JUNE 20-22, 2019, OPLENAC, TOPOLA, SERBIA

THIRD JOINT MEETING OF NATIONAL PHYSIOLOGICAL SOCIETIES

In the organisation of a

SLOVAK AND SERBIAN PHYSIOLOGICAL SOCIETIES

HEALTH RISK, NUTRITION AND DIETARY SUPPLEMENTS: OXIDATIVE STRESS AND POLYPHENOLS IN THE HEART OF SERBIAN WINERIES

FINAL PROGRAM & ABSTRACT BOOK

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Organized by
SLOVAK PHYSIOLOGICAL SOCIETY
SERBIAN PHYSIOLOGICAL SOCIETY

Under the auspices of

Federation of European Physiological Societies (FEPS)
International Union of Physiological Sciences (IUPS)
International Society for Pathophysiology (ISP)
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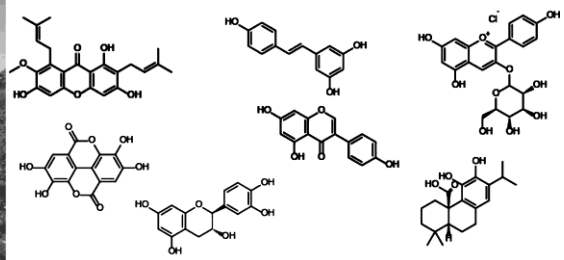

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FOREWORD

Dear Colleagues,

We are very pleased to inform you that third joint scientific meeting of national physiological societies, ie. from Slovakia and Serbia, will be organized in Topola - Oplenac. This meeting already became traditional, and our wish is to attract the physiologists from surrounding countries also. Meeting is directed to investigations from all fields of physiology and biomedicine in general, with special focus on polyphenols action and oxidative stress.

During the years the cooperation between Slovak and Serbian Physiological societies became not just scientifically fruitful but has risen to the level of mutual support and above all friendship. Therefore we are determined to organize this third joint scientific gathering in the beautiful ambience of the "Aleksandrovic" winery on Oplenac hill in Topola center of Sumadija. At this place in the heart of our country there is one of the most eminent wine complexes that, besides the true enjoyment in wine and the entire wine production environment, provide unique opportunity for organizing such a meeting. On this way, it can be achieved an unforgettable approach to the exchange of scientific experiences which as one of the common characteristics has the role of polyphenolic compounds – the main theme of this congress.

We really hope that this meeting is an excellent opportunity for all participants to share their ideas and give their own contribution in this friendly cooperation. Finally, Topola and Oplenac are not only famous for wines and traditional Serbian spirit of life, but they are also the places which are internationally known for the historical objects, museums, churches, surroundings etc.

We appreciate your participation and wishing you warm welcome to Topola and Sumadija.

On behalf of the Program/Organizing Committee

Andrea Calkovska, Dragan M. Djuric,
Olga Pechanova and Vladimir Jakovljevic

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Vranic Aleksandra (Kragujevac)
Vucic Vesna (Belgrade)
Zivkovic Vladimir (Kragujevac)

PROGRAM

Thursday, June 20th, 2019

17.00-17.30
Opening Ceremony/Welcome Messages
Chairpersons: Calkovska A, Pechanova O, Jakovljevic V

17.30-18.00
Plenary Lecture
Pechanova O
Centre of Experimental Medicine, Slovak Academy of Sciences, Bratislava, Slovak Republic
POLYPHENOL-RICH RED WINE EXTRACT: FROM GENTLE PREPARATION TO BIOMEDICAL ANALYSIS

18.00-18.30
Plenary Lecture
Jakovljevic V
Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
Department of Human Pathology, 1st Moscow State Medical, University IM Sechenov, Moscow, Russian Federation
POLYPHENOLS: FROM BASIC TO APPLIED INVESITGATIONS

18.30 Welcome Reception/Cocktail

Friday, June 21st, 2019

Session 1: NOVEL PLANT COMPOUNDS AND CARDIOVASCULAR PHYSIOLOGY

Chairpersons: Zivkovic V, Srejovic I

9.30-9.45
Zivkovic V, Bradic J, Mijailovic Z, Petkovic A, Andjic M, Vucicevic K, Sovrlic M, Barjaktarevic A, Tomovic M, Jakovljevic V
Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
PRECONDITIONING WITH *ALLIUM URSINUM* AS A NEW TOOL FOR FUNCIONAL RECOVERY OF ISOLATED RAT HEART: FOCUS ON HYPERTENSION

9.45-10.00
Mutavdzin S, Gopcevic K, Stankovic S, Jakovljevic Uzelac J, Djuric D
Institute of Medical Physiology "Richard Burian", Faculty of Medicine, University of Belgrade, Belgrade, Serbia
THE EFFECTS OF PYRIDOXINE ADMINISTRATION ON CARDIAC OXIDATIVE STRESS AND MATRIX METALLOPROTEINASES IN STREPTOZOTOCIN INDUCED DIABETES MELLITUS IN WISTAR ALBINO RATS

10.00-10.15
Srejovic I, Bradic J, Mijailovic Z, Petkovic A, Andjic M, Vucicevic K, Sovrlic M, Barjaktarevic A, Tomovic M, Jakovljevic V
Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
EFFECTS OF *GALIUM VERUM* EXTRACT AGAINST ISCHEMIA-REPERFUSION INJURU IN ISOLATED RAT HEART

10.15-10.30
Barancik M, Bartekova M, Fogarassyova M, Dovinova I
Centre of Experimental Medicine, Slovak Academy of Sciences, Bratislava, Slovak Republic
EFFECT OF QUERCETIN ON PROTEINS OF ANTIOXIDANT DEFENSE SYSTEM AND ABC TRANSPORTERS IN RAT HEARTS

10.30-10.45
Petkovic A, Bradic J, Zivkovic V, Srejovic I, Jeremic J, Draginic N, Andjic M, Simonovic N, Jakovljevic V
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
PRECONDITIONING WITH HYPERBARIC OXYGEN AND CALCIUM CHANNEL MODULATORS IN RAT HEART

10.45-11.00
Bradic J, Zivkovic V, Srejovic I, Jeremic J, Andjic M, Tomovic M, Petkovic A, Jakovljevic V
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
NOVEL INSIGHT INTO THE ROLE OF *GALIUM VERUM L*. EXTRACT IN CARDIOPROTECTION DURING ISCHEMIA/REPERFUSION INJURY

11.00-11.15 Pause

Session 2: NOVEL PLANT COMPOUNDS AND APPLIED PHYSIOLOGY

Chairpersons: Ristic-Medic D, Ljujic B

11.15-11.30
Milosavljevic I, Cikiriz N, Jakovljevic B, Bolevich S, Jeremic J, Nikolic Turnic T, Mitrovic M, Srejovic I, Zivkovic V, Bolevich S, Jakovljevic V
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
THE INFLUENCES OF CHOKEBERRY EXTRACT SUPPLEMENTATION ON REDOX STATUS AND BODY COMPOSITION IN HANDBALL PLAYERS DURING COMPETITION PHASE - PILOT STUDY

11.30-11.45
Ljujic B, Stankovic M, Miletic-Kovacevic M, Gazdic Jankovic M, Pejnovic N, Lukic ML
Department of Genetics, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
CIRCULATING INTERLEUKIN-33 LEVELS RELATE TO PLAQUE STABILITY IN PATIENTS WITH CAROTID ATHEROSCLEROSIS

11.45-12.00
Vranic A, Antovic J, Veselinovic M, Pruner I, Petkovic A, Jakovljevic V, Antovic A
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
ALTERATIONS OF FIBRIN STRUCTURE IN WOMEN WITH RHUMATOID ATRHRITIS

12.00-12.15
Ristic-Medic D, Takic M, Zekovic M, Vucic V, Petrovic S, Arsic A, Radjen S
Centre of Research Excellence in Nutrition and Metabolism, Institute for Medical Research, University of Belgrade, Belgrade, Serbia
DIETARY ANTIOXIDANTS NUTRIENTS INTAKE IN PATIENTS WITH CHRONIC RENAL FAILURE

12.30 – Lunch

13.00 – Excursion to Oplenac and Topola

20.00 – Gala dinner

Saturday, June 22nd, 2019

Session 3: GASTROINTESTINAL, PULMONARY AND RENAL PHYSIOLOGY

Chairpersons: Calkovska A, Stojiljkovic N

09.30-09.45
Calkovska A, Nova Z, Topercerova J, Kolomaznik M, Kopincova J, Mokra D, Urbanova A, Mokry J, Skovierova H, Halasova E, Strnadel J
Department of Physiology, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Martin, Slovak Republic
COMPLEX EVALUATION OF THE EFFECT OF BACTERIAL LIPOPOLYSACCHARIDE ON RESPIRATORY SYSTEM IN THREE MODELS

09.45-10.00
Brankovic S, Gocmanac Ignjatovic M, Kostic M, Milutinovic M, Kitic N, Miladinovic B, Kitic D
Department of Physiology, Faculty of Medicine, University of Nis, Nis, Serbia
INFLUENCE OF AQUEOUS FENNEL STEM EXTRACT (*FOENICULUM VULGARE MILLER*) ON SMOOTH MUSCLES OF RAT ILEUM

10.00-10.15
Strbak V
Institute of Experimental Endocrinology, Biomedical Research Center, Slovak Academy of Sciences, Bratislava, Slovak Republic
ROLE OF PANCREATIC THYROTROPIN RELEASING HORMONE IN DIRECTING INSULIN SECRETION TO REGULATORY PATHWAY

10.15-10.30
Stojiljkovic N, Ilic S, Stojanovic N, Petkovic M
Department of Physiology, Faculty of Medicine, University of Nis, Nis, Serbia
ELLAGIC ACID PREVENTS CYCLOPHOSPHAMIDE-INDUCED RAT LIVER OXIDATIVE DAMAGE

10.30-10.45
Radonjic K, Jakovljevic V, Zivkovic V, Srejovic I, Nikolic Turnic T, Milosavljevic I, Jeremic J, Savic M, Sretenovic J, Bradic J, Novokmet S
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
TOXIC EFFECTS OF Ru(II) COMPLEX AND CISPLATIN ON LIVER AND KIDNEY FUNCTION OF WISTAR ALBINO RATS

10.45-11.00
Ilic S, Stojiljkovic N, Randjelovic P, Stojanovic N
Department of Physiology, Faculty of Medicine, University of Nis, Nis, Serbia
WINE COMPOUND QUERCETIN PROTECTS KIDNEY INJURIES CAUSED BY CISPLATIN IN RATS

11.00-11.15 Pause

Session 4: NEUROPHYSIOLOGY AND CELLULAR PHYSIOLOGY

Chairpersons: Jagla F, Rosic G

11.15-11.30
Jagla F
Centre of Experimental Medicine, Slovak Academy of Sciences, Institute of Normal and Pathological Physiology, Bratislava, Slovak Republic
ELECTROPHYSIOLOGICAL CORRELATES OF THE EXECUTIVE FUNCTIONINIG - SENSORIMOTOR INTEGRATION

11.30-11.45
Selakovic D, Jovicic N, Katanic J, Boroja T, Mihailovic V, Kumburovic I, Kumburovic D, Rosic G
Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
THE IMPACT OF ANTIOXIDANT SUPPLEMENTATION WITH *SATUREJA HORTENSIS* L. EXTRACT ON CISPLATIN-INDUCED BEHAVIORAL ALTERATIONS

11.45-12.00
Nesic M, Stankovic M
Department of Physiology, Faculty of Medicine, University of Nis, Nis, Serbia
FUNCTIONAL BRAIN ASYMMETRY IN FACIAL EMOTIONS RECOGNITION AND INDIVIDUAL DIFFERENCES

12.00-12.15
Sretenovic J, Zivkovic V, Srejovic I, Ajdzanovic V, Milosevic V, Milosavljevic Z, Jakovljevic V
Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
MORPHOMETRIC ANALISYS OF PITUITARY GONADOTROPIC CELLS AFTER ADMINISTRATION OF NANDROLONE DECANOATE AND SWIMMING IN ADULT RATS

12.15-12.30
Besterciova D, Rovny R, Marko M, Riecansky I
Institute of Normal and Pathological Physiology, Centre of Experimental Medicine Slovak Academy of Sciences, Bratislava, Slovak Republic
THE ROLE OF THE CEREBELLUM IN MODULATING ACOUSTIC STARTLE RESPONSE

12.30-12.45
Sreckovic N, Matic S, Katanic J, Stanic S, Mihailovic V
Department of Chemistry, Faculty of Science, University of Kragujevac, Kragujevac, Serbia
LYTHRUM SALICARIA L. EXTRACTS AND THEIR PHENOLIC COMPOUNDS IN PREVENTION OF OXIDATIVE DNA DAMAGE

12.45-13.00
Tomovic M, Bradic J, Zivkovic V, Srejovic I, Andjic M, Petkovic A, Jakovljevic V
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
CHEMICAL COMPOSITION AND ANTIOXIDANT ACTIVITY OF *ALLIUM URSINUM L.* EXTRACTS

13.00-13.15 Pause

13.15-15.00
Poster Session (5 min poster presentation with discussion)

Chairpersons: Nesic M, Gazdic Jankovic M, Selakovic D, Milosavljevic I

Andjic M, Draginic N, Radoman K, Jeremic J, Nikolic Turnic T, Srejovic I, Zivkovic V, Kovacevic M, Bolevich S, Jakovljevic V
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
THE EFFECTS OF CHRONIC EVENING PRIMROSE OIL ON THE CARDIODYNAMICS PARAMETERS OF MALE AND FEMALE RATS

Arsic A, Kojadinovic M, Petrovic S, Ristic Medic D, Glibetic M, Vucic V
Center of Research Excellence in Nutrition and Metabolism, Institute for Medical Research, Belgrade, Serbia
SHORT TERM CONSUMPTION OF POMEGRANATE JUICE DECREASES LDL-CHOLESTEROL AND DIASTOLIC BLOOD PRESSURE IN SUBJECTS WITH METABOLIC SYNDROME

Barak O, Janjic N, Drvis I, Mijacika T, Mudnic I, Thom S, Yang M, Madic D, Dujic Z
Faculty of Medicine, University of Novi Sad, Serbia
VASCULAR DYSFUNCTION FOLLOWING BREATH-HOLD DIVING

Dayar E, Cebova M, Kosutova M, Pechanova O
Centre of Experimental Medicine, Slovak Academy of Sciences, Bratislava, Slovak Republic
EFFECTS OF CORNELIAN CHERRIES ON NITRIC OXIDE SYNTHASE ACTIVITY IN THE HEART AND AORTA OF OBESE ZUCKER RATS

Draginic N, Andjic M, Radoman K, Jeremic J, Bradic J, Nikolic Turnic T, Srejovic I, Zivkovic V, Bolevich S, Jakovljevic V
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
CHRONIC FLAXSEED OIL TREATMENT DOES NOT AFFECT CARDIODYNAMICS IN ISOLATED HEART MODEL INDEPENDENTLY OF GENDER

Gocmanac-Ignjatovic M, Brankovic S, Mihailov-Krstev T, Kitic D, Kostc M, Milutinovic M, Miladinovic B
Department of Physiology, Faculty of Medicine, University of Nis, Nis, Serbia
INVESTIGATION OF ANTIMICROBIAL ACTIVITY OF ESSENTIAL OIL AND METHANOL EXTRACTS OF FENNEL FRUIT (*FOENICULUM VULGARE MILLER*)

Golas S, Berenyiova A, Cacanyiova S
Institute of Normal and Pathological Physiology, Center of Experimental Medicine Slovak Academy of Sciences, Bratislava, Slovak Republic
THE ROLE OF PERIVASCULAR ADIPOSE TISSUE AND ENDOGENOUS H_2S IN VASOACTIVE RESPONSES OF MESENTERIC ARTERY IN NORMOTENSIVE AND SPONTANOUSLY HYPERTENSIVE RATS

Jakovljevic Uzelac J, Mutavdzin S, Stankovic S, Labudovic Borovic M, Milic N, Simic T, Djuric D
Institute of Medical Physiology "Richard Burian", Faculty of Medicine, University of Belgrade, Belgrade, Serbia
CARDIAC OXIDATIVE STRESS PARAMETERS AND CARDIOMETABOLIC MARKERS IN MONOCROTALINE-INDUCED HEART FAILURE IN WISTAR ALBINO RATS: INFLUENCE OF SUBCHRONIC VITAMIN B6 APPLICATION

Kolomaznik M, Kopincova J, Topercerova J, Matasova K Jr, Mikolka P, Kosutova P, Zila I, Mokra D, Calkovska A.
Division of Respirology, Martin Biomedical Centre, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Martin, Slovak Republic
N-ACETYLCYSTEINE REDUCES INFLAMMATION AND OXIDATIVE STRESS IN DOUBLE-HIT MODEL OF LUNG INJURY IN RATS

Maricic M, Janjic N, Zubnar A, Karan V, Drapšin M, Klasnja A
Department of Physiology, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
EFFECTS OF TRAINING AND DETRAINING ON MUSCLE STRENGTH IN ROWERS

Mazgutova N, Mikolka P, Czippelova B, Krohova J, Wiszt R, Kosutova P, Pozorciakova K, Ciljakova M, Javorka M
Biomedical Center Martin and Department of Physiology, Jessenius Faculty of Medicine, Comenius University, Martin, Slovak Republic
OXIDATIVE DAMAGE AND ANTIOXIDANT CAPACITY IN OBESE AND OVERWEIGHT ADOLESCENTS

Miletic-Kovacevic M, Pejnovic N, Jovicic N, Gazdic Jankovic M, Lukic M, Kovacevic V, Ljujic B
Department of Histology and embryology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
ROLE OF GALECTIN 3 ON THE COLLAGEN DEPOSITION DEGREE IN HEART TISSUE OF MICE SUFFERING FROM AUTOIMMUNE MYOCARDITIS

Miloradovic Z, Jovovic Dj, Mihailovic-Stanojevic N, Ivanov M, Vajic JU, Karanovic D, Grujic Milanovic J
Institute for Medical Research, University of Belgrade, Serbia
SUPPLEMENTATION OF *OLEA EUROPEA* L. LEAF EXCTRACT DIFFERENTLY AFFECTS SPONTANEOUSLY VERSUS MALIGNANT HYPERTENSIVE RATS

Radovic S, Starovlah I, Nef S, Kostic T, Andric S
Laboratory for Reproductive Endocrinology and Signaling, Laboratory for Chronobiology and Aging, Centre of Excellence CeRES, Faculty of Sciences, University of Novi Sad, Novi Sad, Serbia
FEMINIZATION OF PROGENITOR AND MATURE ADULT LEYDIG CELLS LACKING INSULIN AND IGF1 RECEPTORS

Rankovic M, Bradic J, Radonjic K, Srejovic I, Zivkovic V, Jeremic N, Jakovljevic V
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
DIFFERENCE IN CARDIOTOXICITY INDUCED BY DOXORUBICIN IN MALE AND FEMALE RATS

Ravic M, Plecevic S, Bolevich S, Jeremic J, Bolevich S, Nikolic Turnic T, Jakovljevic V, Jeremic N
Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
SWIMMING ATTENUATES BLOOD PRESSURE AND OXIDATIVE STRESS IN HIGH SALT-INDUCED HYPERTENSIVE RATS

Starovlah I, Radovic S, Kostic T, Andric S
Laboratory for Reproductive Endocrinology and Signaling, Laboratory for Chronobiology and Aging, Centre of Excellence CeRES, Faculty of Sciences, University of Novi Sad, Novi Sad, Serbia
SIGNALING PATHWAYS REGULATING THE MITOCHONDRIAL DYNAMIC AND ACROSOMAL REACTION ARE DISTURBED IN SPERMATOZOA FROM STRESSED ADULT RATS

Stojanovic M, Todorovic D, Mitrovic D, Scepanovic V, Scepanovic R, Scepanovic T, Borozan S, Dragutinovic V, Scepanovic Lj
Institute of Medical Physiology „Richard Burian", Faculty of Medicine, University of Belgrade, Belgrade,
EFFECTS OF SULFUR-CONTAINING AMINO ACIDS ON ACTIVITY OF ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE IN DIGESTIVE SYSTEM OF RATS

Stojanovic N, Stojiljkovic N, Ilic S, Stojanovic S, Randjelovic P
Faculty of Medicine, University of Nis, Nis, Serbia
OLIVE LEAF GLYCOSYLATED SECO-IRIDOID-PHENOL OLEUROPEIN DOES NOT AFFECT MADIN-DARBY CANINE KIDNEY (MDCK) CELL VIABILITY AND LYSOSOMAL FUNCTION

Zubnar A, Nikolic S, Ilincic B, Cabarkapa V, Janjic N, Maricic M, Slavic D, Rakovac A, Karaba Jakovljevic D
Department of Physiology, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
EFFECTS OF VITAMIN D LEVELS ON GLUCOREGULATORY PARAMETERS IN TYPE 2 DIABETES MELLITUS

*** Surnames are given following alphabetical order.*

ABSTRACTS

POLYPHENOL-RICH RED WINE EXTRACT: FROM GENTLE PREPARATION TO BIOMEDICAL ANALYSIS

Pechanova O, Barta A, Cebova M
Centre of Experimental Medicine, Slovak Academy of Sciences, Bratislava, Slovak Republic

The main drawback of using red wine as curative and/or preventive substance is its alcohol content. A simple thermal evaporation removes alcohol, but leads to the production of unidentifiable cleavage products and significant reduction in thermolabile polyphenols. The disadvantage of powder extract received by lyophilzation is its poor solubility in the water due to irreversible changes in colloidal substances. Thus, we have suggested and made a simple device for gentle preparation of polyphenol-rich red wine extract. Furthermore, we used this device for preparation of Alibernet red wine extract (AWE) and we characterized it from the chemical (polyphenolic content, total antioxidant capacity) and biomedical (effects on hypertensive, obese rats) points of view. Briefly, the main part of the device is slowly rotating discs, the lower part of which is immersed in the wine. The fan drives a drying air and the fluid is stretched over the surface of the disks and subsequently evaporates through the large area thus obtained. Evaporation rate is dependent on the number of discs and their total area. AWE obtained in this way was a non-alcoholic, slightly syrupy dark red liquid which, as confirmed by the analysis (GAE/ml), contains tenfold concentrations of polyphenols and ten times higher antioxidant capacity than original wine. Three weeks of treatment of hypertensive, obese rats with AWE led to significant decrease of their serum glucose and trigycerides and pro-inflammatory markers like iNOS and NF-kappaB as well. This confirms that the concentration of wine by this method allows a gentle production of wine extract which is suitable for further use as a food supplement.

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POLYPHENOLS: FROM BASIC TO APPLIED INVESTIGATIONS

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This abstract presents summary of our recent basic and applied investigations regarding the research of different polyphenolic compounds on both animals and humans. We aimed to assess the direct and acute influence of provinols on cardiac function using an isolated rat heart model and showed that provinols may have a beneficial effect on the intact myocardium and coronary circulation. Furhermore, we evaluate the effects of standardized *Aronia melanocarpa* extract (SAE), as a polyphenol-rich diet in rats with metabolic syndrome (MetS). This research involved rats divided randomly into six groups: control with standard diet (Sd), control with Sd and SAE, MetS with (high-fat diet) HFd, MetS with HFd and SAE, MetS with Sd and MetS with Sd and SAE during 4 weeks. After the 4-week protocol, cardiac function, systemic redox state, blood glucose levels and lipid profile were estimated. Our results indicate favorable effects of SAE on heart function, lipid status and attenuation of oxidative stress in rats with MetS, with more prominent impact achieved in combination with Sd. Promising findings of our research suggest cardioprotective potential of SAE supplementation in rats with MetS. In the other study we estimated the impact of 12-week SAE supplementation on lipid profile, oxidative stress markers and routine biochemical parameters in active handball players. Protective effects of SAE supplementation were dominantly manifested by decrease in the level of pro-oxidants, elevation of capacity of antioxidant defense system and increase in high density lipoprotein level. Observed beneficial impact of polyphenols in both rats and athletes provide basis for future studies, which are neccessary to reveal the overall effects of polyphenol consumption.

PRECONDITIONING WITH *ALLIUM URSINUM* AS A NEW TOOL FOR FUNCIONAL RECOVERY OF ISOLATED RAT HEART: FOCUS ON HYPERTENSION

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Taken into consideration that the impact of *Allium ursinum (A.ursinum)* on the cardiac mucle, especially in hypertensive conditions, is almost unkown the goal of this research was to assess the effects of methanol extract of this plant on myocardial ischemia-reperfusion injury in spontaneously hypertensive rats. Twenty male Wistar Kyoto rats were randomly divided into two groups: control and *A.ursinum* group, which included animals treated with 500 mg/kg body weight of the methanol extract of *A.ursinum per os* for 4 weeks. At the end of the treatment hearts from animals in both groups were excised and retrogradely perfused according to the *Langendorff* technique at constant perfusion pressure of 70 cmH_2O. After stabilization period hearts were subjected to 20 minutes ischemia followed by 30 minutes reperfusion. The following parameters of cardiac function were continuously measured: the maximum (dp/dt max) and minimum (dp/dt min) rate of pressure development, systolic (SLVP) and diastolic (DLVP) left vertical pressure and heart rate (HR) were registered. Coronary flow was measured flowmetrically. Levels of superoxide anion redical, hydrogen peroxide, nitrites and index of lipid peroxidation (measured as thiobarbituric acid reactive substances- TBARS) were determined spectrophotometrically in coronary venous effluent. Our results have shown that preconditioning with *A.ursinum* could be promising tool for diminishing of ischemia-reperfusion injury in rat heart in the hypertensive conditions. These findings may be of interest for designing of future basic and clinical investigations in this field.

THE EFFECTS OF PYRIDOXINE ADMINISTRATION ON CARDIAC OXIDATIVE STRESS AND MATRIX MELTALOPROTEINASES IN STREPTOZOTOCIN INDUCED DIABETES MELLITUS IN WISTAR ALBINO RATS

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The aims of this study were examination of antioxidant enzymes (superoxide dismutase (SOD) and catalase (CAT)) activities, and relative activities of matrix metalloproteinase (MMP)-2 and 9 in the cardiac tissue of diabetic *Wistar* male rats, and the effects of pyridoxine administration. There were five groups: C1 – control (physiological saline 1 ml/kg, i.p. one day), C2 – control with daily physiological saline treatment (1 ml/kg, i.p. 28 days), DM – diabetes mellitus (streptozotocin (STZ) 100 mg/kg in physiological saline, i.p., one day), P – pyridoxine (7 mg/kg, i.p. 28 days), and DM + P – diabetes mellitus and pyridoxine group (STZ 100 mg/kg, i.p. one day and pyridoxine 7 mg/kg, i.p. 28 days). After four weeks, the serum (glucose, insulin, homocysteine) parameters and cardiac tissue enzymes activities were measured. All STZ treated animals had elevated glucose level and insulin level was lowered in the DM group. Homocysteine was significantly decreased in the DM + P group. Both SOD and CAT activities were elevated in the DM group while pyridoxine treatment reduced CAT activity. MMP-2 relative activity was increased in the DM and DM + P groups; however it was decreased in the P group. MMP-9 activity was decreased in the DM, while pyridoxine increased its activity. Increased activities of SOD and CAT and altered MMP activities during four week period may be the consequence of oxidative stress caused by DM. Administration of the pyridoxine reduced CAT activity and increased MMP-9 activity, so it can be concluded that pyridoxine has potential beneficial effects in diabetic rats.

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EFFECTS OF *GALIUM VERUM* EXTRACT AGAINST ISCHEMIA-REPERFUSION INJURU IN ISOLATED RAT HEART

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Beside the widespread traditional use of *Galium verum (G. verum)* in the treatment of numerous diseases and conditions, it's effects on heart function and redox status has still not been fully clarified. Therefore the aim of our study was to examine the effects of methanol extract of *G. verum* on ischemia-reperfusion (I/R) injury in isolated rat heart. Twenty male Wistar albino rats were randomly divided into two groups: control and *G. verum* group, which included animals treated with 500 mg/kg body weight of the methanol extract of *G. verum per os* for 4 weeks. At the end of the treatment hearts from animals in both groups were excised and retrogradely perfused according to the *Langendorff* technique at constant perfusion preassure of 70 cmH_2O. After stabilization period hearts were subjected to 20 minutes ischemia followed by 30 minutes reperfusion. The parameters of cardiac function including the maximum and minimum rate of pressure development, systolic and dyastolic left ventricular pressure and heart rate were registered. Coronary flow was measured flowmetrically. Levels of superoxide anion radical, hydrogen peroxide, nitrites and index of lipid peroxidation (measured as thiobarbituric acid reactive substances- TBARS) were determined spectrophotometrically in coronary venous effluent. Our results demonstrated that treatment with methanol extract of *G. verum* preserved cardiac contractility, systolic and diastolic function and diminished production of pro-oxidants. Promising potential of *G. verum* in the present study in a model of pharmacological preconditioning may be a starting point for future researches, which would fully reveal effects of this plant on cardiac function and redox status in various models of I/R injury.

EFFECT OF QUERCETIN ON PROTEINS OF ANTIOXIDANT DEFENSE SYSTEM AND ABC TRANSPORTERS IN RAT HEARTS

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The flavonoid quercetin (QCT) is widely distributed in the form of glycosides in components of the human diet. In the present study, we analyzed the effects of chronic administration of QCT on SOD and members of ABC transporters family (P-glycoprotein, MRP1) in the left (LV) and right ventricle (RV) of rat heart. The effects of QCT were studied in male Wistar control rats and in rats exposed to treatment with doxorubicin (DOX). We found that in both LV and RV, QCT increased SOD activities in control animals, while no changes were observed in DOX-treated rats. Protein levels of SOD isoforms were not changed in LV of control hearts. On the other hand, in LV of DOX-treated hearts QCT significantly attenuated DOX-induced down-regulation of SOD2. In RV of control hearts were effects of QCT associated with up-regulation of SOD2. The investigation of effects of QCT on MRP-1 and P-glycoprotein showed that their levels were increased in LV of control hearts. In RV we observed only up-regulation of MRP-1. Increased MRP-1 levels we found also in LV of DOX-treated rat hearts and co-treatment with QCT further potentiated the MRP-1 up-regulation. The data point to the possible important role of SOD and ABC transporters in processes associated with prolonged effects of QCT and DOX.

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PRECONDITIONING WITH HYPERBARIC OXYGEN AND CALCIUM CHANNEL MODULATORS IN RAT HEART

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This study was aimed to establish the impact of combined therapy with hyperbaric oxygen (HBO2) therapy and verapamil or amlodipine on functional recovery and oxidative stress markers after ischemia in the isolated rat heart. The study included 36 rats (Wistar albino, male gender, eight weeks old, body weight 200 ± 50g). All animals were exposed to HBO2 treatment over 14 days. Afterwards hearts were excised and perfused according to Langendorff technique at a constant coronary pressure of 70 cm H_2O. After stabilization period the hearts were divided into the following groups: HBO2 group (animals exposed to only HBO2 preconditioning); HBO2 + verapamil; HBO2 + amlodipine (animals pretreated with HBO2 and appropriate pharmacological agent). Thereafter, hearts in all groups were subjected to 20-minute global ischemia and 30-minute reperfusion. Parameters of heart function were registered, including maximum and minimum rate of pressure development, systolic and diastolic left ventricular pressure, heart rate and coronary flow. Levels of pro-oxidants such as index of lipid peroxidation, measured as thiobarbituric acid-reactive substances, nitrites, levels of superoxide anion radicals and hydrogen peroxide were determined in coronary venous effluent. Obtained results clearly indicate that blockage of calcium channel in combination with HBO2 prevented ischemia/reperfusion-induced cardiac deleterious effects, thus contributing to improvement of functional recovery of the heart. However, future studies are certainly necessary for better understanding the mechanisms through which combination of these two maneuvers of preconditioning triggers cardioprotection.

NOVEL INSIGHT INTO THE ROLE OF *GALIUM VERUM L.* EXTRACT IN CARDIOPROTECTION DURING ISCHEMIA/REPERFUSION INJURY

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The present study aimed to assess the effects of methanol extract of *Galium verum L.* (*G. verum)* on myocardial ischemia/reperfusion (I/R) injury. Thirty male Wistar abino rats were randomly assigned into three groups: control and rats treated with *G. verum* extract (250 and 125 mg/kg per os) for 4 weeks. After the treatment, animals were sacrificed, hearts were excised and retrogradely perfused according to the Langendorff technique at constant perfusion pressure of 70 cmH_2O. After stabilization, hearts were subjected to 20-minute ischemia and 30-minute reperfusion. Following parameters of cardiac function were registered: maximum and minimum rate of pressure development, systolic and diastolic left ventricular pressure, heart rate and coronary flow. Additionally, cardiac pro-oxidant markers involving superoxide anion radical, hydrogen peroxide, nitrites and index of lipid peroxidaton were estimated. Our results demonstrated that *G. verum* extract preserved cardiac contractility and relaxation and prevented ischemia-induced deterioration of systolic function. Furthermore, *G. verum* extracts alleviated cardiac production of pro-oxidants with more prominent influence achieved with higher dose. Promising results of our study suggest possible role of *G. verum* in triggering cardioprotection, however further studies are necessary to fully reveal therapeutic possibilities of this plant species.

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

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The aim of 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 is consisted of morphofunctional and biochemical testing before and during the supplementation. After three months treatment with dietary supplement contains extract of chokeberry we noticed significant changes in three main ways. After the treatment with chokberry extract the levels of pro-oxidants were decreased, and on contrary the levels of antioxidant enzymes were increased. Additionally, 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 shows that use of dietary supplement with chokeberry extract induces a wide range of beneficial effects in examined group of athletes.

CIRCULATING INTERLEUKIN-33 LEVELS RELATE TO PLAQUE STABILITY IN PATIENTS WITH CAROTID ATHEROSCLEROSIS

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IL-33 is a dual function cytokine with roles in chronic inflammation and fibrosis. The importance of IL-33 in the pathogenesis of carotid atherosclerosis is not defined. We aimed to investigate the circulating IL-33 levels in patients undergoing endarecteromy and their association with carotid plaque structure, degree of carotid stenosis and neurosymptoms. 199 consecutive patients with atherosclerotic carotid stenosis, hospitalized for carotid endarterectomy, and 30 healthy subjects were enrolled in this study. The patients selected for endarterectomy were either symptomatic or asymptomatic. Histopathologic analyses of atherosclerotic carotid plaques were performed to determine plaque types according to AHA classification. Circulating IL-33 levels were determined by ELISA from serum taken prior to surgery. Association between demographic, clinical, cardiovascular risk factors and grade of carotid stenosis, stable/unstable carotid plaques and neurologic events of a study population was analyzed. IL-33 serum levels were significantly higher ($p<0.05$) in patients with stable plaques compared to patients with unstable plaques, however there were no differences ($p>0.05$) in serum level of IL-33 between patients with different grade of carotid stenosis as well as between symptomatic and asymptomatic patients. When serum IL-33 level was analyzed in relation to histological features of the carotid plaques the highest level of IL-33 was found in the group of patients with fibrotic plaques Vc (537.1±178.0 pg/ml), followed by those with fibroatheromatous plaques Va (338.5±152.9 pg/ml). The lowest serum level of IL-33 was detected in the group of patients with atheroma IV (23.7±7.6 pg/ml). Circulating IL-33 is related to carotid plaque stability.

ALTERATIONS OF FIBRIN STRUCTURE IN WOMEN WITH RHUMATOID ATRHRITIS

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To assess fibrin structure in female patients with established rheumatoid arthritis (RA) in relation to menopausal status. Ninety women were included in the study, 42 RA 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. All patients were treated with the standard treatment protocol (methotrexate and prednisolone). Parameters of fibrin structure (lag time, Max Abs, Slope, Max Abs time, Slope time) were measured by clot turbidity and clot lysis time (CLT) was also determined. Moreover, electron microscopy of fibrin clots was performed. All participants were divided in two subgroups according to menopause: (1) premenopausal controls (n=14); (2) postmenopausal controls (n=34); (3) premenopausal patients (n=11); (4) postmenopausal patients (n=31). Premenopausal controls in the subgroup 1 differed significantly from all other subgroups by the longer lag time and Max Abs time ($p<0.05$), lower Max Abs ($p<0.05$) and higher Slope values ($p<0.05$), while CLT was reduced ($p<0.05$). In premenopausal controls fibrin clots were composed of thicker fibers, had larger pores with lower density, so-called looser structure, which is more susceptible to fibrinolysis. On the other hand, postmenopausal controls and both pre- and postmenopausal patients had denser fibrin clots composed of thinner fibers with smaller intrinsic pores. Premenopausal patients with established RA had impaired fibrin structure compared to control subjects, which resembled the clot structure in postmenopausal patients. Larger studies are mandatory to confirm these preliminary findings.

DIETARY ANTIOXIDANTS NUTRIENTS INTAKE IN PATIENTS WITH CHRONIC RENAL FAILURE

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Oxidative stress plays a key role in numerous disease processes including chronic renal disease. The body has developed a sophisticated antioxidant system that depends on antioxidant nutrients. Certain nutrients serve as antioxidants or are components of antioxidant enzymes. Antioxidants include vitamins C and E, carotenoids, and antioxidant enzymes containing Se, Cu, Fe or Zn. Therefore, the aim of our study was to determine the intake of nutrients important for the antioxidant status up to now in 73 patients with chronic renal failure (CRF). The study was designed as a cross-sectional study. We used 24-hour dietary recall as assessment method for daily nutrition intake, two days during the working week and one day for the weekend in 34 pre-dyalysis patients (CRF stage 3-5), and in 37 hemodialysis patients at dialysis day, the day after the dialysis and one day for the weekend. Dietary questionnaires were processed using Diet Assess & Plan, advanced nutritional software tool. Consumption data was converted to nutrient intake estimates according to Serbian Food Composition Database. Mean daily intake of vitamins C and A, and minerals Cu and Fe were below recommendations in patients. There was no significant difference in vitamins C, E, A, and minerals Se, Cu, Fe, Zn intake from food in pre-dyalysis and hemodialysis patients. Adequate dietary intervention with point on antioxidant nutrients intake is necessary for patients with CRF.

COMPLEX EVALUATION OF THE EFFECT OF BACTERIAL LIPOPOLYSACCHARIDE ON RESPIRATORY SYSTEM IN THREE MODELS

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The respiratory system is permanently exposed to bacterial lipopolysaccharide (LPS) called endotoxin. LPS may impair cell survival, induce inflammation and oxidative stress, influence airway smooth muscle (ASM) tone and modulate surfactant production. Main objective is to investigate the mechanisms related to acute lung injury including pulmonary surfactant inactivation after endotoxin-challenge and to study the effects of its treatment by exogenous surfactant combined with antiinflammatory/antioxidant drugs using three *in vivo* and *ex vivo* models: 1. by culturing alveolar epithelial cells (human lung carcinoma A549 cells) and pulmonary capillary endothelial cells, 2. by method of tissue baths to evaluate ASM tone and 3.in rats with pulmonary surfactant inactivation after intratracheal and intravenous endotoxin administration. Partial results show, that A549 cells are relatively resistant to LPS and maintain their integrity even at high LPS concentrations. LPS modulates surfactant protein (SP) gene expression in dose and time-dependent manner. Long term cultured A549 cells seem to produce larger amount of surfactant than short term cells. Moreover, LPS-induced SPs gene expression is modulated in different way. The exogenous surfactant has relaxing effect on the ASM, but does not reverse LPS-induced smooth muscle contraction. Indomethacin inhibits production of bronchodilator prostaglandins and results in an increase of methacholine response of ASM exposed to LPS *in vitro*. Data indicate the involvement of leukotriene and H_1 receptors in airway contractile mechanisms in presence of LPS. Conclusion: study yields in comprehensive picture on the effect of endotoxin on respiratory system and possible therapeutic options.

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INFLUENCE OF AQUEOUS FENNEL STEM EXTRACT (*FOENICULUM VULGARE MILLER*) ON SMOOTH MUSCLES OF RAT ILEUM

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Fennel (*Foeniculum vulgare* Miller) is a member of the Apiaceae family and has been traditionally used both as a medicinal plant and as a spice. The aim of this study was to investigate the effects of aqueous extract of fennel stem on the spontaneous contractions, acetylcholine and potassium chloride induced contractions of the isolated rat ileum *in vitro.* In this study *Wistar* albino rats (200-250 g) were used. The ileum portions were mounted in tissue baths. The aqueous extract of fennel stem was tested for spasmolytic activity using different experimental models: against spontaneous contractions and contractions induced with acetylcholine and potassium chloride. The aqueous extract of fennel stem exhibited dose-dependent effect in all experimental models. Cumulative concentrations of extract of fennel (0.01-3 mg/ml) induced a relaxant effect on spontaneous rat ileum contractions and showed the marked spasmolytic effect. The aqueous extract of fennel stem (1-3mg/ml) also induced a significant depression of the cumulative concentration response curve for acetylcholine (5–1500 nM). The extract of fennel significantly reduced the rat ileum contractions induced by potassium chloride. The results show that the aqueous extract of fennel stem exhibited significant and dose-dependent spasmolytic activity on the spontaneous, acetylcholine and KCl induced rat ileum contractions.

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ROLE OF PANCREATIC THYROTROPIN RELEASING HORMONE IN DIRECTING INSULIN SECRETION TO REGULATORY PATHWAY

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Thyrotropin releasing hormone (TRH; pGlu-His-ProNH2) is colocalized in pancreatic β cells in secretory granules with insulin. TRH secretion from pancreatic islets is stimulated by glucose and inhibited by insulin. Disruption of the TRH gene in knockout mice results in hyperglycemia accompanied by impaired insulin secretory response to glucose. To understand role of TRH we blocked the last step of biosynthesis of α-amidated peptides, including TRH by disulfiram (DS) treatment of adult male rats subcutaneously with 200 mg/kg for five days. TRH in physiological concentration (1 nM) does not affect basal insulin secretion from intact islets. In contrast, basal insulin secretion from islets of DS-treated rats is four times higher compared to controls and could not be stimulated by high-glucose. The addition of 1 nM TRH into medium decreased immediately basal insulin secretion in DS (TRH lacking) islets to control level and normalized also their response to glucose. Absence of the secretory response to glucose in islets from TRH depleted rats is connected with their increase of insulin content. Glucose stimulation together with 1 nM TRH normalized also insulin content in DS islets. Apparently, high insulin content in islets from TRH depleted animals is a result of block of regulatory secretion pathway which is corrected by the addition of TRH. In conclusion, presence of TRH in β-cells ensures appropriate low basal (constitutive) insulin secretion and high response to stimulation. Release of TRH induced by glucose has autocrine effect resulting in directing insulin secretion to regulatory pathway.

ELLAGIC ACID PREVENTS CYCLOPHOSPHAMIDE-INDUCED RAT LIVER OXIDATIVE DAMAGE

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In this study we aimed to evaluate effects of ellagic acid (EA) in preventing cyclophosphamide-induced liver damage. The protective effect of EA was determined based on serum liver function, liver tissue antioxidative capacities and oxidative tissue damage parameters. Also, tissue morphological changes following cyclophosphamide administration were studied using standard histopathological and immunohistochemical analysis. Experimental protocol included 3 groups of 6 rats treated daily by an intraperitoneal injection (*i.p.*), as following: ellagic acid (EA) group - the animals were given EA (10 mg/kg) for 5 days; cyclophosphamide (CP) group - the animals were given CP (200 mg/kg) at 3rd day of experiment; ellagic acid-cyclophosphamide (EACP) group - the animals were given CP (200 mg/kg) at 3rd day of experiment and EA (10 mg/kg) for 5 days. Applied EA was found to prevent rat liver damage induced by cyclophosphamide estimated through the changes in serum liver damage parameters and tissue antioxidant capacities, as well as based on oxidatively modified lipids and proteins. Also, changes in morphology of liver cells and the expression of Bcl-2, HIF-1α and CD15 molecules in livers of animals of different experimental groups are in accordance with the obtained biochemical parameters. The results of our study also indicate that ellagic acid can be used as a supporting agent in clinical practice in patients treated with cyclophosphamide.

TOXIC EFFECTS OF Ru(II) COMPLEX AND CISPLATIN ON LIVER AND KIDNEY FUNCTION OF WISTAR ALBINO RATS

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Ruthenium complexes have been extensively investigated for the design of new antitumor ruthenium-based drugs as alternatives to cisplatin, due to drug resistance and side effects (including hepatotoxicity and nephrotoxicity). The objective of the present study was to evaluate the effects of [Ru(Cl-tpy)(en)Cl][Cl] and cisplatin (reference compound) on serum biochemical parameters of liver and kidney function. The levels of AST and ALT (markers of hepatotoxicity), as well as levels of urea and creatinine (markers of nephrotoxicity) were assessed spectrophotometrically in 36 male Wistar albino rats (8 weeks old, BW 200-250 g, n=12 animals per group). Rats were chronically treated for 4 weeks with [Ru(Cl-tpy)(en)Cl][Cl] (4 mg/kg/week), cisplatin (4 mg/kg/week) and saline (4 mL/kg/week). Our results showed that the levels of AST did not significantly differ between groups, while ALT levels were significantly increased in ruthenium group compared to cisplatin and control group. The levels of urea did not significantly differ between groups, while levels of creatinine were significantly elevated in cisplatin group compared to ruthenium and control group. The results indicates that ruthenium compounds offer the potential of reduced toxicity and may help in tuning the systemic toxicity of ruthenium(II) complexes, as potential antitumor metallodrug.

WINE COMPOUND QUERCETIN PROTECTS KIDNEY INJURIES CAUSED BY CISPLATIN IN RATS

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Quercetin is natural polyphenolic flavonoid present in high concentration in red wine and plenty of fruits and vegetables. Because it's powerful antioxidant and cytoprotective effects, the aim of our study was to investigate the possible effect of quercetin on cisplatin-induced nephrotoxicity in rats. Experiments were done on twenty four male Wistar rats in 4 groups. The CIS group received a single dose of cisplatin (8 mg/kg) intraperitoneally, whereas the CISQ group received quercetin intraperitoneally at a dose of 50 mg/kg for 9 days and a single dose of cisplatin intraperitoneally (8 mg/kg). Animals in the Q group received quercetin (50 mg/kg) and the C group received saline (1 mL/day), both given intraperitoneally for 9 days. Quantitative evaluation of structural and functional alterations in the kidneys was performed by measuring biochemical and parameters of oxidative stress and by histological and morphometric examination of kidneys. Quercetin showed a significant protective effect by decreasing serum levels of creatinine and urea, elevating catalase activity and decreasing concentrations of AOPP and MDA in kidney tissue. Histological sections of kidney showed that quercetin ameliorated degenerative changes of proximal tubules and focal apoptosis of tubulocites. Quercetin also reduced histopathological changes of glomeruli and glomerular basement membrane. Morphometric analysis revealed statistically significant differences in the size of glomeruli (area, perimeter, Feret´s diameter), glomerular basement membrane thickness and cellularity of glomeruli between CIS and CISQ group. The results suggest that quercetin ameliorates oxidative stress and has the nephroprotective action which might be clinically useful.

ELECTROPHYSIOLOGICAL CORRELATES OF THE EXECUTIVE FUNCTIONINIG - SENSORIMOTOR INTEGRATION

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Many contributions are published now in the scientific literature pointing to lifestyle modification as activating nitric oxide synthases. Such modifications can positively affect the cardiovascular and nervous system functioning. Proposed modifications are recommended for early pathophysiological/reversible stages primarily. Results with animal models are really very impressive. There are troubles to manifest similar changes in human studies. Among such lifestyle modifications the nutritional changes are recommended. Nowadays, quite a lot of nutritional supplements, even as the bonuses for several specialized programs of physical fitness trainings are at disposal. Among them, the polyphenols may be mentioned as most frequently discussed in prospective human/clinical studies also. They are commended as regulatory promoters of **i**nterrelations among oxidative stress, lifestyle, nutrition and cognition. The use of the standard human psychophysiological methods can reveal valid indicators of desired effects. The electrophysiological markers of sensorimotor integration may help. This integration form the basis for executive functions which refer to the higher-level cognitive skills used to control and coordinate human cognitive abilities and behaviour. The visual-oculomotor integration reflects the impact on the intentionally as well as reflexively triggered central regulations and also the increase of the overall brain cortex activity. Such an approach may offer more informative correlates of the impact of polyphenol based lifestyle modification as well as to follow the long-term impact on the physical health and cognitive changes.

THE IMPACT OF ANTIOXIDANT SUPPLEMENTATION WITH *SATUREJA HORTENSIS* L. EXTRACT ON CISPLATIN-INDUCED BEHAVIORAL ALTERATIONS

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Cisplatin toxicities are usually accompanied by tissue oxidative damage and cell apoptosis. Anxiogenic effect (neurotoxic manifestation of cisplatin administration) also appears along with the increase in oxidative stress and apoptotic indicators in the hippocamus. Thirty-five Wistar albino male rats were divided into seven groups: control, cisplatin (received a single dose of cisplatin – 7.5 mg/kg), three groups with oral administration of *Satureja hortensis* L. methanolic extract (SH) (low – 50, middle – 100, and high dose – 200 mg/kg) along with cisplatin application and a group with the extract in high dose alone, and a silymarin group (cisplatin and silymarin – 100 mg/kg) for 10-day pretreatment, in order to evaluate the antioxidant effects of SH on cisplatin-induced increase on the anxiety level. The behavioral testing was performed in the open field, the elevated plus maze and tail-suspension test, followed by an investigation of oxidative stress and apoptosis parameters in the hippocampus. Cisplatin administration resulted in anxiogenic-like behavior, increased lipid peroxidation and proapoptotic markers accompanied by the decline in antioxidant and antiapoptotic defense. With no effect when applied solely, when applied along with cisplatin, SH (100 mg/kg) induced the significant anxiolytic effect with concomitant recovery of antioxidant and antiapoptotic activity indicators (equivalent to effect of silymarin), while both lower and higher doses of the extract failed to improve the adverse effects of cisplatin administration. This indicate that the antioxidant supplementation with SH in an optimal dose significantly induced antioxidative and antiapoptotic effect in rat hippocampus following the cisplatin administration, resulting in attenuation of cisplatin-induced anxiogenic effect.

FUNCTIONAL BRAIN ASYMMETRY IN FACIAL EMOTIONS RECOGNITION AND INDIVIDUAL DIFFERENCES

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Numerous studies demonstrate the association of emotion recognition with Functional Brain Asymmetry (FBA). Major reduction-localist hypotheses of FBA in emotion recognition are: the right hemisphere hypothesis; the valence-specific hypothesis; modified valence-specific hypothesis and motivation model. However, recent behavioral studies increasingly report inconsistent data. This experimental study aimed to examine FBA hypotheses and the correlation of basic emotion recognition presented to the right (RVF) or the left visual field (LVF) with handedness and personality traits. Personality traits were assessed in 80 healthy students of the Faculty of Medicine by the Zuckerman-Kuhlman Personality Questionnaire-50-CC (ZKPQ-50-CC), and The Depression, Anxiety and Stress Scale (DASS-21), whereas handedness was assessed by the Edinburgh Handedness (activities: writing, throwing; objects: toothbrush, spoon) Inventory-Short form. Photographs of emotional and neutral faces were displayed (170msec) in the RVF or the LVF in random order, and participants' response accuracy was registered. None of the FBA hypotheses has been confirmed. We found a significant correlation between the recognition accuracy of a happy face presented to the RVF (happy_RVF) and writing (r = -0.31, p = 0.006); sadness_LVF and toothbrush (r = -0.23, p = 0.041); fear_LVF and stress (r = 0.26, p = 0.023); disgust_LVF and stress (r = 0.26, p = 0.018); disgust_RVF and stress (r = 0.24, p = 0.032); and anger_LVF and neuroticism/anxiety (r = 0.25, p = 0.026). Thus, in addition to neurophysiological characteristics of cerebral hemispheres, individual (psychological) differences between people may be of fundamental importance for comprehensive understanding of FBA in emotion recognition.

MORPHOMETRIC ANALISYS OF PITUITARY GONADOTROPIC CELLS AFTER ADMINISTRATION OF NANDROLONE DECANOATE AND SWIMMING IN ADULT RATS

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The study included 32 Wistar albino male rats, 10 weeks old, divided into 4 groups: control (T-N-), nandrolone (T-N+), swimming (T+N-) and swimming plus nandrolone (T+N+) groups. The T+ positive groups swam for 4 weeks, 1 hour/day, 5 days/week. The N+ positive groups received nandolone decanoate (20 mg/kg b.w.) once per week, subcutaneously. Five micrometre thick sections were immunohistochemically stained LH and FSH cells were expose to the morphometric analysis. Circulating level of LH, FSH and testosterone were measured. Body weight did not significant decreased in all experimental groups compared to control. Absolute pituitary weights were decreased in T-N+ and increased in T+ positive groups. Relative pituitary weights were increased in all experimental groups compared to control. Volume density of LH cells was decreased for 48% in T-N+, for 22% in T+N- and for 35% in T+N+ group. Number of LH cells on mm2 was decreased for 36% in T-N+, for 3% in T+N- and for 27% in T+N+ group. Volume density of FSH cells were decreased for 39% in T-N+, for 5.5% in T+N- and for 30% in T+N+ compared to control. Number of FSH cells was decresed for 13% in T-N+, for 1% and 15% in T+N+ group compared to control. Serum level of LH were decreased in N+ positive groups, while FSH level were increased in T+N- group. Serum level of testosterone was increased in all experimental groups compared to contol value. Nadrolone alone or combined with swimming decreased morphometric parameters of gonadotropic cells.

THE ROLE OF THE CEREBELLUM IN MODULATING ACOUSTIC STARTLE RESPONSE

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Dysfunctional cerebellum is associated with several neuropsychiatric disorders. Many of these disorders share some similarities in their pathophysiology. Alterations of the acoustic startle response (ASR) and its modulation seem to play role in the pathogenesis of several neuropsychiatric disorders. ASR is a fast reaction of the organism to a sudden and intensive stimulus. Repeated presentation of startle stimulus leads to habituation of ASR. Presenting a weaker prepulse before a startling pulse causes either an attenuation or an increase of ASR (prepulse inhibition or facilitation, respectively), depending on the onset asynchrony between the prepulse and the pulse. Our study aimed to explore the possible contribution of the cerebellum in controlling ASR and its modulation using anodal transcranial electrical stimulation (tDCS). Seventy healthy adults participated in this study. Acoustic stimulation consisted of presentation of pulses (white noise, intensity 105 dB, duration 40 ms) alone or in combination with prepulses (white noise, 75 dB, 20 ms, prepulse-pulse onset asynchrony 30, 60, 120, 2000, or 4000 ms). tDCS duration was 20 minutes with 2 mA current intensity and with the active electrode placed over the cerebellum (1-2 cm below inion) and the reference electrode on the right arm. In comparison with a control group (sham stimulation, n=35), the stimulated group (n=35) showed enhanced ASR to isolated pulses, while startle in the prepulse-pulse conditions remained unchanged. The results indicate that the cerebellum may control startle reactivity.

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LYTHRUM SALICARIA L. EXTRACTS AND THEIR PHENOLIC COMPOUNDS IN PREVENTION OF OXIDATIVE DNA DAMAGE

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Lithrum salicaria L. (purple loosestrife) is a perennial herbaceous plant (family Lythraceae) traditionally used for treatment of diseases related to an inflammatory background. Phenolics, including *C*-glucosidic ellagitannins and *C*-glucosidic flavonoids, were reported as the main classes of compounds in *L. salicaria*. Our previous studies showed that *L. salicaria* aerial parts (LSA) and root (LSR) methanol extracts contain gallic, caffeic, chlorogenic, and ellagic acid and three flavone *C*-glucosides, orientin, isoorientin, and vitexin. Considering the high content of phenolics in *L. salicaria*, the aim of this study was to estimate the ability of LSA and LSR to protect DNA damage induced by hydroxyl and peroxyl radicals. The DNA damage protective activity of LSA and LSR in a concentrations range of 25 to 400 μg/mL and phenolic compounds detected in these extracts (50 or 100 μg/mL) was assayed *in vitro* using DNA from herring sperm as a model system. Oxidative damage of DNA was generated by Fe^{2+} and H_2O_2-induced hydroxyl radicals and 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH)-induced peroxyl radicals. All applied concentrations of studied extracts and phenolic compounds were able to protect DNA against induced oxidative damage. The highest DNA protection showed extracts applied at concentrations of 25 and 50 μg/mL, while orientin and vitexin were the most effective in DNA oxidative protection among phenolic compounds identified in extracts. Obtained results indicate that tested extracts and phenolic compounds presented in these extracts may be used as natural antioxidants in pharmaceutical products with potential application to reduce oxidative stress in a living system.

CHEMICAL COMPOSITION AND ANTIOXIDANT ACTIVITY OF *ALLIUM URSINUM L. EXTRACTS*

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Allium ursinum L. is a perennial plant species which grows in fens and marshes of Europe and Asia. The aim of this study is to investigate the antioxidant activity and to determine the total phenolic and flavonoid contents aerial part of *A. ursinum* water, chloroform and methanol extracts. Plant material was collected in May 2017. The extracts were prepared separately extracting aerial part with appropriate solvent by heat reflux extraction. DPPH (1,1-difenil-2-picrilhidrazil) test was used for determining the antioxidant activity of all extracts. Total phenolic (TPC) and flavonoid (TFC) contents were measured spectrophotometrically. The highest TPC was observed in the chloroform extract (60.47 ± 5.95 mg GAE/g extract) while the lowest measured value was in the methanol extract (33.29 ± 3.13 mg GAE/g extract). The chloroform extract also shows the highest TFC value (34.76 ± 1.31 mg of quercetin/g of extract) compared to methanol (6.86 ± 0.10 mg of quercetin/g of extract) and aqueous (3.34 ± 0.05 mg of quercetin/g of extract) extract. Antioxidant activity was calculated as a percentage of DPPH radical scavenging activity and expressed as IC_{50} values. Furthermore, examined extracts reduced DPPH with an IC_{50} 111.04 ± 7.69 μg/ml of methanol extract, 154.25 ± 3.50 μg/ml of aqueous extract and 391.79 ± 33.01μg/ml of chloroform extract. These findings demonstrated that aerial part of *A. ursinum* represents a valuable source of phenols and flavonoids and indicate that there is scientific basis for the traditional uses of this plant species in alleviation of oxidative stress.

THE EFFECTS OF CHRONIC EVENING PRIMROSE OIL ON THE CARDIODYNAMICS PARAMETERS OF MALE AND FEMALE RATS

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The aim of the present study was to investigate the effects of treatment with evening primrose oil (EPO) on the cardiodynamic parameters in the isolated rat heart. Fourty Wistar albino rats (24 weeks old) were divided into four groups (10 per group): male rats treated with EPO; female rats treated with EPO; control group of female rats; control group of male rats. Animals in the experimental groups were treated with EPO in a dose of 10 mg/kg body weight once a week for 6 weeks via gavage. After sacrificing the animals, hearts were isolated and perfused according to the Langendorff technique at gradually increased coronary perfusion pressures (40-120 cmH_2O). The following parameters of cardiac function were continuously recorded: maximum and minimum rate of pressure development in the left ventricle (dp/dt max, dp/dt min), systolic and diastolic left ventricular pressure (SLVP, DLVP), heart rate (HR) and coronary flow (CF). Our results illustrated that treatment with EPO significantly improved diastolic function in male rats. Moreover, slightly better impact of EPO administration on cardiac function was achieved in male rats compared to female rats. Based on our findings, we may conclude that EPO treatment didn't change the function of the isolated rat heart, independently of the sex.

SHORT TERM CONSUMPTION OF POMEGRANATE JUICE DECREASES LDL-CHOLESTEROL AND DIASTOLIC BLOOD PRESSURE IN SUBJECTS WITH METABOLIC SYNDROME

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The metabolic syndrome (MS) is a collection of cardio metabolic risk factors that includes insulin resistance and raised fasting plasma glucose, abdominal obesity, disturbances in lipid metabolism and hypertension. Regular consumption of fruits rich in antioxidants, such as pomegranate (*Punica granatum* L) may be associated with lower incidences of cardiovascular and metabolic diseases. In the present study we investigated whether consumption of pomegranate juice 300ml/ day during a short term of 2 weeks may influence on the lipid profile and systolic and diastolic blood pressure, in subjects with MS. Twenty-four subjects with MS were included in this study and randomly divided in two groups. The first group consumed pomegranate juice, and the second group was without treatment. Among lipid parameters, only the level of LDL-cholesterol was significantly lower ($p<0.05$) in intervention group after the supplementation period. Also, we found a significant decrease in diastolic blood pressure in subjects with MS, after 2 weeks of pomegranate consumption. Other investigated parameters in intervention group including triglycerides, total cholesterol and HDL-cholesterol, and all parameters in control group, did not change during the study period. In conclusion, our results indicate that even a short term consumption of pomegranate juice may lead to reduced LDL cholesterol and diastolic blood pressure in subjects with MS, what may have beneficial effect on cardiovascular health in these subjects.

VASCULAR DYSFUNCTION FOLLOWING BREATH-HOLD DIVING

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The pathogenesis of predominantly neurological decompression sickness (DCS) in breath-hold diving is probably multifactorial and cannot be explained only by arterialized venous gas emboli. In SCUBA diving other areas have been investigated with links to DCS including microparticles, impairment of endothelial function and platelet activation, suggesting complex mechanisms. This study focused on the vascular damage and how it fits into the puzzle of DCS genesis in breath-hold diving. Eleven breath-hold divers participated in a field study and completed two different diving protocols separated by two days without diving. Protocol 1 consisted of five deep dives with short surface periods, protocol 2 of repetitive dives lasting for six hours. Endothelium-dependent vasodilator function of the brachial artery was assessed pre- and post-dive using the flow-mediated dilation (FMD) approach. All FMD measures were analysed by two-way within-subject analysis of variance (ANOVA; factors: time – pre-/post-dive, protocol – deep/repetitive dive). Absolute FMD was reduced following both diving protocols ($p<0.001$). There was no interaction ($p=0.288$) and main effect of protocol ($p=0.151$). The same main effect of time persisted following allometric scaling for baseline diameter and including shear rate area under the curve (SRAUC) and baseline diameters as covariates. The SRAUC stimulus remained the same in all measuring conditions ($p=0.529$). Both deep and repetitive breath-hold diving leads to endothelial dysfunction that may play an important role in the genesis of DCS.

EFFECTS OF CORNELIAN CHERRIES ON NITRIC OXIDE SYNTHASE ACTIVITY IN THE HEART AND AORTA OF OBESE ZUCKER RATS

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Treatment of metabolic syndrome with statins may be associated with considerable side effects. Cornelian cherry (CC) which contains polyphenolic compounds may represent promising agents in the treatment of cardiovascular and metabolic diseases with minimal side effects. We aimed to study the effects of CoQ10 and different varieties of CC on nitric oxide synthase (NOS) activity in the cardiovascular system of obese Zucker rats. 12-week-old male obese Zucker rats were divided into the control group and groups treated with CoQ10 (15 mg/kg/day), or different CC varieties namely: Radost, Koralovy Marka, Dive, and Lonicera (10 g/day, n=6 in each group) for 6 weeks. Blood pressure (BP) was measured by tail-cuff plethysmography. Body weight, heart weight (HW) and tibia length were determined. NOS activity was determined in the heart and aorta. CoQ10 did not affect either BP or HW/tibia ratio. From CC varieties, Radost only was able to decrease BP of obese Zucker rats. None of CC varieties were able to affect the HW/tibia ratio. CoQ10 did not affect NOS activity either in the heart or aorta. Interestingly, Radost decreased significantly NOS activity in both heart and aorta. Other three CC varieties increased NOS activity in the aorta, while not affecting the activity in the heart. Our results suggest that three out of four CC varieties were able to increase NOS activity in the aorta which may have further beneficial effects. Interestingly, Radost that decreased NOS activity in the cardiovascular system was paradoxically able to reduce BP in obese Zucker rats. Further studies are needed to explain this effect.

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CHRONIC FLAXSEED OIL TREATMENT DOES NOT AFFECT CARDIODYNAMICS IN ISOLATED HEART MODEL INDEPENDENTLY OF GENDER

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The objective of the present investigation was to assess the effects of 6-week administration of flaxseed oil (FSO) rich in omega-3 fatty acids (α-linolenic acid) on cardiac function with an emphasis on gender specific differences. The present study was carried out on 40 adult Wistar albino rats (24 weeks old) randomly divided into 4 groups: males treated with FSO (300 mg/kg/day); females treated with FSO (300 mg/kg/day); females treated with regular laboratory food for animals; males treated with regular laboratory food for animals. After chronic treatment, animals were sacrificed and the isolated hearts were retrogadely perfused on Langendorff apparatus, at gradually increased coronary perfusion pressures (40-120 cmH_2O) in order to establish coronary autoregulation. Following markers of heart function were evaluated: the maximum and minimum rates of pressure development in the left ventricle (dp/dt max, dp/dt min), systolic and diastolic left ventricle pressure (SLVP, DLVP), heart rate (HR) and coronary flow (CF). Treatment with FSO led to a significant decrease in dp/dt max values compared to control group of female rats at higher pressures (100-120 cmH_2O). Most of measured parameters did not significantly differ when we compared FSO treatment in males and females. Our study results indicate that chronic administration of FSO did not alter cardiac contractility and systolic and diastolic function, except sporadic cases, independently from the gender.

INVESTIGATION OF ANTIMICROBIAL ACTIVITY OF ESSENTIAL OIL AND METHANOL EXTRACTS OF FENNEL FRUIT (*FOENICULUM VULGARE MILLER*)

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The aim of this research was to investigate the antimicrobial activity of essential oil and methanol extracts of fennel (*Foeniculum vulgare* Miller) on selected Gram-positive and Gram-negative bacteria by microdilution method. Plant species *Foeniculum vulgare* Miller, of the *Apiaceae* family, popularly known as fennel has been used for centuries in traditional medicine. Fennel extracts and essential oil manifest antioxidant, antitumor and antimicrobial effects. Polyphenolic compounds are secondary metabolites of plants with important role in the prevention of chronic and infectious diseases. Testing antimicrobial activity of the essential oil and methanol extracts was performed *in vitro* on isolated microbiological strains from the respiratory and gastrointestinal tract of which are formed the suspension 0.5 *McFarland* turbidity. The tested concentrations of extracts were 0.10-100 mg/mL, while tested concentrations of oil were 0.05-50 μL/mL. MIC (minimum inhibitory concentration) and MBC (minimum bactericidal concentration) were determined by a microwell dilution method according to the recommendations of the National Committee for Clinical Laboratory Standards. The results showed that better MIC/MBC concentration were obtained from the 100% methanol extract of the ripe fennel fruit (6.25/25.00 mg/mL on *Streptoccocus pneumoniae* and *Staphylococcus aureus*). The essential oil of unripe fennel fruit showed better MIC concentration (3.13 ml/ml) on *Escherichia coli* and *Proteus mirabilis.* The tested extracts and essential oil have demonstrated a solid antimicrobial activity. Therefore, these extracts and essential oil could play an important role of co-therapeutic agents for the treatment of various bacterial infections.

THE ROLE OF PERIVASCULAR ADIPOSE TISSUE AND ENDOGENOUS H_2S IN VASOACTIVE RESPONSES OF MESENTERIC ARTERY IN NORMOTENSIVE AND SPONTANOUSLY HYPERTENSIVE RATS

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In pathophysiological conditions like essential hypertension the increased oxidative stress occurs which modulates signal pathways in perivascular adipose tissue (PVAT) such as hydrogen sulfide (H_2S) signalization. Consequently, it can change vasoactive responses. We studied the role of PVAT and endogenous H_2S in contractile and relaxation responses of mesenteric artery induced by vasoactive substances in adult normotensive Wistar and spontaneously hypertensive rats (SHR) during physiological and pathophysiological conditions. The changes in isometric tension were evaluated after transmural nerve stimulation (TNS) or after application of exogenous noradrenaline (NA) in MA with preserved or denuded PVAT. To inhibit the endogenous H_2S production the inhibitor of cystathionine γ-lyase, propargylglycine, was used. In SHR, unlike in Wistar rats, PVAT induced pro-contractile effect on responses induced by endogenous NA after TNS. Surprisingly, PVAT revealed a more pronounced anti-contractile effect on responses induced by exogenous NA in SHR compared to Wistar rats. In Wistar rats, H_2S produced by arterial wall and PVAT revealed anti-contractile effect on contractile responses induced by exogenous NA. In SHR, H_2S produced by arterial wall revealed pro-contractile effect, however, this effect was counter-balanced by anti-contractile effect of H_2S produced by PVAT. The results indicated that the pro-contractile effect of PVAT was closely associated with perivascular nerve stimulation, and besides the pro-contractile action of H_2S in the arterial wall, could represent the pathologic features of SHR. On the other hand, we confirmed that the anti-contractile action of PVAT associated with participation of H_2S could probably be part of compensatory vascular mechanisms triggered in SHR.

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CARDIAC OXIDATIVE STRESS PARAMETERS AND CARDIO-METABOLIC MARKERS IN MONOCROTALINE-INDUCED HEART FAILURE IN WISTAR ALBINO RATS: INFLUENCE OF SUBCHRONIC VITAMIN B6 APPLICATION

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Monocrotaline (MCT) induce pulmonary arterial hypertension (PAH), characterized by remodeling mechanisms of the pulmonary arterial vessels with increased pulmonary vascular resistance, and with the occurrence of consequent right ventricular hypertrophy, right-sided heart failure, decompensation and ultimately to fatal outcome. The aim of this study was to test the hypothesis that subchronic application of vitamin B6 could affect heart failure (HF) induced by MCT and with the modulation of oxidative stress parameters and cardiometabolic biomarkers. Biochemical and inflammatory parameters together with histomorphometric analysis were assessed in blank solution-exposed controls (C1 physiological saline 1ml/kg one day n=8; C2 physiological saline 1ml/kg 28 days n=8)**,** MCT-induced HF **(**MCT 50mg/kg, n=8**),** B6 (vitamin B6 7mg/kg/day, n=8) and MCT+B6 (MCT 50mg/kg, vitamin B6 7mg/kg/day, n=8) male Wistar albino rats (b.w. 160 g, at start)**.** Superoxide dismutase (SOD) and glutathione peroxidase (GPX) activities together with parameters of oxidative damage of proteins, thiol- and carbonyl groups, were determined in cardiac tissue. Echocardiography was also performed in order to confirm MCT-induced rat heart failure. The right ventricular (RV) wall hypertrophy, accompanied with significant increase of troponin T and preserved renal and liver plasma markers has been shown in MCT-induced HF. However, these effects were not related to antioxidant effects of vitamin B6, since several parameters of oxidative stress were more pronounced after treatment. In this study application of vitamin B6 did not significantly attenuate hypertrophy of RV wall, but showed a tendency to decrease it, while modulated oxidative stress which is involved in PH pathogenesis and subsequent HF.

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N-ACETYLCYSTEINE REDUCES INFLAMMATION AND OXIDATIVE STRESS IN DOUBLE-HIT MODEL OF LUNG INJURY IN RATS

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We hypothesized that therapy with N-acetylcysteine (NAC) reduces inflammation and oxidative stress in experimental hyperoxia and lipopolysaccharide (double-hit) induced acute lung injury. Material and methods: Adult male rats (Wistar) were anaesthetized, tracheotomised and the endotracheal tube was inserted. Animals were ventilated with following settings: frequency (f) of 50/min, fraction of inspired oxygen (FiO_2) 1.0, inspiration time (Ti) 50 %, tidal volume (V_T) of 6 ml/kg. Bacterial infection was mimicked by intratracheally instillation of LPS (500 μg/kg b.w.; 2.2 ml/kg b.w; E.coli, 055:B5). Animals with hyperoxia and LPS were treated with N-acetylcysteine intravenously. Controls received sterile saline and were ventilated with FiO_2 0.4. After 5 hrs of ventilation the animals were overdosed by anaesthetics. Cytokine induced neutrophil chemoattractant-1 (CINC-1), caspase 3 (Casp-3), hydroxyproline, thiobarbituric acid reactive substances (TBARS), 3-Nitrotyrosine (3NT) and total antioxidant capacity (TAC) were determined in lung tissue. Total count of leukocytes in blood was evaluated. Results: In comparison with control, hyperoxia and LPS increase 3NT ($p=0.015$), Casp-3 ($p=0.001$) and decrease TAC ($p=0.025$) in lung and total count of leukocytes in blood from 3rd hour of experiment. In animals with hyperoxia and LPS, NAC administration significantly reduces Casp-3 ($p=0.001$) and increases TAC ($p=0.024$) and total count of leukocytes (4th hour $p=0.050$, 5th hour $p=0.005$), and tended to reduce CINC-1 and hydroxyproline (both $p=0.055$). N-acetylcysteine therapy improves antioxidant lung capacity and thus reduces inflammation and oxidative stress in experimental double-hit model of acute lung injury.

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EFFECTS OF TRAINING AND DETRAINING ON MUSCLE STRENGTH IN ROWERS

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Annual planning and periodization play a great role in muscle adaptation in rowers. Considering that the training's main effect is to increase specific muscle strength, while in detraining rowers work on general muscle strength and active recovery, the aim of the study was to compare strength of different muscle groups between periods of training and detraining. The study was conducted at the Department of Physiology, Faculty of Medicine Novi Sad, and included 34 male and female rowers, 15 to 18 years of age. Muscle strength was measured using Concept2 DYNO dynamometer. Strength of the arm extensors and flexors as well as the leg extensors was measured twice, at the end of competition season (peak of performance) and before the start of competition season (after detraining). Significant difference was found in absolute strength, relative strength and contraction speed in arm flexors and extensors, as well as in relative strength and contraction speed in leg extensors between training and detraining period ($p<0.05$). No difference was found in leg extensors relative strength between two measurements ($p>0.05$). Periodization of the annual rowing training program has bigger impact on upper limbs adaptation oscillations compared with the lower limbs muscles in the terms of absolute strength.

OXIDATIVE DAMAGE AND ANTIOXIDANT CAPACITY IN OBESE AND OVERWEIGHT ADOLESCENTS

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Obesity is a major cause of morbidity and mortality. It has been reported that obese adolescents are at higher risk for health problems in adulthood. Obesity is characterized by chronic low-grade inflammation with increased oxidative stress. Inflammation is induced by the activation of the immune system in adipose tissue promoting pro-inflammatory status and oxidative stress. Since association between inflammation and oxidative stress was not assessed previously in adolescents with overweight and obesity separately, we focused on analysis of antioxidant capacity, oxidative damage and inflammation in these groups. Adolescents (28 male, 27 female) aged 16.2 years were divided by body mass index into: obese (O, n=19), overweight (OW, n=16) and control (C, n=20) groups. Insulin, leptin, TNFα, IL-6, markers of proteins (3NT) and lipids (TBARS) oxidative damage and total antioxidant capacity (TAC) were determined in plasma. Although inflammatory markers, insulin and leptin levels were significantly increased in OW and O vs. C, increased oxidative damage was detected in O group only (O vs. C: TBARS, 3NT $p<0.01$; O vs. OW: TBARS $p=0.036$). TAC was decreased in O group (O vs. C, $p=0.032$), while no significant difference between OW and C ($p=0.1$) was found. While increased inflammation, insulin, leptin levels are found in both overweight and obese groups, oxidative damage increased and TAC decreased in obesity only. Increased reactive oxygen species production and/or impaired antioxidative mechanisms could be responsible for this observation, requiring further study. Overweight could be a transient state between obesity and normal weight in terms of oxidative damage.

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ROLE OF GALECTIN 3 ON THE COLLAGEN DEPOSITION DEGREE IN HEART TISSUE OF MICE SUFFERING FROM AUTOIMMUNE MYOCARDITIS

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Myocarditis is an inflammatory heart muscle disease characterized by focal or diffuse cell infiltrates. It can progress to fibrosis, tissue remodeling and loss of contractile function. Experimental autoimmune myocarditis (EAM) is an animal model of immune mediated myocarditis and cardiomyopathy. Galectin 3 (Gal-3) belongs to the family of β-galactoside-binding lectins and plays important role in regulation of inflammation and collagen deposition process. C57BL/6 (WT) mice and mice with a targeted deletion of the Gal-3 gene (Gal-3KO) were immunized with the peptide MyHC$\alpha_{334-352}$ myosin on day zero and day seven. Quantity of deposited collagen and expression of IL-10 in the heart of immunized mice was determined by selective histochemical techniques, Sirius Red and Masson trichrome staining, and by immunohistochemistry on the 21st day after immunization. Absolute number and percentage of infiltrating immune cells was determined by flow cytometry. Immunized Gal-3KO mice had a significantly lower percentage of red and blue collagen fibers compared to WT mice on the 21st day after immunization ($p<0.05$). A significantly higher cytoplasmic expression of IL-10 ($p<0.05$) was detected in Gal-3KO mice myocard compared to WT mice. Deletion of Gal-3 gene induced a significantly higher number and percentage presence of myeloid CD11b+IL-10+ cells in the Gal-3KO mouse's heart tissue compared to WT mice three weeks after immunization ($p<0.05$). Obtained results suggest that less amount of deposited collagen in the heart of Gal-3KO mice during EAM is due to the absence of Gal-3 gene expression as well as the higher incidence of antifibrotic cells producing IL-10.

SUPPLEMENTATION OF *OLEA EUROPEA* L. LEAF EXCTRACT DIFFERENTLY AFFECTS SPONTANEOUSLY VERSUS MALIGNANT HYPERTENSIVE RATS

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Antihypertensive and anti-oxidative properties of widely used Olive leaf extract (OLE) are still incompletely defined, especially in different form of hypertension. The main goal of our study was to investigate acute haemodynamic and biochemical effects of OLE in spontaneously as well as malignant hypertensive rats. We used *Olea europea* L. leaf extract EFLA®943 and L-NAME, NO synthesis inhibitor, as an inducer of acute malignant hypertension. SHR were divided in 4 experimental groups: SHR, SHR+OLE, SHR+L-NAME, SHR+L-NAME+OLE. Saline, L-NAME (10mg/kg t.m.) and EFLA®943 (50mg/kg t.m) were given in the femoral vein by bolus. Mean arterial pressure (MAP) and heart rate (HR) were followed during 30minutes. Cardiac output (CO) and TBARS (as marker of lipid peroxidation) were measured, while total vascular resistance (TVR) was calculated. L-NAME significantly increased MAP, TVR and lowered HR in SHR leading to malignant hypertension. SHR treated with OLE showed decreasing of: MAP, HR CO and TBARS. Concomitant OLE with L-NAME treatment decreased MAP, but TVR remained high, CO was diminished and lipid peroxidation was significantly increased. Our results indicate that acute olive leaf treatment had strong antihypertensive properties, diminished total vascular resistance and blunted lipid peroxidation in SHR. In opposite, this extract kept antihypertensive properties, but it was unable to reduce increased both TVR and lipid peroxidation in malignant hypertensive rats. This picture is probably due to strong endothelial dysfunction and furious peroxinitrite formations following NO blockade.

FEMINIZATION OF PROGENITOR AND MATURE ADULT LEYDIG CELLS LACKING INSULIN AND IGF1 RECEPTORS

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Insulin/IGF1 (insulin like growth factor 1) signaling is one of the essential cellular regulators of growth and development. Here, we used prepubertal (P21) and adult (P80) male mice with insulin and IGF1 receptors deletion in steroidogenic cells (*Insr/Igf1r*-DKO). The profile of the key markers of Leydig cell functions, but also the markers of steroidogenic machinery common for all other steroidogenic cells (ovaries, adrenals) were followed in Leydig cells, seminiferous tubules and whole testes. Our study showed, according to the best of our knowledge for the first time, that INSR and IGF1R deletion caused development of estrogenic characteristic of progenitor Leydig cells in prepubertal mice and mature adult Leydig cells in adult mice. The level of androgens significantly decreased in serum, testes and Leydig cells from *Insr/Igf1r*-DKO prepubertal as well as adult mice. This was followed with dramatic reduction of cAMP, *Insl3* and transcripts for all functional markers of Leydig cells. In the same cells, significant increase of ovarian differentiation markers (*Rspo1, Wnt4, Amh, Fshr, Cyp19a1*) was observed. Moreover, Leydig cells from *Insr/Igf1r*-DKO mice produced significantly higher level of estradiol than control, proving physiological significance of the results. Accordingly, insulin and IGF1 receptors are important for differentiation of progenitor Leydig cells and development of functional testosterone-producing adult Leydig cells.

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DIFFERENCE IN CARDIOTOXICITY INDUCED BY DOXORUBICIN IN MALE AND FEMALE RATS

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Doxorubicin (DOX) is an anthracycline antibiotic, routinely used as a chemotherapeutic agent. However, a significant risk of cardiotoxicity limits its use. The aim of this study was to examine the sex differences of doxorubicin-induced cardiotoxicity on isolated rat heart according to *Langendorff* technique. This experimental study was conducted on 24 male and female *Wistar albino* rats (6 per group, 12 weeks old; bw: 200-250 g) divided into CTRL and DOX groups. DOX was dissolved in saline and administered by intraperitoneal injection at a dose of 15 mg/ kg, while control animals were injected with a comparable volume of saline. After 72 hours of DOX injection, all animals were sacrificed and cardiodynamic data were collected. We continuously measured parameters of cardiac function such as: maximum rate of pressure development in the left ventricle (dp/dt max), minimum rate of pressure development in the left ventricle (dp/dt min), systolic left ventricular pressure (SLVP), diastolic left ventricular pressure (DLVP), heart rate (HR) and coronary flow (CF). Administration of DOX significantly reduced cardiodynamic parameters in both male and female rats. The most prominent changes in male rats were observed in the dp/dt max, dp/dt min and SLVP values, whereas DLVP and CF were notably reduced in female rats ($p<0.05$). On the other hand, no major sex differences existed in HR values due to doxorubicin treatment. Results from our study could help to better understanding the impact of sex differences on doxorubicin-induced cardiotoxicity.

SWIMMING ATTENUATES BLOOD PRESSURE AND OXIDATIVE STRESS IN HIGH SALT-INDUCED HYPERTENSIVE RATS

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The aim of our study was to estimate the effects and different duration of swimming training, on blood pressure and oxidative stress parameters on normotensive and salt-induced hypertensive rats. Our research included 6-week-old male Wistar albino rats (n = 60) that were divided in two groups, normotensive and hypertensive rats. Each of these two groups consisted 3 subgroups depending on swimming protocol. Training was maintained 5 days a week for all training session with maximum 6 rats into the pool. Training was constant 60 min/day that last for 6 or 9 weeks. After 6 or 9-week swimming protocol, blood pressure and redox status parameters (TBARS, NO_2^-, O_2^-, H_2O_2, SOD, CAT, GSH) were measured in normotensive and hypertensive rats. Our results confirmed that swimming, as an aerobic exercise, decreases blood pressure and has time-dependent positive system adaptations, especially on the antioxidant parameters.

SIGNALING PATHWAYS REGULATING THE MITOCHONDRIAL DYNAMIC AND ACROSOMAL REACTION ARE DISTURBED IN SPERMATOZOA FROM STRESSED ADULT RATS

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Mitochondria are key component of energy production, oxidative stress, calcium homeostasis, steroid biosynthesis, but also the key component of stress response. However, the molecular adaptation of spermatozoa from stressed males was not described well. The aim of this study was to determine the functionality and molecular adaptation of spermatozoa from stressed rat by applying *in vivo* and *in vitro* approach. For *in vivo* experimental model, psychophysiological stress by immobilization (IMO), was performed for 3 hours in different time during the day (ZT3, ZT11, ZT23), for one (1xIMO) or ten (10xIMO) consecutive days. For *in vitro* approach, epididymal spermatozoa from undisturbed rats were stimulated with stress hormones adrenaline and cortisol. Results showed that number of spermatozoa significantly decreased in all 10xIMO rats comparing to control. Acrosomal status (response to acrosome-reaction-inducer progesterone) significantly decreased in spermatozoa from 1xIMO and 10xIMO rats comparing to control. The same effect was observed in spermatozoa stimulated *in vitro* with stress hormones. RQ-PCR results revealed that transcription of the main mitochondrial biogenesis markers *Ppargc1a*, *Nrf1* and *Nrf2* increased in spermatozoa from 10xIMO rats in ZT3 time point. In the same spermatozoa samples transcription of main markers of mitochondrial architecture *Opa1, Mfn1, Mfn2* increased in ZT3 while decreased in ZT11 time point. Incubation of spermatozoa with adrenaline decreased level of *Ppargc1a* and *Nrf2a* transcripts, while cortisol decreased expression of mitochondrial transcription factor TFAM. In summary, repeated psychophysical stress decreased the number and functionality of spermatozoa and disturbed transcriptional profile of their mitochondrial biogenesis and architecture markers.

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EFFECTS OF SULFUR-CONTAINING AMINO ACIDS ON ACTIVITY OF ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE IN DIGESTIVE SYSTEM OF RATS

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Subchronic methionine loading leads to oxidative stress, which is a potential cause of disorders of many organs, including organs of digestive system. The aim of this stidy was to assess activities of acetylcholinesterase and butyrylcholinesterase in digestive organs of rats in condition of methionine overload and to test the ability of L-cysteine and N-acetyl-L-cysteine to reverse the effects of methionine on this enzymes. This study was conducted on *Wistar albino* rats. Animals were divided into three groups with 8 animals in each group: control group (K) received 0.9% NaCl, M group received methionine, C group received methionine + L-cysteine and N group received methionine + N-acetyl-L-cysteine intraperitoneally. After 21 days the animals were sacrificed and samples of duodenum, ileum, colon and liver were taken for biochemical analysis. Activities of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) were determinated. AChE activity was significantly increased in duodenum ($p<0.05$), colon ($p<0.05$) and liver ($p<0.01$) of rats that were treated with N-acetyl-L-cysteine. L-cysteine caused increasement of AChE activity in colon ($p<0.01$) and liver ($p<0.05$). Activity of BChE was changed mainly in ileum, methionine decreased its activity compared to control group ($p<0.05$) and N-acetyl-L-cysteine diminshed this effect of methionine leading to increased activity of BChE in ileum ($p<0.05$). BChE activity was also increased in colon of rats treated with L-cysteine compared to M group ($p<0.05$). These findings suggest that subchronic treatment with antioxidant sulfur-containing amino acids L-cysteine and N-acetyl-L-cysteine can lead to increased activity of AChE and BChE in condition of methionine overload.

OLIVE LEAF GLYCOSYLATED SECO-IRIDOID-PHENOL OLEUROPEIN DOES NOT AFFECT MADIN-DARBY CANINE KIDNEY (MDCK) CELL VIABILITY AND LYSOSOMAL FUNCTION

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Oleuropein (OLE) is a glycosylated seco-iridoid-phenol, present in olive leaves and fruits, is believed to be one of the main carriers of *Olea europaea* medical properties which include anti-cancer, nephroprotective, cardioprotective, anti-neurodegenerative, etc. Madin-Darby canine kidney (MDCK) cells represent a good substitution model for human collecting tubule cells, which are the target for the adverse action of numerous chemotherapeutics that are excreted by the urine. The aim of the present study was to evaluate the effect of OLE, applied in different concentrations, on MDCK cell mitochondrial and lysosomal function. This was performed by studying cells β-*N* acetyl glucosaminidase (β-NAG) activity and their ability to metabolize/accumulate different supravital dyes under the influence of OLE. The application OLE in a concentration ranging from 10^{-4} to 10^{-8} mol/L did not cause any change in MDCK ability to metabolize MTT, a dye that is metabolized by enzymes in viable mitochondria. Additionally OLE had no significant influence on MDCK cells ability to accumulate neutral red in their lysosomal. Also, the studied activity of β-NAG, a lysosomal derived enzyme, was found to be unaffected by the applied OLE in different concentrations. From the findings of our study, we can conclude that OLE applied on its own does not affect MDCK collecting tubule cells function, suggesting that this glycosylated seco-iridoid-phenol from natural origin could potentially be used for the management of different kidney-related illnesses.

EFFECTS OF VITAMIN D LEVELS ON GLUCOREGULATORY PARAMETERS IN TYPE 2 DIABETES MELLITUS

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Vitamin D affects the function of pancreatic beta cells, but the effects of vitamin D deficiency on glucoregulatory mechanisms are still inconclusive. The aim of this study was to link vitamin D levels with insulin resistance and insulin secretion parameters. The study included 65 male and female participants, 35 newly-diagnosed, therapy-naïve type 2 diabetics and 30 healthy controls. All participants were tested for fasting glucose, hemoglobin A1c, fasting insulin, vitamin D levels, and the HOMA indexes were calculated using HOMA2 calculator. Fasting glucose levels, insulinemia, hemoglobin A1c levels and HOMA IR were all significantly higher in the diabetic group ($p<0,001$), while the vitamin D levels and HOMA S index were significantly lower ($p<0,001$). HOMA-B values did not differ between the two groups ($p=0.31$). Vitamin D levels moderately correlated with HOMA S and HOMA B indexes ($r=0,466$, $p<0,001$; $r=0,394$, $p<0,001$, respectively), whereas a negative correlation was found between vitamin D levels and HOMA IR ($r=−0,285$; $p<0,001$). Multiple regression analysis showed that the vitamin D levels significantly predicted the values of HOMA B index ($p=0,001$), but it had no predictive value on HOMA IR ($p=0,26$). In conclusion, the diabetic group showed statistically lower vitamin D values compared with the healthy control group. Connection between vitamin D, glucose levels, hemoglobin A1c and insulin secretion index underline the role of this vitamin in glucoregulation.

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Registration is following invitation only and includes admission to all sessions, opening ceremony, welcome reception, and receiving meeting materials.

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Official language will be English. No simultaneous translation will be provided.
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The social program will include convivial (welcome reception/cocktail) and cultural (visit to worldwide recognized naïve art gallery, town tour etc.) events. Exciting social event will be offered (gala dinner with multinational music etc.).

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IMPORTANT INFORMATION

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