SYLLABUS

Ph.D.
PHARMACOLOGY AND TOXICOLOGY

NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH GUWAHATI
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Ph.D. Syllabus

PHARMACOLOGY AND TOXICOLOGY

Course No.	Course Name	Credits
	Semester-I	
Core Subjects (All compulsory): Any 4 Credits		
PC- 710	Receptor Mechanism	2
PC-720	Free Radicals in Drug Research	2
PC- 730	Regulatory Toxicology and Drug Safety Evaluation	2
*CS -701	Research Methodology (Compulsory)	2
EL/PC-701	Application of Biotechnology in Parasitic Disease Research	2
EL/PC-702	Phytopharmaceuticals and its Standardization Aspects	2
	Choose any core course of other department (MC/PA/PE/MD)	2

Course No.	Course Name	Credits
	Semester-II	
Core Subjects (All compulsory): Any 4 Credits		
PC- 810	Epigenetics and Diseases	2
PC-820	Diabetes, Pathophysiology and Discovery of new Drugs	2
PC -830	Current topics in Cancer Research	2
***CS -801**	Research and Publication Ethics (Compulsory)	2
	Elective Subjects (Any 2 credits)	
EL/PC- 801	Pharmacological Interventions for Ischemic Brain Injury	2
EL/PC- 802	Nanotoxicology	2
EL/PC -803	Neuropharmacology	
EL/PC- 804	Pharmacological Interventions for Ischemic Brain Injury	2
Choose any core course of other department (MC/PA/PE/MD)		

***Detailed Syllabus is available at Page No. 39-40**

Ph.D. Syllabus
SEMESTER - I

PC- 710 :- Receptor Mechanism (2 Credits)

Chapter 1: Biochemical mechanisms of cell signalling; Plasma membrane and cytosolic receptor structure; Plasma membrane as a signal transduction element; Mechanisms of receptor mediated signalling; Ion gated channels; Ligand activated receptors with intrinsic enzyme activity; Amplification of transmembrane signals.

Chapter 2: Structure of G proteins, subclassification of G proteins; Role of heterotrimeric G proteins in signalling; Generation of intracellular second messengers; Modulation of G protein activity. Calcium as second messenger, PIP2, IP3 receptors, calcium influx and efflux, intracellular sources of calcium and release.

Chapter 3: Molecular and chemical characterization of membrane receptors; Use of monoclonal antibodies in receptor characterization and purification; Immunoprecipitation and electrophoretic analysis of membrane proteins; Peptide mapping; Molecular weight determination; Solubilization of the receptors; Reconstitution of membrane receptors.

Chapter 4: Intracellular signaling: signaling by cAMP, signaling by NF-kB, signaling by STAT, the MAPK signaling pathway, apoptosis, Role of mitochondria in apoptosis and aging, Transcription factors, mechanisms, pharmacological targets and their role in different diseases conditions.

PC- 720 :- Free Radicals In Drug Research (2 Credits)

1. Introduction to free radicals: Free radicals, reacting oxygen species, production of free radicals in cells, damaging reactions of free radicals, defences against free radicals, free radicals in human disease**.**
2. Measurement of free radicals: Lipid peroxidation products, lipid hydroperoxide, malondialdehyde, measurement of antioxidants**.**
3. Antioxidants: Endogenous antioxidants- enzymatic and nonenzymatic; Regulation of antioxidant defences, pharmacological antioxidants**.**
4. Free radicals in neurological and neurodegenerative diseases: Free radical scavengers in the treatment of brain injury. Peroxynitrite induced toxicity: Interaction of nitric oxide with oxygen radicals and scavengers in ischemic damage, role of poly (ADP) polymerase in cell death and PARP inhibitors in ischemic injury. Oxidative stress and MAP kinases. Oxidative stress and apoptosis. Free radicals involvement in other disorders. Free radicals' theory of ageing**.**
5.

PC 730 :- Regulatory Toxicology And Drug Safety Evaluation (2 Credits)

1. **Concept and Development of Regulatory Toxicity Testing Models:** Bio assays and endpoints: Human pharmaceutical products; Exposure characterization; Routes of exposure; ADME profiles.
2. Stages of drug development: Drug laws, FDA, OECD, ICH, Schedule Y; Design of preclinical toxicity studies and clinical development, clinical risk/benefit analysis. Safety evaluation of medical devices and bio materials. Good Laboratory Practices (GLP), issues and implementation.
3. Different methods in toxicity testing: Dose determination, response characterization, NOAEL.
4. MTD and threshold limitations: Hormesis, lower dose extrapolation, in vitro and in vivo correlation, animal to human extrapolation; Flow chart.
5. Mechanism of toxicity: Evaluation across different models: Target organs, cell death, necrosis, apoptosis, oxidative stress, chromosome and DNA damage**.**
6. Acute and chronic toxicity, genetic toxicity: Types of genetic toxicity testing; Principles of detection; Genotoxicity of marketed drugs, test batteries, Salmonella test, micronucleus test, chromosome aberration test, Comet assay, New-bio assays**.**
7. Reproductive toxicity: Germ cell toxicant, effect on gonads, F1generation study. Neonatal toxicity; Transplacental mutagenesis and carcinogenesis**.**
8. Carcinogenicity, carcinogen identification: Carcinogenesis process, drug induced carcinogenicity, lifetime carcinogenicity bio assays, neonatal mouse models; Short and medium term bio assays, limitations and impacts.
9. Regulations, discoverydevelopment gap: Risk characterization; Management and Communication.
10. Future of regulatory toxicology in drug safety evaluation.

EL/PC- 701 - Application Of Biotechnology In Parasitic Disease Research (2 Credits)

EL/PC -701 Application of Biotechnology in Parasitic Disease Research,
2 Credits (Kept as elective)

EL/PC- 702 : - Phytopharmaceuticals and Its Standardization Aspects (2 Credits)

1. Introduction of Phytopharmaceuticals, Nutraceuticals, Herbal Cosmetics, Natural food colours and other value added products from natural resources; product development, advantages, market size and regulations.
2. Identification and Authentication of Plant Drugs: Taxonomical Identification of plant, morphological and anatomical description, Natural habitat, geographical distribution of plant, source (wild or cultivated), Season and time of collection, post-harvest processing.

3. Quality Control of Plant Drugs: Foreign matter, total ash, acid insoluble ash, Pesticide residue, Heavy metals, Microbial load, Chromatographic finger print with respect to four phytochemical reference markers, bio assay for phytochemicals.
4. Process for extraction and subsequent fractionation: Steps involved in processing of plant material by retaining the medicinal and nutritional values (phytochemical active principal ingredient -pAPI). Examples: Spray Drying, Lyophilization and Bead milling.
5. Quality specification of pAPI: Details of solvent used, Extractive values, Solvent residue, Microbial load, Heavy metals, Chromatographic finger print profile with respect to reference markers.
6. Biological Activity/ Efficacy Data of pAPI: Primary screen detail [with reference] (target-based/phenotypic with comparator/ standard drug at appropriate concentration); EC50 of pAPI and bioactive Marker, CC50 (cell line used), Selectivity Index (SI). Secondary screen detail (in-vivo model; if more than one, please provide details for all); ED50/dose for curative efficacy, Criterion for Go/No-Go decision (superiority/non-inferiority with standard of care).
7. Stability data of pAPI: Procedures, predictable chemical and galenical changes, technical limitations, testing methods. Stability data of the finished product in the pack intended for marketing.
8. Bioavailability and pharmacokinetics (PK) aspects for Phytopharmaceuticals with examples. Phytoequivalence, pharmaceutical equivalence. PK in mice/rat (dose and route); primary parameters wrt bioactive marker.

Importance of monographs of standards of medicinal plants and their parts, comparative study of BHP, API, Chinese, Japanese Herbal Pharmacopoeia, USP.

(Syllabus for Compulsory Courses)

Semester-I

CS- 701 :- Research Methodology (2 Credits)

Unit 1: **Objectives and types of research**: Motivation and objectives, research methods vs methodology. Types of research – descriptive vs analytical, applied vs fundamental, quantitative vs qualitative, conceptual vs empirical. Introduction to drug discovery & development research, objectives, flowchart from discovery to post-marketing research, overview of research methodology in various areas of drug discovery and development research.

Unit 2: **Research formulation and Literature review**– Defining and formulating the research problem, selecting the problem, the necessity of defining the problem, the importance of literature review in defining a problem, Literature review - primary and secondary sources, reviews, monographs, patents, research databases, web as a source, searching the web, critical appraisal of literature, identifying gap areas from literature review and research databases, and development of a working hypothesis.

Unit 3: **Research design and methods**: Research design – basic principles, need of research design, features of good design, important concepts relating to research design, observation and facts, laws and theories, prediction and explanation, research databases, development of models, developing a research plan – exploration, description, diagnosis, and experimentation.

Unit 4: **Execution of the research, data collection and analysis**: Aspects of method validation, observation and collection of data, methods of data collection, sampling methods, data processing and analysis strategies and tools, data analysis with statistical packages (GraphPad Prism, SPSS for Student t-test, ANOVA, etc), hypothesis testing, generalization, and interpretation.

Unit 5: **Safety measures in the laboratory: Handling of hazardous chemicals, incompatible chemicals, flammable solvents, toxic chemicals and forms of toxic materials.** Approaches for prevention and management of fire, electrical, chemical, biological, and gaseous hazards, good laboratory practices. General safety rules, waste minimization approaches and safety practices for disposal of chemical waste, biologicals and other laboratory waste.

(Syllabus for Compulsory Courses)

Semester-II

CS- 801 :- Research and Publication Ethics (2 Credits)

Unit 1: **Research Ethics:**

a) Ethics – ethical issues, ethical committees (human & animal)
b) Ethics with respect to science and research
c) Intellectual honesty and research integrity
d) Scientific misconducts: Falsification, Fabrication, and Plagiarism
e) What is plagiarism? Similarity report software like iThenticate/ Turnitin/ Urkund.
f) Redundant publications: duplicate and overlapping publications, salami-slicing
g) Selective reporting, and misrepresentation of data

Unit 2: **Publication Ethics:**

a) Publication ethics: definition, introduction, and importance.
b) Best practices / standards-setting initiatives and guidelines: COPE, WAME, etc.
c) Conflicts of interest
d) Publication and Research misconduct: definition, concept, problems that lead to unethical behavior and vice versa, types
e) Violation of publication ethics, authorship, and contributorship
f) Identification of publication misconduct, complaints, and appeals
g) Predatory publishers and journals.
h) Journal finder/journal suggestion tools.

Unit 3: **IPR and scholarly publishing**:

Intellectual Property Rights (IPR) and patent law, commercialization, copyright, royalty, trade-related aspects of intellectual property rights (TRIPS)

Unit 4: **Report and thesis writing:**

a) Structure and components of scientific reports, types of reports, technical reports, and thesis.
b) Thesis writing – different steps and software tools (Word processing, etc) in the design and preparation of the thesis, layout, structure (chapter plan), and language of typical reports, Illustrations and tables, bibliography, referencing, and footnotes.
c) Oral presentation – planning, software tools, creating and making an effective presentation, use of visual aids, the importance of effective communication
d) Writing a research proposal and research grant
e) Scholarly publishing – IMRaD concept and design of research paper, citation and acknowledgment, reproducibility, and accountability.
f) Graphical Abstract and Artwork preparation

Unit 5: **Databases and Research Metrics**

a) Indexing databases: PubMed, Embase, etc.
b) Citation databases: Web of Science, Scopus, etc.
c) Impact Factor of the journal as per Journal Citation Report, SNIP, SJR, IPP, Cite Score, *etc*.
d) Metrics: h index, g index, i10 index, altmetrics