FACULTY OF MEDICAL SCIENCES, UNIVERSITY OF KRAGUJEVAC,
1st MOSCOW STATE MEDICAL UNIVERSITY I.M. SECHENOV
(SECHENOV UNIVERSITY)
WITH
THE SERBIAN PHYSIOLOGICAL SOCIETY

Сеченовский
Университет

SATELITE SYMPOSIUM

8th International Congress of Pathophysiology

FINAL PROGRAM &
ABSTRACT BOOK

OXIDATIVE STRESS IN HEALTH AND DISEASE: FROM BASIC SCIENCE TO APPLIED INVESTIGATIONS

Under the auspices of
International Society for
Pathophysiology (ISP)

ISP

September 03, 2018

Faculty of Medical Sciences University of Kragujevac,
Kragujevac, Republic of Serbia

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FOREWORD

Dear Colleagues,

We are very pleased to welcome you on The Satelitte Symposium to 8th International Congress of Pathophysiology will be held during September 03, 2018 at the Faculty of Medical Sciences, University of Kragujevac. For the last 16 years, the Serbian Physiological Society with the most improtant support from Faculty of Medical Sciences, University of Kragujevac has developed a series of national and internationally recognized congresses and meetings: the conferences of physiological sciences with international participation on environmental risk factors, oxidative biology and human health (Zlatibor 2001; Belgrade/Zrenjanin, 2003; Kragujevac 2004), the first congress of physiological sciences with international participation (Belgrade, 2005), the satellite symposium of the XIV International Symposium on Atherosclerosis (Belgrade, 2006), the scientific conference with international participation on nutrition, treatment and cardiovascular risk management (Novi Sad, 2007), the scientific conference with international participation devoted to our famous physiologist Richard A. Burian (Belgrade, 2008), second congress of physiological sciences with international participation (Kragujevac, 2009), the scientific conference with international participation on preclinical testing of active substances and cancer research with international symposium on anti-cancer agents, cardiotoxicity and neurotoxicity (Kragujevac, 2011) and under the auspice of EU 7th framework program, the joint scientific meeting of the national physiological societies organized by the Slovak Physiological Society and Serbian Physiological Society (Kovačica 2013), third congress of physiological sciences with international participation (Belgrade, 2014), second European meeting of the International Academy of Cardovascular Sciences (Belgrade, 2015), second joint scientific meeting of the national physiological societies organized by the Slovak Physiological Society and Serbian Physiological Society (Smolenice 2016, Slovakia), the joint scientific meeting of the national physiological societies organized by the Hungarian Physiological Society and Ser-

bian Physiological Society (Subotica 2017), and a few CME meetings in the field of atherosclerosis, vascular biology, risk factors and health. These meetings were recognized internationally, attracted a worldwide scientific audience, and had been supported by the Federation of European Physiological Societies (FEPS), the International Union of Physiological Sciences (IUPS), the International Society for Pathophysiology (ISP), the International Academy of Cardiovascular Sciences (IACS), and the International Atherosclerosis Society (IAS). Such success in former years directed us to plan and organize Satelitte Symposium to 8th International Congress of Pathophysiology. This initiative was primarily recognized from our russian collegues from 1st Moscow State Medical University "IM Sechenov", who supported that idea with significant number of participants. Primary idea with this bilateral initiative isr to attract more collegues from surronding countries to join us at the Symposium, as well as in Bratislava on 8th International Congress of Pathophysiology. This Symposium is focused on oxidative stress from its basic to applied investigations as still very attratctive scientific topic worldwide.

We really hope that this Symposium is a unique opportunity for all participants to exchange their ideas and give their own contribution in this fruitful cooperation. Finally, city of Kragujevac, located in the heart of Serbia is not only the place where you will find typical Serbian spirit of life, but also the place which is known for the worldwide recognized sacral and historical objects and monuments, museums, galleries etc.

We appreciate your participation and wishing you warm welcome to Kragujevac and central part of Serbia.

On behalf of the Program/Organizing Committee
Vladimir Jakovljevic and Sergey Bolevich

SYMPOSIUM CHAIRMEN

Jakovljevic V, Kragujevac, Symposium Co-chairman
Bolevich SB, Moscow, Symposium Co-chairman

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8th International Congress of Pathophysiology – Satellite Symposium Oxidative Stress in Health and Disease: From Basic Science to Applied Investigations, September 03, 2018
Faculty of Medical Sciences University of Kragujevac, Kragujevac, Republic of Serbia

PROGRAM

9.00 – 9.30
OPENING CEREMONY AND WELCOME MESSAGES
Chairmen: Canovic P, Bolevich S, Jakovljevic V

SESSION 1: NEW INSIGHTS INTO METABOLIC PATHWAYS
Chairmen: Jeremic N, Tsymbal AA

9.30 – 9.45
CLINICAL BENEFITS OF n-3-PUFA AND GAMA-LINOLENIC ACID IN PATIENTS WITH RHEUMATOID ARTHRITIS
Jakovljevic V[1,2], Vasiljevic D[3], Vucic V[4], Arsic A[4], Petrovic S[4], Tomic Lucic A[4], Savic M[5], Veselinovic M[6]
[1]Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, [2]Department of Human Pathology, First I. M. Sechenov Moscow State Medical University, Moscow, Russian Federation, [3]Department of Hygiene, Institute for Public Health, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, [4]Centre of Research Excellence in Nutrition and Metabolism, Institute for Medical Research, University of Belgrade, Belgrade, [5]Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, [6]Department of Internal Medicine, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

9.45 – 10.00
EFFECTS AND MECHANISMS OF BIOLOGICAL ACTIVITIES OF ELECTROMAGNETIC WAVES OF THZ DIAPASON (T-RAYS)
Tsymbal A
First I. M. Sechenov Moscow State Medical University, Moscow, Russian Federation

10.00 – 10.15

ROLE OF TLR-4 IN HYPERTENSION INDUCED BY HYPERHOMOCYSTEINEMIA

Jeremic N[1,2], Weber G[1], Tyagi SC[1]

[1]Department of Physiology, University of Louisville, Kentucky, USA, [2]Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

10.15 – 10.30

RELATIONSHIP OF THE PLASMA PHOSPHOLIPID FATTY ACID PROFILE AND THE LEVEL OF HOMOCYSTEINE IN EXPERIMENTAL HYPER-HOMOCYSTEINEMIA: ROLE HMG-COA REDUCTASE INHIBITORS

Nikolic Turnic T[1], Arsic A[2], Vucic V[2], Petrovic S[2], Ristic Medic D[2], Zivkovic V[3], Jeremic J[1], Milosavljevic I[1], Djuric D[4], Jakovljevic V[3,5]

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10.30 – 10.45 Coffee Break/Pause

SESSION 2: NOVEL IMPACT ON OXIDATIVE STRESS IN DIFFERENT PATHOPHYSIOLOGICAL CONDITIONS

Chairmen: Zivkovic V, Kabanov DS

10.45 – 11.00

EFFECTS OF ATORVASTATIN AND SIMVASTATIN ON OXIDATIVE STRESS IN DIET-INDUCED HYPERHOMOCYSTEINEMIA IN WISTAR ALBINO RATS: A COMPARATIVE STUDY

Zivkovic V[1], Nikolic T[2], Srejovic I[1], Milosavljevic I[2], Jeremic N[2], Jeremic J[2], Radonjic K[2], Stankovic S[3], Obrenovic R[3], Djuric D[4], Jakovljevic V[1,5]

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11.00 – 11.15

ROLE OF PRIMARY PROTEINS OF ENDOTOXIN-INDUCED RECEPTOR COMPLEX IN HUMAN NEUTROPHILS PRIMING FOR RESPIRATORY BURST

Kabanov D[1], Grachev S[1,2], Prokhorenko I[1]

[1]Department of Molecular Biomedicine, Institute of Basic Biological Problems, Russian Academy of Science, Pushchino, [2]Department of Pathology, Sechenov's 1st Moscow State Medical University, Russian Ministry of Healthcare, Moscow, Russian Federation

11.15 – 11.30

MODULATION OF N-METHYL-D-ASPARTATE RECEPTORS IN ISOLATED RAT HEART – EFFECTS ON REDOX BALANCE

Srejovic I[1], Zivkovic V[1], Jeremic N[2], Nikolic Turnic T[2], Jeremic J[2], Milosavljevic I[2], Bradic J[2], Petkovic A[2], Djuric D[3], Jakovljevic V[1,4]

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11.30 – 11.45

CARDIOPROTECTIVE EFFECTS OF DATS IN TYPE 1 DIABETIC RATS: ROLE OF OXIDATIVE STRESS

Jeremic J[1], Jeremic N[1], Nikolic Turnic T[1], Ravic M[1], Sretenovic J[2], Zivkovic V[2], Srejovic I[2], Tyagi S[3], Jakovljevic V[2,4]

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11.45 – 12.00 Coffee Break/Pause

SESSION 3: PATHOPHYSIOLOGICAL AND IMMUNOLOGICAL BASIS OF HEALTH AND DISEASE
Chairmen: Srejovic I, Vorobyev SI

12.00 – 12.15
PATHOPHYSIOLOGICAL BASIS FOR THE USE OF PERFLUOROCARBON BLOOD SUBSTITUTES WITH GAS TRANSPORT FUNCTION
Vorobyev SI, Votrin SV, Bolevich SB
[1]Department of Human Pathology of Faculty of Medicine, First I. M. Sechenov Moscow State Medical University, Moscow, Russian Federation

12.15 – 12.30
OXIDATIVE STRESS AS ONE OF PATHOGENIC FACTORS FOR CHROMOSOMAL ABERRATION FORMATION IN CHRONIC LYMPHOCYTIC LEUKEMIA
Zhevak TN[1], Shelekhova TV[2], Chesnokova NP[2], Budnik I[1], Tsareva OE[2], Chanturidze AV[2], Litvitsky PF[1]
[1]Sechenov First Moscow State Medical University, Moscow, [2]Saratov State Medical University n.a. V.I. Razumovsky, Saratov, Russian Federation

12.30 – 12.45
ACTIVITIES OF CARDIAC TISSUE LACTATE AND MALATE DEHYDROGENASE IN DIABETIC RATS
Mutavdzin S[1], Gopcevic K[2], Jakovljevic Uzelac J[1], Despotovic J[1], Labudovic Borovic M[3], Stankovic S[4], Djuric D[1]
[1]Institute of Medical Physiology, "Richard Burian", University of Belgrade, Belgrade, [2]Institute of Chemistry in Medicine "Prof. dr Petar Matavulj", Belgrade, [3]Institute of Histology and Embryology "Aleksandar Dj. Kostic", Faculty of Medicine, University of Belgrade, Belgrade, [4]Emergency Centre, Clinical Centre of Serbia, Belgrade, Serbia

12.45 – 13.00
TRANSGENIC ENHANCED GALECTIN-3 EXPRESSION IN B CELLS IS IN A STRONG POSITIVE CORRELATION WITH TLR4 EXPRESSION ON B CELLS AFTER 16 WEEKS OF HFD
Petrovic I[1], Kovacevic Miletic M[2], Jovicic N[2], Pavlovic S[3], Ljujic B[4], Arsenijevic N[3], Lukic M[3]
[1]Department of Pathophysiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, [2]Department of Hystology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, [3]Center for Molecular Medicine, Faculty of

Medical Sciences, University of Kragujevac, Kragujevac, [4]Department of Genetics, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

POSTER SESSION 13.00 – 14.00
Chairmen: Nikolic Turnic T, Zhevak TN

EFFECTS OF RU(II) COMPLEX AND CISPLATIN ON REDOX STATUS AND CARDIAC INJURY MARKERS IN WISTAR ALBINO RATS: A COMPARATIVE STUDY

Radonjic K[1], Jakovljevic V[2,3], Zivkovic V[2], Srejovic I[2], Nikolic Turnic T[1], Milosavljevic I[1], Jeremic J[1], Savic M[1], Sretenovic J[2], Bradic J[1], Novokmet S[1]

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CARDIOPROTECTIVE EFFECTS OF GALIUM VERUM L. EXTRACT AGAINST MYOCARDIAL ISCHEMIA-REPERFUSION INJURY: ROLE OF OXIDATIVE STRESS

Bradic J[1], Zivkovic V[2], Srejovic I[2], Nikolic Turnic T[1], Jeremic J[1], Ravic M[1], Tomovic M[1], Petkovic A[1], Jakovljevic V[2,3]

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THE IMPACT OF RHEUMATOID ARTHRITIS ON REDOX STATUS IN WOMEN

Vranic A[1], Veselinovic M[2], Jakovljevic V[3,4], Antovic A[5]

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THE EVALUATION OF OXIDATIVE STRESS IN CANCER AND HEALTHY TISSUES OF MICE TREATED WITH RUTHENIUM(II) COMPLEXES

Savic M[1], Milovanovic M[2], Milovanovic J[2,3], Stojanovic B[2,4], Nikolic Turnic T[1], Jakovljevic V[5,6], Novokmet S[1]

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REDOX STATUS OF PREGNANT WOMEN WITH THROMBOPHILIA

Petkovic A[1], Dimitrijevic SA[2], Bradic J[1], Jeremic J[1], Zivkovic V[3], Dimitrijevic BA[2], Milojevic Corbic M[2], Djuric J[2], Jakovljevic V[3,4]

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IMPACT OF HYPERBARIC OXYGENATION COMBINED WITH NICORANDIL ON OXIDATIVE STRESS IN ISCHEMIA-REPERFUSION MODEL OF ISOLATED RAT HEART

Ravic M[1], Simonovic N[2], Jeremic J[1], Mitrovic S[3], Srejovic I[4], Nikolic Turnic T[1], Zivkovic V[4], Jakovljevic V[4,5]

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EFFECTS OF TWO DIFFERENT TYPES OF TRAINING ON MORPHOMETRIC PARAMETERS OF THE LEFT VENTRICLE MIOCARDIUM IN NORMOTENSIVE AND HIPERTENSIVE RATS

Sretenovic J[1], Jakovljevic B[2], Zivkovic V[1], Srejovic I[1], Ajdzanovic V[3], Milosevic V[3], Jakovljevic V[1,4]

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EFFECTS OF DIFFERENT DOSES OF ZINC GLUCONATE ON TOTAL ANTIOXIDANT CAPACITY AND SUPEROXIDE DISMUTASE IN ALLOXAN-INDUCED DIABETIC RABBITS

Stanojevic Ristic Z[1], Valjarevic D[2], Stevic S[1], Mitic R[1]

[1]Department of Pharmacology and Toxicology, Faculty of Medicine, University of Pristina, Kosovska Mitrovica, [2]Department of Mathematics, Faculty of Natural Sciences and Mathematics, University of Pristina, Kosovska Mitrovica, Serbia

COMBINATION OF MENADIONE AND ASCORBATE INDUCES OXIDATIVE STRESS AND MTOR-DEPENDENT CYTOTOXIC AUTOPHAGY

Despotovic A[1], Tovilovic Kovacevic G[1], Zogovic N[1], Harhaji Trajkovic Lj[1], Trajkovic V[2]

[1]Institute for Biological Research "Sinisa Stankovic", University of Belgrade, Belgrade, [2]Institute of Microbiology and Immunology, School of Medicine, University of Belgrade, Belgrade, Serbia

THE EFFECT OF INCREASING WAIST CIRCUMFERENCE ON BIOMARKERS OF OXIDATIVE STRESS AND INFLAMMATION IN OVERWEIGHT YOUNG ADULTS

Kisic B[1], Miric D[1], Ilic A[2]

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PATHOGENETIC ASPECTS OF CEREBRAL MALARIA

Popovska Jovicic B, Rakovic I

Department of Infectious diseases, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

THE EFFECTS OF WHEY AND LOW DOSE OF CHRONIC ALCOHOL INTAKE ON OXIDATIVE PARAMETERS IN RAT LIVER

Radic I[1], Mijovic M[2], Tatalovic N[3], Blagojevic D[3], Adzic M[4], Mitic M[4], Ristic S[5], Velickovic S[1], Miric M[1], Popovic Lj[1], Nestorovic V[6], Lukic V[7], Janicijevic Hudomal S[8]

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THE INFLUENCES OF CHOKEBERRY EXTRACT SUPPLEMENTATION ON REDOX STATUS AND BODY COMPOSITION IN HANDBALL PLAYERS DURING COMPETITION PHASE

Cikiriz N[1], Milosavljevic I[2], Jakovljevic B[1], Bolevich S[3], Jovanovic Lj[4], Jeremic J[2], Nikolic Turnic T[2], Djuric D[2], Jakovljevic V[3,5]

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14.00 – 14.15 Concluding remarks/Closing ceremony

ORAL PRESENTATIONS

CLINICAL BENEFITS OF n-3 PUFA AND ɤ-LINOLENIC ACID IN PATIENTS WITH RHEUMATOID ARTHRITIS

Jakovljevic V[1,2], Vasiljevic D[3], Vucic V[4], Arsic A[4], Petrovic S[4], Tomic-Lucic A[4], Savic M[5], Veselinovic M[6]

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Marine *n*-3 polyunsaturated fatty acids (PUFA) and ɤ-linolenic acid (GLA) are well-known anti-inflammatory agents that may help in the treatment of inflammatory disorders. Their effects were examined in patients with rheumatoid arthritis. Sixty patients with active rheumatoid arthritis were involved in a prospective, randomized trial of a 12 week supplementation with fish oil (group I), fish oil with primrose evening oil (group II), or with no supplementation (group III). Clinical and laboratory evaluations were done at the beginning and at the end of the study. The Disease Activity Score 28 (DAS 28 score), number of tender joints and visual analogue scale (VAS) score decreased notably after supplementation in groups I and II ($p < 0.001$). In plasma phospholipids the *n*-6/*n*-3 fatty acids ratio declined from 15.47 ± 5.51 to 10.62 ± 5.07 ($p = 0.005$), and from 18.15 ± 5.04 to 13.50 ± 4.81 ($p = 0.005$) in groups I and II respectively. The combination of *n*-3 PUFA and GLA (group II) increased ɤ-linolenic acid (0.00 ± 0.00 to 0.13 ± 0.11, $p < 0.001$), which was undetectable in all groups before the treatments. Daily supplementation with *n*-3 fatty acids alone or in combination with GLA exerted significant clinical benefits and certain changes in disease activity.

EFFECTS AND MECHANISMS OF BIOLOGICAL ACTIVITIES OF ELECTROMAGNETIC WAVES OF THz DIAPASON (T-RAYS)

Tsymbal A
First I. M. Sechenov Moscow State Medical University, Moscow, Russian Federation

Nowadays a special attention in the medicine is paid to the non-drug methods of treatment socially meant diseases. Among abiotic factors of the environment the leading place belongs to the electromagnetic waves of different diapasons and frequencies: laser, extremely high frequency (EHF) waves (rays) and etc. Terahertz waves (T-Rays; THz radiations) are named electromagnetic waves with a frequency diapason $10^2 – 10^4$ GHz (or the waves with the length from 3mm till 30 micro millimeters). Scientists' interest of THz waves is connected with the point of its concentration of frequent molecular spectra of radiation and absorption of important cellular metabolites (NO, O_2, CO_2, CO, OH- and others) and the effects appearing with the interaction of the pointed waves and bio-objects. Since 2008-2017 the experiments have been made on white mongrel rat-males with the body mass 180-260g. Totally were used more than 950 sexually mature animals. In our researches the radiation of experimental animals was with THz waves on nitrogen oxide frequencies 150,176-150,664 GHz and atmospheric oxygen 129,0 GHz. The radiation dose was defined with the power density falling on the skin and radiation set time. The duration of radiation was 5, 15 and 30 min. While analyzing the received results was discovered the normalizing influence of electromagnetic radiation THz diapason on the waves of nitrogen oxide 150,176-150,664 GHz and atmospheric oxygen 129,0 GHz of various time regimes on post-stress changes of indices of rat -males' homeostasis. Inter alia (in particular), the THz diapason electromagnetic waves (rays) on the frequencies of active cellular metabolites normalize the changed functional activity of endocrine glands: pituitary, thyroid, adrenal of stressed rats. They effectively prevent from post stress changes in the systems of hemostasis and fibrinolysis, gas and electrolyte composition of blood. Also, they prevent from excessive activation of processes of lipid peroxidation of stressed animals. The radiation of the pointed rays effectively normalize NO concentration in the animals' blood plasma while being stressed. The mechanisms of influence of electromagnetic waves (rays) THz diapason on the frequencies of active cellular metabolites on biological systems appear on molecular, cellular, tissue, organ and organism levels. On the molecular level- the pointed radiation induces the changes of space configuration in the molecules of biopolymers, in particular, albumin protein. On the cellular changes the process of conformational activation of fibrinogen receptors. On tissue it effectively restores the functional condition of vascular endothelium, normalizing its balance production of vasoconstrictor and vasodilator biologically active substances. On organ and organism levels of organizations of live systems activities of the pointed mechanisms are connected with the normalization of activity of endocrine glands and the main indicators of homeostasis.

ROLE OF TOLL LIKE RECEPTOR-4 IN HYPERTENSION INDUCED BY HYPERHOMOCYSTEINEMIA

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A significant number of studies have shown a positive correlation between Hcy plasma levels and hypertension. On the other hand, pathogen recognition receptor, and in particular TLR-4 is a foreign antigen sensor that plays role in innate immune system activation and has recently gained a significant attention in the field of hypertension. Mitochondrial dysfunction and mitochondria-dependent apoptosis have been shown to promote endothelial cell loss leading to endothelial dysfunction that contributes to pathogenesis of hypertension. These events induce mitochondrial dysfunction characterized by excessive mitochondrial fission and mitochondrial apoptosis contributing to vascular remodeling followed by hypertension. The objective of this study is to define the mechanisms of homocysteine effect on aortic wall that promote vascular remodeling and hypertension and explore the role of TLR-4 mutation in alleviation of homocysteine negative effects. For this study we used 5 groups of mice: C57BL/6J, C3H/HEouJ, CBS+/-; C3H/HeJ, and CBS+/-/C3H. For further analysis we used isolated aorta and collected blood. Blood pressure was recorded using noninvasive tail cuff method. Effects of hyperpolarization factor and endothelial-dependent vasodilator on aorta contractility were also performed. We checked expression of mitochondrial fusion and fission proteins, antioxidant markers and expression of collagen/elastin fragments. Data showed that there were increased values of systolic and diastolic pressure in CBS+/- mice (DP: 127.06±18.24; SP: 159.59±15.84) and C3H/HeJ mice had decreased levels of in comparing to other groups (DP: 55.43±16.19; SP: 110.04±5.90). The response to hyperpolarization factor and endothelial-dependent vasodilator were blended in CBS+/- aorta, however mitigated in CBS+/-/C3H. Fusion and fission ratio (Mfn2/DRP1) were increased in C3H/HeJ mice (1.53±0.08) and mostly decreased in CBS+/- mice (0.42±0.05) compering to other groups. These findings indicate the prevalence of mitochondrial fission over mitochondrial fusion in HHcy may explain possible endothelial cell loss and dysfunction followed by collagen accumulation that contributes to vascular remodeling.

RELATIONSHIP OF THE PLASMA PHOSPHOLIPID FATTY ACID PROFILE AND THE LEVEL OF HOMOCYSTEINE IN EXPERIMENTAL HYPER-HOMOCYSTEINEMIA: ROLE HMG-CoA REDUCTASE INHIBITORS

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Polyunsaturated fatty acids (PUFAs), especially the n-3 series, are known for their protective effects. Fatty acid availability from circulation and from intracellular lipid droplets to fuel the heart is critical to maintain its function. Increased reliance on fatty acids to produce energy might predispose the heart to oxidative stress and ischemic damage and contribute to cardiac remodelling and cardiac dysfunction. The present study investigates the relationship of the plasma phospholipid fatty acid profiles and the level of homocysteine in experimental hyperhomocysteinemia caused by excessive intake of methionine for four weeks. Study was conducted on adult male Wistar albino rats (n=48; 4 weeks old; 100±15g body mass), and after the pharmacology treatment (ATO/SIM) and dietary manipulation all animals were sacrified. Biochemical data were collected (Hcy and fatty acid profile). Consumption of high-methione food induced decreases of C18:1n-9 and C18:3n-3 in rats. However, rats fed with high-methione and B-deficinet food had reduced proportions of mono- (C16:1n-7, C18:1n-7) and polyunsaturated fatty acids (PUFAs: C18:3n-3, C20:5n-3, and C22:4n-6) as well as n-6 PUFAs and total PUFAs. Our results indicate that statins in severe hypehomocysteinemia had a strong impact on disturbing of plasma phospholipid fatty acid profile in rats.

THE EFFECTS OF ATORVASTATIN AND SIMVASTATIN ON OXIDATIVE STRESS IN DIET-INDUCED HYPERHOMOCYSTEINEMIA IN WISTAR ALBINO RATS: A COMPARATIVE STUDY

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Taken into consideration the well-known antioxidant properties of statins, the aim of this study was to assess their influence on major markers of oxidative stress (superoxid anion radical, nitric oxide, index of lipid peroxidation), with interest to compare antioxidative potentials of atorvastatin and simvastatin during the different degree of hyperhomocysteinemia in rats. Study was conducted on adult male Wistar albino rats (n=90; 4 weeks old; 100±15g body mass) in which HHcy was achieved by dietary manipulation. For 4 weeks, the animals were fed with one of the following diets: standard rodent chow, diet enriched in methionine with no deficient in B vitamins (folic acid, B6 and B12) or diet enriched in methionine and deficient in B vitamins (folic acid, B6 and B12). At the same time, animals were exposed to pharmacology treatment with atorvastatin in dose of 3 mg/kg/day i.p or simvastatin in dose of 5 mg/kg/day i.p. Levels of superoxide anion radical and TBARS were significantly decreased by administration of simvastatin in normal and high homocysteine groups ($p<0.05$). At 4-wk after feeding with purified diets, concentrations of the antioxidant GSH, CAT and SOD were significantly affected among all groups ($p<0.05$). Our results indicated that statin therapy resulted in variable effects on redox status in hyperhomocysteinemic rats and simvastatin demonstrated a stronger antioxidant effects than atorvastatin.

ROLE OF PRIMARY PROTEINS OF ENDOTOXIN-INDUCED RECEPTOR COMPLEX IN HUMAN NEUTROPHILS PRIMING FOR RESPIRATORY BURST

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A growing body of evidence has indicated that the CD11b/CD18 receptor plays the significant role in the endotoxin signaling machinery because it can influence on TLR4-mediated cell signaling. Involvement of CD14 and TLR4 in a variety of inflammatory responses of white blood cells provides the reason for development of target therapy by blocking monoclonal antibodies (mAbs) specific to human CD14 or TLR4. Moreover, the role of CD11b in the LPS-driven priming of polymorphonuclear leukocytes (PML) is not fully elucidated. So, using receptor-directed mAbs we performed experiments to elucidate the influence of CD14, CD11b or TLR4 blocking on LPS-driven priming of human PML for reactive oxygen species (ROS) production (respiratory burst) triggered by bacterial derived formyl-methionyl-leucyl-phenylalanine (fMLP). PML were isolated from heparinized blood of healthy volunteers by standard procedure and incubated with or without anti-CD14 (UCHM-1, isotype IgG2a), anti-CD11b (clone 44, IgG1) or anti-TLR4 (HTA125, IgG2a), respectively, for 30 min before priming with S- or Re-LPS from *Escherichia coli* O55:B5 or JM103. During our study the similar priming activity of S- or Re-LPS from *E. coli* for fMLP-triggered ROS production by primed PML has been found. Among mAbs used, only the anti-CD14 mAbs down-regulated significantly the priming effect of S- or Re-LPS (by 18% and 13%, respectively; $p < 0.05$), whereas anti-CD11b did not display any blocking activity on LPS effectiveness during PML priming for fMLP-triggered ROS production. Unexpectedly, fMLP-triggered ROS production from LPS primed PML was amplified by prior cell exposure to anti-TLR4 mAbs, but this effect was not significant when compared to control LPS primed cells stimulated by fMLP. ROS production from fMLP-stimulated PML was not influenced by prior cell exposure to anti-CD14, anti-CD11b or anti-TLR4 mAbs. On the contrary, isotype-matched IgG1 or IgG2a decreased fMLP-triggered ROS production from unprimed PML (by 12% and 15% respectively; $p < 0.05$). In spite of this, neither IgG1 nor IgG2a did not influence on Re-LPS capacity to prime PML for fMLP-triggered ROS production. The results obtained in our study support the thesis that mCD14 is the key player in LPS driven PML priming for fMLP-triggered ROS production.

MODULATION OF N-METHYL-D-ASPARTATE RECEPTORS IN ISOLATED RAT HEART – EFFECTS ON REDOX BALANCE

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N-methyl-D-aspartate (NMDA) receptors belong to the ionothropic glutamate receptor family, whose roles in regulation in physiological processes and pathogenesis of various pathological states have been most intensely studied in relation to the central nervous system. On the other hand, roles of NMDA receptors in physiology and pathophysiology of other tissues attract more attention, and their role in cardiovascular tissue is still unclear. The aim of this study was to assess the effects of modulation of NMDA receptors on redox balance in isolated rat heart by glutamate, glycine, glutamate and glycine, verapamil as a calcium channel blocker, alone and in combination with glycine and/or glutamate, MK-801 as a NMDA receptor antagonist, alone and in combination with glycine and/or glutamate. The hearts of male Wistar albino rats were excised and perfused according to Langendorff technique. The oxidative stress biomarkers, including thiobarbituric acid reactive substances, nitrites, superoxide anion radical, and hydrogen peroxide, were each determined spectrophotometrically from coronary venous effluent. The application of glycine and glutamate in combination induced significant increase of NO_2^-, O_2^- and H_2O_2. Application of verapamil, as well as MK-801, induced decrease of observed oxidative stress biomarkers. Based on the obtained results it can be concluded that activation of NMDA receptors allows sufficient influx of calcium to increase the production of oxidative species.

CARDIOPROTECTIVE EFFECTS OF DATS IN TYPE 1 DIABETIC RATS: ROLE OF OXIDATIVE STRESS

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This investigation aimed to examine whether DATS-treatment exerts any protective role on the myocardial ischemia-reperfusion injury using a Langendorff-perfused diabetic rat heart. The present study was performed using 40 male Wistar albino rats (8 weeks old; 200±20g body weight). Rats were randomly divided into 4 groups (10 per group): control healthy rats (CTRL), DATS treated healthy rats (DATS), diabetic (DM) and DM DATS-treated rats (DM+DATS, 40 mg/kg body mass every other day for 3 weeks). DM was induced by intraperitoneal streptozotocin injection at a dose of 60 mg/kg body mass. After confirmation of DM, we started with DATS-treatment (40 mg/kg body mass every other day for 3 weeks). Then, animals were sacrificed and the blood was collected for redox status examination, while isolated rat hearts were subjected to ischemia and reperfusion on Langendorff apparatus. During *ex vivo* protocol, we collected coronary venous effluent from which we measured oxidative stress parameters. Expression of SOD-1 and SOD-2 were studied as well, while animals' hearts were used for histopathological examinations. Oxidative parameters were significantly altered in DATS-treated groups (DATS and DM+DATS). DATS has the protective effects in acute induced ischemia-reperfusion injury in healthy and diabetic rat heart.

PATHOPHYSIOLOGICAL BASIS FOR THE USE OF PERFLUOROCARBON BLOOD SUBSTITUTES WITH GAS TRANSPORT FUNCTION

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One of the main pathophysiological problems in clinical practice is the elimination of hypoxia and the delivery of oxygen to tissues and organs in blood loss through the use of blood substitutes with gas transport function. The influence of the Russian perfluorocarbon blood substitutes with gas transport function on gas transportation as Perfluorane and Fluoroemulsion III is determined by two factors: Oxygen capacity and the dynamics of gas exchange. There tree options that influence on the dynamics of gas exchange in the body. *The change in the blood viscosity*. The introduction of perfluoroemulsion in the bloodstream reduces the blood viscosity. *Secondly*, perfluorocarbons, dissolving in the membrane of erythrocytes, make them more elastic and easily deformable. *Thirdly*, perfluoroemulsion increases the negative charge of erythrocytes, and it increases the degree of repulsion of erythrocytes from each other. *The change in the state of the vascular bed.* Perfluoroemulsion stabilizes and modifies the membranes of the vessel walls, reversibly reduces the transport of calcium into the cell, that manifests in the active vasodilation and antispasmodic action on the wall of spasmodic vessels, firstly. *Secondly*, the size of the corpuscles of perfluoroemulsion - 0.07 μm, to 100 times smaller than erythrocyte. *Thirdly*, perfluoroemulsion eliminates the effects of intravascular coagulation. *Fourthly*, as it has a disaggregation effect on platelets, perfluoroemulsion destroys platelet aggregates. *Sixthly*, the emulsifier of perfluorocarbons - proxanol improves rheology of blood and microcirculation, improves capillary pulse, increases regional blood flow, and reduces total peripheral resistance. *Change of the oxygenation speed and the oxygen release from the blood.* Perfluoroemulsion increases the mass transfer of O_2, firstly. *Secondly*, the increase of the mass transfer of O_2 in the presence of particles of the perfluoro compounds is due to the improvement of the diffusion of O_2 in the perfluoro compounds. *Thirdly*, increasing of the mass transfer of O_2 occurs due to the oxygen extraction enhancement by the particles of the emulsion from the erythrocyte hemoglobin, because each erythrocyte is enveloped in a cloud of particles of the emulsion of the perfluoro compounds moving in the bloodstream. *Fourthly*, the increase of the mass transfer of O_2 is due to the formation in the bloodstream the gas channels from of the particles of the perfluoro compounds. *Change of the gas exchange area*. It is known that when the decreases oxygen tension, total gas diffusion is maintained by increasing the gas exchange area.

OXIDATIVE STRESS AS ONE OF PATHOGENIC FACTORS FOR CHROMOSOMAL ABERRATION FORMATION IN CHRONIC LYMPHOCYTIC LEUKEMIA

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The aim of this study was to establish the serum level of diene conjugates (DC), malondialdehyde (MDA) and nitrite (metabolite of nitric oxide) as markers of oxidative stress, to detect activities of antioxidant enzymes such as ceruloplasmin (CP) and glutathione peroxidase (GPx) as well as to reveal relationship between expressiveness of oxidative stress and frequency of cytogenetic aberrations in B-CLL patients. A total of 64 patients with B-CLL enroled in the study. At first, the types of mutations and their total frequency in B-CLL cells were detected by fluorescence in situ hybridization (FISH) with the use of Deletion Probes for 17p13.1, 11q22.3, 13q14.3 and 6q23.3 as well as Breakapart Probes for 14q32.33 and 8q24.21. Secondly, all patients were divided into four groups according to the disease stage (Rai stages 0-I, II, III and IV) and then into two larger groups (with or without mutations). Serum level of diene conjugates (DC) and malondialdehyde (MDA), activity of ceruloplasmin (CP) and glutathione peroxidase (GPx) in all these patients were detected by spectrophotometry, serum nitrite level was tested using enzyme-linked immunosorbent assay (ELISA). Control group included 30 healthy donors. After that a binomial logistic regression was performed to reveal the relationship between expressiveness of oxidative stress and frequency of cytogenetic aberrations. FISH testing has revealed the following frequency of cytogenetic aberrations in B-CLL patients: chromosomal abnormalities were detected in 42 patients (~65.6%), whereas 22 patients had no aberrations. Del 13q14.3 detectable as single lesion occurred in 19 patients (~29.7%), del 11q22.3 – in 5 patients (~7.8%), del 17p13.1 – in 4 patients (6.25%), combined mutations – in 14 patients (~21.9%). Aberrations of chromosomes 14 and 6 were not detected. Serum levels of DC and MDA were significantly increased in all patient groups as compared to the control group. Serum ceruloplasmin level was also permanently increased in patients with different Rai stages. Glutathione peroxidase activity progressively decreased. A binomial logistic regression was performed to ascertain the effects of DC, MDA, nitrite, CP, and GPx on the likelihood of having a mutation. Oxidative stress plays an important role in pathogenesis of B-CLL and is characterized by excessive accumulation of markers (DC, MDA and nitrite) as well as decreased activity of CP. Increasing DC and decreasing CP were independently associated with an increased likelihood of harboring a mutation in B-CLL patients. Therefore, prevention of oxidative stress consequences may be a beneficial treatment strategy for patients with B-CLL.

ACTIVITIES OF CARDIAC TISSUE LACTATE AND MALATE DEHYDROGENASE IN DIABETIC RATS

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The aim of this study was examination of lactate- and malate dehydrogenase (LDH, MDH) activity and their isoforms distribution in cardiac tissue of diabetic *Wistar* male rats, as well as the effect of folic acid administration. Diabetes mellitus (DM) type I was induced by streptozotocin (STZ). All experimental animals were divided into five groups: C1 – control (physiological saline 1ml/kg, i.p. one day; n=8), C2 – control with daily physiological saline treatment (1ml/kg, i.p. for 28 days; n=10), F – folic acid (5mg/kg in physiological saline, i.p. for 28 days; n=10), DM – diabetes mellitus (STZ 100mg/kg in physiological saline, i.p., one day; n=8), and DM+F – diabetes mellitus and folic acid group (STZ 100mg/kg in physiological saline, i.p. one day and folic acid 5mg/kg in physiological saline, i.p. for 28 days; n=10). After four weeks of experimental period the animals were sacrificed, the serum glycaemia was measured, and animal hearts were isolated and homogenized for spectrophotometric measurement of enzymes activity and determination of enzymes isoforms by reverse electrophoretic activity staining. After administration of STZ, DM was developed (glycaemia level over 11.5 mmol/l) in all treated animals, but there was statistically significant decrease of serum glucose level in the group DM+F in comparison to DM group ($p=0.006$). There was no difference in LDH activity between the groups, while MDH activity was increased in DM in comparison to C1 group ($p=0.043$), and decreased in DM+F group in comparison to all other groups. In all tested groups four LDH and three MDH isoforms were detected in the heart tissue, but there were differences in their distribution among the groups. The obtained results show increased activity of MDH in diabetic rats that may be the consequence of oxidative stress caused by DM. It can also be concluded that the folic acid application has positive effects as it leads to a reduction in glycaemia and in MDH activity.

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TRANSGENIC ENHANCED GALECTIN-3 EXPRESSION IN β CELLS IS IN A STRONG POSITIVE CORRELATION WITH TLR4 EXPRESSION ON β CELLS AFTER 16 WEEKS OF HFD

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The aim of this research was to investigate is there a connection between the expression of galectin-3 and TLR4 receptors in β cells in experimental model of obesity. The study was done on WT C57Bl/6 mice as well as mice with transgenically enhanced expression of galectin-3 in pancreatic β cells. Two experimental groups were on high fat diet (60% calories from fat, HFD) feeding for 16 weeks. Using flow cytometry and immunohistochemical analysis, we found a strong positive correlation of galectin-3 expression and TLR4 expression on pancreatic β cells.Increased expression of galectin-3 positively correlates with upregulation of TLR4 receptors on β cells in experimental model of HFD induced obesity. Activation of TLR4, the receptor for the cell damage patterns, induces inflamazoma activation and increases oxidative stress in β cells, which might be one the mechanisms for β cells damage in development of diabetes type 2.

ANTIBODY-PROTEASES AS BIOMARKERS AND TARGETS OF THE NEWEST GENERATION TO MONITOR AUTOIMMUNE DISORDERS

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The methodological bricks of subclinical diagnostic and predictive protocols should include basic algorithms to differ essentially from those employed in traditional clinical practice, i.e., (i) to confirm a diagnosis of subclinical stage of the disease course and (ii) to select a mode for preventive treatment to quench the chronic autoimmune inflammation. In this sense, among the best-validated proteome-related translational biomarkers, antibodies (Abs) are the best known ones to represent one of the principal immune effectors and thus key mediators of inflammatory responses to generate the events. Meanwhile most of autoimmune disorders are preceded by a symptom-free subclinical stage in which the patients can be identified by specific autoAbs. Proteolytic Abs are multivalent immunoglobulins (Igs) endowed with a capacity to provide a targeted proteolytic effect on the antigenic (Ag) substrate. The property mentioned is appearing to sound as a functional property (functionality) of the Ab molecule. The first example of Ab-proteases was an IgG found in bronchial asthma (BA) and was shown to hydrolyze vasointestinal peptide (VIP) which played a major role in the respiratory disfunction. Similar examples would cover: (i) autoimmune myocarditis (AIM) whilst demonstrating anticardiomyosine (anti-CM) autoAbs to destroy the targeted CM, (ii) antithyroid autoAbs to specifically proteolyze thyroid Ags and (iii) Abs against myelin basic protein/MBP endowing with proteolytic activity to monitor demyelination and to illustrate the evolution of multiple sclerosis (MS). Ab-proteases occur at subclinical and clinical stages and evidently correlate with the severity and course of the disease. The activity of Ab-proteases is first registered at the subclinical stages 1-2 years prior to the clinical illness. The activity of Ab-proteases would confirm a high subclinical and predictive (translational) value of the tools as applicable for personalized monitoring protocols. Ab-proteases can be programmed and re-programmed to suit the needs of the body metabolism or could be designed for the development of principally new catalysts with no natural counterparts. Further studies on targeted Ab-mediated proteolysis may provide a translational tool for predicting the subclinical and clinical courses.

REDOX LIPIDOMICS BIOMARKERS OF PROGRAMMED CELL DEATH IN HEALTH AND DISEASE

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Ferroptosis is a newly discovered and conceptualized type of regulated cell death that has been associated with the pathogenesis of several major diseases such as cancer, acute kidney and brain injury as well as chronic clinical conditions (eg, Parkinson disease). While lipid peroxidation is a hallmark of ferroptosis, its mechanisms are still the matter of scientific debate. There are arguments favoring the participation of poorly controlled free radical oxidation reactions and there are also strong pieces of evidence supporting the strictly controlled enzymatic mechanisms. Among the latter are highly specific oxidation products, *hydroperoxyl - derivatives of phosphatidylethanolamines* generated by two isoforms of 15-lipoxygenases with the assistance of a scaffold protein, phosphatidylethanolamine binding protein 1 (PEBP1). The complex of these two proteins confers remarkable selectivity towards the oxidation substrates and specificity of the products formed. Understanding and deciphering of these mechanisms is essential for the design and development of future small molecule regulators of ferroptosis with a potential to act as a new generation of therapeutic modalities against several common disease conditions.

POSTER PRESENTATIONS

EFFECTS OF Ru(II) COMPLEX AND CISPLATIN ON REDOX STATUS AND CARDIAC INJURY MARKERS IN WISTAR ALBINO RATS: A COMPARATIVE STUDY

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The investigations of ruthenium(II) complexes, as a potential metallopharmaceutics, have shown important antitumor properties in numerous *in vitro* and *in vivo* tumor models, and lower systemic toxicity than platinum(II) compounds. Therefore, the purpose of our study was to assess the effects of [Ru(Cl-tpy)(en)Cl][Cl] and cisplatin (reference compound) on systemic redox status and cardiac injury markers in rats. The levels of oxidative stress and serum cardiac biomarkers were evaluated in 36 male Wistar albino rats (8 weeks old, BW 200-250 g, n=8 animals per group) chronically (4 weeks) treated with [Ru(Cl-tpy)(en)Cl][Cl] (4 mg/kg/week), cisplatin (4 mg/kg/week) and saline (4 mL/kg/week). In collected blood samples, the following pro-oxidative parameters in plasma were measured spectrophotometrically: TBARS, NO_2^-, O_2^-, H_2O_2, while antioxidative defense system in erythrocytes was estimated by determination of SOD and CAT activity, and GSH content. The cardiac biomarkers LDH, CK, CK-MB and cTnT were measured in serum samples spectrophotometrically. Our results showed that pro-oxidative markers (TBARS, NO_2^-, O_2^-) were significantly elevated in cisplatin group compared to ruthenium and control group, while concentrations of antioxidative parameters were significantly decreased. The levels of cardiac biomarkers were significantly reduced in control group in relation to all other groups. The most pronounced effects on CK and cTnT concentrations were observed in ruthenium treated animals, while LDH and CK-MB were highly affected by cisplatin administration. These findings may help in better understanding of effects of ruthenium(II) complexes on the redox status and myocardial injury.

CARDIOPROTECTIVE EFFECTS OF *GALIUM VERUM L.* EXTRACT AGAINST MYOCARDIAL ISCHEMIA-REPERFUSION INJURY: ROLE OF OXIDATIVE STRESS

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The aim of the present study was to evaluate the effects of methanol extract of *Galium verum L.* (*G. verum)* on ischemia-reperfusion (I-R) injury in isolated rat heart. Twenty male Wistar kyoto rats were randomly divided into two groups: spontaneously hypertensive rats (SHR) and SHR rats treated with the *G. verum* extract (500 mg/kg body weight per os) for 4 weeks. Afterwards hearts were excised and retrogradely perfused according to the Langendorff technique at constant perfusion pressure of 70 cmH_2O. After stabilization period, hearts underwent 20-minute ischemia, followed by 30-minute reperfusion. Parameters of heart function such as maximum and minimum rate of pressure development, systolic and diastolic left ventricular pressure, heart rate and coronary flow were registered. Levels of superoxide anion radical, hydrogen peroxide, nitrites and index of lipid peroxidaton (measured as thiobarbituric acid reactive substances) were spectrophotometrically measured in coronary venous effluent. 4-week pretreatment with methanol extract of *G. verum* preserved contractility and lusitropic property of myocardium and led to the recovery of systolic function and coronary flow. Furthermore, applied extract alleviated I-R-induced oxidative stress. However promising potential of *G. verum* in the present study should be thoroughly examined in future researches.

THE IMPACT OF RHEUMATOID ARTHRITIS ON REDOX STATUS IN WOMEN

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Oxidative stress is a dynamic and complex phenomenon occurring in RA and it is involved in the disease pathogenesis in a complex way. Regarding, the aim of this study was to assess oxidative status in female patients with established rheumatoid arthritis (RA). Ninety women were included in the study, 42 patients and 48 age-matched healthy controls (mean age 54.8±9.1 and 54.1±6.2, respectively). The mean disease duration in patients was 12.8±8.0 years and the mean value of DAS28 was 3.8±1.1 at the moment of blood sampling. All patients were treated with the standard treatment protocol. There were no differences between the investigated groups regarding the presence of traditional cardiovascular-risk factors: smoking status, body-mass index (BMI) and lipid profile (triglycerides-, cholesterol-, HDL- and LDL levels). Patients with RA had higher CRP, SR and fibrinogen levels. The following markers of oxidative stress were determined spectrophotometrically: NO_2^-, TBARS, H_2O_2 and O_2^- as well as antioxidative parameters: CAT, SOD and GSH. Increased oxidative stress generated within an inflamed joint can produce connective tissue degradation leading to joint and periarticular deformities in patients with RA. The patients were well characterized for the presence of traditional cardiovascular-risk factors, ongoing medications and had moderate- to high disease activity, which enabled assessment in the real life setting. Further studies are mandatory to confirm these preliminary findings.

THE EVALUATION OF OXIDATIVE STRESS IN CANCER AND HEALTHY TISSUES OF MICE TREATED WITH RUTHENIUM(II) COMPLEXES

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We have compared antitumor and toxic effects of Ru(II) complexes in comparison with oxalilplatin (reference compound) in mice, by evaluating oxidative stress parameters in tumor, heart, hepatic, lung and kidney tissues, and indicated antioxidant effects of Ru(II) complexes. Tumor induction was conducted with 1×10^6 CT26-cells suspended in 100 µl of DMEM and injected subcutaneously into the flank of male Balb/c mice. Treatment groups were as follows: Ru-1, Ru-2, oxaliplatin and control (0.9% NaCl). The complexes were administered at dose of 5 mg/kg, twice weekly for 14-days period. The tumor, heart, liver, lungs, and kidney were isolated and frozen at -80 °C. The tissues were homogenized in phosphate buffer. Markers of oxidative stress (TBARS, H_2O_2) and antioxidant defense system (GSH, SOD and CAT), were determined spectrophotometrically form the homogenate of tissues. The present study showed that Ru-2 caused renal oxidative damage, manifested by an increase in TBARS levels and depletion of GSH in the kidneys. Ru(II) complexes has led to increase activity of SOD, CAT and GSH in lungs, and significantly decreased the levels of TBARS in liver, but increased production of TBARS in heart. SOD activity and H_2O_2 levels were significantly decreased in tumor tissue in all experimental groups compared to control. The use of oxaliplatin has led to a decreased activity of SOD in heart, CAT and GSH in liver, but also increased activity of CAT in lungs and heart. These results could be of importance for better understanding the side effects of Ru(II) complexes, as potential anticancer drugs.

REDOX STATUS OF PREGNANT WOMEN WITH THROMBOPHILIA

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The aim of our study was to establish the redox status of pregnant women with thrombophilia. Investigation included 120 pregnant women who were divided into two groups: thrombophilia and normal pregnancy group. The thrombophilia group consisted of 60 pregnant women with thrombophilia, while the normal pregnancy group included 60 physiologically healthy pregnant women. For biochemical analysis, blood samples were collected at the end of first, second and third trimester of pregnancy. Levels of superoxide anion radical (O_2^-), hydrogen peroxide (H_2O_2), nitrites (NO_2^-) and thiobarbituric acid reactive substances (TBARS) were measured in plasma, while reduced glutathione (GSH), activities of superoxide dismutase (SOD) and catalase (CAT) were measured in erythrocytes. Different dynamics of release of pro-oxidants and antioxidants during the gestation period was observed both in thrombophilia and normal pregnancy group. Higher values of pro-oxidants and lower values of parameters of antioxidant defense system were noticed in women with thrombophilia in comparison with healthy pregnant women in first and second trimester. On the other hand, during the third trimester there wasn't any difference in the measured parameters between thrombophilia and normal pregnancy group. Generally viewed, thrombophilia was associated with impaired antioxidant capacity, which was variously diminished from first to third trimester, in different parameters. This study may be a starting point for further investigators which would clarify the role of thrombophilia on modulation of redox homeostasis.

IMPACT OF HYPERBARIC OXYGENATION COMBINED WITH NICORANDIL ON OXIDATIVE STRESS IN ISCHEMIA-REPERFUSION MODEL OF ISOLATED RAT HEART

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The aim of this study was to estimate the effects of combination therapy with verapamil and hyperbaric oxygenation (HBO) on ischemia-reperfusion injury using the Langendorff heart preparation model. The hearts (n=48 total, 12 per group) were divided into four groups: control, HBO, nicorandil and nicorandil + HBO. Prior to acute verapamil perfusion, animals were exposed to hypebaric oxygen therapy for 3 weeks (2 AT/1 hour per day) and after chronic treatment rats were sacrificed. Isolated hearts were perfused on a Langendorff apparatus and afterward the stabilisation time we started with 5 minutes long verapamil (200 μmol/l) preconditioning, then hearts were subjected to ischemia (20min) and reperfusion (30min). During *ex vivo* protocol we collected coronary effluent from which we measured the oxidative stress parameters (TBARS, NO_2^-, O_2^-, H_2O_2). The fixed hearts samples was used for hematoxylin and eosin staining. Our results show that nicorandil and its combination with HBO improved redox status of ischemic heart and reduced remodelling of cardiac tissues. Results of our study may be a starting point for further researchers which would fully clarify effect of nicorandil and HBO on the ischemic heart.

EFFECTS OF TWO DIFFERENT TYPES OF TRAINING ON MORPHOMETRIC PARAMETERS OF THE LEFT VENTRICLE MIOCARDIUM IN NORMOTENSIVE AND HIPERTENSIVE RATS

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The aim of this study was to show the effects of moderate-intensity and high-intensity training on morfometric parameters of the left ventricle miocardium in normotensive and hypertensive rats. The study included 32-male Wistar albino and spontaneously hypertensive rats, divided into 6 groups: control normotensive (CTRL), normotensive moderate-intensity training (MIT), normotensive high-intensity training (HIIT), control hypertensive (SHR), hypertensive moderate-intensity training (SHR-MIT) and hypertensive high-intensity training (SHR-HIIT). The rats from MIT groups ran on trandmile on speed from 10 to 15m/min, 5 days/week, 1h/day, while HIIT groups ran on speed from 35 to 55m/min, 30s in 5 cycles, with a 3 min period of rest between the cycles. After 4-weeks of training, the rats were sacrificed. Heart biopsy specimens were routinely fixed and embedded in paraffin. Five micrometer thick sections were H&E stained. Captured microscopic images were processed by special software for image analysis to quantify the results. Body weights were decreased in all groups of hypertensive rats compared to normotensive rats. Relative heart weights were increased in hypertensive rats compared to normotensive rats. Longitudinal section diameter of cardiac muscle cells was decreased in SHR-MIT group for 13% compared to MIT, while in SHR-HIIT group the same parameter decreased for 17% compared to HIIT. Cross section muscle cell area was decreased: in SHR for 7% compared to CTRL, in SHR-MIT for 6% compared to MIT, and in SHR-HIIT for 9% in comparison with HIIT. Both types of training caused significant hypertrophy of the left ventricle myocardium in normotensive and hypertensive rats.

EFFECTS OF DIFFERENT DOSES OF ZINC GLUCONATE ON TOTAL ANTIOXIDANT CAPACITY AND SUPEROXIDE DISMUTASE IN ALLOXAN-INDUCED DIABETIC RABBITS

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The aim of this study was to investigate the effects of three different doses of zinc supplementation on plasma total antioxidant capacity (TAC) and change in the activity of superoxide dismutase (SOD) in normally and alloxan induced diabetic rabbits. The 25 New Zealand rabbits were divided into three groups. Zinc is given as zinc gluconate in doses of 5.5 mg/day (I group), 9.2 mg/day (II group) and 18.4 mg/day (III group) during 15 days. The treatment dosages were chosen in relation to the values obtained from human population studies and determinated by used Clarc formula. After washout period (10 $t_{1/2}$), experimental diabetes in all rabbits were induced i.v. injection of alloxan (80 mg/kg BW). The diabetic rabbits with fasting blood glucose values between 9.99 and 14.98 mmol/L were continued the research. All three groups of diabetic rabbits were given appropriate dose of zinc gluconate during 15 days. Blood samples were taken before and after treatment of zinc gluconate in normally and diabetic rabbits. The administration of three different doses of zinc in normally rabbits did not cause any changes in TAS and SOD activity. Also, the TAS was not significantly different after administration of zinc in diabetic rabbits. But, the activity of SOD was significantly increased after administration of zinc in doses of 5.5 mg ($p<0.05$), 9.2 and 18.4 mg/day ($p<0.001$) in diabetic rabbits. In conclusion, these results show that activity of zinc-dependent enzyme SOD increased after administration of different doses of zinc gluconate in diabetic rabbits.

COMBINATION OF MENADIONE AND ASCORBATE INDUCES OXIDATIVE STRESS AND mTOR-DEPENDENT CYTOTOXIC AUTOPHAGY

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The goal of this study was to investigate ascorbate and menadione potential to induce oxidative stress and autophagy in U251 human glioblastoma cells *in vitro*. To this purpose, U251 cells were treated with single and combined doses of ascorbate and menadione. Cell viability was assessed by crystal violet test. Changes in mitochondrial membrane potential, superoxide production, apoptosis, and autophagy were determined by flow citometry using appropriate fluorochromes (JC-1, MitoSox, Annexin-Propidium iodide, and LysoTracker Red, respectively). Activation of the main autophagy repressor mTOR, and its target S6K, expression of proautophagic protein p62, and conversion of LC3I to LC3II were assessed by immunoblot, while transfection with LC3 siRNA was used to determine the role of autophagy in glioma cell death. Treatment with single doses of ascorbate and menadione did not affect the viability of U251 cells, while their combination resulted in significant dose-dependent cytotoxic effect. This was associated with mitochondrial depolarization followed by increase in concentration of mitochondria-derived superoxide, and finally by apoptosis. Menadione and co-treatment induced increase in the content of acidic autophagic-like vesicles and autophagosome-associated LC3II protein, while decreased concentration of autophagic proteolysis substrate p62. The expression of LC3II was additionally elevated in the presence of proteolysis inhibitor, suggesting increase in autophagic flux. Reduced activity of mTOR and S6K indicate that detected autophagy was mTOR-dependent. Induced autophagy was cytotoxic, since its inhibition by LC3 RNA interference recovered viability of glioma cells. To conclude, combination of ascorbate and menadione synergistically induced oxidative stress, apoptosis, and mTOR-dependent cytotoxic autophagy in U251 cells.

THE EFFECT OF INCREASING WAIST CIRCUMFERENCE ON BIOMARKERS OF OXIDATIVE STRESS AND INFLAMMATION IN OVERWEIGHT YOUNG ADULTS

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Obesity is disease characterized by an increased inflammatory state and chronic oxidative stress. Oxidative damage and inflammation are possible mechanisms linking obesity to increased risk of chronic diseases. The aim of the study was to assess the influence of obesity among young adults on lipoproteins levels, inflammatory and oxidative stress markers. The study included 175 young adults. Based on the measured WC (cm) the subjects were divided into 3 groups, I: WC to 79 cm (N 86), II: WC 80 – 94 cm (N 66), III: WC: over 95 cm (N 23). Clinical and biochemical parameters, including lipid profile, levels apolipoprotein B and A1, fasting glucose; the markers of inflammation (high-sensitivity C-reactive protein, IL-6, fibrinogen) and oxidative stress (myeloperoxidase (MPO) activity, malondialdehyde and ferric reducing antioxidant power) were measured. We measured higher levels of total cholesterol, LDL-c, VLDL-c, triacylglycerol, ApoB and lower levels of HDL-c and ApoA1 in the serum of subjects in II and III groups ($p<0.001$). Obese subjects presented lower levels of sulfhydryl groups (-SH) and higher MPO activity and hsCRP ($p<0.001$). There was a positive correlation between MPO activity and hsCRP (0.405, $p<0.01$), WC and ApoB (0.352, $p<0.01$), WC and ApoB/ApoA1 (0.353, $p<0.01$), WC and MPO (0.379, $p<0.01$), and negatively associated between hsCRP and ApoA1 (-0.880 $p<0.01$), MPO activity and ApoA1 levels (-0.296, $p<0.05$). We determined increased levels of inflammation and oxidative damage markers with increasing WC. Interventions that mitigate oxidative damage and/or reduce inflammation could be essential for reducing or preventing obesity and related chronic disease.

PATHOGENETIC ASPECTS OF CEREBRAL MALARIA

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Cerebral malaria is a diffuse encephalopathy that manifests itself by coma and presents the most difficult complication of infection caused by Plasmodium Falciparum. The onset of cerebral malaria presents a multifactorial process, and many aspects of this clinical syndrome remain unknown. In addition to hemolysis, which almost all manifestations have been attributed to, phenomena such as sequestration, cytoadherence, rosette phenomenon and inflammation hold an important place in pathogenesis as well. In the cytoadherence process, a particular role is played by the PfEMP1 protein, called knoblike projections, which is expressed on the surface of the infected erythrocyte 12 to 15 hours after infection. It binds to a variety of receptors on the surface of endothelial cells such as ICAM-1, EPCR, CD36, CD31. A special place in the pathogenesis of cerebral malaria has the binding of PfEMP1 domains called DC 8 and DC13 to the EPCR receptor on endothelial cells. The binding of infected erythrocytes to EPCR blocks the conversion of inactive protein S into active protein S, which contributes to the formation of endothelial activation. The binding of DC 4 to ICAM-1 on endothelial cells holds an important place in the cytoadherence process. By the destruction and lysis of erythrocyte, hemolysin is released as well as GPI which activates macrophages and endothelial cells, especially microglia, to secrete proinflammatory cytokines such as TNFα, IL-1, IL-6, IL-8 which mediate the formation of Nitric oxide (NO). Locally produced NO diffuses into the central nervous system parenchyma and interrupts normal transmission. The onset of cerebral malaria represents a multifactorial process. Despite numerous studies which examine the pathogenic mechanisms of malaria, numerous aspects of this clinical syndrome remain unknown.

THE EFFECTS OF WHEY AND LOW DOSE OF CHRONIC ALCOHOL INTAKE ON OXIDATIVE PARAMETERS IN RAT LIVER

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It is known that ethanol applied chronically at higher doses shows prooxidant effect in the liver tissue, that could lead to the development of alcoholic liver disease. On the other hand, whey is often used as a traditional dietary supplement in the treatment of liver damage. The aim of this study was to assess how low doses of chronic alcohol intake (12% ethanol "*ad libitum"*) and recommended doses of the whey (2g/kg per day), alone or in combination, could affect the oxidative status of the rat liver. Wistar male rats were divided in four groups of six animals: control, ethanol, whey, and ethanol and whey. Activities of manganase superoxide dismutase (MnSOD), copper, zinc superoxide dismutase (CuZnSOD), gluthatione reductase (GR), gluthatione peroxidase (GPx) in the experimental groups compared to the control group did not change after treatment of 6 weeks. Concentration of malondialdehid (MDA) is lower ($p<0.05$) in ethanol and ethanol and whey, co-administered group compared to the whey and the control group. The activity of catalase (CAT) was increased ($p<0.001$) in ethanol and ethanol and whey, co-administered group compared to the control and whey treated group. Our results indicate that the applied dose of 12% ethanol "*ad libitum"* (0,254 g/L) in the blood did not cause obvious oxidative stress, since the level of MDA didn't increase. Ethanol altered activity of CAT which origin is not attributed to the oxidative stress in mitochondria but rather to the microsomal "turnover" of hydrogen peroxide produced in cytoplasmatic ethanol metabolism.

THE INFLUENCES OF CHOKEBERRY EXTRACT SUPPLEMENTATION ON REDOX STATUS AND BODY COMPOSITION IN HANDBALL PLAYERS DURING COMPETITION PHASE

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The aim of our study was to investigate the influence of twelve-week consumption of chokeberry extract on redox status, body composition, lipid profile and biochemical parameters in active handball players. The study included 16 handball players, aged 16-24 years (20.26±2.86 years). The players received 30 mL of liquid chokeberry extract, in the morning before training, once per day for 12 weeks, during regular competition season. The research consistied of morphofunctional and biochemical testing. After three months treatment with dietary supplement contains extract of chokeberry we noticed significant changes in three main ways. The supplementation with chokberry extract decrease the levels of pro-oxidants and increase the levels of antioxidant enzymes. Analysing the dynamic of body composition it can be noticed decrease of body fat, as well as its percent in a body. On the other hand increase of dry muscle mass and high density lipoprotein. At the same time there are decrease of leucocytes and increase of haemoglobin and red cells in blood count. In the overall these result emphatically show that use of dietary supplement with chokeberry extract induce a wide range of beneficial effects in examined group of athletes.

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