

3.1 MEDICINAL CHEMISTRY – I (THEORY)

75 hours ; 3 hours/week

I Basic Principles of Medicinal Chemistry

12 hours;15-16 marks

- History and development of Medicinal Chemistry, definition of hit, lead and drug.
- Effects of the following physicochemical properties of drug molecules on biological activity: Ionisation, hydrogen bonding, solubility, partition coefficient, logP, logD, protein binding, chelation and polar surface area.
- Receptor and drug receptor interactions.
- Drug metabolism: Biotransformation, sites of biotransformation, General pathways of drug biotransformation, role of cytochrome P-450 and monoaminoxygenase in oxidative biotransformation, oxidative, reductive, hydrolytic and conjugation reactions with examples.

A study of development of the following classes of drugs including structure activity relationship (SAR), mechanism of action, synthesis of compounds superscribed by 's', chemical nomenclature, generic names, brand names (a few important marketed products) and side effects.

II Central nervous system depressants

16 hours;20-21 marks

- General Anaesthetics: Definition, mode of action
 - Inhalation anaesthetics: Halothane^s, Methoxyflurane, Nitrous oxide
 - Ultra short acting barbiturates: Methohexital sodium^s, Thiopental sodium
 - Dissociative anaesthetics: Ketamine hydrochloride
- Tranquilizers, sedatives and hypnotics
 - Major tranquilizers*: SAR of Phenothiazines, Promethazine HCl, Chlorpromazine HCl^s, Prochlorperazine, thioridazine HCl
Thioxanthenes: Chlorprothixene, thiothixine, clozapine
Fluorobutyrophenones: Haloperidol^s, Risperidone
Beta amino ketones: Molindone HCl, Benzamamide surpieriide
Minor tranquilizers: SAR of Benzodiazepines, Chlordiazepoxide, Diazepam^s, Orazepam, Chlorazepam, Lorazepam, Flurazepam, Alprazolam^s, Triazolam^s
 - Barbiturates: Classification and SAR, Barbitol^s, Methobarbital^s, Phenobarbital, Amobarbital^s, Butarbital, Pentobarbital, Secobarbital
 - Miscellaneous sedative hypnotics:
 - Amides and imides: Glutethimide^s, Methyprylon, Methaqualone^s
 - Alcohols and their carbamate derivatives: Ethchlorvynol, Ethinamate, Meprobamate^s
 - Aldehydes and their derivatives: Chloral hydrate, Paraldehyde
- Skeletal muscle relaxants: Chlorphenesin^s, Methocarbamol, Chlorzoxazone
- Drugs used in spasticity: Baclofen, Buspirone
- Anticonvulsants: Structural requirement for anticonvulsant activity, mechanism of anticonvulsant action
 - Barbiturates: Phenobarbitone, Mepobarbitone
 - Hydantoin: Phenytoin sodium^s, Ethotoin, Mephenytoin
 - Oxazolidinediones: Trimethadione^s, Paramethadione
 - Succinimides: Phensuximide^s, Methsuximide, Ethsuximide
 - Urea and monoacyl ureas: Phenacemide, Carbamazepine^s
 - Benzodiazepines: Clonazepam^s,
 - Miscellaneous: Primidone, Valproic acid

III Adrenergic agents

9 hours;11-12 marks

A. Adrenergic neurotransmitters and their biosynthesis and metabolism, adrenergic receptors their distribution and actions mediated by them

B. Sympathomimetics

1. Direct acting: SAR, Endogenous catecholamines,
 - a) Alpha adrenergic agonists: Phenylephrine^s, Methoxamine, Naphazoline, Xylometazoline^s, Oxymetazoline, Clonidine^s, Guanabenz, Methyldopa
 - b) Dual agonist/antagonist: Dobutamine
 - c) Beta adrenergic agonists: Isoproterenol^s, Metaproterenol, Terbutalin^s, Albuterol, Salbuterol, Bitolterol, Ritodrine
2. Indirect acting: Hydroxyamphetamine, Propylhexedrine
3. Mixed acting: Ephedrine, Metaraminol

C. Adrenolytics:

1. Alpha blockers:
 - a) Non selective: Tolazoline
 - b) Irreversible blockers: Phenoxybenzamine^s
 - c) Alpha1 blockers: Prazosin^s, Doxazosin, Tamsulosin
 - d) Alpha2 blockers: Yohimbine, Coryanthine
2. Beta blockers: SAR
 - a) Non selective blockers: Propranolol^s, Nadolol, Pindolol, Timolol, Sotalol
 - b) Beta1 blockers: Acebutolol, Atenolol, Esmolol, Metoprolol^s
 - c) Betablockers with alpha1 antagonistic activity: Labetalol, Carvedilol

IV Cholinergic drugs and related agents

12 hours;15-16 marks

1. Cholinergic neurotransmitter: Biosynthesis, metabolism and functions of acetylcholine
2. Cholinergic receptors: Nicotinic, muscarinic and their subtypes

A. Cholinergic agonists:

1. Stereochemistry and SAR, Acetylcholine, Methacholine, Carbachol, Bethanechol, Pilocarpine
2. Cholinesterase inhibitors:
 - a) Reversible: Mode of action, Physostigmine, Neostigmine^s, Ambenonium, Demecarium, Edrophonium, Tacrine
 - b) Irreversible: Mode of action, Isoflurophate, Ecothiophate, Malathion, Parathion, Pralidoxime.

B. Cholinergic blockers: SAR

1. Postganglionic blockers: Structural considerations of solanaceous alkaloids and analogs, Atropine, Hyoscyamine, Scopolamine, Homatropine, Ipratropium
2. Synthetic agents: Clidinium, Dicyclomine^s, Glycopyrrolate, Methantheline, Propantheline, Benztropine, Procyclidine, Tropicamide^s
3. Ganglionic blockers: Mode of action, Trimethaphan, Mecamylamine
4. Neuromuscular blockers: Mode of action, Tubocurarine, Metocurine, Gallamine, Pancuronium, Vecuronium.

V Local anesthetics

4 hours;5-6 marks

A. Definition, classification, and mechanism of action

B. SAR of lidocaine derivatives

C. 1. Benzoic acid derivatives: Hexylcaine, Cyclomethicaine, Piperocaine

2. Aminobenzoic acid derivatives: Benzocaine, Procaine^s, Procainamide
3. Lidocaine derivatives (Anilides): Lidocaine^s, Prilocaine
4. Miscellaneous: Dimethisoquin, Dibucaine

VI Histamine and antihistaminic agents

6 hours;8-9 marks

- A. Histamine: receptors and its actions
- B. Antihistaminics: H1 antagonists
 - a) Aminoalkyl ethers: Diphenhydramine HCl, Bromodiphenhydramine, Doxylamine
 - b) Ethylene diamines: Tripelenamine, Pyrilamine
 - c) Propylamine derivatives: Pheniramine, Chlorpheniramine^s
 - d) Phenothiazine derivatives: Promethazine^s, Trimeprazine
 - e) Piperazine derivatives: Cyclizine, Meclizine, Cetrizine^s
 - f) Miscellaneous compounds: Phenindamine, Cyproheptadine
- C. H2 antagonists: Mechanism, Cimetidine, Ranitidine, Famotidine
- D. Gastric proton pump inhibitors: Mechanism of action, Omeprazole^s, Pentaprazole, Rabiprazole, Lansoprazole.

VII Analgesic agents

9 hours;11-12 marks

- A. 1. Narcotic analgesics: Opioid receptors, SAR, Morphine, Codeine, Diacetyl morphine, Levorphanol, Dextromethorphan^s, Pentazocine, Meperidine, Loperamide, Fentanyl, Methadone^s, Propoxyphene, Tramadol
 2. Narcotic antagonists: Butorphanol, Nalorphine, Levalorphan, Naltrexone, Naloxone
- B. Non narcotic analgesics
 1. Steroidal anti-inflammatory agents: Cortisone, Hydrocortisone, Dexamethasone, Betamethasone, Triamcinolone, Fluocinolone
 2. Non steroidal anti-inflammatory agents: Mechanism of action
 - a) Salicylic acid derivatives: Aspirin
 - b) N-aryl anthranilic acid derivatives: Mefenamic acid^s, Diclofenac, Aceclofenac
 - c) Aryl acetic acid derivatives: Indomethacin, Ibuprofen^s, Piroxicam^s, Naproxen^s
 - d) Aniline and paraaminophenol derivatives: Phenacetin, Acetaminophen^s
 - e) Pyrazolone and pyrazolidine dione derivatives: Antipyrin, Oxyphenbutazone, Phenylbutazone
 - f) Diaryl sulphonamides: Nimesulide^s, Rofecoxib, Valdecoxib

VIII Structure and medicinal uses of important prostaglandins

1 hour;1-2 marks

IX Natural Products

6 hours;8-9 marks

- A. Alkaloids: Definition, Classification, Structural elucidation of ephedrine
- B. Purines: Definition, Structural elucidation of caffeine, Interrelation among caffeine, theophylline, theobromine.
- C. Terpenoids: Definition, classification, isoprene and special isoprene rule, Interrelationship among monocyclic monoterpenoids like limonene, dipentene, alpha terpenoid, alpha terpenion, terpenolene, terpin, terpene hydrate, carvone and cineone.

MEDICINAL CHEMISTRY I (PRACTICALS)

75 hours ; 3 hours/week

I. Identification test and test for purity of*

1. Benzocaine
2. Phenytoin sodium
3. Diclofenac sodium
4. Aminophylline
5. Aspirin
6. Caffeine
7. Paracetamol

II Assay of medicinally useful compounds (in solid dosage form)**

1. Ibuprofen by alkalimetry
2. Analgin by iodimetry
3. Ephedrine HCl/Phenobarbitone by non-aqueous titration
4. Procaine/Benzocaine by diazotisation
5. Chlorpromazine by cerimetry

III Preparation of medicinally useful compounds*

1. Phenytoin from benzoin
2. Paracetamol from p-nitrophenol
3. Benzocaine from p-aminobenzoic acid
4. 4-hydroxycoumarin from resorcinol
5. Mefenamic acid from anthranilic acid
6. Phenothiazine from diphenylamine

IV Degradation of Ephedrine to benzoic acid*

V Determination of partition coefficient and log P for any two drugs**

Note: ** Denotes major experiments * Denotes minor experiments

Scheme of Examination

1 Synopsis	10 Marks
2 Major (indicated by **)	25 Marks
3 Minor (indicated by *)	15 Marks
4 Minor (indicated by *)	10 Marks
5 Practical Viva-voce	10 Marks

Total

70 Marks

MEDICINAL CHEMISTRY I TEXT BOOKS (THEORY)

Latest editions and all volumes of

- 1 Wilson and Giswold's Text book of Organic Medicinal and Pharmaceutical Chemistry, Wolters Kluwer
- 2 William O Foye Principles of Medicinal Chemistry, Lea and Febiger, Philadelphia
- 3 Medicinal Chemistry Ashutosh Kar New age international publishers, New Delhi
- 4 Chemistry of Natural Products by Chatwal and Anand
- 5 Organic medicinal chemistry by Pandey

MEDICINAL CHEMISTRY I REFERENCE BOOKS (THEORY)

Latest editions and all volumes of

- 1 Burger's Medicinal Chemistry, ME Walffed Johnwiley and sons
- 2 Martindale the Extra Pharmacopoeia, JE Reynolds The pharmaceutical press, London
- 3 Beckett and Stenlake Practical Pharmaceutical Chemistry, the sthalone press, University of London
- 4 IP 2014 Govt. of India, Ministry of health
- 5 BS Furniss et al Vogel's TB of Practical Organic Chemistry including quantitative analysis, ELBS/Longman, London
- 6 Mann and Saunders Practical Organic Chemistry Longman Green and Co London
- 7 Organic Chemistry of Drug Synthesis Lednicer Mitzsher
- 8 Current Index of Medical Specialities (CIMS)
- 9 Essentials of Medicinal Chemistry Korolkovas
- 10 Natural Product Chemistry by Agarwal

MEDICINAL CHEMISTRY I REFERENCE BOOKS (PRACTICALS)

Latest editions and all volumes of

- 1 IP
- 2 IL Finar TB of organic chemistry
- 3 AI Vogel TB of Practical organic chemistry
- 4 The Organic chemistry of drug synthesis Lednicer Mitzsher
- 5 Mann and Saunders Practical organic chemistry
- 6 T Robinson Organic constituents of higher medicinal plants
- 7 CIMS

LIST OF MINIMUM EQUIPMENTS REQUIRED

1	Suction pump	01
2	Analytical balance	10
3	Water bath, reflux flask and condenser	10
4	Hot plate	01
5	Mechanical stirrer	02
6	Magnetic stirrer with thermostat	02
7	Distillation unit	01
8	Refrigerator	01
9	Fuming hood	01
10	Oven	01