were submitted to biochemical analyses at baseline, after 3 months and at the end of the treatment. Oxidized LDL, Ox-LDL, were tested by enzyme linked immunosorbant assay (Mercodia AB, Uppsala, Sweden) and glutathione levels (GSH and total glutathione) by Biovision GSH Assay kit (Biovision). Lipid profile (TC, HDL-C, TG) was assessed by automatic analyzer (Olympus AU 2700, Japan) and LDL-C were calculated. Statistical analyses were performed using the SPSS 20.0.

Results: Lipid profile levels (mean±SD [mg/dl]): baseline TC 242.5±60, HDL-C 57.2±13.9, TG 92.8±33.8, LDL-C 167.6±60.6; after probiotics TC 227.7±47.0, HDL-C 56.0±11.8, TG 93.2±28.6, LDL-C 153.4±47.5) showed significant TC reduced compared to baseline after 3 months while, when comparing active treatment and placebo, decrease were not significant. Ox-LDL and GSH were respectively 71.2±25.5 U/l and 271.1±65 ng/ml in basal conditions and decreased to 63.2±20.7 U/l and 218.5±53 ng/ml after probiotic treatment. These decrease were significant intra-group but results were not significant compared with the placebo ones.

Conclusion: The effects of Bifidobacterium lactis and Lactobacillus acidophilus supplementation in children affected by primary hyperlipidaemia are contrasting. A PO and HDL-C levels ameliorate after active treatment; these results are an important points that need to be further investigated.

69 - Anti-inflammatory therapies

EAS-0969.

INTERVENTION WITH ANTI-INFLAMMATORY RVE1 ATTENUATES Atherosclerosis WITHOUT DECREASING PLASMA CHOLESTEROL AND ADDS TO THE ANTI-ATHEROGENIC EFFECT OF ATORVASTATIN

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Objectives: Atherosclerosis is a multifactorial disease that correlates positively and significantly with low-density lipoprotein (LDL) plasma cholesterol and requires inflammatory components. Whereas reduction of plasma LDL cholesterol is effectively achieved by statins, quenching of the inflammatory factors has not been addressed adequately by existing therapies. Resolvins are naturally-occurring, small molecule lipid mediators with the potential to treat multiple inflammatory diseases. Here we investigated the potency of RvE1 supplementation in children affected by primary hyperlipidemia are contrasting. APO A and HDL-C levels ameliorate after active treatment; these results are an important points that need to be further investigated.

Methods: Mice were fed a hypercholesterolemic diet (0.4%) for nine weeks. Subsequently, mice were randomized and treated with low (1mg/kg/day) and high (5mg/kg/day) doses of RvE1, atorvastatin (1.5mg/kg/day), and the combination of atorvastatin and low dose RvE1 for the following 16 weeks to evaluate the anti-atherogenic effects.

Results: Both low and high dose RvE1 treatment significantly (35% and 37%, respectively; p<0.05) attenuated atherosclerotic lesion size, without affecting plasma cholesterol. Plasma cholesterol lowering (24%; p<0.01) atorvastatin reduced the lesion size to a similar extent (27%; p<0.05). Neither RvE1 nor atorvastatin reduced circulating SAA levels. Notably, refined analysis revealed the presence of less severe lesions with RvE1 versus atorvastatin treatment. Importantly, in combination with atorvastatin, RvE1 added to the anti-atherosclerotic effect of atorvastatin, resulting in decreased atherosclerotic lesion area (31%), lesion severity (58%) and increased percentage of lesion-free segments (62%). Furthermore, microarray analysis of aortas from RvE1-treated mice revealed changes in gene expression profiles that are enriched in biological processes involved in stress, defense and immune responses, cell adhesion and superoxide metabolism.

Conclusion: RvE1 attenuates atherosclerosis lesion size and lesion severity without lowering plasma cholesterol and SAA levels. Combined RvE1 and atorvastatin treatment was more effective than each compound alone, indicating the potential of RvE1 to be used on top of atorvastatin treatment.

69 - Anti-inflammatory therapies

EAS-0680.

THE CELLULAR AND MOLECULAR BASIS FOR THERAPEUTIC EFFECTIVENESS OF β-ESCIN

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Objectives: β-escin is a mixture of triterpene saponins isolated from horse chestnut seeds (Aesculus hippocastanum L.). Historically, it was used to treat multiple diverse conditions, including bladder disorders, cough, diarrhea, dysmenorrhea and tinnitus. The anti-edematous, anti-inflammatory and venotonic properties of β-escin that have been particularly well established in ethnomedical tradition are not only recognized and acknowledged by modern medicine, but have remained the most extensively clinically investigated effect of this plant-based drug. Although randomized controlled trials have so far provided strong evidence for the effectiveness of β-escin only for the treatment of chronic venous insufficiency (CVI), growing body of scientific data may soon broaden its indications for use. However, despite the popularity of the drug its pharmacological mechanism of action still remains largely unknown. The aim of this study was to determine the cellular and molecular basis for therapeutic effectiveness of β-escin.

Methods: To investigate the effect of β-escin on human endothelial cells, the following experimental methods were applied: i) gene expression microarrays, ii) global proteomic analysis and iii) in vitro analysis of a broad panel of cellular responses including migration, proliferation, permeability and apoptosis.

Results: We identified several novel pathways responsible for the protective effects of β-escin on the vascular endothelium under inflammatory conditions. We show that this plant-based drug acts as an inhibitor of the TNF-α - regulated inflammation process by negatively affecting the NF-κB pathway, therefore decreasing expression of TNF-α - induced effector proteins. Our results strongly suggest that the observed effects are directly linked to the loss of cell membrane cholesterol caused by β-escin.

Conclusion: This study provides a thorough insight into the molecular and cellular mechanisms of anti-inflammatory properties of β-escin. Moreover, our data suggest novel indications for its clinical use.

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EAS-0534.

MULTIMODAL MELDONIUM’S INFLUENCE ON FUNCTIONAL BRAIN STATE

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Objectives: Cerebral atherosclerosis (CA) is a chronic cerebral vessel disease which presented with leasure of its functions. In therapeutic strategy is necessary take into account heterogenity of CA pathogenesis and use the medicines with multimodal actions (antioxidants, vasoactive, nootropic). The aim of our work is the complex estimation of meldonium influence on functional state of central nervous system in patients with CA.

Materials and methods: In complex clinical analysis were included 25 patients with CA (mean age – 58.3±3.4 years). All patients took meldonium in dose 5 ml (100 mg/ml) intravenously one time a day during 10 days.
Before and after treatment all patients were carried out duplex scanning of cerebral vessels and EEG.

**Results:** In patients with CA meldonium increases linear flow blood velocity in right medium cerebral artery (before treatment 50.23±4.88 sm/s, after - 101.67±7.26 sm/s), in left anterior cerebral artery (before - 77.18±2.33 sm/s, after - 82.86±3.92 sm/s); in basilar artery (before - 26.61±2.21 sm/s, after - 56.28±4.46 sm/s). After meldonium’s course treatment in patients with CA there is significant increasing of the power of beta 1- and beta 2-rhythms in all regions of both hemispheres.

**Conclusions:** The meldoniums’s course treatment improves cerebral blood flow in intracranial carotid and vertebro-basilar vessels and increases the power of rapid EEG rhythms.

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**69 - Anti-inflammatory therapies**

**EAS-0152.**

**FUMARIC ACID ESTERS CAN BLOCK PRO-INFLAMMATORY ACTIONS OF HUMAN CRP AND AMELIORATE METABOLIC DISTURBANCES IN TRANSGENIC SPONTANEOUSLY HYPERTENSIVE RATS**

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**Objectives:** Inflammation and oxidative stress have been implicated in the pathogenesis of metabolic disturbances. Esters of fumaric acid, mainly dimethyl fumarate (DMF), exhibit immunomodulatory, anti-inflammatory, and anti-atherosclerotic effects. In the current study, we tested the hypothesis that DMF treatment of an animal model of inflammation and metabolic syndrome, the spontaneously hypertensive rat (SHR) transgenically expressing human CRP (C-reactive protein) (SHR-CRP strain), will ameliorate inflammation, oxidative stress, and metabolic disturbances.

**Methods:** We studied the effects of DMF (Fumaderm) (10 mg/kg body weight for 4 weeks) in SHR-CRP males versus untreated SHR-CRP controls. All rats were fed a high sucrose diet.

**Results:** Treatment with Fumaderm, compared to untreated controls, was associated with significantly reduced endogenous CRP but not transgenic CRP, with amelioration of inflammation (reduced levels of serum IL6 and TNFa) and oxidative stress (increased activities of anti-oxidative enzymes and reduced levels of TBARS lipoperoxidation products in liver, heart, kidney, and plasma). In addition, Fumaderm treatment reduced visceral fat weight and ectopic fat accumulation in liver and muscle, and increased sensitivity of adipose tissue to insulin action. Analysis of gene expression profiles in the liver with Affymetrix arrays revealed differentially expressed genes from KEGG pathways regulating inflammation and oxidative stress.

**Conclusion:** These findings provide evidence for anti-inflammatory, anti-oxidative, hypolipidemic, and antiatherosclerotic effects of DMF of potential therapeutic significance.

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**69 - Anti-inflammatory therapies**

**EAS-0689.**

**THE ANGIOTENSIN (1-7)/MAS RECEPTOR AXIS AND VASCULAR CELL INFLAMMATION**

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**Objectives:** Angiotensin-(Ang)-(1-7) is an heptapeptide of the renin angiotensin system (RAS) generated from Ang I and Ang II by different enzymatic pathways. Ang-(1-7) binds the G protein-coupled receptor Mas and is considered nowadays as a physiological antagonist of Ang II. In the present study, we investigated the anti-inflammatory potential of Ang-(1-7) in human vascular cells.

**Methods:** In human aortic smooth muscle cells (HASMC), the inductive nitric oxide synthase (iNOS) levels and NO release were determined by Western blotting and the Griess method, respectively. The activation of NAPDH oxidase and NF-kB were analysed by lucigenin-derived chemiluminescence and electromobility shift assay. In human umbilical vein endothelial cells (HUVEC), leucocyte adhesion was measured in a flow chamber, while the expression of adhesion molecules was determined by flow cytometry and indirect immunofluorescence.

**Results:** Pre-incubation of HASMC with Ang-(1-7) (1 nM to 1 μM) reduced in a concentration-dependent manner iNOS induction and NO release stimulated by both Ang II (100 nM; 18 h) and the RAS independent pro-inflammatory cytokine IL1β (2,5 or 10 ng/ml; 18 h). The Mas receptor antagonists A779 (1 μM) or D-Pro7-Ang-(1-7) (1 μM) blocked the anti-inflammatory effects of Ang-(1-7). By using apocynin (30 μM) and PDTC...