

Jadavpur University

Department of Pharmaceutical Technology

Syllabus for M.Pharm in Pharmaceutical Biotechnology

PG / PHAR / T/ 112BPharmaceutical Biotechnology-I

Theory 4 hours/week

Unit I

Molecular and genetic mechanisms, Genes and Chromosome

- (i) Nucleic acids and their structure, Study of Central dogma of life: Replication, transcription, translation, structure and function of different types of RNAs, DNA sequencing methods, chromosomal organization and morphology in prokaryotes and eukaryotes, exons and introns, mobile and organelle DNAs, nucleosome structure and spatial organization. DNA recombination, DNA repair mechanism.
- (ii) Regulation of gene expression in eukaryotes and prokaryotes (bacteria, yeast, insect, mammalian cells) transcriptional control, feedback inhibition; Different models and mechanisms of transcriptional attenuation.

Unit II

Introduction to microbial genetics

- (i) Mechanism of genetic exchange (Conjugation, transduction, Transformation), genetic mapping using transformation and transduction, triple cross experiment, Type and selection of mutants, Cis-trans complementation. Isolation of mutants, factors influencing rate of mutation
- (ii) Transposition: Mechanism and models. Insertion sequences. Composite transposons. Transposon-mediated *in vitro* mutagenesis.
- (iii) Viruses: Structure, classification, genome, replication and growth, purification, quantification. Mechanism of infection by retroviruses. Life cycle of viruses: Lytic and lysogenic phage, Details of lamda genome, viroids and prions.
- (iv) Yeast: Model organism. Importance as genetic tool. Mating type switch. Types of yeast vectors. Important genes. Two hybrid system. Red-white screening.

Unit III

Tools of Genetic Engineering

- (i) Basic concept of r-DNA technology, detail study of enzymes used in molecular biology (restriction endonuclease, DNA polymerase, DNA ligase, reverse transcriptase etc.), Cloning vectors, linkers and adaptors. Animal virus derived vector –SV-40, vaccinia, baculo, pichia and retroviral vectors. Expression vectors, Intein based vectors, Inclusion bodies and methodologies to reduce the formation of

inclusion bodies. Blotting/hybridization techniques and their application. Electrophoretic separation of protein and nucleic acids.

(ii) Polymerase chain Reaction (PCR): basics, types (multiplex, hot start, touch down, nested, real time and reverse transcriptase colony PCR), cloning of PCR products. PCR in molecular diagnostics.

Unit IV

Applications of Genetic engineering in Pharmaceutical Industry

Role of r-DNA technology for the production of biopharmaceuticals (insulin and engineered insulin, tissue plasminogen activator, interferon, erythropoietin, growth hormones), vaccine, diagnostics, antibiotics etc. Stability of r-DNA technology derived products. Priorities for future biotechnological research.

Unit V

Bioprocess Technology

(i) Upstream process: Introduction to microbial growth, media, formulation, sterilization, inoculum preparation.

(ii) Fermentation: Fermentation process design, operation and characteristics of fermentation processes, batch, fed-batch, continuous process etc. Instrumentation and bioprocess control. Mass transfer in bioreactors. Rheology of fermentation fluids.

(iii) Downstream process: Introduction to various downstream processes operations in biopharmaceutical manufacturing such as centrifugation, filtration, tangential flow filtration, cell disintegration, solvent:solvent extraction, supercritical fluid extraction etc.

resistance.

(iv) Antibiotic biosynthesis genes and their use in developing new antibiotic from micro organisms. Methods for isolating new antibiotics, genetic systems and molecular tools for analysis of antibiotic, biosynthesis, cloning and analysis of antibiotic biosynthesis genes, genetically engineered hybrid antibiotics.

Unit VI

Enzyme technology:

(i) Dynamics of enzyme activity, enzyme kinetics, pharmaceutical, therapeutic and clinical applications of enzyme. Protein engineering in enzyme improvements, Immobilization of enzymes, methods of immobilization, whole cell immobilization and its application. Enzyme based assay for small molecule screening.

(ii) Industrial enzymes in drug development: penicillin amidase, lipase, oxidoreductase, nirtilase, protease etc. Use of these enzymes for enantio-selective synthesis of important drug/drug intermediates, future directions.

Unit VII

Introduction to Plant tissue Culture, Tissue culture Media (composition and preparation), protoplast isolation, culture and purification, Production and purification of Plant secondary metabolites. Applications of Plant tissue cultures in Healthcare

PG / PHAR / T/ 127FPharmaceutical Biotechnology-II

Pharmaceutical Biotechnology-II

Unit I

(i) Fundamental concept of immune system:

Basics of immunology, Components of cell mediated and humoral immunity, Components of innate and acquired immunity, MHC genes, antigen processing and presentation, MHC and immune responsiveness and disease susceptibility, different MHC molecules, phagocytosis, Complement and inflammatory responses, haematopoiesis, maturation of different immune cells, Antigens-immunogens, haptens, Active and passive immunization, Adjuvant. Cells and organs of immune system and their functions

(ii) Molecular basis of immune response

Immunoglobulins, class, sub-class and structure, Immunoglobulin superfamily, affinity, avidity, allotype, idiotype, isotype, polyclonal and monoclonal antibody. Antibody genes and antibody diversity. Antigen-antibody reactions. Different immunological techniques such as RIA, ELISA ELISPOT assay, Western blotting, immunofluorescence and flow cytometry.

(iii) Monoclonal antibodies (mAbs): Commercial production and applications of monoclonal antibodies in different areas of healthcare. Pre-clinical safety assessment and PK/PD in clinical development of antibody therapeutics.

(iv) Manufacture, Quality control and Stability of immunological products. Manufacturing process validation, Characterization of rDNA-derived biotherapeutics (Physicochemical characterization, biological activity), process related impurities and contaminants, product related impurities and contaminants etc.

Unit II

Design and Development of protein based biopharmaceuticals and protein engineering

(i) Pharmacokinetics and pharmacodynamics of peptide and protein drugs, direct and indirect link PK/PD models

(ii) Different protein purification techniques and issues to consider in production and purification of proteins

(iii) Mutagenesis and its applications in protein engineering.

(iv) Second generation molecules via site-specific gene alteration, second generation protein program design, examples of engineered proteins of therapeutic potential, methods of protein drug delivery with a special emphasis on nanotechnology, future perspective.

Unit III

Gene Therapy and epigenetics

Introduction of DNA into mammalian cells, transfection techniques, gene silencing techniques, Introduction to siRNA and antisense technology, vectors used in gene therapy, somatic and germ-line therapy *-in-vivo* and *exvivo*, Suicide gene therapy, Gene replacement, Gene targeting, Transgenic plant and animal and their applications in healthcare. cDNA and intragenic arrays, Differential gene expression and protein array. Role of gene therapy in management of communicable, lifestyle and metabolic diseases/disorders. Guidelines for gene therapy.

Unit IV

Cell biology

(i) Cell structure and organization: Cells as a unit of life, prokaryotic and eukaryotic cells, biomembranes, structure and basic functions of various cell organelles

(ii) Tools and techniques of cell biology

Histology, staining, Affinity chromatography, Fluorescence, Confocal, TEM and SEM. Fluorescent dyes and GFP tagged proteins in visualization, FACS, cell fractionation, immunohistochemistry, immunoprecipitation and immunoblotting. Types of different cell culture techniques. Metabolism, regulation and nutritional requirements for mass cultivation of animal cell culture, types of contaminants, techniques of detections and precautionary measures for the management of contaminations in animal cell culture. Kinetics of cell growth and product formation and effect of shear force. Product and substrate transport, Micro and macro-carrier culture, Genetic engineering in animal cell culture, Animal cell preservation. Assays for cytotoxicity.

(iii) Organization of tissues: Cell-cell and cell-matrix interactions, cell adhesion molecules, components of extracellular matrix cellular junctions and role.

(iv) Cell cycle: G₁, G₂, S and M phase of cell cycle. Cell cycle analysis and its applications, programmed cell death apoptosis versus necrosis. Role of telomeres in the cell cycle

(v) Cell signaling: Receptor concept, receptor signaling and expressions, orphan receptor, extracellular signals and cell functions, hormones, second messengers and hormone actions, growth factors.

(vi) Transport across the membrane: Osmosis, active and passive transport, protein transporter ion channels, antiporters, symporters. Applications in the field of medicines.

(vii) Cellular movement and Molecular motors: Types of movement, extravasation, role of cytoskeletal proteins in movement, molecular motors, the movement of cilia and flagella, muscle contractions, myosin and kinesins in the movement of vesicles.

(viii) Protein synthesis and Targeting: Ribosome and endoplasmic reticulum secretory pathways, targeting and sorting of proteins, nuclear localizations signal, organelle specific signal sequence, ATP driven translocation, glycosylation, transport of proteins, endocytosis, exocytosis, macropinocytosis.

(ix) Relevance of cell biology: Stem cells, tissue engineering, infectious disease

(x) Cancer: Tumor cells, cell lines and models, proto-oncogenes and oncogenes, signaling pathways, oncogenic mutations, loss of cell cycle control, carcinogenesis. Characteristics of tumor cells, Factors responsible for MDR in cancer and possible remedies to overcome MDR. Role of biotechnology in the management and diagnosis of cancer, future perspectives of research.

Unit V

Introduction to the human genome project and Pharmacogenomics

Physical mapping and sequencing of genome, sequence analysis, comparative homologies, evolutionary changes and single nucleotide polymorphism, expression and analysis of expressed genes.

Unit VI

Bioinformatics

Introduction to human genome and bioinformatics resources (NCBI, EBI, ExPASy), sequence and structure of database. Genomics and proteionomics (large scale genome sequencing strategies, Comparative genomics, Understanding the DNA microarrays and protein arrays). Molecular modeling and simulation (basic concepts including the concept of force fields).

Pairwise alignment techniques, Multiple sequence analysis, Mutiple sequence alignment, Flexible sequence similarity searching with FASTA3 program package, Use of Clustal W and Clustal X for the multiple sequence alignment, submitting DNA protein sequence to database.

Protein structure prediction:

Protein folding and model generation, secondary structure prediction, Analysing secondary structure, protein loop searching, Loop generation methods Loop analysis Homology modeling, potential applications.

Unit VII

Bioethics

Bioethics, biosafety and IPR related issues for biotechnological product: Introduction, Biological safety cabinet, Primary containment for Biohazards, Biosafety levels, Biosafety levels of Specific microorganisms, Recommended Biosafety level for Infectious Agents and Infected Animals.

Biosafety guidelines: Government of India, Roles of Institutional biosafety committee

PG / PHAR / T/ 129F Pharmaceutical Biotechnology-III

Pharmaceutical Biotechnology-III

Theory 4 hours/week

Unit I

- (i) Biotechnology cytokines and leukotrienes: Cytokine receptor, cytokine as biopharmaceutical, interferons, interleukins and its types. Tumor necrosis factor.
- (ii) Growth factors: Hematopoietic growth factors, Growth factors and wound healing.
- (iii) Secondary metabolite production by plant cells: Conventional methods, Non-classical methods for the production of secondary metabolites, Production of anti-tumor compounds and antimicrobials by plant-cell culture.
- (iv) Oligonucleotides in drug delivery: Types of oligonucleotides (Antisense, ribozymes, siRNA, miRNA, triple helix forming oligonucleotides). Pharmacokinetics considerations of oligonucleotide-based therapeutics for improving their stability.
- (v) Role of biotechnology in concept of target based drug design and target discovery of biopharmaceuticals.

Unit II

- (i) Sterilization and Sterility testing:** Principle, methods and validation of sterilization processes, Industrial sterilizer and air handling (importance of sterile air), Sterility testing of different types of dosage forms and Separation techniques of pyrogen from Pharmaceutical products.
- (ii) Screening of antagonistic organisms and their antagonistic activity:** Classification of antibiotics, Isolation, Purification and Identification of new antibiotics from fermentation broth. Strain Improvement and synthesis of novel antibiotics by recombination.
- (iii) Fermentative production of pharmaceutically important products:** antibiotics (penicillin, streptomycin, erythromycin, cephalosporin; vitamins (B₂, B₁₂, C), amino acids etc. Mechanism of development of drug resistance by microbes and possible remedies to overcome the resistance.
- (iv) Prebiotics, Probiotics and Synbiotics:** Immune Booster, Inrelation to to the liberation of Short Chain Fatty Acids (SCFAs) for the prevention of colon cancer.

Unit III

Biochemistry

- (i) Biochemical energetics: Free energy, concept of standard free energy, laws of thermodynamics, exergonic and endergonic reactions, energy rich compounds, coupling of reactions, biological oxidation and reduction.

(ii) Metabolism of Carbohydrate (Glycolysis, gluconeogenesis, TCA cycle, Pentose phosphate biosynthesis regulation of carbohydrate metabolism, Electron transport chain and oxidative phosphorylation, disorders of carbohydrate metabolism)

(iii) Protein structure, function, Sequencing methods proteins, Biosynthesis of aminoacids, Urea cycle and formation of Uric acid, inborn error of metabolism.

(iv) Nucleic acid structure, function. Purine and Pyrimidine biosynthesis, salvage pathways, Role of ribonucleotidoreductase, Disorders of Purine and Pyrimidine metabolisms

(v) Lipid metabolism: Hydrolysis, absorption and transport of lipids, catabolism of lipids, Keone bodies, biosynthesis of cholesterol, biosynthesis of fatty acids, disorders of lipid metabolisms.

(vi) Coenzymes, classification of vitamins, Role and mechanisms of some important coenzymes, role of cofactors with some examples, marker enzymes and their application.

Unit IV Microbial biotransformation

Introduction, types of reactions mediated by microorganisms, design of biotransformation processes, selection of organisms, biotransformation process and its improvements with special reference to steroids and prostaglandins.

Unit V

Microbial spoilage, Infection risk and Contamination control, Redox potential of Pharmaceuticals

Unit VII

Introduction to Nanobiotechnology: Criteria for suitability of nanostructures for biological applications.

Different nanostructures: Thin films, colloidal nanostructures, nanospheres, nanocapsules.

M. Pharm. First year 2nd semester

PG/PHAR/T/129D Pharmaceutical Biotechnology C

The subject content will be the recent trends and latest development in the field of Pharmaceutical Biotechnology.