Teaching hours: 3Hrs/week

Duration of Exam: 3 Hrs.
Max. Marks: 100

MAT-I MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES

1. Chromatographic techniques - Principles of separation and applications of TLC, Column chromatography, Paper chromatography, Ion exchange chromatography, G.C, HPTLC , HPLC and electrophoresis.

2. Infrared spectroscopy - Introduction, basic theory, modes of vibration, instrumentation, The Hook's Law & calculations of frequencies for different types of bonds, coupled interactions, hydrogen bonding radiation source, sample handling, applications of IR spectroscopy and introduction about FT-IR.

3.Ultraviolet spectroscopy – Introduction, electronic transitions, the origin and designation of UV band, absorption laws, calculation of Lambda maxim, the chromophore concept, factors effecting the position of UV bands, instrumentation, qualitative and quantitative applications.

4. Nuclear Magnetic Resonance spectroscopy –
A. 1H NMR Spectroscopy - Introduction, principle, instrumentation, solvents, chemical shift, spin-spin coupling, coupling constant, spin-spin splitting, chemical equivalence, Pascal triangle. Application including interpretation of Proton-NMR spectra.

B. 13C NMR Spectroscopy – Introduction, peak assignments, off resonance decoupling, selective proton decoupling, chemical shifts and factors affecting them, chemical shift equivalence, and spin coupling. Applications of 13C NMR.

5. Mass Spectrometry - Basic principle and theory involved, Instrumentation, types of ions, fragmentation, rearrangements, recognition of molecular ion peak, mass spectra of representative compounds, chemical ionization mass spectrometry (CIMS), field ionisation mass spectrometry (FIMS), fast atom bombardment mass spectrometry (FAB-MS). Applications.

6. Thermal analysis - Introduction to various thermal methods of analysis, basic principle and theory, Different types of calorimeters and micro calorimeters differential thermal analysis (DTA), differential scanning calorimetry (DSC) and micro calorimetry.

7. Pharmacological evaluation of drugs in biological fluids: Bioassay.

8. Microbiological assays.

9. Radioimmunoassays.

10.Quantitative microscopy of herbal drugs. Lycopodium spore method, stomatal number, stomatal index, palisade ratio, vein-islet number, and vein-termination number.

11. BIOSTATISTICS AND COMPUTER APPLICATION

i). Methods of collection of data, classification of data, graphical representation of data, frequency, polygon, histogram, measure of central tendency, mean mode and median dispersion and standard deviation.

ii). Confidence level, Null hypothesis, Calculation of statistical significance between two means, Analysis of variance.

iii). Association of attributes centigency, classification of attributes, coefficient of association, chi square test.

iv). Theory of probability, simple probability, law of probability, Permutation and combinations, ratios percentages and proportions and statistical difference between proportions. Analysis of variance two way ANOVA and multiple comparison procedures.

v) Correlation and regression, least square method and its application, significance of coefficient of correlation, non linear regression.

vi) Calculation of ED50, LD50, probit analysis.

II COMPUTER APPLICATIONS

BOOK RECOMMENDED

1. R.M.Silverstein, F.X.Webster, Spectrometric Identification of organic compounds, 6th ed. John Wiley & sons, New-York, 1998.
2. Remington, The science and practice of pharmacy, Mack publishing company. Easton Pennsylvania.
3. Organic spectroscopy by Willam Kemp
4. E. Heftmann, A laboratory handbook of chromatography, New - York.
5. H.H.Willard, L.L.Merritt and J.A.Dean, Instrumental methods of analysis, Van Nostrend Reinhold, New York.
6. WWM. Wenland, Thermal analysis, John Willy and sons, New-York.
7. Principle of instrumental analysis,V ed. By Skoog, Holler-Niemen.
8. Modern analytical chemistry by David Harvey. (MC Graw-Hill international edition).

(MAT-II) PRACTICALS

Practicals based on instrumental methods of analysis. A sufficient training will be given through exercises using different kinds of spectral analysis.

Modern Pharmaceutical Analytical Techniques (Theory & Practical) is a common subject in the first year of the all the five branches of Master of Pharmacy

M.PHARM
PHARMACEUTICAL BIOTECHNOLOGY
(MPB)

MICROBIAL AND CELLULAR BIOLOGY INCLUDING BIOPROCESS TECHNOLOGY

(MPB- I)

UNIT I **THEORY 120 Hrs**

Microbiology

Introduction – Prokaryotes and Eukaryotes. Bacteria, fungi, actionomyocytes and virus - structure, chemistry and morphology, cultural, physiological and reproductive features. Methods of isolation, cultivation and maintenance of pure cultures. Industrially important microorganisms - examples and applications, Microbial Screening (Primary and secondary), maintenance of stock culture, strain improvement. Pyrogens: Sources, Chemistry and properties of bacterial pyrogens and endotoxins,Official pyrogen tests.

UNIT II

Molecular Biology

Structure of nucleus and chromosome, Nucleic acids and composition, structure and types of DNA and RNA. Central dogma of molecular biology: Replication, Transcription, and Translation process in prokaryotic & eukaryotic cell.

Gene regulation

Gene copy number, transcriptional control and translational control.

RNA processing

Modification and Maturation, RNA splicing, RNA editing, RNA amplification. Mutagenesis and repair mechanisms, types of mutants, application of mutagenesis in stain improvement, gene mapping of plasmids- types purification and application. Phage genetics, genetic organization, phage mutation and lysogeny.

UNIT III

Cell structure and function

Cell organelles, cytoskeleton & cell movements, basic aspects of cell regulation, bioenergetics and fuelling reactions of aerobics and anaerobics, secondary metabolism & its applications. Cell communication, cell cycle and apoptosis, mechanism of cell division. Celljunctions/adhesion and extra cellular matrix, germ cells and fertilization, histology – thelife and death of cells in tissues.

Cell Cycle and Cytoskeleton

Cell Division and its Regulation, G-Protein Coupled Receptors, Kinases, Nuclear receptors, Cytoskeleton & cell movements, Intermediate Filaments.

Apoptosis and Oncogenes

Programmed Cell Death, Tumor cells, carcinogens & repair.

Differentiation and Developmental Biology: Fertilization, Events of Fertilization, *In*

vitro Fertilization, Embryonic Germ Cells, Stem Cells and its Application.

UNIT IV

Principles of microbial nutrition

Physical and chemical environment for microbial growth, Stability and degeneration of microbial cultures.

Growth of animal cells in culture

General procedure for cell culture, Nutrient composition, Primary, established and transformed cell cultures, applications of cell cultures in pharmaceutical industry and research. Growth of viruses in cell culture propagation and enumeration. *In vitro* screening techniques- cytotoxicity, anti-tumor, anti-viral assays.

UNIT V

Microbial pathology

Identifying the features of pathogenic bacteria, fungi and viruses. Mechanism of microbial pathogenicity, etiology and pathology of common microbial diseases and currently recommended therapies for common bacterial, fungal & viral infections. Mechanism of action of antimicrobial agents and possible sites of chemotherapy.

UNIT VI

Introduction to fermentation technology

Basic principles of fermentation

Study of the design and operation of bioreactor

Ancillary parts and function, impeller design and agitation, power requirements on measurements and control of dissolved oxygen, carbon dioxide, temperature, pH and foam.

Types of bioreactor

CSTR, tower, airlift, bubble column, packed glass bead, hollow fiber, configuration and application

Computer control of fermentation process

System configuration and application

UNIT VII

Mass transfer and Rheology

Mass transfer

Theory, diffusional resistance to oxygen requirements of microorganisms, measurements of mass transfer co- efficient and factor affecting them, effects of aeration and agitation on mass transfer, supply of air, air compressing, cleaning and sterilization of air and plenum ventilation, air sampling and testing standards for air purity.

Rheology

Rheological properties of fermentation system and their importance in bioprocessing.

UNIT VIII

Scale up of fermentation process

Principles, theoretical considerations, techniques used, media for fermentation, HTSTsterilization, advantage and disadvantage, liquid sterilization.

Cultivation and immobilized culture system

Cultivation system - batch culture, continuous culture, synchronous cultures, fed batch culture. Graphical plot representing the above systems.

Introduction to immobilization

Techniques, immobilization of whole cell, immobilized culture system to prepare fine chemicals. Immobilization of enzymes and their applications in the industry. Reactors for immobilized systems and perspective of enzyme engineering.

UNIT IX

Downstream process

Theory, equipment design and operation, methods of filtration, solvent extraction, chromatographic separation, crystallization turbidity analysis and cell yield determination, metabolic response assay, enzymatic assay, bioautographic techniques and disruption of cells for product recovery.

UNIT X

Bioprocessing of the industrially important microbial metabolites

a. Organic solvents – Alcohol and Glycerol
b. Organic acids - Citric acids, Lactic acids,
c. Antibiotics - Penicillin, Streptomycin, Griseofulvin,
d. Vitamins - B12, Riboflavin and Vitamin C
e. Amino acids - Glutamic acids, Lysine, Cyclic AMP and GMP

Biosynthetic pathways for some secondary metabolites, microbial transformation of Steroids; Biotransformation for the synthesis of chiral drugs; Bio catalysis process. Production of single-cell protein, Production of probiotic & postbiotics; Regulation governing the manufacturing of biological products

REFERENCES:-

1. W.B. Hugo and A.D. Russel: Pharmaceutical Microbiology, Blackwell Scientific publications, Oxford London.
2. Prescott and Dunn, Industrial Microbiology, CBS Publishers & Distributors, Delhi.
3. Pelczar, Chan Kreig, Microbiology, Tata McGraw Hill edn.
4. David Freifelder, Molecular Biology, Narosa Publishing House.

5. R. Ian Freshney, Culture of animal cells – A manual of Basic techniques, Wileys publication house.
6. David Baltimore, Molecular cell biology, W H Freeman & Co publishers.
7. Cell biology vol-I,II,III by Julio E. Cells
8. Bergeys manual of systematic bacteriology, Williams and Wilkins- A Waverly company.
9. Peter Stanbury, Allan Whitaker, Stephen Hall, Principles of Fermentation technology, 3rd edition, Elsevier stores.
10. L.E. Casida, Industrial Microbiology, John Wiley & sons Inc.
11. F.M. Asubel, Current protocols in molecular biology, volume I and II, John Wiley Publishers.
12. Biotol Board, Bioreactor design and product yield, Butterworth and Helhemann publishers.
13. A. H. Patel, Industrial microbiology, Macmillan India Limited.

ADVANCED PHARMACEUTICAL BIOTECHNOLOGY INCLUDING IMMUNOTECHNOLOGY (MPB-II)

THEORY **120 Hrs**

UNIT I

Enzyme Technology

Classification, general properties of enzymes, dynamics of enzymatic activity, sources of enzymes, extraction and purification of enzyme; Applications of enzyme in pharmaceutical, therapeutic and clinical. Production of amyl glucosidase, glucoseisomerase, amylase and trypsin.

UNIT II

Genetic Engineering

Techniques of gene manipulation, cloning strategies, procedures, cloning vectors expression vectors, recombinant selection and screening, expression in E.coli and yeast. Site directed mutagenesis, polymerase chain reaction, and analysis of DNA sequences.

Gene library and cDNA

Applications of the above technique in the production of,

Regulatory proteins	- Interferon, Interleukins
Blood products	-Erythropoietin
Vaccines	- Hepatitis-B
Hormones	-Insulin

UNIT III

Therapeutic peptides

Study on controlled and site specified delivery of therapeutic peptides and proteins through various routes of administration.

Transgenic animals

Production of useful proteins in transgenic animals and gene therapy.

Human Genome

The human genome project-a brief study, Human chromosome – Structure and classification, chromosomal abnormalities – Syndromes

UNIT IV

Signal transduction

Introduction, cell signaling pathways, Ion channels, Sensors and effectors, ON and OFF mechanisms, Spatial and temporal aspects of signaling, cellular process, development, cell cycle and proliferation, neuronal signaling, cell stress, inflammatory responses and cell death, signaling defects and diseases.

Oncogenes

Introduction, definition, various oncogenes and their proteins. Tumor suppressor genes.

UNIT V

Microbial Biodegradation

Biodegradation of xenobiotics, chemical and industrial wastes,
Applications of microbes in environmental monitoring.

Biosensors

Definition, characteristics of ideal biosensors, types of biosensors, biological recognition elements, transducers, application of biosensors.

UNIT VI

Fundamental aspects of immunology

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

UNIT VII

Immune Regulation and Tolerance

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

UNIT VIII

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

UNIT IX
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.

UNIT X

Immunological Disorder
Autoimmune disorders and types, pathogenic mechanisms, treatment, experimental models of auto immune diseases, primary and secondary immunodeficiency disorders.

Immunodiagnostics
Antigen antibody interaction – Precipitation reaction, Agglutination reactions, Principles and applications of ELISA, Radio Immuno Assay, Western blot analysis, immune-electrophoresis, immunofluorescence, chemiluminescence assay.

REFERENCES:-

1. Biotechnology-The biological principles: MD Trevan, S Boffey, KH Goulding and P.F. Stanbury.
2. Immobilization of cells and enzymes: Hosevear Kennady cabral & Bicker staff
3. Principles of Gene Manipulating: RW Old and S.B. Primrose.
4. Molecular Cell Biology: Harvey Lodish, David Baltimore, Arnold Berk, S Lawence Zipursky, Paul Matsudaira, James Darnell.
5. Modern Biotechnology: S.B Primrose
6. Gene transfer and expression protocols-methods in Molecular Biology, vol. VII, Edit E.T. Murray
7. Current protocols in Molecular Biology, Vo1.I & II:F.M. Asubel, John wiley

Publishers
8. Current protocols in cellular biology, Vo1.1 & II John wiley publishers.
9. Principles of human genetics; by Curt Stern, published by W.H. Freeman, 1960.
10. J. Kubey, Immunology – an Introduction.
11. S.C. Rastogi, Immuno diagonstics, New Age International.
12. Ashim Chakravarthy, Immunology and Immuno technology, Oxford UniversityPress.
13. E. Benjamini, Molecular Immunology.

PROTEINS AND PROTEIN FORMULATIONS, BIOINFORMATICS AND COMPUTER TECHNOLOGY INCLUDING BIOLOGICAL EVALUATION OF DRUG THERAPY (MPB-III)

UNIT I **THEORY 120 Hrs**

Protein engineering

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

UNIT II

Peptidomimetics

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.

UNIT III

Proteomics

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 IPGs), resolution, reproducibility and image analysis, future developments

UNIT IV

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.

UNIT V

Methods of protein sequencing

Various methods of protein sequencing, characterisation, Edman degradation, Tryptic and/or Chymotryptic Peptide Mapping.

UNIT VI

Introduction to Bioinformatics

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.

UNIT VII

Sequence analysis

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.

UNIT VIII

Protein informatics

Introduction; Force field methods; Energ, buried and exposed residues, side chains and neighbours; Fixed regions, hydrogen bonds, mapping properties onto surfaces; Fitting monomers, rms 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, Topologyfingerprint 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 basedmethods 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.

UNIT IX

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.

UNIT X

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.

REFERENCE:-

1. H. Lodhishet. Al. Molecular Cell Biology, W. H. Freeman and Company
2. Protein Purification – Hand Book – 1998 Amersham pharmacia biotech
3. Engelbert Buxbaum, Fundamentals of Protein Structure and Function, SpringerScience
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.
9. David W. Mount, Bioinformatics Sequence and Genome Analysis, CBS Publishers and Distributors
10. S. C. Rastogiet. al. Bioinformatics- Concepts Skill and Applications, CBS Publishers and Distributors
11. T. E. Creighton, Protein Structure and Molecular Properties, H.Freeman and Company.
12. Andreas D. Baxevanis, B. F. Francis Ouellette, Bioinformatics; A Practical Guide to the Analysis of Genes and Proteins, John Wiley & Sons, Inc.
13. Arthur M. Lesk, Introduction to Bioinformatics, Oxford University Press.
14. Shui Qing Ye. Bioinformatics: A Practical Approach, Chapman & Hall/CRC.
15. David Posada, Bioinformatics for DNA Sequence Analysis, Humana press.
16. Lesk, A.M. Introduction to Bioinformatics. Oxford University Press.
17. Letovsky, S.I. Bioinformatics. Kluwer Academic Publishers.
18. Baldi, P. and Brunak, S. Bioinformatics. The MIT Press.
19. Perkins F.T., Hennessen W. Standardization and Control of Biologicals Produced by Recombinant DNA Technology, International Association of Biological standardization.

PRACTICAL PAPERS

PRACTICALS (MPB-IV)

1. Isolation and Purification of microorganism from the soil
2. Microbial contamination of Water and biochemical parameters.
3. Determination of Minimum Inhibitory concentration by gradient plate technique and serial dilution method.
4. UV- survival curve and Dark repair
5. Sterility test for pharmaceutical preparations
6. Sub culturing of cells and cytotoxicity assays.
7. Construction of growth curve and determination of specific growth rate and doubling time
8. Fermentation process of alcohol and wine production
9. Fermentation of vitamins and antibiotics
10. Whole cell immobilization engineering
11. Thermal death kinetics of bacteria
12. Replica plating and Bio-autography.
13. Isolation and estimation of DNA and RNA
14. Agarose gel electrophoresis.
15. SDS – polyacrylamide gel electrophoresis for proteins
16. Polymerase chain reaction technique.

PRACTICALS (MPB-V)

1. Partial Protein purification
2. Protein Quantification
3. Protein analysis by SDS –PAGE
4. Protein formulation (Protein stability testing
5. Database searching
6. Sequence analysis methods
7. Protein structure prediction (Using Bioinformatics tools)
8. Phylogenetic analysis
9. Primer design using softwares.
10. Introduction to PCR – working of PCR, Programming.
11. Preparation of DNA for PCR applications – Isolation, Purity and Quantification
12. Introduction to RT-PCR – working, programming.
13. Gene DNA amplification by random / specific primers.
14. Western Blotting