

## 4.4 MEDICINAL CHEMISTRY II (THEORY)

75 hours ; 3 hours/week

**A. Introduction to QSAR:** Study of hydrophobic, Electronic & Steric parameters

2 hours;3-4 marks

**B. Prodrugs:** Definition and examples

1 hour;1-2 marks

**C. Introduction to drug discovery-** Definition of lead molecule and its identification methods viz, high throughput screening, wholesale screening, and fragment based lead generation, fast followers

2 hours;3-4 marks

**D. History and development of chemotherapeutic agents:** Structure, uses and synthesis of only those compounds that are underlined and superscripted by 's'.

1. Antifungal agents:

a) Antifungal antibiotics- Nystatin, Griseofulvin, Amphotericin-B, Synthetic anti fungal agents:

b) Substituted imidazoles: Clotrimazole, Miconazole<sup>s</sup>, Ketoconazole, oxiconazole, Intraconazole.

c) Miscellaneous–Zinc propionate, Sodium caprylate, Tolnaftate<sup>s</sup>. 4 hours;5-6 marks

2. Urinary tract anti-infectives:

a) Quinalones: Nalidixic acid, Cinoxacin, Norfloxacin, Ciprofloxacin<sup>s</sup>, Pefloxacin, Ofloxacin, Sparfloxacin

b) Miscellaneous: Nitrofurantoin<sup>s</sup>. 3 hours;4-5 marks

3. Antitubercular drugs:

a) Synthetic antitubercular agents: p-Aminosalicylic acid, Isoniazid, Ethambutol, Pyrazinamide, Ethionamide, Clofazamine, Bedaquiline

b) Antitubercular Antibiotics: Cycloserine, Viomycin sulfate, Capreomycin sulfate, Rifampicin.

c) Combination therapy for TB 4 hours;5-6 marks

4. Antiviral Agents

a) Amantidine hydrochloride, Idoxuridine, Acyclovir, Zidovudine.

b) Anti-AIDS: Zalcitabine, Zalcitabine, Suramin 2 hours;3-4 marks

5. Antiprotozoal agents: Emetine hydrochloride, Metronidazole<sup>s</sup>, tinidazole, ornidazole, secnidazole, Diloxanide furoate, 8-hydroxy quinoline derivatives (clioquinol, iodoquinol) Carbarsone 2 hours;3-4 marks

6. Anthelmintics: Piperazine, Diethyl carbamazine, Pyrantel pamoate, Thiabendazole<sup>s</sup>

Albendazole<sup>s</sup>, Mebendazole 2 hours;3-4 marks

**E. Sulfonamides, Sulfones as antibacterial agents :**

1. SAR and mode of Sulfonamides.

2. Classification of sulfonamides based on duration of action and site of action with examples. Sulfamethiazole, Sulfisoxazole<sup>s</sup>, Sulfapyridine, Sulfamethoxazole<sup>s</sup>, Sulfadiazine, Sulfacetamide, sulfasalazine, Phthalyl sulfathiazole.

3. Folate reductase inhibitors: Trimethoprim, Synergistic action of the combination of sulfamethoxazole and trimethoprim<sup>s</sup>.

4. Sulfone: Dapsone<sup>s</sup> 4 hours;5-6 marks

**F. Antimalarials: Etiology of malaria, History, Mechanism and SAR**

1. Quinolines and analogues: 7-chloro-4-amino quinolines :Chloroquine phosphate<sup>s</sup>, Hydroxychloroquine sulphate, Amodiaquine, 8-amino quinolines: Pamaquine, Primaquine,

9-amino acridines: Quinacrine.

2. Artimicin and its derivatives: Artiether, Artimether, Artisunate

1. Biguanides and Dihydrothiazines: Chloroguanide, Cycloguanil.

2. Miscellaneous: Mefloquine, Pyrimethamine, Trimethoprim. **6 hours;8-9 marks**

### **G. Antibiotics: Classification and Mechanism of action**

1. Beta lactam antibiotics: Pencillins – structures, chemical degradation, bacterial resistance. Penicillin G, Penicillin V, Cloxacillin sodium, Nafcillin sodium, Ampicillin, Amoxycillin.

2. Cephalosporins: Structure and uses of Cephalexin, Cephadrine, Cefadroxil, Cefixime, Cefapryridine, Cefutroxime

3. Monolactams: Sulfazecin, Aztreonam, Tigmonam.

4. Beta lactamase inhibitors: Clavulanic acid and its salts, Thienamycin.

5. Aminoglycosides: Structural features and Mechanism of action, Streptomycin, Amikacin, Neomycin, Kanamycin, Gentamycin, Netilmycin

6. Tetracyclines: Chemistry and SAR, tetracycline, Chlortetracycline, Methacycline, Demeclocycline, Oxytetracycline, Meclocycline, Doxycycline, Minocycline.

7. Macrolide: Structure and specific uses of Erythromycin, Azithrocin, leandomycin.

8. Lincomycins: Lincomycin, Clindamycin.

9. Polypeptides: Gramicidin, Bacitracin, Polymyxin B, Colistin.

10. Miscellaneous: Chlormphenicol<sup>s</sup>, Vancomycin, Novobiocin. **12 hours;15-16 marks**

**H. Antineoplastic agents:** Introduction, mechanism of action and classification with examples.

1. Alkylating agents: Mechlorethamine, Cyclophosphamide, Melphalan, Chlorambucil<sup>s</sup>, Busulfan, Lomustine,

2. Antimetabolites: Mercaptopurine, Thioguanine, 5-Fluorouracil, Methotrexate<sup>s</sup>,

3. Antibiotics: Dactinomycin, Bleomycin, Mitomycin, Streptozocin.

4. Plant products: Etoposide, Taxol, Camphothesin, Vincristine, Vinblastin.

5. Hormones: Dromostanalone, Megestrol,

6. Kinase inhibitors: Imatinibmesylate

6. Miscellaneous: Asparaginase, Cisplatin, Hydroxy urea.

7. Immunotherapy: Interferon alpha 2a and 2b.

**6 hours;8-9 marks**

### **I. Cardiovascular agents:**

1. Antianginal agents and vasodilators: Chemical structure and specific uses of Amyl nitrite, Nitroglycerine, Isosorbide dinitrate.

2. Calcium antagonists: Brief introduction of calcium channels and their blockers. Chemical structures and uses of Verapamil, Diltiazem, Nifedepine, Nimodepine, Felodepine, Dipyridamole, Cyclandelate.

3. Antiarrhythmic drugs: Structure, chemical name, and classification of antiarrhythmics with examples

Class I- Membrane depressant drugs: Quinidine Procainamide, Phenytoin.

Class II-Beta adrenergic blocking agents. Tocainide, propranolol

Class III-Repolarization prolongators. Bretylium, Amiodarone

Class IV-Calcium channel blocker. Diltiazem, Verapamil

4. Antihypertensive agents:

Beta-blockers: Propranolol. Timolol

ACE Inhibitors: Captopril, Enalapril

Diuretics: Hydrochlorthiazide, Spiranolactone

Calcium channel blockers: Nifedepine, Felodipine, Amlodipine

$\alpha_1$  -Antagonist: Prazocin

$\alpha_2$  -agonist: Clonidine, Guanithedine

Angiotensin –II receptor antagonist: Losartan, Valsartan

Miscellaneous: Reserpine, Hydralazine, Minoxidil

5. Antihyperlipidemic agents: Structure and specific uses.

Clofibrate, Lovastatin, Cholesteramine, Colestipol, Atorvastatin

6. Anticoagulants: Dicumorol, Warfarin<sup>s</sup>, Phenindione

**14 hours;17-18 marks**

**J.** Hypoglycemic agents: Insulin and its preparations.

Sulfonylureas–Chlorpropamide<sup>s</sup>, Acetohexamide, Glipizide,

Biguanides-Phenformin, Metformin

Substituted benzoic acid derivatives – Meglitinides, Nateglinide

Thiazolidinediones –Glitazones, Pioglitazone, Ciglitazone, Rosiglitazone

Glipitines – Sitagliptin, Anagliptin

**2 hours;3-4 marks**

**K.** Thyroid harmones : L-thyroxine, L-thyronine,

**1 hour;1-2 marks**

**L.** Antithyroid drugs: Propylthiouracil, Methimazole.

**1 hour;1-2 marks**

**M.** Estrogens and progesterones- Skeletal structure and their uses

**2 hour;3-4 marks**

**N. Diuretics: Introduction**

1. Carbonic anhydrase inhibitors: Acetazolamide<sup>s</sup>, Methazolamide.

2. Thiazide and Thiazide like diuretics: Chlorthiazides, Benzthiazide, Xipamide, Chlorthalidone.

3. High-ceiling or loop diuretics: Furosemide<sup>s</sup>, Ethacrynic acid<sup>s</sup>.

4. Potassium sparing diuretics: Spironolactone, Triamterene, Amiloride.

5. Miscellaneous: Mannitol.

**5 hours;6-7 marks**

**MEDICINAL CHEMISTRY II (PRACTICALS)**  
**75 hours ; 3 hours/week**

**Assay of**

1. Sulphadiazine by diazotization
2. Chloroquine by nonaqueous titration
3. Ascorbic acid by Iodimetry
4. Isonicotinic acid by  $\text{KBrO}_3$  (bromimetry)
5. Benzyl penicillin by Iodometry
6. Metronidazole/Mepacrine by nonaqueous titration
7. Furosemide by neutralization titration
8. Diethyl carbamazine by neutralization titration

**Preparation of medicinally important compounds or intermediates required for synthesis of drugs**

1. PAS from p-nitro salicylic acid
2. Dichloramine T from toluene p-sulphonamide
3. Chloramine T from Dichloramine T
4. Fluorescein from phthalic anhydride
5. Eosin from Fluorescein
6. Sulphacetamide from sulphanilamide
7. Sulphanilamide from Acetanilide
8. INH from  $\gamma$  Picoline
9. Chlorobutanol
10. Benzotriazole
11. 3-Diphenyl quinoline
12. 2,4,5-Triphenyl imidazole from Benzoin

**Green Chemistry Synthesis**

1. Microwave assisted synthesis of 1,4-dihydropyridine/pyrimidine
2. Synthesis of p-bromoacetanilide from aniline using KBr

**Estimation of the functional groups in medicinally important compound**

1. Hydroxyl group in cholesterol
2. Ketone in camphor
3. Hydroxyl group in menthol
4. Amide in nicotinamide

**SCHEME OF EXAMINATION**

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|---|------------|
| 1. Synopsis   | - 10 Marks |
| 2. Assay/Estimation (including standardization)                             | - 30 Marks |
| 3. Preparation including re-crystallisation and Melting Point determination | - 20 Marks |
| 4. Practical viva   | - 10 Marks |

**Total**

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**- 70 Marks**

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## **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

## **LIST OF MINIMUM EQUIPMENTS REQUIRED**

1. Suction Pump	01
2. Analytical Balance	10
3. Physical Balance	Adequate
4. Triple beam balance	10
5. Water Baths Reflux Flask and condenser	10
6. Hot Plate	01
7. Mechanical Stirrer	01
8. Magnetic Stirrers with Thermostat	01
9. Distillation Unit	01
10. Refrigerator	01
11. Fuming Hood	01
12. Microwave Oven	01

