MEDICAL AND PHARMACEUTICAL BIOTECHNOLOGY
(BIOT 3221)

Time Allotted : 3 hrs **Full Marks : 70**

Figures out of the right margin indicate full marks.

Candidates are required to answer Group A and any 5 (five) from Group B to E, taking at least one from each group.

Candidates are required to give answer in their own words as far as practicable.

Group – A
(Multiple Choice Type Questions)

1. Choose the correct alternative for the following: **10 × 1 = 10**

(i) Of the biopharmaceutical proteins that have been produced by recombinant means, the ones that have been expressed in yeast have which one of the expression level percentages ?
(a) 30% (b) 20%
(c) 50% (d) None of (a), (b) & (c).

(ii) Which one of the following DOES NOT constitute a test on a potential new drug in the preclinical phase of drug development?
(a) Pharmacokinetic profile (b) Pharmacodynamic profile
(c) Bioequivalence and bioavailability (d) Global tolerance.

(iii) Glucagon is a hormone that has which one of the following characteristics?
(a) Single chain polypeptide of 29 amino acid residues
(b) Synthesized by the B cells of the Islets of Langerhans
(c) Can cause hypoglycaemia
(d) Has an overall anabolic effect.

(iv) RISC is used to inhibit expression of gene at
(a) DNA level (b) RNA level
(c) Protein level (d) None of the above.

(v) CD4 markers are present on the surface of
(a) Cytotoxic T cells (b) Helper T cells
(c) B cells (d) RBC.

(vi) Glucocorticoids are usually employed as
(a) Immunosuppressive agents
(b) Anti-inflammatory agents
(c) Adrenal insufficiency replacement therapy
(d) All of the above.

(vii) Detection of antibody by Evanescent wave is a type of
(a) Piezoelectric Biosensors (b) Calorimetric Biosensors
(c) Optical Biosensors (d) Amperometric Biosensors.

(viii) "Flipped LDH" is an indicative of
(a) Heart Attack (b) Hepatitis
(c) Haemolytic anaemia (d) Prostate cancer.

(ix) Betamethasone fits which one of the following choices?
(a) Synthetic corticosteroid; used as an anti-inflammatory drug
(b) Used for treatment of Addison's disease
(c) Its biological response includes lipolysis of adipose tissue
(d) Can be used as a local anaesthetic.

(x) Biosensors which detect changes in light is known as
(a) Piezoelectric Biosensors (b) Amperometric Biosensors
(c) Optical Biosensors (d) None of (a), (b) & (c).

Group - B

2. (a) The effectiveness of an intravenous administration of a lifesaving antibiotic is partially dependent on the plasma halflife given by $t_{1/2} = 0.693 \text{ X } V_d/Cl_{int}$. What are typical values of $t_{1/2}$? What is the significance of a low and high $t_{1/2}$ value?

Property	Small molecule pharmaceutical(s)	Biologics/biopharmaceutical
Stability	Stable	Unstable
Specificity	Non-specific	Specific
Distribution	Via circulation, easily distributed	Via circulation and lymphatics, limited distribution
Immunogenicity	No	Yes

Use the above table to briefly comment on the difficulties inherent in the preclinical toxicological assessment of biopharmaceutical drugs.

[(CO2)(Understand-analyse/IOCQ)]

(b) Define a biosimilar drug with examples from two different classes of biologics which were permitted to be developed as biosimilars. Define the following terms consistent with pharmaceutical use as a biosimilar: heterogeneity and interchangeability using examples wherever appropriate. List the factors that contribute to the immunogenic response of either a biologic or biosimilar drug.

[(CO1,CO2)(Understand-analyze/LOCQ)]

(c) A global alliance to fight antimicrobial resistance has been a medical priority for a considerable period of time. One of the commonest classes of antibiotics are the β-lactam antibiotics. Briefly explain the two modes of β-lactam resistance.

[(CO1)(Understand-explain/IOCQ)]

4 + 5 + 3 = 12

3. (a) Recombinant (human) Interferonβ (RhIFN-β) has been found to have therapeutic applications in the treatment of autoimmune diseases including

relapse-remission multiple schlerosis , a chronic disease of the nervous system. How does this disease progress? What are the clinical presentations of this disease? Such recombinant biopharmaceutical products of IFN-β have been clinically approved in two cellular expression systems. What are they? Briefly explain your answers. Suppose the Rh-IFN-β under production was in a *E. coli* expression system. What are the anticipated structural differences between native and recombinant IFN-β? *[(CO1)(Understand-analyze/IOCQ)]*

(b) Using a labelled flowchart overview for the manufacture of a (RhIFN-β) explain the role of E.coli fermentation, use of inclusion bodies (IB) and the downstream processing part of this purification process. How is shelf-life of this recombinant biopharmaceutical stabilized in this purification process?

[(CO1)(Understand-apply/IOCQ)]

(c) Use a table to represent the ADRs (adverse drug responses) associated with administration of IFN-β. Why is it difficult to predict such side effects and what clinical means have been adopted to counteract such ADRs?

[(CO2)(Analyze/IOCQ)]

5 + 4 + 3 = 12

Group - C

4. (a) State the detection of two different types of lymphomas with the help of FACS.

[(CO3)(State/LOCQ)]

(b) Illustrate the process of inhibiting the gene expression with the help of Peptide Nucleic Acids (PNA). *[(CO4)(Illustrate/IOCQ)]*

6 + 6 = 12

5. (a) Comment on the benefits of Pharmacogenomics. *[(CO4)(Comment/IOCQ)]*

(b) Design the gene therapeutic technique of treating SCID with the help of a retrovirus. *[(CO4)(Design/HOCQ)]*

5 + 7 = 12

Group - D

6. (a) (i) Define a thrombolytic agent. Use a diagram to represent a fibrinolytic system in which tissue plasminogen activator (t-PA) is involved. (ii) Ecokinase is a modified recombinant t-PA that has gained regulatory approval for clinical use. Using its flowchart for production explain the importance of the following steps in the production procedure: (A) use of inclusion bodies (B) affinity chromatography and ultrafiltration and (C) excipient addition.

[(CO1)(Understand-apply /IOCQ)]

(b) In a typical biopharmaceutical prep, a tissue homogenate was prepared from pig heart tissue in the preparation of the enzyme aspartate aminotransferase. Cell debris was removed by filtration and nucleic acids removed by treatment with polyethyleneimine, leaving a total extract of 2 dm^3. A sample of this extract (50 mm^3) was added to 3 cm^3 of buffer in a 1 cm path length cuvette and the absorbance at 280 nm was shown to be 1.65. What is the approximate protein

concentration in the extract and hence the total protein content of the extract? Explain the upstream processing steps leading upto the protein estimation.

[(CO1)(Calculate-analyze/IOCQ)]

(2 × 4) + 4 = 12

7. (a) Enlist the characteristics of a protein that make it ideal for use as a biomarker of a disease state. Name the types of biomarkers that are in common use in diagnostic clinical practice. What biomedical characteristics make molecular biomarkers most useful in clinical diagnosis? *[(CO3)(Understand-apply/IOCQ)]*

(b) What are the possible uses of a microarray? Tabulate the differences between a functional and an analytical microarray. *[(CO4)(Understand-LOCQ)]*

(c) What are the reasons for validation of an immunoassay? Using one example highlight the quantitative parameters and boundary values for such a validation. How are these validation procedures confirmed when testing for low levels of antigen in blood serum? *[(CO4)(Understand-Analyze/IOCQ)]*

5 + 3 + 4 = 12

Group - E

8. (a) Name a diagnostic enzyme that is used to detect Myocardial infarction. State it's principle of action in our body. Write down the assay by which you can detect it in blood. *[(CO6)(Understand/LOCQ)]*

(b) Discuss the applications of carbon nanotubes in a biosensor. *[(CO5)(Discuss/IOCQ)]*

(1 + 3 + 3) + 5 = 12

9. (a) Illustrate the process of detecting DNA in a sample with the help of Optical Biosensor. *[(CO5)(Illustrate/HOCQ)]*

(b) Design the working principle of Human Immunodeficiency Virus Rapid Test Kit**.** *[(CO6)(Design/HOCQ)]*

6 + 6 = 12

Cognition Level	*LOCQ*	*IOCQ*	*HOCQ*
Percentage distribution	*21.88*	*58.33*	*19.79*

Course outcomes (CO):

At the end of this course students will be able to:

1. Understand and apply principles and practices of drug development of biopharmaceuticals (e.g. insulin, interferons, EPO); pharmaceuticals of biological origin (e.g. corticosteroids) and microbial origin (e.g. antibiotics) including synthesis, biological and therapeutic characteristics (e.g.PK/PD profiles) of such molecules.
2. Understand the methodological and technological differences between formulation, delivery and post-production quality control of biopharmaceuticals versus small molecule pharmaceuticals.
3. Understand the process of discovery, technological developments and subsequent applications of monoclonal antibodies, DNA/RNA based diagnostics and protein based biomarkers.
4. Understand principles and applications of the following topics with relevance to disease therapeutics: vaccines, gene therapy, proteomics techniques in drug development.
5. Understand the principles of fabrication, operation and clinical applications of biosensors.
6. Understand and apply principles of enzymology for applications in microclinical diagnostics in kits and biochips.

**LOCQ: Lower Order Cognitive Question; IOCQ: Intermediate Order Cognitive Question; HOCQ: Higher Order Cognitive Question.*