Syllabus for the Entrance of Pre-Ph.D. course in Pharmaceutical Sciences: Date of Entrance Examination is 30.6.14.

Guidelines for Paper Setter: The entrance test will be of three hours duration and will be for 100 marks. The question paper will have two parts. Part-I will have 25 objective-type questions carrying 25 marks related to reasoning/aptitude/current affairs/general knowledge etc. and Part-II carrying 75 marks will require the students to answer short answer/essay type questions in the subject concerned.

Syllabus (Page no. 01 to 07):

Infrared Spectroscopy
Introduction, the infrared absorption process, the modes of vibrations, stretching and bending, bond properties and absorption trends, basics of instrumentation techniques, pharmaceutical applications. The Hook’s law and calculation of stretching frequencies for different types of bonds and their bond strengths, coupled interactions, hydrogen bonding, examination of infrared spectrum, survey of important functional groups with examples, radiation source, detectors used, sample handling, quantitative applications, qualitative applications with special reference to stereochemical aspects and hydrogen bonding, Near-IR spectroscopy, absorption and reflectance spectrophotometry, instrumentation, applications, Far Infrared spectroscopy. Introduction to FTIR and its applications.

Ultraviolet / Visible Spectroscopy and Fluorimetry
Introduction, the nature of electronic excitation, the origin of uv band structure, principle of absorption spectroscopy, chromophore- $σ→σ^*$, $η→σ^*$, $π→π^*$ transitions, basics of instrumentation techniques, pharmaceutical applications. Energy level and selection rules, effect of substituents, effect of conjugation, conformation and geometry, the Woodward-Fisher rules, the Fisher-Kuhn rules, applications of UV with reference to different electronic systems. Derivative spectroscopy and its applications. Fluorescence and chemical structure, fluorescence intensity, factors affecting fluorometry, instrumentation, comparison of fluorometry with spectrophotometry, applications of fluorimetry in pharmaceutical analysis.

Nuclear Magnetic Resonance Spectroscopy
Introduction, nuclear spin states, nuclear magnetic moments, absorption of energy, the mechanism of resonance, chemical equivalence, spin-spin coupling, basics of instrumentation techniques, pharmaceutical applications.

$^1$H-NMR spectroscopy
Magnetic equivalence, failure of the N+1 rule, chemical shifts, local diamagnetic shielding, hybridization effects, magnetic anisotropy, mechanism of spin-spin coupling, the origin of spin-spin splitting, Pascal’s triangle, the coupling constant, protons on oxygen, nitrogen and sulphur, diastereomeric protons, chemical shift reagents, long range coupling, spin decoupling methods, nuclear over Hauser effect. Correlation NMR spectrometry: introduction to $^1$H - $^1$H cosy and $^1$H - $^{13}$C cosy and its applications. Introduction and applications of 2D NMR; solid state NMR.

$^{13}$C-NMR spectroscopy
Introduction, peak assignments, off resonance decoupling, selective proton decoupling; chemical shift equivalence; chemical shifts; spin coupling.

Spectrometry of other important nuclei - Introduction to $^{15}$N, $^{19}$F, $^{31}$P, basic concepts.
Mass Spectrometry  
Basic principle and theory involved; instrumentation, type of ions; various ion sources, electron impact source, chemical ionization sources, field ionization sources, desorption sources, mass analysers, double focusing, quadrupole, time of flight, ion trap analyzer, ionization, fragmentation, rearrangements, mass spectra of representative compounds, recognition of molecular ion peak, metastable peak, isotopic peaks, applications.

Raman Spectroscopy -  Introduction, theory and polarization measurement, rules of selection and polarization, instrumentation, applications in pharmaceutical sciences. Comparison of Infrared and Raman spectra.

X-Ray Spectroscopy

Chromatography

Gas Chromatography: Gas liquid chromatography, gas solid chromatography, instrumentation and applications (GC-MS and GC-FTIR). Derivatization as a means of sampling of thermosensitive compounds.

High Pressure Liquid Chromatography: Partition, adsorption, ion exchange, size exclusion; pharmaceutical applications of HPLC and LC-MS. Super critical fluid chromatography; brief introduction to HPTLC.

Electrophoresis: Theory and application of electrophoresis, polyacrylamide and agarose gel electrophoresis, capillary electrophoresis, 2-D electrophoresis.

Thermal Analysis
Introduction to various thermal methods of analysis, basic principles and theory, instrumentation and pharmaceutical applications of thermo gravimetric analysis (TGA), differential thermal analysis (DTA), differential scanning calorimetry (DSC) and microcalorimetry, different types of calorimeters and micro calorimeters, advantages of microcalorimetry over DSC.

Optical Rotatory Dispersion and Circular Dichroism
Definition, theory and instrumentaton of ORD and CD. Cotton effect, Octant rule and its applications.

Reactive intermediates in organic synthesis:
Free radicals: Formation, structure, stability, detection, reactions involving free radicals, addition to carbon-carbon multiple bonds.

Stereochemistry : General concept of Stereoisomerism, axially dissymmetric molecules such as biphenyls and allenes. Stereochemistry of some elements other than carbon: elementary stereochemistry of Nitrogen Sulfur and Phosphorous compounds. Conformational analysis of
cyclohexane, mono and disubstituted cyclohexanes, heterocycles such as tetrahydro-pyrans with special emphasis on monosaccharides, and piperidines.

**Pericyclic Reactions:** Symmetry properties of molecular orbitals. Woodward Hoffmann rules. Correlation diagram, FMO approach and PMO approach for electrocyclic reactions, cycloadditions, and sigmatropic rearrangements, Applications.

**Organic Photochemistry:**

**Combinatorial Chemistry:** Introduction, solid phase and liquid phase synthesis, split, parallel, mix and split synthesis, ular libraries, limitations of combinatorial synthesis. Examples of combinatorial synthesis: benzodiazepines, quinazolines, imidazoles, hydantoins.

**Name reactions; their mechanism and applications in drug synthesis**
- i) Witting
- ii) Knorr Pyrazole synthesis
- iii) Darzen
- iv) Strecker amino acid synthesis
- v) Meerwein Ponndorf- verley
- vi) Oppenauer oxidation
- vii) Wolf Kishner reduction
- viii) Mannich

**Design of synthesis:** An introduction of synthons and synthetic equivalents, general principles of the disconnection approach, functional group interconversions, the importance of order of events in organic synthesis, one group C-X and two group C-X, chemoselectivity, reversal of polarity, use of nitro compounds in organic synthesis and concept of protection and deprotection of functional groups.

Mechanistic and biosynthetic approaches to plant secondary metabolites. Acetate-mevalonate pathway (biosynthesis of gibberellic acid, cholesterol).

Shikimic acid pathway (Biosynthesis of chlorogenic acid, cichorin). Polyketides (Biosynthesis of 6-methylsalicylic acid, petulin, penicillinic acid).

Amino acids and peptides, nucleic acids: General introduction, synthesis, degradative and synthetic approaches supported by spectral data of peptides and amino acids. End group analysis, structural features of Insulin, vasopressin and oxytocin, structural features of DNA & RNA. Compounds derived from Amino acids: Colchicine, Cephalosporin C.


Lipids - Classification, role of lipids, fatty acids and glycerol derived from oils and fats; Physical properties – polymorphism, reactions of fats, rancidity, reversion, polymerisatin, saponification,
addition, hydrogenation, phospholipids, lipid metabolism, intermediary metabolism of fatty acids, synthesis of fatty acids.

**Drug receptor interactions and theories of drug action**
Drug receptor interaction, G-protein coupled receptors, ion channel linked receptors. Ligand gated ion channels, voltage gated ion channels. Ligand-receptors theories: Clarks occupancy theory, rate theory, induced fit theory, macromolecular perturbation theory and activation aggregation theory.

**Approaches to drug design**
Introduction, trends in lead identification, modification of lead, source of a lead: Natural products and folklore medicine, random screening, existing drugs.

**Physicochemical and stereochemical aspects of drug action**
Solubility, Drug absorption, surface area and particle size, hydrogen bonding and biological activity, polymorphism, stereochemistry and pharmacological activity.

**Recombinant DNA Technology:**
Introduction, new therapeutics from r-DNA technology, protein engineering and site directed mutagenesis, genetically engineered drug discovery tools: reagents for structural biology study, enzyme as drug targets, receptors as drug targets, cellular adhesion proteins.

**Rational Design of Enzymes Inhibitors**
Introduction, enzyme inhibitors in medicine and basic research.
*Design of non-covalently binding enzymes inhibitors:* Forces involved in enzyme-inhibitor complexes, Rapid reversible inhibitors, slow, tight and slow-tight inhibitors, transition state analogues, multisubstrate inhibitors.
*Design of covalently binding enzyme inhibitors:* Mechanism based inhibitors, affinity labels and pseudo-irreversible inhibitors.
Current developments with respect to the inhibition of the following enzymes: acetylcholinesterase, angiotensin converting enzyme, HMG CoA reductase, dihydrofolate reductase, GABA transferase, monoamineoxidase.

**Analog Design**
Strategies of analog design: bioisosteric replacement, rigid analogs, homologation of alkyl chains, alteration in chain branching, ring size and ring position isomers, alteration in stereochemistry, fragments of lead molecules, variation in interatomic distances.

**Quantitative structure activity relationships**
Fundamentals of QSAR, Quantitative description of physico-chemical properties: hydrophobicity, partition coefficient, electronic effects, steric effects. Statistical methods in QSAR, Correlation of physicochemical parameters with biological activity: Hansch approach, Free Wilson analysis, Topliss decision tree. 3D QSAR approach, Limitations of QSAR.

**Molecular Modeling:**
Drawing chemical structures, conversion of 2D structures in 3D form, visualization of 3D structures, viewing proteins, geometry optimization, energy minimization procedures, molecular
mechanics methods, quantum mechanics methods, molecular properties, conformational analysis, Pharmacophore concept, Pharmacophoric approach, Pharmacophore elements and representation, Pharmacophore identification, docking, homology modeling, currently used softwares for molecular modeling.

**Prodrug Design**

Concept, definition and characteristics of the prodrug, Prodrugs of various functional groups, design strategies for modification of drug properties, modification of the physicochemical, pharmacokinetic and pharmacodynamic properties of a drug through chemical transformation. Applications of the prodrug approach: increased absorption, aqueous solubility, prolongation of activity, site specific chemical delivery systems, mutual prodrugs. Hard and soft drugs.

**Intellectual Property Rights**

Intellectual Property Concepts and fundamentals: The emergence and growth of the concepts regarding intellectual property (IP), intellectual property protection (IPP) and intellectual property rights (IPR); economic importance, mechanism for protection of intellectual property - patents, copyright, trademarks; role of IP in pharmaceutical industry; global ramifications and financial implications.

**Trade Related Aspects of Intellectual Property Rights**

Intellectual property and international trade, concept behind WTO (World Trade Organization), WIPO (World Intellectual Property Organization), GATT (General Agreement on Tariff and Trade), TRIPs (Trade Related Intellectual Property Rights), TRIMS (Trade Related Investment Measures) and GATS (General Agreement on Trades in Services), status in India and other developing countries, case studies and examples, TRIPS issues on herbal drugs.

**Nuts and Bolts of Patenting**


**Ethics and Values in IP**

IP and ethics, positive and negative aspects of IPR, social responsibility, avoiding unethical practices, eco-responsibility–economic, social and environmental benefits of modern biotechnology.

**Biostatistics**
General concepts, two-tail student t-test and paired sample t-test, two samples t-test, Wilcoxon rank-sum test, Mann-Whitney test, one-way analysis of variance, Kruskal-Wallis test, two-way analysis of variance, multiple comparison procedures in ANOVA: Fischer’s LSD test, Tukey’s studentized range test and Dunnett’s test. Non-linear regression: Introduction, iterative method. Correlation, linear regression, PCA and PLS.

General introduction and classification, isolation and purification methods of alkaloids, structure elucidation of reserpine, atropine and morphine. Classification, method of isolation, chemistry, degradation, synthetic methods, spectral techniques for structural elucidation and biological activity of flavonoids rutin and quercetin.

Study of chemistry, stereochemical aspects and pharmaceutical importance of plant derived steroids -cardiac glycosides (cholesterol, diosgenin).

General introduction and classification terpenoids; Essential Oils; Production of Essential Oils; Chemistry and Analysis of Essential Oils; Biological Activities of Essential Oils; Aromatherapy with Essential Oils; Industrial Uses of Essential Oils, Essential Oils Used in Veterinary Medicine; Trade of Essential Oils; Recent EU Legislation on Flavors and Fragrances of Essential Oils.

Recent advances in the chemistry of naturally occurring anti-neoplastic agents (catharanthus alkaloids, camptothecin); antimalarials (cinchona alkaloids, artemisinin derivatives).

Role of natural products in “Neglected Diseases” (dengue, protozoal diseases including leishmaniasis, trypanosomiasis, schistosomiasis, tuberculosis, leprosy).

**Antibacterial agents**
Introduction, history and development of resistance to known antibacterials such as penicillins. Bacterial DNA-gyrase inhibitors - mode of action of fluoroquinolones and development of newer analogues: Trovafloxacin, Levofloxacín, Gratifloxacin including Ciprofloxacin and Norfloxacin, Oxazolidinones: Inhibitors of DNA Synthesis.

**Anti-cancer drugs**

**Antiviral Agents**
DNA and RNA viruses, retroviruses, strategies to design anti-HIV drugs, viral replication, antiviral agents for RNA-virus infections, development of new drugs and drug discovery Diadanosine, Nevirapine.

**Drugs affecting Adrenergic neurotransmission:** Introduction, history and neurotransmission at sympathetic nervous system; biosynthesis and metabolism of NE; characterization of adrenergic
receptor subtypes and mechanism. Structure activity relationship of adrenergic agonists and antagonists.

**Cardiovascular drugs:**


b. β-blockers, α-blockers and α,β-blockers – Atenolol, Metprolol and analogues, Carvedilol, Prazocin, Trazocin, Labetelol

c. Calcium Channel blockers: 1,4-dihydropyridines (Nifedipine, Nimodipine, Nicardipine), Verapamil, Diltiazem.

d. Lipid lowering and anti-clotting agents – Statins eg., Atorvastatin, Rosuvastatin; Aspirin, Lipitor, Gemfibriogel, abciximab, Probucol, Celcade, clopidgrel.

e. Selective human β3 adrenergic agonists used as antiobesity agents.


g. Anti – arrhythmic agents: Amidorane, Digoxin, Flecainide, Mexiletine, Tocainide, Lidocaine.

h. Peptides with cardiovascular applications.

**Psychopharmacological Agents**

Psychopharmacological agents : Antipsychotic Agents : Biochemical basis of mental disorders, Development of antipsychotic agents, tricyclic antidepressants, Monoamine oxidase inhibitors; Selective serotonin-reuptake inhibitors; Atypical antidepressants, Antianxiety Agents : Chemistry of benzodiazepines; SAR of benzodiazepine derivatives, medicinal chemistry of non-benzodiazepines; serotonin-reuptake inhibitors, development of meprobamate and analogues; atypical anxiolytic agents; including studies of various receptors - GABA, Dopamine, NMDA, Metabotropic glutamate, excitatory amino acid neurotransmitters .

**Drugs affecting hormonal system:** Adrenocorticoids, estrogen, progestins and androgens. Chemical contraceptives; latest advances in drug receptors chemistry.

**Prostaglandins and Other Eicosanoids** - Nomenclature, biosynthesis, design of eicosanoid drugs, biological activity, metabolism, structure activity relationship, eicosanoids approved for human clinical use.