

PHARMACOLOGY — M D

OBJECTIVES

At the end of the 3 years training in pharmacology, the PG Student should be able to

1. Acquire sound knowledge of general pharmacological principles, systemic pharmacology and rational use of drugs.
2. Plan and conduct lecture, practical demonstration, and tutorial classes for students of medical and allied disciplines.
3. Carry out screening of drugs for pharmacological and toxicological profile.
4. Critically review and comment on research papers.
5. Monitor adverse drug reactions, therapeutic drug monitoring, and able to provide drug information service to needy places.
6. Preparation of protocols to conduct experimental studies in animals and human drug trials independently.

The following self learning sessions for PG students will be held

- Post graduate lectures in systemic pharmacology to update various aspects basic pharmacology and applied therapeutics.
- Therapeutic club: To critically analyze the day to day development in therapeutics and new drugs
- Journal club: To familiarize with research methodologies and analysis of results.
- Seminars: To update newer developments in pharmacology/emerging trends/ novel mechanisms of drug action etc.
- Practical exercises: Once in a week, under the supervision of a faculty, with/without the help of animals, various principles/ mode of drug action/ screening of drugs/ drug analysis using various techniques should be performed to develop practical skills to conduct similar experiments in future.
- Thesis: Each PG student will carry out research work under the supervision of a faculty member of the Pharmacology Department. The thesis will be submitted to AIIMS and will be analyzed by suitable experts in that field. The acceptance of the thesis by the institute will be a prerequisite for the candidate to be allowed to appear in the final examination.

M D EXAMINATION**Theory Examination****Paper- I**

General pharmacological principles and allied sciences (section -1)

Paper-II

Systemic pharmacology, chemotherapy and therapeutics (section-2)

Paper-III

Experimental pharmacology, screening of drugs and statistics (section-3)

Paper-IV

Clinical pharmacology and recent advances in pharmacology (section-4)

Practical examination (2 days)

1. One experimental pharmacology exercise on intact animal**
2. One experimental pharmacology exercise on isolated organ**
3. One chemical pharmacology exercise
4. One clinical pharmacology exercise

Oral Examination

1. Microteaching session
2. Thesis presentation and discussion
3. General viva voce

SECTION 1**1.a. General Pharmacological Principles and Applied Sciences****1.b. Toxicology**

Basics of principles of diagnosis and treatment of human poisoning. Clinical features of common poisoning. Antidotes in the management of poisoning. Principles of clinical toxicology. Applied analytical toxicology and toxicovigilance.

Practical skills: Training at poison information centre. Determination of plasma cholinesterase levels in organophosphorus poisoned patients. Spot test for aluminium phosphide poisoning. Estimation of lead in drinking water and patient's urine.

1.c. Molecular Biology in Pharmacology

Gene expression, Pharmacogenomics, Proteomics, techniques involved in studying receptor dynamics. PCR, Northern blot, Southern blot and Western blot. Protein purification. Mono, poly clonal antibodies. Molecular biology in receptor identification. Antisense oligonucleotides, molecular targets of drug action.

1.d. Isolation of Compounds from Herbal Sources

Basic constituents of plants (chemical classification). Isolation of active constituent from plant materials. Percolation and maceration. Qualitative constituent characterisation techniques. Utilisation of HPTLC for the constituent analysis. Estimation of marker compound in biological fluid after crude plant material

administration.

Practical skills: Isolation of active principles from medicinal plants

1.e. Wonder Discoveries in Pharmacology

Nobel laureates in Pharmacology and their revolutionary discoveries

1.f. Teaching and Communication Skills

Delivering lectures, conducting practical/demonstrations for undergraduate and postgraduate students. Maintenance of records of practical exercise. Techniques to retrieve relevant information from various sources. Methodology of preparing research manuscripts. Research presentation in scientific deliberations.

Practical skills: Post graduate teaching of recent developments in pharmacology and therapeutics.

SECTION 2

2.a. Systemic Pharmacology, Chemotherapy and Therapeutics

- Autonomic nervous system
- Central nervous system
- Autacoids
- Drugs affecting kidney function and Cardiovascular system
- Drugs affecting gastrointestinal and respiratory system
- Drugs affecting uterine motility
- Chemotherapy of parasite infections
- Chemotherapy of microbial diseases
- Antineoplastic agents
- Immunomodulators
- Drugs acting on blood and blood forming organs
- Hormones
- Miscellaneous

SECTION 3

3.a. Experimental Pharmacology, Bioassay And Statistics

Experimental methodologies involved in the discovery of drugs (in vivo, in vitro, ex vivo). Animal handling and animal care. Methods of anaesthetising animals and methods of euthanasia. Restraining and blood collecting methods. Drug screening methods involved in the evaluation of anti-ulcer, antidepressant, antianginal, antihypertensive, antiarrhythmic, antidiabetic, anticataract, anti-platelet, anticancer, anti-inflammatory, antidiarrhoeal, antiepileptic, analgesic, antithyroid, antipyretic, antiglaucoma, antihyperlipidemic antiasthmatics drugs and cough suppressants. Drug screening methods used in screening antifungal, antihelminthic, antibacterial, antiviral agents, drugs for heart failure, posterior pituitary, adrenal steroid (gluco & mineralo corticoids), testicular, parathyroid, ovarian, thyroid hormones, Methods involved in testing teratogenicity, carcinogenicity and organ toxicities in animals.

*Practical Skills**:* Effect of antiinflammatory agents on carragennan induced rat paw edema. Evaluation of analgesic activity of morphine using tail flick latency test. Evaluation of cardiotonic drugs on isolated rabbit heart (Langendorff isolated heart preparation). Demonstration of Dale's vasomotor reversal and nicotinic effect of acetylcholine on dog blood pressure. Effect of autonomic drugs on rabbit intestine.

Demonstration of bronchodilation on guinea pig tracheal chain. Effect of sedatives on rodents (rotarod test).

Four point assay of histamine and acetylcholine on guinea pig ileum. Four point assay of 5HT on rat uterus. Estimation of PA_2 value of atropine. Identification of unknown by evaluating its action on dog haemodynamic parameters. Assay of acetylcholine using rat fundus. Estimation of pressor agents on rat blood pressure.

3.b. Instrumentation in Drug analysis

Qualitative testing, titrimetric analysis. Beer and Lambert's law. Basis and working principle of colorimeter, ultraviolet, atomic absorption spectrometers, Fluorescence spectroscopy, NMR and Mass Spectroscopy. Basics of Chromatography. Partition, adsorption and ionexchange chromatography. column chromatography, thin layer chromatography, paper chromatography, immunoabsorbant chromatography, high performance thin layer chromatography, high performance liquid chromatography and gas Chromatography. Radio immunoassay. Processing of biological materials for drug analysis. Calculations in drug analysis. Good laboratory practice. Validation of analytical procedure.

Practical skills: Spectrophotometric & fluorimetric estimations of drugs in biological fluids.

3.c. Biostatistics

Calculation of basic statistical parameters (mean, median, mode, standard deviation, standard error etc.). Null hypothesis, parametric and non parametric tests (Student 't' test, Wilcoxon, ANOVA etc.). Metaanalysis.

Practical skills: Calculation for statistical significance in the given data for Student paired and unpaired t test. Applying ANOVA to the given set of concentration vs time data of two drug formulations to comment about their bio-equivalence.

SECTION 4

4.a. Clinical Pharmacology and Recent Advances

Pharmacokinetics

Basics of pharmacokinetics, calculation of pharmacokinetic estimates (C_{max} , T_{max} , $T_{1/2}$, $AUC_{(0-n)}$, $AUC_{(0-\infty)}$, V_d , K_e , K_a etc.) Compartment models used in pharmacokinetics (oral and intravenous). Compartment fitting (one comp & two comp). Pharmacodynamic /pharmacokinetic (PK/PD) correlation.

Practical skills: Calculation of Pharmacokinetic estimates from given concentration vs time data

Drug Regulations

Drugs and Cosmetics Act, Drug Price Control order, Application for Investigational New Drug (IND), Application for New Drug Discovery (NDD) according to Indian Control Authority & USFDA guidelines. Conducting bio-equivalence studies. Ethical considerations in utilizing human subjects for drug discovery process. Helsinki's declaration. ICH-GCP Guidelines. Ethical guidelines in utilising animals for experimental purposes.

Practical skills: Draft an IND and NDD application for the approval of a numbered compound.

Drug development process

Methods involved in the development of new drugs. Preclinical toxicological studies. Calculation of LD_{50} & ED_{50} . Acute, subacute and chronic toxicity studies. Irwin profile test, Pre-clinical pharmacokinetic

and dynamic studies. Lipinski's rule for drug like molecule, High throughput screening (invitro and invivo) for pre-clinical pharmacokinetic and pharmacodynamic studies.

4.b. Clinical Trials

Types of clinical trials, clinical trial for a new investigational drug in India. Methods involved in the assessment of drugs in human volunteers and bio-equivalence studies. Key points in drafting protocol for a large scale multicentric drug trial in India.

Practical skills: Draft a protocol to conduct phase II clinical trial for a newly discovered non-steroidal anti-inflammatory drug.

4.c. Therapeutic Drug Monitoring (TDM)

Basic principles of TDM. Therapeutic index. Trough level monitoring and dosage adjustments.

Practical skills: Calculation of the next dosage of drug to the patient whose plasma drug level has been estimated

Therapeutic audit: Drug utilisation studies, essential drug concept, rational prescribing

Drug delivery systems: sustained release, enteric coated formulations and liposome etc.

Pharmacovigilance, Pharmacoeconomics, Pharmacogenetics and Drug Information

Practical skills: 50 hours/annum in ADR monitoring. 62 duties/annum in National Poisons Information centre.

Books Recommended

1. Goodman Gillman's The Pharmacological basis of therapeutics. (2001) Ed. Hardman JG, Limbird LE (Tenth Edition) McGraw Hill press New York.
2. Applied biopharmaceutics and pharmacokinetics (1999) Ed. Sargel L. (IV Edition) Prentice-Hall International, London.
3. Fundamentals of experimental pharmacology. (1984) Ed. Ghosh MN. Scientific book agency, Calcutta.
4. Text book of receptor pharmacology. Eds. Forman JC, Johansen TJ CRC Press, New York 1996.
5. Drug Discovery and Evaluation – Pharmacological assays. (1997) Ed. Vogel HG & Vogel WH. Springer-New York.

Journals to be Referred

Trends in Pharmacological Sciences, Annual Review of Pharmacology, Pharmacological Reviews, Indian Journal of pharmacology, Indian Journal of Physiology and Pharmacology, Annals of Pharmacotherapy, Pharmacology and Experimental Therapeutics, Journal of Ethnopharmacology, Nature, Science, European Journal of Clinical Pharmacology, BJCP and other pharmacology related journals.

****Practical Exercise using Animal Experiments is Subject to Ethical Approval**