COURSES OF STUDY

Ph.D.; M.S. (Pharm.); M.Pharm.; M.Tech. (Pharm.);
M.B.A. (Pharm.)

JULY 2018

S.A.S. Nagar

National Institute of
Pharmaceutical Education and Research,
S.A.S. Nagar, Mohali

Courses of Study 2018
Ph.D. Courses

Pharmacoinformatics

Semester-I

PI-710

Strategies in Lead Optimization (2 credits)

1. Introduction:Overview of strategies; Lead optimization;Drugdiscovery cycle; Success story ofcaptopril.
2. *De novo* ligand design: Overview; Active site analysis method; Whole molecule method; Connection methods; Genetic algorithm for ligand building; Limitations; Software.
3. Structure based drug design:Introduction; Bioactive conformation;Ligand anchoring; Desolvation effect; Entropic effect; Role of water;Analog design; Data base searching; *De novo*design;Success stories.
4. Iterative Protein crystallographic analysis: Introduction; Experimental approaches; Role of crystallography in drug design;Conformation and biological ac. Advantages and limitations of crystallography;Applications; Case studies.
5. Docking and Scoring: Molecular recognition. Methods, algorithms, conformational ensemble, molecular determinants forbinding, scoring functions, solvation effect. *In silico* tools, flexible docking, Applications, case studies.
6. Small molecular crystallography: Introduction, direct and indirect design, CSD, bioactive conformation, polar and non-polar molecules, crystal packing and ligand protein interaction. Data base mining, CHO hydrogen bonding, and applications.
7. Peptidomimetics: Introduction, types of peptidomimetics, conformational restriction, template mimetics, peptide bond isosteres, transition state analogs, rational drug design. Case studies.
8. ADMET and Duggability: Property based drug design,absorption, distribution, metabolism, excretionand physicochemical properties. Descriptors, bioisosterism, prodrug and soft drug approaches.
9. Metabolism by Cytochromes: Introductions, significance ofcytochrome P450s,substrates and inhibitors, predicting cytochromeP450 metabolism; Ligand based and structure based models for cytochrome P450. Case studies.
10. Human ether-a-go-go-related gene (hERG): Introduction, cardiac arrhythmias, SAR around hERG, *in silico* approaches. Examples.

PI-720

Computational Bio-pharmaceutics and Pharmacokinetics (2 credits)

1. Preclinical proof-of-concept: Definition, traditional drug development chain, problems in drug development, economical pressures in drug development, new development chain-exploratory Vs confirmatory.
2. Absorption: Introduction, rate limiting steps to oral drug absorption, portal bioavailability, predictive drug absorption models, strategies to improve bioavailability.
3. Permeability: Permeability predictions, models of intestinal drug permeability, drug transporter modelling, case study of P-gp and PEPT1.
4. Distribution: Plasma protein binding, free drug fraction, free drug hypothesis.

5. Metabolism: Integration of nonclinical and clinical data, polymorphism of phase I, II, III, metabolising enzymes and relevance to pharmacokinetics and pharmacodynamics.
6. Physicochemical properties: Introduction, theories of prediction (local Vs Global models), Log P, pKa, Log D, solubility, Peff.
7. Physiologically based pharmacokinetics and pharmacodynamicmodelling: Definition, modelling methodology, extrapolation across doses, routes of exposure and species, application to risk assessment, limitations, pharmacodynamic studies of drug-drug interactions, PK/PD modeling.
8. QSAR studies on drug transporters involved in toxicology: Introduction, the problem of multispecificity, QSAR approaches to design inhibitors of p-glycoprotein (ABCB1), other ABC transporters-ABCG2, ABCC1 and ABCC2, ABCB11), predicting substrate properties, the antitarget concept.
9. Computational modelling of receptor mediated toxicity: Introduction, receptors involved in toxicity of environmental chemicals (estrogen, androgen, thyroid, aryl hydrocarbon), receptors involved in drug metabolism and drug-drug interactions (pregnane X receptor/ steroid and xenobiotic receptor) constitutive androstane receptor, glucocorticoid receptor, clinical drug drug interaction studies.
10. Computational methods for prediction of solid-state: Energetics of molecules in crystals- coulombic interactions, polarisation, dispersions, repulsions. Ab initio method to calculate the structure of the molecule, determination of single crystal structure, the molecular model, intermolecular forces and the search procedure (Cambridge Crystallographic Database).

PI- 750

Big Data and Analytics (2 credits)

1. Introduction to Big Data, characteristics of Big Data, V's of Big Data, impact of Big Data, Big Data in Pharmaceutical Sciences
2. Data science, importance of data science, analytics, types of analytics: prescriptive, predictive, diagnostic, descriptive.
3. Basics of R language, environment setup, data types, variables, operators: arithmetic, relational, logical, assignment; decision making, loops, functions, strings, vectors, lists, matrices, arrays, factors, data frames, data reshaping, R packages
4. Data Interface in R: csv files, excel files, binary files, XML files, JSON, web data, database
5. Charts and graphs in R: pie charts, bar charts, boxplots, histograms, linegraphs, scatterplots
6. R Statistics: mean, median, mode, linear regression, multiple regression, logistic regression, normal distribution, binomial distribution, poisson regression, analysis of covariance, time series analysis, nonlinear least square, decision tree, random forest, survival analysis, chi square tests
7. Big Data analysis using R language
8. Big Data analysis in Pharmacoinformatics

Recommended books:

1. Data Mining and Analysis Fundamental Concepts and Algorithms by Mohammed J. Zaki and Wagner Meira, Jr, Cambridge University Press
2. Data Mining: Practical Machine Learning Tools and Techniques by Ian H. Witten, Eibe Frank, Mark A. Hall and Christopher J. Pal, Morgan Kaufmann
3. A Handbook of Statistical Analyses Using R by TorstenHothorn, Brian S. Everitt, CRC Press
4. An Introduction to Statistical Learning: with Applications in R by Gareth James, Daniela Witten, Trevor Hastie, Robert Tibshirani, Springer