

Syllabus for the Entrance Examination for Ph.D. in Pharmaceutical Sciences

General Aptitude:

General awareness, research methodology, computers in pharmaceutical sciences, biostatistics, current affairs, etc.

Specific to Subject Area: Pharmaceutical Sciences

(Medicinal Chemistry/Pharmaceutical Chemistry)

A. *Pharmaceutical Organic Chemistry*

Stereochemistry- Optical activity, chirality, symmetry elements, chiral molecules-test and biological importance of chirality. Stereospecific and stereoselective synthesis. Resolution of racemic mixtures. Geometric isomerism and Conformational isomerism

Reactive intermediates - structure, generation, stability and reactivity of carbocations, carbanions, carbenes, nitrenes and free radicals.

Alkylation - Alkylation of nucleophilic carbon; enolates and enamines: generation & alkylation of enolates, dianions; oxygen vs. carbon as site of alkylation. Alkylation of aldehydes, esters, amides & nitriles. Enamines and imine anions.

Pericyclic reactions- Molecular orbital symmetry, Woodward-Hofmann rules. Electrocyclic (Diels-Alder reaction) and sigmatropic reactions-Cope, Benzidine rearrangements. Cycloaddition.

Rearrangements- Carbon to carbon migration- Wagner-Meerwein, Pinacol-pinacolone, Benzilic acid, Favorskii. C to N migration -Hoffmann, Curtius, Beckmann, Schmidt, Lossen. C to O migration- Bayer-Villiger, hydroperoxides.

Reduction reactions of carbonyl and other functional groups-Catalytic hydrogenation, reduction by Group III and Group IV hydride donors, dissolving metal reductions, reductive deoxygenation of carbonyl groups.

Synthon approach- Concept, halfreactions, FGI, analysis of target molecule, synthetic strategies. Application to synthesis of benzocaine, propranolol, haloperidol, salbutamol and other drugs. Miscellaneous reactions.

Electrophilic and Nucleophilic addition reactions. Electrophilic Aromatic Substitution – Nitration, halogenation, sulphonation, Friedel-Crafts reactions. *Nucleophilic Aromatic Substitution* and –via diazonium ions.

B. *Spectroscopy*:

Theory, instrumentation and applications of UV, IR, NMR and Mass spectrometric techniques

C. *Pharmaceutical/Medicinal Chemistry*:

Receptors- Types, structures and functions of receptors, signal transduction and G-proteins, theories of drug-receptor interaction, detailed study of adrenergic, cholinergic, histaminergic, dopaminergic and opiate receptors Nitric oxide- interplay of NO & biological systems. NO biosynthesis and cytotoxicity, NO synthetase inhibitors and their therapeutic significance. *Autocoids*-a) Enkephalins & endorphins b) *Prostaglandins & other eicosanoids*. Antiviral agents- DNA & RNA viruses, viral replication, retroviruses, strategies to design anti-HIV drugs, , antiviral drugs. Antineoplastic agents-molecular mechanism of cancer, oncogenes, alkylating agents, antimetabolites, antibiotics, natural products. *Cardiovascular agents*-*Antiarrhythmics* –basis of cardiac arrhythmias, classification of drugs used, mechanism of action, molecular features essential for antiarrhythmic activity. *Antianginal agents*- Pathophysiology of angina, classification and mode of action of drugs used, vasodilators. *Antihypertensive agents*-etiology of hypertension, basis of drug design, agents affecting sympathetic system, agents acting on smooth muscle, ACE inhibitors, diuretics. *Antihyperlipidemic agents*- classes of lipoproteins, hyperlipoproteinemia, development of antihyperlipidaemic agents, mode of action. *Antifertility agents*- methods of fertility control, steroidal and nonsteroidal antifertility agents, abortifacients. *Anti-diabetics agents*, *Chemistry of Natural Products*: Mechanistic and biosynthetic approach to plant secondary metabolites: Acetate-malonate pathway (Biosynthesis of plant fatty acids, biosynthesis and oxidation of ricinoleic acid.) *Polyketides* (Biosynthesis of 6-methylsalicylic acid, petulin, penicillanic acid, griseofulvin, tetracyclines). Acetate-mevalonate pathway (biosynthesis of psoralen, gibberellic acid, cholesterol, conessine). Shikimic acid pathway (Biosynthesis of chlorogenic acid, cichoriin). *Mixed biogenesis of plant products*: Flavonoids and anthocyanins. *Biosynthesis of alkaloids*: Hyoscyamine, Morphine, Vindoline. Compounds derived from Amino acids: Colchicine, Cephalosporin C. *Biosynthesis of porphyrins*: Cobalamine. Study of the chemistry of natural products using degradative and synthetic methods and spectral techniques. Biological significance will also be discussed. Alkaloids: Quinine, Morphine, Reserpine. *Coumarins*: psoralen, xanthotoxin and umbelliferone. Flavonoids: Quercetin and Rutin. *Steroids*: Cholesterol, Vitamin D and Cardiac glycosides. Terpenoids: Zingiberene, Abietic acid and β -amyryn. *Antibiotics*: Chemistry of Penicillins, Cephalosporin, Polypeptides and Chloramphenicol. *Antineoplastic agents obtained from Plants*: Catharanthus alkaloids; Paclitaxel and derivatives; Podophyllotoxin and Etoposide.