مركز الاعتماد وضمان الجودة

Course Syllabus

1	**Course title**	Pharmacokinetics
2	**Course number**	0503590
3	**Credit hours**	3
	Contact hours (theory, practical)	45
4	**Prerequisites/corequisites**	
5	**Program title**	Pharmacology Master Program
6	**Program code**	
7	**Awarding institution**	The University of Jordan
8	**School**	High Studies
9	**Department**	Pharmacology
10	**Course level**	Masters
11	**Year of study and semester (s)**	First semester
12	**Other department (s) involved in teaching the course**	
13	**Main teaching language**	English
14	**Delivery method**	✔☐Face to face learning ☐Blended ☐Fully online
15	**Online platforms(s)**	✔☐Moodle ☐Microsoft Teams ☐Skype ☐Zoom ☐Others……
16	**Issuing/Revision Date**	October 2, 2023

17 Course Coordinator:

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18 Other instructors:

Name:

Office number:

Phone number:

Email:

Contact hours:

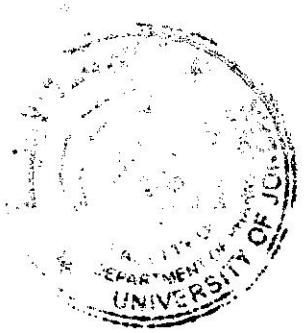
Name:

Office number:

Phone number:

Email:

Contact hours:



19 Course Description:

This course describes the time relationship of drug absorption, distribution, metabolism and excretion in a mathematic way. It is also concerned with the relationship of drug concentration in body fluids (blood and urine) and the drug pharmacokinetic parameters, and the use of such information for dose calculation.

20 Course aims and outcomes:

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A- Aims:

1. Define the basic concepts of pharmacokinetics
2. Design and evaluate dosage regimens of drugs using pharmacokinetics principles
3. Realize the pharmacokinetics principles underlying individualizing dosage regimens

B- Students Learning Outcomes (SLOs):

Upon successful completion of this course, students will be able to:

Self-Reading 1:

Introduction to Pharmacokinetics: At the end of this assignment, the student should be:

1. Familiar with pharmacokinetic terminology.
2. Able to remember many pharmacokinetic terms for his undergraduate study.

Self-Reading 2:

Mathematical Fundamentals in Pharmacokinetics: At the end of this assignment, the student should:

1. Be familiar with all mathematical principles and equations necessary to understand the content of this course.

Topic 1:

One-compartment Open Model: Intravenous Bolus Administration: At the end of this topic, the student should be able to:

1. Define first-order elimination rate constant, apparent volume of distribution, clearance, and elimination half-life from drug plasma concentration versus time data.
2. Calculate first-order elimination rate constant, apparent volume of distribution, clearance, and elimination half-life from drug plasma concentration versus time data.
3. Apply and utilize first-order elimination rate constant, apparent volume of distribution, clearance, and elimination half-life in practical settings.
4. Calculate first-order elimination rate constant from urinary drug excretion data

Topic 2:

Two-compartment Model: Intravenous Bolus Administration: At the end of this topic, the student should be able to:

1. Identify the types of two-compartment open models from drug concentration versus time data.
2. Utilize the equation that represent two-compartment open model in practical settings
3. Use the "Method of Residuals" to calculate the pharmacokinetic parameters for two-compartment open model.

4. Calculate the following volumes of distribution related to two-compartment open model: Apparent volume of distribution at steady-state, Extrapolated volume of distribution. Volume of distribution by area
5. Understand the utilization and significance of Apparent volume of distribution at steady-state, Extrapolated volume of distribution, Volume of distribution by area
6. Predict the concentration of drug in tissue compartment for two-compartment open model.
7. Calculate drug clearance two-compartment open model

Topic 3:

Intravenous Infusion: At the end of this topic, the student should be able to:

1. Describe mathematical equation for intravenous infusion data for one-compartment model drugs.
2. Predict the time to reach Steady-State after intravenous infusion for one-compartment model drugs.
3. Predict drug concentration at steady-state for one-compartment model drugs.
4. Calculate the half-life of elimination after intravenous infusion for one-compartment model drugs.
5. Calculate loading dose plus IV infusion for one-compartment model drugs.
6. Estimate drug clearance and volume of distribution from IV infusion data.
7. Describe mathematical equation for intravenous infusion data for two-compartment model drugs.
8. Describe mathematical equation for intravenous infusion data for two-compartment model drugs.
9. Calculate loading dose after IV infusion for two-compartment model drugs.
10. Calculate volume of distribution at steady-state for two-compartment model drugs.

Topic 4:

Drug Elimination, Clearance and Renal Clearance: At the end of this topic, the student should be able to:

1. Differentiate between drug clearance and drug elimination.
2. Utilize the equation that relate clearance with elimination rate and plasma concentration of the drug for both hepatic and renal clearance.
3. Be aware of clearance models and the calculation of clearance according to them (physiologic/organ clearance, noncompartmental models, and compartmental models
4. Describe the relationship between rate constants, volume of distribution and clearances.
5. Use the Henderson-Hasselbalch equation to calculate the Ionized to Nonionized proportion of acidic and basic drugs, and their implication on drug absorption, distribution and elimination

Topic 5:

Pharmacokinetics of Oral Absorption: At the end of this topic, the student should be able to:

1. Identify the basic principles of physiologically-based absorption kinetics.
2. Estimate the kinetic parameters of oral drug absorption.
3. Understand the significance of absorption rate constants.
4. Identify the causes of zero-order absorption.
5. Identify the significance of first-order absorption.
6. Calculate first-order absorption rate constant from plasma concentration versus time data.
7. Calculate first-order absorption rate constant from drug urinary excretion data.
8. Calculate first-order absorption rate constant using the "method of residuals".
9. Interpret the "lag time" of drug absorption after oral administration.
10. Interpret "flip-flop" of "absorption rate constant" and "elimination rate constant".
11. Determine absorption rate constant by plotting percent of drug unabsorbed versus time.
12. Identify the effect of absorption rate constant and elimination rate constant on C_{max}, t_{max}, and AUC.

Topic 6:

Multiple -Dosage Regimens: At the end of this topic, the student should be able to:

1. Understand drug accumulation after multiple- dosage regimens.
2. Calculate the accumulation half-life of the drug after multiple–dosage regimens.
3. Know the behavior of peak and trough concentration following multiple–dosage regimens, by changing dosing interval while keeping the same total daily dose.
4. Study the kinetics of drugs following repetitive intravenous injections.
5. Study the kinetics of drugs following intermittent intravenous infusion.
6. Calculate dosing regimen schedules.
7. Identify causes of defective dosing regimen schedules.

Topic 7:

Nonlinear Pharmacokinetics: At the end of this topic, the student should be able to:

1. Describe the characteristics of drugs that show nonlinear pharmacokinetics.
2. Identify some examples of drugs that show nonlinear pharmacokinetics.
3. Study saturable enzymatic elimination processes.
4. Calculate pharmacokinetic parameters for drugs eliminated by capacity-limited processes for drugs undergoing one-compartment model, IV bolus injection.
5. Determine K_m and V_{max} for drugs that show nonlinear pharmacokinetics.

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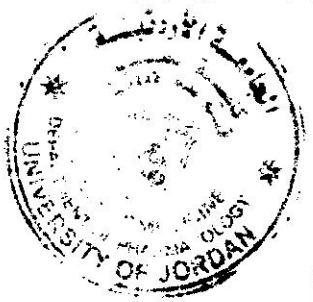
6. Determine K_m and V_{max} from *in vivo* data.
7. Interpret K_m and V_{max}.
8. Describe kinetics of mixed drug elimination.
9. Describe kinetics of zero-order input and nonlinear elimination.
10. Describe kinetics of first-order absorption and nonlinear elimination.
11. Know the meaning of Chronopharmacokinetics.
12. Know the meaning of Time-dependent pharmacokinetics.
13. Describe nonlinear pharmacokinetics due to drug-protein binding



Topic 8:

Physiologic Drug Distribution and Protein Binding: At the end of this topic, the student should be able to:

1. Review physiological factors of drug distribution (diffusion and hydrostatic pressure, Fick's law of diffusion).
2. Describe the relation between distribution half-life, blood flow and drug uptake by organs.
3. Determine the basics of drug accumulation in tissues and in the body as a whole.
4. Describe the effect of drug-protein binding on drug volume of distribution.
5. Study the determinants of the volume of distribution and its calculation.
6. Study the relation between plasma drug protein binding to distribution and elimination.
7. Quantitate the relation between drug volume of distribution and drug elimination half-life.
8. Study the elimination of protein-bound drugs (restrictive versus nonrestrictive elimination).
9. Describe the determinants of drug-protein binding.
10. Know the clinical significance of drug-protein binding.
11. Describe the importance of displacement of drugs from protein binding sites.
12. Study the kinetics of protein binding and drug exposure.

Topic 9:

Drug Elimination and Hepatic Clearance: At the end of this topic, the student should be able to:

1. Describe the relation between route of drug administration and extrahepatic drug metabolism.
2. Know the components of the first-order elimination rate constant.
3. Calculate the fraction of drug excreted unchanged and the fraction of drug metabolized.
4. Review hepatic enzymes involved in the biotransformation of drugs:
   - Mixed-function oxidases reactions
   - Conjugation reactions
   - Metabolism of enantiomers
5. Know the genetic variations of cytochrome P-450
6. Understand drug-drug interaction mechanisms involving drug metabolism
   - Induction and inhibition of drug metabolism
7. Understand transporter-based drug-drug interactions.

8. Describe first-pass effect and its importance.
9. Define liver extraction ratio.
10. Know the relationship between absolute bioavailability and liver extraction.
11. Estimate reduced bioavailability due liver metabolism and variable hepatic blood flow.
12. Understand the relationship between blood flow, intrinsic clearance, and hepatic clearance.
13. Identify" high extraction ratio" and 'low extraction ratio" drugs.
14. Study hepatic clearance of a protein-bound drug.
15. Distinguish between "restrictive" and "nonrestrictive" clearance from binding.
16. Use "hepatic extraction ratio" and "percent plasma protein binding" to assign hepatic clearance of drugs as: Flow-limited, capacity-limited binding sensitive, capacity-limited binding insensitive.
17. Study the kinetics of biliary excretion of drugs.
18. Estimate biliary clearance of drugs.
19. Know the importance of enterohepatic circulation of drugs.
20. Know the role of transporters on hepatic clearance and bioavailability.

Topic 10:

Physiologic Factors Related to Drug Absorption: At the end of this topic, the student should be able to:

1. Identify the various routes of drug administration and know the advantage and disadvantage of each.
2. Identify the various mechanisms of drug passage across cell membranes (passive diffusion, carrier-mediated transport - active transport and facilitated diffusion - and various types of transporters, vesicular transport, convective transport, and ion-pair formation.
3. Know drug interactions in the gastrointestinal tract.
4. Know the processes of oral drug absorption across the various parts of the gastrointestinal tract.
5. Identify factors affecting drug absorption in the gastrointestinal tract (GI motility, gastric emptying time, perfusion of the GIT, absorption through the lymphatic system, effect of food on gastrointestinal absorption.
6. Identify causes of double-peak phenomenon after oral administration.
7. Know the effect of disease states on drug absorption

Topic 11:

Drug Product Performance *in vivo*: Bioavailability and Bioequivalence: At the end of this topic, the student should be able to:

1. Understand the purpose of bioavailability and bioequivalence (BA/BE) studies.
2. Recognize the difference between relative and absolute bioavailability.
3. Recognize the methods for assessing BA/BE (plasma concentration, urinary data).

4. Know the *in vivo* measurement of active moiety in biological fluids.
5. Know bioequivalence studies bases on pharmacodynamics endpoints *in vivo*.
6. Know bioequivalence studies bases on clinical endpoint study.
7. Know *in vitro* studies to assess BE.
8. Understand the processes of design and evaluation of bioequivalence studies.
9. Know that a single reference drug product should be used as a standard drug product to which all generic versions shoud be compared (Reference Listed Drugs – RLD).
10. Familiar with the regulatory recommendations for optimizing bioavailability study design.
11. Know the factors that affect drug bioavailability.
12. Know that the analytical methods used in an *in vivo* BA/BE must be validated for accuracy and sensitivity.
13. Recognize study design for a variety of cases (crossover design, replicated crossover design, narrow therapeutic index drugs, parallel study design, multiple-dose, steady-state study design.
14. Recognize clinical endpoint bioequivalence studies.
15. Determine bioequivalence of drug products in patients maintained on a therapeutic drug regimen.
16. Know the pharmacokinetic evaluation of the results of BE studies.
17. Know the statistical tests needed for evaluation of the results of BE studies.

21. Topic Outline and Schedule:

Week	Lecture	Topic	Student Learning Outcome	Learning Methods (Face to Face/Blended/ Fully Online)	Platform	Synchronous / Asynchronous Lecturing	Evaluation Methods	Resources
1	1.1	Introduction to biopharmaceutics and pharmacokinetics		Self-Reading				
	1.2	Mathematic fundamentals in Pharmacokinetics		Self-Reading				
2	2.1	One-compartment open model:		**Face to Face**				

		Intravenous bolus administration		
2	2.2	One-compartment open model: Intravenous bolus administration	Face to Face	
3	3.1	Multi-compartment Models: Intravenous bolus administration	Face to Face	
	3.2	Multi-compartment Models: Intravenous bolus administration	Face to Face	
4	4.1	Multi-compartment Models: Intravenous bolus administration	Face to Face	
	4.2	Solving problems	Face to Face	
5	5.1	Intravenous infusion	Face to Face	
	5.2	Intravenous infusion	Face to Face	
6	6.1	Drug elimination, clearance and renal clearance	Face to Face	
	6.2	Drug elimination, clearance and renal clearance	Face to Face	

7	7.1	Pharmacokinetic of oral absorption		Face to Face				
	7.2	Pharmacokinetic of oral absorption		Face to Face				
8	8.1	Multiple dosage regimens		Face to Face				
	8.2	Multiple dosage regimens		Face to Face				
9	9.1	Multiple dosage regimens		Face to Face				
	9.2	Solving problems		Face to Face				
10	10.1	Non-linear pharmacokinetics		Face to Face				
	10.2	Non-linear pharmacokinetics		Face to Face				
11	11.1	Physiologic drug distribution and protein binding		Face to Face				
	11.2	Physiologic drug distribution and protein binding		Face to Face				
12	12.1	Drug elimination and hepatic clearance		Face to Face				
	12.2	Drug elimination and hepatic clearance		Face to Face				
13	13.1	Physiologic factors related to drug absorption		Face to Face				

	13.2	Physiologic factors related to drug absorption		Face to Face				
14	14.1	Drug product performance in vivo: Bioavailability and bioequivalence		Face to Face				
	14.2	Drug product performance in vivo: Bioavailability and bioequivalence		Face to Face				
15	15.1	Drug product performance in vivo: Bioavailability and bioequivalence		Face to Face				
	15.2	Revision						

22 Evaluation Methods:

Opportunities to demonstrate achievement of the SLOs are provided through the following assessment methods and requirements:

Evaluation Activity	Mark	Topic(s)	SLOs	Period (Week)	Platform
Exam 1	30				
Exam 2	30				
Final Exam	40				

23 Course Requirements

Students should have a computer, internet connection, access to Microsoft teams, elearningsite access and Calculator with logarithmic functions

24 Course Policies:

A- Attendance policies: According to university requirements

B- Absences from exams and submitting assignments on time: Students should have an acceptable excuse

C- Health and safety procedures:

D- Honesty policy regarding cheating, plagiarism, misbehavior: University regulation will be applied strictly

E- Grading policy: see above

F- Available university services that support achievement in the course: available

25 References:

A- Required book(s), assigned reading and audio-visuals:
Applied biopharmaceutics and pharmacokinetics
Leon Shargel and Andrew B.C. Yu McGraw Hill
Newes edition
ISBN # 978 - 981- 4670 – 24- 1

B- Recommended books, materials, and media:

26 Additional information:

Name of Course Coordinator: Prof. Yacoub Irshaid	Signature: ---------- Date: 3/10/2023
Head of Curriculum Committee/Department: ----------	Signature: ----------
Head of Department: Dr. Alia Shatanawi	Signature: ----------
Head of Curriculum Committee/Faculty: ----------	Signature: ----------
Dean: ----------	Signature: ----------