

Syllabus for Pre-Ph.D. Entrance Examination 2020

Section A : Pharmaceutical Chemistry

Advanced Pharmaceutical Drug Analysis

UV-Visible Spectroscopy: Electromagnetic spectrum, UV-visible range, structural features, absorption of radiant energy, factors influencing absorption of radiant energy: Instrumentation — single-beam spectrophotometer, double-beam spectrophotometer, Assay methods, Applications in pharmaceutical analysis. Infrared Spectroscopy: Molecular vibrations, stretching vibrations, bending vibrations, vibrational frequencies, factors influencing vibrational frequencies, electronic effects, Instrumentation — Single-monochromator IR-spectrophotometer, experimental profile of IR-spectroscopy : Quantitative analysis, applications in the analysis of Pharmaceutical dosage forms, qualitative interpretation of IR-spectra, Recent advances in IR-spectroscopy, e.g. FT-IR, ATR, etc. Optical Rotatory Dispersion: Fundamental principles of ORD, Cotton-effect curves — their characteristics and interpretation, Octet rule and its applications, circular dichroism. Nuclear Magnetic Resonance Spectroscopy: The NMR-phenomenon *viz.* spinning nucleus, effect of an external field, precessional motion, precessional frequency, energy transition, chemical shift, ^3H -NMR (Tritium NMR-spectroscopy), ^{13}C -NMR-spectroscopy, 2D-NMR, interpretations of NMR-spectrum, instrumentation, applications in pharmaceutical analysis. Mass Spectrometry: Basic principles and brief outline of instrumentation, ion formation and types: molecular ion, meta-stable ions, fragmentation processes. Fragmentation patterns and fragment characteristics in relation to parent structure and functional groups; Mass spectrum, its characteristics, presentation and interpretation. Recent advances in MS, *viz.* GC-MS, chemical ionization MS and Fast Atom Bombardment Mass Spectroscopy. High Performance Liquid Chromatography (HPLC): Comparison of GC and HPLC, Instrumentation in HPLC, analytical, preparative, microbore columns, normal and reverse-phase packing materials, reverse-phase HPLC, column selection, mobile phase selection, efficiency parameters, resolution, detectors in HPLC- refractive index, photometric and electrochemical. Applications of these detectors. X-Ray Diffraction Methods: Elementary crystallography, X-ray diffraction, Bragg's law, X-ray powder diffraction, X-ray powder diffractometer — interpretation of data. Gas Chromatography (GC): Theory, Instrumentation- sample injector, columns, detectors, applications. High Performance Thin Layer Chromatography (HPTLC): Principles, instrumentation and applications. Thermal Analysis: Principles and applications of thermogravimetric analysis (TGA), Differential thermal analysis (DTA), and Differential scanning Calorimetry (DSC).

Advanced Organic Chemistry: Chemical Kinetics & Thermodynamics- Kinetic and thermodynamic requirements for reaction, kinetic versus thermodynamic control. Non-kinetic and kinetic methods for determining mechanisms. Stereochemistry- Optical isomerism- Plane, centre & axis of symmetry, chiral molecules-test and biological importance of chirality. Stereospecific and stereoselective synthesis. Resolution of racemic mixtures. Geometric isomerism- Resulting from double bonds, monocyclic compounds, fused ring systems. Conformational isomerism-conformations in cyclic compounds. 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. b) C to N migration -Hoffmann, Curtius, Beckmann, Schmidt, Lossen. c) 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, half-reactions, FGI, analysis of target molecule, synthetic strategies. Application to synthesis of benzocaine, propranolol, haloperidol, salbutamol and other drugs. Miscellaneous reactions. Electrophilic Aromatic Substitution –Nitration, halogenation, sulphonation, Friedel-Crafts reactions. Nucleophilic Aromatic Substitution –via diazonium ions. Electrophilic addition to C=C double bond- halogens, halogen halides, water. Carboxylic acids- formation from alcohols and aldehydes, interconversions of carboxylic acid derivatives. Reagents used in reduction & oxidation.

Advanced 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. Principles of drug design- search for lead compound, pharmacophore identification, methods for lead optimization –synthetic analogs, case studies of cimetidine and oxamniquinone, prodrugs. 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.

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 -amyrin. Antibiotics: Chemistry of Cephalosporin, Polypeptides and Chloramphenicol. Antineoplastic agents obtained from Plants: Catharanthus alkaloids; Paclitaxel and derivatives; Podophyllotoxin, Etoposide and Teniposide. Plant hormones including brassinosteroids. Marine products with therapeutic potential.

Section B : Pharmaceutics

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Product Development:

Preformulation :Objectives, methodology, physico-chemical parameters *viz.* pKa and solubility, partition coefficient, vapour pressure, polymorphism, surface characteristics, compatibility tests, applications of solubility parameters in the development of solid, oral liquid and parenteral dosage forms. Pilot plant scale up techniques : Significance, scale-up techniques for tablets, capsules and liquid orals (involving specific considerations e.g. formula, equipment, product uniformity, stability, processing, physical layouts, personnel required etc.). Production management & documentation : GMP considerations, quality assurance and quality control, process and equipment validation for tablets and parenterals,

basic principles of materials management and cost control, ISO- 9000 series, salient features, intellectual property rights, patent application procedures. Optimization procedures in formulation and processing : Optimization parameters, classical techniques, statistical design and applied optimization methods. Packing materials : Selection and evaluation of materials for containers and closures, pharmaceutical specifications, tests and standards for packing components, Tamper evident packages. Drug stability : Shelf-life determination, overages, accelerated stability testing, effect of packaging components on stability, factors affecting stability of pharmaceutical products. Dosage forms: Theoretical and practical aspects in the manufacture of different dosage forms- Solid dosage forms- tablets, capsules, microcapsules. Liquid dosage forms- suspensions, emulsions- multiphase and microemulsions; solubilization. Parenteral dosage forms- small and large volume parenterals.

Biopharmaceutics & Pharmacokinetics:

General Principles: Drug Absorption, Distribution, Metabolism & Excretion. Factors affecting these processes. Concepts of Bioavailability & bioequivalence. Review of Compartment Approaches : Terminology, Kinetics of single and multiple dose administration, one and two compartment models, basics of Pharmacokinetics and Chronopharmacokinetics. Non-compartmental Pharmacokinetics: Model independent approaches and their advantages, stochastic approach and statistical moment theory, determination of AUC, AUMC, MRT, MDT, MTT and MAT. Advanced techniques like log-trapezoidal, spline, Lagranges, PTTO and hybrid approaches, Computation of statistical moments from plasma and urine data, pharmacokinetic evaluation of Cl, Vd and $t_{1/2}$. Systems theory, theory of Response Mapping Operator (RMO), applications.

Linear Recirculation Models. Non-Linear Pharmacokinetics: Definition, significance and application, determination of non-linearity, computation of non-linear pharmacokinetic parameters (K_m & V_m) by Michaelis-Menten kinetics. Clinical Pharmacokinetics: Kinetics of pharmacological response, explanation of clinical response via pharmacokinetics. Monitoring of Plasma concentration of drug during clinical use, clinical relevance of kinetic studies, turnover concepts. Individualization of dosage regimen, reasons of variability – genetics, age, weight, disease, drug interaction , etc. Pharmacokinetic & Pharmacodynamic Models: basic concepts, applications and limitations with respect to classical compartmental approaches, inter species scaling, integrated PKPD models. *In Vitro –InVivo Correlations* : Drug dissolution, principles and methodology, different methods of *in vitro-in vivo* correlation, their applications and limitations.

Controlled release dosage forms: Bioavailability and pharmacokinetics of oral, parenteral, ocular, transdermal CRDF and IUDs. Computer Applications and Pharmacokinetics : Introduction, strategy for model building, selection and application of suitable pharmacokinetic, statistical and variance models, function minimisation, iterative and noniterative techniques and weighting schemes for nonlinear regression. Critical evaluation of computer fits and computer use in ADME. Literature review on computer software for pharmacokinetics, study of some computer software like- PC-NONLIN, NONMEM/NM-WIN, MicroPharm-K, TOPFIT etc.

Novel Drug Delivery Systems

Fundamentals of Novel Drug Delivery: Rationale of sustained/controlled release(CR), physicochemical and biological factors influencing design and performance of CR products. Pharmacokinetic and Pharmacodynamic basis of NDDS. Bioavailability assessment of CR systems. Regulatory requirements. Theory of mass transfer. Fick's law and its application in NDDS. Triggered, pulsed and programmed drug delivery systems. Polymers in CR: classification, properties biocompatible & biodegradable polymers. Modeling of drug release from porous polymer; drug release from non-porous and hydrophobic polymers. Diffusional release and dissolution controlled release from monolithic devices, microporous systems. Oral Controlled Drug Delivery Systems: Oral systems based on dissolution, diffusion and other mechanism. pH control on exchange resins, gel diffusion, osmotic pumps. Hydrodynamically balanced system, Modulation of GIT transit. Mucosal Drug Delivery System: Mechanism of transmucosal permeation, mucous membrane model, buccal, nasal, pulmonary, rectal and vaginal Drug Delivery systems, Intra Uterine Devices. Ocular Drug Delivery Systems: Fabrication and application of ocuserts. Parenteral Drug Delivery systems: Biopharmaceutical considerations. Solutions, suspensions and emulsions. Implantable therapeutic systems, approaches to develop implants. Transdermal Drug Delivery Systems: Drug absorption through skin, basic components of TDDS, types and techniques for development and evolution. Iontophoresis, Sonophoresis and electroporation, Drug permeation enhancers. Multiple emulsion and Micro emulsion: Multiple w/o/w emulsions as drug vehicles- introduction, composition of multiple emulsion and stability, mechanism of transport of solutes, in vivo studies. Micro emulsion- introduction, structure of micro emulsions, solubilisation and formulation, transport properties and applications. Biochemical and Molecular Biology Approaches to CDDS: Microparticulate Drug Carriers- structural aspects, preparation, characterisation, evaluation and applications of Liposomes, Nanoparticles, microspheres etc. Other vascular systems- general aspects and applications of niosomes, crythroosomes, pharmacosomes, aquasomes and supramolecules. Monoclonal antibodies- preparation and applications. Absorption of proteins and peptide drugs: Consideration in the delivery of proteins and peptides, stability, membrane barriers, delivery systems for proteins and peptides, toxicity aspects; Enzymes and enzyme immobilization. Recent trends in vaccine and vaccine delivery systems.

Section C : Pharmacology

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Advanced Pharmacology:

Principles of Clinical Pharmacology : Definition, scope, development of clinical pharmacology, drug receptors, mechanism of action, drug biotransformation, drug administration in special situations like geriatrics, pediatrics, pregnancy and lactation. Autonomic Pharmacology: Parasympathomimetics, sympathomimetics, Parasympatholytics, sympatholytics, ganglion and neuromuscular blockers. Drug Therapy of Cardiovascular Disorders: Hypertension Congestive Heart Failure, Angina, Arrhythmia, Hyperlipidemia. Drug Therapy of GIT disorders: Peptic Ulcers, emesis, diarrhoea and constipation. Antineoplastic agents: Classification, mode of action, therapeutic

applications. Drug Therapy of Rheumatoid arthritis and gout: Mechanism of inflammation, COX- I and COX-II inhibitors. Chemotherapy of Infectious Diseases: Antibacterial drugs- sulfonamides, quinolones, penicillins, tetracyclines, chloramphenicol, cephalosporins, aminoglycosides, antiviral, antifungal and antiprotozoal chemotherapy, drug therapy of helminthiasis, tuberculosis and leprosy, development of drug resistance. Bioassays: Principles, Types, advantages of bioassays.

Recent Trends in Pharmacology

Drug Therapy of Alzheimer's disease, Drug Therapy of Epilepsy, Depression, Psychosis, Anxiety, Migraine, Parkinsonism, Advances in Receptor Pharmacology (Adrenergic, Cholinergic, 5-HT, GABAergic, Histaminic), Ion Channels, Recent advances in treatment of diabetes mellitus, Recent advances in treatment of asthma, Recent advances in Calcium channel blockers, Potassium channel openers, Angiotensin Converting Enzyme Inhibitors, Immunosuppressive Agents, Platelet Activating Factor and their antagonists, Essential Drugs

Pharmacological Screening of drugs

Study of animal models for screening of following categories of drugs: Analgesics, Anti inflammatory, Local Anesthetics, Antianxiety, Antidepressant, Antipsychotics, Anticonvulsant, Anti Parkinsonism, Antihypertensives, Antidiabetics, Anti-fertility, Nootropics

Section D : Pharmacognosy

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Advanced Pharmacognosy:

Comparative Phytochemistry: Principles of Taxonomy, Study, development, significance of chemotaxonomy with special reference to phytoconstituents *viz.* Alkaloids, glycoside, terpenes, flavonoids, etc. Factors affecting plant drug cultivation: Characteristics of soil, exogenous and endogenous factors essential for plant growth. Fertilizers and their management, Pest Management, Herbal Pesticides & Insecticides. Plant Tissue Culture: History of Plant tissue culture, totipotency, Ingredients used in plant tissue culture media. Callus Culture, Suspension cultures, meristem culture, protoplant cultures, haploid cultures and immobilization, organogenesis. Regeneration of plants from tissue culture,

Biosynthetic potential of tissue culture and factors affecting production of secondary metabolites by tissue culture technique, Application of plant tissue culture in Pharmacognosy/ production of phytopharmaceuticals.

Herbal Drugs Development

Herbal sources of food supplements, Bioavailability enhancers, plant bitters & sweeteners, Herbal Cosmetics: Identification, collection and chemical nature of the natural products used in: Hair care, dandruff, dyeing, Skin care, anti-wrinkles & anti-aging, leucoderma, Scabies, Anticancer Herbal drugs, Herbal Extracts and Their sources, Herbal production, formulation & Development: Introduction, Volume, trade, commerce, resources, status in India and abroad, Traditional versus modern system, Regulatory requirements for manufacture and distribution of herbal formulations, Standardization of Herbal Drugs: Quantitative Pharmacognosy, Modern Instrumental Techniques, Biological response measurements.

Characterization of Plant Constituents

Methods of investigation of biogenetic pathways, Basic principles involved in the phytochemical and biological screening of plant drugs in : Analgesics, anti-inflammatory, cardiogenic, hypoglycemic drugs and plant immunomodulators, Extraction, Isolation and characterization by chemical and spectral means of various active principles having medicinal, industrial and clinical importance from the following categories: Alkaloids, glycosides, steroids, antibiotics, vitamins, terpenoids, lipids, volatile oils, coumarins and photosensitizing agents