KUMARAGURU
college of technology
character is life

B.TECH DEGREE EXAMINATIONS: MAY 2017

(Regulation 2014)

Sixth Semester

BIOTECHNOLOGY

U14BTT603:Biopharmaceutical Technology

COURSE OUTCOMES

CO1: Outline drug standards and pharmacopoeia commission
CO2: Describe the principles of drug action and mechanism of action
CO3: Discuss and obtain knowledge on the drug development and manufacture process
CO4: Explain the principles and materials involved during the drug manufacture in pharmaceutical industries
CO5: Discuss the clinical uses of biopharmaceutical therapeutics

Time: Three Hours **Maximum Marks: 100**

Answer all the Questions:-

PART A (10 x 1 = 10 Marks)

1. A drug (200 mg dose) administered in tablet form and as intravenous injection (50 mg dose) showed AUC of 100 and 200 microgram hr/mL, respectively. The absolute availability of the drug through oral administration is: CO2 [K_3]

   a) 125%. b) 250 %
   c) 12.5% d) 1.25%

2. These are statements related to protein binding of drugs, choose the correct statements from below, CO2 [K_3]

   [P]: Protein binding decreases the free drug concentration in the system.

   [Q]: Protein binding to plasma albumin is an irreversible process.

   [R]: Drugs with low lipophilicity have a high degree of protein binding.

   [S]: Protein binding of one drug can be affected by the presence of other drug.

   a) P & Q b) Q & R
   c) R & S d) P & S

3. Assertion (A): Levo-dopa is preferred over Dopamine because it can cross blood brain barrier CO2 [K_3]

Reason (R): Levo-dopa is a prodrug and Dopamine does not cross blood brain barrier.

a) Both A and R are true and R is the correct explanation of A
b) Both A and R are true but R is not a correct explanation of A
c) A is true but R is false
d) A is false but R is true

4. Which of the following attributes of a drug tends to reduce its volume of distribution, (Vd). CO2 [K_2]

a) High lipid solubility
b) Low ionization at physiological pH
c) High plasma protein binding
d) High tissue binding

5. A laboratory is conducting a study to assess the safety, efficacy, and potency of a group of drugs before allowing the agents to proceed to clinical trials. Figure 2.a shows the dose-response curves for four different drugs (Drugs A, B, C, & D). Decide the correct statement after analysis. CO2 [K_5]

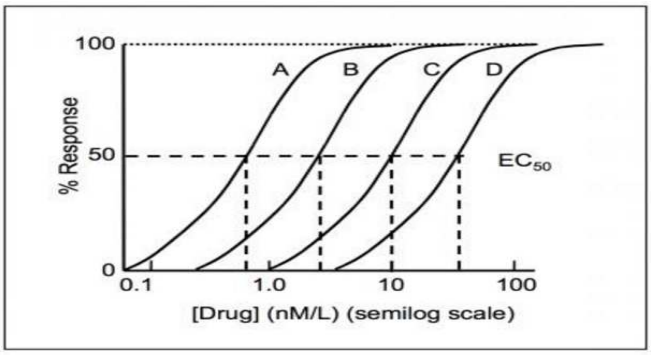

Fig 2.a

a) D has greater potency and efficacy
b) A has greater potency and D have greater efficacy
c) A has greater potency and all have similar efficacy
d) D has greater potency and A has greater efficacy

6. Place in correct order the action of a water-soluble hormone on its target cell. CO2 [K_3]

1. Adenylate cyclase activated, catalyzing conversion of ATP to Camp.
2. Enzymes catalyze reactions that produce physiological response attributed to the hormone.
3. Hormone binds to plasma membrane receptor.
4. Activated protein kinase phosphorylate cellular proteins
5. Hormone-receptor complex activates G-proteins.
6. Cyclic AMP activates protein kinases.

a) 3, 5, 1, 6, 4, 2
b) 3, 1, 5, 6, 4, 2
c) 5, 1, 4, 2, 3, 6
d) 3, 4, 5, 1, 6, 2

7. An inventor was awarded a patent in the USA, on a method for producing recombinant antibody and has practiced the mentioned method only in the USA. Twenty Six years later, another person who wants to manufacture the same recombinant antibody by a different method. She: CO3 [K_4]

a) Would be able to manufacture a generic version if the patent has expired.
b) could do it without major problems
c) would not be able to do it because the method is used in the USA.
d) would not be able to do it because the granted patent was published in the USA.

8. Assertion (A): Ontak is a biologic agent that is approved for the treatment of cutaneous T-cell lymphoma. CO5 [K_5]

Reason (R): Ontak is an interferon so used for cancer treatment.

a) Both A and R are true and R is the correct explanation of A
b) Both A and R are true but R is not a correct explanation of A
c) A is true but R is false
d) A is false but R is true

9. Drugs in suspensions and semi-solid formulations always degrade. CO4 [K_2]

a) first order kinetics
b) second order kinetics
c) zero order kinetics
d) non-linear kinetics

10. Match the activity in List II with the law that mandates it in List I. CO1 [K_3]

List I (LAW)	**List II (MANDATES)**
A. Federal Food Drug and cosmetic Act, 1938	i. Regulates approval of Biologics in India
B. Indian National Biotechnology ACT ,2008	ii. Encourages drug makers to develop drugs that to treat uncommon rare diseases.
C. Indian Pharmacopoiea commission,1945	iii. Prohibits the distribution and use of any new drug without the prior approval of the FDA.
D. Orphan Drug Act	iv. Sets standards for all drugs that are manufactured, sold and consumed in India

	A	B	C	D
a)	iii	i	iv	ii
b)	iv	i	ii	iii
c)	i	iii	ii	iv
d)	ii	i	iv	iii

PART B (10 x 2 = 20 Marks)

(Answer not more than 40 words)

11.	Can therapeutic drug monitoring (TDM) be performed without taking blood samples? Justify from FDA's perspective and your choice of drug sampling.	CO1	[K_4]
12.	What is the significance of plasma level time curve relate to the pharmacologic activity of drug?	CO2	[K_3]
13.	Justify why zone of inhibition in an antibiotic disc is larger for the same drug concentration (10mug/ml) in water than in serum? List the macromolecules which participate in drug- protein binding?	CO2	[K_4]
14.	How can the absorption of drugs from subcutaneous sites be promoted?	CO4	[K_5]
15.	Why is pharmacokinetics important in studying drug interactions?	CO4	[K_3]
16.	When TI is narrow, the drug has to be cautiously administered. Give your reason with definition of therapeutic index.	CO3	[K_3]
17.	What physical and chemical properties of a drug substance are important in designing a drug for (a) oral administration (b) parental administration?	CO4	[K_4]
18.	According to the prescribing information for cimetidine, following IV or IM administration, 75% of the drug is recovered from the urine after 24hrs as parent compound. Following a single oral dose, 48% of the drug is recovered from the urine after 24hrs as the parent compound. From this information determine what fraction of the drug is absorbed systemically from an oral dose after 24hrs.	CO2	[K_4]
19.	Enlist medical applications of Colony Stimulating Factor and differentiate various CSF based on functional uniqueness.	CO5	[K_2]
20.	What is the primary reason that protein drugs such as insulin are not given orally for systemic absorption?	CO5	[K_4]

Answer any FIVE Questions:-

PART C (5 x 14 = 70 Marks)

(Answer not more than 300 words)

Q.No. 21 is Compulsory

21. Working for an innovative pharmaceutical company, you have received a request to develop an oral liquid formulation for a new organ rejection drug. Formulate a drug development strategy. Elucidate the process of drug discovery and development phase in detail with illustrations. CO3 [K_5]

22. i) Write a short note on merger of United States Pharmacopoeia and American Pharmaceutical society National Formulary. (4) CO1 [K_2]

    ii) Explain the role of FDA. (10)

23. i) Write a short account on significance of Cytochrome P^{450} and implications of CYP induction and inhibition. (4) CO2 [K_3]

    ii) Explain biotransformation with appropriate examples. (10)

24. i) What are the main factors that determine uptake and accumulation of a drug into tissues? (4) CO2 [K_5]

    ii) Comparison of plasma concentration of antibiotic as related to Dosage form is given below, (10)

Plasma Concentration (µg/ml)				
Time after Dose (h)	IV Solution (2mg/kg)	Oral Solution (10mg/kg)	Oral Tablet (10mg/kg)	Oral Capsule (10mg/kg)
0.5	5.94	23.4	13.2	18.7
1.0	5.30	26.6	18.0	21.3
1.5	4.72	25.2	19.0	20.1
2.0	4.21	22.8	18.3	18.2
3.0	3.34	18.2	15.4	14.6
4.0	2.66	14.5	12.5	11.6
6.0	1.68	9.14	7.92	7.31
8.0	1.06	5.77	5.00	4.61
10.0	0.67	3.64	3.16	2.91
12.0	0.42	2.30	1.99	1.83
AUC (µg/ml * h)	29.0	145.0	116.0	116.0

The data in Table represents the average findings in antibiotic plasma samples taken from 10 humans (average weight = 70kg), tabulated in a 4way crossover design.

a) Which of the four drug products in Table would be preferred as a reference standard for the determination of the relative bioavailability?

b) From which oral drug product is the drug absorbed more rapidly?

c) What is the absolute bioavailability of the drug from the oral solution?

d) What is the relative bioavailability of the drug from the oral tablet compared to the reference standard?

25. **Case study:** Production of 'Humaspect' CO3 [K_5]

Humaspect is an intact human monoclonal antibody. It is directly produced from a human lymphhoblastoid cell line that was transformed by Epstein-Barr virus. The antibody is labeled with Technium (^{99M}Tc) prior to clinical use. Humaspect specifically binds to a cytokeratine tumor associated complex of antigens known as CTA16.88. These antigens are associated with human large bowel adenocarcinoma. The product's approved therapeutic indication is for the imaging in patients with colorectal cancers. No side-effects or the production process begins by growing the antibody producing lymphoblastoid cell line in a bioreactor of hollow fibre design. The product is a kit with purified antibody and a vial of coupling agent, which allows direct coupling of radiolabel before its clinical use.

Examples of the half-lives show that biological clearing is sometimes dominant and sometimes physical decay is the dominant influence.

Isotope	Half-lives in days		
	$T_{Physical}$	$T_{Biological}$	$T_{Effective}$
^{3}H	4.5×10^{3}	12	12
^{32}P	14.3	1155	14.1
^{90}Sr	1.1×10^{4}	1.8×10^{4}	6.8×10^{3}
^{99m}Tc	0.25	1	0.20

i) What advantage ^{99M}Tc has over other radioactive tracer isotopes? (2)

ii) Define biological half life of a radioisotope. Comment on the biological clearing of ^{99M}Tc. (3)

iii) Write a short note on radioimmunoscintigraphy. (5)

	iv) ^{32}P, is used for some kinds of bone scans. The phosphorous tends to be held in the bones, leading to a long biological half-life, but its physical half-life is short enough to minimize exposure. Similarly, what specificity 'Humaspect' offers?	(2)		
	v) Define radioisotope.	(2)		
26.	i) Compare and contrast good laboratory practice, good clinical practice and good manufacturing practice.	(3)	CO4	[K_3]
	ii) If cGMP non-compliance issues are observed during FDA inspection. Should the product be recalled or should the company go for 'consent decree'? Give your opinion with reason.	(3)		
	iii) Differentiate between an endotoxin and pyrogen and write the significance of LAL test.	(4)		
	iv) Classify clean room facility and its importance.	(4)		
27.	i) Elucidate the steps involved in recombinant insulin production system highlighting the drawbacks of currently available insulin preparations. Explain various insulin preparations available till date with their characteristic features.	(9)	CO5	[K_4]
	ii) Compare and contrast the functions of insulin and glucagon.	(5)		

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