PROTEINS AND PROTEIN FORMULATIONS
(MPB 201T)

Scope

This course is designed to impart knowledge and skills necessary for knowing fundamental aspects of proteins and their formulations is a part of drug research and development process. Basic theoretical discussions of the principles of more integrated and coherent use of information for protein formulation and design are provided to help the students to clarify the various biological concepts of protein.

Objective

At the completion of this course it is expected that students will be able to understand,

- Various methods of purification of proteins
- Peptides in drug development
- Protein identification and characterization
- Protein based formulations
- Sequencing proteins

THEORY 60 Hrs

1. Protein engineering — 12 Hrs

   Concepts for protein engineering. Isolation and purification of proteins, Stability and activity based approaches of protein engineering, Chemical and Physical Considerations in Protein and Peptide Stability, Different methods for protein engineering, gene shuffling, and direct evolution.

2 Peptidomimetics — 12 Hrs

   Introduction, classification; Conformationally restricted peptides, design, pseudopeptides, peptidomimetics and transition state analogs; Biologically active template; Amino acid replacements; Peptidomimetics and rational drug design; CADD techniques in peptidomimetics; Development of non peptide peptidomimetics.

3 Proteomics — 12 Hrs

   Protein identification and characterization: Methods/strategies, protein identification, de novo protein characterization, Isotope labelling, N- and C-terminal tags.

2-Dimensional gel electrophoresis

Methods including immobilized pH gradients (IPGs), resolution, reproducibility and image analysis, future developments

4	Protein formulation Different strategies used in the formulation of DNA and proteins, Analytical and biophysical parameters of proteins and DNA in pre-formulation, Liposomes, Neon-spears, Neon-particulate system, PEGylation, Biological Activity, Biophysical Characterization Techniques, Forced degradation studies of protein.	12 Hrs
5	Methods of protein sequencing Various methods of protein sequencing, characterisation, Edman degradation, Tryptic and/or Chymotryptic Peptide Mapping.	12 Hrs

REFERENCES

1. H. Lodhishet. Al. Molecular Cell Biology, W. H. Freeman and Company
2. Protein Purification – Hand Book, Amersham pharmacia biotech
3. EngelbertBuxbaum, Fundamentals of Protein Structure and Function, Springer Science
4. Sheldon J. Park, Jennifer R. Cochran, Protein Engineering and Design, CRC press.
5. Robert K. Skopes. Protein purification, principle and practice, springer link.
6. David Whitford, Proteins-Structure and Function, John Wiley & Sons Ltd.
7. James Swarbrick, Protein Formulation and Delivery Informa Healthcare USA,Inc.
8. Rodney Pearlman, Y. John Wang Formulation, Characterization, and Stability of Protein Drugs, Kluwer Academic Publishers.

IMMUNOTECHNOLOGY

(MPB 202T)

Scope

This course is designed to impart knowledge on production and engineering of antibodies, the application of antigens, the design of (recombinant) vaccines, strategies for immune intervention, etc. The Immunotechnology – based techniques will be used for therapeutics and diagnostics, industries in the production, quality control and quality assurance, and in R&D.

Objective

After this course, the students will be able to:-

- Understand the techniques like immunodiagnostic tests,
- Characterization of lymphocytes, purification of antigens and antibody, etc.
- Access health problems with immunological background;
- Develop approaches for the immune intervention of diseases

THEORY 60 Hrs

1. Fundamental aspects of immunology 12 Hrs

Introduction, cells and organs of the immune system, cellular basis of Immune response, primary and secondary lymphoid organs, antigen antibody and their structure.

Types of immune responses, anatomy of immune response.

Overview of innate and adaptive Immunity.

Humoral Immunity

B – Lymphocytes and their activation. Structure and function of immunoglobulins, idiotypes and anti idiotypic antibodies.

Cell mediated Immunity

Thymus derived lymphocytes (T cells) – their ontogeny and types, MHC complex, antigen presenting cells (APC), mechanisms of T cell activation, macrophages, dendritic cells, langerhans cells, mechanism of phagocytosis

2 Immune Regulation and Tolerance 12 Hrs

Complement activation and types and their biological functions, cytokines and their role in immune response.

Hypersensitivity

Hypersensitivity Types I-IV, Hypersensitivity reactions and treatment

Autoimmune diseases

3	Vaccine technology Vaccine and their types, conventional vaccines, novel methods for vaccine production, antiidiotype vaccine, DNA vaccine, genetically engineered vaccine, iscoms, synthetic peptides, and immunodiagnostics. Stem cell technology Stem cell technology and applications to immunology	12 Hrs
4	Hybridoma Technology Hybridoma techniques – fusion methods for myeloma cells and B-Lymphocytes, selection and screening techniques. Production and purification of monoclonal antibodies and their applications in Pharmaceutical industry.	12 Hrs
5	Immunological Disorder Autoimmune disorders and types, pathogenic mechanisms, treatment, experimental models of auto immune diseases, primary and secondary immunodeficiency disorders. Immunodiagnosis Antigen antibody interaction – Precipitation reaction, Agglutination reactions, Principles and applications of ELISA, Radio Immuno Assay, Western blot analysis, immune-electrophoresis, immuno fluorescence, chemiluminescence assay, complement fixation reaction.	12 Hrs

REFERENCES

1. J. Kubey, Immunology – an Introduction.
2. S.C. Rastogi, Immunodiagonstics, New Age International.
3. Ashim Chakravarthy, Immunology and Immunotechnology, Oxford University Press.
4. E. Benjamini, Molecular Immunology.

BIOINFORMATICS AND COMPUTATIONAL BIOTECHNOLOGY (MPB 203T)

Scope

This paper has been designed to provide the advanced knowledge to the biotechnology students in invaluable areas of advanced bioinformatics which plays a crucial role in determining its future use and applications in medicine, drug discovery and in pharmaceutical industry.

Objectives

Upon completion of this course it is expected that the students will be able to understand,

- Use of computers in developing a new drugs
- Biological concepts for bioinformatics
- Proteins and their diversity
- Various gene finding methods
- Searching the biological databases
- Target searching
- Various methods of drug designing

THEORY 60 Hrs

1. Introduction to Bioinformatics — 12 Hrs

   Definition and History of Bioinformatics, Internet and Bioinformatics, Introduction to Data Mining, Applications of Data Mining to Bioinformatics,

   Biological Database

   Protein and nucleic acid databases. Structural data bases. Collecting and storing the sequence and Applications of Bioinformatics.

2 Sequence analysis — 12 Hrs

   Sequence alignment, pair wise alignment techniques, multiple sequence analysis, multiple sequence alignment; Flexible sequence similarity searching with the FAST3 program package, the use of CLUSTAL W and CLUSTAL X for the multiple sequence alignment. Tools used for sequence analysis.

3 Protein informatics — 12 Hrs

   Introduction; Force field methods; Energy, buried and exposed residues, side chains and neighbours; Fixed regions, hydrogen bonds, mapping properties onto surfaces; Fitting monomers, R &

S fit of conformers, assigning secondary structures; Sequence alignment-methods, evaluation, scoring; Protein completion, backbone construction and side chain addition; Small peptide methodology, software accessibility, building peptides; Protein displays; Substructure manipulations, annealing.

Protein structure prediction

Protein folding and model generation; Secondary structure prediction, analyzing secondary structures; Protein loop searching, loop generating methods, loop analysis; Homology modeling, concepts of homology modeling, potential applications, description, methodology, homologous sequence identification; Align structures, align model sequence; Construction of variable and conserved regions, threading techniques, Topology fingerprint approach for prediction, evaluation of alternate models; Structure prediction on a mystery sequence, structure aided sequence techniques of structure prediction, structural profiles, alignment algorithms, mutation tables, prediction, validation, sequence based methods of structure prediction, prediction using inverse folding, fold prediction; Significance analysis, scoring techniques, sequence- sequence scoring.

Docking

Docking problems, methods for protein- ligand docking, validation studies and applications; Screening small molecule databases, docking of combinatorial libraries, input data, analyzing docking results.

4	Diversity of Genomes Prokaryotic and Eukaryotic Gene Families. Genome Analysis: Introduction, Gene prediction methods, Gene mapping and applications- Genetic and Physical Mapping, Integrated map, Sequence assembly and gene expression. Completed Genomes Bacterium, Nematode, Plant and Human Evolution of Genomes Lateral or Horizontal Transfer among Genomes, Transcriptome and Proteome-General Account Phylogenetic analysis Evolutionary Change in Nucleotide Sequences, Rates and Patterns of Nucleotide Substitution, Models for Nucleotide Substitution, Construction of Phylogenetic Tree, Genome Annotation technique.	12 Hrs

5	Target searching and Drug Designing Target and lead, timeline for drug development, target discovery, target modulators, In-silico gene expression, microarray, and lead discovery, libraries of ligands, active site analysis, and prediction of drug quality.	12 Hrs

REFERENCES

1. David W. Mount, Bioinformatics Sequence and Genome Analysis, CBS Publishers and Distributors
2. S. C. Rastogiet. al. Bioinformatics- Concepts Skill and Applications, CBS Publishers and Distributors
3. T. E. Creighton, Protein Structure and Molecular Properties, W. H.Freeman and Company
4. Andreas D. Baxevanis, B. F. Francis Ouellette, Bioinformatics; A Practical Guide to the Analysis of Genes and Proteins, John Wiley & Sons, Inc.
5. Arthur M. Lesk, Introduction to Bioinformatics, Oxford University Press.
6. Shui Qing Ye. Bioinformatics: A Practical Approach, Chapman & Hall/CRC.
7. David Posada, Bioinformatics for DNA Sequence Analysis, Humana press.
8. Lesk, A.M. Introduction to Bioinformatics. Oxford University Press.
9. Letovsky, S.I. Bioinformatics. Kluwer Academic Publishers.
10. Baldi, P. and Brunak, S. Bioinformatics. The MIT Press.

BIOLOGICAL EVALUATION OF DRUG THERAPY
(MPB 204T)

Scope

This paper has been designed to provide the knowledge to the biotechnology students to understand the importance of biological and evaluation of drug therapy of biological medicines.

Objective

At the completion of this subject it is expected that students will be able to,

- Understand about the general concept of standardization of biological.
- Understand the importance of transgenic animals and knockout animals.
- Understand the biological medicines in development of various diseases.
- Learn the biological evaluation of drugs in vitro and in vivo

THEORY 60 Hrs

1. Biological Standardization 12 Hrs

General principles, Scope and limitation of bio-assay, bioassay of some official drugs.

Preclinical drug evaluation

Preclinical drug evaluation of its biological activity, potency and toxicity-Toxicity test in animals including acute, sub-acute and chronic toxicity, ED50 and LD50 determination, special toxicity test like teratogenecity and mutagenecity.

Guidelines for toxicity studies

Various guidelines for toxicity studies. Animal experiments assessing safety of packaging materials.

2 Pyrogens 12 Hrs

Pyrogens: Sources, Chemistry and properties of bacterial pyrogens and endotoxins, Official pyrogen tests.

Microbiological assay

Assay of antibiotics and vitamins.

Biological evaluation of drugs

Screening and evaluation (including principles of screening, development of models for diseases: In vivo models / In vitro models / cell line study).

3	Biologic Medicines in Development for various diseases - By Therapeutic Category - Genetic Disorders - Eye related Disorders - Digestive Disorders - Diabetes/Related Conditions - Cardiovascular Disease - Cancer/Related Conditions - Blood Disorders - Autoimmune Disorders - Infectious Diseases - Neurologic Disorders - Skin Diseases - Organe Transplantation Biologic Medicines in Development for various diseases – by Product Category - Antisense - Vaccines - Recombinant Hormones/Proteins - Monoclonal Antibodies (mAb) - Interferons - Growth Factors - Gene Therapy - RNA Interference	12 Hrs
4	Regulatory aspects : drugs, biologics and medical devices An introduction to the regulations and documents necessary for approval of a medical product. Regulatory consideration Regulatory consideration for pre-clinical testing and clinical testing of drugs, biologics and medical devices. New Drug Applications for Global Pharmaceutical Product Approvals	12 Hrs
5	Bioavailability Objectives and consideration in bio-availability studies of Biopharmaceuticals, Concept of equivalents, Measurements of bio-availability.	12 Hrs

Determination of the rate of absorption, Bioequivalence and its importance, Regulatory aspects of bio-availability and bioequivalence studies for conventional dosage forms and controlled drug delivery systems of Biopharmaceuticals.

Pharmacokinetics

Pharmacokinetics:- Basic consideration, Pharmacokinetic models, Application of Pharmacokinetics in new drug development of Biopharmaceuticals and designing of dosage forms and Novel drug delivery systems of Biopharmaceuticals.

REFERENCES

1. Perkins F.T., Hennessen W. Standardization and Control of Biologicals Produced by Recombinant DNA Technology, International Association of Biological Standardization
2. J.H. Burn., Biological Standardization, Oxford University Press
3. Drug Discovery and Evaluation in Pharmacology assay: Vogel
4. Chow, Shein, Ching, Design and analysis of animal studies in pharmaceutical development,
5. Nodine and Siegler, Animal and Clinical pharmacologic Techniques in Drug Evaluation.
6. Screening methods in pharmacology (vol I & II), R.A. Turner.

PHARMACEUTICAL BIOTECHNOLOGY PRACTICAL - II
(MPB 205P)

1. Protein identification
2. Protein characterization
3. Protein biochemistry
4. Recombinant DNA Technology
5. Protein expression
6. Protein formulations
7. Database searching
8. Sequence analysis methods
9. Protein structure prediction
10. Gene annotation methods
11. Phylogenetic analysis
12. Protein, DNA binding studies
13. Preparation of DNA for PCR applications – Isolation, Purity and Quantification
14. Introduction to PCR – working of PCR, Programming.
15. Introduction to RT-PCR – working, programming.
16. Primer design using softwares.
17. Gene DNA amplification by random / specific primers.
18. Southern Hybridization
19. Western Blotting
20. Gene transformation