ELECTIVE 1 & ELECTIVE 2

SYLLABUS

(Supplement from School of Pharmaceutical Sciences & Technology)

Ph.D.

in

PHARMACEUTICAL SCIENCES

To be Effective from Academic Year 2020-21 and Onwards

SARDAR BHAGWAN SINGH UNIVERSITY

BALAWALA, DEHRADUN 248001, UTTARAKHAND, INDIA

SEMESTER 1

Course Code & Name	Sub-code by Department	Course	Credit Points	Hours/Week	Marks
PHDC 713D Elective 1 D. Others[@]	PSPE01	Advanced Pharmaceutical Development	2	2	50
	PSPL 01	Pharmacological Screening Methods And Drug Evaluation			
	PSPG 01	Conventional Herbal Formulations			
	PSPC 01	Advanced Analytical Techniques and Drug Discovery			
PHDC 714 Elective 2: Subject in the Field of Discipline[$]	PSPE 02	Computer Aided Pharmaceutics and Drug Delivery	4	4	100
	PSPE 03	Pharmaceutical Nanotechnology			
	PSPL 02	Advanced Pharmacology			
	PSPL 03	Pharmacological and Toxicological Screening Methods			
	PSPG 02	Herbal Extracts and Stability Studies			
	PSPG 03	Advanced Herbal Formulations			
	PSPC 02	Advanced Medicinal Chemistry and Drug Design			
	PSPC 03	Moderninstrumental Methods of Drug Analysis			

[@] Supervised Self Study [03 Seminars, 03 Assignments, 01 Problem Solving Class/Two Week (n=8); All these under the supervision of Approved Supervisor/Co-supervisor]

[$] Supervised Self Study [05 Seminars, 05 Assignments, 01 Problem Solving Class/Week (n=15); All these under the supervision of Approved Supervisor/Co-supervisor]

PHDC 713D: Elective 1D: Others

PHDC 713D PSPE 01 ADVANCED PHARMACEUTICAL DEVELOPMENT

2 CREDIT POINTS

1. Optimization of Pharmaceutical Formulations (15 h)

Computer based optimization of pharmaceutical formulations, basic concepts, optimization designs, screening designs, response surface methodology, QbD by design, QbD guidelines of ICH, USFDA and EMA, computational fluid dynamics in formulation development, modeling of dissolution/drug release, artificial neural networks, expert systems

2. Latest Developments in Pharmaceutics and Drug Delivery (15 h)

3D printing of various dosage forms, robotics in automation of pharmaceutical operations, pharmaceutical automation, robotic drug delivery, role of artificial intelligence in pharmaceutics and drug delivery.

3. Dissolution of Drugs (10 h)

Drug dissolution, theories of drug dissolution/drug release, evaluation of dissolution/drug release, pharmacopoeial/nonpharmacopoeail methods for conventional and novel drug delivery systems, modeling of dissolution/drug release.

PHDC 713D PSPL 01 PHARMACOLOGICAL SCREENING METHODS AND DRUG EVALUATION 02CREDIT POINTS

1. Detailed study of guidelines for maintenance, breeding techniques and experimentation using laboratory animals. CPCSEA, OECD, ICH, GLP and ICMR Guidelines according to official compendia. Recent advances in Transgenic and Knockout animals and their applications. Limitations of animal experimentation and alternative to animal experiments. **(10 h)**

2 Acute, sub-acute and chronic- oral, dermal and inhalational studies as per OECD guidelines.Preclinical screening of the following classes of drugs using in vivo, in vitro, and other possible animal alternative models.CNS Pharmacology: behavioural, anxiolytics, anti-psychotics. Drugs for neurodegenerative diseases. Respiratory Pharmacology: anti-asthmatics and anti allergics. Cardiovascular Pharmacology: antihypertensives, antiarrythmics, antiatherosclerotic agents. **(10 h)**

3. Preclinical screening of new substances for the pharmacological activity using in vivo, in vitro and other possible animal alternative models: Drugs for metabolic disorders like anti-diabetic, antidyslipidemic agents. Anti-cancer agents. Hepatoprotective screening methods. Immunomodulators, Immunosuppressants and immunostimulants. Immunoassays. **(10 h)**

PHDC 713 PSPG 01 CONVENTIONAL HERBAL FORMULATIONS
02 CREDITPOINTS

1. **Tablets** (**5 h)**
   Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

2. **Herbal Formulations for Transmucosal Drug Delivery** (**5 h)**
   Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

3. **Solid Dispersions** (**5 h)**
   Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

4. **Pellets (5 h)**
   Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

5. **Hydrogels as Delivery Systems in Herbal Medicine (5 h)**
   Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

6. **Emulsions and Self-Emulsifying Delivery Systems (5 h)**
   Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

PHDC 713D PSPC 01 ADVANCED ANALYTICAL TECHNIQUESAND DRUG DISCOVERY 02 CREDIT POINTS

1. Drug discovery (10 h)

Stages of drug discovery, lead identification, validation and importance of biological drug targets. Basic Principle and Applications of QSAR, combinatorial chemistry, High Throughput Screening in Drug Discovery.

2. Instrumentation Techniques (10 h)

UV-Visible Spectroscopy: Theory, Instrumentation and Application. Infrared Spectroscopy: Theory, Instrumentation and Application. NMR Spectroscopy: Theory, Instrumentation and Application. Mass Spectroscopy: Theory, Instrumentation and Application.

3. Chromatographic Techniques (10 h)

High Performance Liquid Chromatography: Theory, Instrumentation and Application. Gas Chromatography: Theory, Instrumentation and Application. High Performance Thin Layer Chromatography: Theory, Instrumentation and Application.

Elective 2: Subject in the Field of Discipline of Pharmaceutical Sciences (Pharmaceutics)

PHDC 714 PSPE 02 COMPUTER AIDED PHARMACEUTICS AND DRUG DELIVERY 4 CREDIT POINTS

1. **History of Computers in Pharmaceutical Development (5 h)**
   History of computers in pharmaceutical sciences, pharmaceutics and drug delivery

2. **Computer Aided Formulation Development (15 h)**
   Computer based optimization of pharmaceutical formulations, basic concepts, optimization designs, screening designs, response surface methodology, QbD by design, QbD guidelines of ICH, USFDA and EMA, computational fluid dynamics in formulation development, modeling of dissolution/drug release, artificial neural networks, expert systems.

3. **Computer Aided Manufacturing of Pharmaceuticals (10 h)**
   3D printing of various dosage forms, robotics in automation of pharmaceutical operations, pharmaceutical automation, robotic drug delivery, role of artificial intelligence in pharmaceutics and drug delivery.

4. **Computer Aided Biopharmaceutics and Pharmacokinetics (15 h)**
   Computer aided biopharmaceutical characterization, pharmacokinetic simulations, simulation of gastrointestinal absorption, applications of simulations (IVIVC, Biowaiver, virtual trials, fasted-fed state absorption estimations, etc.), simulation softwares, modeling of drug disposition, PBPK modeling.

5. **Pharmaceutics Informatics and Modeling of Drug Delivery Systems (15 h)**
   Pharmaceutics informatics, molecular modeling of self assembled drug delivery systems, modeling of drug-polymer interactions in drug delivery systems, modeling of nanoparticles.

PHDC 714 PSPE 03 PHARMACEUTICAL NANOTECHNOLOGY

4 CREDIT POINTS

1. Introduction to Nanotechnology: (10 h)

Definition of nanotechnology, History, Properties, Role of size and size distribution of nanoparticles properties, classification, Pharmaceutical applications of nanotechnology, Future prospects of nanotechnology in pharmacy.

2. Preparation/ Synthesis of nanomaterials: (10 h)

Physical, chemical and biological methods. Methods of synthesis of metal nanoparticles, magnetic nanoparticles, lipid nanoparticles, polymeric nanoparticles.

3. Nanopharmaceuticals: (10 h)

Formulation and evaluation: Nanosuspension, microemulsions, nanoemulsions, nanogels, nanocarrier systems, nanoencapsulations, dendrimers in drug delivery, self-assembly structures such as liposomes, micelles, aquasomes, niosomes, pharmacosomes, liquid crystalline systems, co crystals.

4. Nanomaterials in biological therapy: (10 h)

Nanotechnology in Brain targeting, Oral drug delivery, Pulmonary and nasal drug delivery,ocular drug delivery, cardiovascular drug delivery, topical delivery, disease diagnosis, Targeted release and triggered release.

5. Characterization of nanomaterials: (10 h)

Structural characterization: XRD, electron microscopy, FTIR, XPS. *Surface characterization*

Scanning electron microscopy, Transmission electron microscopy, atomic force microscopy,

Size analysis: Size reduction, PDI, size separation, *stability*, method of analysis regarding *integrity and drug release*.

6. Nanobiotechnology: (10 h)

Cellular level events in targeting, passive and active targeting strategies in cancer, viruses as nanomaterials for drug delivery, gene delivery in gene therapy, nanotechnology in immunotherapy.

Elective 2: Subjects in the field of Discipline of Pharmaceutical Sciences (Pharmacology)

PHDC 714 PSPL 02 ADVANCED PHARMACOLOGY 4 CREDIT POINTS

1. **Fundamentals of Molecular mechanism of drug action (15 h)**
   Intercellular and intracellular signaling pathways. Drug receptor interaction theories, Receptor occupation and response relationship, Cellular signaling systems such as G-proteinscoupled receptors, Tyrosine kinase receptors and nuclear receptors, Cyclic nucleotides and intracellular signaling pathways associated with these receptors.

2. **Endogenous bioactive molecules and Novel target sites (15 h)**
   Cytokines, neuropeptides and their modulators, neurosteroids, nitric oxide, phosphodiestrase enzyme and protein kinase C, arachidonic acid metabolites, COX-2 regulators and their role in inflammation, endothelium derived vascular substances and their modulators. Pharmacology of atrial peptides, reactive oxygen intermediates, antioxidants and their therapeutic implications.

3. **Recent trends on different classes of receptors and drugs acting on them (15 h)**
   Excitatory amino acid receptors, Angiotensin receptors, Kinin receptors, Adrenoceptors, Low molecular weight heparins and GP II/IIIa receptor antagonists, Cholinergic receptors, Dopamine receptors, Serotonin receptors, steroidal receptors, Opioid receptors, Purinergic receptors, Ion channel and their modulators: calcium, potassium, sodium and chloride channels.

4. **Apoptosis (10 h)**
   Basic functions, mechanisms and role of caspases. Pharmacological and clinical implications. Adhesion therapy and cardiac and vascular remodelling, Basic Concepts of Chronopharmacology and their implications to Drug Therapy.

5. **Immunopharmacology (5 h)**
   antibody dependent and cellular cytotoxicity. Monoclonal antibodies and its importance, Gene therapy: Concept of gene therapy and recent development in the treatment of various hereditary diseases.

PHDC 714 PSPL 03 PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING METHODS 4 CREDIT POINTS

1. Detailed study of guidelines for maintenance, breeding techniques and experimentation using laboratory animals: CPCSEA, OECD, ICH, GLP and ICMR Guidelines according to official compendia. **(12 h)**

2. Recent advances in Transgenic and Knockout animals, their production, maintenance and applications. Extrapolation of in vitro data to preclinical and preclinical to humans. Alternatives to animal experimentation, Animal cell lines and their uses, Radioligand binding assays, Patch clamp and ELISA, Stem cell research, Introduction to Pharmacogenomics, Proteomics and Array technology. **(12 h)**

3. Pharmacological activity of new substances and safety assessment tests. Acute, sub-acute (Repeated dose), sub chronic and chronic toxicity studies as per OECD guidelines. Genotoxicity studies (Ames test, in vitro and in vivo Micronucleus and Chromosomal aberrations studies), In vivo carcinogenicity studies as per OECD. **(16 h)**

4. Preclinical screening of new substances for the following pharmacological activities using in vivo, in vitro, and other possible animal alternative models: CNS Pharmacology: behavioural, anxiolytics, anti-psychotics. Drugs for neurodegenerative diseases.Respiratory Pharmacology: anti-asthmatics and anti allergics. Cardiovascular Pharmacology: antihypertensives, antiarrythmics, antiatherosclerotic agents. Drugs for metabolic disorders like anti-diabetic, antidyslipidemic agents. Anti-cancer agents. Hepatoprotective screening methods. Immunoassays. **(8 h)**

5. Safety pharmacology studies- origin, concepts and importance of safety pharmacology. Tier1- CVS, CNS and respiratory safety pharmacology. Toxicokinetics- Toxicokinetic evaluation in preclinical studies, saturation kinetics, Importance and applications of toxicokinetic studies. **(12 h)**

Elective 2: Subject in the Field of Discipline of Pharmaceutical Sciences (Pharmacognosy)

PHDC 714 PSPG 02 HERBAL EXTRACTS AND STABILITY STUDIES
4 CREDIT POINTS

1. Preparation of Extracts and their Standardization (20 h)

Principles of extraction, extraction techniques for plant materials: liquid-liquid extraction, solid-liquid extraction, maceration, hydrodistillation, Soxhlet extraction; nonconventional methods for extraction: ultrasounds, pulsed electric field, extrusion, microwave, ohmic heating, supercritical fluids, accelerated fluids, pressurized liquid, and enzyme-assisted, optimization of extraction process, recent advances in extractions with emphasis on selection of method and choice of solvent for extraction, successive and exhaustive extraction, methods of fractionation, separation of phytoconstituents by latest CCCET, SCFE techniques including preparative HPLC and flash column chromatography, Why standardization of extracts?, Types of extracts, standardized extracts, quantified extracts, other extracts, (EU classification), marker extracts, active constituents extracts, qualitative and quantitative methods of standardization of herbal extracts

2 Isolation of Phytoconstituents from Herbs (20 h)

Solvent methods, precipitation methods, dialysis, fractional distillation, crystallization, chromatographic methods (adsorption, gel, ion exchange, macroporous adsorption resin, partition), HPLC, UHPLC, Column, TLC, HPTLC, optical performance laminar chromatography, , droplet counter current chromatography, high speed counter current chromatography, high performance capillary electrophoresis, affinity chromatography, gas chromatography

3. Stability and Analytical Challenges of Herbal Substances and Products (20 h)

Stability of herbal drug products and phytoconstituents, selection of analytical method for stability testing, storage conditions (ICH, WHO, Indian)

Challenges and possible solutions: Quality of herbal drugs, drug-drug interactions, herb-drug interactions, marker selection, the lack of knowledge of therapeutic markers; non-availability of known therapeutic markers at the commercial scale; batch to-batch variation in quality of herbal raw materials, mistaken identities of many herbs; nonuniform chemical constitutents, pharmacopoeial standards, varied agriculture practices, contamination of raw material (heavy metals, microbes, pesticides, fertilizers; and practices of adulteration), substitution of appropriate test parameters for testing of stability samples, monitoring by sensitive analytical method, chromatographic

fingerprint of the stability sample, thus posing severe analytical challenges physical and all chemical parameters during stability studies on a herbal medicinal product, biological assays in the stability testing program, in vitro models for fast evaluation of biological activities, extrapolatable to the in vivo model for the tested activity, biotechnology or nanobiotechnology role in inventing novel enzyme based or other in vitro models and their in vivo correlation

PHDC 714 PSPG 03 *ADVANCED HERBAL FORMULATIONS*

4 CREDIT POINTS

1. Principles of Sustained, Controlled and Targeted Delivery of Herbal Actives

(6 h)

Types of modified drug delivery systems, rationale for developing modified drug delivery systems, approaches for developing modified drug delivery systems, targeted drug delivery systems for herbal extracts and traditional medicines, targeted drug delivery systems for herbal phytoconstituents

2. Formulation and Delivery Issues for Active Ingredients of Herbal Medicines, Nutraceuticals and Cosmetics - Comparisons to Small Molecule Drugs

(6 h)

Incompatibility within formulation, stability of herbal actives, solubility issues, permeability issues, bioavailability and pharmacokinetics, factors affecting bioavailability and pharmacokinetics of herbal actives, modifications of half life of herbal actives, enhancement of bioavailability of herbal actives

3. Natural Polymers and Excipients for Designing Herbal Formulations

(6 h)

Plant based polysaccharides and their derivatives, gums, mucilages, anionic polymers, cationic polymers, anticancer drug delivery with polysaccharides, online resources, modifications of natural polymer, drug delivery applications in formulations, controlled release, smart drug delivery, micro/nano carriers, microneedles, theranostics etc.

4. Liposomes and Proliposomes (6 h)

Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

5. Nanoparticles Mediated Delivery of Herbal Actives: Solid Lipid Nanoparticles, Polymeric Nanoparticle, Metallic Nanoparticles, Inorganic Nanoparticles, Polymeric Conjugates (Nanocomposites)

(6 h)

Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

6. Transferosomes, Ethosomes and Novel Transdermal Patches

(6 h)

Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

7. Dendrimers (6 h)

Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

8. Carbon Nanotubes (6 h)

Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

9. Plant Derived Bioadhesives for Wound Healing/Regenerative Medicine (6 h)

Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

10. Chemo-Herbal Combination Drug Delivery (6 h)

Introduction (with rationale), physicochemical/biological/physiological principles, formulation, manufacturing/preparation process (step by step), challenges for herbal actives, delivery aspects, clinical trials, marketed products

Elective: 2 Subject in the Field of Discipline of Pharmaceutical Sciences

(Pharmaceutical Chemistry)

PHDC 714 PSPC 02 ADVANCED MEDICINAL CHEMISTRY AND DRUG DESIGN 4 CREDIT POINTS

1. Drug discovery: Stages of drug discovery, lead identification, validation and importance of biological drug targets: enzymes, proteins, nucleic acid, ion channels etc. Special emphasis of Protein Data Bank **(12 h)**

2. Different descriptors and statistical parameters of QSAR. Importance of Energy Minimization process in drug discovery. Importance of small molecule-receptor docking and protein-protein docking.Homology modeling and generation of 3D-structure ofprotein.Pharmacophore mapping and virtual screening. Prediction and analysis of ADMET properties of newmolecules.

   (12 h)

3. Green Chemistry: a. Introduction, principles of green chemistry b. Microwave assisted reactions: Merit and demerits of its use, increased reaction rates, mechanism, superheating effects of microwave, and effects of solvents in microwave assisted synthesis. c. Ultrasound assisted reactions: Types of sonochemical reactions. Continuous flow reactors: Working principle, advantages andsynthetic applications. **(12 h)**

4. Introduction of Combinatorial chemistry and HTS. Principles of solid phase peptide synthesis, t-BOC and FMOCprotocols, various solid supports and linkers. Photochemical Reactions Basic principles of photochemical reactions.Pericyclic reactions Mechanism, Types of pericyclic reactions such as cyclo addition, electrocyclic reaction and sigmatrophic rearrangement reactionswith examples. **(12 h)**

5. Catalysis: Types of catalysis, heterogeneous and homogenous catalysis, advantages and disadvantages. b. Wilkinson catalysts, chiral ligands and chiralinduction, Ziegler-Natta catalysts. Transition-metal and Organo-catalysis in organic synthesis. e. Biocatalysis: Use of enzymes in organic synthesis,immobilized enzymes/cells in organic reaction. **(12 h)**

PHDC 714 PSPC 03 MODERNINSTRUMENTAL METHODS OF DRUG ANALYSIS 4 CREDIT POINTS

1. UV-Visible Spectroscopy (10 h)

Brief review of electromagnetic spectrum; Chromophore concept, absorption laws and limitations; Choice of solvent and solvent effect; Instrumentation and applications; Interpretation of spectra; multi component assay; difference and derivative spectra; Woodward-Fisher rule for calculating absorption maxima.

2. Infrared Spectroscopy and Raman Spectroscopy (10 h)

Infrared Spectroscopy:Basic principles, Instrumentation, sampling technique, applications, Interpretation of spectra; FT-IR, ATR (Attenuated Total Reflectance), Near Infrared spectroscopy: Theory and Applications.

Raman Spectroscopy: Theory, Principle and Applications

3. Nuclear Magnetic Resonance Spectroscopy (10 h)

Theory, Principle, Instrumentation; solvents, chemical shift, factors affecting chemical shift; spin-spin coupling; Spectral interpretation; FT-NMR, 2D-NMR: applications in pharmacy; C-13 NMR- Introduction, natural abundance and its structural applications.

4. Mass Spectroscopy (10 h)

Basic principles, Instrumentation, ion formation and types; Fragmentation process and pattern; Chemical ionization mass spectroscopy (CIMS), Fast atomic bombardment MS (FAB MS); Matrix assisted laser desorption ionization (MALDI), Time of flight (TOF); Applications and spectral interpretation.

5 Advanced Chromatographic Techniques (10 h)

HPLC: Principle, Instrumentation, solvents, types of column, column efficiency; Applications, resolution, asymmetry factor; Theory of Band broadening; Van Deemter equation; Gas Chromatography: Principle, Instrumentation; derivatization and applications

HPTLC: Introduction, Principle, Instrumentation, Applications

6 Thermal Analysis and X-Ray diffraction (10 h)

Thermal Analysis: Theory, Instrumentation and applications of Thermo Gravimetric Analysis (TGA), Differential Thermal Analysis (DTA), Differential Scanning Calorimetry (DSC).

X-Ray Diffraction: Introduction, generation of X-Rays, X-Ray diffraction, Bragg's Law; Applications