MSc exam scope 2021/2022
DRUG DISCOVERY AND DEVELOPMENT

Subject	Example topics
GENERAL (2 questions)	1. Present a Drug Discovery and Development process. Name each stage and give the approximate duration and cost of it. 2. Define a term and show differences between: i) validated hit ii) lead structure iii) candidate (pre-clinical candidate/development candidate). 3. Name and shortly describe three main patentability requirements. How long does patent protection last? Is there any special prolongation designed for pharmaceuticals? What is data exclusivity and market exclusivity? 4. Describe potential funding sources (public, private) that could be used to support a drug discovery or early development program. What are the advantages and disadvantages of them? 5. Give examples of "hard law" and "soft law" which are in force regulating the drug approval process. 6. Explain the term "drug-likeness" and discuss how drug-like property optimization during drug discovery process may enhance the probability of becoming successful drug product for a compound. What are the main parameters used to describe "drug-likeness"? 7. Name and describe the chemical interactions that are important for drug binding to a target and influence its physicochemical properties. 8. Explain how the solubility, ionization state and lipophilicity influence membrane permeability. 9. Explain how the solubility, ionization state and lipophilicity influence membrane permeability. Describe methods used for permeability determination. 10. Describe the aims, design, data analysis and results of TQT studies. 11. Describe the clearance concept. 12. What liver models do you know? Compare them in brief. 13. Discuss factors that may have an influence on permeation during in vitro assessment. 14. Explain how the compound safety and toxicity can be assessed in in vitro conditions. 15. Explain how the compound safety and toxicity can be screened in silico. 16. What are the main differences between Physiologically-based Pharmacokinetic (PBPK) modelling approach and Classical Compartment analysis? 17. Describe phase I of clinical trials: number of subjects, scope, major objectives and impact on the next stages of drug development 18. What are the differences between generic and biosimilar drugs? 19. Name primary and secondary parameters of bioequivalence and explain their meaning. 20. Define term "controlled release" and demonstrate this feature on the examples of different dosage forms. 21. Describe quality control assays for tablets. 22. Explain differences between critical quality attributes (CQA) and critical process parameters (CPP). What is the system that these parameters belong to? 23. What is PAT (process analytical technology) and where is it applicable? 24. Name major types and provide examples of excipients used for manufacturing of oral solid dosage forms. 25. Describe stability assays for selected dosage forms. What are the physical principles in the background of these assays? 26. Name and describe compendial dissolution testing methods used for solid dosage forms.

	27. Provide brief characteristics of drugs targeting α-adrenoceptors (indications, division, examples). 28. Provide brief characteristics of drugs targeting β-adrenoceptors (indications, division, examples). 29. Discuss biological targets that are affected by drugs lowering blood pressure. 30. Provide brief characteristics of drugs targeting serotonin receptors (indications, division, examples). 31. Provide brief characteristics of antibacterial drugs (division, mechanisms of action, examples). 32. Provide brief characteristics of antiarrhythmic drugs (division, mechanisms of action, examples). 33. Provide brief characteristics of drugs targeting histamine receptors (indications, division, examples). 34. Provide brief characteristics of drugs used to treat oncological diseases (division, examples, selected recent achievements)
MODEL INFORMED DRUG DEVELOPMENT (1 question)	1. Define QSP and give a few examples of its potential implementation to the drug development process. 2. Discuss causes and consequences of nonlinear pharmacokinetics. 3. What is allometry and how can it be used in pharmacokinetic studies? 4. Discuss the advantages and limitations of pharmacodynamic models that you know. 5. Discuss the concept of physiologically-based pharmacokinetic modeling. 6. What is hepatic intrinsic clearance and how can it be determined? 7. Discuss and assumptions and usage of perfusion-limited and permeability-limited PBPK models. 8. What is a reason to describe an organ as a permeability-limited tissue in a PBPK approach? Give examples of such situations. 9. Describe briefly the human GI tract anatomical structure and microstructure and how it influences the small molecules absorption after oral dosing. 10. Drug transporters are proteins involved in active transport of small molecule drugs. Define their role in the drug disposition using examples from various tissues. 11. Discuss factors (different than formulation) that can influence the effectiveness of inhalational therapy. 12. Discuss formulation parameters influencing therapeutic effectiveness in pulmonary drug delivery. 13. Discuss the reasons for the importance of the size of particle or droplet in the process of pulmonary drug delivery. 14. Describe briefly the human skin anatomical structure and microstructure and how it influences the small molecules absorption after topical administration. 15. Discuss factors that can influence skin permeability in vivo. 16. Define solid particles solubility and discuss how solubility as a complex physical process occurs in the GI tract 17. Explain the basic concepts and physiological parameters influencing supersaturation and precipitation of drugs in the GI tract and discuss how do these processes influence drug absorption 18. Explain what is a flip-flop kinetics and how it can be examined. 19. Define renal clearance and describe how it can be estimated in practice. 20. Discuss the differences and the use of whole-body (full) PBPK model and minimum-PBPK models.

	21. Describe statistical procedure used for establishing bioequivalence. Explain differences between average, population and individual bioequivalence measures. 22. What are the data necessary to establish Level A IVIVC (in vitro in vivo correlation)? Explain differences between convolution and deconvolution approach to establish Level A IVIVC according to the relevant FDA guideline(s). 23. Explain major benefits of continuous vs. batch manufacturing processes 24. Describe BCS system, its applications and extensions. 25. Explain differences between model dependent and model independent methods for dissolution profiles comparisons. Provide at least one example for each category.
MEDICINAL CHEMISTRY (1 question)	1. Describe and compare the concepts of structure-based drug design and ligand-based drug design in search for new drugs. 2. Describe methods of protein structure prediction. 3. Present classification of scoring functions. 4. Describe how to include flexibility of protein side-chains and protein backbone in docking. 5. Present background and application of molecular dynamics simulations. 6. Name and describe main and miscellaneous drug targets, give the corresponding examples of drugs. 7. Discuss the concept of pharmacophore features and pharmacophore model in medicinal chemistry. 8. Explain the concept of bioisosteres, give examples of bioisosteres used in medicinal chemistry. 9. Describe the role of hERG in the drug discovery process, compounds' structural and physicochemical properties that predispose them to inhibition of hERG and strategies to counteract the inhibition. 10. Describe physicochemical properties (pKa, logP, HBD/HBA) in the context of pharmacodynamic and pharmacokinetics of drugs. 11. Describe CYP-450 enzymes, their role in the drug discovery process and methods used to measure their activity. 12. Describe major processes in drug metabolism, examples of chemical groups/ moieties especially susceptible to metabolism, strategies used to prevent excessive metabolism and methods of determination of metabolic stability. 13. Toxicophores - examples of drug toxicity related to chemical reactivity. 14. Describe plasma protein binding importance for pharmacodynamic and pharmacokinetics of drugs and methods of its determination. 15. Discuss the possible application of fluorine and deuterium in the process of optimization of physicochemical and pharmacokinetic properties of compounds. 16. Describe main reactions causing instability of compounds in plasma and solution and structural modifications that may be used to improve stability. 17. Discuss internet tools and databases useful in search for synthetic methods and compounds' characteristics in medicinal chemistry. 18. Describe methods used for purification of compounds during synthesis. 19. Describe methods used for identification of the structure of newly synthesized compounds.

	20. Describe methods used for identification of impurities in the synthesized compounds. 21. Discuss protection and deprotection of fragile chemical groups in medicinal chemistry, give examples of most frequently used protecting groups. 22. Basic chemical processes in synthesis of biologically active compounds. Describe three selected processes based on your practical experience in medicinal chemistry. 23. Discuss the most important challenges of scaling up in organic synthesis.
EXPERIMENTAL PHARMACOLOGY (1 question)	1. Describe the main principles and discuss the advantages and limitations of PAMPA and Caco-2 in vitro permeability assays. 2. Describe at least one in vitro method for the determination of plasma protein binding. 3. What are the main differences between liver microsomes and S9 fraction of the liver? 4. Describe the principles of the Ames test. 5. Describe the principles and applications of MTS assay. 6. Describe the difference between affinity and functional studies in molecular pharmacology and characterize the parameters used to describe drug activities (Ki, EC50, Emax). 7. Discuss the phenomenon of functional selectivity of GPCR ligands. 8. Compare the properties and pharmacological utility of primary cells and continuous cell lines cultures. 9. Discuss the principles of high-throughput screening in the drug development process. 10. Describe the methods used for the transfection of animal cells. 11. Give three examples of in vivo tests/models, which can be used to determine antidepressant-like properties of a novel compound and describe them shortly. 12. Give three examples of in vivo tests/models, which can be used to determine anxiolytic-like properties of a novel compound and describe them shortly. 13. Give three examples of in vivo tests/models, which can be used to determine procognitive properties of a novel compound and describe them shortly. 14. Give three examples of in vivo tests/models, which can be used to determine analgesic properties of a novel compound and describe them shortly. 15. Give three examples of in vivo tests/models, which can be used to determine antiarrhythmic properties of a novel compound and describe them shortly. 16. List and describe the tests used to verify the cardiovascular safety of a novel compound in vivo. 17. List and describe the tests used to verify the CNS safety of a novel compound in vivo. 18. Discuss the proper design of an in vivo experiment. 19. What is toxicometric evaluation in safety testing of new compounds? Discuss the method for determining the toxicity class according to the OECD 420 procedure. 20. Discuss the basic principles of toxicokinetic studies. How toxicokinetics differs from pharmacokinetics?