

Contents

<i>Preface</i>	<i>v</i>
<i>Syllabus</i>	<i>xi</i>
1. Introduction to Medicinal Chemistry	1–3
2. History of Medicinal Chemistry	4–8
3. Physicochemical Parameters in Relation to Biological Activity	9–33
1. Introduction	9
2. Physicochemical Properties	9
2.1 Ionization and pK_a value	9
2.2 Solubility	11
2.3 Partition co-efficient	12
2.4 Hydrogen Bonding	15
2.5 Protein Binding	18
2.6 Chelation/Complexation	19
2.7 Bioisosterism	21
2.8 Stereoisomerism and Biological Activity	28
4. Drug Metabolism	34–62
1. Introduction	34
1.1 Sites of Bio-transformation	35
1.2 Pathways of Drug Metabolism	35
1.3 Phase I and Phase II Metabolic Pathways	36
1.4 Enzymes Involved in Drug Metabolism	37
2. Phase I Reactions	38
2.1 Oxidative Reactions	38
2.2 Reduction Reactions	45
2.3 Hydrolytic Reactions	47
3. Phase II (or) Conjugation Reactions	48
3.1 Glucuronic acid Conjugation (Glucuronidation)	48
3.2 Sulfate Conjugation	50
3.3 Conjugation with α -amino acids	52
3.4 Conjugation with Glutathione	53
3.5 Acetyl conjugation	55
3.6 Methylation	56
4. Factors Affecting Drug Metabolism	57

5. Adrenergic Drugs	63–100
1. Introduction	63
1.1 Adrenergic Nerve Transmission	63
1.2 Biosynthesis	64
1.3 Metabolism of Catecholamines	66
1.4 Adrenergic Receptors	67
2. Sympathomimetic Agents	70
2.1 Introduction	70
2.2 Structure Activity Relationship	70
2.3 Classification of Adrenergic Agonists	73
3. Sympatholytic (or) Adrenergic Blocking Agents	87
3.1 α -Adrenergic Blocking Agents	87
3.2 β -Adrenergic Blocking Agents	92
6. Cholinergic and Anticholinergic Drugs	101–133
1. Introduction	101
1.1 Neurotransmitter Acetylcholine	101
1.2 Biosynthesis and Catabolism of Acetylcholine	101
1.3 Cholinergic Receptors	102
2. Cholinomimetic (or) Parasympathomimetic Agents	104
2.1 Introduction	104
2.2 Structure Activity Relationship	104
2.3 Classification	107
3. Cholinergic Blocking Agents (or) Antispasmodics	120
3.1 Introduction	120
3.2 Structure Activity Relationship	120
3.3 Therapeutic Uses	121
3.4 Classification	122
3.4.1 Solanaceous Alkaloid	122
3.4.2 Synthetic Cholinergic Blocking Agents	126
7. Sedative and Hypnotics	134–156
1. Introduction	134
2. Classification	134
2.1 Barbiturates	135
2.2 Nonbarbiturates	144
8. Antipsychotics	157–171
1. Introduction	157

2. Classification	157
2.1 Typical Antipsychotics	158
2.2 Atypical Antipsychotics	169
9. Anticonvulsants	172–185
1. Introduction	172
2. Mechanism of Action	173
3. Classification	173
3.1 Barbiturates	174
3.2 Hydantoins	176
3.3 Oxazolidinediones	178
3.4 Succinimides	179
3.5 Urea and Monoacylurea	181
3.6 Imino stilbenes	181
3.7 Benzodiazepines	183
3.8 Miscellaneous	183
10. General Anaesthetics	186–196
1. Introduction	186
2. Mechanism of Action	186
3. Classification	188
3.1 Inhalation Anaesthetics	188
3.2 Intravenous Anaesthetics	193
11. Narcotic Analgesics	197–213
1. Introduction	197
2. Classification	197
2.1 Morphine and its Related Compounds	198
2.2 Morphinan Analogues	206
2.3 Morphan Analogues	207
2.4 4-Phenyl Piperidine Analogues	207
2.5 Phenylpropylamine Analogues	210
3. Narcotic Antagonists	212
12. Anti-Inflammatory Drugs	214–224
1. Introduction	214
2. Mechanism of Action	214
3. Structure Activity Relationship	216
4. Classification	217
4.1 Heteroaryl Acetic Acid Analogues	217

4.2 Aryl Acetic acid Analogues	218
4.3 Aryl Propionic acid Analogues	219
4.4 Oxicams	221
4.5 Salicylic acid Analogues	221
4.6 p-Aminophenol Analogues	222
4.7 Pyrazolones and Pyrazolidinones	223
4.8 N-Aryl anthranilic Acid Derivatives	223
<i>Index</i>	225–226

Syllabus

BP402T Medicinal Chemistry I (Theory)

Unit I	10 hrs
Introduction to Medicinal Chemistry	
History and Development of Medicinal Chemistry	
Physicochemical Properties in Relation to Biological Action	
Ionization, Solubility, Partition coefficient, Hydrogen bonding, Protein binding, Chelation, Bioisosterism, Optical and Geometrical isomerism.	
Drug Metabolism	
Drug Metabolism Principles: Phase I and Phase II	
Factors Affecting Drug Metabolism including Stereo Chemical Aspects	
Unit II	10 hrs
Drugs acting on Autonomic Nervous System	
Adrenergic Neurotransmitters:	
Biosynthesis and Catabolism of Catechol amines.	
Adrenergic Receptors (Alpha and Beta) and their Distribution.	
Sympathomimetic Agents: SAR	
Direct acting: Norepinephrine, Epinephrine, Phenyl ephedrine*, Dopamine, Methyl dopa, Clonidine, Dobutamine, Isoproterenol, Terbutaline, Phenylephrine, Salbutamol*, Bitoterol, Naphazoline, Oxymetazoline and Xylometazoline.	
Indirect acting Agents: Hydroxy Amphetamine, Pseudoephedrine, Propylhexedrine.	
Agents with Mixed Mechanism: Ephedrine, Metaraminol	
Adrenergic Antagonists:	
Alpha Adrenergic Blockers: Tolazoline*, Phentolamine, Phenoxybenzamine, Prazosin, Dihydroergotamine, Methysergide.	
Beta Adrenergic Blockers: SAR of β -blockers, Propranolol*, Metipranolol, Atenolol, Betazolol, Bisoprolol, Esmolol, Metoprolol, Labetolol, Carvediol.	
Unit III	10 hrs
Cholinergic Neurotransmitters: Biosynthesis and catabolism of Acetyl choline, Cholinergic Receptors (Muscarnic & Nicotinic) and their distribution.	
Parasympathomimetic Agents: SAR	

Direct Acting Agents: Acetylcholine, Carbachol*, Bethanechol, Methacholine, Pilocarpine.

Indirect Acting/Cholinesterase Inhibitors (Reversible & Irreversible)

Physostigmine, Neostigmine*, Pyridostigmine, Edrophonium chloride, Tacrine hydrochloride, Ambenonium chloride, Isoflurophate, Echothiophate iodide, Parathione, Malthionine.

Cholinesterase Reactivator: Pralidoxime chloride

Cholinergic Blocking Agents: SAR of Cholinolytic agents.

Solanaceous Alkaloids and Analogues: Atropine sulphate, Hyoscyamine sulphate, Scopolmaine hydrobromide, Homatropine hydrobromide, Ipratropium bromide.

Synthetic Cholinergic Blocking Agents: Tropicamide, Cyclopentolate hydrochloride, Clidinium bromide, Dicyclomine hydrochloride*, Glycopyrrolate, Methantheline bromide, Propantheline bromide, Benztropine mesylate, Orphenadrine citrate, Biperidine hydrochloride, Procyclidine hydrochloride*, Tridihexethyl chloride, Isopropamide iodide, Ethopropazine hydrochloride.

Unit IV

08 hrs

Drugs acting on Central Nervous System

A. Sedative and Hypnotics

Benzodiazepines: SAR, Chlordiazepoxide, Diazepam*, Oxazepam, Clorazepate, Lorazepam, Alprazolam, Zolpidem

Barbiturates: SAR, Barbital*, Phenobarbital, Mephobarbital, Amobarbital, Butabarbital, Pentobarbital, Secobarbital

Miscellaneous:

Amide and Imide: Glutethimide

Alcohols and their Carmbamate Derivatives: Meprobamate, Ethchlorvynol

Aldehyde and their Derivatives: Triclofos sodium, Paraldehyde.

B. Antipsychotics

Phenothiazines: SAR, Promazine hydrochloride, Chlorpromazine hydrochloride*, Trifluromazine, Thioridazine hydrochloride, Piperacetazine hydrochloride, Prochlorperazine maleate, Trifluperazine hydrochloride.

Ring Analogue of Phenothiazines: Chlorprothixene, Thiothixene, Laoxpine succinate, Clozaoine.

Flurobutyphenone: Haloperidol, Droperidol, Risperidone.

Beta amino Ketone: Moilndone hydrochloride

Benzamide: Sulpiride

C. Anticonvulsants: SAR and Mechanism of Action

Barbiturates: Phenobarbitone, Methobarbital.

Hydantoins: Phenytoin*, Mephenytoin, Ethotoin.



Oxazolidine dione: Trimetahdione, Paramethadione.

Succinimides: Phensuximide, Methsuximide, Ethosuximide

Urea and Monoacyl Ureas: Phenacemide, Carbamazepine*.

Benzodiazepine: Clonazepam

Miscellaneous: Primidone, Valproic acid, Gabapentin, Felbamate.

Unit V

07 hrs

Drugs acting on Central Nervous System

General Anaesthetics

Inhalation Anaesthetics: Halothane*, Methoxyflurane, Enflurane, Sevoflurane, Isoflurane, Desflurane.

Ultra Short acting Barbiturates: Methohexital sodium*, Thiameyal sodium, Thiopental sodium,

Dissociative anaesthetics: Ketamine hydrochloride*

Narcotics and Non-narcotic Anaesthetics

Morphine and Related Drugs: SAR of Morphine analogues, Morphine sulphate, Codeine, Meperidine hydrochloride, Anileridine hydrochloride, Diphenoxylate hydrochloride, Loperamide hydrochloride, Fentanyl citrate*, Methadone hydrochloride, Propoxyphene hydrochloride, Pentazocine, Levorphanol tartarate.

Narcotic Antagonists: Nalorphine hydrochloride, Levallorphan tatarate, Naloxone hydrochloride.

Anti-inflammatory Agents: Sodium salicylate, Aspirin, Mefenamic acid*, Neclofenamate, Indomethacin, Sulindac, Tolmetin, Zomepirac, Diclofenac, Ketonolac, Ibuprofen*, Naproxen, Piroxicam, Phenacetin, Acetaminophen, Antipyrine, Phenylbutazone.