SHIVAJI UNIVERSITY, KOLHAPUR

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2009

STRUCTURE and SYLLABUS

for

Ph.D. COURSE WORK

(PHARMACY)

Under

FACULTY OF ENGINEERING & TECHNOLOGY
Ph.D. (Pharmacy) Paper II Subject List

Select any one subject of the following subject with consent of guide

1. Advances in Pharmaceutical Sciences (Pharmacological Screening and Assays)
2. Advances in Pharmaceutical Sciences (Separation Techniques)
3. Advances in Pharmaceutical Sciences (Molecular modelling)
4. Advances in Pharmaceutical Sciences (Isolation And Characterization Of Phytoconstituents)
5. Advances in Pharmaceutical Sciences (Optimization Technology)
6. Advances in Pharmaceutical Sciences (Biopharmaceuticals)

Paper - II

ADVANCES IN PHARMACEUTICAL SCIENCES

Note: A candidate has to take any one subject with consent of research guide.

ADVANCES IN PHARMACEUTICAL SCIENCES (PHARMACOLOGICAL SCREENING AND ASSAYS)

Teaching Scheme: Examination Scheme:
Theory: 4 hrs/week Theory Examination: 100 Marks

Unit-1. General principles of screening, correlations between various animal models and human situations, animal ethics and regulations. Specific use of reference drugs and interpretation of screening results. Human equivalent dose calculations, animal equivalent dose calculation.

Unit-2. Pharmacological screening models for therapeutic areas such as hypertension, cerebral ischaemia, pain, epilepsy, depression, Parkinson’s disease, Alzheimer’s disease and diabetes.

Unit-3. Pharmacological screening models for infectious diseases.

Unit-4. Correlation between in-vitro and in-vivo screens; Special emphasis on cell based assay, biochemical assay, radioligand binding assay, high through put screening, high through put pharmacokinetic analysis.

References:
6. Bacq ZM, Capek, Fundamentals of Biochemical Pharmacology
9. Kulkarni SK, Handbook of Experimental Pharmacology, Vallabh Prakashan, Delhi
10. Seth UK, Dadkar NK, and Kamat UG: Selected Topics in Experimental Pharmacology, Kothari Book Depot, Bombay
ADVANCES IN PHARMACEUTICAL SCIENCES (SEPARATION TECHNIQUES)

Teaching Scheme: Examination Scheme:

Theory: 4 hrs/week Theory Examination: 100 Marks

Unit-1. Chromatography – Principles, retention parameters, stationary phases, separation and purification methods of Column chromatography, HPLC, vacuum liquid chromatography (VLC), Gas chromatography, Ion exchange, ion-pair, ion suppression, molecular Sieve and affinity FPLC. Chiral separation, chiral stationary phases and its application in pharmaceutical industry.


Unit-3. Hyphenated Techniques: GC-MS, LC-MS, LC-MS-MS, LC-MS-NMR, LC-MS-IR, LC-S-IR-NMR.

Unit-4. TLC, HPTLC, over pressure layer chromatography (OPLC), centrifugal chromatography and Capillary electrophoresis – Theory and principle, retention parameters, classification and comparative account with respect to HPLC.

References:
5. LC/MS –A Practical User’s Guide by M.Macmaster, John Wily and Sons Inc.
8. Tandem Techniques(Separation Science Series) by R.P. Scott, John Wily and Sons Inc.
ADVANCES IN PHARMACEUTICAL SCIENCES (MOLECULAR MODELLING)
Teaching Scheme:                           Examination Scheme:
Theory: 4 hrs/week                         Theory Examination: 100 Marks


Unit-2: Bioinformatics: Sequence analysis, protein structure, homology modeling, 3D structure prediction from sequence, chemoinformatics and combinatorial databases. Advanced applications: Free energy calculations from simulations, free energy of solvation, chemical reactions, molecular docking, modern drug design with simulations and quantum chemistry. Introduction to Protein folding, Experimental techniques for studying protein folding, Computational methods for studying protein folding.

Unit-3: Introduction to structure and ligand based drug design and Simulation methods: Pharmacophore model, Homology Model Building, Complementary-based docking, Molecular-dynamics and Monte-Carlo based docking, Fragment based methods, Build-up methodology & bridging methodologies with suitable case studies, Molecular dynamics, equilibration, thermodynamical properties from simulations, stochastic dynamics, energy conservation, conformational analysis.

Unit-4: Molecular Interactions and Recognition: Electrostatics, VDW interactions, hydrophobic effect, molecular recognition (binding energy) Inhibitors types: allosteric, transition state, covalent vs non-covalent, selective and competitive.

References:

ADVANCES IN PHARMACEUTICAL SCIENCES (ISOLATION AND CHARACTERIZATION OF PHYTOCONSTITUENTS)
Teaching Scheme:                           Examination Scheme:
Theory: 4 hrs/week                         Theory Examination: 100 Marks

Unit-1: Extraction techniques such as Soxhlet extraction, microwave extraction, supercritical fluid extraction, solid phase extraction. Isolation and estimation of Secondary metabolites- Alkaloids, Glycosides, Tannins, Flavonoids, Polyphenolics, Terpenoids, Steroids, Organic acids and Proteins.

Unit-2: Isolation and estimation of phytopharmaceuticals:
1) Artimesia -Artimicinine
2) Mapia foetida-Camptothecin
3) Bacopa monnieri-Bacosides
4) Curcuma longa-Curcumin
5) gymnema sylvestre-Gymnemic acid
6) Mucuna pruriuens –L-Dopa
7) Psoralea corylifolia- Psoralin
8) Taxus baccata-Taxol
9) Tinospora cordifolia- Cordifolioside
Unit-3. Structural elucidation of important phytoconstituents belonging to different groups.
1. Alkaloids – Atropine, Morphine.
2. Glycosides – Strophanthinidin.
4. Terpenes – Citral.

Unit-4. Overview of various methods used in characterization including UV, IR, Proton NMR, C13NMR, Mass spectroscopy and crystallographic characterization. Spectral characterization of taxol, pinocembrin, curcumin and digoxin.

References
4. Medicinal and Aromatic Plant abstracts (MAPA) CSIR, New Delhi.
5. Evans, W.C., Trease and Evans Pharmacognosy, W.B. Saunders & co., London.
7. Indian Herbal Pharmacopoeia.
13. Panda, Herbal Soaps and Detergents.

ADVANCES IN PHARMACEUTICAL SCIENCES (OPTIMIZATION TECHNOLOGY)

Teaching Scheme: Examination Scheme:
Theory: 4 hrs/week Theory Examination: 100 Marks

Unit-1. Experiments and optimization process: Design of experiments (DOE) and its need. Identifying formulation and process variables. How to design experiments. Fundamentals of optimization process, need, parameters and methods. Understanding of correlation, linear and non-linear regression analysis & mathematical models.

Unit-2. Experimental designs: Design of experiments with special reference to small and large number of variables. Formulation optimization a case study using Factorial Design, Box design, Doehiert Hexagon or Uniform Shell design, Mixture design, Simplex Lattice design, Extreme-Vertices design, Evolutionary methods, D-Optimal, grid search. Generating contour plot and response surfaces, understanding.


Unit-4. Optimization of fermentation and extraction processes: Fermentation: Ethyl Alcohol, Antibiotics, Vitamins, Amino-acids and Pharmaceutical solvents-raw materials, process and process validation Extraction of phytoceuticals and optimization of the extraction process.
References:
3. Modern Pharmaceutics; By Gillbert and S. Banker.
7. Klir G.J. and Folger T.A, Fuzzy sets, Uncertainty and Information, PHI

ADVANCES IN PHARMACEUTICAL SCIENCES (BIOPHARMACEUTICALS)

Teaching Scheme: Examination Scheme:
Theory: 4 hrs/week Theory Examination: 100 Marks


Unit-2. Bioprocess Technology and Bioengineering Aspects: Strategies of biopharmaceutical production using microbiological processes and mammalian cell culture, Operating considerations for bioreactors for suspension and immobilized cultures, Aeration, mixing and hydrodynamics in bioreactors, Fed-batch cultivation of mammalian cells for the production of recombinant proteins, Optimization of high cell density perfusion bioreactors, Selection, scale-up, operation and control of bioreactors

Unit-3. Recent technologies in optimizing Quality Policies/Processings: Characterization and Bioanalytical Aspects of Recombinant Proteins as Pharmaceutical Drugs, Blotting Technique, ELISA technique (Electrochemiluminescence (ECL) - Meso Scale Discovery (MSD)), PCR, Gel-Permeation chromatography, Size-Exclusion chromatography, MALDI-TOF analyzers, FACS-calibur, Patent procedures and international protection


References:
2. Biotechnology and Biopharmaceuticals- Rodney J.Y. Ho and Milo Gibaldi., 2003 Wiley-Liss
6. Svensson’s course site: http://www.uiowa.edu/~c046138/KINETICS_HOMEPAGE.htm
Select any one subject of the following Electives with consent of guide

1. Open elective (Polymorphs And Salts In The Pharmaceutical Industry)
2. Open elective (Chemotherapy of Parasitic and Microbial Infections)
3. Open elective (Synthetic strategies in synthesis of complex organic molecules)
4. Open elective (Clinical Research)
5. Open elective (Spectral Analysis)
6. Open elective (Drug Regulatory affairs)
7. Open elective (Quality Assurance & Quality Control)
8. Open elective (Process Analytical Technology)
9. Open elective (Industrial Pharmacognosy)

Paper – III

OPEN ELECTIVE

Candidate should select any one subject from the following with the recommendation of the research guide.

OPEN ELECTIVE (POLYMORPHS AND SALTS IN THE PHARMACEUTICAL INDUSTRY)

Teaching Scheme: 
Theory: 3 Hrs. per week
Tutorial: 1 Hr. per week

Examination Scheme: 
Uni. Exam: 80 marks
Term Work: 20 Marks

Unit-1. Introduction and relation to Drug Discovery and Development. Polymorphism, physicochemical properties and bioavailability with appropriate examples.


Unit-4. Regulatory Concerns, Patent Implications and uncertainties involved in prediction of polymorphism.

References:
7. Teva Pharma, Sertraline hydrochloride polymorphs, U.S. patent 6,452,054.
8. Teva Pharma, Clopidogrel hydrogensulfate polymorph, WO 03/051362.
OPEN ELECTIVE (CHEMOTHERAPY OF PARASITIC AND MICROBIAL INFECTIONS)

Teaching Scheme:
- Theory: 3 Hrs. per week
- Tutorial: 1 Hr. per week

Examination Scheme:
- Uni. Exam: 80 marks
- Term Work: 20 Marks

Unit-1: Introduction to parasitic and infectious diseases, life cycle of the parasites causing following infections, immunology of these infectious diseases.

Unit-2: Biology of tuberculosis, amoebiasis, filariasis, leishmaniasis and HIV infection.

Unit-3: Mechanism of action of drugs used in treatment of above infections. Mechanism of drug-resistance in tuberculosis, leishmaniasis and malaria.

Unit-4: Targets for development of treatment of above infections.

References:
1. Infectious disease secrets, By Robert H. Gates
7. Shailza Singh, Balwant Kumar Malik, Durlabh Kumar Sharma, Molecular drug targets and structure based drug design: A holistic approach.
10. Ariens: Medicinal Chemistry Series
11. Bunerworther Progress in Medicinal Chemistry Series

OPEN ELECTIVE (SYNTHETIC STRATEGIES IN SYNTHESIS OF COMPLEX ORGANIC MOLECULES)

Teaching Scheme:
- Theory: 3 Hrs. per week
- Tutorial: 1 Hr. per week

Examination Scheme:
- Uni. Exam: 80 marks
- Term Work: 20 Marks

Unit-1: Retrosynthetic analysis, disconnections and reliability of reactions, synthons: Donor and acceptor, functional group interconversions, one group carbon-heteroatom and carbon-carbon disconnections, chemo-, region- and stereo-selectivity considerations, natural reactivity and umpolung, 1, 3 and 1, 5- difunctional compounds.

Unit-2: Principles of synthetic planning: Logic-centered molecular synthesis; Dislocation, synthetic tree, synthons, logical imposition of boundary conditions, direct associated approach; structural-functionality relationships, functionality and unsaturation levels; Polar reactivity analysis; Control elements, consonant and dissonant circuits; Protocol for synthetic design.

Unit-3: General synthetic reaction patterns and strategies: Aliphatic nucleophilic and electrophilic substitutions, aromatic nucleophilic and electrophilic substitutions, addition to carbon-carbon and carbon-heteroatom multiple bonds, elimination, rearrangements,
oxidations and reductions. Chemistry of protecting groups: protection for alcohols, carbonyl groups, carboxylic groups and amino groups.

**Unit-4.** Chiral synthesis: The chiral pool approach, stereoselective transformation, chiral auxiliary, chiral catalyst, enzymes as chiral catalysts. Asymmetric synthesis of Ibuprofen, levofloxacin and esomeprazole.

**References:**
4. Ledinicer: Organic Drug synthesis Vol. 1, 2, 3, 4 (John Wiley & Sons N.Y.)
5. Stuart Warren: Organic Synthesis- The Disconnection, approach (John Wiley & Sons)
7. Burger: Medicinal Chemistry (John Wiley & Sons N.Y.)

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**OPEN ELECTIVE (CLINICAL RESEARCH)**

**Teaching Scheme:**
- **Theory:** 3 Hrs. per week
- **Tutorial:** 1 Hr. per week

**Examination Scheme:**
- **Uni. Exam:** 80 marks
- **Term Work:** 20 Marks


**References**

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**OPEN ELECTIVE (SPECTRAL ANALYSIS)**

**Teaching Scheme:**
- **Theory:** 3 Hrs. per week
- **Tutorial:** 1 Hr. per week

**Examination Scheme:**
- **Uni. Exam:** 80 marks
- **Term Work:** 20 Marks

**Unit-1.** Ultra violet and visible spectroscopy: Energy levels and selection rules, Woodward-Fieser and Fieser-Kuhn rules; Influence of substituent, ring size and strain on spectral characteristics; Solvent effect; Stereochemical effect; Non-conjugated interactions. Spectral correlation with structure. Spectral interpretations with drug examples.

Unit-3. Nuclear magnetic resonance spectrometry (NMR): Magnetic nuclei, chemical shift and shielding, relaxation processes, chemical and magnetic non-equivalence, local diamagnetic shielding and magnetic anisotropy, spin-spin splitting, Pascal’s triangle, coupling constant, mechanism of coupling, quadrupole broadening and decoupling, effect of conformations and stereochemistry on the spectrum, diastereomeric protons, virtual coupling, long range coupling-epi, peri, bay effects. Shift reagents-mechanism of action, spin decoupling and double resonance. Spectral interpretations with drug examples.

Unit-4. Mass Spectrometry (MS): Molecular ion and metastable peak, fragmentation patterns, nitrogen and ring rules, McLafferty rearrangement, electron and chemical ionization modes, applications. Spectral interpretations with drug examples.

References:
2. M.Orchin and H.H-Jaffe - Theory and applications of ultra violet spectroscopy (John Wiley Md Sons, N.Y.)
4. Willard, Merritt, Dean - Instrumental Methods of Analysis (CBS Publishers and Distributors, Delhi)
7. Higuchi : Instrumental Methods of Analysis (CBS Publishers)
8. Analytical Chemistry by open learning series

OPEN ELECTIVE (DRUG REGULATORY AFFAIRS)
Teaching Scheme: Examination Scheme:
Theory: 3 Hrs. per week Uni. Exam: 80 marks
Tutorial: 1 Hr. per week Term Work: 20 Marks

Unit-1. Concept and historical development of pharmaceutical product registration. Effect of GATT and WTO on commerce of pharmaceuticals. Introduction to IPR, Schedules, NDA, ANDA.


Unit-3. Introduction to Bioethics, Ethical issues in Clinical studies, ICMR ethical guidelines for biomedical research, Institutional Ethics committee – composition, role & responsibility, IRB, SOPs – Ethics committee.

Unit-4. Schedule Y with appendices, CDSCO, ICMR guidelines, Other Indian Regulatory Authorities: DCGI/DBT/BARC. Introduction, Historical perspective (Nuremberg, Tuskegee, Belmont, Helsinki), ICH, ICH – GCP and its difference with Indian GCP. Requirements for BA / BE studies.

References:
2. FDA Regulatory Affairs by Douglas J Pisano & David Mantus.
3. FDA Guidelines.
4. ICH Guidelines.
5. ICMR ethical guidelines
6. Drugs & Cosmetics Act
OPEN ELECTIVE (QUALITY ASSURANCE & QUALITY CONTROL)

Teaching Scheme: Examination Scheme:
Theory: 3 Hrs. per week Uni. Exam: 80 marks
Tutorial: 1 Hr. per week Term Work: 20 Marks


Unit-2. Quality Control Laboratory - Responsibilities and laboratory practices, Routine controls on instruments, standard test procedure sampling plans. Quality control documentation and audits of quality control facilities.

Unit-3. Introduction to validation – Equipment validation, Calibration of equipments, Method validation, Personnel & Process validation, Aseptic validation, Validation of water and air handling systems.

Unit-4. Regulatory Audits, Regulatory Affairs and compliance – QA in Bioanalytical Laboratory, Medical diagnostic laboratory and Clinical Departments. Quality assurance in: Queries and Query resolution, fraud and misconduct, auditing and inspection. Development, Submission and storage of Quality assurance reports.

References:
1. A Practical guide to Quality management in Clinical Trial research, Graham D. Ogg, CRC Taylor and Francis.
3. Validation and Qualification in Analytical Laboratories, Ludwig Huber, Marcel Dekker series.
5. Pharmaceutical Process Validation by Berry IR and Nash RA (Eds.) Marcel Dekker Inc., NY.

OPEN ELECTIVE (CONTROL PROCESS ANALYTICAL TECHNOLOGY)

Teaching Scheme: Examination Scheme:
Theory: 3 Hrs. per week Uni. Exam: 80 marks
Tutorial: 1 Hr. per week Term Work: 20 Marks

Unit-1. Background of PAT, Goals of PAT, PAT Framework and Process Understanding. Principles and Tools of PAT.


References:
10. Brown, S., presented at InCINC’94 "Has the 'Chemometrics Revolution' ended? Some views on the past, present and future of chemometrics." Department of Chemistry and Biochemistry, University of Delaware 3. Wold, S., presented at InCINC’94 Chemometrics; what do we mean with it, and what do we want from it?" Institute of Chemistry, Umea University, Umea, Sweden.

OPEN ELECTIVE (INDUSTRIAL PHARMACOGNOSY)
Teaching Scheme: Examination Scheme:
Theory: 3 Hrs. per week Uni. Exam: 80 marks
Tutorial: 1 Hr. per week Term Work: 20 Marks

Unit-1. Cultivation of commercially important plant drugs, factors affecting quality of plant and animal drugs like Ashwagandha, Glycerrhiza, Dioscorea, Belladonna, Hyoscyamus, Cinchona, Opium, Digitalis, Senna, Plantago, Mentha, Rauwolfia, medicinal yams, Guggul, Gymnema, Insulin.

Unit-2. WHO guidelines on good agricultural and collection practices (GACP) for medicinal plants. Problems and recent trends in pest management, scope of biological control and use of environment friendly pesticides especially plant derived products, Pyrethroids, pheromones and juvenile hormones.

Unit-3. Technology for Commercial Utilization of following aromatic plants and derived products - Lemon grass, Geranium, Basil, Vetiver, Patchouli, Celery and Davana, Valerian.


References:
4. Medicinal and Aromatic Plant abstracts (MAPA) CSIR, New Delhi.
5. Evans, W.C., Trease and Evans Pharmacognosy, W.B. Saundar & co., London.
7. Indian Herbal Pharmacopoeia.
13. Panda, Herbal Soaps and Detergents.