MODERN PHARMACEUTICAL ANALYSIS

THEORY

GOALS:

The important goals of this course are to give through understanding of the spectroscopy, Mass and chromatographic techniques so that the post graduate students can work in the pharmaceutical companies and research laboratories. Goal of this course is also to train the students structural elucidation of organic compounds.

OBJECTIVES:

On completion of the course, the student shall be able to-

- Know the fundamentals principles, instrumentation and applications of UV-Visible, IR, NMR, Mass spectroscopy, ORD and chromatographic techniques.
- Know ORD, Electrophoresis and statistical analysis.
- Shall be able to analyze drugs and pharmaceuticals using the above instruments.
- Shall be able to interpret the structure of the organic compounds with the given spectral data.
- Shall be able to appreciate the importance of modern instruments in the quality control and research

COURSE CONTENTS
THEORY: 75 hr (3hr/week)

1. UV-VISUAL SPECTROSCOPY: Brief review of electromagnetic spectrum, UV-Visible range, energy, wavelength and color relationships. Interaction of electromagnetic radiation (UV-Visible) with matter and its effects. Chromophores and their interaction with E.M.R. Absorption spectra of organic compounds and complexes illustrating the phenomenon and its utilization in qualitative and quantitative studies of drugs. Shifts and their interpretation (including solvent effects). Empirical correlation of structure with absorption phenomena (Woodward's rules etc), Quantitative estimations, Modern instrumentation. Beer-Lambert Law, Absorption spectra of biomolecules. Theoretical aspects of simultaneous estimation of drugs **6 Hours (10-12 marks)**

2. INFRARED SPECTROSCOPY: Nature of infra-red radiation. Interaction of I.R radiation with oraganic molecules and effects on bonds, Hookes' law. Symmetry rules for observing IR spectrum of molecules. Molecular Infrared spectra. Brief outline of classical I.R instrumentation and particle details of obtaining spectra, including sample preparation for spectroscopy, qualitative interpretation and quantitative applications of FTIR spectra. Theory and applications of FT-IR, ATR and micro ATR. Significance of NIR. **5 Hours (08-10 marks)**

3. OPTICAL ROTATORY DISPERSION: Fundamentals principles of ORD. Cotton effect curves, their characteristics and interpretation. Octant rule and its application with examples. Circular dichroism and its relation to ORD. **3 Hours (05-07 marks)**

4. NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY: Fundamentals principles of NMR (Magnetic properties of nuclei; applied field and precession; absorption and transition; frequency). Chemical shifts concept; isotopic nuclei, Reference standards: Proton Magnetic spectra, their characteristics, presentation terms used in describing spectra and their interpretation (Signal No., Position, Intensity). Brief outline of instrumental arrangements and some practical details. Signal multiplicity phenomenon in high resolution PMR. Spin-spin coupling. Application of Signal Split and coupling constant data to interpretation of spectra. De-coupling and shift reagent methods. Brief outline of principles of FT-NMR with reference to ^{13}C NMR: Spin-spin and spin-lattice relaxation phenomenon. Free induction decay (FID) proton noise de-coupling signal, average time domain and frequency domain signals nuclear overhauser enhancement ^{13}C NMR spectra, their presentation, characteristics, interpretation, examples and applications. Brief indication of application of magnetic resonance spectral data of other nuclei by modern NMR instruments. Introduction to 2-D NMR techniques, TOCSY, NOESY, COSY and INADEQUATE. Methods for Structure determination of small molecules by NMR. **14 Hours (24-27 marks)**

5. MASS SPECTROMETRY: Basic principles and brief outline of instrumentation. Ionization techniques Molecular ion, Meta stable ions, fragmentation processes. Fragmentation patterns and fragmentation characteristics in relation to parent structure and functional groups. Relative abundances of isotopes and their contribution to characteristic peaks. Mass spectrum, its characteristics, presentation and its interpretation. Interfacing a LC and GC in MS **9 Hours (15-17 marks)**

6. CHROMATOGRAPHIC TECHNIQUES: Classification of chromatographic methods based on mechanism of separation. Chromatographic theory, efficiency parameters, Selection of adsorbents and mobile phase for TLC. HPTLC- instrumentation and applications, Progammed multiple development techniques. **4 Hours (07-09 marks)**

7. GAS CHROMATOGRAPHY: Instrumentation, packed and open tubular columns, Liquid stationary phases, derivatization techniques, detectors and critical comparison. Head space GC and temperature programmed GC. Interfacing a GC in FTIR and optical emission spectroscopy. **5 Hours (10-12 marks)**

8. LIQUID CHROMATOGRAPHY: Instrumentation in HPLC, Analytical, preparative and micro-bore columns, ion-exchange columns, size-exclusion columns and chiral columns, Reverse phase HPLC, column selection, mobile phase selection, detectors and its comparison Super fluid critical chromatography and affinity chromatography. Salient features of UPLC. Interfacing a LC in MS & NMR **8 Hours (15-17 marks)**

9. ELECTROPHORESIS: Theory and factors affecting electrophoresis, Moving boundary electrophoresis, zone electrophoresis, Isotachophoresis, Isoelectric focusing and immunoelectrophores, continuous electrophoresis (preparative) application. 2D Gel electrophoresis. **2 Hours (04-06 marks)**

10. X-RAY DIFFRACTION METHODS: Introduction, Generation of X-rays, Elementary crystallography, Miller Indices, X-ray diffraction, Bragg's law, X-ray powder diffraction, X-ray powder diffractometer, obtaining and interpretation of X-ray powder diffraction data and application in polymorphism. **4 Hours (07-09 marks)**

11. THERMO ANALYTICAL METHODS OF ANALYSIS: Thermo gravimetric analysis, Differential Scanning Calorimetry, application in drug interaction and interpretation.

3 Hours (05-07 marks)

12. STATISTICAL ANALYSIS: Introduction, significance of statistical methods, Normal distribution, probability, Degrees of freedom, measures of variation-standard deviation, variance, standard error, tests for statistical significance- students 'T' test, chi-square test. **5 Hours (08-10 marks)**

13. TEACHING SKILLS, RESEARCH METHODOLOGY AND LITERATURE SOURCES: Fundamentals of teaching and learning; art and science of teaching. Thesis writing and presentation of the work. Citation of references. **3 Hours (05-07 marks)**

14. ETHICS IN PHARMACY:

Research Ethics

- Animal and experimental research/humanness
- Human experimentation
- Human volunteer research-informed consent
- Clinical trials
- Gathering all scientific factors
- Gathering all value factors
- Identifying areas of value-conflict, setting priorities
- Working out criteria towards decision
- ICMR/CPCSEA/INSA Guidelines for human / animal experimentation **2 Hours (04-06 marks)**

PRACTICALS: **150 hr (6hr/week)**

Major experiments:

1. Atleast 4 simultaneous estimation of fixed dose combinations by UV-Visible spectroscopic methods.
5. UV-Visible spectrum scanning of certain organic compounds- absorption and correlation of structures. Comparison of UV spectrum of drugs.
6. Comparison of three different analytical methods for three official drugs.
7-8. Experiments based on HPLC and GC. (2 expts)
9. Experimants based on IR
10-15. Structural interpretation of at least 6 different compounds/drugs by UV, IR and Mass data

Minor experiments:

16. Effect of pH and solvent on U.V Spectrum of certain drugs.
17-20. Monograph analysis of paracetamol IP. (minor expts)
21. Separation of amino acids by electrophoresis
22. Any other relevant exercises based on theory.

Text Books

1. Spectrometric Identification of Organic Compounds, 7th Edition Robert M. Silverstein et.al
2. *Fundamentals of Applied Statistics by Gupta* Sc *Kapoor* Vk.
3. Instrumental methods of analysis SKOOG and West and Holler
4. *Willard*, H.H.; *Merrit*, L.L.; *Dean*, J.A.; *Settle*, F.A. *Instrumental Methods of Analysis*,7TH Ed CBS publishers and Distributors, New Delhi,.
5. A.H. Beckett and J.B. Stenlake Practical Pharmaceutical Chemistry, Fourth edition, Part-II
6. Kalsi, P. S. Spectroscopy of Organic compounds, New Age Publishers, New Delhi.
7. http://icmr.nic.in/bioethics/final_cpcsea
8. http://icmr.nic.in/ethical_guidelines

Reference Books

1. *X-Ray methods — Clive* Whiston — *John* Wiley & Sons. 1987
2. Statistics by Gofeti Radhakrishna
3. Biostastistics by Sadkar
4. Instrumental methods of analysis Scoog and West
5. Instrumental Method of Analysis - modern methods Part-B, Vol-2, pages 11to 54 Editor by J.W.*Munson* (Marcel Dekker) 4.
6. Kemp William, Organic spectroscopy, Pal Grave, New York.
7. Kalsi, P. S. Spectroscopy of Organic compounds, New Age Publishers, New Delhi.
8. Willard HH, Merritt LL Dean, JA, Settle FA: Instrumental methods of. Analysis, 7th edition, CBS publishers and Distributors, New Delhi,.
9. Robert M. Silverstein, Spectrometric Identification of Organic Compounds, Willey
10. Stahl, E.*:* Thin-Layer Chromatography, A Laboratory Handbook, 2nd. Edit.,
11. Modern NMR Techniques for Chemistry Research. A. E. Derome. Pergamon Press

Journals:

At least one International journal is to be subscribed

Teaching/ Learning activities:

1. Journal Club: Minimum of one presentation per term per student and evaluation is compulsory.
2. Seminar: Minimum of one seminar per term per student.
3. Field visits/ Industrial visits: Minimum of one visit during first year.
4. Conferenc/ meeting in their respective discipline.

Scheme of the examination:

Subjects	**Sessionals**	**Seminar/record marks**	**Annual Examination Marks**	**Total marks**
Theory	**30**	**20 (Journal Club/ Seminar)**	**100 (3 Hours)**	**150**
Practical Record	**30**	**20 (Seminar/record marks)**	**100 (6 Hours)**	**150**

University practical Examination

Synopsis	10 marks
Major Experiment	40 marks
Minor Experiment	30 marks
Viva-Voce	20 marks
Total	100 marks

M. PHARM

INDUSTRIAL PHARMACY

GOAL : To produce a competent Industrial Pharmacist

OBJECTIVE : Upon completion of the course, the candidate shall have

Knowledge – an understanding of the concept and design of various pharmaceutical dosage forms

Skill – the ability to formulate and evaluate various dosage forms

Attitude - the ability to work independently and as a member of the team
- the ability to plan his / her work for efficient use of time and resources
- the ability to identify the cause and to solve the problem
- the ability to think and evaluate scientifically and critically

TITLE OF PAPERS

Paper I	**Modern Pharmaceutical Analysis**	**(T:3 Hrs/wk, P:6Hrs/wk)**
Paper II	**Advanced Industrial Pharmacy**	**(T:2 Hrs/wk, P:6Hrs/wk)**
Paper III	**Biopharmaceutics and Pharmacokinetics**	**(T:2 Hrs/wk, P:6Hrs/wk)**
Paper IV	**Advances in Drug Delivery Systems**	**(T:2 Hrs/wk, P:6Hrs/wk)**

Appendix – I : List of required equipments:

The following common and specialized equipments and charts are to be provided by the course conducting departments/institution**.**

Common Equipments:

Single pan balances (analytical)	-	1
Single pan balances (electronic/digital)	-	2
Hot air oven	-	2
Magnetic stirrers	-	4
Mechanical stirrers-1, 2, 5 lt	-	1 each
Double pan balances (analytical)	-	1
Electrically operated with thermostat water baths		4
Distillation assembly, 5 lt	-	1
Hot plates	-	2
Refrigerator	-	1
Melting and boiling point apparatus	-	2 each
TLC Kit and plates	-	5
Sieves of different mesh sizes (22, 44, 60, 80, 120)		2 each

Special equipments

Monsanto & Pfizer hardness tester	-	2 each
Disintegration test apparatus	-	2
Dissolution test apparatus (single jar)	-	4
Dissolution test apparatus (6 jars)	-	1
UV-Visible spectrophotometer	-	1
Tablet compression machine single station	-	1
Rotary tablet compression machine	-	1
Capsule filling machine	-	1
Stability chambers	-	3
Coating & polishing pan	-	1
Vacuum pump with accessories	-	1
Pocket / pen pH meters	-	2

Vacuum filtration unit	-	1
Rotary evaporator	-	1
Rotary shaker bath	-	1
Filtration sets	-	2

Desirable:

High Performance Liquid Chromatography (HPLC)	-	1
Computers with UPS and a printer	-	2

Glassware:

Common laboratory glassware for regular experiments: Beakers, measuring cylinders, conical flasks, RB & FB flasks (1 & 2 lt capacity), filtration unit, distillation unit, thermometers 110, 360 degree Celsius.

Chemicals and Reagents:

Common pharma grade pure drug samples, polymers and other adjuvants, solvents etc for the purpose of formulation required for the regular practicals.

PAPER - II ADVANCED INDUSTRIAL PHARMACY

1. **Scope and objectives of the subject**: The subject provides a good manufacturing of the concepts, techniques and applications of production and operation management.

2. Objectives

2.1 Knowledge upon the completion of the course, the student shall be able to

- Know about industrial safety, effluent treatment and environmental control.
- Know about intellectual property rights.
- Know about documentation of records.
- Know about stability and its testing.

2.2 Skills: **Upon the completion of the course, the student shall be able to**

- Use laboratory scale production equipments.
- Communicate of laboratory results.
- Interpret the laboratory data.
- Present different production schedule plans for a specified period.

2.3 Attitude: **Upon the completion of the course, the student shall be able to**

- Create intuitiveness and ability to interact.
- Plan his work for efficient use of time and resources.
- Identify the cause and solve the problem.
- Think and evaluate scientifically and critically.

3. Teaching/ Learning Activities:

3.1 **Journal Club**: weekly, Journal club meetings to be held to discuss the recent development in the subject published in the national and international journals.

3.2 **Seminars**: Seminars (5-6 in a year) shall be arranged from experts in the field.

3.3 **Industrial visits**: Visits to pharmaceutical industries to understand shop floor activities.

3.4 **Conferences and meetings**: Staff and students are to be encouraged to participate in seminars, workshops and conferences in the area of this subject.

THEORY **50 hours (2 Hrs./Week)**

1. **Preformulation studies** **06 Hrs**

(Marks allotment : 15)

Introduction, Consideration of physicochemical properties of new drug molecules for different dosage forms. Aqueous solubility, organic solubility, intrinsic solubility, methods of enhancement of solubility-surfactants, pH, co-solvency, solid dispersion, complexation. Techniques for the study of crystal properties and polymorphism - DSC, TGA, PXRD, Optical microscopy, hot stage microscopy. Excipient compatibility studies, Preformulation stability studies.

2. **Pilot plant scale-up techniques** **06 Hrs**

(Marks allotment : 15)

Scale of batches for product development, layout of pharmaceutical pilot plant, organization structure, personnel, activities. Pilot plant of tablets, capsules, solutions, dispersions, semisolids, and parenterals. Protocols for technology transfer. Process automation technology (PAT) in Pharmaceutical manufacturing. Introduction to SUPAC guidelines.

3. **Drug stability kinetics - principles and applications** **05 Hrs**
(Marks allotment : 15)

Chemical kinetics, complex chemical reactions, degradation pathways of drugs, factors affecting chemical stability, influence of temperature on drug degradation, influence of pH of the vehicle on drug degradation. Solid state drug stability, dosage form stability, accelerated stability testing, shelf life calculations.

4. **Stability testing - drugs and dosage forms** **04 Hrs**
(Marks allotment : 10)

Solid state drug stability, dosage form stability, accelerated stability testing, shelf life calculations, strategies for prolonging shelf life. Effect of packaging materials on dosage form stability. Basic principles of ICH, stability testing of new drug substance and formulations, photostability testing and oxidative stability, role of containers in stability testing. WHO stability guidelines.

5. **Plant location, layouts, industrial hazards and plant safety** **05 Hrs**
(Marks allotment : 15)

Pharmaceutical industry – location, layout, utilities, services. Accidents, mechanical hazards, electrical hazards, chemical hazards, gas hazards, dust explosion, fire and explosion hazards, prevention and control of all these hazards, safety management.

6. **Environmental pollution, control, effluent analysis and treatment** **06 Hrs**
(Marks allotment : 15)

Water pollution and control, air pollution and control, noise pollution and control, solid waste management, effluent analysis, effluent treatment in formulation plants, effluent treatment in synthetic drug industry, effluent treatment in fermentation industries. Different types of water used in pharma industry, preparation, and standards prescribed for water as per EPA, USA, WHO, and BIS.

7. **Documentation and records** **03 Hrs**
(Marks allotment : 10)

Material identification system, master formula records, control record, master production and control records, batch production and control records, equipment cleaning and usage log books, records related to container, closure and labeling, production record review, distribution records and complaint files.

8. **IPRs and Regulatory guideline** **7 Hrs**
(Marks allotment : 15)

Definition, Need for patenting, Types of Patents, Conditions to be satisfied by an invention to be patentable, Introduction to patent search. Parts of patents. Filing of patents. The essential elements of patent; Guidelines for preparation of laboratory note book, Non-obviousness in Patent. Brief introduction to Trademark protection and WHO Patents. IPR's and its types, Major bodies regulating Indian Pharmaceutical sector, CDSCO, WHO, USFDA, EMEA, TGA, MHRA, MCC, ANVISA regulatory requirements for contract research organization. Regulations for Biosimilars. Role of GATT, TRIPS, and WIPO.

9. **Quality by design, design of experiments, formulation by design 4 Hrs**
(Marks allotment : 10)

USFDA's view of QbD, Elements of QbD, QbD tools, Design of experiments –Methods and applications. Optimization techniques: Concept of optimization, optimization parameters, classical optimization. Statistical design (Simplex and factorial design).

10. **Generic drug products 4 Hrs**
(Marks allotment : 10)

Various stages of drug - New chemical entity (NCE), new drug, investigational new drug (IND), new drug applications (NDA), active pharmaceutical ingredient (API), abbreviated new drug application (ANDA), generic drug product. Hatch-Waxman act. Drug regulations of IND, NDA, ANDA, orphan drugs. Differences between generic drug products and brand name products. Generic drug product development and its approval.

REFERENCE BOOKS

1. Rawlins EA. Bentley's textbook of pharmaceutics. 8th Ed. New Delhi: ELBS Publication; 2010.
2. Remington: The Science and practice of pharmacy, Laura Moore Fox. 21st Ed. New York: Lippincott Williams & Wilkins; 2006.
3. Loyd VA, Nicholas GP, Howard CA. Pharmaceutical dosage forms and drug delivery systems. 9th Ed. New York: Lippincott Williams & Wilkins; 2010.
4. Subrahmanyam CVS, Thimmasetty CVS. Pharmaceutical regulatory affairs. Delhi: Vallabh Prakashan; 2012.
5. Ahuja A. Textbook of pharmaceutical management. New Delhi: Birla Publications; 2005.
6. Banker, Rhodes. Modern pharmaceutics. Vol 121, 4th Ed. New York: Marcel Dekker Inc; 2009.
7. Martin A. Martin's Physical pharmacy & pharmaceutical sciences. 6th Ed. New York: Lippincott Williams & Wilkins; 2011.
8. Herbert. Pharmaceutical dosage form- Tablets, Vol 1,2,3, 2nd Ed. New York: Marcel Dekker Inc; 2005.
9. Kohli DPS. Drug formulation manual. 3rd Ed. New Delhi: Eastern publishers; 2006.
10. Yalkowsky SH. Techniques of solubilization of drugs. Vol-12. New York: Marcel Dekker Inc; 1981.
11. Guarino RA. New drug approval process. Vol 100. New York: Marcel Dekker Inc; 2002.

12. Subrahmanyam CVS. Pharmaceutical production and management. Delhi: Vallabh Prakashan; 2007.
13. Evans, Anderson, Sweeney, Williams. Applied production and operations management. 3rd Ed. St.paul: West publishing company Ltd; 1984.
14. Peter FD. Management - task, responsibility and practices. Bangalore: Allied publication; 1986.
15. Tomski HW. A textbook of pharmacy management. London: Kogan Page ltd; 1976
16. Harold K, Cyril OD, Heinz W. Essentials of management. New Delhi: McGraw-Hill Book Company; 1986.
17. Lachman L, Liberman HA, Kanig JL. Theory and practice of industrial pharmacy. 3rd Ed. Bombay: Varghese Publishing House; 1986.
18. Sidney H, Willig. Good manufacturing of pharmaceuticals - A plan for total quality control from manufacturer to consumer. 5th Ed. New York: Marcel Dekker Inc; 2001.

JOURNALS

1. Indian Journal of Pharmaceutical Sciences.
2. Indian Drugs.
3. Journal of Scientific and Industrial Research.
4. RGUHS Compendium of Pharmacy Research Publication
5. Indian Journal of Pharmaceutical Education & Research

URLs

1. www.ich.org
2. www.fda.gov
3. www.who.int
4. www.gatt.org
5. http://www.wipo.int
6. http://www.wto.org
7. http://www.madridprotocol.info/
8. http://www.who.int/medicines/areas/policy/WHO_EDM_PAR_2002.3.pdf
9. http://www.tripsagreement.net/
10. http://www.law.cornell.edu/treaties/berne/overview.html
11. www.uspto.gov
12. www.ipo.gov.uk
13. www.ipindia.nic.in
14. www.copyright.gov
15. www.iso.org
16. www.iso.com
17. www.isoindia.org
18. www.bis.org.in

PRACTICALS

Suggested practical experiments

1. Study on the effect of pH on the solubility of drugs.

2. Study on the effect of surfactants to improve the solubility of drugs.

3. Study on the effect of cosolvents to improve the solubility of drugs.

4. Study on diffusion of drugs through various polymeric membranes.
5. Study on the effect of pH on the stability of drug in solution at elevated temperature.
6. Accelerated stability study of aspirin or any other drug in solution dosage form.
7. Stability studies of drug in dosage form as per ICH guidelines.
8. Determination of p*Ka* of a drug (8-hydroxyquinoline/pimozide/meloxicam or any other) using spectrophotometry.
9. Study on the methods of effluent testing.
10. Study on the effect of particle size on dissolution/ compatibility/flow properties.
11. Testing of drug degradation compounds using TLC.
12. Compatibility evaluation of drugs and excipients using spectrophotometry.
13. Designing of plant layouts for tablets, liquid orals, and parenterals (3 experiments)
14. Dissolution of drugs in different pH media for comparison of performance with innovator.
15. Study of the effects of pH on rheological characteristics of carbopol gels using Brookefield viscometer.

SCHEME OF EXAMINATION

1. Synopsis	- 20 marks
2. Major experiment	- 35 marks
3. Minor experiment	- 25 marks
4. Viva-voce	- 20 marks
Total:	**100 marks**

PAPER III - BIOPHARMACEUTICS AND PHARMACOKINETICS

Goal: To train the students in the area of biopharmaceutics and pharmacokinetics to work efficiently in the R&D Dept of industry, to take part in clinical research (clinical trials)

Objectives: Upon completion of the course, the candidate shall have the ability to:

- Calculate Pharmacokinetics parameters from the given data.
- Apply the principle of Pharmacokinetics in new drug development as well as in the design of new formulations.

COURSE DESCRIPTION

THEORY **50 Hours (T:2Hours/Week)**

1. **ABSORPTION OF DRUGS** **(8 Hrs.)**
   (Marks allotment : 20)

   Structure of cell membrane, Gastro-intestinal absorption of drugs, mechanisms of drug absorption, Factors affecting drug absorption: Biological, Physiological, Physico-chemical and Pharmaceutical. Absorption of drugs from non-per oral routes, Methods of determining absorption: *In-vitro, in-situ* and *in-vivo* methods.

2. **BIOAVAILABILITY** **(7 Hrs.)**
   (Marks allotment : 15)

   Objectives and consideration in bioavailability studies, Concept of equivalence, Measurement of bioavailability, Determination of the rate of absorption, Bioequivalence protocol and its importance, Bioequivalence studies.

3. **DISSOLUTION** **(3 Hrs.)**
   (Marks allotment : 10)

   BCS Classification, Noyes-Whitney's dissolutions rate law, Study of various approaches to improve dissolution of poorly soluble drug, *In-vitro* dissolution testing models, *In-vitro* release kinetic models, similarity and dissimilarity factors, biowaivers, *In-vitro- In –vivo* correlation.

4. **PHARMACOKINETICS** **(10 Hrs.)**
   (Marks allotment : 25)

   Basic considerations, Pharmacokinetic models, Compartment modeling: One compartment model - IV bolus, IV infusion, Extravascular; Multi Compartment models; Two compartment model - IV bolus, IV infusion, Extravascular, Three Compartment model in brief, Application of Pharmacokinetics in new drug development and designing of dosage forms and Novel drug delivery systems.

5. **NON-LINEAR PHARMACOKINETICS** **(3 Hrs.)**
   (Marks allotment : 10)

   Causes of non-linearity, Detection of non – linearity, Michaelis-Menten equation, Estimation of K_m and V_{max} with respect to individualization of a drug therapy.

6. **NON-COMPARTMENT PHARMACOKINETICS** **(3 Hrs.)**

(Marks allotment : 10)

Statistical moment theory, MRT for various compartment models, Physiological pharmacokinetic models.

7. DRUG DISTRIBUTION (3 Hrs.)

(Marks allotment : 10)

Factors affecting drug distribution, Volume of distribution, Protein binding- factors affecting, significance and kinetics of protein binding and drug displacement interactions.

8. BIOTRANSFORMATION (3 Hrs.)

(Marks allotment : 5)

Phase I (oxidative, reductive and hydrolytic reactions) and Phase II reactions (conjugation), factors affecting biotransformation.

9. EXCRETION OF DRUGS (3Hrs.)

(Marks allotment: 5)

Renal and non-renal excretion. Concept of clearance- renal clearance, organ clearance and hepatic clearance.

10. DOSAGE REGIMEN (7 Hrs.)

(Marks allotment : 20)

Multiple dosing with respect to I.V and oral route, concept of loading dose, maintenance dose, accumulation index, adjustment of dosage in renal and hepatic impairment, individualization of therapy, Therapeutic Drug Monitoring.

PRACTICALS **(T:6 Hours/Week)**

1. Improvement of dissolution characteristics of slightly soluble drugs by Solid Dispersion.
2. Improvement of dissolution characteristics of slightly soluble drugs by Solvent deposition.
3. Improvement of dissolution characteristics of slightly soluble drugs by complexation.
4. Improvement of dissolution characteristics of slightly soluble drugs by solvent evaporation.
5. Comparison of dissolution studies of two different conventional marketed products of same drug. - 2 experiments
6. Influence of polymorphism on solubility.
7. Influence of polymorphism on dissolution.
8. Protein binding studies of a highly protein bound drug.
9. Protein binding studies of a poorly protein bound drug.
10. Permeation study of drug through biological membrane.
11. Calculation of Ka, Ke, $t_{1/2}$, C_{max}, and T_{max} for two sets of data. -2 experiments

12. Calculation of bioavailability from urinary excretion data for two drugs. -2 experiments

13. Calculation of AUC and bioequivalence from the given data for two drugs. -2 experiments

SCHEME OF EXAMINATION

1.	**Synopsis**	**-**	**20 Marks**
2.	**Experiment**	**-**	**40 Marks**
3.	**Calculation**	**-**	**20 Marks**
4.	**Viva-voce**	**-**	**20 Marks**
	Total	**-**	**100 Marks**

REFERENCE BOOKS

1. Biopharmaceutics and Clinical Pharmacokinetics by Milo Gibaldi, 4th edition, Philadephia, Lea and Febiger, 1991.
2. Bio pharmaceutics and Pharmacokinetics-A Treatise, By D. M. Brahmankar and Sunil B.Jaiswal, Vallabh Prakashan Pitampura, Delhi
3. Applied Biopharmaceutics and Pharmacokinetics by Shargel. L and Yu ABC, 2nd edition, Connecticut, Appleton Century Crofts, 1985.
4. Textbook of Biopharmaceutics and Pharmacokinetics, Dr. Shobha Rani R. Hiremath, Prism Books Pvt Ltd, Bangalore, 2000
5. Biopharmaceutics and Clinical Pharmacokinetics by Milo Gibaldi, 2nd edition, Marcel Dekker Inc., New York,1982.
6. Current Concepts in Pharmaceutical Sciences: Biopharmaceutics, Swarbrick. J, Lea and Febiger, Philadelphia,1970.
7. Cilincal Pharmacokinetics, Concepts and Applications: By Malcolm Rowland and Thomas, N. Tozen, Lea and Febrger, Philadelphia, 1995.
8. Dissolution, Bioavailability and Bioequivalence, By Abdou H.M, Mack, Publishing Company, Pennsylvania 1989.
9. Biopharmaceutics and Clinical Pharmacokinetics-An introduction 4th edition Revised and expanded by Rebort F Notari Marcel Dekker Inc, New York and Basel, 1987.
10. Biopharmaceutics and Relevant Pharmacokinetics by John. G. Wagner and M. Pernarowski, 1st edition, Drug Intelligence Publications, Hamilton, Illinois,1971.
11. Encyclopedia of Pharmaceutical Technology, Vol 13, James Swarbrick, James, C. Roylan, Marcel Dekker Inc, New York 1996.

URL's

1. European Journal of Bio pharmaceutics and Pharmacokinetics, Publisher- Elsevier Science, www.elsevier.com.
2. Indian Drugs.

3. Indian Journal of Pharmaceutical Sciences.
4. http://www.columbia.edu/itc/gsas/g9600/2004/GrazianoReadings/Drugabs.pdf
5. http://www.google.co.in/url?sa=t&rct=j&q=absorption%20of%20drugs&source=web&cd=9&sqi=2&ved=0CG4QFjAI&url=http%3A%2F%2Fdaactarbhatti.weebly.com%2Fuploads%2F3%2F5%2F1%2F6%2F3516207%2Fabsorption_of_drugs_by_dr._soban.ppt&ei=30AiUI-1N8-srAf1_ICwBg&usg=AFQjCNF0Vj-xdwOpxKTzhkKhPHlmjs1HKg
6. http://www.iuphar.org/pdf/hum_55.pdf
7. http://www.synchronresearch.com/pdf_files/ba-be-trials.pdf
8. http://fip.org/files/fip/BPS/Dissolution/FIP_AAPS_Guidelines%20for%20Dissolution.pdf
9. http://www.dissolutiontech.com/DTresour/200702Articles/DT200702_A02.pdf
10. http://www.pharmpress.com/files/docs/clinical_pharmacokinetics_samplechapter.pdf
11. http://rmipharmacokinetics.com/uploads/Public_Documents/Introduction%20To%20Pharmacokinetics.pdf
12. http://www.pharmpress.com/files/docs/clinical_pharmacokinetics_samplechapter.pdf
13. http://archive.ajpe.org/legacy/pdfs/aj650212.pdf
14. http://www2.courses.vcu.edu/ptxed/m2/powerpoint/download/Lamb%20Drug%20Distribution.pdf
15. http://physiologie.envt.fr/spip/IMG/pdf/Volumes_of_distribution.pdf
16. http://books.mcgraw-hill.com/medical/goodmanandgilman/pdfs/CHAPTER3.pdf
17. http://el.trc.gov.om:4000/htmlroot/MEDICAL/tcolon/pharmacology/General/E-Books/Metabolism%20Excretion.pdf
18. https://apps.who.int/chd/publications/referral_care/referencepdf/15app2.pdf

PAPER IV- ADVANCES IN DRUG DELIVERY SYSTEMS

GOAL

To train the students in the area of novel drug delivery systems.

OBJECTIVE

Upon the completion of the course, the student shall have an understanding of the need, concept, design and evaluation of various sustained and controlled release dosage forms.

COURSE DESCRIPTION

THEORY **50 Hours (T:2Hours/Week)**

1. CONCEPTS OF CONTROLLED RELEASE DRUG DELIVERY SYSTEMS

(Marks allotment :20) (7 Hrs.)

Introduction, concept, advantages & disadvantages. Factors to be considered for designing controlled release dosage forms. Dissolution, Diffusion, Combination of dissolution and diffusion controlled drug delivery systems. Evaluation of CRDF.

2. POLYMER SCIENCE (3 Hrs.)

(Marks allotment : 5)

Polymer: Introduction, classification, general synthesis and evaluation techniques. Appplication of polymers in drug delivery.

3. **APPROACHES TO CONTROLLED DRUG DELIVERY SYSTEM (8 Hrs.)**

(Marks allotment : 20)

Classification of rate-controlled drug delivery systems. Rate-programmed release, activation-modulated and feedback regulated drug delivery systems. Effect of system parameters on controlled drug delivery. Hydrodynamically balanced systems, Osmotic pressure controlled, pH controlled, ion exchange controlled systems.

4. MUCO ADHESIVE DRUG DELIVERY SYSTEMS (8 Hrs.)

(Marks allotment : 15)

Concepts, advantages and disadvantages, structure of oral mucosa, transmucosal permeability, theories of muco adhesion and muco adhesive polymers, mucosal membrane models, permeability enhancers. Development and evaluation of buccal, nasal, pulmonary, rectal, vaginal and ocular drug delivery systems and their applications.

5.TRANSDERMAL DRUG DELIVERY SYSTEMS (7 Hrs.)

(Marks allotment : 15)

Rationale behind transdermal drug delivery, Permeation through skin, factors affecting permeation, basic components of TDDS, formulation approaches used in development of TDDS and their evaluation, permeation enhancers. Iontophoresis, sonophoresis and magnetophoresis.

6. **PARENTERAL CONTROLLED RELEASE DRUG DELIVERY SYSTEMS**

(Marks allotment: 15) (5 Hrs.)

Approaches for injectable controlled release formulations. Development and evaluation of Implantable drug delivery systems, subcutaneous, intramuscular and intrauterine implants.

7. **NANO DRUG DELIVERY SYSTEMS (7 Hrs.)**

(Marks allotment : 25)

Formulation, development and evaluation of Nanoparticles- Polymeric nano particles, Nano crystals, Solid Lipid Nanoparticles (SLN), Metal Nanoparticles. Vesicular Systems-Liposomes, Transferosomes, Ethosomes, Niosomes, Virosomes. Carbon Nano Tubes (CNT) and Dendrimers. Safety issues related to nano drug delivery systems.

8. TARGETED DRUG DELIVERY (5 Hrs.)

(Marks allotment : 15)

Concept, advantages and disadvantages, types of targeting and applications. Monoclonal antibodies-hybridoma cell production, diagnostic and therapeutic applications – cancer and autoimmune diseases. Problems related to monoclonal antibodies.

PRACTICALS **(T:6Hours/Week)**

1. Comparative evaluation of marketed sustained release tablets and data treatment.
2. Preparation and evaluation of matrix tablets using natural polymers.
3. Preparation and evaluation of matrix tablets using synthetic polymers.
4. Preparation and evaluation of microspheres by solvent evaporation.

5. Preparation and evaluation of muco- adhesive microspheres by ionic gelation method.
6. Preparation and evaluation of microspheres by temperature change method.
7. Preparation and evaluation of microcapsules by wax embedded method.
8. Preparation and evaluation of buccal patches.
9. Preparation and evaluation of buccal tablets.
10. Preparation and evaluation of transdermal films.
11. Evaluation of the effect of various permeation enhancers on transdermal drug delivery.
12. Preparation and evaluation of hydrodynamically balanced tablets.
13. Preparation and evaluation of ocular *insitu* gel.

SCHEME OF EXAMINATION

1. Synopsis	- 20 marks
2. Experiment	
a) Formulation	- 35 marks
b) Evaluation	- 25 marks
3. Viva-voce	- 20 marks
Total:	**100 marks**

REFERENCES

1. Chien YW., Novel drug delivery systems, 2nd edition, revised and expanded, Marcel Decker, Inc., New York, 1992.
2. Robinson JR., Lee VHL. Controlled drug delivery systems, Marcel Decker, Inc., New York,1992.
3. John Wiley and sons, Inc, Encyclopedia of controlled delivery, Editor-Edith Mathiowitz, Published by Wiley Interscience Publication, New York/Chichester/Weinheim
4. Jain NK., Controlled and novel drug delivery, CBS Publishers & Distributors, New delhi,First edition 1997 (reprint in 2001)
5. Vyas SP., Khar RK., Controlled drug delivery-concepts and advances, Vallabh Prakashan, New Delhi, first edition 2002.
6. Indian Pharmacopoeia 2010. Volume-I, II & III, Indian Pharmacopoeia Commission. New Delhi.
7. United States Pharmacopoeia, US Publications, US
8. British pharmacopoeia
9. Howard C. Ansel, Nicholas G., Popovid loyd, Allen junior BI. Pharmaceutical dosage forms & drug delivery systems. Waverly pvt, Ltd, New Delhi, Sixth edition
10. Leon Lachman, Lieberman, Kanig JL., Theory and Practice of Industrial Pharmacy, Varghese Publishing House, Bombay, 3rd Edition, 1987.
11. Banker and Rhodes, Modern Pharmaceutics, Marcel Decker Inc., New York, 2nd Edition, 1990.

12. Ansel HC., Introduction to Pharmaceutical Dosage Forms and Drug Delivery Systems, Lippincott Williams and Wilkins, New York, 7th Edition, 2000.
13. Remington, the Science and Practice of Pharmacy, Lippincott Williams, 21st Edition, 2000.
14. Patrick J. Sinko. Lippincott Williams and Wilkins. Martin's physical pharmacy and pharmaceutical sciences. Fifth edition.
15. Wilium Alfred Martin P, Bustamante AH., Chun. Physical Pharmacy, B. I. Waverly Pvt Ltd, new Delhi, 4th edition 1995
16. S.Bharath. Pharmaceutical Technology-Concepts and Applications, Pearson Education in South Asia, First edition,2013.

JOURNALS

1. Indian Journal of Pharmaceutical Sciences (IPA)
2. Indian drugs (IDMA)
3. Journal of Pharmaceutical Education and Research
4. Dissolution Technologies
5. Journal of Controlled Release (Elsevier Sciences), desirable
6. Drug Development and Industrial Pharmacy (Francis and Taylor) desirable
7. European journal of Pharmaceutical sciences
8. European Journal of Biopharmaceutics
9. International Journal of Pharmaceutics
10. Journal of Pharmaceutical Sciences
11. DARU: Journal of Pharmaceutical Sciences
12. Asian Journal of Pharmaceutical Sciences
13. AAPS Pharma Sci Tech
14. Advances in Drug Delivery Reviews
15. Rajiv Gandhi Journal of Pharmaceutical sciences

URL's

http://www.pharmtech.com/
http://www.pharmacytimes.com/
http://pharmacie-globale.info/

http://www.pharmacy.org/
http://www.dissolutiontech.com/
http://onlinelibrary.wiley.com
http://www.uspharmacist.com
http://www.pharmpress.com/
http://www.elsevier.com/

M . P H A R M
PHARMACOLOGY

GOAL: To produce competent Pharmacologists.

OBJECTIVES: Upon completion of the course, the candidate shall have knowledge of understanding the concepts of drug action and its mechanisms involved

Skill: the ability to screen new molecules for their potential pharmacological effects and toxicity

Attitude: the ability to

1. Work independently and as a member of a team
2. Plan his / her work for efficient use of time and resources
3. Identify the cause and to solve the problem
4. Think and evaluate scientifically, ethically and critically

TITLE OF PAPERS

PAPER I	**Modern Pharmaceutical Analysis**	**(T:3Hrs/wk,P:6Hrs/wk)**
PAPER II	**Advanced Pharmacology and Toxicology**	**(T:2Hrs/wk, P:6Hrs/wk)**
PAPER III	**Pharmacological Screening Methods and Clinical Evaluation**	**(T:2Hrs/wk, P:6Hrs/wk)**
PAPER IV	**Molecular Biology**	**(T:2Hrs/wk, P:6Hrs/wk)**

List of special equipment

1.	Student's Physiograph	3 nos
2.	Semi auto Analyzer	1 no
3.	Langendorf's Heart Perfusion Apparatus	2 nos
4.	Students Organ Bath (Temperature Controlled)	6 nos
5.	Elevated Plus Maze	1 no
6.	ECG Equipment for Rats	1 no
7.	Condon's Manometer (for rat BP)	3 nos

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** 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, TGFβ/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	**12**
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- l and Cox-2.	**4**
3. **Pharmacotherapy [28 hrs]** 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	**28**

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

6

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, Williamsand 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. Waynforth 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 pathopysiologic 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+xylazine by intraperitoneal)
4. Blood sampling methods in experimental animals (cardiac puncture, retroorbital, tail vein, cephanous, marginal ear vein)
5. To identify the cholinergic, adrenergic, serotoninergic, vasodilator and cardiotonic 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 canulation).
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, Delhii, 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.

PAPER III PHARMACOLOGICAL SCREENING METHODS & CLINICAL EVALUATION

Proposed	Hours
GOALS: To understand the process of drug development and estimation of drugs using bioassays. To understand and apply pharmacokinetics to rational drug therapy. **OBJECTIVES:** Upon completion of the course, the candidate is expected to know 1. The regulations and ethics concerning animal studies and experiments on human beings. 2. Carry out screening of new drugs. 3. Participate in drug development process. 4. Know alternatives to animal screening procedures / techniques 5. To perform Bioassays official in IP/BP/USP. 6. Concepts of kinetics and various pharmacokinetic models	
COURSE DESCRIPTION **THEORY** **50 Hours (2 Hrs/wk)**	
1. Drug Design: [6 Hours] a. Drug discovery and development – introduction b. Modern methods of drug discovery (Introduction, Target identification, Target validation, Lead compound identification and Optimization). c. Study of laboratory animals including physiological parameters Regulations and ethics requirements. Transgenic animals and other genetically prone animal models (Viz Nude Mice, SH rats and humanized mice).	**6**
2. Preclinical models employed in the screening of new drugs belonging to following categories: [20 Hours] Antipsychotic agent; Antianxiety agents; Nootropic drugs; Antidepressant drugs; Antiparkinsonian agents; Analgesics; Antiepileptics; Antiinflammatory agents; Antiulcer agents; Antianginals and myocardial infarction; Antiarrythmics; Antiatherosclerotic drugs; Antimalarials; Antidiabetics;	**20** **6**

Antihypertensives; Anticancer.

3. Modern techniques to elucidate the mechanisms of drug actions: [6 Hours]

a. Cell culture and maintenance:
Concepts of in-vitro screening, Different cell lines (animal &human) used in screening techniques. Primary and secondary cultures, Principles of techniques involved in cell culture and its maintenance.
b. Introduction and applications of Biomarker analysis
c. Introduction to Translational pharmacology
d. Alternatives to animal screening procedures, cell-line, patch-clamp technique, in-vitro models.
e. High throughput screening (HTS): Introduction, Basic principles involved in cell based assays, receptor binding assays and ultra high through put screening.

7

1. **Definition and Scope of Pharmacokinetics. 1 hour**

Absorption, Distribution, Metabolism, Elimination and transporters

Individualization: variability, genetics, age and weight, disease, interacting drugs, and monitoring of the same. **1 hour**

Pharmacokinetic models: compartmental models, noncompartmental models and physiologic model. Nonlinear pharmacokinetics, multiple dosing and dosage regimen.

3

Clinical Research: Introduction and Ethics [3 Hours]

a. Definition and scope of clinical research. Role of sponsor, study director or principal investigator; Clinical Research Associate in conduct of Clinical Research
b. Study design, ethics in patient selection and preserving their rights. Institutional Ethics Review committee its constituent members and its role in clinical research. Introduction to informed consent and its importance.

3

4. Phases of Clinical Trial and Clinical Trial Design [3 Hours]

a. Calculation of Human Equivalent Dose; Phase 0, Phase I, Phase II, Phase III, Phase IV and Phase V Clinical trial.
b. Randomized Clinical Trial, Uncontrolled Trials, Protocol Development, End points, Patient Selection and blinding, special designs like cross over design, factorial design, Equivalence design, confounding in clinical trials and ways to minimize it, Missing data and its management, occurrence of ADRs, interim monitoring and stopping of trials,

5

5. Regulatory Affairs in Clinical Research [5 Hours]

a. Pharmacovigilance
b. Laws governing Clinical Research: preparation of Drug master files (1ND, NDA and ANDA) Schedule Y, Code of Federal Regulations (CFR-USFDA) CDSCO (ICMR), EMEA
c. International Guidelines to meet the standards in Clinical Research: ICH guidelines for efficacy testing of drugs: clinical aspects and data management strategies (E1 – E14]

BOOKS:

1. Drug Discovery and Evaluation Pharmacological Assay by Vogel H G and Vogel W H (Springer publication)
2. Evaluation of drug activities Pharmacometrics by D R Laurence and A L Bacharach Vol. 1 and 2.
3. Drug Screening Methods by SK Gupta, Jaypee Brothers, New Delhi.
4. Alternatives to animals in toxicity testing. Scientific American 26:(1989), 16-22.
5. Remington's Pharmaceutical Sciences 24th edn.
6. Methods of clinical trials by Alan Spreit and Simon.
7. Clinical Pharmacology by P N Bennett and Brown

8. The Oxford textbook of Clinical Pharmacology and drug therapy by D.G. Graham-Smith and J.K.Aronson.
9. Modern Methods of Drug Discovery by Hillisch, A and Hilgenfeld, R

Reference Books:

1. Short Protocols in Pharmacology and Drug Discovery edited by Enna SJ, et al., John Wiley & Sons Inc.
2. Modern drug research- Paths to better and safe drugs (Medicinal Chemistry vol. 9) by Y C Martin, E. Kutter and V. Austel
3. Practical approaches in toxicity studies by Poole and Leslie
4. Pharmacological Experiments in Intact preparations, Edinburgh University Pharmacology staff, Livingstone, (1968)
5. Pharmacological Experiments on Isolated preparations, Edinburgh University Pharmacology staff, Livingstone, E & S Livingstone Edinburgh & London (1970).
6. Screening Methods in Pharmacology, Academic Press, New York and London (1965).
7. Biopharmaceutics and Clinical Pharmacokinetics by Milo Gibaldi, Lea and Febiger Book. 3rd Edition (1984).

Journals:

1.Indian Journal of Pharmacology [Essential]

2. British Journal of Pharmacology.

3. Drug Metabolism and Pharmacokinetics.

Practicals : [6 hours/week]

1. Bioassay of acetylcholine/histamine using guinea pig/rat ileum preparation.
2. Bioassay of oxytocin using rat uterine preparation.
3. PA_2 values of various antagonists using suitable isolated tissue preparations.
4. *In-vitro* Absorption study using Inverted rat intestine
5. Exercise on determination of pharmacokinetic parameters using UV/visible spectrophotometer/HPLC
6. Screening of anxiolytic drugs
7. Screening of antidepressant drugs
8. Antipyretic activity by yeast induced pyrexia in rats.
9. Anti-inflammatory activity by rat paw oedema method.
10. Analgesic by hot plate, tail flick, tail dip, paw pressure test, plantar test and/or writhing methods.
11. Skeletal muscle relaxant activity by rotarod method.
12. Anticonvulsant
13. Pole climbing
14. Actophotometer
15. Exercise on Biostatistics using software
16. Enzyme based *in vitro* bioassays (5-LO, COX, DPPH, AchE, hyaluronidase inhibition assays)
17. Antioxidant activity of Super oxide dismutase (SOD), Catalase, lipid peroxidation and Reduced glutathione in tissue homogenate

PAPER-IV. MOLECULAR BIOLOGY

Proposed	Hours
GOALS: To understand the cell biology & genetics that forms the basis for new drug discovery. **OBJECTIVES:** Upon completion of the course, the candidate is expected to know basic cell biology. Recombinant DNA technology, transfer of genes to mammalian cells.	
COURSE DESCRIPTION **THEORY** 1. **Cellular structure and functions: (8 hours)** a. **Cell structure**: cell wall, cytoplasm and its components, nucleus and its components b. **Plasma membrane**: Structure, transport of small molecules and drugs across it, endocytosis, transport proteins and their inhibitors c. **Extra cellular matrix, cell signaling and communication** between cells and their environment, ion-channels, Organization of signal transduction pathways, third messengers, d. Biosensors-introduction and applications. **2. Mechanisms of Cellular Regulation: (10 hours)** a. **Excitation, contraction and secretion** b. **Cell proliferation:** Phases and checkpoints of Cell cycle, Positive and negative regulators of cell cycle c. **Cell renewal:** Stem cells and maintenance of adult tissues, proliferation of different stem cells, medical application of adult stem cells, embryonic stem cells, somatic cell nuclear transfer, induced pluripotent stem cells and their therapeutic applications in medicine. d. **Cell death (Apoptosis):** Events of apoptosis, regulators of apoptosis, intrinsic and death pathways of apoptosis. e. Animal cell culture **3. Gene manipulation and its applications (32 hours)** a. Role of genes within cells, DNA- the primary genetic material, Elucidation of genetic code, Gene expression, Genetic elements that control gene expression, microarrey. (5 hrs) b. Recombinant DNA Technology: Principles, process and applications. Gene cloning: Isolation, cloning vectors, enzymes used in molecular cloning, PCR (Polymerase chain reaction), LCR (Ligation chain reaction) and their applications. The formation and uses of RFLP's (Restriction Fragment Length Polymorphism). (8 hrs) c. Recombinant DNA / Human Genetics: DNA sequencing, Mapping and cloning of Human disease genes, DNA-Based diagnosis of genetic diseases. (4 hrs) d. Human genome project. (1 hrs) e. Gene therapy and Antisense technology (2 hrs). f. Biotechnology related techniques: Protein engineering, Peptide chemistry and peptidomimetics, Nucleic acid technologies, catalytic antibodies, glycobiology. (6 hrs) g. Principles of cell based assays and their application: MTT assay, COMET assay, DNA ladder, Radio-ligand binding assay, RT-PCR,	**8** **10** **32**

Western blotting, Immunoblotting, Immunofluorescence, Flow cytometry.
(6 hrs)

BOOKS:

1. Molecular biology of the CELL. Alberts B. et.al (Eds). Garlound Publishing Inc. New York and London.
2. Pharmaceutical Biotechnology. Crommelin DJA and Sindelar RD. (Eds). Harward Academic Publishers, Australia, UK.
3. Biopharmaceuticals: Biochemistry & Biotechnology. Gary Walsh. (Eds). John Wiley and Sons.
4. Recombinant DNA. James D. Watson, Michael Gilman, Jan Witowski, Mark Zollet (Eds). Scientific American Books, New York
5. The Cell: A Molecular Approach. Geoffrey M Cooper and Robert E Hausman (Eds). 5th ed
6. S P Vyas and D V Kohli, Pharmaceutical Biotechnology
7. Kumarsan
8. Satynarayan

PRACTICALS **(6 Hrs/wk)**

1. Drug rnutagenicity study using mice bone-marrow chromosomal aberration test.
2. Drug mutagenicity study using mice bone-marrow micronucleus test.
3. Ame's test (Salmonella typhimurium)
4. Drug cytotoxicity using a cell line (MTT or any other assay)
5. Polyacrylamide Gel Electrophoresis
6. Western Blotting.
7. Isolation and estimation of DNA and RNA.
8. Restriction digestion of DNA.
9. Ligation of DNA.
10. Isolation of plasmids.
11. Estimation of proteins by Braford /or Lowrays

Scheme or examination:

Synopsis	20 marks
Major experiment	35 marks

Minor experiment	25 marks	
Viva-voce	20 marks	
Total	100 marks	