Effects of a new combination of Berberine, Monacolin k and Morus Alba on lipid profile and HDL functions in healty subjects: a pilot study

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Cholesterol efflux capacity (CEC) is the main atheroprotective function of high density lipoproteins (HDL) and represents their ability to accept cholesterol from macrophages therefore counteracting foam-cell formation. Cholesterol efflux to HDL mainly occurs through the activity of the membrane transporters Scavenger Receptor class B type I (SR-BI), ATP Binding Cassette A1 (ABCA1) and G1 (ABCG1). Each transporter recognizes specific HDL subclasses. Interestingly, serum-HDL CEC has been inversely related to early atherosclerosis and cardiovascular risk, independently of HDL cholesterol (HDL-C) levels.

Several nutraceuticals (NUT) have been suggested to improve plasma lipid profile with a possible positive influence on cardiovascular risk. Recently, a NUT combination of Berberine, Monacolin K and Morus Alba extract showed a marked hypocholesterolemic and hypoglycemic effects. The aim of this study was to evaluate the effect of the NUT combination of Berberine (531.25 mg), Red yeast rice powder (220 mg; 3.3 mg monacolin K) and leaf extract of Morus Alba (200 mg) on HDL function measured as CEC.

To achieve this aim a pilot study has been conducted in 9 healthy volunteers treated 4 weeks with the above NUT combination. This product has recently been approved in Italy (LopiGLIK^{TM}, Akademy Pharma). CEC measurement was performed on serum subjects after PEG precipitation of apoB containing lipoproteins. The individual cholesterol efflux pathways were evaluated by using specific cell-based radio isotopic assays.

The NUT combination reduced total cholesterol (from 225±28.2 mg/dl to 194±10.7 mg/dl, $p<0.005$), LDL cholesterol (from 141±25.8 mg/dl to 117±12.4 mg/dl, $p<0.05$) and HDL-C (from 60±11.6 mg/dl to 53±9.8 mg/dl, $p<0.005$). After treatment no differences were observed on plasma triglycerides level and fasting plasma glucose. NUT combination did not influence CEC via aqueous diffusion or via the ABCA1 transporter. On the contrary, after treatment with NUT combination, subject serum-HDL displayed a significantly higher CEC both through SR-BI and ABCG1 pathways with an average increase of 27% and 13%, respectively (from 1.93% ± 0.66 to 2.26% ± 0.54 for SR-BI and from 4.45 ± 0.83 to 5.03 ± 1.24 for ABCG1; $p<0.05$). The results of this pilot study suggest that 4 weeks of treatment with a NUT combination of Berberine, Monakolin K and Morus Alba extract favorably modifies plasma lipid profile in terms of total and LDL cholesterol. The most striking result is that, despite the lack of increase in HDL-C plasma level, these NUT improve CEC, the main antiatherogenic property of HDL. Few studies previously showed a positive effect of nutraceuticals on CEC, and this effect was paralleled by increased HDL plasma concentrations. Conversely, the administration of the present NUT combination seems to ameliorate HDL functionality independently of HDL quantity. In particular, the treatment selectively increased serum-HDL CEC trough SR-BI and ABCG1, suggesting a redistribution of HDL subfractions towards particles specifically inducing SR-BI- and ABCG1-mediated cholesterol efflux. The increase of HDL CEC through these two pathways could be an important mechanism of atheroprotection by opposing to foam cell formation, and by activating anti-inflammatory intracellular signaling known to be mediated by SRBI and ABCG1. Both the improved HDL functionality and the decreased plasma LDL cholesterol levels may contribute to a reduction of serum ability to induce macrophage cholesterol accumulation. Our present observation underlies the importance of measuring functional HDL-related parameters, beyond the simple evaluation of HDL plasma levels. All together these findings show for the first time the capacity of a NUT combination to improve serum-HDL quality and functions independently of HDL plasma concentrations. Although the number of subjects was limited, these findings are very promising and create the premises for a future extended clinical trials.