Study program: Integrated academic studies of Pharmacy

Type and level of the study program: integrated academic studies

Course title: DRUG ANALYSIS (PhV-DRAN)

Teacher: Jelena M. Cvejić Hogervorst, Milica T. Atanacković Krstonošić, Mira P. Mikulić

Course status: compulsory

ECTS Credits: 5

Condition: Pharmaceutical chemistry III; Pharmacognosy II

Course aim

The main aim of the subject Drug analysis is introduction with analysis and control procedure of drug substance and final drug product, domestic and international regulatory rules and validation of analytical methods. Also, the aim is to gain knowledge about applications of analytical methods in pharmaceutical analysis, methods of analysis of various pharmaceutical forms and relationship between purpose of analysis and selection of analytical technique. Analysis of major active component(s), excipients and impurities. Student develops skills for practical laboratory work. In laboratory, analyses of certain pharmaceutical forms are performed using pharmacopoeia procedures or adapted specifications and practical knowledge and skills are gained. Development of critical way of thinking and ability for scientific and research work.

Expected outcome of the course:

It is necessary that student learns about application and choice analytical methods in analysis of actual samples. Knowledge about methods and phases of creation of specification of certain drug. Pharmacopoeia, specifications, law and regulatory rules. Approach to analysis as function of characteristics and quality of analyzed pharmaceutical form/drug substance. Methods of evaluation of analytical error and statistical data analysis. Real sample preparation and analysis of pharmaceutical forms.

Practical application of learned skills. Ability for choosing appropriate analytical method. Searching, interpretation and handling information necessary for appropriate analysis of samples. Preparation and defining procedure considering the aim and the purpose of the analysis. Practical performance of sample analysis. Data analysis, error evaluation and final results expression.

Course description

Theoretical education

1. Introduction in drug analysis. Law and regulatory rules. International Conference on Harmonization (ICH). Good laboratory practice (GLP). ISO 17025 General requirements for the competence of testing and calibration laboratories. Pharmacopoeia-monographs. **2.** Physical and chemical properties of drug molecules, identification of drug substances, pH value, ionization of drug molecules and pKa value. Partition coefficient. Drug stereochemistry, polarimetry, refractometry. Physical constants- specific optical rotation, melting point, freezing point. Determination of melting point - eutecticum, Lefler's block, method of modification. Physical and chemical profile of certain drug molecules. Instrumental methods of analysis - spectroscopy and chromatography**. 3.** Impurities in drug substances and products - organic and non-organic impurities. Residual solvents. Enantiomer impurities. Degradation products. **4.** Application of titration techniques in pharmaceutical analysis. Titrations- direct acid/basic, indirect in aqueous phase, non-aqueous titrations, complexometric, redox, iodometric, potentiometric titrations. Carl-Fischer titrations, flow injection analysis (FIA). Applications. **5.** Application of instrumental methods in pharmaceutical analysis - ultraviolet and visible spectroscopy (UV/Vis)-differential spectroscopy, multicomponent analysis. Interferences, correction techniques, derivative spectroscopy, determination of pKa value and solubility, dissolution test. Infrared spectroscopy (IR). **6.** Application of separation techniques in pharmaceutical analysis- review of separation methods. HPLC-special applications, chromatography with anionic/cationic ionic coupling agent (analysis of adrenaline and ascorbic acid), exclusion chromatography (analysis of hyaluronic acid), ion-exchanging chromatography (analysis of catecholamines), derivatization, separation of enantiomers with GC- derivatization (analysis of pseudoephedrine in syrup), chiral selectivity, analysis of atropine in eye drops, quantification of ethanol in formulation, manufacturing and degradation residues, pivalic acid in dipivefrin eye drops, dimethylaniline in bupivacaine injections. Determination of residual solvents-pharmacopoeia procedure, "head space" and "purge trap" analysis. Thin-layer chromatography-limit tests, determination of impurities in pharmaceutical products. Known and unknown impurities, combined tests. Capillary electrophoresis. Extraction methods. Solid phase extraction. **7.** Drug analysis in pharmaceutical forms - sample preparation from different matrices. Characteristics of analysis of different pharmaceutical forms - tablets, capsules, drops, injections, suppositories, syrups, solutions… **8.** Validation of analytical methods- Strategy for validation. Validation parameters - accuracy and precision, repeatability and reproducibility, range, linearity, limit of detection and quantification, robustness. Validation process. Example. **9.** Providing drug quality - Drug quality. Drug specification, definition. Specification in different phases of drug development. Manufacturing and distribution of drugs. **10**. Quality control of drug products - Activities of quality control. Procedure of quality control- laboratory analysis. Releasing drug to the market, drug embargo, reclamation and drug withdrawal. Drug registration.

Practical education: exercises, other forms of education, research related activities

Laboratory practice involves quality control of solvents, active drug substances and different pharmaceutical forms and evaluation of obtained results in accordance with appropriate regulation.

1. Quality control of solvents- Characters, identification, physical and chemical properties (pH, relative density), microbiological purity. Distilled water, 96% ethanol, European Pharmacopoeia regulation. **2.** Quality control of chemical substances, secondary/active - appearance, identification, physical and chemical properties, impurities (organic, non-organic, residual solvents, enantiomer purity, polymorphism), assay, labelling. Sodium chloride, boric acid, European Pharmacopeia regulation. **3.** Quality control of liquid preparations for cutaneous application - appearance, identification, physical and chemical properties, impurities (organic, non-organic, residual solvents), assay, microbiological purity. Iodi solutio aquosa, Iodi solutio aethanolica, Acidi borici sol., European Pharmacopoeia regulation or manufacturer specification. **4.** Quality control of parenteral preparation - appearance, identification, physical and chemical properties, purity, assay, content uniformity, sterility, bacterial endotoxins. Nirypan injections, Glucose infusion, manufacturer specification. **5.** Quality control of liquid preparations for oral use - appearance, identification, physical and chemical properties, purity, assay, content uniformity, preservative content, microbiological purity. Cliacil® syrup, manufacturer specification. **6.** Quality control of tablets and capsules - appearance, identification, physical and chemical properties, purity, assay, content uniformity, dissolution test, microbiological purity. Glibenclamide tablets, Ampicillin capsules, manufacturer specification. **7.** Quality control of rectal preparations - appearance, identification, impurities, assay, content uniformity, disintegration, dissolution test, microbiological purity. Glycerol suppositories, paracetamol suppositories, manufacturer specification. **8.** Quality control of eye preparations - appearance, identification, impurities, assay, sterility, particle size, microbiological purity. Atropine sulphate eye drops, Oculentum simplex, manufacturer specification. **9.** Validation of analytical methods - Concept of validation, purpose of validation of analytical methods. Analytical procedures that require validation. International regulations for validation of analytical methods, validation protocol. Validation of methods for quality control of pharmaceutical forms (HPLC). Validation documentation. **10**. Additional analysis methods, UV/Vis spectroscopy- content of ascorbic and acetylsalicylic acid in effervescent tablet, multicomponent analysis. Menthol content in preparations lozenges, derivatization. **11.** Drug registration. Requirements, procedure and conditions *for* releasing drug on the market, required documentation.

Literature

Compulsory

1. Watson DG. Pharmaceutical analysis - A textbook for pharmacy students and pharmaceutical chemists. Edinburgh: Churchill Livingstone; 1999.

Additional

2. Ahuja S, Scypinski S. Handbook of modern pharmaceutical analysis. 2nd ed. Amsterdam: Elsevier; 2011.
3. Cairns D. Essentials of pharmaceutical chemistry. 2nd ed. UK: Pharmaceutical Press; 2003.
4. Snyder LR, Kirkland JJ, Glajch JL. Practical HPLC method development. 2nd ed. John Wiley & Sons; 1997.

Number of active classes				Other:
Lectures: 30	Practice: 60	Other types of teaching:	Research related activities:	

Teaching methods: lectures; laboratory work.

Student activity assessment (maximally 100 points)

Pre-exam activities	**points**	**Final exam**	**points**
Lectures	10	Written	60
Practices	10	Oral	
Colloquium	20	.....	
Essay			