

PAPER II. ADVANCED PHARMACOLOGY AND TOXICOLOGY

Revised Syllabus

Hours

GOAL: To understand the mechanism of drug action in detail and toxicity of drugs.

OBJECTIVES: Upon completion of the course, the candidate shall be able to

- know the chemical mediators and mechanisms by which the drugs act
- know the drug therapy of certain disorders
- understand gene therapy
- understand different types of toxicities

COURSE DESCRIPTION

THEORY

50 Hours (2Hrs/wk)

- | | |
|--|------|
| a. Molecular Mechanisms in Cell regulation | 12 |
| b. Signaling molecules and their receptors: | |
| i. Molecules: Nitric oxide, carbon monoxide, neurotransmitters, cytokines, peptide hormones, growth factors and eicosanoids. | |
| ii. Receptors: | |
| 1. Cell surface Receptors: Ion channels, G-protein coupled receptors, tyrosine kinase receptors, cytokine receptors, non-receptor protein tyrosine kinases | |
| 2. Nuclear receptors: Steroid hormone receptors, thyroxine receptors, other nuclear receptor families | |
| c. Signal transduction: | |
| d. Intracellular signal transduction: cAMP, cGMP, IP3-DAG, calcium pathway, PI3K/Akt, m-TOR, MAPK, JAK/STAT, TGF β /Smad, NFB signaling, Hedgehog-Wnt, Notch pathways including Adrenergic and cholinergic transmissions. Other peripheral mediators: 5-HT and Purines, Cannabinoids, Peptides and proteins | |
| i. Cytoskeleton signal transduction: Integrins and signal transduction, regulation of actin cytoskeleton | |
| 2. Chemical Mediators | |
| Biosynthesis, pathophysiological roles, receptors and drugs affecting the receptors for following | |
| a. Mediators of inflammation and allergy: Histamine, Bradykinin, PAF, Eicosanoids: prostaglandins, thromboxanes, leukotrienes and related compounds, EDRF and vascular substances, oxygen free radicals, Cytokines, Cox-1 and Cox-2. | 4 |
| 3. Pharmacotherapy [28 hrs] | 28 |
| The student is expected to understand Pathophysiology, Pharmacotherapy and critical analysis of rational use of drugs in the following disorders. | |
| a. Introduction to Pharmacotherapeutics | |
| b. CVS: Hypertension, Ischaemic heart disease, CCF, Cardiac arrhythmias and dyslipidaemia. | 4 hr |
| c. Respiratory: Asthma and COPD | 1 hr |
| d. CNS: Parkinson's disease, Alzheimer's disease, Schizophrenia, Affective disorders, Epilepsy, insomnia, anxiety and pain management | 6 hr |
| e. Musculoskeletal: Rheumatoid & Osteoarthritis, hyperuricaemia, Myasthenia gravis. | 2 hr |
| f. GIT: Peptic ulcer, GERD, Inflammatory bowel diseases, constipation, diarrhoea. | 3 hr |
| g. Endocrine: Obesity, Diabetes mellitus, Osteoporosis, Thyroid and parathyroid disorders, | 4 hr |
| h. Infectious: UT infections, RT infections, GI infections (Bacterial and protozoal), Malaria, Tuberculosis, AIDS, Malignant: Leukaemia, Lymphomas and solid tumours. | 8 hr |

4. Toxicity studies: [6 Hours]

- a. Acute, sub-acute and chronic studies: Protocols, objectives, methods of execution and regulatory requirements.
- b. Reproductive toxicology assessment: Male reproductive toxicity, spermatogenesis, risk assessment in male reproductive toxicity, female reproductive toxicology, oocyte toxicity, alterations in reproductive endocrinology, relationship between maternal and developmental toxicity
- c. Mutagenicity: In vitro tests for gene mutations in bacteria, chromosome damage, gene mutations in vivo (micronucleus tests and metaphase analysis) in rodents.
- d. Carcinogenicity studies: In vivo and In vitro studies
- e. Toxicological requirements for biological and bio-tech products: Safety analysis, concept of safety Pharmacology, antibodies, transmission of viral infections, residual DNA

Text Books:

1. Goodman and Gilman's The Pharmacological Basis of Therapeutics. (International Edition) McGraw Hill, New York (2001), 10th Edition.
2. Pharmacology by Rang HP, Dale MM and Ritter JM. Churchill Livingstone, London, 6th Edition, 1999.
3. Basic and Clinical Pharmacology by Bertram G Katzung (International Edition) Lange Medical Book/McGraw-Hill, U.S.A. (2001) 8th Edition.
4. Clinical Pharmacy by D.R. Laurence, P.N. Bennett & Mi. Brown, 8th Edition Churchill Livingstone 1997.
5. Clinical pharmacy and therapeutics –Eric T, Herfindal, Williams and Wilkins Publications
6. Clinical pharmacy and therapeutics –Roger and Walker, Churchill Livingstone Publication
7. Experimental and surgical techniques in the rat, 2nd edition H.B. Waynfirth and P.A Flecknell.

Reference Books:

8. Harrison's Principles of Internal Medicine. (2 Volumes 2001) by Braunwald, Fauci, Kasper, Hauser, Longo Jameson, McGraw Hill, New York, 15th Edition.
9. Pharmacotherapy; A pathophysiologic approach-Joseph T. Dipiro et.al Appleton and Lange
10. General and applied toxicology by B. Ballantyne, T. Marrs, P. Turner (Eds) The Macmillan Press Ltd, London.
11. Harrison's Principles of Internal Medicine. (2 Volumes 2001) by Braunwald, Fauci, Kasper, Hauser, Longo Jameson, McGraw Hill, New York, 15th Edition.

Journals:

1. Trends in Pharmacological Sciences. [Essential]
2. Indian Journal of Pharmacology [Essential]
3. Journal of Pharmacology and Experimental Therapeutics [Essential]
4. Indian Journal of Physiology and Pharmacology. (Desirable)
5. Annual Reviews of Pharmacology and Toxicology. [Desirable]
6. Pharmacological Reviews. [Desirable]
7. J-PET Journal of Pharmacology and experimental Therapeutics.

PRACTICALS

1. Animal house: Design and facilities to maintain the animals
2. Routes of administration of drugs like oral, intravenous, intraperitoneal, intramuscular, subcutaneous including conversion of human dose to animal
3. Anaesthetics for animals (isoflurane by inhalation, ketamine+xylozine by intraperitoneal)

4. Blood sampling methods in experimental animals (cardiac puncture, retroorbital, tail vein, cephanous, marginal ear vein)
5. To identify the cholinergic, adrenergic, serotonergic, vasodilator and cardiotoxic drug /blockers using isolated mammalian heart preparation in Langendorff's setup.
6. To assess the effect of drugs on angiogenesis using chorio- allantoic membrane (CAM) assay
7. To identify the Anti-dysrhythmic activity in rats using ECG
8. To identify the effect of various autonomic drugs on rat blood pressure (carotid and jugular cannulation).
9. To identify the effect of various drugs on rabbit/rat/chick jejunum preparation.
10. To identify the Acetylcholine, noradrenaline, adenosine and serotonin like drug /blockers using rat anococcygeus muscle preparation.
11. To identify the following receptors by using suitable tissue preparations:
 - i. the alpha action of a drug
 - ii. the beta action of a drug
 - iii. the muscarinic action of a drug
 - iv. the nicotinic action of drug
 - v. the 5 HT action of a drug

Books for Practicals

1. Fundamentals of experimental pharmacology by M.N Ghosh, scientific book agency, Calcutta.
2. Hand book of experimental pharmacology by SK Kulkarnan, Delhi, Vallabh Prakash
3. Short Protocols in Pharmacology and Drug Discovery edited by Enna SJ, et al., John Wiley & Sons Inc.
4. General and applied toxicology by B. Ballantyne, T. Marrs, P. Turner (Eds) The Macmillan Press Ltd, London.