St.James College of Pharmaceutical Sciences St.James medical Academy River Bank, Chalakudy			
Programme:	Pharm .D/ Pharm. D. (Post Baccalaureate)	Sem.:	IV YEAR/ I Pharm.D (P.B)
Name of Course: (*Subject*)	Biopharmaceutics and Pharmacokinetics	Course Code:	4.5
Teaching faculty of the course	Dr. Smitha .K. Nair		

Summary of the Lecture Plan

Topic	Lectures	Hours
Biopharmaceutics	Introduction to Biopharmaceutics	1
	GI structure, Physiology and transit of drugs through GIT	2
	Absorption of drugs from gastrointestinal tract: factors and mechanisms involved.	4
	Drug Distribution: processes and factors associated.	4
	Drug Elimination pathways	3
Pharmacokinetics	Introduction to Pharmacokinetics	1
	Mathematical Models in Pharmacokinetics	1
	Drug level in blood - Basic Considerations	1
	Rates and orders of pharmacokinetics process	1
	Pharmacokinetics Models	2
	Compartment model: Basic Considerations	1
	Non- compartment analysis & Physiological Models	2
One Compartment Open Model	Introduction: Concept of Pharmacokinetic Compartmental Models	1
	Pharmacokinetics of open one compartment model: Intravenous Injection (Bolus) using blood level data.	3
	Pharmacokinetics of open one compartment model: Intravenous Injection (Bolus) using urinary excretion data.	3
	One compartment open model: Intravenous infusion.	2
Multi compartment Model	Introduction: Two compartment model	1
	Pharmacokinetics Two Compartment Open Model: IV injection (using blood level data).	2
	Pharmacokinetics Two Compartment Open Model: IV injection (using urinary excretion data)	2
	Two compartment open model – IV infusion	2
	Two compartment open model – oral administration	3

Multiple - Dosage Regimens	Principles of super position	1
	Pharmacokinetics of Repititive Intravenous injections – One Compartment Model	2
	Pharmacokinetics of Repititive Extravascular dosing – Open One Compartment model.	2
	Pharmacokinetics of Repititive Intravenous injections – Open Two Compartment Model	2
	Pharmacokinetics of Repititive Extravascular dosing – Open Two Compartment Model	2
	Dosage adjustment	1
Nonlinear Pharmacokinetics	Introduction to Nonlinear pharmacokinetics.	1
	Factors causing Nonlinearity.	2
	Michaelis- Menton equation and capacity limited pharmacokinetics.	2
	Methods for estimation of Michaelis –Menten's constants	3
Noncompartmental Pharmacokinetics	Non Compartmental Pharmacokinetics: Need for Non- compartment model, introduction to Statistical Moment Theory	2
	Determination of Mean Residence Time (MRT) of drugs using statistical moment theory : I.V bolus administration of a drug with characters of one compartment model	2
	Determination of Mean Residence Time (MRT) of drugs using statistical moment theory : Extra vascular administration of a drug with characters of one compartment model	2
	Determination of Mean Residence Time (MRT) of drugs using statistical moment theory : I.V bolus administration of a drug with characters of two compartment model	2
	Determination of Mean Residence Time (MRT) of drugs using statistical moment theory : Extra vascular administration of a drug with characters of two compartment model	2
	Physiologic pharmacokinetic(Perfusion) model	2
Bioavailability and Bioequivalence	Bioavailability and Bioequivalence: Introduction	1
	Bioavailability Study protocol	3
	Methods of Assessment of Bioavailability	3
	Bioequivalence Study protocol	3

Major issues or Core aspects to be addressed/ covered:

Topic Title :Biopharmaceutics
1. Introduction to biopharmaceutics
2. GI structure, Physiology and transit of drugs through GIT : parts of GIT, anatomy of GIT
3. Absorption of drugs from gastrointestinal tract
A. Mechanisms drug absorption – passive diffusion, pore transport, facilitated diffusion, active transport, electrochemical diffusion, ion-pair transport, endocytosis
B. Factors influencing GI absorption of drugs from dosage form – i). Pharmaceutical factors affecting drug absorption: physicochemical properties of drug, drug dissolution and dissolution rate, theories of dissolution, influence of drug pKa and and GI pH on drug absorption, dosage form factors (characteristics and pharmaceutical ingredients). ii). Patient related factors influencing GI absorption of drugs: Gastric emptying time, Intestinal transit time, GI pH, GI contents, age, disease states, presystemic metabolism etc.
4. Drug Distribution: processes 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 and its significance.
5. Drug Elimination pathways and factors affecting drug elimination – Renal excretion of drugs and factors affecting renal excretion, non-renal routes of drug excretion, Phase I and Phase II Metabolism
Topic Title:Pharmacokinetics
1.Introduction to Pharmacokinetics
2.Mathematical Models in Pharmacokinetics : equations to define plasma drug concentration as a function of time in various routes of administration (i.v. bolus, iv infusion and extravascular),and in single/multiple dose.
3. Drug level in blood - Basic Considerations: Understanding the significance of Plasma drug concentration, plasma concentration-time profile
4. Rates and orders of pharmacokinetics process: Definition, equations and unit for zero & first order processes, equation and unit for half-life
5. Pharmacokinetics Models: concept,types, usefulness, limitations of various models
6. Compartment model: Basic concepts, types, limitations,applications
7. Non- compartment analysis & Physiological Models:Basic concept, applications, limitations

Topic Title: One Compartment Open Model
1. Introduction: Concept of Pharmacokinetic Compartmental 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. Determination of elimination rate constant, biological half-life & apparent volume of distribution; applications. iv. Sample calculation
3. Pharmacokinetics of open one compartment model: Intravenous Injection (Bolus) using urinary excretion data. i. Using urinary excretion data: scheme, graphical presentation, mathematical construct defining excretion rate (including derivation), determination of elimination rate constant, biological half-life , limitations, merits. ii. Sigma minus method - mathematical construct defining Amount Remaining to be Excreted (ARE) (including derivation), determination of elimination rate constant, biological half-life , cumulative amount of drug excreted unchanged at different times, limitations, merits. iii.Sample calculation.
4. One compartment open model: Intravenous infusion. I. Continuous i.v. infusion: scheme, graphical representation, mathematical constructs defining drug plasma level during infusion, steady state plasma drug concentration(Css); II. loading dose calculation for specific Css, fixing infusion rate for specific Css; iv iv sample calculation.
Topic Title: Multi compartment Model
1. 1. Pharmacokinetics Two Compartment Open Model: IV injection (using blood level data): i. Scheme, graphical representation, mathematical construct to define drug plasma level in central compartment and peripheral compartment ii. derivation of equation to define drug plasma level in central compartment. iii. Construction of extrapolated line and line of residuals iv. Determination of biological half-life (β half-life) and distribution half-life (α half-life) and other pharmacokinetic parameters
2. Two compartment open model – IV infusion
i. scheme, graphical representation, mathematical constructs defining drug plasma level during infusion, steady state plasma drug concentration(Css); ii. loading dose calculation for specific Css, fixing infusion rate for specific Css; iv iv sample calculation.
3. Two compartment open model – oral administration 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 Loo Reigelmann method.

Topic Title: Multiple - Dosage Regimens
Concepts of multiple dosage regimen
1. 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
2. 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
3. Pharmacokinetics of Repititive Intravenous injections – Open Two Compartment Model: i. Bi-exponential equation to describe plasma drug level and derivation of the equation; equation to describe Css, Css(min), bi-exponential conc.-time plot
4. Pharmacokinetics of Repititive Extravascular dosing – Open Two Compartment Model: i. Equation to describe plasma drug level and derivation of the equation, Css, Css(min), conc. at any time during dosing interval at steady state, conc.-time plot , minimum and average conc. at steady state, AUC 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
Topic Title: Non compartmental Pharmacokinetics
1. Non Compartmental Pharmacokinetics: Need for non-compartment models, introduction to Statistical Moment Theory
2. Determination of Mean Residence Time (MRT) of drugs using statistical moment theory : I.V bolus administration of a drug with characters of one compartment model
3. Determination of Mean Residence Time (MRT) of drugs using statistical moment theory : Extra vascular administration of a drug with characters of one compartment model
4. Physiologic pharmacokinetic(Perfusion) model : Concept, description, merits, demerits and applications of the model
Topic Title: Bioavailability and Bioequivalence
1. Bioavailability and Bioequivalence: Introduction Definition of terms: Bioavailability, Relative and Absolute bioavailability, Bioequivalence

2. Bioavailability Study protocol and study design a. Single and Multiple dose studies- their merits and demerits b. Selection of Volunteers for the study as per legal requirements c. Duration of the study , estimation of Pharmacokinetic Parameters and interpretation of results
3. Methods of Assessment of Bioavailability a. Pharmacokinetic Methods: Plasma level versus time Studies, Urinary excretion versus time studies b. Pharmacodynamic studies : Measurement of Pharmacologic and Therapeutic responses
4. Bioequivalence Study protocol a. Selection of Volunteers for the study as per legal requirements, study design b. Duration of the study , estimation of Pharmacokinetic Parameters and interpretation of results

Sample Questions

Topic Title: Biopharmaceutics
1. What is the major mechanism of absorption of most drugs?
2.Writte anote on passive transport?
3. What is 'sink condition'? Explain its significance in drug dissolution.?
4.Physicochemical factors influencing GI absorption of drug?
5.Patient relaed factors influencing oral absorption of drug?
6.PH partion hypothesis ?
7.Factors influencing drug distribution?
8.Physiological Barriers present in body?
9.Plasma protein binding?
10.Mechanisam and determination of renal clearance?
11.Factors influencing renal elimination of drug?
Topic Title: Pharmacokinetics
1. Define pharmacokinetics. Name and define the three pharmacokinetic parameters that define a typical plasma level vs time curve
2. What are pharmacokinetic models?
3.What are compartment model?
4. What are noncompartment model?
5. . What are hysiological model?
6.In comparison to a mammillary model, the caternary model is less useful. Explain why.
Topic Title One Compartment Open Model

1. In compartment modeling, what is meant by the term “open”?
2.Kinetics of one compartment open model I V bolus
3.What is steady state plasma drug concentration(Css); Deduce the equation to define plasma concentration of drug while the drug is administetred as i.v. infusion
4. Explain sigma-minus method for estimation of elimination half-life. Mention its merits and demerits over excretion rate methods.
Topic Title: Multi compartment model
1. Distinguish “α –phase” and “β –phase
2. What is method of residuals
3 What are hybrid rate constants? Explain
4 What are micro constants? Explain
5. Following a 650 mg i.v. bolus dose of a drug to a 65 kg subject, the plasma drug conc. was found to decline biexponentially following the equation, $C = 67e^{-14t} + 33e^{-3t}$ Where t = time in hrs and C = plasma drug conc. in mcg/ml. Calculate V_c, V_d, k_{12}, k_{21}, K, and $t_{½}$.
6.Determination Ka by Loo Reigelmann method
Topic Title:Multtiple dosage regimen
1. With a neat scheme explain pharmacokinetics of a drug administered repetitively through i.v. route assuming the body impart 2 compartmental kinetic model to the drug.
2.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.
Topic Title:Non linear pharmacokinetics
1.What are the causes of nonlinearity?
2 Discuss nonlinearity in pharmacokinetics with the help of Michaelis –Menten equation
3. Discuss methods for estimation of Vmax, Km
4. Discuss various factors responsible for nonlinearity in pharmacokinetic processes
Topic Title: Noncompartmental Pharmacokinetics
1. Write a note on Physiologic pharmacokinetic model
2. Write a note on concept of statistical moments
3. Explain the determination of MRT for I.V. bolus administration of a drug with one compartment characters

4. Explain the determination of MRT for E.V. administration of a drug with one compartment characters
5 Explain the determination of MRT for E.V. administration of a drug with two compartment characters
6 Explain the determination of MRT for E.V. administration of a drug with two compartment characters
Topic Title:Bioavilability and Bioequvilence
1.Define bioavilability ,Bioequvilence ,Absolute bioavilability, Relative bioavilability
2.Write a note on Selection of human volunteers for bioavailability studies
3. Write in detail Methods of Assessment of Bioavailability
4.Design of single dose bioequvielence study