



GOCE DELCEV UNIVERSITY - STIP
FACULTY OF MEDICAL SCIENCES



International symposium at
Faculty of medical sciences

CURRENT ACHIEVEMENTS AND FUTURE PERSPECTIVES IN MEDICAL AND BIOMEDICAL RESEARCH



STIP, 24 NOVEMBER 2015
MULTIMEDIA CENTRE – UGD, STIP

INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES
“Current achievements and future perspectives in medical and biomedical research”

SCIENTIFIC PROGRAM

November 24, 2015 - Stip

8:30 – 9:00

Registration

9:00 – 9:15

Rector / Vice rector/Dean

SESSION 1

Chair: Prof. Emilija Janevik Ivanovska

Co-chair: Ass. Prof. Elena Drakalska

9:15 – 9:35

Ass. Marija Darkovska Serafimovska
Macedonian agency of drug and medical
devices, Director
University Goce Delcev Stip
Republic of Macedonia

Step forward of Macedonian agency for medicines and medical devices, establishment and strategic plan for development

9:35 – 9:55

Assoc. Prof. Zorica Arsovska Sarafinovska
Institute of Public Health of the
Republic of Macedonia, Skopje,
University Goce Delcev Stip
Republic of Macedonia

Adherence to Therapy: A Modern Pharmacotherapeutic Approach

9:55 – 10:15

Prof. Biljana Gjorgjeska
University Goce Delcev Stip
Republic of Macedonia

Use of disinfectants and antiseptics in selected health institutions in Republic of Macedonia

10:15 – 10:35

Assoc. Prof. Bistra Angelovska
University Goce Delcev Stip
President of Pharmaceutical Chamber
of Macedonia. Republic of Macedonia

Code of Ethics for Pharmacists – Pharmaceutical Chamber of Macedonia

10:40 – 11:10

Coffee break

Poster presentation

Chair: Prof. Milka Zdravkovska

Co-chair: Ass. Prof. Darinka Gjorgieva Ackova

10:10 – 11:50

Prof. Neven Zarkovic
Rudjer Boskovic Institute, Croatia

4-Hydroxynonenal – major bioactive marker of lipid peroxidation

11:50 – 12:10

Assoc. Prof. Tatjana Ruskovska University
Goce Delcev Stip Republic of Macedonia

Nicotinamide adenine dinucleotide biosynthesis and consumption in dysfunctional white adipocytes

12:10 – 12:30

Prof. Rubin Gulaboski University
Goce Delcev Stip Republic of Macedonia

New insights into the chemistry and functions of Coenzyme Q

12:30 – 12:50

Assoc. Prof. Darko Bosnakovski
University Goce Delcev Stip
Republic of Macedonia

Genetically modified systems to study muscular dystrophies

12:50 – 14:00

Coffee break

Poster presentation

Chair: Assoc. Prof. Cena Dimova
Co-chair: Ass. Prof. Nevenka Velickova

- 14:00 – 14:40 Prof. Lia Rimondini**
Università del Piemonte Orientale,
Novara, Italy
Counteracting microbial biofilm formation onto dental materials
- 14:40 – 15:00 Prof. Elizabeta Zisovska**
Agency for Quality and Accreditation of
Healthcare Institutions, Skopje,
Republic of Macedonia
The endless potential of the umbilical cord blood for investigation, research and treatment
- 15:00 – 15:20 Ass. Misko Milev**
University Goce Delcev Stip
Republic of Macedonia
The cytokinesis-blocked micronucleus assay: Good choice for detection and evaluation of genotoxicity in human cells
- 15:20 – 15:40 Prof. Lence Miloseva**
University Goce Delcev Stip
Republic of Macedonia
Multiple predictive model for clinical and subclinical depression in adolescence
- 15:40 – 16:00 Coffee break** **Poster presentation**

SESSION 4

Chair: Assoc. Prof. Darko Bosnakovski
Co-chair: Ass. Prof. Katarina Smilkov

- 16:00 – 16:40 Prof. Adriano Duatti**
University of Ferrara, Ferrara, Italy
Molecular imaging and radionuclide therapy of prostate cancer
- 16:40 – 17:00 Assoc. Prof. Vaso Taleski**
University Goce Delcev Stip
Republic of Macedonia
Where Nanotechnology and Nanomedicine meet – Applications and Potential Risks
- 17:00 – 17:20 Dr. Aleksandar Cvetkovski**
University Goce Delcev Stip
Republic of Macedonia
The role of molecular cocrystals in drug development
- 17:20 – 17:40 Prof. Emilija Janevik Ivanovska**
University Goce Delcev Stip
Republic of Macedonia
Drug development based on radiolabeled antibodies
- 17:40 – 18:00 Closing remarks**

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INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES

“Current achievements and future perspectives in medical and biomedical research”

November 24, 2015 – Stip

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- 2. Adherence to Therapy: A Modern Pharmacotherapeutic Approach**
Author: Zorica Arsovska Sarafinovska
- 3. Use of disinfectants and antiseptics in selected health institutions in Republic of Macedonia**
Author: Biljana Gjorgjeska
- 4. Code of Ethics for Pharmacists – Pharmaceutical Chamber of Macedonia**
Author: Bistra Angelovska
- 5. 4-Hydroxynonenal – major bioactive marker of lipid peroxidation**
Authors: Neven Zarkovic, Kamelija Zarkovic
- 6. Nicotinamide adenine dinucleotide biosynthesis and consumption in dysfunctional white adipocytes**
Authors: Prof. Tatjana Ruskovska, David Bernlohr
- 7. New insights into the chemistry and functions of Coenzyme Q**
Authors: Rubin Gulaboski, Valentin Mirceski, Ivan Bogeski, Sasa Mitrev, Kokoskarova Pavlinka, Velo Markovski, Reinhard Kappl, Markus Hoth
- 8. Genetically modified systems to study muscular dystrophies**
Author: Darko Bosnakovski
- 9. Counteracting microbial biofilm formation onto dental material**
Author: Lia Rimondini
- 10. The endless potential of the umbilical cord blood for investigation, research and treatment**
Author: Elizabeta Zisovska
- 11. The cytokinesis-blocked micronucleus assay: Good choice for detection and evaluation of genotoxicity in human cells**
Authors: Misko Milev, Velickova N., Petrova B., Gorgieva P., Nedeljko B.,
- 12. Multiple predictive model for clinical and subclinical depression in adolescence**
Authors: Lence Miloseva, Tatjana Vukosavljevic-Gvozden
- 13. Molecular Imaging and therapy with radionuclides of prostate cancer**
Author: Adriano Duatti
- 14. Where Nanotechnology and Nanomedicine meet – Applications and Potential Risks**
Authors: Vaso Taleski, Darko Bosnakovski, Milka Zdravkovska, Velo Markoski, Zdenka Stojanovska, Svetlana Jovevska
- 15. The role of molecular cocrystals in drug development**
Author: Aleksandar Cvetkovski
- 16. Drug development based on radiolabeled antibodies**
Author: Emilija Janevik-Ivanovska

INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES
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POSTER PRESENTATIONS

- 1. Correlation between dynamic balance and gait parameters in patients with ischemic stroke in the chronic period**
Authors: Danche Vasileva, Daniela Lubenova, Marija Mihova, Ivan Maznev, Lence Nikolovska, Zhu Jihe;
- 2. Effect of kinesitherapy on physical activity in patient with Guillain-Barré syndrome**
Authors: Antoaneta Dimitrova, Kristin Petrova Grigorova, Daniela Lubenova, Danche Vasileva, Milena Nikolova;
- 3. Case Report :
Oligoasthenoteratozoospermia, treatment with acupuncture**
Authors: Jihe Zhu, Blagica Arsovska, Dance Vasileva, Andrijana Sterjovska-Aleksovska, Kristina Kozovska;
- 4. Treatment of cervical spondylosis with acupuncture**
Authors: Kristina Kozovska, Jihe Zhu, Blagica Arsovska, Andrijana Sterjovska-Aleksovska;
- 5. Effect of kinesitherapy on static and dynamic balance in patient after vertebral basilar system stroke**
Authors: Milena Nikolova, Antoaneta Dimitrova, Danche Vasileva, Daniela Lubenova, Kristin Petrova Grigorova;
- 6. Malignant pleural effusions in lung cancer: the condition during the disease**
Authors: Marija Karakolevska-Ilova, Elena Simeonovska Joveva, Aleksandar Serafimov, Lidija Petrovska;
- 7. Systemic fungal infections in hematological malignancies**
Authors: Petar Kuzmanovski, Velo Markoski;
- 8. Morbidity and mortality of malignant neoplasms in Macedonia**
Authors: Viktorija Vukovikj, Velo Markoski;
- 9. Cognitive behavioral program in treating insomnia among elderly patients**
Authors: Kneginja Richter, Lence Miloseva, Guenter Niklewski, Anja Piehl;
- 10. Regulations and legal aspects in management of medical waste**
Authors: Biljana Shikoska, Cena Dimova, Gjorgji Schumanov;
- 11. Control of the psychiatric disorders in the Republic of Macedonia**
Authors: Leonid Ramov, Velo Markoski;
- 12. Monitoring of the renal function in Indometacin treated patients with rheumatoid arthritis**
Authors: Drita Yzeiri Havziu, M.Hiljadnikova-Bajro, T. Kadifkova Panovska;
- 13. Incidence of breast cancer in Macedonia**
Authors: Dijana Stojanova, Velo Markoski;
- 14. HPV virus as a cause of cancer of the cervix in R.Macedonia**
Authors: Stefanija Joveva, Velo Markoski, Vaso Taleski;
- 15. Analysis of the Pap test results by age groups in the area of Kriva Palanka**
Authors: Robert Nikolovski, Kristina Denchovska, Goran Mladenovski, Velo Markovski;
- 16. Giant rhinophyma treated by excision and full thickness skin grafting**
Author: Emilija Lozanovska Doneva;
- 17. Incidence of patients with chronic renal failure in Skopje**
Authors: Simona Kamceva, Velo Markoski;
- 18. Calculation of effective dose to family members of patients with thyroid diseases**
Authors: Marina Zdravevska Kochovska, Emilija Janjevik Ivanovska, Meri Angeleska, Sasho Nikolovski, Zlatko Filipovski;

- 19. Contemporary Microbiological Diagnostic Tests for Rapid Identification and Detection of Resistance of Mycobacterium tuberculosis**
Authors: Oliver Taleski, Vaso Taleski;
- 20. Analysis of clinical features and complications in patients with β -thalassemia in the region of Strumica**
Authors: Silvana Sinokapovska, Cena Dimova;
- 21. Lymphoepithelioma : A case report**
Authors: Vase Stojcheska, Rade Filipovski, Dobri Stoimenov, Nikica Atanasova, Goran Karaivanov, Ana Doneva, Irena Shulevska, Silvana Kraveva;
- 22. F-ra Capitulum Radii L.Dex. – A Case report**
Authors: Svetlana Jovevska, M.Idrizovikj;
- 23. Patient with intracranial hemorrhage and arteriovenous malformation detected with transcranial color duplex sonography – case report**
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- 24. Hereditary supracondylar spur of the humerus: Case report**
Authors: Strahil Todorov, Christian Lozanoski, George Zafirovski;
- 25. Prosthetic rehabilitation in patient with advanced degree of functional disorders (case report)**
Authors: Natasa Denkova, Katerina Zlatanovska, Ana Radeska-Panovska, Sanja Nashkova, Ivona Kovacevska;
- 26. Marginal Implants Bone Loss – a Case Report**
Authors: Kiro Papakoca, Ana Radeska-Panovska, Katerina Zlatanovska;
- 27. Ectodermal Dysplasia, a Case Report: Challenge for Prosthodontic Solution**
Authors: Emilija Bajraktarova Valjakova, Bajevska Jagoda, Vesna Korunoska Stevkovska, Biljana Kapusevska, Nikola Gigovski, Aneta Mijoska, Katerina Zlatanovska, Cvetanka Bajraktarova Mishevska;
- 28. Alveolar socket preservation and shaping using temporary prosthetic construction – cases presentation**
Authors: Nikola K. Gigovski, Vesna Korunoska- Stevkoska, Emilija Bajraktarova, Aneta Mijoska, Ana Radeska-Panovska, Ana Gigovska;
- 29. Porcelain veneers produced by refractory die method**
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- 30. Correlation of Two Different Local Hemostatic Modalities in Oral Surgery Patients with Oral Anticoagulants**
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- 31. Assessment of orthodontic treatment need among school children by using iotn (index of orthodontic treatment need)**
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- 33. Poor oral hygiene and show of caries in 12 year old children**
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- 35. Oral surgery treatment in the patients with combination syndrome**
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- 36. Iatrogenic mistakes, cause for a failure at surgical treatment of a chronic periapical processes**
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- 37. Evaluation of Different Preparation of Artificial Teeth and Acrylate Prosthetic Base**
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- 38. Analysis of the dimensional stability of elastomeric silicone impression materials**
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- 40. Mobile dental NOG-types used in working dental models**
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- 41. Determining normal tissue toxicity of non-radioactively Lu/Y-labeled rituximab-conjugates in rat animal model**
Authors: Darinka Gjorgieva Ackova, Katarina Smilkov, Icko Gjorgoski, Emilija Janevik-Ivanovska;
- 42. Genetically Engineered Mouse Models For Human Pancreatic Cancer: A Review Of The KC, KPC And iKRas*P53* Models**
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- 44. HER2 Transgenic Mouse Models: A Way To HER2+ Breast Cancer Targeted Therapy**
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- 49. An overview of phytosomes as a novel herbal drug delivery system**
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- 50. Determination of active pharmaceutical ingredient – chloropyramine in dragées**
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- 51. Comparison of volatile aroma compounds between cultivated and spontaneous flowering stems of *Sideritis scardica* Griseb. from R. Macedonia**
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- 52. Bioactive compounds of cold-pressed oil from the seeds of Gojy Berry (*Lycium barbarum*)**
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- 53. Development and validation of HPLC method for determination of flavonoids in herbal preparations**
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- 54. Atomic emission spectrometry with inductively coupled plasma (ICP-AES) analysis of trace elements in *Camellia sinensis* teas**
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- 55. Determination of trace elements analyzed by atomic emission spectrometry with inductively coupled plasma (ICP-AES) in *Matricaria chamomilla* L. teas present on macedonian market**
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- 56. Human health risks from heavy metals via consumption of contaminated food**
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- 57. Development of an ultrasonic method for effective extraction of capsaicin as a potent bioactive compound**
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- 63. Oxidative stress, oxidative DNA damage and prostate cancer**
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- 64. RNA interference (RNAi) mechanism as a basis for future successful treatment of chronic hepatitis B infection**
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- 65. Anti-cancer target therapy based on drugs conjugated to hyaluronic acid**
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- 66. Cancer specific conjugated monoclonal antibodies for anticancer therapy**
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- 67. Accreditation of the Laboratory of Radiopharmacy – requested requirements or need of challenge**
Authors: Apostolova Paulina, Delipetrev Katarina, Smilkov Katarina, Gjorgieva Ackova Darinka, Sterjova Marija, Janevik Ivanovska Emilija;
- 68. Quality control of PET radiopharmaceuticals, with reference to its specifics vs quality control of conventional pharmaceuticals**
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- 69. Production of [11C] Choline in The University Institute for PET – new perspective in diagnostics of prostate malignancy in R. of Macedonia**
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- 70. PET radiopharmaceuticals in the diagnosis of neurological diseases**
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- 71. Achievements and perspectives in formulation of stable immunoconjugate of the HER2-targeting trastuzumab – potential for rapid labelling with Gallium-68**
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Faculty of Medical Sciences

University Goce Delcev – Stip, Macedonia

INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES

**“Current achievements and future perspectives in
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Freeze-drying approach to enhance antibody stability

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Abstract

Preparations containing antibodies are more easily formulated in solution, but their stability is often impaired, concerning the fact that aqueous solutions are prone to numerous physical and chemical changes, such as denaturation, aggregation, adsorption, hydrolysis, deamidation, nonreducible cross-linking, formation/exchange of disulfide bonds, isomerization, fragmentation, Maillard-reaction, etc. Freeze-drying is often used in biopharmaceutical production, because the chemical and physical degradation rate can be significantly reduced in dry state. This process enables preservation of the desired characteristics of the product for a longer period of time, thus increasing its shelf life. Part of the challenges associated with the first phase of the freeze-drying process can be addressed with its corresponding design, i.e. defining the freezing rate, but also addition of bulking crystalline agents as mannitol, glycine or disaccharides (sucrose, trehalose), that can provide fine, microporous structure. Recent research had shown that slow freezing, which includes gradual cooling of the sample to a given temperature with a certain rate, and fast freezing, including direct introduction of the sample to a previously cooled freeze-dryer, are the most favored.

Our experience was in designing a freeze-drying process in order to formulate freeze-dried kit, containing conjugated Anti-CD-20 antibody, ready-to label with radioactive isotopes. Using freeze-dryer able to control process parameters, (Labconco Free Zone Stoppering Tray Dryer, USA), two types of freeze-drying protocols were applied, a protocol with direct freezing to the initial temperature of -40 °C and a protocol with gradual freezing from 5 °C to -40 °C, at a rate of 0,40 °C/min. Appearance after reconstitution of the finished product and presence of aggregates were evaluated, as well as the IR and Raman spectra.

Results have shown that the protocol using gradual freezing from 5 °C to -40 °C, at a rate of 0,40 °C/min was more successful in maintaining the stability of the antibody during freeze-drying, giving clear solution after reconstitution, no presence of aggregates and IR and Raman spectra most similar to the spectra of the native conjugated form.

The research performed, enabled formulation of ready-to label anti-CD-20 antibody, intended for preclinical research for Non-Hodgkin's lymphoma therapy.

Keywords: antibodies, lyophilization, stability.