

1. COURSE DESCRIPTION – GENERAL INFORMATION			
1.1. Course teacher	Professor Biljana Nigović, PhD	1.6. Year of study	4 <sup>th</sup>
1.2. Name of the course	<b>Pharmaceutical analysis</b>	1.7. Credit value (ECTS)	10,5
1.3. Associate teachers	Associate Professor Renata Jurišić Grubešić, PhD Associate Professor, Ana Mornar Turk, PhD Associate Professor Jadranka Vuković Rodriguez, PhD Miranda Sertić, PhD	1.8. Type of instruction (number of hours L+E+S+e-learning)	60+60+15
1.4. Study programme (undergraduate, graduate, integrated)	Integrated study of Pharmacy	1.9. Expected enrolment in the course	130
1.5. Status of the course	Compulsory	1.10. Level of use of e-learning (1, 2, 3 level), percentage of instruction in the course on line (20% maximum)	2 <sup>nd</sup>
2. COURSE DESCRIPTION			
2.1. Course objectives	Students will learn about the system of analytics and quality control of medicines; they will understand the development and validation of analytical methods for pharmaceutical samples according to the methodology of the European Pharmacopoeia; know modern analytical techniques for identification, purity testing and determination of pharmaceuticals. The acquired knowledge and skills provide a basis for electives courses Analytics in the development of pharmaceutical products and Quality assurance and registration of medicines.		
2.2. Enrolment requirements and required entry competences for the course	Analytical chemistry I and II – exams passed Medicinal chemistry II – course attended		
2.3. Learning outcomes at the level of the study programme to which the course contributes	<ul style="list-style-type: none"> <li>Proposing procedures related to the analysis and quality control of medicines.</li> <li>Applying analytical methods to ensure the quality of medicines in accordance with good laboratory practice and the relevant European directives.</li> </ul>		
2.4. Expected learning outcomes at the level of the course (4-10 learning outcomes)	Student will be able to: <ol style="list-style-type: none"> <li>Describe and use pharmacopoeia monographs for the analysis of active pharmaceutical substances and excipients, and quality control of medicines;</li> </ol>		

	<ol style="list-style-type: none"> <li>2. Explain the analysis of pharmaceuticals using spectroscopic (IR, NIR, UV Vis, fluorescence, Raman spectroscopy, AES, AAS, ICP, NMR, MS, X-ray), chromatographic (HPLC, GC, TLC, HPTLC, gel and ion chromatography, GC-MS, LC-MS), electrophoretic, electrochemical and thermoanalytical techniques;</li> <li>3. Compare the possibility of different analytical techniques and choose the appropriate technique to address specific problems in pharmaceutical analysis;</li> <li>4. Define the sources and types of impurities in pharmaceuticals and choose the methods for their control in accordance with the relevant ICH guidelines and European directives;</li> <li>5. Apply analytical methods for identification, purity testing and quantitative determination of pharmaceutical ingredients and calculate the content of impurities and the percentage of the declared content in pharmaceutical dosage forms;</li> <li>6. Explain analysis of polymorphs, hydrates, enantiomers, and biological medicines by various analytical techniques and correlate their quality control in terms of bioavailability, stability of the pharmaceutical product and adverse drug effects.</li> </ol>
<p>6.1. Course content broken down in detail by weekly class schedule (syllabus)</p>	<p>LECTURES:</p> <ul style="list-style-type: none"> <li>• Introduction to analytical studies of pharmaceuticals and legislation.</li> <li>• European Pharmacopoeia. National Pharmacopoeia. Pharmacopoeia monographs. Chemical Reference Standard, Biological Reference Preparations, and reagents.</li> <li>• Infrared spectroscopy (IR) in the identification of pharmaceutical substances as the fingerprint method. Interpretation of the IR spectra of the drug molecule. Identification of active pharmaceutical substances and excipients by chemical reactions according to the regulations of the European Pharmacopoeia.</li> <li>• Impurities in pharmaceutical substances: sources, types and control.</li> <li>• UV-Vis spectrophotometry: identification, purity testing, quantitative analysis and determination of physico-chemical properties of drugs.</li> <li>• Physical and chemical properties of drug molecules important in the selection and development of analytical methods.</li> <li>• The chromatographic parameters and separation efficiency. Quantitative analysis of pharmaceutical substances and pharmaceutical dosage forms using internal and external standard method, calibration and normalisation procedures.</li> <li>• Gas chromatography (GC): determination of volatile impurities and residual solvents, types of stationary phases and detectors, derivatization in GC analysis.</li> <li>• Pharmaceutical analysis using high performance liquid chromatography (HPLC). Reversed-phase and normal-phase chromatography. The effect of the drug's molecular structure on the retention time. Isocratic and gradient</li> </ul>

elution. HPLC analysis with the addition of ionic reagents.

- The analysis of anions and cations by ion chromatography. HPLC analysis of peptide drugs. Gel chromatography in analysis of the biological medicines. Supercritical fluid chromatography.
- Thin layer chromatography (TLC) in pharmacopoeia methods. High Performance TLC (HPTLC) in pharmaceutical analysis.
- Validation of analytical procedures. Analytical parameters in the validation process.
- Structural analysis of pharmaceuticals using NMR spectroscopy.
- The application of mass spectrometry (MS) in pharmaceutical analysis: types of ionization, fragmentation of drug molecules, selective ion mass analyzer.
- Hyphenated techniques in pharmaceutical analysis: LC-MS techniques in the characterization of drug impurities and metabolites, GC-MS technique in bioanalytics and identification of degradation products.
- Determination of the physical constants of pharmaceutical substances and limit tests according to the regulations of the European Pharmacopoeia.
- Atomic emission (AES) and atomic absorption spectroscopy (AAS) and inductively coupled plasma (ICP) emission spectroscopy/mass spectrometry for determination of metal content in the pharmaceutical substances by standard addition method and direct calibration.
- Near-infrared spectroscopy (NIR): the determination of moisture and particle size, identification and determination of the content of active substance in the multicomponent dosage forms, the control of bend uniformity of compositions for pharmaceutical formulations.
- Raman spectroscopy in pharmaceutical analysis.
- Fluorescence spectrophotometry: application and examples of quantitative determination of pharmaceuticals.
- Electrophoresis in pharmaceutical analysis. Capillary electrophoresis (CE): factors affecting the migration velocity and separation, types of CE, drug impurity profiling.
- Electroanalytical methods in pharmacopoeial procedures of analysis.
- Thermoanalytical methods in pharmaceutical analysis: thermogravimetry, differential thermal analysis, differential scanning calorimetry and thermal microscopy.
- Analytical methods for studying and characterizing polymorphs, spectroscopic techniques, solid-state NMR and X-ray powder diffraction.
- Methods for the analysis of hydrate drug forms and the determination of water by Karl-Fischer titration.
- Methods for the analysis of enantiomers: polarimetry, circular dichroism, single crystal X-ray diffraction. Chiral chromatography and testing enantiomeric purity.
- Titrimetric methods of analysis in the pharmacopoeia procedures. Flow injection analysis.
- Determining the quality of excipients. Determination of total organic carbon in pharmaceutical water.
- Analysis of biological medicines: peptide mapping and amino acid analysis, immunoassays. Tests for sterility, pyrogenic substances and bacterial endotoxin in pharmaceutical preparations. Analysis of radiopharmaceuticals.
- Quality control of medicines. Pharmaceutical quality assurance. Good manufacturing practice. Good laboratory practice.

#### SEMINARS:

- The calculation of limit values of inorganic contaminants in pharmaceutical substances.

	<ul style="list-style-type: none"> <li>• Quantitative determination of active pharmaceutical substances and excipients using titrimetric analytical methods according to pharmacopoeia regulations.</li> <li>• Quantitative determination of active pharmaceutical substances and determination of the percentage of the declared content in pharmaceutical formulations using UV-VIS technique.</li> <li>• Determination of validation parameters: accuracy, precision, limit of detection and limit of quantification.</li> <li>• Calculation of capacity factor, column effectiveness, selectivity coefficient and permitted impurity content in chromatographic procedures of pharmaceutical analysis.</li> <li>• Determination of the percentage of the declared content of active pharmaceutical substances in pharmaceutical dosage forms using calibration curve, internal and external standard by liquid and gas chromatography.</li> <li>• Determination of chiral drug optical purity. Determination of drug impurities using potentiometry and standard addition method.</li> <li>• Determination of metal content in the pharmaceuticals using standard addition method and direct calibration method of AAS and AES technique.</li> </ul> <p>LABORATORY EXERCISES:</p> <ul style="list-style-type: none"> <li>• Identification of excipients using selective chemical reactions and by determining the melting point.</li> <li>• Identification of ephedrine and calcium pantothenate by specific optical rotation determination.</li> <li>• Identification of active pharmaceutical substances (atropine, barbital, benzocaine, phenobarbital, furosemide, propranolol, nifedipine, morphine, quinine, codeine, amoxicillin, oxytetracycline, etc.) using IR, UV-Vis spectrophotometry and thin layer chromatography.</li> <li>• Identification of active pharmaceutical substances in analgoantipyretic tablets by TLC.</li> <li>• Identification of acetylsalicylic acid and ascorbic acid in tablets by HPLC.</li> <li>• Testing of clarity and degree of opalescence for resorcinol and calcium gluconate solutions.</li> <li>• Testing of proteolytic impurities in chloramphenicol, caffeine, zinc oxide, procaine and sulfacetamide.</li> <li>• Limit tests of inorganic impurities such as chloride in dextrin, sulfates in potassium bicarbonate and calcium in tartaric acid.</li> <li>• Impurity testing of atropine, cephalexin and lactose using UV-Vis spectrophotometry.</li> <li>• Impurity testing of nifedipine and chloramphenicol using TLC.</li> <li>• Impurity testing of chiral drug substances, ascorbic acid, chloramphenicol, codeine and morphine using polarimetry.</li> <li>• Impurity testing of acetylsalicylic acid using high performance liquid chromatography</li> <li>• Impurity testing of ethanol by gas chromatography.</li> <li>• Determination of theobromine, acetylsalicylic acid, sodium chloride in eye drops, calcium lactate and ascorbic acid using titrimetric methods.</li> <li>• Determination of chloramphenicol, rifampicin and ketoprofen using UV-Vis spectrophotometry.</li> <li>• Determination of cephalexin monohydrate using HPLC.</li> <li>• Determination of the percentage of the declared content of ibuprofen in the dosage form by HPLC .</li> <li>• Validation of the analytical method for the determination of chloramphenicol by UV-Vis spectrophotometry.</li> </ul>		
6.2. Type of instruction	<b>lectures</b>	independent study	6.3. Comments:

6.2. Type of instruction	<b>seminars</b> and workshops <b>exercises</b> online in entirety mixed e-learning field work		multimedia and the internet <b>laboratory</b> work with the mentor (other)		6.3. Comments:	
6.4. Student responsibilities						
6.5. Screening of student's work (specify the proportion of ECTS credits for each activity so that the total number of CTS credits is equal to the credit value of the course)	Class attendance	2	Research		Practical training	
	Experimental work	2	Report			
	Essay		Seminar essay		(Other--describe)	
	Tests	1	Oral exam	3.5	(Other—describe)	
	Written exam	2	Project		(Other—describe)	
2.10. Grading and evaluation of student work over the course of instruction and at a final exam	Entry and final test for laboratory exercises, experimental work grade, written and oral exam.					
2.11. Required literature (available at the library and via other media)	<b>Title</b>					
	B. Nigović, Predavanja iz analitike lijekova, Faculty of Pharmacy and Biochemistry, 2013.					
	B. Nigović, Seminari iz analitike lijekova, Faculty of Pharmacy and Biochemistry, 2013.					
	B. Nigović, R. Jurišić-Grubešić, J. Vuković-Rodriguez, A. Mornar Turk, M. Sertić, Praktikum iz analitike lijekova, skripta, Faculty of Pharmacy and Biochemistry, 2014.					
	D. G. Watson, Pharmaceutical analysis, A Textbook for Pharmacy Students and Pharmaceutical Chemists, 3rd Edition, Elsevier, 2012.					
European Pharmacopoeia 6th edition, Council of Europe, Strasbourg, 2008.						
2.12. Optional literature	Satinder Ahuja, Stephen Scypinski, eds., Handbook of modern pharmaceutical analysis, Academic Press, San Diego, 2001.					
2.13. Methods of monitoring quality that ensure acquisition of exit competences	Outcomes 1, 5 and 7 are checked during the experimental work and final test from exercises. Outcomes 2, 3, 4, 6 are checked by written and oral exam.					