University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Methodology of scientific research

Teachers: Savić M. Miroslav, Krajnović M. Dušanka, Kotur-Stevuljević M. Jelena, Bogavac-Stanojević B. Nataša

Course status: Mandatory common, module: Doctoral academic studies

Semester: I	**Year of studies:** I
ECTS points: 5	**Course code:** Д1О31

Requirements: none

Course aims:

The aim of this course is to provide participants with general scientific skills in order to formulate a scientific problem and plan the experiment, as well as to understand the complete process of preparation and publication of scientific research results

Course outcomes:

By the end of this course participants will be able to summarize and apply the principles of the methodology of scientific-researh work and scientific writing

Course contents:

Science and scientific method. Problem and scientific problem. Hypothesis. Hypothesis verification: scientific observation and scientific experiment. Common methodology of scientific research in biomedicine. Classification of research. Experimental research in laboratory. Animal experiments. Types of studies in epidemiological investigations. Ethics and biomedical investigations. Ethical codex of scientific-researh work. Generation of biomedical information. Communications. Networks. Internet. Internet search engines. Authorship/co-authorship. Role and duties of principal investigator. Protection of intellectual property. Classification of scientific work. Writing of scientific and professional papers. Literature citing. Review process. Oral presentation of scientific work (adaptation to audience and situation). Designing PowerPoint slides for a scientific presentation. Introduction to writing of project proposals. Master's thesis and doctoral dissertation.

Recommended literature:

1 Cargill, M, O'Connor P. Writing scientific research articles: Strategy and steps. John Wiley & Sons, 2013.

2. Baumgartner TA, Hensley LD. Conducting and Reading Research in Health and Human performance. Mc Graw Hill, Boston, 2006

3. Machin D, Campbell MJ. Design of studies for medical research. John Wiley & Sons, Hoboken, 2005.

4. Peat J, Elliot E, Baur L, Keena V. Scientific writing – easy when you know how. BMJ Books, London, 2002.

5. Albert T. The A-Z of medical writing. BMJ Books, London, 2000.

6. Hudson Jones A, McLeallan F. Ethical Issues in Biomedical Publication. Baltimore: John Hopkins University Press, 2000.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures and study-research work

Grading system:

Seminar: 30 points; written exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Statistics in research

Teachers: Bogavac-Stanojević B. Nataša, Kotur-Stevuljević M. Jelena

Course status: Mandatory common, module: Doctoral academic studies

Semester: I	**Year of studies:** I
ECTS points: 5	**Course code:** Д1О32

Requirements: One semester of undergraduate studies in mathematics and statistics
pharmaceutical / medical biochemistry / medicine

Course aims:

Understanding advanced statistical methods. Applying advanced statistical analyses in scientific research.

Course outcomes:

After completing the course students will be trained to:

- Recognizing the type of statistical analysis
- Interpret the significance of the obtained statistical indicators and discuss the results,
- Understand the importance of the application of statistical methods in the scientific research,
- Use statistical software in the data analysis

Course contents:

One-way analysis of variance (ANOVA). Two-way analysis of variance. ANOVA with replication. Post-hoc tests. Simple linear regression analysis. Multiple regression analyses. Logistic regression. Analysis of covariance. Nonparametric analysis of variance. Nonparametric correlation. Chi-square test. Confidence interval.

Student's research: Solving different statistical problems and tasks.

Recommended literature:

1. Sheskin DJ. Handbook of parametric and nonparametric statistical procedures Chapman & Hall/CRC, Washington, D.C., 2000.
2. Vitingoff E, Shiboski SC, Glidden DV, McCulloch CE. Regression Methods in Biostatistics,Springer Science + Business Media, New York, 2005.
3. Selvin S. Statistica Analysis of Epidemiological Data, Oxfor University Press, Oxford, 1996.
4. Tamhane AJ, Dunlop DD. Statistics and Data Analysis, Prentice Hall, Upper Saddle River, NJ, 2000.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures, computer exercises, solving practical problems

Grading system:

The presence at lectures: 30 points; Written Exam: 70 points.

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Seminar 1

Teachers: Ivanović P. Darko, Zečević L. Mira, Malenović M. Anđelija, Stojanović S. Biljana, Miletić Đ. Ivanka, Šobajić S. Slađana, Stanković M. Ivan, Đorđević I. Brižita, Vuleta M. Gordana, Milić R. Jela, Primorac M. Marija, Savić D. Snežana, Vasiljević D. Dragana, Krajišnik R. Danina, Đekić M. Ljiljana, Spasić M. Slavica, Jelić-Ivanović D. Zorana, Spasojević-Kalimanovska V. Vesna, Stojanov D. Marina, Ignjatović D. Svetlana, Topić S. Aleksandra, Dopsaj B. Violeta, Bogavac-Stanojević B. Nataša, Kotur-Stevuljević M. Jelena, Tasić M. Ljiljana, Marinković D. Valentina, Krajnović M. Dušanka, Miljković R. Branislava, Vezmar Kovačević D. Sandra, Vučićević M. Katarina, Kovačević N. Nada, Petrović D. Silvana, Maksimović A. Zoran, Kundaković D. Tatjana, Drobac M. Milica, Ugrešić D. Nenad, Stepanović-Petrović M. Radica, Savić M. Miroslav, Ilić V. Katarina, Novaković N. Aleksandra, Tomić A. Maja, Leposavić M. Gordana, Arsenović-Ranin M. Nevena, Stojić-Vukanić M. Zorica, Plećaš-Solarović A. Bosiljka, Pešić P. Vesna, Nedeljković S. Miodrag, Milenković T. Marina, Antić Stanković A. Jelena, Parojčić V. Jelena, Ibrić R.Svetlana, Đuriš D.Jelena, Grbić V. Sandra, Đurić R. Zorica, Vladimirov M.Sote, Agbaba D. Danica, Bulat L. Zorica,

Matović J. Vesna, Antonijević M. Biljana, Vujanović L. Dragana, Đukić M. Mirjana

Course status: Mandatory common, module: Doctoral academic studies

Semester: I	**Year of studies:** I
ECTS points: 5	**Course code:** Д1О33

Requirements: none

Course aims:

This course aims to enable the participant to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; apply the principles of making a successful oral presentation in English.

Course outcomes:

By the end of this course participants will be able to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; apply the principles of making a successful oral presentation in English

Course contents:

Collecction of pertinent literature (by use of bibliographic databases, web sites of publishers, general search engines). Preparation of personal databases. Contextual analysis of key publications in a field. Preparation and presentation of the published results.

Recommended literature:

1. Alley M. The craft of scientific presentations. Critical steps to succeed and critical errors to avoid. Springer-Verlag New York, Inc., 2003.
2. Original scientific papers and review articles in the field of the participant's research activity.

The total of active learning classes	**Lectures:** 30
	Individual research work: 60

Teaching methods:

Study-research work

Grading system:

Seminar: 70 points; written exam: 30 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Seminar 2

Teachers: Ivanović P. Darko, Zečević L. Mira, Malenović M. Anđelija, Stojanović S. Biljana, Miletić Đ. Ivanka, Šobajić S. Slađana, Stanković M. Ivan, Đorđević I. Brižita, Vuleta M. Gordana, Milić R. Jela, Primorac M. Marija, Savić D. Snežana, Vasiljević D. Dragana, Krajišnik R. Danina, Đekić M. Ljiljana, Spasić M. Slavica, Jelić-Ivanović D. Zorana, Spasojević-Kalimanovska V. Vesna, Stojanov D. Marina, Ignjatović D. Svetlana, Topić S. Aleksandra, Dopsaj B. Violeta, Bogavac-Stanojević B. Nataša, Kotur-Stevuljević M. Jelena, Tasić M. Ljiljana, Marinković D. Valentina, Krajnović M. Dušanka, Miljković R. Branislava, Vezmar Kovačević D. Sandra, Vučićević M. Katarina, Kovačević N. Nada, Petrović D. Silvana, Maksimović A. Zoran, Kundaković D. Tatjana, Drobac M. Milica, Ugrešić D. Nenad, Stepanović-Petrović M. Radica, Savić M. Miroslav, Ilić V. Katarina, Novaković N. Aleksandra, Tomić A. Maja, Leposavić M. Gordana, Arsenović-Ranin M. Nevena, Stojić-Vukanić M. Zorica, Plećaš-Solarović A. Bosiljka, Pešić P. Vesna, Nedeljković S. Miodrag, Milenković T. Marina, Antić Stanković A. Jelena, Parojčić V. Jelena, Ibrić R.Svetlana, Đuriš D.Jelena, Grbić V. Sandra, Đurić R. Zorica, Vujić B. Zorica, Čudina A. Olivera, Bulat L. Zorica, Matović J. Vesna, Antonijević M. Biljana, Vujanović L. Dragana, Đukić M. Mirjana

Course status: Mandatory common, module: Doctoral academic studies

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** Д1О34

Requirements: none

Course aims:

This course aims to enable the participant to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; upgrade his/her capacities for giving a successful oral presentation in English.

Course outcomes:

By the end of this course participants will be able to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; apply the principles of making a successful oral presentation in English

Course contents:

Collecction of pertinent literature (by use of bibliographic databases, web sites of publishers, general search engines). Preparation of personal databases. Contextual analysis of key publications in a field. Preparation and presentation of the published results.

Recommended literature:

1. Alley M. The craft of scientific presentations. Critical steps to succeed and critical errors to avoid. Springer-Verlag New York, Inc., 2003.

2. Original scientific papers and review articles in the field of the participant's research activity.

The total of active learning classes	**Lectures:** 30
	Individual research work: 60

Teaching methods:

Study-research work

Grading system:

Seminar: 70 points; written exam: 30 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Seminar 3

Teachers: Ivanović P. Darko, Zečević L. Mira, Malenović M. Anđelija, Stojanović S. Biljana, Miletić Đ. Ivanka, Šobajić S. Slađana, Stanković M. Ivan, Đorđević I. Brižita, Vuleta M. Gordana, Milić R. Jela, Primorac M. Marija, Savić D. Snežana, Vasiljević D. Dragana, Krajišnik R. Danina, Đekić M. Ljiljana, Spasić M. Slavica, Jelić-Ivanović D. Zorana, Spasojević-Kalimanovska V. Vesna, Stojanov D. Marina, Ignjatović D. Svetlana, Topić S. Aleksandra, Dopsaj B. Violeta, Bogavac-Stanojević B. Nataša, Kotur-Stevuljević M. Jelena, Tasić M. Ljiljana, Marinković D. Valentina, Krajnović M. Dušanka, Miljković R. Branislava, Vezmar Kovačević D. Sandra, Vučićević M. Katarina, Kovačević N. Nada, Petrović D. Silvana, Maksimović A. Zoran, Kundaković D. Tatjana, Drobac M. Milica, Ugrešić D. Nenad, Stepanović-Petrović M. Radica, Savić M. Miroslav, Ilić V. Katarina, Novaković N. Aleksandra, Tomić A. Maja, Leposavić M. Gordana, Arsenović-Ranin M. Nevena, Stojić-Vukanić M. Zorica, Plećaš-Solarović A. Bosiljka, Pešić P. Vesna, Nedeljković S. Miodrag, Milenković T. Marina, Antić Stanković A. Jelena, Parojčić V. Jelena, Ibrić R.Svetlana, Đuriš D.Jelena, Grbić V. Sandra, Đurić R. Zorica, Vujić B. Zorica, Čudina A. Olivera, Bulat L. Zorica, Matović J. Vesna, Antonijević M. Biljana, Vujanović L. Dragana, Đukić M. Mirjana

Course status: Mandatory common, module: Doctoral academic studies

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** Д2О31

Requirements: none

Course aims:

This course aims to enable the participant to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; upgrade his/her capacities for giving a successful oral presentation of results of personal reserch activities

Course outcomes:

By the end of this course participants will be able to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; apply the principles of making a successful oral presentation in English

Course contents:

Collecction of pertinent literature (by use of bibliographic databases, web sites of publishers, general search engines). Preparation of personal databases. Contextual analysis of key publications in a field. Preparation and presentation of the published results.

Recommended literature:

1. Alley M. The craft of scientific presentations. Critical steps to succeed and critical errors to avoid. Springer-Verlag New York, Inc., 2003.

2. Original scientific papers and review articles in the field of the participant's research activity.

The total of active learning classes	**Lectures:** 30
	Individual research work: 60

Teaching methods:

Study-research work

Grading system:

Seminar: 70 points; written exam: 30 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Seminar 4

Teachers: Ivanović P. Darko, Zečević L. Mira, Malenović M. Anđelija, Stojanović S. Biljana, Miletić Đ. Ivanka, Šobajić S. Slađana, Stanković M. Ivan, Đorđević I. Brižita, Vuleta M. Gordana, Milić R. Jela, Primorac M. Marija, Savić D. Snežana, Vasiljević D. Dragana, Krajišnik R. Danina, Đekić M. Ljiljana, Spasić M. Slavica, Jelić-Ivanović D. Zorana, Spasojević-Kalimanovska V. Vesna, Stojanov D. Marina, Ignjatović D. Svetlana, Topić S. Aleksandra, Dopsaj B. Violeta, Bogavac-Stanojević B. Nataša, Kotur-Stevuljević M. Jelena, Tasić M. Ljiljana, Marinković D. Valentina, Krajnović M. Dušanka, Miljković R. Branislava, Vezmar Kovačević D. Sandra, Vučićević M. Katarina, Kovačević N. Nada, Petrović D. Silvana, Maksimović A. Zoran, Kundaković D. Tatjana, Drobac M. Milica, Ugrešić D. Nenad, Stepanović-Petrović M. Radica, Savić M. Miroslav, Ilić V. Katarina, Novaković N. Aleksandra, Tomić A. Maja, Leposavić M. Gordana, Arsenović-Ranin M. Nevena, Stojić-Vukanić M. Zorica, Plećaš-Solarović A. Bosiljka, Pešić P. Vesna, Nedeljković S. Miodrag, Milenković T. Marina, Antić Stanković A. Jelena, Parojčić V. Jelena, Ibrić R.Svetlana, Đuriš D.Jelena, Grbić V. Sandra, Đurić R. Zorica, Vujić B. Zorica, Čudina A. Olivera, Bulat L. Zorica, Matović J. Vesna, Antonijević M. Biljana, Vujanović L. Dragana, Đukić M. Mirjana

Course status: Mandatory common, module: Doctoral academic studies

Semester: IV	**Year of studies:** II
ECTS points: 5	**Course code:** Д2О32

Requirements: none

Course aims:

This course aims to enable the participant to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; upgrade his/her capacities for giving a successful oral presentation of results of personal reserch activities; prepare publications containing the results obtained in the performed personal investigation

Course outcomes:

By the end of this course participants will be able to: search the scientific literature effectively and thoroughly; perform a critical analysis of publications relevant for his/her study field; apply the principles of making a successful oral presentation and preparing publications containing the personal results

Course contents:

Collecction of pertinent literature (by use of bibliographic databases, web sites of publishers, general search engines). Preparation of personal databases. Contextual analysis of key publications in a field. Preparation and oral and written presentation of the personal results.

Recommended literature:

1. Alley M. The craft of scientific presentations. Critical steps to succeed and critical errors to avoid. Springer-Verlag New York, Inc., 2003.
2. Original scientific papers and review articles in the field of the participant's research activity.

The total of active learning classes	**Lectures:** 30
	Individual research work: 60

Teaching methods:

Study-research work

Grading system:

Seminar: 70 points; written exam: 30 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Principles of Modern Pharmaceutical Analysis

Teachers: Darko P. Ivanović, Mira L. Zečević, Anđelija M. Malenović, Biljana S. Stojanović

Course status: Mandatory modules, module: Drug Analysis

Semester: I	**Year of studies:** I
ECTS points: 10	**Course code:** ДАЛ1ОМ1

Requirements: no

Course aims:

Acquiring knowledge in the field of pharmaceutical analysis necessary for characterization of the medicine, from the pharmaceutical substance until final dosage form.

Course outcomes:

Knowledge of all types of tests for pharmaceutical substances and dosage forms which characterize their quality, as well as knowledge of appropriate methods that are used to for quality control.

Course contents:

Analysis of physicochemical properties of pharmaceutical substances (solid state analysis, polymorphism, pKa values, solubility in different media, molecular stereochemistry, etc.) important for quality assessment of the substance. Methods for monitoring the physical and chemical stability of the pharmaceutical substances. Study of relationship between the chemical structure of substances and the development and implementation of new methods in the analysis of the tested compounds, as well as their related substances. Modern methods in testing of the potential drug related substance. The origin of residual solvents in pharmaceutical substances, procedures for testing and determination of the limits of residual solvents. Methods for determination and monitoring the water content in the pharmaceutical substance. Targeted degradation study, isolation and identification of the impurities. Modern methods for impurity structure confirmation. Chemical and safety aspects of impurity testing. The origin and qualification of impurities. Genotoxic impurities - classification, assessment of genotoxic potential; characteristics of methods for monitoring and analysis of genotoxic impurities. Forced degradation studies, methodology, performance conditions and ways of interpreting the results. Degradation mechanisms and analysis of degradation pathways of different structures. Drug degradation profile view. Determination of the kinetics of a chemical reaction. Active pharmaceutical substance testing. Pharmacopoeia and compendial tests. Quality assessment of the dosage form during development and preformulation studies. Testing of the final dosage form. The scientific aspect of method validation. Evaluation and interpretation of obtained results. Verification of compendial methods. Transfer of compendial methods.

Recommended literature:

1. Ahuja, S. Scipynski, S., Editors: Handbook of Modern Pharmaceutical Analysis. Academic Press, San Diego, 2001.

2. Ermer, J., McB. Miller, J. H., Editors: Method Validation in Pharmaceutical Analysis, WILEY–VCH Verlag GmbH & Co. KGaA, Weinheim, 2005.

3. Ohannesian, L, Streeter, A. J. Editors: Handbook of Pharmaceutical Analysis, Marcel Dekker, Inc., New York, USA 2002.

4. Pedersen, O.: Pharmaceutical Chemical Analysis: Methods for Identification and Limit Tests, Taylor & Francis Group, LLC 2006.

5. Ahuja, S.: Impurities Evaluation of Pharmaceuticals, Marcel Dekker, Inc., New York, 1998.

6. Yoshioka, S., Stella, V. J.: Stability of drugs and dosage forms, Cluwer, Academic publishers, New York, 2002.

The total of active learning classes	**Lectures:** 60
	Individual research work: 60

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Chemometrics in Drug Analysis

Teachers: Darko P. Ivanović, Mira L. Zečević, Anđelija M. Malenović, Biljana S. Stojanović

Course status: Mandatory modules, module: Drug Analysis

Semester: I	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1ОМ2

Requirements: no

Course aims:

Acquiring knowledge about different chemometrical approaches impirtant for application in different area of drug analysis.

Course outcomes:

Success in defining nature of problem and proper selection of exeprimental design. Interpretation of experimentali obtained results and presentation of relevant conclusion.

Course contents:

Chemometrics – teoretical principles. Chemometrics approach in anaysis of experiments – significance. Analysis of experiments with one factor. Analysis of experiments with multiple factors. Application of experimental design in screening experiments. Design chosing and interpretation of obtained results. Analysis of full factorial and fractional factorial design. Solving problems with highly fractionated designs. response surface methodology and interpretation of obtained results. Central composite desgn, Box–Behnken design and full factorial design in method optimization. Qualitative and quantitative factors analysis by applying D optimal design. Multicriterium and multifactors optimization. Deringer desirability function ans sensitivity analysis. Robustness testing in method development and optimization. Calculation of parcial and total robustness criterium. Experimental design (Plackett-Burman design and fractional factorial design in robustness testing with suitable statistical analysis (Dong algorithm and analysis of non-significance interval for significance factors) followed by appropriate graphical evaluation (Pareto charts, half-normal probability and normal probability plots). Process improvement by application of ceratin experimental design. Visualisation of obtained results (3-D graphs, 2-D graphs, etc). Estimation of model adequacy. Model validation. Estimation of scientific significance of experimental design application. Problem solving – ase study with analysis. Presentation of the best solution and discussion.

Recommended literature:

1. Deming, S. N., Morgan, S. L.: Experimental design: a chemometric approach, Elsevier, Amsterdam, Netherlands, 1993.

2. Brereton, R. G.: Chemometrics: Data Analysis for the Laboratory and Chemical Plant, John Wiley & Sons, Chichester, England 2003.

3. Mason, R. L, Gunst, R. F.,Hess, J. L.: Statistical Design and Analysis of Experiments, John Wiley & Sons, New Jersey, USA 2003.

4. Hinkelmann, K., Kempthorne, O.: Design and Analysis of Experiments, John Wiley & Sons, New Jersey, USA 2005.

5. Vander Heyden, Y., Nijhuis, A., Smeyers–Verbeke, J., Vandeginste, B.G.M., Massart, D.L.: Guidance for Robustness/Ruggedness Tests in Method Validation, J. Pharm. Biomed. Anal., 24, 723–753, 2001.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Separation Methods in Drug Analysis

Teachers: Darko P. Ivanović, Mira L. Zečević, Anđelija M. Malenović, Biljana S. Stojanović

Course status: Mandatory modules, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 10	**Course code:** ДАЛ1ОМ3

Requirements: no

Course aims:

Acquiring knowledge of the different types of separation methods and exploring the possibilities of their application in drug analysis.

Course outcomes:

Successful implementation of the acquired knowledge to solve specific problems in drug analysis.

Course contents:

Liquid chromatography, advantages, disadvantages, and application in drug analysis. Separation mechanisms for different types of chromatography (adsorption, partition, gel, ion-exchange and affinity chromatography). The chromatographic parameters and criteria to assess the quality of the chromatographic separation. The elementary and global separation criteria. The chromatographic response functions for the interpretation of the chromatographic analysis quality. The assessment and analysis of the acceptability of the chromatographic separation. The analysis of the Van Deemter 's equation coefficients. Fitting of the retention data in localized and non-localized adsorption models. The characteristics of the stationary phase: geometry of the particles, stationary phase chemistry, chemical modifications, and the hybrid and the polymeric stationary phase. The mobile phase modifications (ion-pair chromatography, ion suppression). The micellar and mikroemulziona liquid chromatography and improvement of the method selectivity. Hydrophilic interaction chromatography, advantages, limitations, and application in drug analysis. Hydrophobic interaction chromatography, advantages, limitations, and application in drug analysis. Ultra High Performance Liquid Chromatography - UHPLC, characteristics and analytical application in drug analysis. Hyphenated techniques - liquid/mass, liquid/mass/mass (LC -MS, LC-MS/MS) and their application in drug analysis. Development of liquid chromatographic method compatible with mass spectrometry. Preparative liquid chromatography and its importance in the isolation of impurities and degradation products. Gas chromatography and gas chromatography/mass analysis of the genotoxic impurities and residual solvents .

Recommended literature:

1. Snyder, L. R., Kirkland, J. J., Dolan, J. W.: Introduction to modern liquid chromatography. Third Edition, John Wiley & Sons, Inc., New York,USA 2010.

2. Ahuja, S.: Chromatography and separation science. Volume 4 of Separation science and technology, Academic Press, San Diego, USA 2003.

3. Ed. Kazakevich, Y., Lobrutto, R.: HPLC for pharmaceutical scientist. John Wiley & Sons, Inc., New York,USA 2007.

4. Scott, R. P. W.: Liquid chromatography column theory, John Wiley & Sons, Inc., Chcihester, England 1991. 5. Kromidas, S.: HPLC made to measure. John Wiley & Sons, Inc., New York,USA 2006.

6. Fowlis, I. A.: Gas Chromatography, Second Ed., John Wiley & Sons, Inc., Chichester, England, 1995.

The total of active learning classes	**Lectures:** 60
	Individual research work: 60

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	DOCTORAL ACADEMIC STUDIES	

Course title: Multivariate Analysis in Drug Analysis

Teachers: Biljana S. Stojanović, Vladimir R. Vasić

Course status: elective, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1И1

Requirements: no

Course aims:

Gaining knowledge of multivariate analysis that is applicable in different areas of pharmaceutical analysis.

Course outcomes:

Ability to independently apply multivariate analysis for obtaining results of high quality in pharmaceutical analysis, then ability to apply statistical models for statistical inference, as well as ability to create statistical models for real life problems along with appropriate assessment of suitability of their application.

Course contents:

Introduction to multivariate analysis. Multivariate statistical analysis techniques. Multiple linear regression and appliances. Generalized linear models. Factor analysis (identification of factors, types of factor analysis, model of factor analysis, a method of performing factor analysis and the use of different statistical tools for factor analysis). Principal Component Analysis (concept, number of key components, algorithms for key components, evaluation and diagnosis, complementary methods). Principal component analysis in the evaluation of the results obtained by spectroscopic methods. Calibration (concept, characteristic of regression models). Robust regression. The method of partial least squares. Classification (linear classification methods, tree of classification, artificial neuron networks, vector machine, evaluation of methods, etc.). Cluster Analysis and basic methods. Appliance of cluster analysis in separation methods. Pattern recognition and appliance for the characterization of chromatographic analysis. The application of multivariate analysis techniques for screening and quantification in complex samples. Interpretation and presentation of obtained results. Mastering the different software tools for multivariate analysis. Creation of statistical models for particular situations with a presentation and critical analysis of the obtained models.

Recommended literature:

1. Filzmoser, P. Varmuza, K: Multivariate Statistical Analysis in Chemomterics, CRC Press, Taylor and Francis Group, New York, USA, 2008.

2. Harrell, F.E. Ir. Regression Modeling Strategies with Applications to Linear Models, Logistic Regression and Survival Analysis, Springer, New York, 2001.

3. Basilevsky, A. Statistical Factor Analysis and Related Models: Theory and Applications, Wiley Interscience, New York, 1994.

4. Kvalheim, O. M., Chan, H., Benzie, I. F. F., Szeto, Y., Tzang, A. H., Mok, D. K., Chau, F: Chromatographic profiling and multivariate analyisi for screening and quantifying contributions from individual components to the bioactive signature in natural products. Chemom. Intell. Lab. Syst. 107 (2011) 98–105.

5. Tabachnick, B, Fidell, L.: Using Multivariate Statistics (5. izdanje), Boston: PEARSON, 2007

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, workshops, seminars, interactive classes and internet.

Grading system:

Pre-exam activities: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Quantitative Structure–Retention Relationships

Teachers: Darko P. Ivanović, Mira L. Zečević, Anđelija M. Malenović, Biljana S. Stojanović

Course status: elective, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1И2

Requirements: no

Course aims:

Acquisition of knowledge in the field of Quantitative Structure–Retention Relationships in different chromatographic systems.

Course outcomes:

Ability of standalone analysis of Quantitative Structure–Retention Relationships of active pharmaceutical ingredients, as well as adequate selection of the most suitable separation system for the analysis.

Course contents:

Basic structural descriptors and their calculation. Thermodynamic basis of Quantitative Structure–Retention Relationships. The methods of determination of a molecule lipophilicity and its significance. The determination of log P values using experimental and computational methods. Estimation of the lipophilicity of xenobiotics. Various methodologies in the analysis of Quantitative Structure–Retention Relationships (chemometrics, multiple regression analysis, artificial neural networks, etc.). Estimation of retention prediction on the basis of created mathematical models or artificial neural networks. Application of various types of chromatography in the determination of the retention behavior of the analytes (reversed–phase liquid chromatography, normal–phase liquid chromatography, hydrophilic interaction liquid chromatography, micellar liquid chromatography). Analysis of Quantitative Structure–Retention Relationships in isocratic and gradient elution. Characterization of the stationary phases and appropriate selection of the stationary phase type for the chromatographic analysis of the specific molecules. Application of Quantitative Structure–Retention Relationships in proteomics Quantitative Structure–Retention Relationships of enantiomers and the specificity of its determination. The creation of quantitative relationship between retention behavior of the analyte and its biological effect.

Recommended literature:

1. Kaliszan, R.: QSRR: Quantitative Structure–(Chromatographic) Retention Relationship. Chem Rev. 2007 (107) 3212¬23246.

2. Put, R. Vander Heyden, Y.: Review on Modelling aspects in Reversed–Phase Liquid Chromatographic Quantitative Structure–retention Relationship. Anal. Chim. Acta 2007 (602) 164¬172.

3. Heberg, K.: Quantitative Structure–(Chromatographic) Retention Relationships. J. Chromatogr. A 2007 (1158) 273–305.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, workshops, seminars, interactive classes and internet.

Grading system:

Pre-exam activities: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Biological Material for Biopharmaceutical Testing

Teachers: Mira L. Zečević, Anđelija M. Malenović

Course status: elective, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1И3

Requirements: no

Course aims:

Acquiring the knowledge required for the successfull preparation of biological samples for biopharmaceutical studies

Course outcomes:

The selection and application of the appropriate procedure for the preparation of biological samples, and the ability to assess the adequacy of the chosen method.

Course contents:

The analysis of the problems that might occur during the testing of the pharmaceutical compounds and their metabolites in samples of biological material. The modes of collection and storage of biological material samples (plasma, serum, urine, saliva, etc.), their impact on the process of analysis, as well as the reliability of the results. Methods and procedures for the preparation of samples for bioanalytical testing; selection of the appropriate procedure depending on the type of biological material sample, instrumental methods that might be applied for the testing and the characteristics of the analyte. The extraction of drug metabolites from the biological material. The basic principles of solid-phase extraction and liquid-liquid extraction, and their appropriate modifications. The types of solid-phase extractions, various adsorbents and solvents that might be used as eluents, factors affecting the extraction, the automation of the process. The optimization of solid-phase and liquid-liquid extraction. Quality assurance and quality control during sample preparation. The sample collection using the Dry Matrx Spots - DMS method, critical steps that might affect the reliability of the analysis and storage of these samples. Preparation and analysis of DMS samples.

Recommended literature:

1. Mitra, S. (Editor): Sample Preparation Techniquues in Analytical Chemistry. John Wiley & Sons, New Yersey, USA, 2003.

2. Kataoka, H.: Recent Advances in Solid–Phase Microextraction and Related Techniques for Pharmaceutical and Biomedical Analysis. Curr. Pharm. Anal 2005 (1) 65–84.

3. Wells, D.: High Throughput Bioanalytical Sample Preparation, Elsevier, Amsterdam, 2003.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, consultations, seminars, interactive teaching.

Grading system:

Pre-exam activities: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Chiral Drug Analysis

Teachers: Mira L. Zečević, Anđelija M. Malenović, Biljana S. Stojanović

Course status: elective, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1И4

Requirements: no

Course aims:

Acquiring additional knowledge about the investigation of physicochemical properties of chiral compounds and the methods that can be applied for identification and assay of pharmacologically active chiral compounds.

Course outcomes:

Acquired knowledge application to the selection of the appropriate approach and method which should be applied to the chiral compounds analysis.

Course contents:

Importance of chirality in pharmaceutical research and development, and therapeutical application as well. Evaluation of physicochemical properties of chiral compounds (solubility, specific optical rotation, polymorphism and pseudopolymorphism, racemization, etc). Determination of composition of chiral compounds by means of solid state analysis methods. Chiral compounds analysis by means of high performance liquid chromatography. Direct and indirect enantiomeric analysis. Stationary phase chemistry (Brush type stationary phases, etc). Types and properties of mobile phase chiral modifiers. Evaluation of the quality of chromatographic enantiomeric separation. Specificity of development and optimization of the chromatographic methods for enantiomeric analysis. Determination of enantiomers in biological material by means of liquid chromatography. Other separation methods that can be applied to chiral compounds analysis: gas chromatography, supercritical fluid chromatography − SFC, capillary electrophoresis – CE), capillary electrochromatography – CEC). Selection of the appropriate approach and method which should be applied to the analysis of the specific chiral compounds. Method development for qualitative and quantitative pharmaceutical analysis of chiral compounds.

Recommended literature:

1. Buch, K. W., Buch, M. A.: Chiral Analysis, Elsevier, San Diego, USA 2006.

2. Subramanian, G.: Chiral Separation Techniques, Third Edition, WILEY–VCH Verlag GmbH & Co., Germany 2007.

3. Ahuja, S., Rasmussen, H.: HPLC Method Development for Pharmaceuticals, Volume 8 of Separation Science and Technology, Academic Press, San Diego, USA 2003.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet.

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Conducting Research in the Analysis of Medical Devices

Teachers: Anđelija M. Malenović

Course status: elective, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1И5

Requirements: no

Course aims:

Acquiring the knowledge related to the assessment of the quality and safety of medical devices, as well as the introduction to the most important methods and procedures used for quality control and evaluation of the reliability of medical devices.

Course outcomes:

Application of acquired knowledge in assessment of the adequacy of the data on the characteristics, safety and quality of medical devices.

Course contents:

The analysis of the requirements that medical devices, in vitro diagnostic medical devices and active implantable medical devices must meet in terms of quality and safety. Factors affecting quality and safety. Classification rules for medical devices and their implementation. The types and characteristics of the materials used for medical devices production; special emphasis on biomaterials. The characterization of biomaterials by dynamic mechanical analysis, differential scanning calorimetry and differential thermal analysis / thermogravimetric analysis. Safety assessment of medical devices by testing cytotoxicity, sensitization, irritability, acute and subchronic toxicity, genotoxicity and hemocompatibility. Analytical testing of medical devices:testing of materials, known impurities and agents used during production, testing of the extractabls. The examination of degradation products and impurities that may arise under the action of the immune system, or of the intracellular and extracellular biological fluids. Calculation of the patient exposure upper theoretical limit. Defining the principles for the appropriate test selection and conduction of medical device testing. The application of risk management to medical devices. Basic requirements for conformity assessment of medical devices.

Recommended literature:

1. Directive 90/385/EECof the European parliament and of the council on active implantable medical devices. 2. Directive 98/79/EC of the European parliament and of the council on in vitro diagnostic medical devices. 3. Directive 93/42/EEC of the European parliament and of the council concerning medical devices

4. Richard, F.: Reliable design of medical devices. Second edition. Taylor & Francis Group, Boca Raton, Florida, USA, 2006.

5. Nicholson, J.W.: The chemistry of medical and dental materials. The Royal Society of Chemistry, Cambridge, UK, 2002.

6. Shayne, C. G., McCord, M.G.: Safety Evaluation in the Development of Medical Devices and Combination Products. Third Edition, Informa Healthcare USA, Inc., New York, USA, 2008.

7. ISO 14971:2000(E), Medical Devices – Application of Risk Management to Medical Devices.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Grading system:

Pre-exam activities: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Spectroscopic Methods in Drug Analysis

Teachers: Mirjana B. Medenica, Mara M. Aleksić

Course status: elective, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1И6

Requirements: no

Course aims:

Acquirement of additional knowledge of different spectroscopic methods in the analysis of small molecules and macromolecules.

Course outcomes:

Knowledge of the theory and application of modern spectroscopic methods. The ability to choose the adequate spectroscopic method for the corresponding pharmaceutical analysis. Successful implementation of the acquired knowledge to solve specific problems in drug analysis.

Course contents:

Introduction to different spectroscopic methods. Quantitative analysis of multicomponent mixtures by using UV/VIS spectrophotometry - mathematical correction techniques and their analysis. The application of IR (Infrared Spectroscopy), NIR (Near Infrared Spectroscopy), and Raman spectroscopy: qualitative analysis, solid-state analysis, analysis of traces of various foreign contaminations, analysis of biopharmaceutical products, etc. Atomic absorption spectrometry for the analysis of metals in different pharmaceutical products, as well as for the purity degree analysis. Detection and analysis of metal traces in various samples (active pharmaceutical substance, pharmaceutical product, biological material) using the inductively coupled plasma spectrometry - ICP with the theoretical principles of the method. The application of nuclear magnetic resonance - NMR for the confirmation of chemical structure, in the qualitative and quantitative analysis of pharmaceutical substances and products with the theoretical principles. One-dimensional (1D) and two dimensional (2D) NMR spectra. Theoretical principles of mass spectroscopy. Types of ionization (chemical ionization, electron ionization, electrospray ionization, chemical ionization at atmospheric pressure). Types and characteristics of the mass analyzer. Types of ions in the mass spectra and the characteristics of the mass spectra. Hyphenated methods with mass detector and their application in drug analysis. Other hyphenated techniques, so-called hybrid methods (ICP-MS, GC-AAS, GC-ICP, GC-MS, HPLC-ICP).

Recommended literature:

1. Lee, D. C., Webb, M. (Editors): Pharmaceutical Analysis, Blackwell Publishing Ltd., CRC Press, Boca Raton, USA, 2003.
2. Hoffman, E., Stroobant, V.: Mass spectrometry: Principles and Applications. Wiley, New York, 2007.
3. Watson, D. G.: Pharmaceutical Analysis, Second edition, Elsevier, Edinburg, 2005.
4. Vandecasteele, C., Block, C. B.: Modern Methods for Trace Element Determination, John Wiley and Sons, New York, 1995.
5. Siuzdak, G.: The Expanding Role of Mass Spectrometry in Biotechnology, Second edition, MCC Press, England, 2006.
6. Skoog, D. A., Holler, F. J. and Nieman, T. A.: Principles of Instrumental Analysis, Fifth edition, Sounders College Publishing, Philadelphia, 1998.
7. Keeler, J.: Understanding NMR spectroscopy, Second edition, Wiley, New York, 2010.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, workshops, seminars, interactive classes and internet.

Grading system:

Pre-exam activities: 50 points Final exam: 50 points

University of Belgrade Faculty of Pharmacy	DOCTORAL ACADEMIC STUDIES	

Course title: Thermal Analysis Methods in Drug Analysis

Teachers: Mira L. Zečevič, Anđelija M. Malenović, Aleksandra S. Daković

Course status: elective, module: Drug Analysis

Semester: II	**Year of studies:** I
ECTS points: 5	**Course code:** ДАЛ1И7

Requirements: no

Course aims:

Gaining the knowledge about the examination of physical characteristics and physical stability of pharmaceutical substances using methods of thermal analysis, as well as the possibilities of applying these methods in the development of pharmaceutical dosage forms and their quality control.

Course outcomes:

The application of acquired knowledge in order to select the appropriate method of thermal analysis to examine the physical characteristics and monitoring physical stability of pharmaceutical substances. Critical evaluation of the possibilities of application of these methods in process control of pharmaceutical dosage forms.

Course contents:

The principles and theoretical foundations of thermal analysis. The most commonly used thermal analysis methods in the pharmaceutical field : thermogravimetry - TG), derivative thermogravimetry - DTG , thermogravimetric analysis - TGA, differential thermal analysis - DTA and differential scanning calorimetry - DSC. The basic principles of TG, TGA and DTA. The effect of the sample carrier, gas type, gas pressure and gas flow rate on the analysis. Preparation of sample for thermogravimetric analysis. The types of scale to be used in the TGA apparatus. Advantages and disadvantages of the application of TGA in analytics drugs. Interpretation of the thermogram . The application of TGA on pharmaceutical substances stability evaluation, hydrate characterization, characterization of creams, tablets, and controlled-release tablets. Principles and types of differential scanning calorimetry. Practical problems in the application of DSC. Calibration of DSC apparatus. Interpretations of the results. The examination of the polymorphic forms, hydrates, solvates, amorphous forms, the glass transition; the interpretation of the results. Confirmation, clarification and replenishment of the results obtained by different methods of thermal analysis.

Recommended literature:

1. Craig, D. Q. M., Reading, M.: Thermal Analysis of Pharmaceuticals. CRC Press is an imprint of Taylor & Francis Group, an Informa business, Boca Raton, USA, 2007.

2. Ed. Haines, P. J.: Principles of Thermal Analysis and Calorimetry. RSC, Cambridge, UK 2002.

3. Ed. Gabbott P.: Principles and Applications of Thermal Analysis, Blackwell Publishing Ltd ,Oxford, UK 2008.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, consultations, seminars, interactive teaching.

Grading system:

Pre-exam activities: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Method Development Strategy for Drug Analysis

Teachers: Darko P. Ivanović, Mira L. Zečevic, Anđelija M. Malenović, Biljana S. Stojanović

Course status: Mandatory modules, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2ОМ1

Requirements: no

Course aims:

Acquiring necessary knowledge for the successful method development and establishment and for drug analysis involving scientific approach in definition of critical steps.

Course outcomes:

Successful acquired knowledge application in evaluation of critical phases in method development and establishment, as well as ability to resolve defined problems with adequate risk assessment.

Course contents:

Development of liquid chromatographic method for the determination of purity level of starting material for active pharmaceutical substance synthesis. Development of liquid chromatographic method for the drug concentration analysis in in process samples, and for the evaluation of purity level of intermediers. Development of liquid chromatographic method for the for the finalised drug product with special reflection to the achiral and chiral compounds analysis. Considerations related to the quality and method characteristics (nature of the sample to be analysed, type of the detectors, solution stability, stationary phase selection and mobile phase selection, etc. development of other methods involved in drug quality assessment (spectroscopic methods, titrimetric methods, etc.). The actions involved in embedding of quality into method with the assistance of design – QbD (eng. Quality by Design), as well as the ways of applied method adequacy assessment. Development of alternative method. Method robustness and ruggedness assessment. The choice of optimal method that satisfies in advance assigned criteria and the ways how to asses risk in method application. Defining critical method parameters. Special aspects of method development which involve analysis of impurities of different origin with particular reference to genotoxic impurities. Development of separation methods which are compatible with mass detection for the analysis of genotoxic impurities. Development of Stability Indicating methods. Drug stability evaluation, obtained results interpretation. The recommendation for the application of appropriate method for the analysis in relation to the nature of samples.

Recommended literature:

1. Juran, J. M., Blanton Godfrey, A. 5th edition: Juran s quality handbok, McGraw–Hill, New York, USA, 1999. 2. Ed. Kazakevich, Y., Lobrutto, R.: HPLC for pharmaceutical scientist. John Wiley & Sons, Inc., New York,USA 2007.

3. Freitag, R. (Ed.): Moder Advances in Chromatography. Springer, Berlin, Nemačka, 2002.

4. Vogt, F.G., Kord, A.S.: Development of Quality-by-Design Analytical Methods. J. Pharm. Sci. 2011 (100) 797–812.

5. Cimarosti, Z., Bravo, F., Stonestreet, P., Tinazzi, F., Vecchi, O., Camurri, G.: Application of Quality by Design Principles to Support Development of a Control Strategy for the Control of Genotoxic Impurities in the Manufacturing Process of a Drug Substance, Org. Process. Res. Dev. 2010 (14) 993–998.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet.

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Arificial Neural Networks

Teachers: Mira L. Zečević, Anđelija M. Malenović, Biljana S. Stojanović

Course status: elective, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2И1

Requirements: no

Course aims:

Gaining knowledge about arificial inteligence in aim to solve different problems in drug analysis.

Course outcomes:

Ability to solve problems through choice of appropriate neural networ, than network testing and dinal validation of results. Showing and interpretation of obtained results.

Course contents:

Basic principles of artificial neural networks. Analogy artificial neurons with biological neurons. Compounds of artificial neurons and basic characteristics of all compounds. Types of artificial neural networks and possibilities for application (prediction, classification, grouping of results, etc.) Methods for network training. Creation of plan of experiments suitable for application of artificial neural networks by applying experimental design methodology. Networks with one layer. Multiple layer perceptron networks. Self-organizing maps. Other types of artificial neural networks. Algorithms for networks training (Back Propagation, Conjugate Gradient descent, Quick Propagation and Quasi Newton, etc). Error function. Optimization of artificial neural networks. Confirmation of successful application of neural networks for certain problem. Application of artificial neural networks for solving different problems in drug analysis (optimization of chromatographic methods, modeling of chromatographic behavior, prediction of retention behavior). Comparing application of artificial neural networks and multiple regression analysis in quantitative relationship between molecular structure and retention behavior. Application of artificial neural networks in prediction of drug substance behavior during period of storage and expiration date. Application of different statistical programs in creation and testing of artificial neural networks and estimation of obtained results.

Recommended literature:

1. Bishop, C. M.: Neural networks for pattern recognition. Oxford, University press, Great Britain 1994.

2. Medsker, L. R., Jain, L. C.: Recurrent neural networks: Design and Application. CRC Press, Washington, USA 2001.

3. Arbib, M. A.: Brain Theory and Neural Networks, 2nd, Massachusetts Institute of Technology, 2003, Madison, USA.

4. Freeman, J. A., Skapura, D. M.: Neural Networks: Algorithms, Applications and Programming Techniques. Addison-Wesley Publishing Company, 1991, New York, USA.

5. Ed. Kwon, S. J.:Artificial Neural Networks, Nova Publishers, 2011.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, workshops, seminars, interactive classes and internet.

Grading system:

Pre-exam activities: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	DOCTORAL ACADEMIC STUDIES	

Course title: Evolutionary Algorithms in Drug Analysis

Teachers: Biljana S. Stojanović, Zorica V. Stanimirović

Course status: elective, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2И2

Requirements: no

Course aims:

Training of the candidate to recognize, model and resolve complex problems of optimization in Drug Analysis by applying evolutionary and other algorithms.

Course outcomes:

The ability of clear definition of complex systems and processes, creation of appropriate mathematical models and successful application of evolutionary and other algorithms for obtaining optimal and high quality problem solutions.

Course contents:

Elementary problems of mathematical modeling, problem definition and presentation of mathematical formulation. The complexity of mathematical model and its interpretation. Basis of exact and heuristic optimization methods which could be successfully applied in resolving of optimization problems in drug analysis. Elementary and advanced concept of evolutionary algorithms. Presentation of solutions and different forms of coding function. Generation of initial population, resolving of problems of incorrect individuals. Definition of fitness function. Evolutionary operations of selection, recombination and mutation – elementary and advanced operation types and their modifications. Other aspects of evolutionary algorithms, strategies for prevention of premature convergence and preservation of genetic material diversity. Creation of evolutionary algorithm concept which is adjusted to the problem that should be resolved. Hybridization with exact and heuristic methods aiming to improve the efficiency of algorithm and solution quality.

Examples and the possibility of evolutionary algorithms application in drug analysis. Development and optimization of complex chromatographic methods applying evolutionary algorithms. Resolving of different problems in spectroscopic methods applying evolutionary algorithms. Evaluation of problems solutions and data interpretation. Individual resolving and analysis of defined problems.

Recommended literature:

1. Leardi, R.: Geneticalgorithmsinchemistry. J. Chromatogr. A 2007 (1158) 226–233.

2. Haupt, R. L., Haupt, S. E.: PracticalGeneticAlgorithms. WILEY–INTERSCIENCE, AJohn Wiley &Sons, Inc. Publication, New Yersey, U. S. A. 2004.

3. Leardi, R. Ed.: Natureispiredmethodsinchemometrics: geneticalgorithmsandartificialneuralnetworks. Elsevier, Amsterdam, 2003.

4. Coley, D.: AnIntroductiontoGeneticAlgorithmsforScientistsandEngineers, WorldScentific, Singapore/New Jersey/London/HongKong, 2003.

5. Glover, F., KochenbergerG.: HandbookofMetaheuristics, KluwerAcademicPublishers, Boston/ Dordrecht/London, 2003.

6. Michalewicz, Z., Fogel, D.B.: How tosolveit: modernheuristics, Springer 2004.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, workshops, seminars, interactive classes and internet.

Grading system:

Pre-exam activities: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Proteomic, Metabolomic and (Pharmaco)metabonomic Analysis

Teachers: Mira L. Zečević, Anđelija M. Malenović, Biljana S. Stojanović

Course status: elective, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2И3

Requirements: no

Course aims:

Understanding of modern pharmaceutical analysis principles in the field of peptide and protein, proteomic, metabolomic and (pharmaco)metabonomic analysis.

Course outcomes:

Basic knowledge needed for metabolomic profiling and establishing a relationship between phenotype or phenotype response and genetic or nutritional disorder, in order to give the right treatment regimen.

Course contents:

Pharmacometabolomics (or pharmacometabonomics) are a part of the scientific field Metabolomics and refer to quantification of metabolites, originated after the application of specific active pharmaceutical substance. Interpretation of the obtained results may provide an evidence of the influence of the applied substance to metabolic pathway. On the other hand, metabolites may be monitored during the research and development phase in order to predict and estimate the metabolism of the pharmaceutical substances. Both approaches include the use of appropriate bioanalytical methods for metabolic profiling in tissues and biological liquids (blood, plasma, urine, etc.). Most applicable methods are liquid chromatography and gas chromatography combined with mass spectrometry and nuclear magnetic resonance. Obtained data are most adequately analyzed by means of chemometrics, because it allows individual patient's response prediction. Metabolomic profiling and establishing a relationship between phenotype or phenotype response and genetic or nutritional disorder enables giving of the right treatment regimen. The main goal of pharmacometabolomics and complementary scientific areas like pharmacogenomics is to provide therapy individualization by treatment results predicting in terms of efficiency and safety.

Recommended literature:

1. Weckwerth, W.: Metabolomics, Methods and Protocols. Humana Press, New Jersey, 2007.

2. Evans, G.: A Handbook of Bioanalysis and Drug Metabolism., CRC Press, New York 2004.

3. Lovrić, J.: Introducing Proteomics: From Concepts to Sample Separation, Mass Spectrometry and Data Analysis, John Wiley–Blackwell, New Jersey 2011.

4. Assfalg, M., Bertini, I., Colangiuli, D., Luchinat, C., Schäfer, H., Schütz, B. Spraul, M.: PNAS 2011 (105) 1420–1424.

5. Lindon, J. C., Holmes, E., Nicholson, J. K.: Pharm. Res. 2006 (23) 1075–1088.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet.

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Pharmacological Profile of the Drug

Teachers: Miroslav S. Savić

Course status: elective, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2И4

Requirements: no

Course aims:

Acquiring knowledge for understanding the basic characteristics of drugs based on in vitro and in vivo data obtained from preclinical studies.

Course outcomes:

Ability to independently interpret the results obtained during preclinical investigation of drugs. Ability for critical appraisal of the completeness of the available pharmacological profile of a drug. Appraisal of preclinical research data in the context of the findings of research in humans.

Course contents:

The process of drug discovery. Strategy for investigation and development of new drugs. Drug target sites. Integration of multi-celled organism. Interaction drug – mechanism of biological regulation. Biological membranes and the effect of the drug. Receptors, ion channels, enzymes, transporters. In vitro investigation of drug affinity and efficacy. Efficacy and potency. Agonists, inverse agonists, antagonists. Relathionship between dose and effect. Tolerance and resistance. Principles of investigation on animals. Legislation and ethical issues in relation to work with experimental animals. Methods of genetic engineering in assessment of pharmacological profile of drug. Primary pharmacodynamic investigations. Secondary pharmacodynamic investigations. Safety pharmacology. Pharmacokinetic profile of drug. Toxicological profile of drug. Acute toxicity. Repeated dose toxicity. Mutagenicity. Teratogenicity. Carcinogenicity. Interpretation of the results obtained from toxicological studies and data extrapolation on humans. Estimation of efficacy and safety of drugs. Preclinical profile of biological drugs. Planning of clinical investigations of drugs. Phases in clinical investigation. Pharmacoepidemiological investigation. Pharmacological profile in special populations (children, pregnancy, lactation, elderly, patients with excretory organ disease).

Recommended literature:

1. Rang, H. P.: Drug discovery and development. Churchil Livingstone, Edinburgh, 2006.

2. Kenakin T. A Pharmacology Primer: Theory, Applications and Methods, 2nd edition. Academic Press, London, 2006.

3. Hacker M, Bachmann K, Messer W. Pharmacology Principles and Practice. Academic Press, Amsterdam, 2009.

4. Rang, H. P., Dale, M. M., Ritter, J. M., Flower, R. J., Henderson, G. Rang and Dale's Pharmacology, 7th ed. Elsevier Churchill Livingstone, Edinburgh, 2011.

5. Brunton, L., Chabner, B. A., Knollman, B. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 12 ed. McGraw–Hill, New York, 2010.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures and study-research work

Grading system:

Seminar: 30 points; written exam: 70 points

University of Belgrade Faculty of Pharmacy	DOCTORAL ACADEMIC STUDIES	

Course title: Advanced Pharmaceutical Dosage Forms

Teachers: Snežana D. Savić, Svetlana R. Ibrić

Course status: elective, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2И5

Requirements: no

Course aims:

Acquiring knowledge in the field of formulation development and control of conventional and modern pharmaceutical dosage forms.

Course outcomes:

Dealing with development approaches and recognizing of formulation difference between conventional and modern pharmaceutical dosage forms: preformulation (phisicochemical and biopharmaceutical characterization of active pharmaceutical ingredient, excipients selection) and formulation consideration of conventional and modern pharmaceutical dosage forms intended for different administration routes; acquiring knowledge about the techniques of preparation/obtaining and common methods for characterization/control of conventional and modern pharmaceutical dosage forms during the development phase in laboratory; getting familiar with technological producing processes of conventional and some modern pharmaceutical dosage forms and methods for their pharmacotechnological examination. Knowledge about manufacture methods, development and formulation of biotechnological drugs.

Course contents:

Selection of excipients for the formulation of conventional and modern pharmaceutical dosage forms. Formulation and control of the dosage forms intended for per oral administration. Formulation and control of the sterile dosage forms: parenteral administration and ophthalmic preparations. Pharmaceutical preparations for dermal application and specific administration routes. Formulation and control of modified-release preparations. Formulation and techniques of preparation of microparticle drug delivery systems. Preformulation and formulation considerations, preparation techniques and characterization of colloidal carriers: micellar systems, microemulsions, liquid crystal phases, liposomes, nanoparticle systems.

Properties of biotechnological drugs. Development of biotechnological drugs. Prokaryotic and eukaryotic cells in biotechnological drug production. Production of biotechnological drugs from plants. Development of industrial production process and production process. Formulations with proteins and peptides. Scientific, technological and economic aspects of vaccine development, including DNA vaccines also. Inhaled preparations based on biomacromolecules. Proteins and phospholipids (injectable forms, formulation and preparation, characteristics of the products). Polymeric systems for per os administration of proteins and peptides. Characterization of the recombinant proteins as drugs. Biogeneric drugs.

Recommended literature:

1. Gibson, M.: Pharmaceutical preformulation and formulation, 2nd ed. Informa healthcare, New York–London, 2009.

2. Rathbone, M. J., Hadgraft, J., Roberts, M. S., Lane, M. E.: Modified Release Drug Delivery Technology, Second Edition, Volume 1, Informa healthcare, New York–London, 2008.

3. Rathbone, M. J., Hadgraft J., Roberts M. S., Lane M. E.: Modified–Release Drug Delivery Technology, Second Edition, Volume 2, Informa healthcare, New York–London, 2008.

4. Bauer, K. H., Fröming, K. H., Führer, C.: Lehrbuch der Pharmazeutischen Technologie. 8th ed., Nova Stuttgart, 2006.

5. Ed.:Kayser, O., Müller, R. H.: Pharmaceutical Biotechnology, Drug Discovery and Clinical Application. Wiley-VCH Verlag GmbH&Co. KgaA, Weinheim, Nemačka, 2004.

6. Walsh, G: Pharmaceutical Biotechnology, Concept and Application. Wiley & Sons Ltd., Chichester, England, 2007.

7. Groves, M.J.: Pharmaceutical Biotechnology, Taylor & Francis Group, CRC Press, Boca Raton, U. S. A. 2006.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet.

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Biological Drug Analysis

Teachers: Biljana S. Stojanović, Nevena M. Arsenović Ranin, Zorica M. Stojić Vukanić

Course status: elective, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2И6

Requirements: no

Course aims:

Acquiring knowledge about the characteristics of methods used for biological drug analysis.

Course outcomes:

Ability to select an adequate method for biological drugs analysis.

Course contents:

Protein structure and properties. Properties and classification of biological drugs. Immunogenicity of biological drugs. Biosimilars, properties and comparison to generic drugs. Biotechnological drug development. Chromatography and other techniques used for protein purification. Chromatographic methods used for the analysis of biological drugs, i.e. proteins and peptides (size-exclusion chromatography, ion-exchange chromatography, reversed-phase chromatography, hydrophilic interaction liquid chromatography and affinity chromatography). Development of chromatographic methods used for biological drug analysis. Mass spectrometry methods used for protein characterization (electrospray ionization, matrix-assisted laser desorption/ionization). Benefits from hyphenation with „time of flight"– TOF detector. Determination of protein molecular mass. Protein characterization by means of mass spectrometry. Characterization of drug-protein interactions by means of affinity HPLC/MS. Microwaves application in protein and peptide analysis. Application of electrophoresis and multidimensional chromatography in protein analysis. Comparison of methods used for biological and conventional drug analysis. Comparison of biological and conventional drugs. Regulatory requirements concerning quality of biological drugs. Monitoring of biological drug quality assurance. Stability of biological drugs and protocols of stability studies for biological methods. Literature overview about specific biological drug analysis, presentation and critical review on the proposed procedure.

Recommended literature:

1. Groves, M.J.: Pharmaceutical Biotechnology, Taylor&Francis Group, CRC Press, Boca Raton, U. S. A. 2006.

2. Ed. Kazakevich, Y., Lobrutto, R.: HPLC for pharmaceutical scientist. John Wiley & Sons, Inc., New York,USA 2007.

3. Quality of Biotechnological Products:Stability Testing of Biotechnological/Biological Products, ICH Q5C Guideline, 1995.

4. Pramanik, B. N., Mirza, U. A., Ing, Y. H., Liu, Y. H., Bartner, P. L., Weber, P. C., Bose, A. K.: Microwave-enhanced enzyme reaction for protein mapping by mass spectrometry: A new approach to protein digestion in minutes, Protein Science 11 (2002), 2676–2687.

5. Walsh, G: Pharmaceutical Biotechnology, Concept and Application. Wiley & Sons Ltd., Chichester, England, 2007.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Lectures, workshops, seminars, interactive teaching and internet.

Grading system:

Pre-exam engagements: 30 points Final exam: 70 points

University of Belgrade Faculty of Pharmacy	**DOCTORAL ACADEMIC STUDIES**	

Course title: Drug analysis in Pharmacokinetics Investigation

Teachers: Miljković P. Branislava, Vezmar Kovačević D. Sandra, Vučićević M. Katarina

Course status: elective, module: Drug Analysis

Semester: III	**Year of studies:** II
ECTS points: 5	**Course code:** ДАЛ2И7

Requirements: no

Course aims:

The aim of the course is to provide students with relevant tools needed for planning, conducting and interpretating the results of bioanalytics methods during pharmacokinetic studies.

Course outcomes:

On completion of the course, the student will be able independently to account for the need of bioanalytical methods within pharmacokinetic studies, to plan and carry out optimal techniques, and interpret, critically appraise and present the results of bioanalytical analysis during pharmacokinetic studies.

Course contents:

Significance of pharmacokinetics in drug development. Biological materials used in pharmacokinetic investigation. Planning the process of biological samples preparation and analysis methodology for pharmacokinetic studies. Methods for biological samples preparation and optimization of the separation methods. Optimization of drugs' and metabolites' analysis in biological samples. Parameters of bioanalytical analysis validation in pharmacokinetic studies according to the regulatory authorities. Representation of validation parameters. Preparing the report as a part of pharmacokinetic clinical studies. Bioanalytical aspects of bioavailability and bioequivalence studies. Calculation of pharmacokinetic parameters of interest for the bioequivalence studies. Bioanalytical aspects in terapeutic drug monitoring. Factors that contribute to pharmacokinetic variability, and interpretation of measured drug levels. Pharmacokinetic analysis of measured drug concentrations. Interpretation of measured drug concentration during terapeutic drug monitoring. Critical appraisal of pharmacokinetic and studies of bioequivalence based on the results. Adjustment of dosing regimen based on the measured drug concentration levels.

Recommended literature:

1. Xu A.Q, Madden T. Analytical Methods for Therapeutic Drug Monitoring and Toxicology. Wiley, 1st ed. 2011.

2. Burton M.E. (Editors): Shaw L.M, Schentag J.M, Evans W.E. Applied Pharmacokinetics and Pharmacodynamics: Principles of Therapeutic Drug Monitoring. Lippincott Williams & Wilkins; 4th ed, 2005.

3. Chow S.C, Liu J. Design and Analysis of Bioavailability and Bioequivalence Studies. CRC Press, New York, 3rd ed, 2009.

4. Rowland M, Tozer T.N. Clinical Pharmacokinetics and Pharmacodynamics: Concept and Applications, Lippincott Williams & Wilkins, 4th ed, 2011.

The total of active learning classes	**Lectures:** 30
	Individual research work: 30

Teaching methods:

Theoretical lectures, workshops, seminars, interactive classes and internet.

Grading system:

Pre-exam activities: 30 points Final exam: 70 points