SEMESTER – IV

DRUG SYNTHESIS AND MECHANISM OF ACTION

THEORY

Programme: M.Sc. **Max.Hours : 60**
Course Code: P20/CHE/DSC/402 **Hours per week: 4**
Course: DSC –2 **Max.Marks: 100**
No. of credits : 4

COURSE OBJECTIVES:

- Drugs acting on metabolic process, cell wall and specific enzymes Sulphonamides were used to successfully treat many infections which later yielded to penicillin and so their role deserves wider acknowledgement

- Intercalation is the insertion of molecules between the planar bases of deoxyribonucleic acid (DNA). This process is used as a method for analyzing DNA and it is also the basis of certain kinds of poisoning.

- Drugs interact with receptors by bonding at specific binding sites. Most receptors are made up of proteins, and the drugs can therefore interact with the amino acids to change the conformation of the receptor proteins.

- Enantiomers of chiral drugs have the same chemical connectivity of atoms; they exhibit marked differences in their pharmacology, toxicology, pharmacokinetics, metabolism etc

COURSE OUTCOME:

CO1: Explain the basic concepts of mechanism of drug action
CO2: Outline the discovery and mechanism of action of the drugs acting on metabolic processes or antifolates
CO3: Describe the structure of bacterial cell wall and discuss the synthesis and mechanism of action of penicillins and cephalosporins on the bacterial cell wall
CO4: Discuss the synthesis and mode of action of drugs acting on specific enzymes
CO5: Discuss the classification and mechanism of action of drugs acting on genetic material
CO6: Give an overview of the nervous system, describe the structure of neuron and nerve transmission
CO7: Discuss about the classification, synthesis and mode of action of drugs acting on the various receptors
CO8: Give an overview of chiral drugs, explain the role of chirality on biological activity and discuss the synthesis and pharmacological activity of some important chiral drugs

MODULE1: DRUGS ACTING ON METABOLIC PROCESS, CELL WALL AND SPECIFIC ENZYMES (15 HRS)

Basic concepts of mechanism of drug action: Introduction to macromolecular targets, carbohydrates, proteins, lipids and nucleic acids as possible drug targets. Classification of drugs. Enzyme inhibition and its types.

a)**Drugs acting on metabolic process**:
Antifolates –Discovery and mechanism of action of sulphonamides, Synthesis of sulfomethoxazole, sulfodoxine, sulfaguanidine and dapsone.

Diaminopyrimidines -trimethoprim, bacterial resistance to sulfonamides and drug synergism

b)Drugs acting on cell wall: Structure of bacterial cell wall, β-Lactam antibiotics – mechanism of action of penicillins and cephalosporins. Synthesis of pencillin-G and cephalosporin-C, cefalexin and cycloserine.Resistance to pencillins, broad spectrum penicillins – cloxacillin, methicillin, ampicillin, amoxicillin and carbenicillin.β-Lactamase inhibitors- Structural formulae and mode of action of clavulanic acid and sulbactum c)Drugs acting on specific enzymes: H^+/K^+ -ATPase inhibitors- synthesis of Omeprazole and Carbonic anhydrase inhibitors-synthesis of Acetazolamide.

MODULEII: DRUGS ACTING ON GENETIC MATERIAL AND IMMUNE SYSTEM (15 HRS)

Drugs acting on genetic material:Introduction, classification and mechanism of action.

a) DNA-intercalating agents-Anticancer and antimalarial agents. Structural formulae of Daunomycin, Adriamycin and Amsacrine. Synthesis of Amscarine, Nitracrine, Quinacrine and Chloroquine.

b) DNA- Binding and nicking agents: Antiprotozoal drugs. Synthesis of Metronidazole, Dimetridazole and Tinidazole.

c) DNA-Alkylators: Synthesis of Cyclophosphamide and Bisulphan.

d) DNA-Polymerase inhibitors: Antiviral agents- Synthesis of Acyclovir and AZT.

e) DNA-Topoisomerase inhibitors: Anti bacterialagents.Synthesis of Ciprofloxacin and Norfloxacin. Structural formulae ofloxacin and Lomefloxacin.

f) Inhibitors of transcribing enzymes: Anti-TB and antileprosy agents-structural

g) formulae of Rifamycins and partial synthesis of Rifampicin.

h) Drugs interfering with translation process: Antibacterial drugs- Structural formulae of Erythromycin, 5-Oxytetracycline and Streptomycin. Synthesis of Chloromycetin

Drugs acting on immune system: Introduction to immune system. Immunosupressing agent-structural formula of Cyclosporin.Immunoenhancers-use of vaccines and strucrural formula of levamisol.

MODULE III: DRUGS ACTING ON RECEPTORS AND ION CHANNELS (15 Hrs)

Introduction to nervous system: structure of neuron, nerve transmission. Definition and examples of agonist, antagonist, neurotransmitters and receptors. Drugs acting on receptors:

a) **Adrenergic receptors** - Introduction and classification. α-Adrenergic-receptor agonists and antagonists- Synthesis and biological activity of Nor-adrenaline, Methyl L dopa and Tetrazosin.

   β-Adrenergic-receptor - agonists and antagonists – Synthesis and pharmacological activity of Salbutamol, Tetrabutalin, Propranolol and Atenolol.

b) **Cholinergic-receptors**: Introduction and classification.Cholinergic-receptor agonists and antagonists- Structural formulae of Nicotine, Atropine and Tubocurarine. Synthesis of Acetyl choline and Succinyl choline

c) **Dopamine receptors**: Introduction and classification.Dopamine- receptoragonists and antagonists- Biosynthesis of Dopamine. Synthesis of L-Dopa and Chlorpromazine.d)Serotonin receptors: Introduction and classification.Serotoninreceptoragonists and antagonists-synthesis and pharmacological activity of Serotonin and Metoclopramide.

d) **Histaminereceptors:**Introduction and classification.Histamine receptor agonists and antagonists-synthesis and biological action of Histamine, Chloropheneramine, and Ranitidine.

e) **Hormones and their receptors**: Introduction to estrogen receptors, Structural formulae of Tamoxifen

Drugs acting on ion channels: Introduction to ion channels, drugs acting on Ca^{2+}, Na^{+} and Cl^{-}channels and their mode of action. Structural formulae of Tetracaine and synthesis and of Nifedipine, Diltiazem, Tetracine and 4-Aminopyridine.

MODULE IV:CHIRAL DRUGS **(15 Hrs)**

Introduction to chiral drugs.Three-point contact model, Eutomer, Distomer and eudesmicratio.Pfeiffer's rule. Role of chirality on biological activity: Distomers – a) with no side

effects b)with undesirable sideeffectstherapeutic value
d)combination products having therapeutic advantages e) metabolic chirality inversion. Synthesis and pharmacological activity of S-buprofen, S- Metaprolol, Ininavir sulfate, Levocetrazine, 2S-Verapamil, S,S-Ethambutol , (+)Lomefloxacin, Fluvastatin, Dextropropoxyphen, (+)Ephedrine, (+)Griseofulvin, Dexormaplatin, R-Indacrinone, Nateglinide, Oxybutynin hydrochloride, S,S- Captopril and S,S,S- Enalaprilate.

Reference Books:

1. Burger's medicinal chemistry and drug discovery. By Manfred B. Wolf.
2. Introduction to Medicinal chemistry. By Graham Patrick.
3. Introduction to drug design. By R.B.Silverman
4. Comprehensive medicinal chemistry. Vol 1-5 by Hanzsch.
5. Principles of medicinal chemistry. By William O. Foyeetal.
6. Biochemical approach to medicinal chemistry. By Thomas Nogrady.
7. Pharmaceutical Chemistry and Drug synthesis By Roth and Kleeman
8. Drug design By E.J. Arienes
9. Principles of Medicinal Chemistry. Vols.1 & 2 By Kadametal
10. Medicinal chemistry An introduction By Gareth Thomas
11. Wilson and Gisvold,s text book of Organic, Medicinal and Pharmaceutical chemistry By J.N.Delgado and W.A.Remers.
12. Organic Pharmaceutical chemistry By Harikishansingh.
13. Medicinal Chemistry ByAshutoshkar
14. Medicinal Chemistry By G.Chatwal
15. Organic Drug synthesis By LedneiserVol 1-6
16. Strategies for organic drug synthesis and design By Daniel Ledneiser
17. Top Drugs: Top synthetic routes By John Saunders
18. Chirotecchnology By Roger A. Sheldon

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MODEL QUESTION PAPER

THEORY

Course Code: P20/CHE/DSC/402 **Max. Marks: 60**
Credits -4 **TIME: 2½ hrs**

SECTION –A

I. Answer the following **4 x 10 = 40 M**

1. a) What is enzyme inhibition and write the different types of Enzyme inhibition (CO1)
   b) Outline the synthesis of sulfomethoxazole and dapsone (CO2)

OR

2. a) Formulate Folate mechanism in bacteria. (CO3)
   b) What are H+/K+ ATPase inhibitors? Give the synthesis of Omeprazole (CO4)

3. a) What are DNA intercalating agents? Give two examples (CO5)
   b) Briefly discuss the mechanism of Action of AZT and write its synthesis (CO5)

OR

4. a) How do you plan for the synthesis of Ciprofloxacin? What is its mechanism of action? (CO5)
   b) What are Immunosupressing agents? Explain by taking one example. (CO5)

5. a) Discuss about Dopamine receptors and their classification. Write a short note on the Synthesis of Chlorpromazine (CO7)
   b) Outline the Structural formulae of Tamoxifen? (CO7)

OR

6. a) What are the different types of ion channels? Write the synthesis of tetracaine? (CO7)
   b) Explain the Synthesis and pharmacological activity of Propranolol and Atenolol (CO7)

7. a) Explain the following terms (CO7)
   i) Eutomer ii) Distomer iii) Eudesmic ratio (CO7)
   b) Write the synthesis and pharmacological activity of S- Metaprolol (CO7)

OR

8 a) Outline the synthesis and pharmacological activity of
   i) S-Ibuprofen ii) (+) Ephedrine (CO7)
   b) Explain the metabolic Chirality inversion (CO8)

SECTION –B

II Anwer any five **5 x 4 =20 M**

9. Write about Macromolecular targets. (CO1)
10. Outline the synthesis of Acetozolamide (CO4).
11. What are antiprotozoal drugs? Write the Synthesis of Metronidazole. (CO5).
12. Write the structural formula and importance of Erythromycin and Streptomycin (CO5).
13. Give the definition and examples of agonist and antagonist. (CO6)
14. What are cholinergic receptors? Write their classification (CO6)
15. Explain Pfeiffer's rule and three-point contact model? (CO7)
16. Outline the synthesis and pharmacological activity of Indinavir Sulfate(CO7)