Course Syllabus

Code - Course Title	**FTE635 - Oral Drug Absorption and Evaluation Techniques**
Course Type	I. SEMESTER
Laboratory + Practice	3+0
ECTS	**7.5**
Language of Instruction	Türkçe
Course Type	Elective Courses
Course Instructor(s)	PROF. DR. MUSTAFA SİNAN KAYNAK

Mode of Delivery	The mode of delivery of this course is face to face.
Place of Delivery	On Campus
Used Educational Platforms	Online,Face-to-face
Prerequisites	There is no prerequisite or co-requisite for this course.
Courses Recomended	BFK501 Biopharmaceutics, BFK502 Pharmacokinetics and FTE542 Biopharmaceutics and Pharmacokinetics are recommended. The gastrointestinal anatomy and physiology, biopharmaceutics classification system, bioavailability-bioequivalence and basic pharmacokinetics topics covered in these courses are assumed as prior knowledge in this course.
Recommended Resources	PRIMARY TEXTBOOKS1. Dressman JB, Reppas C (eds.). Oral Drug Absorption: Prediction and Assessment, 2nd ed. Informa Healthcare, New York, 2010. ISBN 978-1-4200-7733-9.2. Dressman JB, Lennernäs H (eds.). Oral Drug Absorption: Prediction and Assessment, 1st ed. Marcel Dekker, New York, 2000. ISBN 0-8247-0272-7. (The first edition is used for the chapters on animal and human perfusion methods and on deconvolution.)SUPPLEMENTARY TEXTBOOKS3. Ducharme MP, Shargel L, Yu ABC. Shargel and Yu's Applied Biopharmaceutics and Pharmacokinetics, 8th ed. McGraw Hill, 2022.4. Taylor KMG, Aulton ME (eds.). Aulton's Pharmaceutics: The Design and Manufacture of Medicines, 7th ed. Elsevier, 2026.5. Derendorf H, Schmidt S (eds.). Rowland and Tozer's Clinical Pharmacokinetics and Pharmacodynamics, 5th ed. Wolters Kluwer, 2019.REGULATORY GUIDELINES (current versions are followed during the course)6. ICH M9 Biopharmaceutics Classification System-Based Biowaivers and its Questions and Answers document (Step 4, 2019).7. ICH M13A Bioequivalence for Immediate-Release Solid Oral Dosage Forms and its Questions and Answers document (Step 4, 2024).8. ICH M13B Bioequivalence for Immediate-Release Solid Oral Dosage Forms: Additional Strengths Biowaiver (Step 4, 2026).9. ICH M12 Drug Interaction Studies (Step 4, 2024).10. ICH M15 General Principles for Model-Informed Drug Development (Step 4, 2026).11. EMA. Guideline on the reporting of physiologically based pharmacokinetic (PBPK) modelling and simulation, EMA/CHMP/458101/2016.12. FDA. The Use of Physiologically Based Pharmacokinetic Analyses - Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls (draft guidance, 2020).PHARMACOPOEIAS13. European Pharmacopoeia (Ph. Eur.), current edition.14. USP-NF, current version. Relevant general chapters: 1087 Intrinsic Dissolution, 1088 In Vitro and In Vivo Evaluation of Oral Dosage Forms, 1092 The Dissolution Procedure, 1236 Solubility Measurements.In addition, a reading list of selected current peer-reviewed articles on the method covered is provided each week.
Work Placement	Practical training is not required for this programme.

Aims of the Course	This course provides a comparative examination of the in vitro, cell culture-based, ex vivo, in situ and in vivo methods used to determine the intestinal absorption of orally administered drugs, with respect to their physiological relevance, experimental throughput, data quality and regulatory acceptance criteria. Its aim is to enable the student to select an appropriate combination of methods for a given active substance and research question and to defend that selection on the basis of current regulatory guidelines and the scientific literature; to calculate permeability data and interpret them together with their sources of uncertainty; to establish correlations between methods of different scales in order to predict the fraction absorbed in humans; and to design an original absorption assessment strategy.

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Weeks	Learning Outcomes	Topics	Teaching Methods
Week - 1	**LO-1** **LO-3**	Introduction: determinants of oral absorption and the problem of method selection; scope of the course and map of prerequisite knowledge	Lecture, Discussion
Week - 2	**LO-1**	Physiological relevance of methods: regional pH, transit time, surface area, transporter distribution, mucus layer and food effect	Lecture, Discussion
Week - 3	**LO-2**	Regulatory framework: ICH M9, M13A, M13B, M12 and M15 guidelines; FDA and EMA acceptance criteria for permeability and absorption assessment; EMA draft guideline on gastrointestinal interactions	Discussion, Critique/Critical Reading, Document/Text/Data Analysis
Week - 4	**LO-3**	In vitro methods I: PAMPA and its variants, artificial membrane systems; physicochemical prediction (pKa, log P, log D, pH-partition hypothesis)	Lecture, Case Study
Week - 5	**LO-3** **LO-6**	In vitro methods II: biorelevant media (FaSSGF, FaSSIF, FeSSIF), the solubility-permeability interplay and biphasic systems	Lecture, Case Study
Week - 6	**LO-5**	Cell cultures I: the Caco-2 model - establishment of the cell line, transepithelial electrical resistance (TEER), calculation of apparent permeability (Papp), method validation and limitations	Lecture, Problem Solving
Week - 7	**LO-5** **LO-8**	Cell cultures II: MDCK and MDCK-MDR1 models, efflux ratio, carrier-mediated transport (P-gp, BCRP, PEPT1, OATP) and inhibition assays; organoid/enteroid and gut-on-chip systems	Lecture, Critique/Critical Reading
Week - 8	**LO-3**	Ex vivo methods: the Ussing chamber, the everted gut sac technique and criteria of tissue viability	Lecture, Case Study
Week - 9	**LO-4**	In situ methods I: the Doluisio technique and closed-loop perfusion; theoretical basis and kinetic analysis	Lecture, Problem Solving
Week - 10	**LO-4** **LO-7**	In situ methods II: single-pass intestinal perfusion (SPIP) - experimental design, selection of the perfusion medium and selection of markers	Lecture, Proje Design/Management
Week - 11	**LO-4**	Evaluation of SPIP data: net water flux correction, calculation of effective permeability (Peff), regional and dose-dependent differences, sources of uncertainty and the role of the analytical method in the result	Problem Solving, Document/Text/Data Analysis
Week - 12	**LO-3** **LO-8**	In vivo methods: regional perfusion and intubation techniques in humans, mass balance and radiolabelled studies, imaging methods	Lecture, Critique/Critical Reading

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Week - 13	**LO-6**	Deriving the absorption profile from in vivo data: deconvolution, the Wagner-Nelson and Loo-Riegelman methods, fraction absorbed (Fa); in vitro-in vivo correlation (IVIVC/IVIVR) and absorption modelling with PBPK/PBBM	Lecture, Problem Solving
Week - 14	**LO-7** **LO-8**	Method selection case study and journal club: student presentations and defence of the designed absorption assessment strategy	Discussion, Critique/Critical Reading, Research and Inquiry

Learning Outcomes

#	Learning Outcome
1	Critically evaluates the physiological, physicochemical and biopharmaceutical variables governing oral absorption in terms of the extent to which a given method represents these variables.
2	Compares the acceptance criteria of current regulatory guidelines regarding permeability and absorption assessment, and justifies the biowaiver eligibility of a given active substance.
3	Selects and defends the method appropriate to a given research question by comparing in vitro, cell culture-based, ex vivo, in situ and in vivo permeability methods in terms of physiological relevance, experimental throughput, cost and regulatory acceptance.
4	Calculates effective permeability in single-pass intestinal perfusion and closed-loop methods using net water flux correction, and analyses the sources of uncertainty in the result.
5	Interprets apparent permeability, efflux ratio and transepithelial electrical resistance data in cell culture-based permeability experiments, and distinguishes carrier-mediated transport from passive diffusion.
6	Integrates data obtained from methods of different scales within an in vitro-in situ-in vivo correlation framework and predicts the fraction absorbed in humans.
7	Designs a multi-step absorption assessment strategy for a given active substance and justifies the experimental design, analytical method, sample size and ethical requirements.
8	Critically evaluates a published study on oral absorption methods in terms of method validity, data quality and generalisability, and communicates the findings in the form of a scientific report and presentation.

Sustainable Development Goals

✓ Health and Quality of Life ✓ Quality Education ✓ Industry, Innovation and Infrastructure

Course Theme

✓ Health Sciences and Medical Technologies

AKTS Workload

Activity	Duration (Hour)	Count	Workload
Teorik Derse Katılım	3.00	14	42
Sınıf Dışı Çalışma (Ön Hazırlık & Pekiştirme Amaçlı)	5.50	14	70
Ödevler	6.00	2	12

AKTS Workload

Activity	Duration (Hour)	Count	Workload
Proje - Rapor - Sunum Hazırlama	26.50	1	26
Ara Sınav Hazırlığı (sınav süresi dahil)	12.00	1	12
Final Sınavı Hazırlığı (sınav süresi dahil)	18.00	1	18
Uygulama (Laboratuvar, Müzik/Enstrüman Uygulaması, Atölye/Saha Çalışması vb.)	0.00	0	0
Staj Uygulaması	0.00	0	0
		Calculated ECTS	**7.5**

Assessment Method and Passing Requirements

✓ Open-Ended Test ✓ Project ✓ Homework ✓ Presentation