BP 604T

Roll No. | | | | | | | | | | |

SHAMBHUNATH INSTITUTE OF PHARMACY
Biopharmaceutics & Pharmacokinetics
B. Pharm, IIIrd Year (VIth Sem.)
Ist Sessional Examination 2019-2020

Time: 1.5 Hours. *Max. Marks: 30*

SECTION-A

1. Attempt all the questions: (1X5=5)

Q.N	QUESTION	Marks	CO	BL
a)	Define bioavailability. Ans. The proportion of the dose of a drug that rea ches the systemic circulation intact after ad ministration by a route other than intraveno us called as bioavailability.	1	3	1
b)	Define absolute and relative bioavailability. Ans. Absolute bioavailability may be calculated by comparing the total amount of intact drug that reaches the systemic circulation after the administration of a known dose of the dosage form via a route of administration, with the total amount that reaches the systemic circulation after the administration of an equivalent dose of the drug in the form of an intravenous bolus injection. Relative bioavailability is a measure of the fraction (or percentage) of a given drug that is absorbed intact into the systemic circulation from a dosage form relative to a recognized (i.e. clinically proven) standard dosage form of that drug.	1	3	1
c)	Name the various drug binding sites on HSA. Ans. Four different sites; Warfarin, Diazepam, Digitoxin, Tamoxifen	1	1	1
d)	Classify the drug transport mechanisms. Ans. Passive transport i) Simple diffusion or passive diffusion ii) Osmosis iii) Facilitated diffusion Active transport i) Primary active transport ii) Secondary active transport	1	1	1
e)	Define disposition. Ans. It is defined as the processes that tend to lower the plasma concentration of drug.	1	1	1

SECTION-B

2. Attempt any two of the following: (2X5=10)

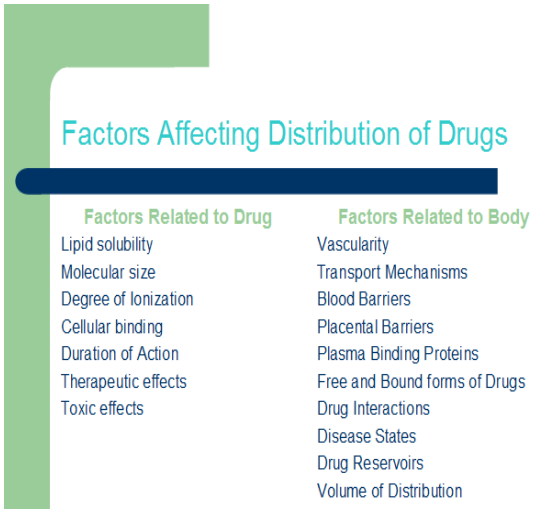
Q.N	QUESTION	Marks	CO	BL
a)	What are the different sites of presystemic metabolism of orally administered drugs? Ans. The 3 primary systems which affect presystemic metabolism of a drug are: Luminal enzymes • Digestive enzymes • Bacterial enzymes Gutwall enzymes Hepatic enzymes	5	1	1

b)	Discuss the limitations and significance of pH-partition hypothesis. Ans. Limitations: • Presence of virtual membrane pH • Absorption of ionized drug • Influence of GI surface area and residence time of drug • Presence of aqueous unstirred diffusion layer • Significance: It provides a basic framework for understanding drug absorption.	5	1	3
c)	Describe the anatomy and physiology of blood brain barrier. What characteristics of a drug are necessary to penetrate such a barrier? Ans. The blood-brain barrier is formed by endothelial cells of the capillary wall, astrocyte end-feet ensheathing the capillary, and pericytes embedded in the capillary basement membrane. This system allows the passage of some molecules by passive diffusion, as well as the selective transport of various nutrients, ions, organic anions, and macromolecules such as glucose, water and amino acids that are crucial to neural function.	5	1	1
d)	Explain the kinetics of protein-drug binding. What are the different plots for it? Explain. Ans. P+D----PD Ka= [PD]/[P][D] P_T= [PD]+ [P] 4 different plots are as follows: 1. Direct plot 2. Scatchard plot 3. Klotz plot 4. Hitchcock plot	5	2	1

SECTION-C

5. Attempt any one of the following: (1x5=5)

Q.N	QUESTION	Marks	CO	BL
a)	What do you understand by sink conditions? How is it maintained and responsible for complete passive absorption of drugs from the GIT? Ans. One of the requirements to conduct an appropriate drug dissolution test is to use a sufficient volume of dissolution medium, which should be able to dissolve the expected amount of drug released from a product. This ability of the medium to dissolve the expected amount of drug is known as a "sink condition". It is important to note that a dissolution test should not be conducted in a volume of the medium which would not dissolve the expected amount of the drug completely and freely.	5	1	3
b)	Why is distribution of a drug not uniform throughout the body? List the factors influencing drug distribution. Ans. Distribution of a drug not uniform	5	1	2

	throughout the body because of different following factors which influence drug distribution:  			

6. Attempt any one of the following: (1x5=5)

Q.N	QUESTION	Marks	CO	BL
a)	A protein bound drug is both pharmacokinetically as well as pharmacodynamically inert. Explain. **Ans.** A protein bound drug is both pharmacokinetically as well as pharmacodynamically inert i.e. a protein bound drug is neither metabolized nor excreted nor is it pharmacologically active. A bound drug is also restricted since it remains confined to a particular tissue for which it has greater affinity. Moreover, such bound drug because of its enormous size cannot undergo membrane transport & thus its half life is increased. However this binding is rapidly reversible and non-specific – that is many drugs may bind to the same protein. Drug–plasma protein binding forms a "reservoir" of drug, but only the free (unbound) drug is available to the tissues to exert a therapeutic effect. Binding of drug generally is reversible process (hydrogen bond, hydrophobic bond, ionic bond, vander waal's forces). Irreversible drug binding though rare (covalent binding) is often a reason for carcinogenicity or tissue toxicity of drug ;for example covalent binding of paracetamol metabolites to liver results in hepatotoxicity.	5	1	2
b)	What are the two major rate- limiting steps in the distribution of drugs? Under what circumstances are they applicable? Ans. Distribution is the reversible transfer of a drug from one location to another within the body. Once a drug enters into systemic circulation by absorption or direct administration, it must be distributed into interstitial and intracellular fluids. Each organ or tissue can receive different doses of the drug and the drug can remain in the different organs or tissues for a varying amount of time. The distribution of a drug between tissues is dependent on vascular permeability, regional blood flow, cardiac output and perfusion rate of the tissue and the ability of the drug to bind tissue and plasma proteins and its lipid solubility.	5	1	1

7. Attempt any one of the following: (1x5=5)

Q.N	QUESTION	Marks	CO	BL
a)	Explain the various theories of drug dissolution. Ans. Dissolution is a process in which a solid substance solubilises in a given solvent.	5	1	1

	The important theories of drug dissolution are: • Diffusion layer model The diffusion layer model proposed originally by Nernst and Brunner (Brunner, 1904; Nernst, 1904) is widely used to describe the dissolution of pure solid substances. In this model, it is assumed that a diffusion layer (or a stagnant liquid film layer) of the thickness h is surrounding the surface of a dissolving particle. The reaction at the solid-liquid interface is assumed to be instantaneous. Thus, equilibrium exists at the interface, and hence the concentration of the surface is the saturated solubility of the substance (Cs). • Danckwert's model Danckwert's model suggests that the transport of solute is achieved by the macroscopic packets that reach the solid surface, absorb solutes at the surface, and deliver them to the bulk solution. • Interfacial barrier model The interfacial barrier model assumes that the reaction at the solid surface is significantly slower than the diffusion across the interface. Therefore, no equilibrium exists at the surface, and the liberation of solutes at the solid-liquid interface controls the overall rate of the transport process.			

b)	Why is *in- vivo* drug dissolution always faster than *in-vitro* dissolution? What conditions should be simulated in order to obtain a good relationship? Ans. *In- vivo* drug dissolution always faster than *in-vitro* dissolution because it follows sink condition. *in vitro – in vivo* correlation (IVIVC) allows prediction of the *in vivo* performance of a drug based on the *in vitro* drug release profiles. To develop an effective IVIVC, the physicochemical and biopharmaceutical properties of the drug as well as the physiological environment in the body must be taken into consideration. Key factors include drug solubility, pKa, drug permeability, octanol-water partition coefficient and pH of environment. In general, construction of an IVIVC involves three stages of mathematical manipulation: construct a functional relationship between input (*in vitro* dissolution) and output (*in vivo* dissolution); establish a structural relationship using data collected; parameterize the unknowns in the structural model.	5	1	2