ANTIRADICAL AND ANTIHYPERGLYCEMIC ACTIVITY OF RASPBERRY POMACE

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Plant foods and products are rich sources of a variety of biologically active compounds possessing wide range of biological activities such as hypolipidemic, antiplatelet, antitumor, antioxidant, and immunostimulating properties. Enzyme inhibitors have potential value, in many areas of disease control and treatment. α-Glucosidase is a therapeutic target for type II diabetes, and α-glucosidase inhibitors have been used in the clinic as alternative treatments for this disease. There is a growing interest to reduce waste and to study the possibility of using by-products, such as pomace from fruit processing industry, for isolation of bioactive compounds. For this purpose, raspberry pomace, Meeker variety, was extracted and screened for the presence of biologically active compounds with antiradical and α-glucosidase enzyme-inhibitory activity. In order to characterize the raspberry pomace as a source of bioactive compounds, total polyphenol (6.15 mg/g pomace), flavonoid (3.87 mg/g pomace) and anthocyanin (0.66 mg/g pomace) contents in the extract were determined spectrophotometrically, while the presence of vitamin C (1.41 mg/g pomace) was determined by HPLC. Raspberry pomace extract exhibited antihyperglycemic activity, inhibiting α-glucosidase activity at the concentration range from 0.04 to 0.63 mg/ml. Inhibitory activity reached 50 % applying 0.2 mg/ml of raspberry pomace extract. Antiradical activity of raspberry pomace extract, evaluated by ABTS assay, was 1.17 mM Trolox equivalents at the concentration of 3.33 mg/ml. Results obtained in this study show that rasberry pomace is a natural source of effective and safe bioactive compounds for development of functional foods to treat diabetes and oxidative stress related diseases.

DOWNREGULATION OF *CYP26B1* RNA BY WILLOW BARK, ITS ETOH-FRACTION AND BY THE ANTIDEPRESSANT IMIPRAMINE

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CYP26B1 is a member of the cytochrome P450 26 family which catabolizes retinoids. Recently it was shown that *CYP26B1* mRNA was increased in murine atherosclerosis and expressed in macrophage-rich areas of human atherosclerotic lesions. A role of the CYP26B1 enzyme activity on atherosclerosis development by altering the availability of retinoid ligands was suggested and investigations on pharmacological CYP26PB1 inhibitors in the treatment of atherosclerosis and its complications proposed (1). The Netherlands study of depression and anxiety (NESDA) demonstrated a higher likelihood of subclinical atherosclerosis in persons with current depressive or anxiety disorders compared to healthy controls (2) substantiating a low grade inflammation in depression further. We examined whether the anti-inflammatory agent willow bark, its salicin rich ethanol fraction and the tricyclic antidepressant imipramine target the gene-expression of *CYPB26B1* and retinoid ligands in peripheral blood of rats in the Porsolt-Swimming Test (FST). Male Sprague Dawley rats (n = 12 per group) were treated for 14 days p. o. with the willow bark extract STW 33-I (group A), its salicin rich fraction (group B), imipramine (group C). All three groups showed a reduction of the immobility time in the Porsolt swimming test, in comparison to an untreated control group as described earlier (3). Gene expression in peripheral rat blood of groups A, B, C (n = 4 per group) were analysed by Agilent whole genome microarray, reverse transcriptase-PCR and compared to those of untreated controls (n = 4) (3).

Transcripts of *CYP26B1* were strongly down regulated (-12 to — 20 fold, $p < 0.01$) in all three groups based on microarray analysis. RT-PCR revealed the down regulation in all groups, however, significantly only in group B, in which the strongest (20-fold) regulation based on the microarray-analysis was found. Also transcripts of retinoid x receptors (RXRA, RXRB) were down regulated (- 1.6 to — 2.0, $p < 0.05$) in group A and C based on microarray data. We can report that the gene expression of *CYP26B1* and of retinoid ligands is targeted by willow bark, its salicin rich ethanol fraction and imipramine in the peripheral blood of rats, but to a variable extent. Further studies are recommended to fully understand the mode of action of willow bark and its constituents on the retinoid acid metabolism for their further systematic development as co-medication in indications with a prevailing low grade inflammation.

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BIOSAFETY ASSESSMENT OF SILYMARIN AND ARGININE COMBINATION IN HEALTHY MEN

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Silymarin (SMN) in milk thistle is used as a heptoprotective against alcohol and drug toxicity. Silymarin is also being investigated for its cancer preventive and cholesterol lowering properties (1). L-arginine (L-Arg), a semi-essential amino acid, is recommended as an immune and vitality enhancer (2) but with some urinary side effects (3). This controlled intervention trial aimed to investigate the effect on metabolic parameters of a beverage containing SMN and L-Arg in 20 healthy men aged 41–59 years. The design of the study is shown in Fig.

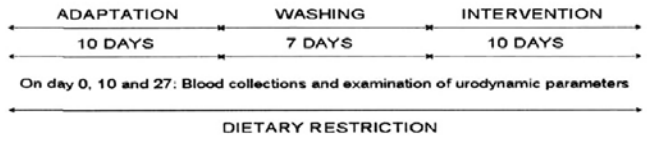

Fig. Design of the intervention study.

The subjects drank 500 ml/day beverage without SMN and Arg for 10 days followed by the beverage with 400 mg SMN and 295 mg L-Arg for 10 days. Blood and urine samples were collected on days 0, 10 and 27. Total antioxidative capacity, plasma/erythrocyt oxidative stress and clinical chemistry safety markers, urination parameters including IPSS, voiding parameters-rate of urine flow (Q_{max}), average flow (Q_{ave}), total volume and postvoid residual volume (RV) parameters were measured. The data suggest that the combination of SMN plus L-Arg alters the antioxidant status of erythrocyte, other clinical markers or urinary parameters were unchanged. Overall, the drink was well-tolerated with no adverse effects.

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