



# **SYLLABUS**

## **Ph.D. Pharmacology & Toxicology**

## Ph.D Pharmacology & Toxicology

Course Code	Course Name	Credits
<b>Semester I</b>		
PC 710	Signaling Mechanisms Of Receptors And Neurotransmitters In Brain	02
PC 720	Basics And Advances In Neuoscience	02
PC 820	Pharmacological Interventions for Ischemic Brain Injury	02
PC 830	Parasitology/Microbiology, Community & Pharmacy	02
GE 710	Research and Publication Ethics	02
	<b>Total Credits</b>	<b>10</b>
<b>Semester II</b>		
PC 840	Regulatory Toxicology And Drug Safety Evaluation	02
PC 860	Epigenetics and Diseases	02
PC 870	Preclinical Pharmacological Models Of Screening	02
GE 820	Research Methodology	02
	<b>Total Credits</b>	<b>08</b>

## Ph.D Pharmacology & Toxicology Semester I

<b>PC 710: Signaling Mechanisms Of Receptors And Neurotransmitters In Brain (2 Credits)</b>	
1	<b>Receptor in CNS and molecular signaling mechanisms:</b> Cholinergic receptors, ion-channel/ligand-gated ion-channel receptors in CNS and their signal transduction mechanisms; Amplification of transmembrane signals
2	<b>Neurotransmitters and neuromodulators:</b> Neuromodulation of glial function and alterations in astrocytic signaling during neurodegeneration; Therapeutic strategies to control these alterations; Role of metal ions in brain physiology and pathology.
3	<b>Neurotransmitter receptor mechanisms:</b> Signaling mechanisms of ionotropic and metabotropic neurotransmitter receptors; Pathophysiological implications of neurotransmitter receptors. Calcium as second messenger in neuronal signaling.
4	<b>Orphan GPCRs in CNS diseases:</b> GPCRs and orphan GPCRs implicated in inflammatory neurodegenerative degenerative disorders and their signaling mechanisms.
5	<b>Insulin receptor in the brain:</b> Mechanisms of activation and the role in the CNS pathology and approaches for its regulation.

### ***Recommended Books and Readings:***

- 1 Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel.
- 2 Foundations of Neuroscience. By: Casey Henley. Elsevier 2021
- 3 Understanding G protein-coupled receptors and their role in the CNS (Molecular and Cellular Neurobiology). By: Menelas N. Pangalos and Ceri H. Davies. OUP Oxford Publisher 2002.
- 4 The Molecular and Clinical Pathology of Neurodegenerative Disease. By: Patrick A. Lewis, Jennifer E. Spillane. Elsevier Publishers 2018.
- 5 Neurodegenerative Diseases: Clinical Aspects, Molecular Genetics and Biomarkers. By: Daniela Galimberti, Elio Scarpini. Springer Publishers, 2<sup>nd</sup> Edition, 2018
- 6 Neuroinflammation. By Alireza Minagar. Elsevier Publishers, latest Edition, 2011
- 7 Neuroinflammation and Neurodegeneration. By: Phillip K. Peterson and Michal Toborek. Springer Publishers 2014.
- 8 Scientific Journals

# Ph.D Pharmacology & Toxicology Semester I

## PC 720: Basics And Advances In Neuroscience (2 Credits)

1	<b>Fundamentals of neuroscience:</b> Neurons and Networks, The Electrical Properties of the Neuron, Action potentials and their role in the nervous system, Basics of synapses, Excitation & Inhibition, Potentiation & Depression, Role of neuromodulation in the firing of synapses.
2	<b>Systems neuroscience:</b> Organization of the brain structures, Communication between neuron, Sensory and motor systems, Aplysia and hippocampal physiology, Uses of neural networks.
3	<b>Brain &amp; neuronal plasticity:</b> Brain and neuronal plasticity and cellular and molecular mechanisms of learning and memory, Homeostatic plasticity.
4	<b>Developmental neurobiology:</b> Principles of neural development, Examples of the classes of molecules involved in core processes and how they control and drive these processes. A description of how these core processes combine to develop a neural system such as the thalamocortical pathway.
5	<b>CNS disease models and techniques in neuroscience:</b> Behavioral assessment models and circuit-based correlations, Circuit selectivity for stimulation and inhibition, chemo- and opto-genetics. Electrophysiological methods, Brain imaging.
6	<b>Degenerative and demyelinating diseases:</b> Molecular and cellular mechanisms of neuronal cell death with reference to Alzheimer's, Parkinson, motor neuron and prion diseases; Amyloid precursor protein and its metabolism, Presenilin biology, Cytoskeleton and its involvement in neurodegeneration; Free radical damage; Clinical and pathological features of neurodegenerative diseases, Genetics of neurodegenerative diseases.
7	<b>Neuroimmunology:</b> Components and operations of the immune system in the brain, neuroinflammation and repair in diseases.

### **Recommended Books and Readings:**

- 1 Eric R. Kandel, James H. Schwartz, and Thomas M. Jessell. Principles of Neural Science
- 2 Benjamin Reddi and Roger Carpenter. Neurophysiology: A Conceptual Approach, 5<sup>th</sup> Edition.
- 3 Manter And Gatz's Essentials Of Clinical Neuroanatomy And Neurophysiology 10<sup>th</sup> Edition By Gilman.
- 4 Dale Purves (Editor), George Augustine (Editor), David Fitzpatrick (Editor), William Hall (Editor), Neuroscience.

# Ph.D Pharmacology & Toxicology Semester I

## PC 820: Pharmacological Interventions for Ischemic Brain Injury (2 Credits)

1	<b>Stroke:</b> Etiology & risk factors, Laboratory evaluation and Clinical management.
2	<b>Pathophysiology of ischemic brain injury:</b> Infarct vs Penumbra, Neuronal cell death cascade.
3	Blood Brain Barrier breakdown and post-ischemic inflammatory response.
4	<b>Excitotoxicity of ischemic brain injury:</b> Excitatory amino acid (EAA) and their receptors, Role of excitotoxicity in neurodegeneration, EAA antagonists, Problems associated with EAA antagonists.
5	<b>Disrupted ionic homeostasis in ischemic stroke:</b> Emerging mechanisms and therapeutic targets.
6	<b>Oxidative and nitrosative stress:</b> Free radicals (FRs) generation in brain and their role in neurodegeneration, Role of nitric oxide in ischemic brain injury, FRs measurement and potential therapeutic agents targeting oxidative/nitrosative stress.
7	<b>Neuronal cell death pathways:</b> Intrinsic and extrinsic pathways of apoptosis, Necrosis, Necroptosis, Autophagy, Ferroptosis and Pyroptosis.
8	<b>Other neuroprotective approaches:</b> Calpain inhibitors, PARP inhibitors, MAP kinase inhibitors, Nrf2 Activation, PPAR agonism.
9	Experimental models for testing neuroprotective drugs, Neuronal culture, Brain slices and Animal models for focal and global ischemia.

### Recommended Books and Readings:

- 1 Neuroprotective Therapy for Stroke and Ischemic Disease. Editor: Paul A. Lapchak, John H. Zhang. Electronic ISSN:2363-9598. Print ISSN: 2363-958X <https://doi.org/10.1007/978-3-319-45345-3>. Publisher Name: Springer, Cham.
- 2 Advancement in the Pathophysiology of Cerebral Stroke. Editors: Ranjana Patnaik, Amit Kumar Tripathi, Ashish Dwivedi. Hardcover ISBN: 978-981-13-1452-0. eBook ISBN 978-981-13-1453-7. DOI: <https://doi.org/10.1007/978-981-13-1453-7>. Publisher Name: Springer, Singapore.
- 3 Advances in the Preclinical Study of Ischemic Stroke. Editor: Maurizio Balestrino. Hardcover ISBN:978-953-51-0290-8. eBook (PDF)ISBN:978-953-51-5240-8. DOI: <https://doi.org/10.5772/1082>. Publisher Name: IntechOpen Limited United Kingdom.

## Ph.D Pharmacology & Toxicology Semester I

### PC 830: - Parasitology/Microbiology, Community & Pharmacy (2 Credits)

1	<b>Parasitic, microbial and viral infections, community and pharmacy:</b> The general perceptions, linkages and relevances; Basic principles of epidemiology; Epidemiology of infectious/tropical diseases; Community related issues involved in the epidemiological studies; Community participation in epidemiological studies; Role of epidemiological studies on disease treatment, control and prevention.
2	<b>Emerging and re-emerging infections:</b> Role of vectors and population migration; Impact of travel on the transmission patterns of infectious diseases; Mapping and managing of the drug-resistant pathogens.
3	<b>Biomedical and biocultural definitions of parasitic and microbial diseases:</b> The perceptions of community; Community or selected schools participation/involvement in the control and treatment of infectious diseases; Role of NGOs and media; Modern and traditional medicines for the treatment of tropical diseases
4	<b>Mothers definition of malaria:</b> Mothers beliefs and behaviours in relation to malaria in children; Home management of childhood malaria, diarrhoea and respiratory infections; The decision-making dynamics in treatment seeking behaviours, antimalarials available in retail outlets and home; Impact of parasitic and microbial diseases on the education of children.
5	<b>Women and tropical diseases:</b> Introduction; Women's participation in the treatment and management of infectious diseases; The relationship between gender and tropical diseases: Risk factors of infection, social costs and access to care, knowledge and resources; Assessment of women' need as related to infectious diseases, their involvement in the identification of their own needs, setting their own goals and targets; Training of women to train themselves.
6	<b>Mass chemo and immunoprophylaxis against tropical diseases:</b> Evaluation of their impact and the understanding of the cost-effectiveness.
7	<b>Determination of disease burden, the disability-adjusted life years, and the understanding of the economical aspects of tropical diseases:</b> Details of studies the social and economic burden of malaria and tuberculosis.

# Ph.D Pharmacology & Toxicology Semester I

## GE 710: - Research and Publication Ethics (2 Credits)

1	<p><b>Philosophy and Ethics:</b> 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.</p>
2	<p><b>Publication Ethics:</b> 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.</p>
3	<p><b>Open Access Publishing:</b> Open access publications and initiatives. SHERPA/RoMEO online resource to check publisher copyright &amp; 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.</p> <p><b>Publication Misconduct:</b></p> <p><b>a.</b> Group discussions: Subject specific ethical issues, FFP, authorship. Conflicts of interest. Complaints and appeals: examples and fraud from India and abroad.</p> <p><b>b.</b> Software tools: Use of plagiarism software like Turnitin, Urkund and other open source software tools.</p>
4	<p><b>Databases and Research Metrics</b></p> <p>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.</p>

### Recommended Books and Readings:

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/EthicsBook.pdf>
9. Scientific Journals

## Ph.D Pharmacology & Toxicology Semester II

<b>PC 840: Regulatory Toxicology And Drug Safety Evaluation (2 Credits)</b>	
1	<b>Concept and development of regulatory toxicity testing models:</b> Bioassays and endpoints, Human pharmaceutical products; Routes of exposure; Toxicokinetic.
2	<b>Regulating guidelines:</b> Drug laws, FDA, OECD, ICH, NDCT-CDSCO. Design of preclinical toxicity studies and clinical development, Safety evaluation of medical devices and biomaterials. Good Laboratory Practices (GLP) and Good Laboratory Practices (GCP).
3	<b>Different methods in toxicity testing:</b> Dose determination, Response characterization, NOAEL.
4	<b>MTD and threshold limitations:</b> Hormesis, Lower dose extrapolation, in vitro and in vivo correlation, Animal to human extrapolation.
5	<b>Mechanism of toxicity:</b> Evaluation across different models: Target organs, Cell death, necrosis, Apoptosis, Oxidative stress, Chromosome, and DNA damage.
6	Acute, sub-acute and chronic toxicity as per OECD guidelines.
7	<b>Genotoxicity study:</b> Types of genetic toxicity testing; Principles of detection; Ame's test, Micronucleus test, Chromosome aberration test, Comet assay, Genotoxicity of marketed drugs.
8	<b>Reproductive toxicity:</b> Germ cell toxicants, Effect on gonads, F1 generation study, Neonatal toxicity, Transplacental mutagenesis.
9	<b>Carcinogenicity, carcinogen identification:</b> Guidelines for carcinogen risk assessment Carcinogenesis process, Drug induced carcinogenicity, Lifetime carcinogenicity bioassays, Neonatal mouse models; Short- and medium-term bioassays, Limitations and impacts.
10	<b>Regulatory issues for nanotechnologies:</b> Regulatory framework for the emerging technologies; Identifying and defining nanomaterials; Risk assessment of nanomaterials.
11	Future of regulatory toxicology in drug safety evaluation.

### **Recommended Books and Readings:**

- 1 <https://dbtindia.gov.in/latest-announcement/guidelines>.
- 2 <https://dst.gov.in/sites/default/files/Draft-Guidelines%20.pdf>.
- 3 <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/>
- 4 Regulatory Toxicology by Shayne C. Gad Taylor & Francis.
- 5 Principles and Methods of Toxicology by A. Wallace Hayes.
- 6 Drug safety evaluation, third edition by Shayne C. Gad Wiley  
ISBN:9781119097419, 111909741X



## Ph.D Pharmacology & Toxicology Semester II

<b>PC 860: Epigenetics And Diseases (2 Credits)</b>	
1	Toxicogenomics, Pharmacogenomics, Pharmacogenetics, and Personalized medicine.
2	<b>Proteomics in Drug Discovery:</b> Two-dimension gel electrophoresis; In-gel digestion etc. Microarray technology (principle and application): Hybridization and types of arrays, tiling array, Protein arrays.
3	<b>Chromatin structure and functions:</b> Nucleosome, Euchromatin & Heterochromatin, Regulation and alteration of chromatin higher order structure.
4	Epigenomics and Histone modifications; RNA Splicing and implications in epigenetics.
5	<b>Epigenomic plasticity:</b> how aging and environmental factors can alter the epigenome.
6	Role of epigenetic modifications in cancer, neurodegenerative diseases, and Diabetes etc.
7	<b>Lost in translation:</b> Non-coding RNAs in epigenetics, MicroRNA and the environment, MicroRNA Control of epigenetic mechanisms.
8	Advance techniques in genome-wide analysis of histone modifications, Epigenome Wide Association Studies, Next-generation sequencing, Potential pitfalls in current epigenetic research.
9	Model systems to study epigenetic regulations, Bioinformatics research tools.
10	Nucleic acid based Therapeutics, Targeted Delivery.

### ***Recommended Books and Readings:***

- 1 Epigenetics in Biology and Medicine Edited by Manel Esteller Published by Taylor & Francis Ltd.
- 2 Epigenetics in Human Disease edited by Trygve Tollefsbol; 2nd Edition, 2018. Published by Elsevier.
- 3 Genetic and Epigenetic Insights into the Developmental Origins of Health and Disease. edited by Tesfaye B. Mersha, Fasil Tekola-Ayele, Daniel Enquobahrie Frontiers Media SA.
- 4 Epigenetics: Current Research and Emerging Trends. Edited by: Brian P. Chadwick Published: 2015 Book: 978-1-910190-07-4. Ebook: 978-1-910190-08-1.
- 5 RNA and the Regulation of Gene Expression: A Hidden Layer of Complexity. Edited by: Kevin V. Morris Published: 2008 Book: 978-1-904455-25-7. Ebook: 978-1-913652-26-5.

## Ph.D Pharmacology & Toxicology Semester II

### PC 870: Preclinical Pharmacological Models of Screening (2 Credits)

1	General principles of in-vitro preclinical screening; Extrapolation of preclinical data to predict clinical implications and its limitations.
2	<b>Primary cell culture and immortalized cell lines:</b> Preparation of primary cell lines, immortalized cell lines and their maintenance; Three-dimensional cell-culture models including organoids and spheroids etc., Implications of cell-based assay in preclinical screening.
3	Modeling of different diseases using cell lines, Correlation between neuroinflammation and neurodegenerative diseases using in vitro models; Different cell-based models including glial, astrocytic, and neuronal cell lines implicated in neuronal disorders, iPSC and co-culture system.
4	General principles of in-vivo pharmacological preclinical screening for CNS drugs; In vivo models to study different diseases including Alzheimer's disease, Parkinson's disease, multiple sclerosis, Non-alcoholic Fatty Liver Disease (NAFLD), Cirrhosis, Respiratory inflammation including asthma and COPD and Cancer.
5	Genetically modified animals used to study different models of diseases, mapping the pathways from genes to disease pathology.

#### **Recommended Books and Readings:**

- 1 Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel.
- 2 The Molecular and Clinical Pathology of Neurodegenerative Disease. By: Patrick A. Lewis, Jennifer E. Spillane. Elsevier Publishers 2018.
- 3 Neurodegenerative Diseases: Clinical Aspects, Molecular Genetics and Biomarkers. By: Daniela Galimberti, Elio Scarpini. Springer Publishers, 2nd Edition, 2018.
- 4 Neuroinflammation. By Alireza Minagar. Elsevier Publishers.

## Ph.D Pharmacology & Toxicology Semester II

<b>GE 820: Research Methodology (2 Credits)</b>	
1	<b>Concept of Research:</b> - Meaning and importance of Research- Objectives and types, Motivation in Research
2	<b>Analysis of literature review:</b> - Primary and Secondary sources, Web sources –critical literature review
3	<b>Hypothesis:</b> Different types, Significance, Development of working hypothesis, Null hypothesis.
4	<b>Introduction to research methods/ methodology:</b> - 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	<b>Data Collection and Statistical Analysis:</b> 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	<b>Data Reporting and Scientific Writing: -</b> 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	<b>Principal of Analytical Instrumentation and their Implication: -</b> 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 and Readings:**

- 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