

RAFFLES UNIVERSITY

Japanese Zone, NH-48, Neemrana-301705

Ph.D. Course Work Syllabus

PHARMACEUTICS

Paper Code-(Ph.D-102)

Continuous Assessment: 40 Marks

Presentation: 60 Marks

Credit: 4

Contact Hours: 4 Hrs/ week

1.Preformulation Studies: Molecular optimization of APIs (drug substances), crystal morphology and variations, powder flow, structure modification, drug-excipient compatibility studies, methods of determination.

2.Formulation Additives: Study of different formulation additives, factors influencing their incorporation, role of formulation development and processing, new developments in excipient science. Design of experiments – factorial design for product and process development.

3 Compression and compaction: Physics of tablet compression, compression, consolidation, effect of friction, distribution of forces, compaction profiles. Solubility.

4 Study of consolidation parameters; Diffusion parameters, Dissolution parameters and Pharmacokinetic parameters, Heckel plots, Similarity factors – f_2 and f_1 , Higuchi and Peppas plot, Linearity Concept of significance, Standard deviation, Chi square test, students T-test, ANOVA test.

5. A. Sustained Release(SR) and Controlled Release (CR) formulations: Introduction & basic concepts, advantages/ disadvantages, factors influencing, Physicochemical & biological approaches for SR/CR formulation, Mechanism of Drug Delivery from SR/CR formulation. Polymers: introduction, definition, classification, properties and application Dosage Forms for Personalized Medicine: Introduction, Definition, Pharmacogenetics, Categories of Patients for Personalized Medicines: Customized drug delivery systems, Bioelectronic Medicines, 3D printing of pharmaceuticals, Telepharmacy.

B. Protein / Peptide Drug Delivery Systems: Concepts, delivery techniques, formulation, stability testing, causes of protein destabilization, stabilization method

REFERENCES

1. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice Of Industrial Pharmacy, 3rd ed., Varghese Publishers, Mumbai 1991.
2. Sinko PJ. Martin's physical pharmacy and pharmaceutical sciences, 5 Th ed., B.I. Publications Pvt. Ltd, Noida, 2006.
3. Lieberman HA, Lachman L, Schwartz JB. Pharmaceutical dosage forms: tablets Vol. I-III, 2 nd ed., CBS Publishers & distributors, New Delhi, 2005.
4. Connors KA. A Text book of pharmaceutical analysi Wells JI. Pharmaceutical preformulation: The physicochemical properties of drug substances. Ellis Horwood Ltd., England, 1998.
5. Y W. Chien, Novel Drug Delivery Systems, 2nd edition, revised and expanded, Marcel Dekker, Inc., New York, 1992.
6. Robinson, J. R., Lee V. H. L, Controlled Drug Delivery Systems, Marcel Dekker, Inc., New York, 1992.
7. N.K. Jain, Controlled and Novel Drug Delivery, CBS Publishers & Distributors, New Delhi, First edition 1997 (reprint in 2001).
8. S.P.Vyas and R.K.Khar, Controlled Drug Delivery - concepts and advances, Vallabh Prakashan, New Delhi, First edition 2002
9. Encyclopaedia of Pharmaceutical technology, Vol I – III. Modern Pharmaceutics; By Gillbert and S. Banker.
10. Remington's Pharmaceutical Sciences.
11. Advances in Pharmaceutical Sciences Vol. 1-5; By H.S. Bean & A.H. Beckett.
12. Physical Pharmacy; By Alfred martin
13. Bentley's Textbook of Pharmaceutics – by Rawlins.
14. Good manufacturing practices for Pharmaceuticals: A plan for total quality control, Second edition; By Sidney H. Willig
15. Applied production and operations management; By Evans, Anderson, Sweeney and Williams.

JOURNALS

1. Indian Journal of Pharmaceutical Sciences (IJPS)
2. Indian drugs (ID)
3. Journal of controlled release (Elsevier Sciences) desirable
4. Drug Development and Industrial Pharmacy (Marcel & Decker) desirable

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Ph.D. Course Work Syllabus

PHARMACOGNOSY

Paper Code-(Ph.D-102)

Continuous Assessment: 40 Marks

Presentation: 60 Marks

Credit: 4

Contact Hours: 4 Hrs/ week

1. Monographs of herbal drugs: General parameters of monographs of herbal drugs and comparative study in IP, USP, Ayurvedic Pharmacopoeia, Siddha and Unani Pharmacopoeia, American herbal pharmacopoeia, British herbal pharmacopoeia, WHO guidelines in quality assessment of herbal drugs.

2. Plant drug cultivation: General introduction to the importance of Pharmacognosy in herbal drug industry, Indian Council of Agricultural Research, Current Good Agricultural Practices, Current Good Cultivation Practices, Current Good Collection Practices, Conservation of medicinal plants- Ex-situ and Insitu conservation of medicinal plants.

3. A. Marine natural products: General methods of isolation and purification, Study of Marine toxins, Recent advances in research in marine drugs, Problems faced in research on marine drugs such as taxonomical identification, chemical screening and their solution.

B. Herbal drug industry: Infrastructure of herbal drug industry involved in production of standardized extracts and various dosage forms. Current challenges in upgrading and modernization of herbal formulations. Entrepreneurship Development, Project selection, project report, technical knowledge, Capital venture, plant design, layout and construction. Pilot plant scale –up techniques, case studies of herbal extracts. Formulation and production management of herbals

4. Extraction and Phytochemical studies: Recent advances in extractions with emphasis on selection of method and choice of solvent for extraction, successive and exhaustive extraction and other methods of extraction commonly used like microwave assisted extraction, Methods of fractionation. Separation of

phytoconstituents by latest CCCET, SCFE techniques including preparative HPLC and Flash column chromatography

5. Testing of natural products and drugs: Herbal medicines - clinical laboratory testing. Stability testing of natural products, protocols.

REFERENCES

1. Pharmacognosy - G. E. Trease and W.C. Evans. Saunders Edinburgh, New York.
2. Pharmacognosy-Tyler, Brady, Robbers
3. Marine Natural Products-Vol.I to IV.
4. Chemistry of Marine Natural Products- Paul J. Schewer 1973.
5. Natural products: A lab guide by Raphael Ikan , Academic Press 1991.
6. Herbal drug industry by R.D. Choudhary (1996), Eastern Publisher, New Delhi.
7. Quality control of herbal drugs by Pulok K Mukarjee (2002), Business Horizons Pharmaceutical Publisher, New Delhi
8. Indian Herbal Pharmacopoeia (2002), IDMA, Mumbai.
9. Text book of Pharmacognosy by C.K. Kokate, Purohit, Gokhlae (1996), Nirali Prakashan, New Delhi.
10. Text book of Pharmacognosy and Phytochemistry by Vinod D. RangarI (2002), Part I & II, Career Publication, Nasik, India.
11. Plant drug analysis by H.Wagner and S.Bladt, Springer, Berlin.
12. Standardization of Botanicals. Testing and extraction methods of medicinal herbs by V. Rajpal (2004), Vol.I, Eastern Publisher, New Delhi
13. Herbal Medicine. Expanded Commission E Monographs by M.Blumenthal, (2004), IST Edition
14. Cultivation of Medicinal Plants by C.K. Atal & B.M. Kapoor.
15. Cultivation and Utilization of Aromatic Plants, C.K. Atal & B.M. Kapoor
16. Cultivation of medicinal and aromatic crops, AA Farooqui and B.S.Sreeramu. University Press, 2001

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Ph.D. Course Work Syllabus

PHARMACEUTICAL CHEMISTRY

Paper Code-(Ph.D-102)

Continuous Assessment: 40 Marks

Presentation: 60 Marks

Credits: 4

Contact Hours: 4 Hrs/ week

1.A.UV-Visible spectroscopy: Introduction, Theory, Laws, Instrumentation associated with UV-Visible spectroscopy, Choice of solvents and solvent effect and Applications of UV-Visible spectroscopy, Difference/ Derivative spectroscopy.

B.IR spectroscopy: Theory, Modes of Molecular vibrations, Sample handling, Instrumentation of Dispersive and Fourier - Transform IR Spectrometer, Factors affecting vibrational frequencies and Applications of IR spectroscopy, Data Interpretation.

C.Spectrofluorimetry: Theory of Fluorescence, Factors affecting fluorescence (Characteristics of drugs that can be analysed by fluorimetry), Quenchers, Instrumentation and Applications of fluorescence spectrophotometer.

D.Flame emission spectroscopy and Atomic absorption spectroscopy: Principle, Instrumentation, Interferences and Applications.

2. Study of mechanism and synthetic applications of following named Reactions: Ugi reaction, Brook rearrangement, Ullmann coupling reactions, Dieckmann Reaction, Doebner-Miller Reaction, Sandmeyer Reaction, Mitsunobu reaction, Mannich reaction, Vilsmeier-Haack Reaction, Sharpless asymmetric epoxidation, Baeyer-Villiger oxidation, Shapiro & Suzuki reaction, Ozonolysis and Michael addition reaction.

3. Drug discovery: Stages of drug discovery, lead discovery; identification, validation and diversity of drug targets. Biological drug targets: Receptors, types, binding and activation, theories of drug receptor interaction, drug receptor interactions, agonists vs antagonists, artificial enzymes.

4. Study of Natural products as leads for new pharmaceuticals for the following class of drugs

- a) Drugs Affecting the Central Nervous System: Morphine Alkaloids
- b) Anticancer Drugs: Paclitaxel and Docetaxel, Etoposide, and Teniposide
- c) Cardiovascular Drugs: Lovastatin, Teprotide and Dicoumarol
- d) Neuromuscular Blocking Drugs: Curare alkaloids
- e) Anti-malarial drugs and Analogues
- f) Chemistry of macrolid antibiotics (Erythromycin, Azithromycin, Roxithromycin, and Clarithromycin) and β - Lactam antibiotics (Cephalosporins and Carbapenem)

Structural Characterization of natural compounds

Structural characterization of natural compounds using IR, ¹HNMR, ¹³CNMR and MS Spectroscopy of specific drugs e.g., Penicillin, Morphine, Camphor, Vit-D, Quercetin and Digitalis glycosides

5. Molecular Modeling and Docking

- a) Molecular and Quantum Mechanics in drug design.
- b) Energy Minimization Methods: comparison between global minimum conformation and bioactive conformation
- c) Molecular docking and drug receptor interactions: Rigid docking, flexible docking and extra-precision docking. Agents acting on enzymes such as DHFR, HMG-CoA reductase and HIV protease, choline esterase (AchE & BchE)

REFERENCES

1. Spectrometric Identification of Organic compounds - Robert M Silverstein, Sixth edition, John Wiley & Sons, 2004.
2. Principles of Instrumental Analysis - Douglas A Skoog, F. James Holler, Timothy Nieman, 5th edition, Eastern press, Bangalore, 1998.
3. Instrumental methods of analysis – Willards, 7th edition, CBS publishers.
4. Practical Pharmaceutical Chemistry – Beckett and Stenlake, Vol II, 4th edition, CBS Publishers, New Delhi, 1997.
5. Organic Spectroscopy - William Kemp, 3rd edition, ELBS, 1991
6. Medicinal Chemistry by Burger, Vol I–VI.
7. Wilson and Gisvold's Text book of Organic Medicinal and Pharmaceutical Chemistry, 12th Edition, Lppincott Williams & Wilkins, Woltess Kluwer (India) Pvt.Ltd, New Delhi.
8. Comprehensive Medicinal Chemistry – Corwin and Hansch
9. Chemistry of natural products Vol I onwards IWPAC.

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PHARMACOLOGY

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Continuous Assessment: 40 Marks

Presentation: 60 Marks

Credits: 4

Contact Hours: 4 Hrs/ week

1.General Pharmacology

a.Pharmacokinetics: The dynamics of drug absorption, distribution, biotransformation and elimination. Concepts of linear and non-linear compartment models. Significance of Protein binding.

b.Pharmacodynamics: Mechanism of drug action and the relationship between drug concentration and effect. Receptors, structural and functional families of receptors, quantitation of drug receptors interaction and elicited effects.

2.Neurotransmission

a. General aspects and steps involved in neurotransmission.

b. Neurohumoral transmission in autonomic nervous system (Detailed study about neurotransmitters- Adrenaline and Acetyl choline).

c. Neurohumoral transmission in central nervous system (Detailed study about neurotransmitters- histamine, serotonin, dopamine, GABA, glutamate and glycine].

d. Non adrenergic non cholinergic transmission (NANC). Cotransmission

Systemic Pharmacology

A detailed study on pathophysiology of diseases, mechanism of action, pharmacology and toxicology of existing as well as novel drugs used in the following systems

Autonomic Pharmacology

Parasympathomimetics and lytics, sympathomimetics and lytics, agents affecting neuromuscular junction

Central nervous system Pharmacology

General and local anesthetics Sedatives and hypnotics, drugs used to treat anxiety. Depression, psychosis, mania, epilepsy, neurodegenerative diseases. Narcotic and non-narcotic analgesics.

3. Laboratory Animals

Common laboratory animals: Description, handling and applications of different species and strains of animals.

Transgenic animals: Production, maintenance and applications

Anaesthesia and euthanasia of experimental animals.

Maintenance and breeding of laboratory animals.

CPCSEA guidelines to conduct experiments on animals

Good laboratory practice.

Bioassay-Principle, scope and limitations and methods

4. Clinical Trials: Types and Design

Experimental Study- RCT and Non RCT,

Observation Study: Cohort, Case Control, Cross sectional

Clinical Trial Study Team

Roles and responsibilities of Clinical Trial Personnel: Investigator, Study Coordinator, Sponsor, Contract Research Organization and its management

Clinical Trial Documentation- Guidelines to the preparation of documents, Preparation of protocol, Investigator Brochure, Case Report Forms, Clinical Study Report Clinical Trial Monitoring- Safety Monitoring in CT

Adverse Drug Reactions: Definition and types. Detection and reporting methods. Severity and seriousness assessment. Predictability and preventability assessment, Management of adverse drug reactions; Terminologies of ADR.

5. Toxicokinetics : Toxicokinetic evaluation in preclinical studies, saturation kinetics Importance and applications of toxicokinetic studies. Alternative methods to animal toxicity testing.

REFERENCES

1. The Pharmacological Basis of Therapeutics, Goodman and Gillman's
2. Principles of Pharmacology. The Pathophysiologic basis of drug Therapy by David E Golan, Armen H, Tashjian Jr, Ehrin J, Armstrong, April W, Armstrong, Wolters, Kluwer-Lippincott Williams & Wilkins Publishers.
3. Basic and Clinical Pharmacology by B.G Katzung
4. Hand book of Clinical Pharmacokinetics by Gibaldi and Prescott.
5. Applied biopharmaceutics and Pharmacokinetics by Leon Shargel and Andrew B.C.Yu.
6. Principles of toxicology by Karen E. Stine, Thomas M. Brown
7. Animal Models in Toxicology, 3rd Edition, Lower and Bryan
8. Textbook of Clinical Trials edited by David Machin, Simon Day and Sylvan

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PHARMACEUTICAL ANALYSIS

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Continuous Assessment: 40 Marks

Presentation: 60 Marks

Credits: 4

Contact Hours: 4 Hrs/ week

1.Spectroscopy : Introduction, theory, principle, factors affecting, instrumentation and applications of following

- a. UV/Visible spectroscopy
- b. IR spectroscopy
- c. Spectrofluorimetry
- d. Flame emission spectroscopy and Atomic absorption Spectroscopy
- e. NMR spectroscopy
- f. Mass spectroscopy

2.Chromatography: Principle, apparatus, instrumentation, chromatographic parameters, factors affecting resolution, isolation of drug from excipients, data interpretation and applications of the following:

- a. Thin Layer chromatography
- b. High Performance Thin Layer Chromatography
- c. Ion exchange chromatography
- d. Column chromatography
- e. Gas chromatography
- f. High Performance Liquid chromatography
- g. Ultra High Performance Liquid chromatography
- h. Affinity chromatography
- i. Gel Chromatography

3. Impurity and stability studies: Definition, classification of impurities in drug Substance or Active Pharmaceutical Ingredients and quantification of impurities as per ICH guidelines

Impurities in new drug products: Rationale for the reporting and control of degradation products, reporting degradation products content of batches, listing of degradation products in specifications, qualification of degradation products.

4. Analytical method validation: General principles, Validation of analytical method as per ICH guidelines and USP. Computerized system validation: Electronic records and digital significance-21 CFR part 11 and GAMP 5

5. Testing of natural products and drugs: Effect of herbal medicine on clinical laboratory testing, Adulterant Screening using modern analytical instruments, Regulation and dispensing of herbal drugs, Stability testing of natural products, protocol.

Monographs of Herbal drugs: Study of monographs of herbal drugs and comparative study in IP, USP, Ayurvedic Pharmacopoeia, American herbal Pharmacopoeia, British herbal Pharmacopoeia, Siddha and Unani Pharmacopoeia, WHO guidelines in quality assessment of herbal drugs.

REFERENCES

1. Spectrometric Identification of Organic compounds - Robert M Silverstein, Sixth edition, John Wiley & Sons, 2004.
2. Principles of Instrumental Analysis - Douglas A Skoog, F. James Holler, Timothy Nieman, 5th edition, Eastern press, Bangalore, 1998. Instrumental methods of analysis – Willards, 7th edition, CBS publishers.
3. Practical Pharmaceutical Chemistry – Beckett and Stenlake, Vol II, 4th edition, CBS Publishers, New Delhi, 1997.
4. Organic Spectroscopy - William Kemp, 3rd edition, ELBS, 1991.
5. Vogel's textbook of quantitative chemical analysis - Jeffery J Bassett, J. Mendham, R. C. Denney, 5th edition, ELBS, 1991.
6. Practical Pharmaceutical Chemistry - Beckett and Stenlake, Vol II, 4th Edition, CBS publishers, New Delhi, 1997
7. Validation Standard Operating Procedures: A Step by Step Guide for Achieving Compliance in the Pharmaceutical, Medical Device, and Biotech Industries, Syed Imtiaz Haider.