ICCN Poster Presentations

Nutrition and cardiovascular disease

Antioxidants modulate the nitric oxide system and SOD activity and expression in rat epithelial lung cells

Z Madar*[1], N Maayan[1], O Sarit[1] and A Eliraz[2]
[1]*The Hebrew University of Jerusalem, The Institute of Biochemistry, Food Science and Nutrition, Rehovot, Israel*
[2] *Pulmonary Unit, Kaplan Hospital, Rehovot, Israel.*

Nitric Oxide (NO) plays a key role in many physiological processes and is synthesized by the enzyme Nitric Oxide Synthase (NOS). There is increasing evidence that NO produced in human airways is involved in pathological events, such as asthma. This work investigated the effect of various antioxidants on NO production and on iNOS and SOD expression and activity in stimulated epithelial lung cells, as a model for asthma. L-2 cells were stimulated with combinations of TNFα, INFγ and LPS for 24h, followed by incubation with increasing concentrations of N-acetyl-l-cystein (NAC), resveratrol, Genistein, Quercetin, soy saponin 2, 3-dihydro-2, 5-dihydroxy-6-methyl-4H-pyran-4-one (DDMPl) and with an olive leaf polyphenol extract. NO production was determined by measuring nitrate and nitrite concentrations using the Griess reaction. Expression of iNOS and SOD were detected using western blot analysis. SOD activity was measured by an ingel activity assay. cGMP was also detected using radioimmunoassay kit. In stimulated cells, the concentration of nitrites in the medium increased 4 fold compared to control cells. Resveratrol and the olive leaf extract reduced nitrite levels in the medium by 37% and 41% respectively. Quercetin and genistein reduced nitrite levels by approximately 50%. However, NAC increased levels by 48% and DDMP had no effect. Significant reductions in iNOS expression were measured following treatment with polyphenol extract and resveratrol. SOD expression was higher in stimulated cells when compared to controls and significant increases were detected by olive leaf extract, quercetin and genistein. Total SOD activity, as well as cGMP levels were not affected by cytokine stimulation or by any treatment. The presence of resveratrol as well as a polyphenol extract in a cellular model of asthma significantly reduced iNOS expression and medium nitrite concentrations. These compounds presumably act by different mechanisms. The polyphenol extraction affects the antioxidant enzyme MnSOD while resveratrol does not. These results indicate that treatment with these active compounds may be beneficial in inflammatory lung diseases.

Long- term effects of policosanol on older patients with Type 2 diabetes

R Mas*[1], G Castaño[2], J Fernández[1], [R] R Gamez[1], J Illnait[1], L Fernandez[2], E Lopez[2], M Mesa[2], E Alvarez[1] and S Mendoza[1]
[1] *Center of Natural Products, National Center for Scientific Research;*
[2] *Surgical Medical Research Center* [3] *Havana City, Cuba*

Diabetes and hypercholesterolemia are major coronary risk factors. Coronary risk of diabetics is also greater than non-diabetics. The main goal of dyslipidemia control in diabetics is to lower elevated low-density lipoprotein-cholesterol (LDL-C) levels. Policosanol is a cholesterol-lowering drug purified from sugar cane wax, which significantly reduces LDL-C levels and inhibits platelet aggregation. Previous short-term studies have shown the efficacy and tolerability of policosanol at 10 mg/day on patients with Type 2 diabetes, but no previous study on the effects of long-term treatment or lower doses has been reported. This study was undertaken to investigate the long-term efficacy, safety and tolerability of policosanol on patients with Type 2 diabetes. After 5 weeks on a step one cholesterol lowering diet, 239 patients with Type 2 diabetes were randomized to policosanol 5 mg/day or placebo for 2 years. Analysis was by Intention-to-treat. Baseline characteristics were well matched in both groups. After one year, policosanol reduced significantly ($p < 0.0001$ *versus* baseline and placebo) low-density lipoprotein-cholesterol (LDL-C) (21.1 %), total cholesterol (TC) (17.5 %) and triglycerides (TG) (16.0 %), whereas increased ($p < 0.01$ *versus* baseline and placebo) high-density lipoprotein-cholesterol (HDL-C) levels (10.7 %). Treatment effects on LDL-C, HDL-C and TC persisted, even moderately enhanced, during the study, the effect on TG being persistent too Thus, at study completion, policosanol lowered ($p < 0.0001$ *vs* baseline and placebo) LDL-C (29.5 %), TC (21.9 %), TG (16.9 %) and raised ($p < 0.0001$ *vs* baseline and placebo) HDL-C (12.4 %). No significant changes on lipid profile variables of placebo group occurred during the study. Of 239 randomized patients, 63 (26.4 %) discontinued the study, 43/120 placebo (35.8 %) and 20/119 policosanol patients (16.8 %). Of them, 35 patients (28 placebo, 7 policosanol) withdrew from the study due to some AE. The frequency of serious adverse events (SAE), most vascular, in policosanol patients (6/119, 5.0 %) was lower than in respective placebo (26/120, 43.3 %). Five patients, all placebo, died during the study, four of them due to myocardial infarction. No drug-related impairment of safety indicators, particularly on glycemic control, was observed. Nevertheless, a reduction of systolic and diastolic blood pressure was observed in policosanol patients compared with placebo. The overall frequency of policosanol patients reporting mild and/or moderate was similar than in placebo. It is concluded that policosanol was long-term effective, safe and well tolerated on patients with dyslipidemia due to Type 2 diabetes.