SRF
SOCIETATEA ROMÂNĂ DE FIZIOLOGIE

UMF
UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE IULIU HAȚIEGANU CLUJ-NAPOCA

Al XIV-lea Congres al Societății Române de Fiziologie

Fiziologia azi: între concept, inovație tehnologică și aplicația clinică

17-19 octombrie 2024, Cluj-Napoca

Hotel Univers T: Amfiteatrul Terra

EVENT Management Eveniment

Romanian Society of Physiology (SRF)

The 14th Congress of the Romanian Society of Physiology:
„Physiology today: between concept, technological innovation and clinical application”

CONGRESS PROGRAM

17-19 October 2024
Cluj-Napoca

Comitet ştiinţific / Programme committee

Preşedinte/Chairman: Dan Dobreanu, UMFST "George Emil Palade", Tg. Mureş, România

Adrian Bălşeanu, UMF Craiova, România
Walther Bild, UMF "Grigore T. Popa, Iaşi, România
Cătălin Bogdan, UMF Craiova, România
Simona Clichici, UMF "Iuliu Haţieganu", Cluj-Napoca, România
Adriana Filip, UMF "Iuliu Haţieganu", Cluj-Napoca, România
Carmen Panaitescu, UMF "Victor Babeş", Timişoara, România
Alina Scridon, UMFST "George Emil Palade", Tg. Mureş, România
Veronica Sfredel, UMF Craiova, România
Şoimiţa Suciu, UMF "Iuliu Haţieganu", Cluj-Napoca, România
Gabriela Tanasie, UMF "Victor Babeş", Timişoara, România
Ana-Maria Zăgrean, UMF "Carol Davila", Bucureşti, România

Comitet de organizare /Organizing committee
Disciplina Fiziologie, UMF "Iuliu Haţieganu", Cluj-Napoca/
Physiology Department, UMF "Iuliu Haţieganu", Cluj-Napoca

Preşedinţi/Chairs: Şoimiţa Suciu, Simona Clichici

Răzvan-Geo Antemie
Ioana Bâldea
Cristina Bidian
Meda Cosma
Hana Decean
Adriana Filip
Irina Haranguş
Oana Hoteiuc
Cezar Login
Mihai Lupu
Teodora Mocan
Daniela Mitrea
Iuliana Nenu
Cristina Olănescu Vaida-Voevod
Nadina Pop
Lavinia Sabău
Lăcrămioara Samoilă
Alexandra Sevastre-Berghian
Ramona Simedrea
Alina Toader

SCIENTIFIC PROGRAM OF SRF CONGRESS: „Physiology today: between concept, technological innovation and clinical application”

17-19 October 2024
UNIVERS T HOTEL, TERRA AMPHITEATRE

Thursday, 17 October 2024

14,00 – 14,30 Opening ceremony

14.30 - 15.30 Are nanomaterials suitable for medical applications? From concept to technological innovation

Chairs: ***Simona Clichici, Luminița David***

14.30 - 14.50 *Teodora Mocan (Cluj-Napoca)* - Nano-biotic systems. New concepts and trends at international level

14.50 - 15.10 *Bianca Moldovan et al. (Cluj-Napoca)* Green synthesis of bimetallic „core-shell” Ag@Au nanoparticles using bioactive compounds from Lycium Barbarum L. fruits and in vitro evaluation of their antioxidant capacity

15.10 - 15.30 *Ioana Bâldea et al. (Cluj-Napoca)* Combined magnetic hyperthermia and chemotherapy mediated by iron oxide nanoclusters linked with doxorubicin induces cell cycle arrest and apoptosis on breast cancer spheroids

15.30 - 16,00 *Dan Dobreanu (Tg. Mureș)* Focus: Is there still a need to understand physiology in the treatment of dyslipidemias?
(Session carried out with the support of the company Sanofi)

16,00 - 16.30 Coffee break

16,30 – 18.00 Experimental studies – are they useful today?

Chair: ***Adriana Filip, Bogdan Cătălin***

16.30 - 16.45 *Vlad Toma et al (Cluj-Napoca)* Exploring oxygen carriers for hemorrhage management: vascular response to sheep hemoglobin administration

16.45 - 17.00 *Victor Ojog et al. (Chișinău)* Contractile activity of portal vein in experimental acute pancreatitis

17.00 - 17.15 *Patricia Dulf et al. (Cluj-Napoca)* Implications of oxidative stress and autophagy in anthracycline-induced cardiotoxicity and the protective role of natural antioxidants

17.15 - 17.30 *Anca Stoica et al. (Cluj-Napoca)* Conjugating non-steroidal anti-inflammatory drugs for alleviating side effects - a model of acute inflammation *in vivo*

17.30 - 17.45 *Alina Hanga-Fărcaș et al. (Oradea)* Phytochemical compounds applied in bone regeneration

17.45 - 18.00 *Victor Ojog et al. (Chișinău)* The contractile reactivity of the isolated portal vein in different concentrations of Ca2+ ions in experimental hypertension

18.00 - 18.30 *Dan Dobreanu (Tg. Mureș)* Is still pathophysiology the ABC of understanding atrial fibrilation? (Session carried out with the support of the company Berlin Chemie)

18.30 - 19.30 – Is there a need for artificial intelligence and predictive models in medicine?

Chairs: *Walther Bild, Ion Grabovschi*

18.30 – 18.50 *Walther Bild et al. (Iași)* Artificial intelligence in biomedicine – how does it work?

18.50 - 19.10 *Ion Grabovschi et al. (Chișinău)* Severe trauma machine learning prediction model

19.10- 19.30 *Nenu Iuliana et al. (Cluj-Napoca*) Improving prognostic precision in hepatic resection for hepatocellular carcinoma: the superior role of liver stiffness measurement with Fibroscan

20.00 - Welcome cocktail

Friday, 18 October 2024

9,00 – 11.00 Advances in neurosciences (part I)

Chairs: *Ana-Maria Zăgrean, Tudor Badea*

9.00 - 9.40 *Tudor C. Badea (Brașov)* Characterization of a newly discovered Glucose Transport regulator expressed in projection sensory neurons

9.40 - 10.00 *Ana Maria Zăgrean (București)* Oxytocin mediated neuroprotection in hypoxic-ischemic conditions: timing and mechanisms

10.00 - 10.15 *Cătălin Bogdan (Craiova)* Cerebral water channels regulate amyloid burden and cognitive abilities in a mouse model of Alzheimer's disease

10.15 - 10.30 *Ioan-Alexandru Florian et al. (Cluj-Napoca)* Initial results of the gliostat study: a potential cure for glioblastoma?

10.30 - 10.45 *Lázaro Arturo Góngora Hernández et al. (Cluj-Napoca)* Epigenetic modulation by oleocanthal: implications for stress response and neurodegenerative diseases

10.45-11.00 *Vlad Sever Neculicioiu et al. (Cluj-Napoca) Cornus mas* as a potential modulator in a sleep deprived rat model

11.00 – 11.15 Coffee break

11.15 - 11.30 *Teodora Mocan (Cluj-Napoca)* The importance of physiological and pathological mechanisms related to gut microbiota in maintaining health
(Session carried out with the support of the company Innergy)

11.30 – 12.45 Advances in neurosciences (part II)

Chairs: ***Adrian Bălşeanu, Tibor Szilagyi***

11.30 -11.45 *Ştefan Martin et al. (Tg. Mureş)* Testing Muscle Fatigue Threshold on Cycling: The Use of Surface Electromyography as a Complementary Method to Ventilatory Thresholds

11.45 - 12.00 *Nadina Pop (Cluj-Napoca)* Local topical treatment of peropheral nerve lesions: utopia or reality?

Alina Cătălina Buican et al. (Craiova) Effects of C3a Antagonist on behavior in a cuprizone-induced demyelination model

12.00 - 12.15 *Sofia Timpuriu (Bucureşti)* Theragnostic - Somatostatin receptors and their application

12.15-12.30 *Claudia-Andreea Moldoveanu (Cluj-Napoca)* Unlocking early diagnosis: exploring blood-brain biomarkers in Parkinson's Disease for enhanced intervention strategies

12.30-12.45 *Adrian Lupuşor (Chişinău)* Could circadian rhythm disruption contribute to sleep apnea headache?

12.45 - 13.15 Posters session (I)

Evaluation committee: ***Ana-Maria Zăgrean, Alina Scridon, Adriana Filip***

**Silviu Filipiuc et al. (Iaşi) In vitro* testing of lidocaine and cannabidiol absorption from complex topical formulations

**Irina Burlacu et al. (Craiova)* Sweet, spice and everything nice: a review of therapeutic options for post-stroke depression in diabetic patients

**Andrei Ganenco et al. (Chişinău*) Establishing predictors extracted from breathing pattern parameters in predicting sympathovagal balance

**Andrei Greşita - In vitro* evaluation of bioprinted alginate-collagen scaffolds laden with astrocytes

**Mădălina Muşat et al. (Craiova)* The impact of ketamine on behavioral responses, neuroinflammation, and liver injury in a depressed murine model

**Corina Pal et al. (Tg. Mureş)* Dipper status variations in spontaneous low level blood pressure patients

**Alina Cătălina Buican et al. (Craiova)* Effects of C3a Antagonist on Behavior in a Cuprizone-Induced Demyelination Model

13.15 – 14.00 Lunch break

14.00 – 15.30 The impact of discoveries in physiology and pathophysiology on cardiovascular diseases

Chairs: ***Alina Scridon, Dan Dobreanu***

14.00 - 14.15 *Danina M. Muntean et al. (Timişoara)* Methilene blue reduces oxidative stress and monoamine oxidase expression in human cardiovascular adipose tissue: what's new about an old molecule?

14.15-14.30 *Marcel Perian (Tg. Mureş)* Blood pressure and dipper status. Measurements and interpretations

14.30-14.45 *Vasile Bogdan Halațiu (Tg. Mureș)* Non- antiarrhythmic agents with antiarrhythmic properties

14.45-15.00 *Alina Scridon (Tg. Mureș)* New antithrombotics: where to?

15.00-15.15 *Dan Alexandru Cozac et al. (Tg. Mureș)* Preoperative inflammatory biomarkers as predictors of postoperative atrial and ventricular ectopy and complications following coronary artery bypass grafting

15.15-15.30 *Cristian Militaru (Craiova)* Septal ablation with alcohol, a minimally invasive gradient reduction intervention in hypertrophic obstructive cardiomyopathy

15,30 – 16.00 Coffee break

16.00 – 17.00 Modelling and modulating the respiratory immune response

Chairs: *Carmen Panaitescu, Corina Bocșan*

16.00 - 16.20 *Carmen Panaitescu et al. (Timișoara)* Modulating the allergic immune response towards tolerance by allergen immunotherapy: a 21st century challenge

16.20-16.40 *Pătrașcu et al. (Timișoara)* Lessons learned from modulating the immune response in SARS CoV2 infection

16.40-17.00 *R.I. Zimbru et al. (Timișoara) In vitro* modulation of bronchial responsiveness

17.00 - 18 *Prof. Dr. Adrian Șalic (Boston)* How do cells communicate?

18.00-19.00 Intracellular insights in cell functioning in health and disease

Chairs: *Gabriela Tănăsie, Ioana Bâldea*

18.00 – 18.15 *Gabriela Tănăsie et al. (Timișoara) In vitro* functional studies regarding cryopreserved mesenchymal stem cells healing properties in various culture conditions

18.15 - 18.30 *Camelia Coadă et al. (Cluj-Napoca, Bologna)* Global miRnome analysis reveals specific profiles associated with the progression of endometriosis towards endometriosis-related ovarian cancer

18.30 -18.45 *Alkora Balan et al. (Tg. Mureș)* Aging-associated atrial and circulating microRNA changes

18.45-19.00 *Bogdan Dume et al. (Cluj-Napoca)* Targeting constitutive HIF-1α expression to overcome doxorubicin resistance in B16.F10 melanoma cells

19.00 SRF General Assembley

20.00 Dinner Gala

Saturday, 19 October 2024

08.30 – 10.00 Immune disorders in pathological conditions

Chairs: *Olga Orășan, Adriana Muntean*

8.30 - 8.45 *Olga Orășan et al. (Cluj-Napoca)* IgG4 related diseases. When are they suspected? How do we treat them?

8.45 - 9.00 *Adriana Muntean et al. (Cluj-Napoca)* Inflammation in allergic rhinitis

9.00 - 9.15 *Roxana Schurger-Cimponeriu et al. (Cluj-Napoca)* Immune thrombocytopenic purpura and thrombosis-a paradoxical association
9.15 - 9.30 *Iulia Szabo (Cluj-Napoca)* Immune dysfunction in systemic sclerosis: from bench to bedside

9.30 - 9.45 *Aliona Dobrovolskaia et al. (Chişinău)* Diagnostic and predictive value of cytokine levels in pregnancies complicated by preeclampsia in pregnant women over 35 years old

9.45 - 10.00 *Teodora Larisa Florian (Cluj-Napoca)* Effect of Biological Therapies on Key Inflammatory Cytokines in Psoriasis

10.00 – 10.30 Coffee break

10.30 – 10.50 *Dan Dobreanu (Tg. Mureş)* ARNI decoded: from physiological principles to clinical practice (Session carried out with the support of the company Novartis)

10.50 - 11.05 *Lăcrămioara Samoilă (Cluj-Napoca)* The mechanism of action of Brolucizumab in retinal pathology (Session carried out with the support of the company Novartis)

11.05 – 11.50 The interaction of alcohol with the central nervous system

Chairs: *Cătălin Bogdan, Karoly Orban-Kis*

11.05 - 11.35 *Prof. Dr. Mickael Naasela (Lille)* Interests and mechanisms of action of psychedelics (psilocybin and LSD) in alcohol addiction: from preclinical to clinic

11.35–11.50 *Eugeniu Coreţchi (Chişinău)* Alcohol's impact on central nervous system excitability

11.50 - 12.20 Posters session (II)

Evaluation committee: *Ana-Maria Zăgrean, Alina Scridon, Adriana Filip*

**Szilvia Toth et al. (Cluj-Napoca)* Hematologic alterations associated with nonsteroidal anti-inflammatory drug (NSAID) therapy in rheumatoid arthritis

**Alexandra Sevastre-Berghian et al. (Cluj-Napoca)* Neuroprotective effects of Cynara Scolymus L. extracts in Aβ1–42-induced neurotoxicity in SK-N-SH neuronal cells and Wistar rats

**Alexandra Sevastre-Berghian et al. (Cluj-Napoca)* Neuroprotective effects of Cynara Scolymus L. extracts in Aβ1–42-induced neurotoxicity in SK-N-SH neuronal cells and Wistar rats

**Mariana Mureşan et al. (Oradea)* Preliminary study in the evaluation of the antioxidant potential of Cichorium intybus L extracts

**Corina Bocşan et al. (Cluj-Napoca)* Retrospective analysis of allergen-specific immunotherapy efficacy and safety in a Romanian cohort of allergic patients

**Mekan Jumamyradov et al. (Tg. Mureş)* Abdominal aortic constriction in adult Wistar rats – an animal model of pressure overload cardiac hypertrophy and subsequently heart failure

**Teodora Bonci et al. (Cluj-Napoca)* Efectul antiinflamator al terapiei complementare cu vitamina D în astmul bronşic indus experimental

**Ramona -Niculina Jurcău et al. (Cluj-Napoca)* Auriculopuncture effectiveness on anxiety, heart rate and salivary cortisol, in dental patients

**Andreea Vădan et al. (Cluj-Napoca) In vivo* hepatoxicity evaluation of differently shaped hybrid gold-iron oxide nanoparticles

12.20 – 13.45 Teaching and learning: where do we stand?

Chairs: *Şoimiţa Suciu, Pompei Bolfă*

12.20 - 12.50 *Prof. Hwee-Ming Cheng (Kuala Lumpur)* The PHYsherman: catching students'attention

12.50 - 13.05 *Prof. Pompei Bolfă (Ross University School of Veterinary Medicine, Saint Kitts)* Boosting veterinary student success: the impact of test-enhanced learning

13.05 - 13.20 *Boris Dragan (Chişinău)* Chronic stress and its inducing factors in medical students

13.20 - 13.45 *Prof. Pompei Bolfă (Ross University School of Veterinary Medicine, Saint Kitts)* The vital role of diversity, equity, and inclusion (DEI) in shaping the future of health professions

13,45 - 14,00 Discussions

14,00 - Closing ceremony

ORAL PRESENTATIONS

Nano-biotic systems. New concepts and trends at international level

Teodora Mocan

„Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca.

Nanotechnologies applied in medicine represent a field on the rise, the variety of structures and applications being constantly growing and developing. The efficacy of nanomedicine and its potential have been demonstrated by numerous experimental and clinical studies. Equally, the knowledge in the field of functional medicine and in the potential of biotics to intervene as a modulator of various pathological mechanisms is gaining ground, making its presence felt through extensive trials and by the inclusion in the main ones of new clinical guidelines for the recommended management of human pathologies. This presentation presents some of the main new hybrid, nano-biotic approaches that have appeared in the literature, together with the physiological considerations underlying the proposed designs as well as the results obtained.

Keywords: Nanostructures, biotics

Green synthesis of bimetallic „core-shell" Ag@Au nanoparticles using bioactive compounds from *Lycium Barbarum* L. fruits and *in vitro* evaluation of their antioxidant capacity

Moldovan B.[1], David L.[1], Morosan V.[1], Baldea I.[2]. Filip G.A.[2]

1) Faculty of Chemistry and Chemical Engineering," Babeş-Bolyai" University, Cluj-Napoca, Romania; 2) Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Introduction: Nanobiotechnology facilitates the production and application of nanosized materials which interact with the human body. Phenolic compounds from fruits can be successfully used in the synthesis of hybrid nanomaterials. *L. barbarum* L. fruits are rich in antioxidant bioactive compounds, efficient in reducing damages generated by oxidative stress. Therefore, functionalization of noble metal nanoparticles with natural antioxidants from fruits reduce ROS production. The use of bimetallic nanoparticles by controllable integration of two metals into single nanostructures is a great approach, as the properties of both metals can be exploited.

Objectives: The aim of the study was to elaborate a „green" method for the phytosynthesis of bimetallic „core-shell" Ag@Au nanoparticles and to evaluate their antioxidant capacity.

Materials and methods: The AgNO3 solution was used as source of silver ions for the phytomediated synthesis of silver nuclei, to obtain core-shell bimetallic nanoparticles. Over the solution of AgNPs thus obtained, HauCl4 sol. was added to deposit the colloidal gold over the obtained Ag cores. The formation of nanoparticles was confirmed by UV-VIS spectroscopy. To evaluate their cytotoxicity, normal human dermal fibroblasts (Bj, ATCC, CRL-2522™) cell line was used. The antioxidant capacity was evaluated on human umbilical vein endothelial cells (HUVEC-ECCAC). Colorimetric MTS and viability testing with trypan blue was applied. For MTS, cell survival was assessed by colorimetric measurement of formazan, using the CellTiter 96® cell proliferation assay. Oxidative stress parameters: MDA, SOD and CAT enzymatic activity were spectrophotometrically determined.

Results: The extracellular synthesis of a nanostructured biomaterial based on bimetallic Ag@Au nanoparticles using polyphenols from goji has been achieved. Modern techniques (TEM, FT-IR) confirmed the spherical shape and a mean diameter of 11 nm of the nanoparticles, as well as the presence of bioactive compounds on their surface. The crystal structure of nanoparticles was confirmed by X-ray powder diffraction. The in vitro protective role of the phytosynthesized nanostructures on the induced oxidative stress was evaluated on human umbilical vein endothelial cells exposed to hyperglycemia. The antioxidant defence markers: MDA as a marker of lipid peroxidation and SOD and CAT activities were assessed. The bimetallic nanoparticles had an antioxidant effect, by improving MDA level and inducing a significant recovery of the activity of the antioxidant enzyme CAT and a mild one of SOD.

Conclusions: A novel „green" method for the synthesis of bimetallic nanoparticles using the polyphenols rich goji fruits was developed. Investigation of their antioxidant behaviour suggest that the nanoparticles present promising antioxidant activity and hence have a great potential in the development of therapeutic agents against oxidative tissue injuries.

Keywords: bimetallic nanoparticles, goji fruits, antioxidant activity

Combined magnetic hyperthermia and chemotherapy mediated by iron oxide nanoclusters linked with doxorubicin induces cell cycle arrest and apoptosis on breast cancer spheroids

Baldea I[1*], Petran A[2], Muntean M[3], Florea A[3], Cenariu M[4], Razniceanu V[1], Sevastre-Berghian A[1] and Iacovita C[5]

1) Department of Physiology, University of Medicine and Pharmacy Iuliu Hatieganu, Cluj-Napoca, Romania; 2) National Institute of Research and Development of Isotopic and Molecular Technologies, Cluj-Napoca, Romania; 3) Departmen of Molecular Biology, University of Medicine and Pharmacy Iuliu Hatieganu, Cluj-Napoca, Romania; 4) Department of Biochemistry, University of Agicultural Sciences and Veterinary Medicine; 5) Department of Biophysics, University of Medicine and Pharmacy Iuliu Hatieganu, Cluj-Napoca, Romania

Introduction: Magnetic hyperthermia (MH) is an therapeutic procedure that involves magnetic nanoparticles administration either local or general, then exposure to an external alternating magnetic field (AMF). This leads to hyperthermia in the treated tumor resulting in the death of tumor cells. Objective: To increase the efficiency and selectivity of tumor killing by combined, synergic effects of the two oncologic therapies: chemotherapy induced by doxorubicin and magnetic hyperthermia. Materials and Methods: Iron oxide magnetic nanoclusters (MNC) were synthetized by solvothermal method and functionalized with polydopamine polymers and further linked with doxorubicin in a ratio 20:1. Biological studies were conducted on tumor spheroid models containing either MDA-MB-231 or MDA-MB-231/ADM (resistant to doxorubicin) and normal dermal fibroblasts (BJ) and endothelial cells (HUVEC). Cell toxicity, nanoparticles uptake and apoptosis were evaluated. Results: nanoparticle clusters, showed spherical shapes and size ~200 nm. MNC w/wt doxorubicin exhibited no cytotoxicity up to 100 μg/ml. Magnetic hyperthermia induced significant cell toxicity and death through membrane apoptosis. Hyperthermia using MNC linked with doxorubicin, further increased apoptosis and induced selective cell cycle arrest of tumor cells. Acknowledgements: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, Romania, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2021-0498, within PNCDI III.

The effect of gold and silver nanoparticles capped with Cornus mas L. extract on PI3K-AKT signaling pathway genes expression in oral dysplastic keratinocytes

Filip GA[1], Clichici S[1], Muresan CI[2], Nistor A[2], Baldea I[1], Moldovan B[3], David L[3], Vulturar R[1], Suharoschi R[2]

1) Morpho-functional Department, Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca; 2) Molecular Nutrition and Proteomics Laborator, Institute of Life Science, University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca; 3) Faculty of Chemistry and Chemical Engineering, Babes-Bolyai University, Cluj-Napoca

Introduction/Objectives: The study aims to investigate the ability of gold (AuCM) and silver nanoparticles (AgCM) capped with Cornus mas L. (CM) extract to influence the gene expression involved in PI3K-AKT pathway in human dysplastic oral mucosa cells (DOK). Materials and methods: DOK cultures were treated with AuCM, AgCM and CM extract. Untreated cells were used as controls. Viability, cell death by FACS (apoptosis/necrosis) and the gene expression by using RT2 PCR Profiler high-throughput technique were evaluated. Thus, the 96-well PCR plates containing RT2 qPCR Primer Assays for a set of 84 genes, five housekeeping genes, and three controls were assayed on qPCR (Roche LC480). Results: In dysplastic cells, AgCM and AuCM significantly decreased cell viability and induced cell death at doses higher than 20 μg/ml compared to CM. Forty-seven genes with different expression levels were found, 27 genes being over-expressed while 20 genes were under-expressed. The results were integrated with other two signaling pathways (p53 and WNT) with potential therapeutic approach in cancer chemotherapy. Higher values of gene over-expression were identified for MTOR, GSK3B, EIF4B, and RAC1 genes. The mTOR was under-expressed while GSK3B gene was over-expressed. Among the under-expressed genes, we outline those with more than 2-fold activity suppression respectively EIF4E, RHOA, and RPS6KA1. Conclusions: In dysplastic cells, AgCM and AuCM significantly decreased cell viability and induced cell death at doses higher than 20 μg/ml. The suppression of GSK-3B activity under therapeutic interventions suggested that gold and silver nanoparticles treatments can be associated with inhibition of cancer progression.

Exploring oxygen carriers for hemorrhage management: vascular response to sheep hemoglobin administration

Toma V.A.[1,2,3*], Moldoveanu C.A.[1,2], Lehene M.[4], Muntean M.[5], Florea A.[5], Roman I.[2], Dandea Ş.[6], Sevastre B.[6], Silaghi-Dumitrescu R.[4]

1) Babeş-Bolyai University, Faculty of Biology and Geology, Department of Molecular Biology and Biotechnology,

Cluj-Napoca, Romania; 2) Institute of Biological Research, Cluj-Napoca, branch of INCDSB Bucharest, Department of Biochemistry and Experimental Biolo

Introduction: In the search of the semi¬artificial oxygen carriers as blood substitutes, polymerized sheep hemoglobin (SpolyHb) was noticed as a valuable candidate in terms of oxygen delivery, redox impact, and toxicity. However, its effect on vascular homeostasis remains incompletely understood.

Objectives: To evaluate the vascular effect of SpolyHb, the activities involved biochemical analyses (inflammatory response, oxidative stress), ultrastructural investigations, and immunohistochemical exam of the aorta exposed to SpolyHb.

Materials and Methods: It was conducted an in vivo experiment utilizing Wistar rats (8/group) subjected to hemorrhagic shock conditions and perfused with SpolyHb. For comparison, another group received i.v. Dextran 40, while the Control group underwent hemorrhagic shock without fluid perfusion. SpolyHb and Dextran 40 exposure was limited to 24 hours. Subsequently, animals were deeply anesthetized (ketamine-xylazine), and samples of the abdominal aorta (2-2.2 cm) were collected for electron microscopy, iNOS immunohistochemistry, and assessment of inflammation status via ELISA for IL-6, IL-10, IL-1beta, IL-1alpha, and prostaglandin E2. Kinetic assays were conducted for catalase and peroxidase, and levels of reduced and oxidized iron were estimated using colorimetric methods. Matrix metalloproteinases were assessed using a gelatin zymography protocol.

Results: In summary, exposure to SpolyHb led to a reduction in proinflammatory cytokines, matrix metalloproteinases, and an increase in IL-10, while Dextran 40 maintained vascular inflammation similar to the Control group. Both exposed groups (Dextran 40 and SpolyHb) exhibited a significant increase in oxidative stress. However, ultrastructural investigations revealed only slight endothelial damage in the hemorrhage group, while Dextran and SpolyHb did not have prominent detrimental effects on the vascular endothelium. Following exposure to SpolyHb, highlights of the vascular effects included no hypertension, slight endothelial damage with slight iNOS changes, and a decrease in vascular inflammation mediated by IL-10.

Conclusion: SpolyHb was more performant than Dextran 40 and MMP changes open new research topics in HBOC physiology.

Keywords: hemoglobin, oxygen carriers, aorta.

Acknowledgments: This research received support from a GTC grant from Babes-Bolyai University (Grant No. 32939/22.06.2023) and part of the study was sustained by the AOSR-TEAMS-III 2024-2025 grant.

Contractile activity of portal vein in experimental acute pancreatitis

Ojog V, Lozovanu S, Ganenco A, Borș P

Department of Physiology and Biophisics , Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Introduction: Trypsin, released into the blood in acute pancreatitis, probably impairs the intracellular homeostasis of Ca2+ ions, including vascular smooth muscles.

Objectives: The aim of the study was to highlight the contractile properties of the smooth muscle of the portal vein in response to changes in the concentration of Ca^{2+} ions.

Materials and methods: The study was performed on 24 Wistar rats. The rat portal vein was placed in the thermostatic bath, perfused with Krebs-Henseleit solution, where it was subjected to passive expansion with a force of 4 mN. In both groups (control and experimental pancreatitis) the reactivity of smooth muscle to Ca^{2+} under conditions of changing Ca^{2+} ions was determined. Spontaneous contractions of the isolated portal vein were determined in isometric mode. Acute pancreatitis was produced by the Malhasean method.

Results. The segment of the portal vein possesses spontaneous contractility, which in the conditions of experimental isolation manifests itself in a certain rhythmicity with variable force of contraction. The amplitude of contraction in experimental pancreatitis largely depended on the concentration of Ca^{2+} ions in the perfusate. The decrease in the concentration of Ca^{2+} ions in the perfusate suppressed the amplitude of contraction compared to the initial value. This suppression phenomenon was very expressive in the response to increased concentration of Ca^{2+} ions, amplitude of contraction decreased approximately 3 times in experimental pancreatitis. The frequency of spontaneous contractions of the portal vein in pancreatitis was decreased at the normal concentration of Ca^{2+} and especially at the increase of the concentration of this ion. The results of the experiments had found that the segments of the portal vein responded to the increase in the concentration of Ca^{2+} ions by decreasing the duration of relaxation, which indicates that Ca^{2+} ions were rapidly expelled or inactivated by a currently unidentified mechanism.

Conclusion: Experimental trypsinemia, like in acute pancreatitis, due to the proteolytic damage of the glycocalyx or/and by the action on trypsin on PAR-2 (protease-activated receptors), obviously changes the reactivity of smooth muscle of portal vein to Ca2+ ions, which requires some corrections in the treatment of acute pancreatitis.

Keywords: portal vein, smooth muscle, hypertrypsinemia.

Implications of oxidative stress and autophagy in anthracycline-induced cardiotoxicity and the protective role of natural antioxidants

Dulf PL[1], Coadă CA[1*], Florea A[2], Moldovan R[3], Baldea I[3*], Dulf DV[1,4], Blendea D[5,6], Filip GA[3]

1) Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; 2) Department of Molecular Sciences, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; 3) Department of Functional Biosciences, Iuliu Hatieganu University

of Medicine and Pharmacy, Cluj-Napoca, Romania; 4) Municipal Clinical Hospital, Cluj-Napoca, Romania; 5) Internal Medicine Department, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; 6) Department of Cardiology, Heart Institute, Cluj-Napoca, Romania

Introduction: Doxorubicin (DOX) is an effective anticancer drug, but its use is limited by a dose-dependent heart toxicity.

Objective: This study aimed to explore the potential cardioprotective effects of quercetin (Q), a natural antioxidant, in chronic DOX treatment.

Material and methods: A total of 32 Wistar rats were randomly divided into four groups: Control, DOX, DOX/Q-50 and DOX/Q-100, treated with saline, 2.5mg/kg body-weight DOX, 2.5mg/kg body-weight DOX + 50mg Q and 2.5mg/kg body-weight DOX + 100mg Q, respectively, for two weeks. Rats were monitored using cardiac ultrasound (US) and markers for cardiac injury. Oxidative damage and ultrastructural changes in the heart were investigated.

Results: Chronic DOX treatment led to a decline in cardiac function and elevated values of NT pro-BNP, troponin I and CK-MB. Q treatment slightly improved certain US parameters, and normalized serum NT pro-BNP levels. Furthermore, DOX induced SOD1 depletion with consequent NRF2 activation and DNA damage as shown by an increase in γH2AX and 8HOdG. Q treatment alleviated these alterations.

Conclusion: Oral administration of Q alleviated serum markers associated with DOX-induced cardiotoxicity. Furthermore, it exhibited a favorable impact on the cardiac US parameters. This suggests that Q may have potential cardioprotective properties.

Conjugating non-steroidal anti-inflammatory drugs for alleviating side effects - a model of acute inflammation *in vivo*

Stoica A.D.[1,5], Toth S.H.[1,2], Moț A.C.[3], Sevastre B.[4], Bizău, M.I.[1], Grigor, A.G.[1], Sevcencu, C.[1,5]

1) Doctoral School of Integrative Biology, Babes-Bolyai University, Cluj-Napoca, Romania; 2) Departament of Molecular Biology and Biotechnology, Faculty of Biology and Geology, Babes-Bolyai University, Cluj-Napoca, Romania; 3) Departament of Chemistry, Faculty of Chemistry and Chemical Enginering, Babes-Bolyai University, Cluj-Napoca, Romania; 4) Faculty of Veterinary Medicine, University of Agricultural Sciences and Veterinary Medicine, 400372, Cluj-Napoca, Romania; 5) National Institute of Research and Development of Isotopic and Molecular Technologies, Cluj-Napoca, Romania

Introduction: Non-steroidal anti-inflammatory drugs are a class of drugs used in the medical and pharmaceutical industry due to their antipyretic, analgesic, and anti-inflammatory effects. These drugs are among the most prescribed drugs in the world. They are used to relieve fever, pain, and inflammation in various conditions, such as rheumatoid arthritis (RA) and osteoarthritis (OA). The mechanism of reducing inflammation and pain with the help of NSAIDs is based on the reduction of the synthesis of prostaglandins (PGs). The enzyme that mediates the synthesis of these molecules is called cyclooxygenase, known as COX. It is present in the human body under two isoforms: one constitutive, COX-1, and one inducible, COX-2. This action is crucial in moderating the clinical effects of NSAIDs, given the importance of prostanoids such as PGE2, PGI2, and TXA2 in regulating key cellular functions locally.

Objective: The aim of this study is to evaluate and compare the efficacy of free and conjugated NSAIDs (diclofenac and ibuprofen) in a carrageenan-induced acute inflammation model in the laboratory rat. The study aims to determine whether conjugated diclofenac and ibuprofen offers additional therapeutic advantages and minimal side effects in the treatment of inflammation compared to standard drugs.

Materials and methods: The experiment was performed over a period of 24 hours. Treatment with standard Ibuprofen, standard Diclofenac, and the conjugated forms (10 mg/kg) were administered once, via oral gavage, 30 min after induction of acute inflammation by subplantar injection of 100 µl carrageenan into the left hindpaw of each subject. The morphological evaluation of the paw injected with the inflammatory agent was analyzed and measured using the plethysmometer every 30 minutes for 3 hours and subsequently at 24 hours. Statistical analysis was performed using GraphPad Prism.

Results: The reduction of plantar edema following diclofenac administration was visible after one hour of administration, faster than diclofenac-BSA. In the groups treated with Ibuprofen and Ibuprofen-BSA, the volume of edema is considerably reduced, highlighting the anti-inflammatory efficiency of these treatments. Treatment with Ibuprofen resulted in a reduction in reduced glutathione (GSH) levels, superoxide dismutase (SOD) activity, and total antioxidant capacity (TAC), indicating increased oxidative stress. In contrast, the Ibuprofen-BSA conjugate maintained GSH levels and SOD activity close to those of the control group and significantly improved the total antioxidant capacity compared to plain Ibuprofen, indicating a protective effect against inflammation-induced oxidative stress. The increase in GSH levels in the group treated with conjugated diclofenac suggests an improvement in intracellular antioxidant capacity. This may indicate that conjugated diclofenac helps maintain a better redox balance in cells, thereby protecting against oxidative stress caused by inflammation.

Conclusions: The conjugation of NSAIDs, ibuprofen and diclofenac, with bovine serum albumin showed a reduction of side effects, a superior ability to maintain cellular redox balance and reduction of oxidative stress at the cellular level, but also a slower release of the active substance to reduce inflammation, a fact which may constitute an improved safety profile.

Key words: nonsteroidal anti-inflammatory drugs, acute inflammation, paw edema

Acknowledgements: This research was funded by a grant from the Ministry of Research, Innovation and

Digitization, CNCS-UEFISCDI, project number PN-III-P1-1.1-PD-2021-0286, within PNCDI III.

Phytochemical compounds applied in bone regeneration

Alina Hanga-Farcas[1], Luminita Fritea[2], Gabriela Adriana Filip[3], Simona Clichici[3], Laura Gratiela Vicas[4], Vlad-Alexandru Toma[5], Remus Moldovan[6], Nicoleta Decea[6], Mariana Eugenia Muresan[2]

1) Doctoral School of Biomedical Science, University of Oradea, 410087 Oradea, Romania; 2) Department of Preclinical Discipline, Faculty of Medicine and Pharmacy, University of Oradea, Romania; 3) Department of Physiology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; 4) Department of Pharmacy, Faculty of Medicine and Pharmacy, University of Oradea, Romania; 5) Department of Molecular Biology and Biotechnology, Faculty of Biology and Geology, Babes Bolyai University, Cluj-Napoca, Romania; 6) Department of Physiology, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj Napoca, Romania 2 Department of Pathology, USAMV, Cluj Napoca, Romania

Bone defects are often considered an issue in orthopedic clinical practice and the materials used for their treatment present some disadvantages. Thus, recently various studies have been performed on evaluating the modulation of bone signaling pathways by some phytochemical compounds. The influence of *Juglans regia* L. extract compared to ellagic acid was assessed in rats by analyzing antioxidant, anti-inflammatory and bone regeneration biomarkers such as: malondialdehyde, superoxide dismutase, catalase, TNF-α, IL-6, RANKL and hydroxyproline. Scanning electron microscopy images of the skulls were also performed in order to highlight the bone neoformation.

Keywords: *Juglans regia* L. extract, ellagic acid, bone regeneration

The contractile reactivity of the isolated portal vein in different concentrations of Ca^{2+} ions in experimental hypertension

Ojog V, Lozovanu S, Ganenco A, Borș P

Department of Physiology and Biophysics, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republica of Moldova

Introduction: Portal hypertension syndrome is a major public health problem due to the increased frequency of liver cirrhosis.

Objectives: Current study investigation highlighted the contractile reactivity of the vascular smooth muscle of the portal vein at different concentrations of Ca^{2+} ions in portal hypertension.

Material and methods: We determined contractile activity of 20 longitudinal segments of the portal vein from Wistar rats. Portal hypertension was induced by applying partial ligature of the portal vein in the prehepatic region. In both groups (control (C) and experimental portal hypertension (PH)) contractility was determined under conditions of modification of Ca^{2+} ions.

Results: 1. At the concentration of 2.5 mM Ca^{2+}, the following parameters increased in the PH group compared C group: contraction force (30%), duration of twitch (about 2 times), duration of contraction (51%), duration of relaxation (3 times). Other parameters decreased: area of contraction (10%), intensity of structure functioning (ISF) (55%) and especially frequency (60%). 2. When concentration of Ca2+ was halved, the contraction force increases substantially (185%), the duration of twitch (44%), as well as the duration of relaxation (71%) and duration of contraction (19%). Contraction frequency decreased by 4 times and ISF by 30%. 3. When Ca2+ ions are increased threefold or four times, a decrease in contraction force (19% and 22%), frequency (59% and 56%), ISF (69% and 65%) and area of contraction (32% and 50%) compared to the control group at the same concentrations of Ca2+ ions. Duration of twitch (31% and 29%), duration of contraction (73% and 61%) and duration of relaxation (30% and 22%) increased in PH group compared C group. Within each group, we observed that with the decrease in Ca^{2+} concentration, there was a smaller decrease in the force of contraction in the group with portal hypertension (34%), compared to the control group (65%) compared to the initial concentration of Ca^{2+} ions

Conclusion: Portal vein coarctation causes an increase in spontaneous contraction force, probably due to cellular hypertrophy of the portal venous smooth muscle. The reactivity of the portal vein to changes in the concentration of Ca2+ ions is diminished, which may be the consequence of the recovery of the mechanisms for maintaining intracellular Ca^{2+} homeostasis.

Keywords: portal hypertension, vascular smooth muscle, $Ca2^{+}$ concentration

Artificial intelligence in biomedicine – how does it work?

Walther Bild, Razvan Nicolae Rusu, Ionut Raducu Popescu

„Gr. T. Popa" University of Medicine and Pharmacy Iasi

Artificial intelligence (AI) is rapidly transforming the landscape of biomedical research, offering unprecedented opportunities for accelerating scientific discovery and improving healthcare outcomes. However, many medical professionals, biologists and researchers throughout the field are not familiar with the possibilities of the machine learning algorithms, particularly deep learning models. AI is being applied across the biomedical spectrum, from drug discovery and genomics to medical imaging and personalized medicine. Most of the people involved in medicine and biology use the LLMs, but the possibilities of analysis for vast and complex biological datasets with greater speed and accuracy are yet to

be perceived. Key areas of impact include the identification of novel drug targets, prediction of protein structures, analysis of electronic health records, and early disease detection through advanced image processing. AI also shows promise in optimizing clinical trials and enhancing precision medicine approaches. However, the integration of AI in biomedical research also raises important ethical and practical challenges. These include concerns about data privacy, algorithmic bias, interpretability of AI models, and the need for robust validation of AI-derived findings. The present paper intends to fully use the AI assistance in order to offer readers some insight into how the LLM model operate, what truly AI implication means and what are the limits of such computerized aids.

Severe trauma machine learning prediction model

Grabovschi I[1], Baltaga R[2], Arnaut O[1]

1) Department of Human Physiology and Biophysics, State University of Medicine and Pharmacy "Nicolae Testemițanu", Chișinău, Republic of Moldova; 2) Department of Anaesthesiology and Reanimatology No. 1 "Valeriu Ghereg", State University of Medicine and

Introduction/Background: Severe trauma continues to be a medical crisis, and in certain instances, mortality rates still increase despite recent progresses in prevention and treatment. Early collection of physiological, anatomical, and comorbidity data can offer valuable clues about how the patient may recover, both during their stay in the hospital and in different periods after dischargement.

Objectives: The aim of this research was to develop a predictive survival model for severe trauma patients based on physiological, anatomical and comorbidities performed at ICU admission.

Materials and methods: Data from 2651 patients admitted in the ICU of the Emergency Medicine Institute with severe trauma for the period 2014-2024 was selected according to the inclusion criteria. Total number of included subjects was divided into train and test groups in order to consider verification and validation of the results from the test group. Treatment outcome (survival or death) was predicted using several predictive models obtained by different machine learning algorithms as logistic regression, random forest, XGB, lightGBM, SVM, StackingClassifier and GridSearchCV, SHAP analysis being performed to estimate the contribution of each considered variables.

Results: The algorithms were compared by accuracy, balanced accuracy, f1 score, recall, prediction precision. The best characteristics were observed for logistic regression algorithm (accuracy 0.979, balanced accuracy 0.978, f1 score 0.966, recall 0.975, and prediction precision 0.957, AUC=0.998, precision recall curve for logistic regression: f1=0.966 AUC=0.997). It allowed the identification of physiological, anatomical and comorbidities factors with predictive potential on the treatment outcome in patients with severe trauma.

Conclusion: The results obtained from statistical processing allow us to consider the logistic regression algorithm as appropriate. Its implementation in daily practice in other hospitals may be possible only after validation.

Keywords: machine learning, severe trauma, predictive model.

Improving prognostic precision in hepatic resection for hepatocellular carcinoma: the superior role of liver stiffness measurement with Fibroscan

Nenu I[1,2], Topor I[1], Chereș I[3], Topor M[3], Ștefănescu H[2], Groza A[3], Al Hajjar N[1,2], Filip GA[1], Spârchez Z[1,2], Procopeț B[1,2]

1) "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 2) "Prof. Dr. O. Fodor" Regional Institute of Gastroenterology, Cluj-Napoca, Romania; 3) Artificial Intelligence (Intelligent Systems Group), Department of Computer Science

Background: Liver stiffness measurement (LSM) using Fibroscan (FS) plays a critical role in clinical settings for selecting hepatocellular carcinoma (HCC) patients eligible for hepatic resection. Its importance lies in its superior ability to assess portal hypertension and predict clinical outcomes compared to traditional serum liver tests. This study aimed to evaluate the effectiveness of LSM in identifying clinically significant portal hypertension (CSPH) and predicting post-hepatectomy liver failure (PHLF). Additionally, a machine learning-based predictive model for PHLF was developed and validated.

Method: A total of 128 patients with compensated cirrhosis and HCC, who underwent hepatic resection at the Regional Institute of Gastroenterology and Hepatology Cluj-Napoca between 2016 and 2023, were included in the study. CSPH was defined using criteria such as hepatic venous pressure gradient (HVPG) ≥ 10 mmHg, or the presence of esophageal varices, splenomegaly, and thrombocytopenia (< 100,000/mm^3). LSM was primarily evaluated against other non-invasive tests for its ability to predict CSPH and PHLF, utilizing area under the receiver operating characteristic (AUROC) curves and logistic regression analysis.

Results: LSM significantly outperformed other non-invasive tests in predicting CSPH (AUROC=0.913, 95% CI: 0.84-0.98; p<0.05), demonstrating its reliability. Notable predictive trends for PHLF were also observed with LSM. Furthermore, a machine learning model based on LSM data improved predictive accuracy for PHLF (logistic regression accuracy of 0.937).

Conclusion: LSM via Fibroscan is a highly effective tool for identifying CSPH and predicting PHLF in HCC patients.

Characterization of a newly discovered Glucose Transport regulator expressed in projection sensory neurons

Tudor C. Badea

Diabetic and Peripheric Neuropathies (DR and DPN) are frequent in patients with Type II Diabetes, begin early, together with Insulin Resistance (IR), and are caused by metabolic disbalances due to excess Glucose. DR and/or DPN eventually progress to blindness, severe neuropathy and impairment of autonomic functions. Import of Glucose happens through Glucose Transporters (GluTs) which are constitutively present on plasma membrane or translocate to it upon Insulin stimulation (or neuronal activity). We recently found that the dispanin Tusc5 is expressed in Retinal Ganglion Cells (RGCs) and Dorsal Root Ganglia (DRGs), major targets of DR and DPN. In adipocytes, Tusc5 mediates Insulin-dependent GluT4 translocation to the surface and increase of Glucose import. Our preliminary experiments using mouse genetics and biochemistry suggest that Tusc5 plays a similar role in RGCs. We propose that the Tusc5 pathway may be used to target drugs with neuroprotective effects in the context of Diabetes.

Initial Results of the GlioStat Study: A Potential Cure for Glioblastoma?

Florian Ioan-Alexandru, Șușman Valeriu-Sergiu, Ede Bodoki, Soriță̆u Olga, Peștean Petru-Cosmin, Iacob Bogdan-Cezar, Bărăian Alexandra-Iulia, Buruiană Andrei, Florian Ioan-Ștefan

UMF "Iuliu Hatieganu", Cluj-Napoca; USAMV Cluj-Napoca; IOCN

Background: GlioStat (pattent pending) is an innovative solution that aims to improve glioblastoma (GBM) chemotherapy. It involves the creation of a specialized drug reservoir that is tailored for post-surgical recovery, addressing the limitations of current treatments. Objectives: Our research aimed to ensure the sustained release of the antitumor drug ruxolitinib (RUX), which is designed to target residual infiltrative cancer cells, while minimizing the risk of side effects. We have successfully developed and characterized four distinct molecularly imprinted polymers (MIPs), with one of them advancing to in vivo experimentation, in order to achieve this goal.

Material and Methods: A single MIP was chosen for further in vivo studies based on the results of the Alamar Blue viability assay conducted on C6 GBM cell cultures. This assay considered both the effectiveness of the MIP and the potential harm caused by any remaining monomers. During a 96-hour period, MIP 2 exhibited the most favorable risk-benefit profile, demonstrating superior efficacy against GBM C6 cells. On the other hand, the non-imprinted counterpart (NIP 2) showed very low levels of toxicity. The protocol required the administration of anesthesia to the male Wistar rats, followed by immobilization on a corkboard, without the need for a stereotactic headholder. Following the shaving of the head and local disinfection using an iodine solution, a linear sagittal incision was performed to expose the parietal bones. A burr hole measuring 3x3 mm was created using a pneumatic drill on the right parietal bone, exposing the dura mater. Afterward, we administered 20,000 C6 GBM cells in a 5-microliter solution into the cerebral parenchyma at a depth of 3 mm. Control was conducted both clinically and through imaging. A second therapeutic intervention was conducted for the animals that developed tumors. The rats were prepared in a similar manner as previously, undergoing anesthesia and disinfection. The burr hole was opened, and the tumor was partially removed using a technique known as „microscooping." Then, a small volume of MIP2 solution (4 mg/mL) was injected into the surrounding tissue of the tumor. Next, a 5 µL solution of thrombin (100 IU/mL) was added to create the fibrin network.

Results: The in vitro evaluation showed that GBM cell lines treated with MIP 2 had apoptosis and necrosis percentages similar to those treated with temozolomide. During the in vivo evaluation, animals treated with MIP2 showed a significant increase in survival time compared to the untreated controls and animals treated with free RUX. The survival time extended from 20 to 50 days.

Conclusions: Our research has resulted in a drug delivery system for GBM that has the potential to greatly improve postoperative survival rates. Further in vivo testing is necessary to validate our findings.

Keywords: Glioblastoma (GBM); Ruxolitinib (RUX); Molecularly Imprinted Polymers (MIP).

Epigenetic modulation by oleocanthal: implications for stress response and neurodegenerative diseases

Góngora Hernández L. A.[1], Toma V. A.[1,2,3*]

1) Babeș-Bolyai University, Faculty of Biology and Geology, Department of Molecular Biology and Biotechnology, Cluj-Napoca, Romania; 2) Institute of Biological Research, Cluj-Napoca, branch of INCDSB Bucharest, Department of Biochemistry and Experimental Biology, Cluj-Napoca, Romania; 3) Academy of Romanian Scientists, Ilfov 3, Bucharest, Romania

Introduction: Chronic stress is a well-established contributor to various chronic diseases, particularly neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. Recent studies suggest that oleocanthal, a phenolic compound from extra virgin olive oil (EVOO), exhibits significant epigenetic modulatory effects. These effects are crucial for mitigating the pathological impacts of stress and neuroinflammation. Oleocanthal's ability to influence gene expression through DNA methylation, histone modification, and non-coding RNAs (ncRNAs) positions it as a promising candidate for neuroprotection.

Objectives: This study aims to comprehensively analyze the role of oleocanthal in modulating epigenetic processes associated with stress adaptation and neurodegenerative diseases. Specifically, it investigates oleocanthal's effects on neuroinflammation, oxidative stress, and synaptic plasticity, key factors in the pathogenesis of neurodegeneration.

Materials and Methods: A systematic review and meta-analysis were conducted using peer-reviewed research articles. The studies focused on oleocanthal's impact on epigenetic mechanisms, including DNA methylation patterns, histone modifications (H3K9me3, H3K27me3, H3K18ac), and the regulation of miRNAs involved in stress and neurodegenerative pathways. The integration of bioinformatics tools allowed for a detailed pathway analysis, particularly focusing on the glucocorticoid receptor (GR) signaling, NF-κB, Nrf2, and MAPK pathways.

Results: Oleocanthal significantly modulates epigenetic marks, including the methylation of genes like FKBP5 and NR3C1, which play crucial roles in glucocorticoid receptor sensitivity and stress response. Furthermore, oleocanthal decreases the expression of pro-inflammatory cytokines and oxidative stress markers through the activation of Nrf2 and inhibition of NF-κB and MAPK pathways. These epigenetic alterations contribute to the reduction of neuroinflammation and the promotion of neurogenesis, enhancing cognitive resilience against stress-induced damage and reducing the risk of neurodegenerative disease onset.

Conclusion: Oleocanthal's role as an epigenetic modulator underscores its potential as a nutraceutical intervention for neurodegenerative diseases, particularly those exacerbated by chronic stress. The findings suggest that oleocanthal could be integrated into therapeutic strategies aimed at modulating stress-related epigenetic changes, offering a novel approach to neuroprotection. Future studies should explore the clinical applicability of oleocanthal in human populations, focusing on its long-term impact on neurodegeneration and cognitive function.

Keywords: oleocanthal, neuroinflammation, DNA methylation

Acknowledgments: This research received support from a GTC grant awarded by Babes-Bolyai University (Grant No. 32939/22

Cornus mas as a potential modulator in a sleep deprived rat model

Vlad Sever Neculicioiu[1], Alexandra Sevastre-Berghian[2], Horațiu Alexandru Colosi[3], Dan Alexandru Toc[1], Carmen Costache[1], Ioana Colosi[1], Ana-Maria Vlase[4] and Simona Clichici[2]

1) Department of Microbiology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 2) Department of Physiology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 3) Division of Medical Informatics and Biostatistics, Department of Medical Education, „Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 4) Faculty of Pharmacy, "Iuliu Haţieganu" University of Medicine and Pharmacy, V. Babeş Street, 400000 Cluj Napoca, Romania

Background. Sleep is vital for overall health, yet sleep deprivation is increasingly common in today's 24/7 society, affecting at least one-third of adults. Research links insufficient sleep to numerous adverse health outcomes, including cardiovascular disease, obesity, metabolic disorders, psychiatric conditions, cancer, and higher mortality rates. Sleep plays a complex, bidirectional role with oxidative stress and inflammation - while some oxidative eustress promotes sleep, deprivation triggers oxidative damage, highlighting sleep's antioxidant role. Interest in herbal medicines has grown recently due to their affordability and potential health benefits.

Objectives. The main objective of this study was to evaluate the modulatory potential of a cornelian cherry (*Cornus mas)* fruit extract on behavioural, oxidative and inflammatory alterations induced in a sleep deprived rodent model.

Materials and methods. A total of 28 adult Wistar male rats were randomised in four groups (n=7): Control, Cornus mas (CM), Sleep deprivation (SD), Sleep deprivation + Cornus mas (SD+CM). CM and SD+CM groups received 1.2mL/kg bw/day of *Cornus mas* fruit extract through oral gavage for seven consecutive days. SD and SD+CM groups were sleep deprived through the modified multiple small platforms (MMSP) protocol of REM sleep deprivation for seven days. The *Cornus mas* extract was characterised through total polyphenol content (Folin-Ciocalteu method - 25.5 g GAE/ 1000 mL) and in vitro antioxidant effect (DDPH assay - 4.84 mg TE/ mL). Behavioral alterations were evaluated through the Open Field Test (OFT) and Elevated Plus Maze (EPM). Oxidative stress parameters (GSH, GSSG, GSH/GSSG ratio and MDA) were evaluated in the prefrontal cortex, hippocampus, serum and pro-inflammatory cytokines (IL-1β, TNF-α) were evaluated through ELISA in the prefrontal cortex and hippocampus.

Results. Sleep deprivation induced behavioural alterations in the OFT and EPM and these changes were partially modulated by the fruit extract. SD significantly elevated systemic oxidative stress (decreased GSH) and *Cornus mas* presented a trend towards normalising these values. However, no significant changes were found in the brain regarding oxidative stress parameters or cytokine levels.

Conclusion. Although *Cornus mas* extract modulated certain behavioural changes induced by sleep deprivation, the underlying mechanisms require further investigation and may not be directly related to its antioxidant or anti-inflammatory properties.

Testing Muscle Fatigue Threshold on Cycling: The Use of Surface Electromyography as a Complementary Method to Ventilatory Thresholds

Martin ȘA[1], Martin-Hadmaș RM[2], Gavra GM[3], Scridon A[4]

1) Department of Physiology and Advanced Medical and Pharmaceutical Research Center (CCAMF) of "George Emil Palade" University of Medicine, Pharmacy, Science and Technology from Târgu Mureș, Romania; 2)Department of Community Nutrition and Food Hygiene, Faculty of Medicine, "George Emil Palade" UMFST

Introduction. During physical exercise, muscle fiber electrical activity drops with sustained contractions, indicating changes in motor unit activation. The process is influenced by energy availability, and therefore reduced ATP production will impair muscle response. Although heart rate often guides training intensity in young athletes, significant differences have been observed in performance by following heart rate, muscle activation, or power output data.

Objective. The study aimed to assess the use of surface electromyography (EMG) as a complementary method to measure muscle fatigue during cycling.

Material and Method. We conducted a 4-month prospective observational study on a sample of 25 athletes, both male and female. All participants underwent an incremental physical exercise test to measure their maximum aerobic capacity (VO2max), and ventilatory thresholds: aerobic threshold (AT) and respiratory compensation point (RCP). Muscle activation rate, amplitude, EMG maximum reached point (EMGMRP), and EMG fatigue threshold (EMGFT) were measured in the vastus lateralis using surface EMG.

Results. Both ventilatory thresholds were correlated with power output (both $p< 0.05$). Power output increased with oxygen uptake ($r = 0.89$, $p = 0.0001$) and oxygen pulse ($r = 0.79$, $p = 0.0001$). Oxygen uptake increase was consistently followed by a significant rise in power output at both the EMGFT ($r = 0.73$, $p = 0.0001$) and EMGMRP ($r = 0.84$, $p = 0.0001$). Both VT1 and VT2 correlated with EMGFT and EMGMRP (both $p< 0.05$), while the aerobic-anaerobic cardiopulmonary exercise zone strongly correlated with EMGFT ($r = 0.64$, $p = 0.0001$).

Conclusions. Surface EMG is a valuable complementary method that can be used to determine specific fatigue thresholds. Surface EMG accurately captures changes in muscle.

Effects of C3a Antagonist on Behavior in a Cuprizone-Induced Demyelination Model

Alina Cătălina Buican-Chirea[1,2], Kevyn Ianis Boboc[1], Mădălina Iuliana Mușat[1,2], Bogdan Cătălin[1,3], Tudor Adrian Bălșeanu[1,3]

1) Experimental Research Centre for Normal and Pathological Aging, University of Medicine and Pharmacy of Craiova; 2) U.M.F. Doctoral School Craiova, University of Medicine and Pharmacy of Craiova, Craiova, Romania; 3) Department of Physiology, University of Medicine and Pharmacy of Craiova, Craiova, Romania

Introduction: Multiple sclerosis (MS) is a multifaceted disease, with several aspects yet to be fully understood. A significant component of its pathology involves heightened inflammation, which includes complement activation, leading to increased cell death and tissue destruction. Cuprizone, a selective and sensitive copper-chelating agent, is employed to induce toxic demyelination, mimicking the demyelination observed in MS.

Methods: Over a three-week period, CX3CR1(+/+, +/-) mice were allocated into two groups: those fed with cuprizone and those receiving both cuprizone and an intraperitoneal administration of a C3a antagonist. Behavioural assessments, including open field, novel object recognition, and the Three-Chamber Sociability and Social Novelty Test, were conducted prior to and following the cuprizone and C3a antagonist treatments.

Results: The administration of the C3a antagonist may potentially reduce inflammation, resulting in milder behavioural changes compared to the group solely fed with cuprizone.

Conclusion: Further research is warranted to investigate the effects of cuprizone and C3a antagonist at the cellular level, ensuring benefits at both the cytological and behavioural levels.

Keywords: cuprizone, CX3CR1, mice model.

Local topical treatment of peropheral nerve lesions: utopia or reality?

Nadina-Liana Pop, Alexandrina Nan, Daniela Gheza

UMF Iuliu Hatieganu Cluj-Napoca, Institutul Național de Cercetare-Dezvoltare pentru Tehnologii Izotopice și Moleculare Cluj-Napoca

Peripheral nerve injuries can significantly affect, in the medium or long term, the quality of life of patients, the development of a conservative treatment that addresses both the symptomatology and the regeneration of the damaged peripheral nerve representing a necessity. The research conducted evaluated the effectiveness of topical daily topical administration of a simple capsaicin cream and a cream with capsaicin-functionalized magnetic nanoparticles for 30 days in functional recovery following experimentally induced right sciatic nerve injury in White Wistar rats, healthy, male. To quantify the level of nerve recovery and regeneration, the following parameters were dynamically analyzed: sciatic functional index, animal behavior associated with pain and total body weight. The obtained evaluations were analyzed statistically, by comparison with a control group, which suffered the same sciatic nerve injury, but which did not receive any kind of treatment. Statistical analysis confirmed optimal functional recovery for both treatment methods, showing that topical application of capsaicin cream and capsaicin-functionalized magnetic nanoparticle cream, administered daily for 30 days at the lesion level, significantly reduced the level of pain in the animals, they improved the values of the sciatic functional index, the animals gaining weight by the end of the experiment, suggesting a reduction in general stress. Thus, the designed capsaicin-functionalized magnetic nanoparticle cream could represent a new research direction in the field of peripheral nerve injury treatment and recovery.

Theragnostic - Somatostatin receptors and their application

Sofia-Maria Timpuriu[1,2], Catalina Ciornei[1], Cristian Scheau[1], Ioana-Anca Badaru[1], Antoaneta Punga[1], Radu Vrabie[1], Maria Marinescu[1], Silviu Vlasceanu[1,3], Ioana-Raluca Papacocea[1]

1) UMF "Carol Davila", Physiology Department III, Bucharest, Romania; 2) National Institute of Geriatrics and Gerontology "Ana Aslan", Bucharest, Romania; 3) National Institute of Pneumology "Marius Nasta", Bucharest, Romania

Introduction: Somatostatin receptors (SSTR) mediate the effects of two structurally similar families of peptides, somatostatins (SRIF-14, SRIF-28) and cortistatins (CST-14, CST-17, CST-29). Five receptors have been identified that all have nanomolar affinity for somatostatins and cortistatins: SSTR2, SSTR2, SSTR3, SSTR4, SSTR5. These receptors are members of the superfamily, 7-transmembrane receptors (GPCR) linked to G proteins and are physiologically expressed in various tissues (in the central and peripheral nervous system, in the endocrine pancreas and gut, thyroid, prostate, placenta, adrenals, kidneys and skin) as well as on multiple tumor types: neuroendocrine tumor (NET), small cell lung cancer, breast tumor and malignant lymphoma. SSTR2 is predominantly overexpressed in tumors.

Along the time, many potential methods of diagnosis and treatments (Theragnostics) which target SSTR2 were developed for these tumors. From Octreotite/Octreotate, the first class of SSTR analogues (administered per os), we evolved to i.v administred radiolabeled somatostatin receptors analogues such as ([^{177}Lu]Lu-DOTATOC/TATE) or the latest compound ([^{177}Lu]Lu DOTA-JR11, a radiolabeled SSTR antagonist, with a better affinity for SSTR.

Aim: To describe the clinical applicability of somatostatin receptors in two patients with neuroendocrine tumors.

Material and methods: We present cases of 2 patients diagnosed with two aggressive NET (metastatic parganglioma and pheochromocytoma respectively) with high expression of somatostatin receptors (objectified on histological report and on [68Ga]Ga-DOTATOC scan), non-responsive to conventional treatment, but responsive to peptide receptor radionuclide therapy (PRRT), targeting SSTR.

Both patients had a good prognosis, with a progression free survival time of 10 respectively 14 months.

Conclusion: Somatostatin receptors have a large distribution and express on different types of tissues. Therefore, they have a high and efficient theragnostic applicability (diagnosis and treatment) in patients with tumors overexpressing SSTR.

Preoperative inflammatory biomarkers as predictors of postoperative atrial and ventricular ectopy and complications following coronary artery bypass grafting

Cozac D.A[1,2], Palfi N.R[1], Somkereki C.[1], Scridon A.[1,2]

1) Emergency Institute for Cardiovascular Diseases and Transplantation of Targu Mures, Romania; 2) Physiology Department, University of Medicine, Pharmacy, Science and Technology of Targu Mures, Romania

Background: Cardiac arrhythmias are among the most frequent postoperative complications following coronary artery bypass grafting (CABG) surgery. The occurrence of premature atrial contractions (PACs) and premature ventricular contractions (PVCs) after CABG has been linked with worse short- and long-term outcomes. However, at this point, clinicians lack reliable biomarkers for identifying patients who will develop postoperative arrhythmias. Given the role of inflammation in cardiac electrical remodeling and arrhythmia occurrence, we aimed to determine whether the extent of preoperative inflammation influences the postoperative atrial and ventricular ectopic status of patients undergoing elective CABG.

Materials and Methods: A prospective cohort study was conducted in 102 patients scheduled for an elective CABG procedure. Blood samples were collected one day before surgery and the levels of several inflammatory and endothelial dysfunction biomarkers (i.e., high-sensitivity C-reactive protein [hs-CRP], von Willebrand factor [vWF], transforming growth factor-beta [TGF-β], interleukins (IL)-2, 6, and 8) were determined using Multiplex. Continuous 24-hour ECG Holter monitoring was performed preoperatively and on days 2, 3, and 4 post-CABG to assess PAC and PVC burden. The impact of preoperative biomarkers on postoperative ectopic activity and the influence of arrhythmic burden on post-CABG outcomes were evaluated.

Results: Preoperative plasma levels of vWF, TGF-β, and IL-8 positively correlated with postoperative PAC burden (all $p< 0.05$). Conversely, preprocedural hs-CRP, TGF-β, IL-6, and IL-8 plasma levels positively correlated with postoperative PVC burden (all $p< 0.05$). No significant correlation was found between preoperative inflammatory biomarkers levels and any of the studied postoperative outcomes (i.e., acute kidney injury, acute liver dysfunction), nor between preoperative inflammatory biomarkers levels and the duration of inotropic support or hospitalization (all $p >0.05$).

Conclusion: This study indicates that specific preoperative inflammatory biomarkers are strongly linked to an increased risk of postoperative atrial and ventricular ectopy, pointing towards a potential utility in identifying patients at higher risk for these arrhythmias following CABG. However, none of the tested biomarkers predicted other post-CABG complications, suggesting that the preexisting inflammatory status is likely to play a minor role in post-CABG evolution, if any. Keywords: coronary artery bypass surgery; endothelial dysfunction; inflammation; postoperative cardiac arrhythmias.

Septal ablation with alcohol, a minimally invasive gradient reduction intervention in hypertrophic obstructive cardiomyopathy

Cristian Militaru

UMF Craiova, SCJU Craiova

The presentation initially aims to explain the pathophysiological phenomena that produce dynamic systolic obstruction in the ejection tract of the left ventricle in patients with obstructive hypertrophic cardiomyopathy. Later, septal ablation with alcohol will be presented, a modern, minimally invasive technique, which involves the injection of pure alcohol at the level of a septal artery, thus producing a controlled infarction and implicitly reducing the thickness of the interventricular septum. Finally, a case from SCJU Craiova of septal ablation with alcohol will be presented. The ultrasound, coronary images and pressure curves from the ventricle and the aorta during the procedure will be presented. The presenter is an interventional cardiologist and performed such procedures for the first time locally.

Modulating the allergic immune response towards tolerance by allergen immunotherapy: a 21st century challenge

Panaitescu C.[1,2], Tatu C.[1,2], Haidar L.[1,2], Buzan M.R.[2]

1) Department of Functional Sciences, Physiology Discipline, Faculty of Medicine, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania; 2) Center of Immuno-Physiology and Biotechnologies, Department of Functional Sciences, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

Allergies affect millions of individuals worldwide, leading to a significant burden on healthcare systems and quality of life. Immunotherapy, particularly allergen immunotherapy (AIT), has emerged as a cornerstone in the long-term management of allergic diseases. Unlike conventional treatments that merely alleviate symptoms, AIT aims to modify the underlying immune response, offering a disease-modifying approach to allergies.

AIT is the only therapy able to modulate the immune tolerance through controlled exposure to allergens, thereby leading to a decreased hypersensitive response. By inducing regulatory T cells (Tregs) and shifting the immune balance from a Th2 to a more balanced, regulated response, AIT has been shown to reduce symptom severity, medication use and the risk of developing new allergies or allergic asthma, while promoting long-lasting immune tolerance.

The landscape of AIT is ever evolving, as new delivery methods, shorter treatment protocols, and emerging therapies such as peptides are being studied and translated into the clinic. Recent advances in AIT have led to the development of novel therapies that aim to enhance efficacy and reduce adverse effects. Among these are synthetic peptides, which represent an exciting frontier in AIT. Peptide-based therapies are designed to target specific epitopes on allergens, avoiding full allergenic proteins and reducing the risk of anaphylaxis. These peptides help modulate the immune system more precisely and safely, leading to a more controlled and focused immune response. Early clinical trials are showing encouraging outcomes, positioning peptides as a critical advancement in allergy treatment.

By understanding these advancements, clinicians will be better equipped to manage allergic diseases and overcome the challenges posed by 21st century allergy trends.

Keywords: allergen immunotherapy (AIT), immune tolerance, peptide-based therapies

Lessons learned from modulating the immune response in SARS-CoV-2 infection

Patrascu R.[8] , Laitin S.M.D.[1,2], Baditoiu L.M.[1,3], Laza R.[2,4], Besliu R.S.[5], Gug M.[6], Dumitru C.S.[7]

1) Epidemiology University Clinic, Department XIII, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania; 2) Clinical Hospital of Infectious Diseases and Pneumology "Dr. Victor Babes" Timisoara, Romania; 3) Multidisciplinary Research Center on Antimicrobial Resistance, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania; 4) Infectious Diseases University Clinic, Department XIII, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania; 5) Epidemiology Clinic, "Pius Brinzeu" Emergency Clinical County Hospital Timisoara, Romania; 6) Doctoral School, Department of Microscopic Morphology, Discipline of Genetics, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania; 7) Department of Microscopic Morphology/Histology, Angiogenesis Research Center, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania; 8) Department of Functional Sciences, Physiology Discipline, Faculty of Medicine, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Eftimie Murgu Square No. 2, 300041 Timișoara, Romania

Introduction: The COVID-19 pandemic has had a significant impact on global health, with serious outcomes, such as lung damage, being major determinants of patient morbidity and mortality. Immunization has been essential in attenuating these outcomes. This study aimed to evaluate the impact of COVID-19 vaccination on disease severity, particularly focusing on pulmonary involvement, among hospitalized patients, thus developing conclusions regarding a model of no-vaccination vs. post-vaccination immune response.

Materials and Methods: A retrospective cohort study was conducted at "Victor Babes Hospital", Timisoara, involving 3,005 patients diagnosed with COVID-19 between December 2020 and March 2022. Patients were stratified into vaccinated and unvaccinated groups.

Results: The study found that vaccinated patients had significantly lower rates of severe pulmonary involvement compared to unvaccinated patients. Specifically, only 151 vaccinated patients experienced severe lung damage, compared to 849 in the unvaccinated group ($p < 0.0001$). Vaccinated individuals also had shorter hospital stays (9±5.2 days vs.

13±9.3 days, p = 0.0020) and lower complication rates (35% vs. 53%, p < 0.0001). Additionally, chronic pulmonary diseases and stroke were less prevalent among vaccinated patients, highlighting the protective effect of vaccination.

Conclusions: COVID-19 vaccination significantly reduces the severity of disease, particularly in preventing severe pulmonary damage, which is a major determinant of patient outcomes. These findings underscore the importance of ongoing vaccination efforts and the need for booster doses to maintain immunity, especially as new variants emerge. The study supports the continued prioritization of vaccination in public health strategies to mitigate the long-term impact of COVID-19. Furthermore, these findings show an overall model of the boosted and faster immune response in vaccinated patients, with shorter hospital stays and fewer complications.

Keywords: COVID-19, vaccination, immune response, pulmonary damage

In vitro modulation of bronchial responsiveness

Zimbru R.I.[1,2], GeorgescuM.[1,2], Zimbru E.L.[1,2], Haidar L.[1,2], Tănasie G.[1,2]

1) Department of Functional Sciences, Physiology Discipline, Faculty of Medicine, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania; 2) Center of Immuno-Physiology and Biotechnologies, Department of Functional Sciences, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

Introduction: Allergic asthma is characterized by airway hyperresponsiveness and chronic inflammation, often triggered by environmental allergens such as house dust mites (HDMs) and ragweed (RW) pollen. The rising incidence of co-sensitization to these allergens, combined with obesity-related factors such as a high-fructose diet (HFrD), complicates asthma pathology. This study explores the interaction between co-sensitization and HFrD on airway reactivity and systemic inflammation in rats.

Objectives: The primary aim was to investigate the effects of co-sensitization to HDMs and RW pollen in rats, especially when combined with a high-fructose diet. The study focused on airway hyperresponsiveness and serum biomarkers to assess the severity of allergic asthma under these conditions.

Materials and Methods: Sprague Dawley rats were sensitized to HDMs, RW pollen, or both, and were divided into groups with and without a high-fructose diet. Airway reactivity was measured using an isolated organ bath system with methacholine, while serum biomarkers such as C-reactive protein (CRP), total IgE, and lipid profiles were analyzed. Histopathological examination was conducted to assess airway inflammation and structural changes.

Results: Co-sensitization to HDMs and RW pollen led to significant airway hyperresponsiveness, especially in rats fed a high-fructose diet. The combination of allergens and diet resulted in increased CRP, IgE levels, and severe bronchoconstriction, with notable smooth muscle hypertrophy and bronchial wall thickening. Rats on the high-fructose diet exhibited worsened dyslipidemia and obesity, which amplified the inflammation and severity of asthma symptoms.

Conclusion: Co-sensitization to HDMs and RW pollen exacerbates allergic asthma, and when combined with a high-fructose diet, it significantly worsens airway reactivity and systemic inflammation. This interaction suggests that obesity and dietary factors play a critical role in the progression of allergic asthma, highlighting the need for further research into diet-related interventions for managing asthma.

Keywords: asthma, obesity, airway reactivity

In vitro functional studies regarding cryopreserved mesenchymal stem cells healing properties in various culture conditions

Tanasie Gabriela[1,2], Cristea Mirabela[2], Tatu Carmen[1,2], Nistor Daciana[1,2], Bojin Florina[1,2], Anghel Simona[2], Teusan-Botea Matei[1], Zimbru Razvan[1], Carmen Panaitescu[1,2], Virgil Paunescu[1,2]

1) Center of Immuno-Physiology and Biotechnologies, Department of Functional Sciences, University of Medicine and Pharmacy Victor Babes Timisoara; 2) OncoGen Center, Clinical County Emergency Hospital Pius Brinzeu Timisoara

Introduction: Tissue repair is a complex process involving inflammation, new matrix synthesis and remodeling and is directed by various signaling molecules, growth factors and cell types. The understanding of repair mechanisms has led to the development of new therapies for tissue engineering and regenerative medicine. Research is needed in this area to fully exploit the clinical potential of the cryopreserved cells.

Objectives: The study aims to compare the clonogenicity, proliferation potential and the adhesion on different substrates of the mesenchymal stem cells (MSCs) cryopreserved at early passages (P3), respectively more advanced passages (P15). Also was analysed how some biochemical factors influence the tissue repair process.

Materials and Methods: Hoffa-type MSCs previously isolated from 4 patients undergoing arthroscopic surgery, were expanded several passages and cryopreserved in the biobank of the OncoGen Centre. The clonogenic potential was measured by colony-forming unit-fibroblasts (CFU-F) number. The cells proliferation was evaluated in an Xcelligence system. The ability of the MSCs to repair a mechanically produced lesion (the scratch-assay) was assessed using the ImageJ software. For the cells viability was used acridine orange/ethidium bromide staining. The functionality of MSCs was studied after addition of chemical and cell-derived factors in culture media: fetal calf serum (FCS), FGF, ascorbic acid, TGF beta 3, supernatant derived from a bronchial epithelial cells (BEC) line, a primary culture of tumour-associated fibroblast (TAF) and the tumoral CaCo2 cell line. The MSCs adhesion

to different substrates (fibronectin, collagen, TNF alpha) was tested using a flow chamber device where progressive tangential stress was applied.

Results: CFU-F number for MSCs at P3 was significantly higher compared with P15. The absence of FCS showed a decrease in growth rate regardless the passage. No significant changes in growth rate noticed after FGF addition. The TGF beta 3 and ascorbic acid did not have positive effects on wound healing; moreover, TGF beta 3 is able to induce apoptosis. The factors derived from other cells type culture increased the scratch-assay results in this order: TAF>CaCo2>BEC. The MSCs adhesion to collagen and fibronectin was reduced for P15, especially at high tangential stress values; adherence to TNF alpha was relatively similar for both passages.

Conclusion: The potential of MSCs use in tissue repair seems to decrease in parallel with the number of passages. Progressively, the cells lose their clonogenic capacity, proliferative potential and the ability to adhere to the extracellular matrix substrates, but they keep for a longer time adherence to inflammatory substrates. The presence of FCS in the culture medium favours cell proliferation and repair of mechanical injury by MSCs. Signals derived from other cell types improve the invasive properties of MSCs, especially those derived from tumour cells.

Global miRnome analysis reveals specific profiles associated with the progression of endometriosis towards endometriosis-related ovarian cancer

Coada CA[1], Ravegnini G[2], Mantovani G[3], de Leo A[4,5], de Biase D[2,4], Costantino A[4], Gorini F[2], Dondi G[3], Di Costanzo S[3], Giorgi FM[2], Tallini G[4,5], Angelini S[2], Astolfi A[5], Strigari L[6], De Iaco P[3,5], Perrone AM[3,5]

1) University of Medicine and Pharmacy „Iuliu Haţieganu", Cluj-Napoca, Romania; 2) Department of Pharmacy and Biotechnology (FABIT), University of Bologna, Bologna, Italy; 3) Division of Oncologic Gynecology, IRCCS Azienda Ospedaliero-Universitaria Bologna, Bologna, Italy; 4) Solid Tumor Molecular Pathology Laboratory, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; 5) Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy; 6) Department of Medical Physics, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Introduction: Endometriosis (EMS) is a chronic gynecological condition affecting 6-10% of reproductive-age women. Albeit benign, it presents cancer-like features and may progress towards epithelial ovarian cancer (EOC), known as endometriosis-related ovarian cancer (EROC), sometimes with the presence of transitional lesions (TL) such as atypical EMS and/or borderline lesions. MiRNAs are small noncoding RNAs which regulate the expression of multiple genes, playing a role in various biological processes including tumorigenesis.

Objectives: We aimed to identify miRNAs that may drive or modulate the malignant transformation of ovarian EMS into TL and ultimately EROC.

Materials and methods: MiRNA profiling was evaluated in 81 samples (EMS, TL and EROC) from 44 patients through the Illumina NextSeq 500 high-throughput platform. Bioinformatic pipelines were employed for the alignment, clustering and differential expression analyses (DEA). The p-values were adjusted for multiple comparisons using the Benjamini-Hochberg procedure. The threshold was set to 0.05.

Results: Principal component analysis and unsupervised clustering revealed two distinct clusters formed by ovarian EMS and EROC samples. TL also formed a cluster between EMS and EROC samples. DEA of TL vs ovarian EMS revealed 30 significantly upregulated miRNAs, while comparison of EROC vs TL samples yielded 118 significantly upregulated miRNAs and 72 significantly downregulated miRNAs (BH adjusted p-value<0.05). Finally, DEA of EROC vs ovarian EMS lesions yielded the greatest differences with 199 upregulated and 120 downregulated miRNAs. Evaluation of miRNAs commonly deregulated between the three groups showed a total of 14 shared upregulated miRNAs with a progressing increase in expression levels, from ovarian EMS to TL and ultimately to EROC. Moreover, a panel of miRNAs were able to differentiate ovarian EMS from EROC samples with excellent values of specificity, sensitivity, and accuracy.

Conclusion: The transition from ovarian EMS to TL and EROC is marked by the deregulation of specific miRNAs, some of which can be used to stratify benign and malignant tissues with excellent accuracies.

Keywords: endometriosis-related ovarian cancer; microRNA; diagnosis

Aging-associated atrial and circulating microRNA changes

Balan AI[1,2], Halaţiu VB[1], Bobârnac RL[1], Cozac DA[1], Bănescu C[2], Scridon A[1,2]

1) Department of Physiology Faculty of Medicine, University of Medicine, Pharmacy, Science and Technology "George Emil Palade" of Târgu Mureş, Romania: 2) Center for Advanced Medical and Pharmaceutical Research, Târgu Mureş, Romania

Introduction: Recent research has highlighted the importance of microRNAs (miRNAs) in cardiovascular diseases (CVD). However, miRNA dysregulation with advancing age and its role in the development of aging-related CVD is not elucidated. This study aimed to explore the expression profiles of several miRNAs in the heart and blood of rats across different age groups, to provide insights into their potential roles in cardiac aging.

Materials and method: Thirty-nine Wistar Kyoto (WKY) rats were randomized into three groups: young (14 weeks of age; n = 16), adult (28 weeks of age; n = 12), and aging (48 weeks of age; n = 11) WKYs. Blood and atrial tissue samples

were collected from each animal. Circulating expression of 11 CVR related target (miR-100-5p, miR-106b, miR-150, miR-203, miR-21, miR-26b, miR-29a, miR-30e, miR-328, miR-9-5p, and miR-99b-5p) and one control (U6 snRNA) miRNAs was evaluated and compared between the different age groups.

Results: Atrial level of miR-203 decreased progressively ($p = 0.03$), while that of miR-30e increased progressively ($p = 0.01$) with advancing age. Circulating levels of miR-106b were significantly higher in the young compared to aging ($p = 0.02$), but not with adult ($p > 0.05$) rats. Atrial and circulating levels of the other miRNAs remained unchanged with advancing age (all $p > 0.05$).

Conclusions: The progressive decrease of miR-203 and the progressive increase of miR-30e in the atrial tissue observed with advancing age suggests that these miRNAs could be involved in aging-related atrial remodeling. Meanwhile, the reduction in circulating, but not atrial miR-106b, suggests that certain miRNAs may reflect general changes in gene regulation and may not reflect atrial remodeling. These findings could provide a foundation for further research into the potential role of miRNAs in aging-related CVD.

Keywords: aging; atrial tissue; cardiovascular disease; blood biomarkers; microRNA

Targeting constitutive HIF-1α expression to overcome doxorubicin resistance in B16.F10 melanoma cells

Bogdan Dume[1], Alina Sesărman[2], Manuela Banciu[2,3], Emilia Licărete[2]

1) Doctoral School in Integrative Biology, Faculty of Biology and Geology, "Babes-Bolyai" University, Cluj-Napoca, Romania; 2) Department of Molecular Biology and Biotechnology, Center of Systems Biology, Biodiversity and Bioresources, Faculty of Biology

Introduction: Melanoma is one of the deadliest type of skin cancer and its incidence has risen over the last decades. B16. F10 murine melanoma cells exhibit resistance to conventional chemotherapy agents such as doxorubicin, rendering them highly aggressive and metastatic. One mechanism contributing to this resistance is the constitutive expression of hypoxia-inducible factor 1-alpha (HIF-1α), a key transcription factor that regulates the expression of target genes involved in oxygen homeostasis in response to hypoxia. The role of HIF-1α in oncogenic processes involves regulation of angiogenesis and cell survival, proliferation, migration and invasion. Therefore, targeting HIF-1α could be a promising strategy to overcome this resistance. Objectives: Sensitizing B16.F10 melanoma cells to doxorubicin by concomitant administration of doxorubicin and HIF-1α specific siRNA *in vitro*.

Materials and methods: Under hypoxic (1% O2) conditions, HIF-1α gene was knocked down by transfecting B16.F10 melanoma cells with HIF-1α specific siRNA. Scrambled siRNA was used as negative control for transfection. The mRNA and protein expressions of HIF-1α were detected through RT-qPCR and Western blotting. Furthermore, cell proliferation, migration, and invasion were assessed using BrdU cell proliferation assay kit, wound healing assay, and transwell invasion assay. Enzymatic activity of matrix metalloproteinase (MMP)-2 and MMP-9 from conditioned media were determined by gelatin zymography.

Results: Both RT-qPCR and Western blot results indicated that the mRNA and protein expression of HIF-1α were significantly reduced. Furthermore, knockdown of HIF-1α significantly inhibited the proliferation, migration and invasion of melanoma cells and reduced the enzymatic activity of MMP-2.

Conclusion: Concomitant administration of HIF-1α specific siRNA and doxorubicin holds significant therapeutic potential, offering a dual-faceted attack on B16.F10 murine melanoma cells by simultaneously inhibiting a key survival factor and enhancing the efficacy of existing chemotherapeutic agents.

Keywords: melanoma, HIF-1α siRNA, doxorubicin
Funding: This work was funded by UEFISCDI (Romanian Ministry of Research and Innovation), under Grant PN-III-P1-1.1-TE-2019-1320.

IgG4 Related Diseases. When are they suspected? How do we treat them?

Olga Hilda Orășan, Codruța Pocol

University of Medicine and Pharmacy „Iuliu Hațieganu", Cluj-Napoca, Romania; 4th Medical Clinic, Cluj-Napoca, Romania

IgG4 represents between 3-6% of total serum Ig G values, higher values being found in men and in elderly patients. Recent studies have shown that IgG4 related diseases are actually immune mediated vasculitis of variable vessels affecting different organs and tissues. The salivary and lacrimal glands, pancreas, biliary tract, are the most often affected organs, but the disease can involve any organ.

IgG4 related disease with autoimmune pancreatitis (AIP) are more common in men, which usually develop more severe forms with visceral damage. This is an uncommon type of chronic pancreatitis that has typical biological features represented by increased IgG4 level. Histological, there are found storiform fibrosis, obliterative phlebitis and lymphoplasmocytic infiltration, but they are not typical for IgG4 related diseases. As a consequence, IgG4 related disease doesn't have a typical histopathological diagnosis, but levels of IgG4 are an excellent indicator for it and for the disease activity. Increased IgG4 serum levels can also be found in other autoimmune diseases, gastrointestinal and lymphoproliferative disorders, allergies, eczemas, asthma or different types of cancers. Consequently, it's critical to measure serum IgG4 levels, assess all affected organs, and search for other causes of IgG4 serum increase might occur. Patients with IgG4 related diseases are asymptomatic for extended periods (months or years), but organic lesions may become significant during this time. The patients with

IgG4 autoimmune pancreatitis might experience jaundice, weight loss, abdominal pain and complications like chronic pain, pancreatic insufficiency or fibrosis, therefore it is critical to diagnose as soon as possible. CT and MRI are used in the imaging diagnosis of IgG4 autoimmune pancreatitis. Pancreatic cancer represents the most relevant differential diagnosis for IgG4 mediated autoimmune pancreatitis. Treatment options include corticosteroids (which are both the first therapeutic option and also a diagnostic test) and B-cell depletion and inhibitory therapy.

As a conclusion, the identification and treatment of IGg4 related diseases constitutes a medical emergency due to its clinical repercussions.

Inflammation in allergic rhinitis

Ioana Adriana Muntean[1], Ioana Corina Bocșan[2], Irena Nedelea[1], Carmen Teodora Dobrican-Baruta[1], Diana Deleanu[1]

1) Universiatea de Medicina si Farmacie „Iuliu Hatieganu" Cluj Napoca, Disciplina Imunologie-Alergologie; 2) Universiatea de Medicina si Farmacie „Iuliu Hatieganu" Cluj Napoca, Disciplina Farmacologie

Allergic rhinitis (RA) is classically described as a symptomatic disease of the nose induced by an IgE-mediated inflammation, after exposure to the allergen of the nasal mucosa in patients sensitized to that allergen. Symptoms of allergic rhinitis include nasal itching, anterior/posterior watery rhinorrhea, nasal obstruction, sneezing, generally reversible spontaneously or with treatment. Inflammation plays a crucial role in the pathogenesis of allergic rhinitis, influencing the severity of symptoms and response to treatment.

This pathogenetic model involves the immunological processes underlying other atopic conditions and involves the activation of the adaptive immune system with the exacerbation of Th2-type immune responses and inflammation. A number of steps in the sensitization process are responsible for triggering the Th2-dominant response. Protease allergens activate and damage nasal epithelial cells, which then secrete alarmins such as interleukins (IL) IL-25, IL-33, thymic stromal lymphopoietin (TSLP) and other injury-associated molecular patterns (DAMPs) that stimulate innate lymphoid cells type 2 (ILC2) responsible for the secretion of some pro-inflammatory cytokines that create a microenvironment in the damaged tissue responsible for the proliferation of Th2 lymphocytes; directly or indirectly via antigen-presenting cells (APCs) located within and beneath the nasal epithelium. Activated T lymphocytes proliferate into memory Th2 cells, which secrete IL-4, IL-5, IL-9, and IL-13. A series of pro-inflammatory cytokines are responsible for maintaining inflammation at the level of the nasal mucosa: IL-4, IL-5, IL-13, together with the cell adhesion molecules, are responsible for the inflammatory cell-type infiltrate predominantly through eosinophils.

Understanding the inflammatory mechanisms brings information about the evolution of allergic rhinitis to bronchial asthma and can lead to the development of effective prevention strategies and therapeutic methods.

Keywords: allergic rhinitis, inflammation, cytokines, adhesion molecules

Immune thrombocytopenic purpura and thrombosis-a paradoxical association

Shurger-Cimponeriu R[1,2], Parvu A[1,2], Popovici C[1,2], Bojan AS[1,2]

1) "Iuliu Hatieganu" University of Medicine and Pharmacy; 2)"Ion Chiricuta" Institute of Oncology, Cluj-Napoca, Romania

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by immune-mediated platelet destruction and reduced platelet production leading to low levels of platelets counts. Common bleeding complications include petechiae, purpura, nose bleeding, heavy menstrual bleeding. The mechanism for thrombocytopenia in not fully understood, but autoantibodies targeting surface complexes such a glycoproteins GPIIb/IIIa and GPIb/IX are responsible for early platelet destruction. Treatment includes corticosteroids, immune globulins, thrombopoetin receptor agonists and splenectomy. Despite severly low levels of the platelet counts patients diagnosed with ITP have an increased risk of developing arterial/venous thrombotic events, comparing to the general population. The main difficulty in treating any thrombosis is the increased risk of bleeding due to the low platelet counts. Cardiac risk factors, type 2 diabetes, hypertension, hypercholesterolemia, family or personal history, prior splenectomy are considered to be risk factors. One of the theories regarding the mechanism of thrombosis would be the platelet microparticles which can increase the synthesis of thrombin, playing a function in clot formation. Additionally, some ITP patients had higher levels of von Willebrand factor antigen. The activation of immune system with increased secretion of pro-inflammatory cytokine such as interleukin 6 and interleukin 21 and anti-inflammatory cytokines suggest that thrombosis in ITP may have an inflammatory cause. The aim of this presentation is to summarize the findings regarding thrombotic events in primary immune thrombocytopenia.

Immune dysfunction in systemic sclerosis: from bench to bedside

Iulia Szabo

Department of Rheumatology, County Emergency Hospital, Cluj-Napoca, Romania

Background: Altered innate and adaptive immune responses provide a link between microvascular injury and fibrosis in systemic sclerosis (SSc) pathophysiology. Peripheral

blood mononuclear cells (PBMCs) drive the secretion of cytokines known for their pro-inflammatory and pro-fibrotic effects. The distinct cytokine profiles observed in both serum and PBMCs highlight the crucial role of targeting immune dysregulation in SSc.

Objectives: The current study aimed to: (1) assess various cytokine profiles in primary PBMCs upon stimulation with lipopolysaccharide (LPS) and heat-killed Candida albicans, (2) investigate the cytokine expression levels in correlation to disease duration and various clinical phenotypes, as well as (3) explore the involvement of the IL-1 signaling pathway in SSc inflamatory responses.

Material and methods: An inception cohort comprising 18 SSc patients and 17 age and gender matched healthy controls (HCs) were initially enrolled, followed by a validation study that included 74 SSc patients and 65 HCs. In the inception cohort, PBMCs were isolated and further subjected to stimulation with LPS and heat-killed Candida albicans, while in the validation cohort Influenza B and C, Respiratory syncytial virus type A (RSV-A), Poly(I:C) and CpG were aditionally used for the polyclonal activation of myeloid cells. Cytokine production was measured after 24 h and 7 days, respectively, using ELISA kits for interleukin (IL)-1β, IL-1 receptor antagonist (IL-1Ra), IL-6, tumor necrosis factor (TNF), IL-10, IL-17, and interferon-gamma (IFN-gamma).

Results: In the inception cohort, IL-1β, IL-6, and TNF levels were increased in SSc patients compared with HCs irrespective of the stimulus used. IL-1Ra and Il-17 concentrations were not statistically different between groups, even though a trend toward higher levels in patients compared with their matched controls was also observed. Most cytokines demonstrated a stable course with disease progression, except for IL-10 levels, which declined over time. In the validation cohort, baseline IL-1Ra values (RPMI), as well as those resulting from incubation with LPS, heat-killed Candida albicans, Poly(I:C), Influenza B, and RSV-A, were significantly elevated in the SSc group. A decreased IL-1Ra/IL-1β ratio was obtained following stimulation with LPS (IL-1Ra/IL-1β = 19) and heat-killed Candida albicans (IL-1Ra/IL-1β = 7).

Conclusions: This study emphasized the role of cell-mediated immunity in the pathogenesis of SSc by demonstrating a generally elevated cytokine response in patients versus controls. The sustained PBMC reactivity seen in our patients at baseline and up to 16 years after diagnosis supports the hypothesis that an innate immune memory could be present in SSc. The low IL-1Ra/IL-1β ratio observed in our study emphasizes the therapeutic potential of targeting IL-1 signaling pathway.

Keywords: systemic sclerosis, immune dysregulation, IL-1

Diagnostic and predictive value of cytokine levels in pregnancies complicated by preeclampsia in pregnant women over 35 years old

Dobrovolskaia Aliona

USMF Nicolae Testemițanu, Chisinau, Republic of Moldova

Introduction: The National Bureau of Statistics of the Republic of Moldova records a reduction in the birth rate. In the dynamics of the years 2015 - 2022, the reduction in the number of births was 33.5 %, at the same time, the demographic forecast for the period until year 2035 states that the number of births will be too lower to recover the population decline. Objectives Analysis of the clinical evolution of pregnancies obtained by in vitro fertilisation method in pregnant women over 35 years old, as well as the interpretation of the cytokine levels determined in maternal blood and amniotic fluid in pregnant women whose pregnancies were complicated by preeclampsia.

Materials and methods: The sample of the study, according to the determined purpose, included 222 pregnant women over the age of 35, divided into 2 groups according to the criterion of the method of conception through the IVF method, or by natural means, with the monitoring of the evolution and the determination of how many 28 biomarkers (6 immune mediators, including cytokines and 11 categories of oxidants and antioxidants of oxidative stress) in biological material, collected from maternal serum and amniotic fluid in the second trimester of pregnancy.

Results: Of the total of 222 pregnancies, including 14 twins and births monitored in the research, 5 preeclampsias (2.3 %) were recorded, which started in the period of 34-36 weeks of gestation, being assessed as late preeclampsia. In all pregnant women, pregnancy-induced hypertension developed in anticipation of preeclampsia was diagnosed at 22-24 weeks of gestation.

Conclusions: Carrying out the comparative analysis with similar markers determined in pregnant women from the same batch with the evolution of pregnancy without particularities, had been found in the blood serum of pregnant women with complications of preeclampsia: - IL 6 and IL - 10, have a significant increase; - pro-oxidants: with increased circulating levels of lipid hydroperoxide products of lipid peroxidation; - antioxidants: amplification of mediators of total antioxidant activity, histidine peptides, superoxide dismutase, glutathione reductase, a fact that may suggest environmental involvement and instability for oxidative stress, from the second trimester of pregnancy. In the amniotic fluid of pregnant women with complications of preeclampsia: - IL-8 and IL-12 identified in the second trimester of pregnancy have statistically higher significant values in the amniotic fluid of pregnant women whose pregnancy was complicated by preeclampsia. - antioxidants: AAT-isopropyl, Carnosine, Catalase, determined in the amniotic fluid of pregnant women diagnosed with preeclampsia or identified with increased values compared to the same markers determined in the amniotic fluid of pregnant women with normal pregnancies from the same batch of study. Keywords preeclampsia, pregnant women over 35 years old.

Effect of biological therapies on key inflammatory cytokines in psoriasis

Teodora-Larisa Florian[1], Ioan-Alexandru Florian[2], Stefan Cristian Vesa[3], Lehel Beni[2], Meda Orăsan[4]

1) Department of Physiology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 2)

Department of Neurosciences, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 3) Department of Pharmacology, „Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 4) Department of Pathophysiology, „Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Introduction: The role of inflammatory cytokines in the clinical progression of psoriasis is of significant interest.

Objectives: This study aims to investigate the relationship between inflammatory cytokine levels (such as TNF-α, IL-23, IL-17A, and IL-17F) and disease duration and severity scores in psoriasis. Additionally, it seeks to determine if a reduction in any of these cytokines is associated with an improvement in disease severity scores. Furthermore, the study aims to analyze whether any of the four biological agents used are associated with a greater decrease in overall cytokine levels.

Materials and Methods: We recruited a total of 23 adult patients who were receiving treatment with ixekizumab, secukinumab, guselkumab, or adalimumab. We assessed the severity of their psoriasis using the Psoriasis Area Severity Index (PASI) and the impact on their quality of life using the Dermatology Life Quality Index (DLQI). Additionally, we measured the levels of the cytokines mentioned earlier at the beginning of therapy and after 3 months of continuous treatment. The study enrolled participants who met specific criteria: having psoriasis, being over 18 years old, and requiring biological therapy due to a lack of response to standard treatment.

Results: Biological therapies led to improvements in PASI and DLQI scores, along with reductions in levels of TNF-α, IL-23, and IL-17F. The duration of the disease and the scores for PASI and DLQI did not show any correlation with cytokine levels, except for the DLQI score and IL-23 level, which exhibited an interestingly inverse relationship.

Conclusion: Biologic therapies are effective in ameliorating both clinical and immunological parameters in psoriasis. IL-23 has the potential to serve as a valuable biomarker for assessing treatment response in psoriasis.

Keywords: psoriasis; inflammatory cytokines; biological therapy.

The mechanism of action of Brolucizumab in retinal pathology

Samoila Lacramioara, Samoila Ovidiu, Clichici Simona

UMF „Iuliu Hatieganu", Cluj-Napoca

Introduction. Real-world studies concerning different populations are valuable and bring new information regarding different regimens of Brolucizumab injections and their adverse reactions. This highliths the powerfull mechanism of Brolucizumab in retinal pathologies requiring anti VEGF treatments.

Objectives. The present study investigates the efficacy of a pro-re-nata regimen (PRN) for neovascular Age-related Macular Degeneration (nAMD). Separate from the main statistics we report the use of Brolucizumab in central serous chorioretinopathy (CSC).

Materials and methods. A retrospective observational single-center study was conducted on 82 eyes treated with Brolucizumab between 2021 and 2023, for nAMD. All procedures were in accordance with the ethical standards of the institutional research comity of the University of Medicine and Pharmacy Iuliu Hatieganu and the Declaration of Helsinki.

Results. Patients were injected with intravitreal Brolucizumab at intervals of at least 2 months after the loading phase. In 9 (3-20) months follow-up, only 0.26% adverse reactions were noticed, with good resolution of retinal fluid (significant reduction of CST on SD-OCT, -72.50μ, $p<0.05$), and especially for subretinal fluid. 54% of the eyes remained fluid- free. The interval of injection (INTOI, a parameter calculated by averaging the results of the division of the follow-up period to the number of injections received by each patient) was 2.6899 (corresponding to an injection interval of 11 weeks). This could become an important parameter for the characterization of Brolucizumab and any other Anti-VEGF therapy and could provide a more precise interval of injection in the future. Four patients also received Brolucizumab for the treatment of chronic CSC (3 doses each). All showed good response, 3 of them remaining fluid-free.

Conclusions. Brolucizumab was safe and efficient in retinal pathologies, showing powerfull blocking effect on VEGF molecules.

Keywords. Brolucizumab, Age-Related Macular Degeneration, Central Serous Chorioretinopathy.

Boosting Veterinary Student Success: The Impact of Test-Enhanced Learning

Bolfa P, Karnik PS, French H, Gilbert R

Ross University School of Veterinary Medicine, St. Kitts and Nevis

Background: Frequent, low-stakes tests have been shown to enhance long-term retention of knowledge and assist in learning new information (Test Enhanced Learning or TEL). Numerous meta-analyses of the educational literature have determined that TEL improves academic performance across subjects via long-term retention and facilitates subsequent learning of new material. Furthermore, there is strong evidence that practice tests reduce test anxiety to some extent despite being more stressful than other study activities. A consistent finding has been that the beneficial impact of TEL is greatest for students experiencing test anxiety. The Veterinary Educational Assessment (VEA ®) is administered by the International Council for Veterinary Assessment and is used as a tool to assess candidate knowledge of veterinary anatomy, physiology, pharmacology, microbiology, and pathology; at Ross University it is a low-stakes test for students, used primarily as an institutional benchmark. The VEA® also is a predictor of student performance in the North American

Veterinary Licensing Examination (NAVLE), which is required for licensure to practice within the US and Canada. Summary of Work: Ross University School of Veterinary Medicine (RUSVM) implemented TEL in the form of weekly quizzes in all major subjects at the start of January 2020. Preclinical subjects taught in the first four semesters of the of the DVM program at RUSVM from September 2018 through August 2023 were classified as being taught before the implementation of weekly quizzes or after, and also as to whether teaching during that term was disrupted by the COVID-19 pandemic. Courses were then aligned with the appropriate administration of the Veterinary Educational Assessment and the discipline area within the VEA®. The percentage of questions answered correctly within that discipline area was the major outcome. A total of 200 courses were included; 74 were taught before the introduction of weekly quizzes and 126 after; 75 were disrupted by COVID-19 control measures and 125 were independent of such interference. Analysis was by multiple linear regression. Weekly quizzes at the time of teaching each subject had a significant positive impact on related VEA scores ($P < 0.0001$). COVID-19 related disruption to teaching had a negative impact ($P < 0.0001$). In addition, there was an independent positive effect showing improvement over time ($P < 0.0001$). Take Home Message: Test-Enhanced Learning has a positive academic impact in a veterinary medical school setting.

Chronic stress and its inducing factors in medical students

Dragan B, Timotin I

Department of Physiology and Biophysics, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Introduction. The study at medicine faculty is considered one of the most demanding, both in terms of the volume of information, knowledge, and skills required, and the psychological demands, competitive environment, and encounters with human suffering. All of the aforementioned factors and circumstances can lead to chronic stress among medical students which contribute to a decrease in the quality of life for medical students.

Objectives. Assessment of the level of chronic stress and the prevalence of its inducing factors among medical students.

Materials and methods. Perceived chronic stress was assessed in a group of students (N = 240, age 19-29 years) of medical school. We utilized the MSSQ (Medical Student Stressor Questionnaire) for assessments. It measures stress factors within 6 domains. Assessment of stress levels: Score 0.00-1.00 - Low stress; Score 1.01-2.00 - Moderate stress; Score 2.01-3.00 - High stress; Score 3.01-4.00 - Severe stress.

Results: Percentage distribution of stress levels in the analyzed group: mild - 10.4%, moderate - 25%, high - 49.6%, severe - 15%. We observed that stress factors have different prevalence among subjects with high and severe stress levels: I - Academic Related Stressor: high stress level (47%); severe (13%) II - Interpersonal and Intrapersonal Related Stressor: high stress level (18%); severe (3%) III – Teaching and Learning Related Stressor: high stress level (22%); severe (8%) IV - Social Related Stressor: high stress level (20%); severe (2%) V – Drive & Desire Related Stressor: high stress level (12%); severe (4%) VI - Group Activities Related Stressor: high stress level (20%); severe (3%)

Conclusions: The MSSQ test scores in correlation with related stressors (6 domains) highlighted the prevalence of three domains of stress-inducing factors among medical students: academic related stressors (domain I), teaching and learning related stressors (domain II) and group activities related stressors (domain VI). Keywords: stress, medical students, MSSQ

The vital role of diversity, equity, and inclusion (DEI) in shaping the future of health professions

Pompei Bolfa[1] and María José Navarrete Talloni[1]

1) Ross University School of Veterinary Medicine, Biomedical Sciences Department. Basseterre, Saint Kitts

Diversity, Equity, and Inclusion (DEI) are crucial in health professions to ensure comprehensive, culturally competent care and foster innovation. In medicine, diverse teams better address health disparities and improve patient outcomes. For instance, African American physicians are more likely to treat underserved populations, enhancing access to care. In nursing, DEI initiatives have led to increased representation of minority groups, resulting in improved patient satisfaction and communication in diverse communities. In pharmacy, culturally diverse teams enhance medication adherence by considering cultural beliefs and practices. Mental health professions benefit from DEI by providing more effective counseling for diverse populations and addressing cultural stigmas surrounding mental health.

The veterinary profession, while historically less diverse, recognizes the importance of DEI. Diverse veterinary teams can better serve multicultural pet owners, understanding varying cultural attitudes towards animals. Additionally, increased diversity in veterinary research and ONE HEALTH oriented research leads to more comprehensive studies on zoonotic diseases affecting different populations and therefore improving public health.

Ross University School of Veterinary Medicine (RUSVM) exemplifies the commitment to DEI in veterinary education. Located in St. Kitts, RUSVM provides a unique, multicultural learning environment. The school‘s diverse student body and faculty contribute to a rich educational experience, preparing the students to serve in various global settings. RUSVM‘s emphasis on DEI not only enhances the learning environment but also equips future veterinarians with the cultural competence necessary to address the evolving needs of a diverse clientele and animal populations worldwide.

This presentation will introduce fundamental concepts of Diversity, Equity, and Inclusion (DEI) and highlight concrete examples of initiatives we have implemented locally at RUSVM. We will also highlight the advantages of being part of a network of schools operating under shared DEI principles. Through these examples and our collaborative efforts, we aim to demonstrate and affirm the significant value that diversity brings to the veterinary medical profession. The audience will gain insights into practical DEI applications and their positive impacts on our academic community and the broader field of veterinary medicine.

Keywords: diversity, health professions, veterinary medicine.

Alcohol's impact on central nervous system excitability

Coreţchi E.

Universitatea de Stat de Medicină și Farmacie „Nicolae Testemițanu"

Introduction: Alcohol is recognized as a psychoactive substance with central nervous system depressant properties that exhibit a high degree of dependence. The consumption of alcohol has the potential to give rise to severe health complications. Moldova ranks among the global frontrunners in terms of per capita alcohol consumption. Specifically, the volume of pure alcohol drank per individual aged 15 and above was about 12.9 liters in 2019. Alcohol usage is responsible for 26.1% of recorded mortality cases. For Europe, 5.5% of the overall mortality rate, or approximately 291,000 individuals, experience fatalities attributed to alcohol-related causes daily.

Objectives: The present study was designed to evaluate and describe changes in the excitability of the central nervous system (CNS) to alcohol content and the effects of changes in excitability in various regions of the CNS

Materials and methods: The PubMed database was used for this work. 164 scientific articles from the period 2014-2024 were analyzed. The articles were selected based on the keywords: CNS, alcohol, and excitability, and 85 articles met the selection criteria and were in an open-access format.

Results: Low Ethanol (<20mM) and medium ethanol (20–50mM) affect the cerebellum and both increase the frequency of spontaneous inhibitory postsynaptic currents (sIPSC) in cerebellar granule cells, increase tonic GABA current in extrasynaptic GABAA receptors and reduce the size of the spike complex in Purkinje cells. The cerebral cortex, especially the frontal cortex, regulates alcohol's effects on cognition. At low alcohol concentrations, it increases GABA response, represses excitability, and inhibits NMDA receptor-mediated ESPCs. Medium concentrations suppress activity in prefrontal cortex neurons and have inhibitory effects via glycine receptors. The amygdala is the site of the f anxiolytic effects of low alcohol levels, which play a role in neuroadaptation for negative reinforcement in alcohol addiction. On the thalamus, a medium concentration has an inhibitory impact leading to a sedative or hypnotic effect.

Conclusion: Among the ways that drinking alcohol changes the excitability of the CNS are by increasing tonic GABA currents in extrasynaptic GABA receptors and decreasing the size of the spike complex in Purkinje cells, which shows that it can inhibit. NMDA receptors have a high affinity for the excitatory neurotransmitter glutamate. Long-term exposure to ethanol increases NMDA receptors in the brain, which can cause seizures during ethanol withdrawal. Activation of GABA causes chloride ion influx, leading to hyperpolarization, reducing the excitability of postsynaptic neurons, and inhibiting the release of stimulating neurotransmitters.

Keywords: central nervous system, alcohol, excitability.

Unlocking early diagnosis: exploring blood-brain biomarkers in Parkinson's Disease for enhanced intervention strategies

Moldoveanu C.A.[1,2], Jurca A.[1], Colnita A.[3], Roman I.[2], Sevastre B.[4], Toma V.A.[1,2*]

1) Department of Molecular Biology and Biotechnology, Babes-Bolyai University, Cluj-Napoca, Romania; 2) Institute of Biological Research, the branch of NIRDBS Bucharest, Romania; 3) NIRD for Isotopic and Molecular Technologies, Cluj-Napoca, Romania; 4) Faculty of Veterinary Medicine, University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania

Introduction. Introduction. Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra, leading to motor and non-motor symptoms. Although the pathogenetic mechanisms of PD are complex and multifactorial, there is a growing interest in identifying biomarkers that allow early diagnosis, especially in the silent stages of the disease when clinical symptoms are not yet evident.

Objectives. This research aimed to explore the blood-brain link in the context of Parkinson's disease through an in vivo experiment using MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), a neurotoxic agent known to induce Parkinson's symptoms.

Materials and Methods. In this study, mice received intraperitoneal injections of MPTP x HCl at 25 mg/kg in seven doses over 14 days. Samples were collected seven days after the final dose to evaluate MPTP effects. Confirmatory assays, including ELISA for alpha-synuclein and dopamine, and histological evaluations using immunohistochemistry for alpha-synuclein, validated the model. After confirming PD induction, a comprehensive analysis of biological markers was conducted, focusing on metalloproteinases (MMP-9) and glycoproteins in blood, as well as cytokines (IL-1α, IL-1β, IL-6, IL-10, and PGE2) in brain tissue. Techniques like Raman spectroscopy and GFAP analysis identified correlations between these markers. The study measured proteins, cytokines, and other biomarkers in blood and brain tissue to detect early-stage PD changes, with principal component analysis (PCA) performed to correlate the results.

Results. Preliminary findings reveal specific blood biomarkers that correlate with brain changes, paving the way for a new pre-diagnostic marker panel. These candidates may help identify patients in the silent stages of the disease, enabling early, personalized interventions. Notably, IL-10 levels increased in the striatum after MPTP exposure and inhibited blood MMP-9, while IL-6, IL-1β, and PGE2 activated MMPs. IL-1β, IL-10, and PGE2 levels decreased in the cortex, and IL-1α declined in both cortical and striatal regions. In contrast, IL-6 levels rose in both brain areas. Overall, the silent pathology at the cellular level was linked to decreased serum MMP-9, suggesting its potential as a prediagnostic blood marker for Parkinson's disease.

Conclusion. This study underscores the critical interaction between the circulatory and central nervous systems in the context of Parkinson's disease and highlights new research avenues for early disease identification. The discovery of blood-based biomarkers that reflect neurodegenerative changes could revolutionize diagnostic and therapeutic strategies, leading to more effective management of Parkinson's disease. The findings from this research offer promising prospects for future research and the development of preventive strategies targeting vulnerable populations.

Keywords: Metalloproteinases, Parkinson's disease, Oxidative stress

Acknowledgements: This research received support from a GTC grant from Babes-Bolyai University (Grant No. 32939/22.06.2023) and AOSR-TEAMS-III 2024-2025 grant. Part of the research was sustained through the PN-III-P1-1.1-TE-2021-0753 grant and Babes-Bolyai University Research Fellow 2023-2024.

Could circadian rhythm disruption contribute to sleep apnea headache?

Lupusor A., Cebuc M., Lozovanu S., Moldovanu I., Vovc V.

Human Physiology and Biophysics Department, "Nicolae Testemitanu" State University of Medicine and Pharmacy of the Republic of Moldova; Institutul de Neurologie și Neurochirurgie „D. Gherman"

Introduction/Background: Sleep apnea headache (SAH) is classified as a secondary headache by the International Classification of Headache Disorders (ICHD-3). Among the probable etiologies of SAH are hypoxemia, hypercapnia, dysregulation of sleep architecture, increased sympathetic tone, arterial hypertension, etc.; however, the exact cause remains to be elucidated. The ICHD-3 criteria emphasize the morning nature of the headache syndrome in SAH, so we can hypothesize that circadian rhythm disruption (CRD) may represent a potential pathogenetic co-factor for this type of headache.

Objectives: Analyzing circadian rhythm disruptions as the potential physiopathological mechanism behind sleep apnea headache.

Materials and methods: This literature review, based on the PRISMA 2020 guidelines, was accomplished via the PubMed and Scopus databases using the keywords: „sleep apnea", „sleep apnea headache", and „circadian rhythm disruption/disorders"; articles in English published in the timeframe 2017-2024 were selected.

Results: CRD and sleep apnea syndrome (SAS) are becoming ubiquitous in modern societies due to obesity, informational and emotional overwhelming, and artificial light. CRD in patients with SAS can be determined through different pathophysiological mechanisms: (1) sleep fragmentation due to hypoxemia and hypercapnia disrupts sleep architecture. The decrease in the duration of nocturnal REM and NonREM3 sleep phases triggers daytime pathological hypersomnolence with REM-rebound. Thus, in these patients, the circadian rhythm will be disturbed for the recurrence of day-time sleep intervals, fragmented and superficial sleep at night-time; (2) increased sympathetic tone and nocturnal hypercortisolemia, due to the autonomic nervous system activation, will alter the nocturnal body's recovery mechanisms. Idem, the nocturnal brain circuitry involved in emotional processing will not be spared. As a result, the restoration cycles of the body specific to night-sleep will be altered; (3) due to the frequent hypoxia/reoxygenation episodes, the oxidative stress worsens, which results in prolonged pro-inflammatory periods.

Conclusions: The above-mentioned mechanisms, in conjunction to those involved in the pathophysiology of SAS, can trigger SAH directly through pro-algesic mechanisms: qualitative and quantitative changes in sleep architecture, hypersympathetic tone, oxidative stress, etc. At the same time, the latter contribute to the onset of CRD. Accordingly, circadian rhythm disturbances could simultaneously act as both aggravating and reinforcing factors for these mechanisms in the pathophysiology of SAH.

Keywords: „sleep apnea", „sleep apnea headache", and „circadian rhythm disruption/disorders".

Nanomaterials: a double-edged sword

Simona Clichici

Department of Physiology, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca

In recent years. nanomateriales, structures with dimensions between 1 and 100 nanometers, have attracted attention due to their unique, specific properties and a wide range of biomedical applications. At the same time, they can become both friends and enemies, depending on how they are used and managed. In healthcare, nanomaterials have been used in areas such as: targeted drug delivery systems, improving the efficacy of treatments and reducing side effects; diagnostics, becoming highly sensitive diagnostic tools; tissue engineering, with the development of scaffolds for tissue repair and regeneration. Nanomaterials have been extensiveley used for environmental applications, electronics and computing. Despite their benefits,

nanomaterials have potential risks for human health and for the environement, from the point of view of toxicity, pollution, long-term and persistent accumulation. It is essential to find a balance between innovation and safety, with appropriate safeguards, so that the technological benefits outweight the side effects of nanomaterials.

Cerebral water channels regulate amyloid burden and cognitive abilities in a mouse model of Alzheimer's disease

Bogdan Catalin[1], Marina Daniela Manescu[2], Valentin Octavian Mateescu[2], Gabriela Camelia Rosu[2], Ianis Kevyn Stefan Boboc[1], Anca-Maria Istrate-Ofiteru[2], Ilona Mihaela Liliac[2], Costin Teodor Streba[3], Samir Kumar-Singh[4], Daniel Pirici[2]

1) Department of Physiology, University of Medicine and Pharmacy of Craiova, Romania; 2) Department of Histology, University of Medicine and Pharmacy of Craiova, Romania; 3) Department of Pulmonology, University of Medicine and Pharmacy of Craiova, Romania; 4) Laboratory of Cell Biology and Histology, Molecular Pathology Group, Faculty of Medical and Health Sciences, University of Antwerp, Belgium

Recent research has linked water buildup and insufficient removal of amyloid-β to changes in cerebral water channels. However, direct evidence between in vivo blocking and opening cerebral aquaporins has not been conducted.

By comparing the behavioural of APPPS1 mice before and after we chemically blocked or opened aquaporins for 28 days, we observed an increase in the total amyloid deposits when blocking and a decrease while opening the channels. Opening the channels also decrease in Aβ40/Aβ42 ratio. The opening of aquaporin decreases anxiety levels and improve memory, as tested by the open field and novel object recognition tests.

We provide behavioural and cellular evidence that regulating aquaporins can be an viable solution for amyloid clearing in Alzheimer's diseas.

In vitro testing of lidocaine and cannabidiol absorption from complex topical formulations.

Filipiuc S.I.[1], Ababei D.C.[2], Urîtu C.M.[1], Filipiuc L.E.[1] Tamba B.I.[1], Bild W.[3]

1) Advanced Research and Development Center for Experimental Medicine (CEMEX), Grigore T. Popa University of Medicine and Pharmacy Iasi, Romania; 2) Pharmacodynamics and Clinical Pharmacy Department, Faculty of Pharmacy, Grigore T. Popa University of Medicine and Pharmacy Iasi, Romania; 3) Physiology Department, Faculty of Medicine, Grigore T. Popa University of Medicine and Pharmacy Iasi, Romania

Introduction: Chronic pain affects over a third of the global population aged over 25. Regardless of the cause, it has a negative impact on all aspects of life, leading to reduced productivity and overall well-being. Systemic treatments are effective, but prolonged use is associated with significant side effects. In contrast, local treatments offer only short-term effectiveness, necessitating frequent reapplication. While lidocaine is known as an effective local anesthetic, it also exhibits an analgesic effect through a central mechanism that remains unclear. Cannabidiol (CBD) has shown pain-relieving properties both when applied topically and used systemically, making it a promising option for topical products with either localized effects or systemic absorption. Objectives: The objectives of the study are to evaluate the versatility of the inclusion technique using beta-cyclodextrin-based nanoparticles and to assess the in vitro absorption of lidocaine and CBD from complex topical formulations.

Methods: To demonstrate the versatility of the system, we created lidocaine nanoparticles and we applied the same method for CBD. To do this, we used the beta-cyclodextrin encapsulation technique previously developed and patented for lidocaine. We incorporated the resulting nanoparticles into a gel base for topical application. We tested the formulation in vitro using a Franz Cell system with Strat-M synthetic membranes. The diffusion medium was analyzed to measure the amounts of lidocaine and CBD that passed through the membranes at 1h, 2h, and 24 hours. Quantitative analysis was performed using a spectrophotometer UV-VIS.

Results: The results showed that the largest amount of lidocaine diffused through the membranes in the first two hours, while CBD showed a significant diffusion rate from 2 to 24 hours.

Conclusions: The results confirm that the inclusion technology in beta-cyclodextrin previously developed can also be successfully applied to CBD. Additionally, such a formulation with CBD could generate a long-lasting effect.

Keywords: Canabidiol, lidocaine, nanoparticles

Sweet, spice and everything nice: a review of therapeutic options for post-stroke depression in diabetic patients

Burlacu Irina, Gresita Andrei, Sfredel Veronica

Universitatea de Medicina si Farmacie Craiova, Facultatea de Medicina

Introduction: Post-stroke depression is a common and severe complication affecting between 30% and 50% of patients who have experienced a stroke. This condition not only exacerbates cognitive and emotional function but also interferes with the recovery process, significantly impacting quality of life. Managing post-stroke depression becomes even more complex in diabetic patients, a population presenting additional risks and unique challenges. Diabetes can affect the response to antidepressant treatments through drug interactions and side effects that may alter glycemic control. This review aims to explore the efficacy of various therapeutic interventions, including conventional antidepressant treatments and adjunctive strategies, and discuss the challenges and limitations associated with each therapeutic option in the context of diabetes.

Objectives: The aim of the review is to analyze and synthesize the existing literature on conventional antidepressant treatments and adjunctive interventions for post-stroke depression in diabetic patients. Objectives include evaluating the effectiveness of antidepressant medications, adjunctive

therapies, and identifying specific clinical challenges faced by this patient group.

Materials and Methods: The review is based on a selection of relevant studies published in the scientific literature. Data from research articles, systematic reviews, and meta-analyses were analyzed to assess the impact of different therapeutic interventions on post-stroke depression in the context of diabetes. Both the effectiveness of treatments and potential adverse effects and interactions with diabetes medications were evaluated.

Results: The literature analysis suggests that conventional antidepressant treatments can be effective but often require adjustments in the context of diabetes. Adjunctive interventions, such as antipsychotic augmentation and phytotherapy, have shown promising results but require more clinical evidence. Challenges include managing side effects and complex drug interactions.

Conclusions: The review highlights the need for a personalized approach in treating post-stroke depression in diabetic patients. Although existing therapeutic options offer positive perspectives, further studies are needed to improve treatment strategies and minimize risks associated with antidepressant treatments in this complex context. Keywords: post-stroke depression, diabetes mellitus

Establishing predictors extracted from breathing pattern parameters in predicting sympathovagal balance

Ganenco A, Lozovanu S, Vovc V, Timotin I

Catedra de fiziologie a omului și biofizică, Universitatea de Stat de Medicină și Farmacie „Nicolae Testemițanu", Chișinău, Republica Moldova

Introduction: Studies on the influence of physiological, pathological, neuropsychological, and environmental factors on heart rate variability (HRV) aim to determine what can improve HRV and create strategies to support the low-HRV risk group.

Objectives: Increased HRV is related to activation of the parasympathetic system, and establishing factors that improve HRV is the primary goal in identifying positive predictors of HRV.

Materials and methods: The current study aimed to create predictive models, using the data obtained by descriptive analysis of the values of the breathing pattern (BP) parameters and HRV in 2 respiratory models, the resting respiratory model and the respiratory model with a frequency of 6 breaths per minute and the equal duration of inspiration and expiration, namely 5 s. The standardized values of the BP parameters, further considered as factors that can quantify sympathovagal balance, allowed us to create predictive models and select those parameters that have predictive value for quantification of low frequency to high frequency ratio (LF/HF) as indicative of sympathetic to parasympathetic autonomic balance. Due to the possible complex interactions between the measured factors, the multivariate analysis was performed next. We used the Backward method to establish predictors extracted from the BP parameters recorded in the 2 breathing patterns in order to quantify the role of each of the respiratory pattern parameters in predicting the sympathovagal balance expressed by the LF/HF ratio of the HRV when the breathing pattern changes.

Results: We can consider the model of paced breathing with constant duration of the respiratory phases of 5s to 5s as being optimal in LF/HF prediction. The most evident parameter of the BP recorded in those two respiratory models, with predictive value in the variation of the sympathovagal ratio LF/HF, is the respiratory minute volume (l/min), recorded in resting breathing.

Conclusion: Modulation of two parameters of the BP, tidal volume and duration of a respiratory cycle by performing paced breathing with 6 breaths per minute and the equal duration of inspiration and expiration, 5 to 5 s, can improve autonomic balance on account of increased parasympathetic dominance in healthy individuals. Keywords: breathing pattern, heart rate variability, sympathovagal balance

In vitro evaluation of bioprinted alginate-collagen scaffolds laden with astrocytes

Andrei Gresita[1,2], Shebin Tharakan[2], Elina Sarecha[2], Michael Hadjiargyrou[2*], Eugen Petcu[2]

1) Department of Physiology, Physiopathology, and Neuroscience, University of Medicine and Pharmacy of Craiova, Craiova, Romania; 2) Department of Biomedical Sciences, College of Osteopathic Medicine; Department of Biological & Chemical Sciences, New York

The increasing prevalence of ischemic stroke (IS), a principal cause of morbidity globally, accentuates the imperative need for novel therapeutic treatments. This investigation describes the development and utilization of three-dimensional (3D) bioprinted alginate-collagen scaffolds with the aim to promote neuroregeneration and functional recovery post-IS. Central to this investigation is the proposition that alginate-collagen scaffolds possess the intrinsic capacity to support cellular development, a premise that underpins their potential utility as versatile approaches for neurorehabilitation. Specifically, the study demonstrates that biocompatible scaffolds can be effectively laden with glial cells with successful outcomes *in vitro*. This versatility suggests a broad applicability of the scaffolds in promoting neural repair and recovery. Using a BioX 3D printer, two scaffold architectures were engineered to optimize cellular distribution and proliferation, structural support, and eventually microvascular development. Immortalized murine astrocytes were engrafted into these scaffolds, with assessments of their viability, proliferation, and migration conducted over 14 days. The scaffolds also underwent rigorous evaluation for biocompatibility, structural integrity, and ability in supporting astrocyte survival and functionality. The study demonstrates

astrocyte survival and viability within the 3D bioprinted matrices, with peak growth observed on the seventh day of the study. The intricate 3D nanofilament architecture facilitated equitable cell dispersion and maintained structural integrity. The alginate-collagen scaffolds, present a promising "vehicle" for future *in vivo* studies that could enhance neuroregeneration and functional recovery following IS.

The impact of Ketamine on Behavioral Responses, Neuroinflammation, and Liver Injury in a Depressed Murine Model

Mădălina Iuliana Mușat[1,2], Smaranda Ioana Mitran[2,3], Eugen Osiac[4], Bogdan Cătălin[2,3]

1) U.M.F. Doctoral School Craiova, University of Medicine and Pharmacy of Craiova; 2) Experimental Research Centre for Normal and Pathological Aging, University of Medicine and Pharmacy of Craiova; 3) Department of Physiology, University of Medicine and Pharmacy of Craioa; 4) Department of Biophysics University of Medicine and Pharmacy of Craiova

Introduction: Depression has been increasingly associated with non-alcoholic fatty liver disease (NAFLD), with individuals affected by depression and concurrent comorbidities often exhibiting inadequate responses to conventional antidepressant treatments. The growing prevalence of depression, along with comorbid conditions, has emphasized the critical need for the development of robust animal models to facilitate advanced scientific investigation. Although ketamine has been recognized for its effectiveness in alleviating depression, its therapeutic effects in the setting of depression linked to liver pathology remain insufficiently studied. This research aimed to assess the effects of ketamine treatment in a murine model of concurrent depression and liver injury.

Methods: Depressive-like behavior and NAFLD were induced in mice through the chronic unpredictable mild stress (CUMS) protocol and a methionine-choline deficient (MCD) diet. Clinical assessments and behavioral tests, including the sucrose preference test, open field test, novel object recognition test, and Crawley's sociability test, were conducted to validate the depression model and evaluate the effects of ketamine on behavior. Hepatic ultrasonography was employed to assess liver status. The areas of NeuN+, GFAP+, and Iba1+ signals in the cortex and hippocampus were quantified for each animal using a Zeiss LSM 900 Airyscan 2 confocal microscope.

Results: Behavioral tests have shown changes in animals similar to the clinical elements of depression and anxiety. After ketamine treatment, mice showed behavioral improvements. Ketamine alleviated anhedonia and anxiety-like behavior, regardless of liver injury, but did not improve memory recognition in animals with liver damage. However, it did enhance sociability in older subjects. Ketamine demonstrated greater efficacy in young compared to aged animals. Acute administration of ketamine did not affect the severity of liver injury, but it can lead to inhibition of activity in cortex and hippocampus.

Conclusion: Despite their limited ability to replicate clinical characteristics, animal models of depression remain useful in quantifying the molecular interactions of ketamine therapy.

Keywords: depression, anxiety, stress, liver injury, ketamine

Dipper status variations in spontaneous low level blood pressure patients

Corina Mihaela Pal, Marcel Perian

UMFST George Emil Palade din Targu Mures

Background: The lack of the dipper status has been associated in multiple studies with an increase in cardivascular risk, but there are only few studies carried on hypotensive patients or presenting spontaneous low blood pressure values.

Objectives: The aim of our study is to evaluate the variations of the dipper status in non-treated spontaneous low level blood pressure patients . Materials and methods The study was carried on 66 patients, 53 women and 13 men, symptomatic and non-symptomatic, presenting with low blood pressure levels at TopMed medical center of Targu Mures. The patients underwent 24h ABPM investigation, using Contec ABPM50 devices. All patients on anti-HTA or nitrate medication were excluded. The recordings were analysed with the Contec prprietary ABPM software and exported to MS Excel.

Results: Of our 66 patients, 80.3% were ladies and 19.7% were men. The mean age was 63 years +/- 17. In our lot, 34 patients (51.51%) were non-dippers, while 32 (48.49%) were dippers, P=0.9.

Conclusions: 1. Our study found no significant differences in dipper status among naturally low level blood pressure patients. 2. The data we analysed showed a greater incidence of low level blood pressures among ladies (80.3% vs 19.7%. 3. Our study included a relative reduced number of patients, more research is needed to confirm our results. 4. Our study has not included young patients (below 22 years) so it cannot be extrapolated to this population segment.

Keywords: Dipper, hypotention, ABPM

Hematologic alterations associated with nonsteroidal anti-inflammatory drug (NSAID) therapy in rheumatoid arthritis

Toth, Sz.[1], Moț, A. C.[2], Vădan, A.[1], Popa, A.[3] Sevastre, B.[4], Sevcencu, C.[1, 5], Stoica, A. D.[3, 5*]

1) Doctoral School of Integrative Biology, Babes-Bolyai University, Cluj-Napoca, Romania; 2) Departament of Chemistry, Faculty of Chemistry and Chemical Enginering,

Babes-Bolyai University, Cluj-Napoca, Romania; 3) Departament of Molecular Biology and Biotechnology, Faculty of Biology and Geology, Babes-Bolyai University, Cluj-Napoca, Romania; 4) Faculty of Veterinary Medicine, University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania; 5) National Institute of Research and Development of Isotopic and Molecular Technologies, Cluj-Napoca, Romania

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease that develops with advancing in age and is characterized by chronic pain, stiffness and swelling of any joints. The disease if frequently treated with anti-rheumatic drugs and nonsteroidal anti-inflammatory drugs (NSAIDs). In addition, prolonged NSAID oral administration causes gastro-intestinal (GI) mucosal lesions and hemorrhages, as cyclooxygenases involved in mucosal hemostasis are inhibited. Thus, when GI complications occur, these conditions can lead to anemia. Due to chronic inflammation and autoimmune factors, patients with RA may be already at risk of anemia. While NSAIDs are effective for pain management and reducing inflammation, they can potentially induce or exacerbate anemia, due to their effects on the GI mucosal barrier and on blood cells.

Objective: The present study explores the hematological alterations induced by newly developed Ibuprofen (Ibu)-BSA and Diclofenac (Diclo)-BSA conjugates in a collagen-induced arthritis (CIA) rat model in comparison with market samples, Ibuprofen and Diclofenac.

Materials and methods: The experiment lasted 28 days after the first injection of Wistar rats with Collagen type II. Treatment with standard Ibuprofen, standard Diclofenac, and the conjugated forms (10 mg/kg) were administered orally for fourteen days after the second injection. At the end of the experiment, blood samples were collected and a complete blood count was performed. Statistical analysis was performed using GraphPad Prism.

Results: Our results showed that the Diclo-BSA conjugate proved to be most efficient in reducing the lymphocyte count (4.73±0.62 109/L), while standard Ibuprofen significantly reduced neutrophil count compared to the inflammation group (5.63±0.64 109/L and 1.16±0.11 109/L). The monocyte count was significantly ($p<0.05$) elevated in case of Ibu-BSA-treated subjects (0.61±0.08 109/L) compared to the inflammation group (0.2±0.004 109/L), Ibuprofen-treated group (0.18±0.03 109/L), and Diclo-BSA-treated group (0.16±0.02 109/L). Moreover, Ibu-BSA significantly reduced red blood cell count (8.35±0.24 109/L), hemoglobin concentration (14.52 ±16.71 g/L), platelet count (481±16.71 109/L) and plateletcrit (0.33±0.01 %) compared to the inflammation group (8.34 ±0.12 109/L, 15.2±0.19 g/L, 528±13.81 109/L and 0.37±0.01 %, respectively). The novel conjugates did not significantly alter the lastly mentioned cell counts compared to the untreated inflammation group.

Conclusions: Based on our discoveries, Ibu-BSA and Diclo-BSA conjugates did not significantly influence hematological parameters related to NSAID GI side effects. Thus, the obtained conjugates can be potential candidates for RA management that alleviate the NSAID-induced hematological alterations, namely anemia and thrombocytopenia. Key words: nonsteroidal anti-inflammatory drugs, rheumatoid arthritis, hematology

Efectul antiinflamator al terapiei complementare cu vitamina D în astmul bronșic indus experimental

Bonci Teodora Irina

Universitatea de Medicină și Farmacie „Iuliu Hațieganu" Cluj-Napoca

Astmul bronșic este o afecțiune cronică pulmonară, heterogenă din punct de vedere clinic, dar și al mecanismelor imuno-inflamatorii. În ultimele decade s-a observat creșterea prevalenței bolii, iar controlul acesteia este un subiect de interes global în cercetare. Administrarea vitaminei D (VD) per os este o intervenție facilă în domeniul sănătății publice și din acest motiv a devenit tema multor tipuri de studii în legătură cu astmul bronșic. Prezentul studiu și-a propus să cerceteze rolul VD în inflamația bronșică de tip astmatic indusă experimental. Inflamația a fost provocată cu ovalbumină pură (OVA) folosind un model murin de astm bronșic validat în literatură pentru specia de șoarece BALB/c. Animalele au fost sensibilizate prin injecție intraperitoneală cu OVA, ulterior prin instilarea intranazală a soluției de OVA s-a urmărit provocarea inflamației bronșice. Animalele au fost împărțite în patru loturi (n=5), după cum urmează: control negativ (fără astm, fără tratament), control pozitiv (cu astm, fără tratament cu VD), lot cu tratament de prevenție cu VD (doza 50 μg/kg zilnic, inițiată înainte de inducerea experimentală a inflamației bronșice), lot cu tratament de salvare cu VD (doza 100 μg/kg administrat doar etapa de provocare). S-au recoltat ser, lichid de lavaj bronhoalveolar (LLBA) și omogenat tisular pulmonar (OTP) pentru analiza produșilor finali stabili ai oxidului nitric (NOx) precum și pentru identificarea ELISA a citokinelor interleukina-4 (IL-4), interleukina-5 (IL-5), transforming growth factor beta-β1 (TGF-β1). Fragmente de țesut pulmonar au fost incluse în parafină pentru analiza histologică și imunohistochimică pentru NF-κB p65. Validarea modelului s-a realizat prin analiza histopatologică. Inflamația acută de tip astmatic a determinat creșterea semnificativă a nivelului IL-4 în LLBA la șoarecii din grupul control pozitiv, comparativ cu cei din lotul martor ($p< 0,05$). Tratamentul cu VD a avut un efect antiinflamator, producând o scădere a nivelului IL-4 din LLBA la șoarecii tratați cu VD. Inflamația experimentală a determinat creșterea nivelurilor citokinelor IL-4, IL-5 și TGF-β1 în OTP, iar tratamentul cu VD a avut un efect antiinflamator, producând o scădere a nivelurilor de IL-4, IL-5 și TGF-β1 în OTP. În toate tipurile de probe biologice, nivelul NOx a fost mai mare la șoarecii din grupul control pozitiv ($p < 0,05$), iar la animalele tratate preventiv cu VD fost observată o reducere importantă a NOx în ser, LLBA și OTP ($p < 0,05$). În ceea ce privește grupul cu terapie de salvare, VD a determinat scăderea NOx în toate tipurile de probe, dar cu semnificație statistică numai pentru ser și LLBA

($p < 0,05$). În concluzie, suplimentarea cu VD a avut un efect antiinflamator, prin ameliorarea nivelului NOx din ser, LLBA și OTP. Acest efect a fost semnificativ statistic în special când VD a fost administrată drept terapie de prevenție.

Neuroprotective effects of Cynara Scolymus L. extracts in Aβ1–42-induced neurotoxicity in SK-N-SH neuronal cells and Wistar rats

Sevastre-Berghian A.C.[1], Ielciu I.[1], Bab T.[3], Olah N.K.[2], Barbălată C.[1], Tomuță I.[1], Toma I.[1], Toma V. A.[5], Sevastre B.[4], Hasas A.D. [4], Filip G.A.[1], Clichici S.[1], Suciu S.[1], Hanganu D.[1], Bodoki A., Roman I.[5], Baldea I.[1]

1) University of Medicine and Pharmacy „Iuliu Hațieganu", Cluj-Napoca, Romania; 2) PlantExtrakt Ltd., Rădaia, Cluj-Napoca, Romania; 3) Babes-Bolyai University, Cluj-Napoca, Romania; 4) University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania; 5) Institute of Biological Research, Cluj-Napoca, Romania;

Introduction: Alzheimer's disease (AD), a progressive neurodegenerative disorder, is the most common cause of dementia in the middle-aged and elderly, worldwide. Objectives: Our study aimed to evaluate the effects of aCynarae folium extracts (CFE) on Aβ1–42-induced neurotoxicity in SK-N-SH neuronal cells and Wistar rats

Materials & Methods: Acute toxicity of the extracts was tested both on cell cultures and animals (according to OECD Guidlines for testing chemicals (2022). Moreover, Wistar rats were divided into 6 groups (n=7/group): control, Aβ1–42 (2 μg/rat), Aβ1–42 + CGA, Aβ1–42 + CFE, Aβ1–42 + CFL, DMSO. On the 15th day, one dose of Aβ1–42 was intracerebroventricularly administered. CGA (60 mg/kg b.w), CFE, CFL (200 mg/Kg b.w.) were orally administered for the first 14 days, and from the 16th day, for 14 more days. Brain oxidative stress markers and inflammatory cytokines along with Tau protein were analyzed by Elisa and immunohistochemistry.

Results: The optimized extract of Cynarae folium and the liposomes loaded with the optimized extract showed no toxicity, diminished lipid peroxidation, neuroinflammation, modulated specific protein expression and enhanced the antioxidant capacity, The effects weere evaluated both in vitro and *in vivo* studies.

Conclusion: Our findings indicate that CFE administration might represent a good option in neurodegenerative disorders, exerting its beneficial effect by increased antioxidant defense and decreased neuroinflammation.

Acknowledgment: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2021-0159, within PNCDI III (TE60/2022)

Key words: oxidative stress, neuroinflammation, Cynara Scolymus L. extracts

Abdominal aortic constriction in adult Wistar rats – an animal model of pressure overload cardiac hypertrophy and subsequently heart failure

Mekan Jumamyradov

Universitatea de Medicină, Farmacie, Științe și Tehnologie „George Emil Palade" din Târgu Mureș

Background: Despite significant therapeutic advances in the treatment of heart failure (HF), the prevalence and the morbi-mortality of HF continue to rise, highlighting the need for new therapeutic targets. The development of new potential therapeutic strategies necessitates testing in appropriate animal models.

Objectives: The purpose of this work is to describe a model of aortic banding in rats to induce pressure overload cardiac hypertrophy and subsequently HF with reduced systolic function.

Materials and methods: The aortic constriction procedure is performed on adult Wistar rats. (200-300 g). During the entire procedure, the animals are anesthetized with Isoflurane (4 L/min, 2.5%). After confirming the deep anesthesia, the abdominal area is prepared by hair removal, skin sterilization with iodine, and isolating the area with a sterile field. A 2 cm incision is made with a scalpel perpendicular to the midline of the abdomen. The moisture of the intraperitoneal organs is maintained by the application of saline solution. The tissues are carefully delineated, and the aorta is visualized in the depth of the abdominal region. Adjacent to the origins of the renal arteries, the aorta is isolated, beneath which a 4/0 silk wire. A 22G needle is placed with the blunt tip parallel to the trajectory of the aorta, and a double knot is made that tightens, encompassing both the aorta and the 22G needle. Subsequently, the needle is withdrawn, resulting in a constriction with a diameter of 0.7 mm. The abdominal cavity is closed with simple sutures using 6/0 absorbable surgical thread. All animals will receive a post-operative dose of anti-inflammatory medication for analgesic effect. If it is considered that all aseptic and antiseptic measures have been fully respected, there is no need for post-operative antibiotic injection.

Results: Successful constriction is confirmed by pulsed wave Doppler after one week. The correct placement of the constriction wire leads to an increased flow velocity in the transverse aorta above the renal arteries. Every two weeks post-constriction, an echocardiogram is performed, and after 6 to 8 weeks, impaired cardiac function is evidenced by decreased ejection fraction and increased wall thickness.

Conclusion: Easily reproducible animal models are critical in experimental research for studying the pathophysiology of various pathologies, but especially for testing potential new therapeutic targets and translating the results obtained to humans.

Key-words: abdominal aortic constriction; animal model; echocardiography; heart failure;

Auriculopuncture effectiveness on anxiety, heart rate and salivary cortisol, in dental patients

Ramona-Niculina Jurcău[1*], Ovidiu Mureșan[2], Ioana-Marieta Jurcău[3], Răzvan Titus Pîrvan[4]

1) Department of Pathophysiology, Faculty of Medicine, „Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 2) Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, „Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; 3) Emergency Clinical Hospital for Children, Cluj-Napoca, Romania; 4) Faculty of Medicine, University of Oradea, Romania

Background. The interaction between dentist and patient can reveal the presence of anxiety and psychological stress, aspects which represents a frequently problem in dental offices. On the other hand, auriculopuncture (AP) has shown to reduce anxiety.

Objectives. Evaluation of AP effectiveness on anxiety, heart rate and salivary cortisol in dental patients.

Materials and methods. Participants (no=44, age 19-49years) were randomized into 3 groups: control (C no=10); with AP for one month (A1 no=17); with AP for two months (A2 no=17). AP was applied one session a week keeping the needels on place 4days, without any anxiolytic medication. Evaluations: anxiety, heart rate, salivary cortisol.

Results. Anxiety was significantly improved in A1 (0.05) and A2 (0.001), compared to C and in A2 (0.05) compared to A1. Compared to C, heart rate (HR) and salivary cortisol (SC) were significantly lower in A1 (HR=0.05, SC=0.05) and A2 (HR=0.01, SC=0.005).

Conclusion. Applying AP for two months had a more intense anxiolytic and antistress effect than applying it for only one month. AP has an important anxiolytic effect and may reduce dental psychological stress. AP could be a practical method for modulating stress in dental offices.

Keywords: auriculopuncture, anxiety, heart rate, salivary cortisol.

In vivo hepatoxicity evaluation of differently shaped hybrid gold-iron oxide nanoparticles

Vădan A.[1], Stoica A. [2,3], Toth S.[1], Ciorîță A.[2,3], Marica R.[4], Dobre C.[2], Arik F.[5], Klein S.[5], Boca S.[3,6]

1) Doctoral School of Integrative Biology, Faculty of Biology and Geology, Babeș-Bolyai University, Cluj-Napoca, Romania; 2) Department of Molecular Biology and Biotechnology, Faculty of Biology and Geology, Babeș-Bolyai University, Cluj-Napoca, Romania; 3) National Institute for Research and Development of Isotopic and Molecular Technologies, Cluj-Napoca, Romania; 4) Faculty of Veterinary Medicine, University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania; 5) Physical Chemistry I, Department of Chemistry and Pharmacy, Friedrich-Alexander University Erlangen-Nürnberg, Germany; 6) Interdisciplinary Research Institute in Bio-Nano-Sciences, Babeș-Bolyai University, Cluj-Napoca, Romania

Introduction: there is an extensive use of gold-iron oxide nanoparticles (Au-Fe3O4 NPs) in the biomedical field due to their interesting physicochemical properties. However, a major barrier to the introduction of Au-Fe3O4 NPs into clinical applications is their safety to the organism. Hence, the investigation of their toxicity is crucial. Moreover, the assessment of their physiological effects in experimental models might provide more comprehensive and relevant data about nanoparticle-cell interactions.

Objectives: the aim of this study was to monitor in vivo the toxicity of hybrid gold-iron oxide nanoparticles having two different shapes: flower-like and dumbbell. In order to achieve the proposed goal, the following objectives have been set: to evaluate the toxicity induced by nanoparticles in the liver and plasma; to monitor the toxicity evolution during the experiment by administering various nanoparticle doses at different time intervals.

Materials and methods: for this, membrane integrity (ALAT, ASAT, LDH), concentration of Fe, markers for oxidative stress, hematological parameters, histopathological and electron microscopy images were analyzed.

Results: the observed changes in almost all parameters were in a dose-dependent manner. The overall results showed a depletion of antioxidant pool in the blood plasma. In the liver, there was an activation of the antioxidant system, which protected the cells from the harmful effects of reactive oxygen species (ROS). The changes in enzyme levels that are markers of cellular damage and histopathological examination indicated no obvious alterations.

Conclusion: the findings from the current investigation clearly indicate an influence of the nanoparticle shape on the enzyme kinetics, antioxidant status, and structural changes of the liver, dumbbells triggering transitory changes in plasma and liver due to initial exposure of the nanoparticles to the biological system while nanoflowers having a greater impact on altering plasma redox state.

Acknowledgements. S. Boca acknowledges financial support from MCID through the "Nucleu" Program within the National Plan for Research, Development, and Innovation 2022–2027, project PN 23 24 01 02. A. Stoica acknowledges financial support from the Ministry of Research, Innovation and Digitization, CNCS-UEFISCDI, project number PN-III-P1-1.1-PD-2021-0286, within PNCDI III.

Keywords: hepatotoxicity, dose-dependent, gold-iron oxide nanoparticles

Preliminary study in the evaluation of the antioxidant potential of Cichorium intybus L extracts

Olimpia Daniela Frenț[1], Eleonora Marian[1], Claudia Mona Morgovan[2], Laura Grațiela Vicaș[1], Tunde Jurca[1], Annamaria Pallag[1], Mariana Mureșan[3], Ioana Lavinia Dejeu[1]

1) Department of Pharmacy, Faculty of Medicine and Pharmacy, University of Oradea, Oradea, Romania; 2) Chemistry Department, Faculty of Informatics and Sciences, University of Oradea, Oradea, Romania

Introduction: In carrying out the research, we followed the comparative study of the content in phytocompounds of the extracts obtained by two extraction methods.

Materials and methods: In this sense, we harvested the Cichorium intybus L. plant from Bihor, Romania. Through the determinations made, we performed an evaluation of the content of total polyphenols, flavonoids and the content of metals in the plant Cichorium intybus L. The extraction method involved is the Soxhlet method using two different solvents, namely 50% methanol and chloroform.

Results: Following the extraction with the two solvents, a comparison was made of the total phenolic and flavonoid content, as well as the antioxidant capacity of the extracts using the DPPH and FRAP methods. Thus, the methanolic chicory extract had a higher total content of polyphenolic compounds (57.98 ± 0.60 mg GAE/g dry fiber) and flavonoids (5.94 ± 0.08 mg QE/g dry fiber) compared with the extract in chloroform (55.28 ± 1.11 mg GAE/g dry plant) and (5.54 ± 0.13 mg QE/g dry plant). We can say that methanol is a solvent that ensures a better extraction compared to chloroform. We state that the chloroform extract of chicory showed a higher percentage of inhibition (74.10 ± 0.22%) compared to the methanolic extract (67.47 ± 0.22%) antioxidant capacity using the DPPH method. Following the application of the FRAP method, the methanolic chicory extract demonstrated a higher antioxidant capacity (856.80 μmol TE/g dry plant) than the chloroform extract (771 μmol TE/g dry plant).

Conclusions: Based on this reasearch, it was mentioned that Cichorium intybus L has antioxidant potential which helps us to encourage the use of the plant in phytopharmaceutical products with biological activity.

Key words: Cichorium intybus L., antioxidant capacity, plant extracts

Retrospective analysis of allergen-specific immunotherapy efficacy and safety in a Romanian cohort of allergic patients

Bocsan IC[1], Popa R[1], Muntean IA[2], Varga MA[3], Barbinta C[3], Buzoianu AD[1]

1) Department of Pharmacology, Toxicology and Clinical Pharmacology, „Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj Napoca, Romania; 2) Department of Allergology and Immunology, „Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj Napoca, Romania; 3) Almedo Clinic, Cluj-Napoca, Romania

Allergen immunotherapy (AIT) is the only therapeutic option that modify the course of allergic diseases. AIT significantly improves rhinitis and asthma symptoms, reduces the need for symptomatic medication and prevents the development of other sensitizations. The present retrospective study assesess the efficacy and safety of AIT in patients with allergic rhinitis.

Material and method: 101 patients with allergic rhinitis±asthma, who followed oral or subcutaneous AIT were included in the study. Allergen immunotherapy and clinical evaluation were performed during 2012-2021. Clinical evaluation age, gender, the onset of allergic diseases, the presence and severity of symptoms, the presence of asthma symptoms at the onset of AIT, family and personal history related to allergic diseases. The presence of allergy was assessed through skin prick tests for standard allergens. The efficacy of AIT was documented after 1 year of treatment and at the end of the treatment, using total symptoms score. The adverse reactions that occured during the build up and maintenance phases of AIT have been evaluated.

Results: Twenty five percent of patients were children. The average age of onset o allergic rhinitis was 19.17 ± 11.09 years. Most of them (88.1%) had moderate to severe forms of allergic rhinitis, with a basal total symptom score of 9.97 ± 2.43. One third of the patients followed sublingual AIT, and 64 patients received the subcutaneous form of it. The mean duration of AIT was 38.28 ± 14.53 months. One patient had a systemic anaphylactic reactions during the build-up phase of AIT, while patients receiving sublingual AIT presented only mild-moderate local adverse reaction. The total symptom score decreased significantly both at 1 year and at the end of treatment. The effectiveness was not influenced by type of AIT

Parteneri SRF

SRF
SOCIETATEA ROMÂNĂ DE FIZIOLOGIE

BERLIN-CHEMIE MENARINI

sanofi

AstraZeneca

Terapia
a SUN PHARMA company

NOVARTIS | Reimagining Medicine

NOVARTIS

Boehringer Ingelheim

15 Years INNERGY
Inner balance for a quality life

VIATRIS