St.James College of Pharmaceutical Sciences St.James medical Academy River Bank, Chalakudy			
Programme:	B. Pharm	Sem.:	VI
Name of Course: (*Subject*)	Biopharmaceutics and Pharmacokinetics	Course Code:	BP 604 T
Teaching faculty of the course	Dr. Smitha.K. Nair & Ms. Dony Lonappan		

Summary of the Lecture Plan

Topic	Lectures	Hours
Introduction to Biopharmaceutics	Mechanisms of drug absorption through GIT	1
	Factors influencing drug absorption though GIT	3
	Absorption of drug from Non per oral extra-vascular routes	1
	Distribution of drugs Tissue permeability of drugs and binding of drugs	2
	Protein binding of drugs, factors affecting protein-drug binding and Kinetics of protein binding	2
	Clinical significance of protein binding of drugs, Apparent volume of drug distribution	1
Biotransformation	Phase I Bioransformaion	2
	Phase II Bioransformaion	2
	Renal excretion of drugs, factors affecting renal excretion of drugs	1
	Renal clearance and Non renal routes of drug excretion of drugs	1
	Objectives of bioavailability studies, absolute and relative bioavailability, measurement of bioavailability,	1
	In-vitro drug dissolution models, in- vitro, in-vivo correlations	1
	bioequivalence studies, methods to enhance the bioavailability	2
Pharmacokinetics	Introduction to Pharmacokinetics models ,Compartment model	2
	Non compartment models, physiological models	1
	One compartment open model Intravenous Injection (Bolus)	2
	One compartment open model Intravenous infusion	1
	One compartment open model extra vascular administrations	2

	calculations KE from plasma and urinary excretion data	2
Multicompartment models	Two compartment open model. IV bolus	2
	Multiple – Dosage Regimens	2
	Repititive Intravenous injections – One Compartment Open Model	2
	Repititive Extravascular dosing – One Compartment Open model	2
Nonlinear Pharmacokinetics	Introduction	1
	Factors causing Non-linearity	3
	Michaelis-menton method of estimating parameters	3

Major issues or Core aspects to be addressed/ covered:

Topic Title: Introduction to Biopharmaceutics
1. Absorption of drug from gastrointestinal tract mechanisms and factors involved
A. Mechanisms of drug absorption: transcellular/intracellular transport paracellular /intercellular transport, vesicular transport
B .Factors influencing GI absorption of drug from dosage form:
i)Pharmaceutical factors affecting drug absorption: Drug solubility and dissolution ,particle size ,polymorphism and amorphism , pseudo polymorphism, salt form of drug , lipophilicity, Pka of drug and GI pH, Dosage form factors (characteristics and pharmaceutical ingredients)
ii) Patient related factors influencing GI absorption of drug: Gastric emptying time, Intestinal transit time, GI pH, Disease state, age ,Pre systemic metabolism etc
C. Absorption of drug from per oral route
2.Drug distribution : Process and factors associated
Tissue permeability and physicochemical properties of the drug, physiological barriers to drug distribution, tissue binding of drugs and perfusion rate, factors affecting drug distribution, volume of distribution, protein binding of drug , kinetics and its significance
Topic Title : Biotransformation
1.Phase I Biotransformation : Types of phase I Biotransformation process, oxidation reduction , hydrolysis ect
2.Phase II Biotransformation:Types of phase II Biotransformation process like conjugation reactions
3. Drug Elimination
i) Renal excretion of drugs and renal clearance
ii) Factors affecting renal excretion of drugs
iii) Non renal routes of drug excretion of drugs
4. Bioavailability and Bioequivalence
1. Bioavailability and Bioequivalence: Introduction i) Definition of terms: Bioavailability, Relative and Absolute bioavailability, Bioequivalence

ii) methods for the enhancement of the bioavailability of drugs

2. Methods of Assessment of Bioavailability
   i)Pharmacokinetic Methods: Plasma level versus time Studies, Urinary excretion versus time studies
   ii)Pharmacodynamic studies : Measurement of Pharmacologic and Therapeutic responses
   iii) In-vitro drug dissolution models

3. In- vitro- In-vivo correlations: Objective, types and different levels

4. Bioequivalence Study protocol
   i) Selection of Volunteers for the study as per legal requirements, study design
   ii) Duration of the study , estimation of Pharmacokinetic Parameters and interpretation of results

Topic Title: Pharmacokinetics

1. Introduction: Concept of Pharmacokinetic Compartmental Models:
   i)Basic considerations, definition of pharmacokinetics, concept of compartment, model, open & closed compartments;
   ii) Assumptions , concepts ,basic considerations ,types, advantages and limitations of compartment model, Non compartment models, physiological models.

2. Pharmacokinetics of open one compartment model: Intravenous Injection (Bolus) using blood level data.
   i. Scheme, graphical representation, rate of change of drug plasma level & equation to define it;
   ii. mathematical construct to define drug plasma level (including derivation);
   iii. plotting of drug plasma concentration vs time data in Cartesian as well as semilog paper
   iv. determination of elimination rate constant, biological half-life & apparent volume of distribution

3. Pharmacokinetics of open one compartment model: Intravenous Injection (Bolus) using urinary excretion data.
   i. Using urinary excretion data
   ii. Rate of excreation method – scheme, graphical presentation, mathematical construct defining excretion rate (including derivation), determination of elimination rate constant, biological half-life & apparent volume of distribution, limitations, merits.
   iii. Sigma minus method - mathematical construct defining Amount Remaining to be Excreted (ARE) (including derivation), determination of elimination rate constant, biological half-life & apparent volume of distribution, cumulative amount of drug excreted unchanged at different times, limitations, merits.

4. One compartment open model: Intravenous infusion.
   i. Short term constant rate infusion: Scheme Graphical representation, mathematical construct (including derivation) defining drug plasma level during infusion, on completion of infusion and post infusion.
   ii. Continuous i.v. infusion: scheme, graphical representation, mathematical constructs defining drug plasma level during infusion, steady state plasma drug concentration(Css);
   iii)loading dose calculation for specific Css, fixing infusion rate for specific Css

5. One compartment open model: extra vascular administrations
   i) Scheme, graphical representation, rate of change of drug plasma level & equation to define it
   ii) Determination of elimination rate constant, biological half-life ,Cmax, Tmax
   iii) Determination of Ka using method of residual and Wagner Nelson method

Topic Title: Multi compartment model

1. Pharmacokinetics Two Compartment Open Model: IV injection (using blood level data):
   i. Scheme, graphical representation, description of distribution and post distribution phases.
   ii. Mathematical construct to define drug plasma level in central compartment and peripheral compartment;
   iii. Derivation of equation to define drug plasma level in central compartment.
   iv. Construction of extrapolated line and line of residuals
   v. Determination of biological half-life (β half-life) and distribution half-life (α half-life)
   vi. Determination of different pharmacokinetic parameters

2. Concepts of multiple dosage regimen

3. Pharmacokinetics of Repititive Intravenous injections – Open One Compartment Model:
   i. Derivation of equations describing amount of drug in the body, plasma drug concentration during multiple dosing
   ii. Equation to define amount and concentration at steady state; maximum, minimum and average concentration at steady state.

4. Pharmacokinetics of Repetitive Extravascular dosing – Open One Compartment model:
   i. Pharmacokinetics of repetitive extravscular dosing – concentration – time profile, deducing equation to describe plasma drug concentration (Cn) from corresponding equation for i.v. dosing utilizing Bennet's multiple dosing function, equation for C_{ss}, $C_{ss(min)}$
   ii. Accumulation factor – definition, relation of dosing interval and half-life on drug accumulation at steady state .

Topic Title: Nonlinear Pharmacokinetics

1. Introduction to Nonlinear pharmacokinetics: Definition, concept, distinction between dose independent and dose dependent pharmacokinetics,

2. Methods to assess nonlinearity in pharmacokinetics, Factors responsible for nonlinearity

3. Methods for estimation of Michaelis –Menten's constants: Graphical methods, methods based on different doses

Sample Questions

Topic Title: Introduction to Biopharmaceutics
1. Mechanisms of absorption of drug from GIT
2. Explain any five pharmaceutical factors influencing GI absorption of drug
3. Patient related factors influencing absorption
4. What is 'sink condition ?
5. BCS classification of drug ?
6. Define distribution ? Explain different physiological barriers for the distribution of drug.
7. Define apparent volume of distribution and explain the significance of Vd.
8. Plasma protein binding
9. Factors influencing protein drug binding
10. Kinetics of protein binding
11. Significance of protein binding
Topic Title
1. Define Biotransformation ?
2. Classify Phase I Biotransformation and give five examples of oxidation reaction
3. Explain Glucuronidation reaction
4. Explain conjugation with Glutathaione and mercapturic acid formation
5. Explain Methylation
6. Mechanism of renal excretion of drug ?
7. Factors influencing renal excretion of drug
8. Explain any two non renal route of elimination
9. Entero hepatic recycling
10. Define Bioavailability , Bioequivalence, , absolute bioavilability and relative bioavailability
11. Methods for the measurement of bioavailability
12. List out the in-vitro drug dissolution models and explain Type I dissolution apparatus with diagram
13. IVIVC
14. Protocol for bioequivalence studies
15. Design of bioequivalence studies
16. Explain any five methods to enhance the bioavailability of drug
Topic Title : Pharmacokinetics
1. Define pharmacokinetics. Name and define the different pharmacokinetic and pharmacodynamics parameters that define a typical plasma level vs time curve.
2. What are pharmacokinetic models?

3. What is the importance of developing pharmacokinetic models
4. Compartment modeling
5. Explain the term MRT
6. Kinetics of One compartment open model. Intravenous Injection (Bolus)
7. What is steady state plasma drug concentration (Css); Deduce the equation to define plasma concentration of drug while the drug is administered as I.V infusion.
8. Explain sigma-minus method for estimation of elimination half-life. Mention its merits and demerits over excretion rate methods.
9. What is method of residuals? Explain.
10. Describe a method for estimation of absorption rate constant from plasma drug concentration vs time data.
11. What is Flip – Flop Phenomenon
Topic Title : Multi compartment models
1. Explain concept of multiple compartment models.
2. Explain the hybrid rate constants (α and β) and micro rate constants (k_{12}, k_{21})
3. Kinetics of two compartment open model
4. With a neat scheme explain pharmacokinetics of a drug administered repetitively through i.v. route assuming the body impart one compartmental kinetic model to the drug.
5. Kinetics of Repititive extravascular dosing in One Compartment Open Model
6. Explain two compartment pharmacokinetics with a neat scheme
Topic Title: Nonlinear Pharmacokinetics
1. Why 'nonlinear pharmacokinetics' is called 'capacity limited kinetics'?
2. Discuss various factors responsible for nonlinearity in pharmacokinetic processes
3. Discuss methods for estimation of Vmax, Km
4. Discuss nonlinearity in pharmacokinetics with the help of Michaelis –Menten equation