. Breuer)



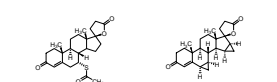
Chapter 16

Cisplatin and Its Analogues for Cancer Chemotherapy (S. Kerpel-Fronius)



Chapter 17

The History of Drospirenone (R. Wiechert)



Analogue-based Drug Discovery

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