



Syllabus
Ph.D. Medicinal Chemistry

CREDIT SYSTEM FOR Ph.D. STUDENTS
(In accordance with NIPER Ordinance)

1. The student who has pursued the M.S. (Pharm.) degree from NIPER shall be required to complete Doctoral courses of minimum 12 credits

2. The student with qualifications from other Institutes [i.e. other than NIPER(s)] shall be required to complete a minimum of 28 credits, out of these 16 credits shall be from specialization and remaining 12 credits shall be from Doctoral courses.

NIPER Students (Total 12 Credits)	<u>Odd Semester</u> 01 Compulsory Subject (02 Credits)	<ul style="list-style-type: none"> • These credits will be obtained from Doctoral Courses.
	<u>Even Semester</u> 01 Compulsory Subject (02 Credits)	

Non - NIPER Students (Total 28 Credits)	<u>Odd Semester</u> 01 Compulsory Subject (02 Credits)	<ul style="list-style-type: none"> • The student shall be required to complete a minimum of 28 credits, out of these 16 credits shall be from specialization and remaining 12 credits shall be from Doctoral courses.
	<u>Even Semester</u> 01 Compulsory Subject (02 Credits)	

GUIDELINES FOR SUBJECT SELECTION – Ph.D. PROGRAMME

<u>Compulsory Subjects for all departments (Total Credits : 04)</u>			
Total Credits for NIPER Students		04	
Total Credits for Non NIPER Students		04	
Odd Semester			
S.No.	Subject Code	Subject	Credit
1.	GE 710	Research and Publication Ethics	02
Even Semester			
S.No.	Subject Code	Subject	Credit
2.	GE 820	Research Methodology	02
NOTE: Earning credits in aforementioned subjects is mandatory and the earned credits will be counted in preparation of final result.			
<u>Doctoral Courses Offered By Various Departments</u>			
Total Credits for NIPER Students		08	
Total Credits for Non NIPER Students		24	
Medicinal Chemistry : Odd Semester			
S.No.	Subject Code	Subject	Credit
1.	MC 710	Stereo selective and Stereospecific Synthesis	02
2.	MC 720	Synthetic Strategies in the Total Synthesis of Complex Organic Molecules	02
3.	MC 730	Organometallic and Sustainable Chemistry in the Synthesis of Pharmaceuticals	02
Total Credits			06
Medicinal Chemistry : Even Semester			
S.No.	Subject Code	Subject	Credit
1.	MC 810	Principles of Peptide Chemistry	02
2.	MC 820	Carbohydrates: Occurrences, Structure, Reactions, Syntheses, Functions and Applications in Present Day Drugs	02
3.	MC 830	Advanced Topics in Drug Action and Drug Design	02
Total Credits			06
Pharmaceutics : Odd Semester			
S.No.	Subject Code	Subject	Credit
1.	PE 710	Implications of Solid State Properties in Drug Delivery	02

2.	PE 720	Advanced Polymeric Formulations	02
3.	PE 730	Advanced Delivery Approaches for Neurological Disorders	02
Total Credits			06
Pharmaceutics : Even Semester			
S.No.	Subject Code	Subject	Credit
1.	PE 810	Novel Approaches for Targeted Drug Delivery	02
2.	PE 820	Advanced Materials as Theranostics	02
3.	PE 830	Cosmeceutical Formulation Development	02
Total Credits			06
Pharmacology and Toxicology : Odd Semester			
S.No.	Subject Code	Subject	Credit
1.	PC 710	Signalling Mechanisms of Receptors and Neurotransmitters in Brain	02
2.	PC 720	Basics and Advances in Neuroscience	02
3.	PC 820	Pharmacological Interventions for Ischemic Brain Injury	02
4.	PC 830	Parasitology/Microbiology, Community & Pharmacy	02
Total Credits			08
Pharmacology and Toxicology : Even Semester			
S.No.	Subject Code	Subject	Credit
1	PC 840	Regulatory Toxicology And Drug Safety Evaluation	02
2	PC 860	Epigenetics and Diseases	02
3	PC 870	Preclinical Pharmacological Models Of Screening	02
Total Credits			06
Regulatory Toxicology : Odd Semester			
S.No.	Subject Code	Subject	Credit
1	RT 710	Recent advances in Regulatory Toxicology	02
Total Credits			02
Biotechnology : Odd Semester			
S.No.	Subject Code	Subject	Credit
1	BT 710	Interfacial Enzymology	02
2	BT 720	Therapeutic and Diagnostic approaches in Neglected Tropical Diseases	02
Total Credits			04

Biotechnology : Even Semester			
S.No.	Subject Code	Subject	Credit
1	BT 810	Protein Structure and Stability	02
2	BT 820	Host-Pathogen Interaction in Infectious Disease	02
3	BT 830	Targeting metabolic disorders by Natural Products	02
4	GE 830	Cell Based Therapies	02
5	GE 840	Cell-Based Therapies: Laboratory Experience Prerequisite: GE 830 Cell-Based Therapies	02
Total Credits			10

All the PhD Students have to complete 12 credits from the doctoral courses mentioned above. Further, the Non NIPERian students shall be required to earn 16 credits more from specialization of the concerned department. For these 16 credits, the PhD student may also refer to subjects of M.S. (Pharm.) Programme of the concerned department.

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Course Code	Course Name	Credits
Semester I		
MC 710	Stereoselective and Stereospecific Synthesis	2
MC 720	Synthetic Strategies in the Total Synthesis of Complex Organic Molecules	2
MC 730	Organometallic and Sustainable Chemistry in the Synthesis of Pharmaceuticals	2
GE 710	Research and Publication Ethics	2
	Total Credits	08
Semester II		
MC 810	Principles of Peptide Chemistry	02
MC 820	Carbohydrates: Occurrences, Structure, Reactions, Syntheses, Functions and Applications in Present Day Drugs	02
MC 830	Advanced Topics in Drug Action and Drug Design	02
GE 820	Research methodology	02
	Total Credits	08

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Odd Semester

MC 710 - Stereoselective and Stereospecific Synthesis (2 Credits)

1.	General concept: Differentiation of molecules, group selectivity, topicity and prochirality, substrate and product selectivities
2.	Chirality and drug action: Terminologies and definitions, significance of drug stereochemistry on drug action and metabolism.
3.	Fundamentals of chirality generation: Necessary conditions for stereoselectivity, concept of enantio/diastereo-differentiation, methods of inducing stereoselectivity, strategies for stereoselective synthesis, kinetics and thermodynamics of stereoselective reactions.
4.	Approaches for chiral synthesis: Chiral pool approach, various chiral auxiliaries, self-generation of chiral center.
5.	Asymmetric catalysis: Stereoselective catalytic reduction-homogeneous hydrogenation (chiral ligands, effect of solvent/ pressure/ temperature/ addendum, substrate dependence of enantioselectivity, mechanistic aspects), stereoselective heterogeneous hydrogenation, transfer hydrogenation, hydrosilylation, hydrocyanation, stereoselective oxidation enantio / diastereoselective epoxidation and dihydroxylation.
6.	Concepts on catalytic asymmetric induction: Ligand accelerated catalysis; Self replication of chirality-catalytic self-replicating molecules, control of chirality memory, P stacking effect, selectivity and mechanism of catalytic asymmetric synthesis.
7.	Stereoselective C-C bond formation: Nucleophilic addition to C=X (X=C, O, S, N), Stereoselective hydroformylation, Pericyclic reaction asymmetric induction in [3+2] and [2+2] cycloaddition, stereoselective carbene addition, chirality transfer in Sigmatropic rearrangements. Determination of enantiomeric purity: Various tools, chiral derivatizing agents, chiral shift reagents, chiral solvating agents.
8.	Applications: Chiral auxiliary based and catalytic asymmetric synthesis of natural and unnatural amino acids and other bio-molecules.

MC 720 – Synthetic Strategies in the Total Synthesis of Complex Organic Molecules (2 Credits)

1	Retrosynthetic analysis, disconnections and reliability of reactions, synthons: Donor and acceptor, functional group interconversions, one group carbon-heteroatom and carbon-carbon disconnections, two group carbon-heteroatom and carbon-carbon disconnections, chemo-, regio- and stereo-selectivity considerations, natural reactivity and umpolung, 1,3 and 1,5-difunctional compounds.
2	General synthetic reaction patterns and strategies: Aliphatic nucleophilic and electrophilic substitutions, aromatic nucleophilic and electrophilic substitutions, addition to carbon-carbon and carbon-heteroatom multiple bonds, eliminations, rearrangements,

	Oxidations and reductions.
3	Chemistry of protecting groups: Protection for alcohols, carbonyl groups, carboxylic groups and amino groups.
4	Applications of synthetic strategies in the total synthesis of selected organic molecules: (a) Cholesterol (b) Estrone (c) Reserpine (d) Penicillin (e) Prostaglandin (f) Progesterone (g) Longifolene (h) Taxol

MC 730 - Organometallic and Sustainable Chemistry in the Synthesis of Pharmaceuticals (2 Credits)

1.	Carbon-carbon coupling reactions: Suzuki, Hiyama, Stille, Negishi, Kumada coupling reactions; Mechanistic aspects of these reactions, comparison in mechanism, relative reactivities of organometallic coupling partners; Palladium and other metal catalysis, controlling parameters; Heck (α - and β -arylation) and Sonogashira coupling reactions; Palladium- and Copper catalysis, mechanism; Synthesis of biaryls, multi-substituted alkenes, alkynes, and various scaffolds.
2.	Carbon-heteroatom coupling reactions: Ullmann, Chan-Lam, and Buchwald-Hartwig reactions. Mechanistic aspects, comparison; Synthesis of various amines, ethers, thioethers, and heterocycles.
3.	Cross-coupling of unactivated arenes: Direct arene C-H bond arylation; oxidative couplings; two- and multi-fold C-H bond arylations; various approaches and mechanistic aspects; synthesis of biaryls and various scaffolds.
4.	Application of coupling reactions (as mentioned in 1-3) in the synthesis of pharmaceutically relevant compounds, Importance in the drug discovery research.
5.	Metathesis: Grubbs (first and second generation) and Schrock catalysts, Advantages and disadvantages, Importance of Ru and molybdenum catalysis; Olefin, alkyne, ring closing, ring opening and multiple metathesis; Mechanism of these reactions, aspects of reaction conditions, and structural aspects of reactants.
6.	Application of metathesis-reactions in the synthesis of various structural motifs including heterocycles, natural products, and pharmaceuticals; Importance in the drug discovery research.
7.	Green chemistry: 12 Principles of Green Chemistry, metrics, perspective of pharmaceutical industries; Green discoveries; greener reactions, catalysis, alternative reaction media, greener technologies; Sustainable synthesis of pharmaceuticals.
8.	Click chemistry: Click reaction-criteria, water as solvent, various classes of reactions, thermodynamics; Huisgen cycloaddition and its modification, and nucleophilic ring opening of epoxide and aziridine.
9.	Alkyne-azide click chemistry in the drug discovery research: Synthetic and medicinal chemistry advantageous aspects of the reaction; Combinatorial, structure-based and In situ approach of click chemistry in drug discovery research.
10.	Multicomponent reactions (MCR): Ugi, Passerini, Biginelli, Hantzsch, Mannich, Petasis, Strecker, Kabachnik Fields reactions, Mechanism of these reactions, Conceptual discovery of MCR, Ugi-deprotection-cyclization (UDC) approach and synthesis of various biologically relevant scaffolds, multi-MCRs in synthesis, Diversity-oriented and convergent synthesis of pharmaceutically-relevant compounds. Interface.

GE 710 - Research and Publication Ethics (2 credits)

1. **Philosophy and Ethics:** Ethics: definition, moral philosophy, nature of moral judgements and reactions. Scientific Conduct: Ethics with respect to science and research. Intellectual honesty and research integrity. Scientific misconducts: Falsification, Fabrication, and Plagiarism (FFP). Redundant publications: duplicate and overlapping publications, salami slicing. Selective reporting and misrepresentation of data. An overview of referencing softwares.

2. **Publication Ethics:** Publication ethics: definition, introduction and importance. Best practices / standards setting initiatives and guidelines: COPE, WAME. Conflicts of interest. Publication misconduct: definition, concept, problems that lead to unethical behavior and vice versa, types. Violation of publication ethics, authorship and contributorship. Manipulation of data and deception of other kinds. Identification of publication misconduct, complaints and appeals. Predatory publishers and journals.

3. **Open Access Publishing:** Open access publications and initiatives. SHERPA/RoMEO online resource to check publisher copyright & self-archiving policies. Software tool to identify predatory publications developed by SPPU. Journal finder / journal suggestion tools viz. JANE, Elsevier Journal Finder, Springer Journal Suggester, etc.

Publication Misconduct:

a. Group discussions: Subject specific ethical issues, FFP, authorship. Conflicts of interest. Complaints and appeals: examples and fraud from India and abroad.

b. Software tools: Use of plagiarism software like Turnitin, Urkund and other open source software tools.

4. **Databases and Research Metrics**

Database: Indexing database. Citation databases: Web of Science, Scopus, etc. Research Metrics: Impact Factor of journal as per Journal Citation Report, SNIP, SJR, IPP, Cite Score. Metrics: h-index, g index, i10 index, altmetrics.

Recommended books:

1. Bird, A. (2006). Philosophy of Science. Routledge.
2. MacIntyre, Alasdair (1967) 4 Short History of Ethics. London.
3. P. Chaddal, (2018) Ethics in Competitive Research: Do not get scooped; do not get plagiarized, ISBN:978-9387480865
4. National Academy of Sciences, National Academy of Engineering and Institute of Medicine. (2009). On Being a Scientist: A Guide to Responsible Conduct in Research: Third Edition. National Academies Press.
5. Resnik, D. B. (2011). What is ethics in research & why is it important. National Institute of Environmental Health Sciences, 1-10.
6. Retrieved from <https://www.niehs.nih.gov/research/resources/bioethics/whatis/index.cfm>
7. Beall, I. (2012). Predatory publishers are corrupting open access. Nature, 489 (7415), 179-179. <https://doi.org/10.1038/489179a>
8. Indian National Science Academy (INSA), Ethics in Science Education, Research and Governance (2019), ISBN:978-81-939482-1-7. <http://www.insaindia.res.in/pdf/Ethics Book.pdf>
9. Scientific Journals

Ph.D Medicinal Chemistry

Even Semester

MC 810 - Principles of Peptide Chemistry (2 Credits)

1.	Importance of peptides in drug discovery. Advantages and disadvantages of peptide drugs, Technology in peptide lead discovery,
2.	Protection and deprotection: General aspects, need for protection, minimal versus global protection, protection of amino group by acid and base labile groups, protection of carboxyl group, concept of orthogonal protection in peptide synthesis.
3.	Importance of side-chain functional group protection and details of protective groups used for masking individual amino acids, methods used for deprotection.
4.	Various methodologies employed for coupling reaction.
5.	Side reactions in peptide synthesis: Deletion peptides, side reactions initiated by proton abstraction, protonation, over-activation and side reactions of individual amino acids.
6.	Segment and sequential strategies for solution phase peptide synthesis with case studies.
7.	Principle of Merrifield solid phase peptide synthesis.
8.	Various solid supports and linkers, activation procedures, peptide bond formation.
9.	Deprotection and cleavage from resin: Low and high HF cleavage protocols, formation of free peptides and peptide amides, purification and case studies, Site-specific chemical modifications of peptides.
10.	t-BOC and Fmoc protocols.

MC 820 - Carbohydrates: Occurrences, Structure, Reactions, Syntheses, Functions and Applications in Present Day Drugs (2 Credits)

1.	Overview: Introduction; importance of carbohydrates in food & nutrition and biology.
2.	Sources, Structure & Shape: This will complement course # MC-630 in certain respects. Methods of structure elucidation.
3.	Recognition of carbohydrates by proteins: Relevance in disease; discussion on the process of infection by microorganisms and possible methods of intervention; specific examples- cholera, flu, etc.
4.	Reactions at the anomeric centre: Methods of glycosylation; details on the various types of glycosyl donors used; their preparation and methods of activation.
5.	Reactions at centres other than the anomeric centre: Selective transformations; strategies for selective and global protection & deprotection of carbohydrates and their

	Significance.
6.	Chemical synthesis: Highlights on the need for synthesis; various approaches adopted for the chemical methods of oligosaccharide synthesis with examples
7.	Enzymatic & chemo-enzymatic oligosaccharide syntheses: Scope & limitation; discussion with examples relevant to medicinal chemists.
8.	Solid-phase oligosaccharide synthesis: Relevance & its importance; different strategies used; applications
9.	Carbohydrate-based drugs: Discussion on various drugs (aminoglycoside antibiotics including glycopeptides, enediynes, macrolides, anthracyclines, etc; alkaloid, steroid and terpenoid glycosides; polyphenol glycosides etc.) that contain carbohydrate moiety (moieties) including polysaccharide therapeutics.
10.	Polysaccharide vaccines: Relevance; discussion on the isolation and modification of bacterial polysaccharides, specifically capsular polysaccharides; protein conjugation

MC 830 - Advanced Topics in Drug Action and Drug Design (2 Credits)

1.	Molecular basis of drug action: Receptor specificity and signal transduction, Channel containing receptors, intracellular receptors, Receptor desensitization, Drug action in cell not mediated through receptors.
2.	Drug metabolism: Inhibitions, induction, species and sex differences in drug metabolism, age on drug metabolism, CYP 450, Glutathione S-transferases, UDP-Glucuronosyl transferase. Metabolite identification and metabolite as a new drug candidate
3.	Resistance, Allergy, Tolerance: Immunologic basis of drug allergy, origin of drug resistance, resistance to the β -lactam antibiotics, resistance via mutation and selection, resistance via gene transfer, resistance via gene amplification, biochemical mechanism of drug resistance, characteristics of tolerance and the dependence, tolerance by indirect mechanisms, cellular tolerance mechanisms, relationship between tolerance and dependence.
4.	Mutagenesis, carcinogenesis, teratogenesis: DNA target for mutagenetic agents, mechanisms of chemical mutagenesis, types of mutations, biologic consequences of mutation, genetic reversion, mechanisms of chemical carcinogenesis, principal groups of chemical carcinogens, drug metabolizers and carcinogens, principles of teratogenesis.
5.	Lipophilicity and drug action: Thermodynamics of van der Waals interactions, thermodynamics of hydrophobic interactions, Molecular lipophilicity potential. Physicochemical and biological factors that influence drug permeability by passive diffusion, lipophilicity of metabolites.
6.	Drug-Receptor thermodynamics: Thermodynamic models of drug-receptor interactions, Effector-receptor interactions. Basics of correlations, relevance to enthalpy-entropy compensation.
7.	Drug action of some agents: Steroid biosynthesis and action, neurotransmitter action and metabolism, membrane-active agents, hormonal modulators, microtubule action.
8.	Case study 1: PfDHFR-Thymedylate synthase, mechanism of protein synthesis, action of anti-folates, selective prevention of protein synthesis in <i>plasmodium falciparum</i> , enzyme action associated with dihydrofolate reduction.
9.	Case study 2: Mechanism based inhibition, carbene reactive metabolites, epoxide reactive metabolites, nitroso reactive metabolites, S-oxidation vs epoxidation in thiophene.

10.	Case study 3: Drug action of agents acting at Glycogen Synthase Kinase (GSK), seven different methods of lead action on GSK3, drug design strategies for anti-diabetic drugs acting at GSK3.
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GE 820 - Research methodology (2 Credits)

1	Concept of Research: - Meaning and importance of Research- Objectives and types, Motivation in Research
2	Analysis of literature review: - Primary and Secondary sources, Web sources –critical literature review
3	Hypothesis: Different types, Significance, Development of working hypothesis, Null hypothesis.
4	Introduction to research methods/ methodology: - Selection and formulation of research problem, Research designing and development of models. Experimentation, determining the experimental and sample designs. Scientific method vs Arbitrary Method.
5	Data Collection and Statistical Analysis: Sources and types of data, Methods of Collecting Data: Observation, field investigations, Direct studies – Reports, Records or Experimental observations, Graphical representation, Descriptive Analysis, Inferential Analysis, Correlation analysis, Discussion, and interpretation of results.
6	Data Reporting and Scientific Writing: - I. Organization of the Research Report Preliminaries, Contents of Report, Bibliography, Appendices, Style Manuals, Criteria for the evaluation of the Research Report. II. Preparation of manuscript for Publication of Research paper, presenting a paper in scientific seminar/conference, Preparation of Project Proposal.
7	Principal of Analytical Instrumentation and their Implication: - Spectroscopic and microscopic techniques including cell and tissue imaging, Live Cell Cytometry studies, Omics techniques. Characterization and implication of API excipients and their formulations in research.

Recommended books:

1. Kothari, C.R., 1990. Research Methodology: Methods and Techniques. New Age International. 418p.
2. Sinha, S.C. and Dhiman, A.K., 2002. Research Methodology, Ess Ess Publications. 2 volumes.
3. Wadehra, B.L.2000. Law relating to patents, trademarks, copyright designs and geographical indications. Universal Law Publishing.
4. Relevant research and review articles.