Faculty of Medicine / PHARMACY / PHARMACEUTICAL CHEMISTRY III

Course:	PHARMACEUTICAL CHEMISTRY III			
Course ID	**Course status**	**Semester**	**ECTS credits**	**Lessons** (Lessons+Exercises+Laboratory)
6771	Mandatory	6	9	4+0+3
Programs	PHARMACY			
Prerequisites	Pharmaceutical chemistry I; Pharmaceutical chemistry II			
Aims	Course aims are providing students with: - Knowledge about chemical structures of drugs affecting CNS and cardiovascular system; - A comprehensive understanding of the underlying principles of drug action; - Identification of fundamental pharmacophores for drugs of selected pharmacotherapy groups; - Structure-activity relationships in relation to drug-target interaction; - Physicochemical properties of drug molecules in relation to drug ADME; - Chemical pathways of drug metabolism.			
Learning outcomes	Having successfully completed this module student will be able to: • Answer rationally the “why” and “how” questions related to drug action; • Relate the structure and physical properties of drugs to their pharmacological activity; • Demonstrate an understanding of concepts such as drug metabolism, bioavailability and pharmacokinetics and the role of medicinal chemistry in improving these parameters; • Describe the current challenges and opportunities in medicinal chemistry in light of contemporary developments in the field of drug discovery; Think critically and solve problems related chemistry of drugs; • The gained knowledge is the basis for the following courses: pharmacology, drug metabolism, pharmaceutical technology and pharmaceutical analysis.			
Lecturer / Teaching assistant	PharmD, PhD, Nemanja Turković, PharmD, Sehija Dizdarević, PharmD, Jadranka Orović			
Methodology	Lectures, exercises, work in a small group, consultations, presentation in front of a group, method of practical student activities			
Plan and program of work				
Preparing week	Preparation and registration of the semester			
I week lectures	Analgesics. Opioid receptors, morphine: mechanism of action, chemical properties, stability, metabolism, adverse effects. Endogenous opioid peptides, structure-activity relationships of opioid agonists and antagonists, morphine-like drugs. Synthetic opioid series (methadone, fentanyl, meperidine, tramadol...). Opioid antidiarrheals.			
I week exercises	Analyses of physical and chemical properties of chemical compouds; the way of analyses; The reactivity of functional groups; Felling’s and Tollens’s tests; Distinction between citric and tartaric acid, reactions of selected amines; Parris reaction, methylxanthines.			
II week lectures	Nonsteroidal anti-inflammatory drugs (NSAID), cyclooxygenase (COX-1, COX-2) activities, and adverse effects. General structure-activity relationships, physicochemical properties of synthetic drugs. Classification: derivatives of aryl alkanoic acid, aryl- and heteroarylpropionic acids, oxicams, selective COX-2 inhibitors. Antirheumatic drugs, drugs for the treatment of gout. Analgoantipyretics.			
II week exercises	Identification of inorganics anions and cations.			
III week lectures	General anesthetics, historical aspect (ether, chloroform). Clinically useful inhalation agents (fluorinated hydrocarbons, ethers), hepatotoxicity. Clinically useful intravenous general anesthetic agents (propofol, ketamine, etomidate, ultrashort-acting barbiturates). Local anesthetics, toxicity, side effects, mechanism of action, structure-action relationship. The most important local anesthetics (benzocaine, bupivacaine, chlorprocaine, lidocaine...).			
III week exercises	Identification of inorganic compounds by reactions of cations and anions.			
IV week lectures	Drugs affecting cholinergic neurotransmission. Cholinergic neurotransmission, biosynthesis of acetylcholine, storage and release, chemistry, metabolism, structure-activity relationships. Cholinergic receptors (muscarinic and nicotinic receptors), muscarinic agonists, reversible acetylcholinesterase inhibitors, Alzheimers disease therapy.			
IV week exercises	Pharmaceutical purity, the origin of impurities, in vitro stability, photochemical degradation, limit tests, methods used to test the purity of pharmaceutical substances.			
V week lectures	Irreversible inhibitors of acetylcholinesterase, muscarinic antagonists, structure-activity relationships. Antiparkinsonian drugs: anticholinergics, L-DOPA. Nicotinic antagonists-neuromuscular blocking drugs (depolarizing and no depolarizing neuromuscular blockers, steroid structure drugs).			
V week exercises	Impurities, examples from the pharmacopoeia, analysis of the instability of pharmaceutical substances, workshop for students - a sample of the instability of substances, the formation of potential degradation products and related compounds.			
VI week lectures	Antidepressants: tricyclic antidepressants, selective reuptake inhibitors (noradrenaline, 5-HT,			

	noradrenaline and serotonin, dopamine and noradrenaline). Monoamine oxidase inhibitors (nonselective, reversible MAO-A inhibitors). Anxiolytic drugs: GABAA receptors, benzodiazepines, structure-activity relationship. Non-benzodiazepine agonists acting on benzodiazepine receptors, other anxiolytics. Non-benzodiazepine sedative-hypnotics.
VI week exercises	Limit tests, control of personal errors, non-specific impurities: clarity and degree of opalescence of liquid, degree of coloring of liquid, insoluble matter, soluble matter, loss on drying, volatile matter and residual solvents, non-volatile matter, residue after annealing, sulfate residue.
VII week lectures	Antisizure drugs, mechanism of action: hydantoins, oxazolidinediones, succinimides, carbamazepine, barbiturates, benzodiazepines, valproic acid and its derivatives, miscellaneous antiepileptic drugs. Hypnotics: barbiturates, benzodiazepine sedative-hypnotics. Antipsychotics: first generation (phenothiazine, thioxanthene, structure-activity relationship; butyrophenone, benzamide derivatives). Second generation (benzazepine and analogues). Specific drugs, other chemical classes of antipsychotics.
VII week exercises	Limit tests for metals and anions (heavy metals: lead, iron, alkaline earth metals and related impurities: barium, calcium, magnesium; potassium, ammonia, aluminum, arsenic, chlorides, oxalates, sulfates, phosphates). Examination of organic impurities in medicinal substances - physical methods, chemical methods.
VIII week lectures	Antihistamines: histamine, chemistry, synthesis, metabolism, structure-activity relationships. Histamine receptors, first-generation H1 antihistamines (ethylene diamines, ethanolamine ethers, alkyl amines, tricyclic H1 antihistamines); second generation of non-sedating H1 antihistamines. Antihistamines for local use, histamine release inhibitors. Antiulcer drugs: H2 antihistamines, proton pump inhibitors.
VIII week exercises	A practical task for every student - laboratory examination of limit tests of solutions.
IX week lectures	Drugs affecting adrenergic neurotransmission. Biosynthesis, storage and release of catecholamine, metabolism, adrenergic receptors. Structure-activity relationships of adrenergic agonists, alpha1-agonist (phenylethanolamines, 2-arylimidazoline). Beta2-adrenergic agonists (phenylethanolamines: short-acting, long-acting; resorcinol and para monophenol derivatives).
IX week exercises	Titrations in non-aqueous medium - determination of weak organic bases, determination of salts of weak organic bases, determination of alkaline salts of weak organic acids, determination of weak organic acids.
X week lectures	Adrenergic antagonists: general structure of beta1-adrenergic receptor blockers (arylethanolamines and aryloxypropanolamines) and stereochemistry. Classification: nonselective (propranolol and other drugs) and cardioselective beta blockers; lipophilicity and metabolism of beta blockers. Medicines with mixed action - α/β adrenergic antagonists: labetalol, carvedilol. Blockers of alpha1-adrenergic receptors: natural and semi-synthetic ergot alkaloids, non-selective alpha-antagonists (phenoxybenzamine); selective alpha1-antagonists (prazosin and related drugs).
X week exercises	Titrations in non-aqueous medium - practical examples.
XI week lectures	Antihypertensive drugs. Classification: adrenergic neuron blocking drugs (reserpine, guanidine derivatives); centrally acting sympatholytic (methyldopa, clonidine); selective alpha1-antagonists (prazosin and related drugs); blockers of beta1-adrenergic receptors; vasodilators (directly acting - hydralazine; drugs that act on ion channels for potassium: minoxidil, diazoxide; drugs that act by releasing NO - nitroprusside); calcium channel blockers; drugs that act on the renin-angiotensin system
XI week exercises	Identification of substances with nitrogen: barbiturate derivatives (barbitone, barbitone-Na, phenobarbitone, phenobarbitone-Na), xanthine derivatives (caffeine, theophylline, theobromine, pentoxifylline), primary aromatic amines (anesthesin, sulfopreparations, urotropin); aminoalcohols, anilides, imidazoline and 3-imidazolin-5-one derivatives (aminophenazone, propyphenazone, phenazone, metamizole sodium, paracetamol, phenacetin, lidocaine hydrochloride; xylometazoline hydrochloride, ephedrine hydrochloride.
XII week lectures	Agents affecting the renin-angiotensin pathway, mechanism of action, structure-activity relationships. Angiotensin-converting enzyme inhibitors: captopril, dicarboxylate-containing inhibitors, phosphonate-containing inhibitors (fosinopril). Angiotensin II receptor blockers, mechanism of action, physical-chemical properties, structure-action relationship.
XII week exercises	Identification of nitrogen-free substances: aromatic acids and derivatives (salicylic acid, Na-salicylate; acetylsalicylic acid, phenylsalicylate, benzoic acid, Na-benzoate), aliphatic acids and derivatives (citric acid, Na-citrate, tartaric acid, Ca-gluconate, ascorbic acid), carbohydrates (glucose, lactose, sucrose, starch).
XIII week lectures	Antiarrhythmic drugs. Normal physiologic action of hearth. Classification of antiarrhythmic drugs: class I-sodium channel blockers (IA, IB, IC), class II (beta1-adrenergic receptor blockers), class III (potassium channel blockers); class IV (calcium channel blockers). Vasodilators: coronary (organic nitrates, nitric oxide donors-molsidomine) and peripheral. Calcium channel antagonists. Mechanism of calcium transport and deposition, chemical division: 1,4-dihydropyridines (physical-chemical properties, structure-activity relationship), verapamil, diltiazem.

XIII week exercises	Anxiolytic drugs-benzodiazepines, antidepressants, reuptake inhibitors of serotonin and adrenaline.
XIV week lectures	Cardiac glycosides: chemistry (cardenolide, bufadienolide), biochemical mechanism, Digitalis, Strophantus. Diuretics. Drug classes: osmotic diuretics, carbonic anhydrase inhibitors, benzothiadiazine (thiazide diuretics), Henle loop diuretics, mineralocorticoid receptor antagonists, potassium-sparing diuretics. Antihyperlipoproteinemic drugs. Lipoprotein and transport of cholesterol and triglycerides, classification of hyperlipoproteinemia. Bile acid adsorbents, fibrates, HMGCoA reductase inhibitors, cholesterol absorption inhibitors-ezetimibe. Platelet aggregation inhibitors (phosphodiesterase inhibitors, glycoprotein IIb/IIIa receptor antagonists), thrombolytics. Anticoagulants (per os, heparin and analogues).
XIV week exercises	Cardiovascular drugs-adrenergic drugs, beta-blockers, vasodilators.
XV week lectures	Review of material and preparation for the exam.
XV week exercises	Diuretics, antihypertensives, vasodilators, ACE inhibitors, antiarrhythmics.
Student workload	

Per week	**Per semester**
9 credits x 40/30=12 hours and 0 minuts 4 sat(a) theoretical classes 3 sat(a) practical classes 0 excercises **5 hour(s) i 0 minuts** of independent work, including consultations	Classes and final exam: **12 hour(s) i 0 minuts x 16 =192 hour(s) i 0 minuts** Necessary preparation before the beginning of the semester (administration, registration, certification): **12 hour(s) i 0 minuts x 2 =24 hour(s) i 0 minuts** Total workload for the subject: **9 x 30=270 hour(s)** Additional work for exam preparation in the preparing exam period, including taking the remedial exam from 0 to 30 hours (remaining time from the first two items to the total load for the item) **54 hour(s) i 0 minuts** Workload structure: **192 hour(s) i 0 minuts (cources), 24 hour(s) i 0 minuts (preparation), 54 hour(s) i 0 minuts (additional work)**
Student obligations	Lectures and laboratory work attendance.
Consultations	
Literature	1. Foyes Principles of Medicinal Chemistry. 7th ed. Williams DA, Lemke TL, editors. Baltimore: Lippincott Williams & Wilkins; 2013. 2. Wilson and Gisvolds Textbook of Organic Medicinal and Pharmaceutical Chemistry. 12th ed. Beale JM, Block JH, editors. Philadelphia: Lippincott Williams & Wilkins; 2011. 3. Radulović D, Vladimirov S. Farmaceutska hemija I. Beograd; 2005. 4. European Pharmacopoeia. 11th Edition. Strasbourg: Council of Europe; 2023. 5. Z. Vujić, J. Brborić, O. Čudina, S. Erić, B. Ivković, K. Vučićević, B. Marković; Priručnik za praktičnu nastavu iz farmaceutske hemije I i II, Beograd, 2004.
Examination methods	Class attendance (0-5). Laboratory work (0-25); Colloquia (0-20); Written exam (0-50). Pass rate for exam: 50, cumulative.
Special remarks	
Comment	

Grade:	F	E	D	C	B	A
Number of points	less than 50 points	greater than or equal to 50 points and less than 60 points	greater than or equal to 60 points and less than 70 points	greater than or equal to 70 points and less than 80 points	greater than or equal to 80 points and less than 90 points	greater than or equal to 90 points