

THIRD Year B. Pharmacy

1. Name of subject : **MEDICINAL CHEMISTRY-I**
2. Departmental objectives:
 - A. **Learning Objectives:**
 - i. To relate the structure and physical properties of drugs to their pharmacological activity.
 - ii. To demonstrate an understanding of concepts such as drug metabolism, bioavailability and pharmacokinetics and the role of medicinal chemistry in improving these parameters.
 - iii. To understand the basic biological and pharmacological interactions by using both natural products and synthetic bioactive molecules
 - iv. To learn about the characterization of drugs and drug-like molecules.
 - v. To understand principles of drug action and the role of bonding in drug-target interactions, identification of targets for drug action.
 - vi. To describe the mechanism of action, synthesis and medicinal uses of different class of chemotherapeutic agents.
 - vii. To differentiate drugs according to their action and give examples of each class of drug.
 - viii. To describe the synthetic routes used to prepare some selected drug compounds.
 - ix. To understand simple methods of synthesis, purification and characterization of an organic medicinal compound in the laboratory.
 - x. To train the students in basic & newer approaches in synthesis of drug molecules chemical entities.
 - B. **Learning Outcomes:**
 - i. Learn the classification of chemotherapeutic agents based on their chemical group, their mode of action and medicinal uses.
 - ii. Understands and describes the synthesis, structure activity relationships and mode of action of drugs used in the treatment of diseases.
 - iii. Use of corresponding knowledge for the development of biologically and clinically active drugs.
 - iv. Employ scientific methodologies such as experimental design, and the critical analysis of data.
 - v. Based on a knowledge of the biochemical details for specific drug mechanisms, to develop the ability to distinguish superior therapeutic drug mechanisms
 - vi. Describe the synthesis of important target compounds.
3. Annual objectives (for each year, if the subject is spread over different years): NA

4. Content distribution as per the list of topics, time allotted for each topic, distribution for 'Must know', 'Desirable to know' and 'Nice to know' and the probable weightage.

Sl No	Topic	Hours	Learning content distribution			Weightage (Marks)
			Must know	Desirable to know	Nice to know	
I	Basic Principles of Medicinal Chemistry	12	a) 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. b) Receptor and drug receptor interactions. c) Drug metabolism: Biotransformation, sites of biotransformation, General pathways of drug biotransformation, role of cytochrome P-450 and monoamine oxygenase in oxidative biotransformation, oxidative, reductive, hydrolytic and conjugation reactions with examples.	d) History and development of Medicinal Chemistry, definition of hit, lead and drug.		15-16
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	A) General Anaesthetics: Definition, mode of action Inhalation anaesthetics: Halothane ^s , Nitrous oxide Methoxyflurane, 1. Ultra short acting barbiturates: Methohexital sodium ^s , 2. Thiopental sodium 3. Dissociative anaesthetics: Ketamine HCl			20-21

		<p>B. Tranquilizers, sedatives and hypnotics</p> <p>1. <i>Major tranquilizers:</i> SAR of Phenothiazines, Promethazine HCl, Chlorpromazine HCl^s, Prochlorperazine, thioridazine HCl Thioxanthenes: clozapine, Chlorprothixene, thiothixine, Fluorobutyrophenones: Haloperidol^s, Risperidone Beta amino ketones: Molindone HCl, Benzamide surpierre</p> <p><i>Minor tranquilizers:</i> SAR of Benzodiazepines, Chlordiazepoxide, Diazepam^s, Orazepam, Chlorazepam, Lorazepam, Flurazepam, Alprazolam^s, Triazolam^s</p> <p>2. Barbiturates: Classification and SAR, Barbitol^s, Methobarbitol^s, Phenobarbitol, Amobarbitol^s, Butarbitol, Pentobarbitol, Secobarbitol</p> <p>3. Miscellaneous sedative hypnotics: a) Amides and imides: Glutethimide^s, Methypylon, Methaqualone^s b) Alcohols and their carbamate derivatives: Ethchlorvynol, Ethinamate, Meprobamate^s c) Aldehydes and their derivatives: Chloral hydrate, Paraldehyde</p> <p>C. Skeletal muscle relaxants: Chlorphenesin^s, Methocarbamol, Chlorzoxazone</p>			
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			D. Drugs used in spasticity: Baclofen, Buspirone E. Anticonvulsants: Structural requirement for anticonvulsant activity, mechanism of anticonvulsant action 1. Barbiturates: Phenobarbitone, Mepobarbitone 2. Hydantoins: Phenytoin ^s , Ethotoin, Mephentyoin 3. Oxazolidinediones: Trimethadione ^s , Paramethadione 4. Succinimides: Phensuximide ^s , Methsuximide, Ethsuximide 5. Urea and monoacyl ureas: Phenacemide, Carbamazepine ^s 6. Benzodiazepines: Clonazepam ^s , 7. Miscellaneous: Primidone, Valproic acid			
III	Adrenergic agents	9	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) <i>Alpha adrenergic agonists:</i> Phenylephrine ^s , Methoxamine, Naphazoline, Xylometazoline ^s , Oxymetazoline, Clonidine ^s , Guanabenz, Methyldopa b) <i>Dual agonist/ antagonist:</i> Dobutamine c) <i>Beta adrenergic agonists:</i> Isoproterenol ^s , Metaproterenol, Terbutalin ^s , Albuterol,			11-12

			Salbuterol, Bitolterol, Ritodrine 2. Indirect acting: Hydroxyamphetamine, Propylhexedrine 3. Mixed acting: Ephedrine, Metaraminol C. Adrenolytics: 1. <i>Alpha blockers:</i> a) Non selective: Tolazoline b) Irreversible blockers: Phenoxybenzamine ^s c) Alpha ₁ blockers: Prazosin ^s , Doxazosin, Tamsulosin d) Alpha ₂ blockers: Yohimbine, Coryanthine 2. <i>Beta blockers: SAR</i> a) Non selective blockers: Propranolol ^s , Nadolol, Pindolol, Timolol, Sotalol b) Beta ₁ blockers: Acebutolol, Atenelol, Esmolol, Metoprolol ^s c) Betablockers with alpha ₁ antagonistic activity: Labetalol, Carvedilol			
IV	Cholinergic drugs and related agents	12	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			15-16

			<p>action, Isoflurophate, Ecothiophate, Malathion, Parathion, Pralidoxime.</p> <p>B.Cholinergic blockers:</p> <p>SAR</p> <p>1.Postganglionic blockers: Structural considerations of solanaceous alkaloids and analogs, Atropine, Hyoscyamine, Scopolamine, Homatropine, Ipratropium</p> <p>2.Synthetic agents: Clidinium, Dicyclomine^s, Glycopyrrolate, Methantheline, Propantheline, Benztropine, Procyclidine, Tropicamide^s</p> <p>3.Ganglionic blockers: Mode of action, Trimethaphan, Mecamylamine</p> <p>4.Neuromuscular blockers: Mode of action, Tubocurarine, Metocurine, Gallamine, Pancuronium, Vecuronium.</p>			
V	Local anesthetics	4	<p>A. Definition, classification, and mechanism of action</p> <p>B. SAR of lidocaine derivatives</p> <p>C. 1. Benzoic acid derivatives: Hexylcaine, Cyclomethicaine, Piperocaine.</p> <p>2. Aminobenzoic acid derivatives: Benzocaine, Procaine s, Procainamide</p> <p>3. Lidocaine derivatives (Anilides): Lidocaines, Prilocaine</p> <p>4. Miscellaneous: Dimethisoquin, Dibucaine</p>			5-6

VI	Histamine and antihistaminic agents	6	<p>B. Antihistaminics:</p> <p>H1 antagonists</p> <p>a) Aminoalkyl ethers: Diphenhydramine HCl, Bromodiphenhydramine, Doxylamine</p> <p>b) Ethylene diamines: Tripelenamine, Pyrilamine</p> <p>c) Propylamine derivatives: Pheniramine, Chlorpheniramine^s</p> <p>d) Phenothiazine derivatives: Promethazine^s, Trimeprazine</p> <p>e) Piperazine derivatives: Cyclizine, Meclizine, Cetrizine^s</p> <p>f) Miscellaneous compounds: Phenindamine, Cyproheptadine</p> <p>C.H₂ Antagonists: Mechanism, Cimetidine, Ranitidine, Famotidine</p> <p>D. Gastric proton pump inhibitors: Mechanism of action, Omeprazole^s, Pantoprazole, Rabeprazole, Lansoprazole.</p>	A. Histamine: receptors and its actions	8-9
VII	Analgesic agents	9	<p>A. 1. Narcotic analgesics: Opioid receptors, SAR, Morphine, Codeine, Diacetylmorphine, Levorphanol, Dextromethorphan^s, Pentazocine, Meperidine, Loperamide, Fentanyl, Methadone^s, Propoxyphene, Tramadol</p> <p>2. Narcotic antagonists: Butorphanol, Nalorphine, Levalorphan, Naltrexone, Naloxone</p> <p>B. Non narcotic analgesics: 2. Non steroidal anti-inflammatory agents: Mechanism of action</p>	1. Steroidal Antiinflammator agents: Cortisone, Hydrocortisone, Dexamethasone, Betamethasone, Triamcinolone, Fluocinolone	11-12

			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			
VII	Structure and medicinal uses of important prostaglandins	1	Structure and medicinal uses of important prostaglandins			1-2
IX	Natural Products	6	A. Alkaloids: Definition, Classification, B. Purines: Definition, Interrelation among caffeine, theophylline, theobromine C. Terpenoids: Definition, classification, isoprene and special isoprene rule, Interrelationship among monocyclic monoterpenoids like limonene, dipentene, alphaterpenoid, alpha terpenion, terpenolene, terpin, terpene hydrate, carvone and cineone.	Structural elucidation of ephedrine. Structural elucidation of caffeine,		8-9

5. Blueprint of question paper, for each QP..

Sl No	Chapter	Marks distribution					Total Marks
		Must Know	Desirable to Know	Long Essay	Short Essay	Short Answer	
I	Basic Principles of Medicinal Chemistry	Physico-chemical properties of drug molecules	History and development of Medicinal Chemistry, definition of hit, lead and drug.	10	--	2	12
II	Central nervous system depressants	Definition, Mechanism of action, classification with structures and synthesis SAR.		10	--	2+2	14
III	Adrenergic agents	Definition, Mechanism of action, classification with structures and synthesis SAR		-	5	2	7
IV	Cholinergic drugs and related agents	Definition, Mechanism of action, classification with structures and synthesis SAR			5	2+2	9
V	Local anesthetics	Definition, Mechanism of action, classification with structures and synthesis SAR		-	5		5
VI	Histamine and antihistaminic agents	Definition, classification with structures and synthesis	Histamine structure, biosynthesis and biological activity. Histamine	-	5	2	7

			receptors and its actions				
VII	Analgesic agents	Definition, Mechanism of action, classification with structures and synthesis SAR and synthesis	.Steroidal Antiinflammatory agents: Cortisone, Hydrocortison, Dexamethasone Betamethasone Triamcinolone, Fluocinolone	--	5	2+2	9
VIII	Structure and medicinal uses of important prostaglandins	Structure and medicinal uses of important prostaglandins		--	--	2	2
IX	Natural Products	Definition, classification with structures and synthesis	Structural elucidation of ephedrine. Structural elucidation of caffeine,	-	5		5
Total				20	30	20	70

* 80 % of the questions shall be from the Must Know area and 20 % shall be from the Desirable to know area of the Curriculum.

6. Question paper layout to show which question number will represent which chapter (s)

Long Essay:

2X 10 = 20

1	Basic Principles of medicinal chemistry
2	Central nervous system depressant

Short Essays:

5x 6 = 30

3	Adrenergic drugs
4	Cholinergic drugs and related agents
5	Local anaesthetics
6	Histamine and antihistaminic agents
7	Analgesic agents
8	Natural products

Short Answers:

2X10 = 20

9	Basic Principles of medicinal chemistry
10	Central nervous system depressant
11	Central nervous system depressant
12	Adrenergic drugs
13	Cholinergic drugs and related agents
14	Cholinergic drugs and related agents
15	Histamine and antihistaminic agents
16	Analgesic agents
17	Analgesic agents
18	Structure and medicinal uses of important prostaglandins

7. Scheme of Practical / Clinical Teaching and Assessment:

List the expected practical / clinical competencies.

State the objectives for each competency.

Assign content for the objectives.

Describe the teaching – learning processes.

Sl No	Skills	Duration	Learning methods
1	Demonstrate the methods of synthesis of simple organic compounds used as drugs or starting materials.		
2	Demonstrate the various methods of filtration, crystallization, purification.		
3	Reason critically and logically and make independent judgments		
4	Employ scientific		

	methodologies such as experimental design, and the critical analysis of data		
5	Interact effectively as part of a team in order to work towards a common outcome		
7	Demonstrate an understanding of the chemical industry and the way it operates, especially the pharmaceutical industry and others involving synthesis such as the petrochemical, polymer and agrichemical industries		

Scheme of examination with the distribution of marks as per the prioritisation of competencies.

Sl No	Competency	Assessment criteria	Marks
A	Knowledge	Synopsis	10
B	Cognitive and intellectual skills		
C	Subject specific practical skills	Major & Minor Experiment-I, Minor experiment-II	25+15+10
D	Transferable professional skills	Viva-voce	10
		Total	70

8. Suggested references (as per Vancouver style):
- Basic references
 - Advanced references (may also include journals / web / other electronic sources)

MEDICINAL CHEMISTRY II TEXT BOOKS (THEORY)

Latest editions and all volumes of

1. Foye's principles of Medicinal chemistry
2. Wilson and Griswold's Text book of Organic and Pharmaceutical chemistry
3. Rama Rao Nadendla, Medicinal Chemistry

MEDICINAL CHEMISTRY II REFERENCE BOOKS (THEORY)

Latest editions and all volumes of

1. Burger's medicinal chemistry
2. The Martindale's Extra Pharmacopoeia
3. A.I.Vogel, Text Book of practical organic chemistry including the qualitative analysis
4. A.H.Becket and J.B.Stanlake, Practical Pharmaceutical chemistry
5. M Raghuprasad, Advanced medicinal chemistry: A laboratory guide
6. J.G.Mann and Saunders, Practical organic chemistry, ELBS Longman, London
7. I.P.1985, Ministry of Health, Govt. of India
8. LedniserMitzsher, Organic drug synthesis, Vol.1 and 2
9. I.L. Finar, Text Book organic chemistry
10. T. Robinson, Organic constituents of higher plants
11. Feiser and Feiser Steroids
12. Drug design by Ariens
13. Smith and Williams, Introduction to principles of drug design
14. Purcell, Strategy of drug design
15. CIMS

MEDICINAL CHEMISTRY II REFERENCE BOOKS (PRACTICALS)

1. A.I.Vogel, Text Book of practical organic chemistry
2. A.H. Beckett and Stanlake, Practical pharmaceutical chemistry
3. J.G.Mann and Saunders, Practical organic chemistry
4. Jayaveera KN, Practical medicinal chemistry
5. Raghuprasad M, Advanced medicinal Chemistry
6. Feiser and Feiser, Steroids
7. IP 1985
8. I.L.Finar, Textbook of organic chemistry
9. CIMS