

Euro Diabetes 2019: The international debate on the enhancement of high-density lipoproteins quantity and quality to treat dyslipidemia and hypertension by policosanols- Kyung-Hyun Cho- Yeungnam University

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Metabolic syndrome is closely associated with higher risk of hypertension, cardiovascular disease, diabetes and stroke. It has been reported that Cuban policosanols improve lipid parameters and HDL functionality in human participants. The aim of the present study was to investigate the long-term effects of policosanols supplementation on blood pressure (BP) and the lipid profile in healthy Korean participants with prehypertension.

This randomized, double-blinded, and placebo-controlled trial included 84 healthy participants who were randomly assigned to three groups receiving 10 mg of policosanols, 20 mg of policosanols, or placebo up to 24 weeks.

The BP, lipid profile, and anthropometric factors were measured pre- and post-intervention and then compared. Based on an average of three measurements of brachial BP, the policosanols 20 mg group showed the most significant reduction in average systolic BP (SBP) from 138 ± 12 mmHg at week 0 to 126 ± 13 mmHg at week 24 ($p < 0.0001$). The policosanols 10 mg group showed a 4% reduction in SBP from 135 mmHg at week 0 to 128 mmHg at week 24 ($p = 0.016$), whereas the placebo group showed no change in BP between weeks 0 and 24.

The policosanols consumption for 12 weeks, the policosanols 20 mg group exhibited the most significant reduction of BP, up to 7.7% reduction of average systolic BP (SBP) from 136.3 ± 6.1 mmHg (week 0) to 125.8 ± 8.7 mmHg ($p < .001$). Between group comparisons using repeated measures ANOVA analysis showed that the policosanols 20 mg group had a significant reduction of SBP ($p = .020$) and a reduction of DBP ($p = .035$). The policosanols 10 mg and 20 mg groups showed significant reductions in aortic SBP of 7.4% and 8.3%, respectively. The policosanols groups showed significant reductions of total cholesterol (TC) of 9.6% and 8.6% for 10 mg and 20 mg of policosanols, respectively. Lipoprotein functionality improved by policosanols to be more anti-atherogenic; LDL showed more anti-oxidant while HDL showed more anti-glycation properties

In conclusion, consumption of policosanols resulted in significant reductions of peripheral SBP and DBP, aortic SBP and DBP, and mean arterial pressure (MAP) and serum TC and LDL-C with elevation of %HDL-C.

In the current study, 8 weeks of policosanols consumption resulted in a reduction in blood pressure and visceral fat amount in healthy female subjects with prehypertension. The lowering effects of policosanols on blood pressure were accompanied by lowering of serum total cholesterol and triglyceride levels as well as increased HDL-C levels via inhibition of serum CETP activity. One of the interesting findings of this study is that policosanols could enhance cholesterol efflux in a dose-dependent

manner by stimulating the expression of ABCA-1. Cholesterol efflux is a key feature of HDL that exerts regression activity via removal of cholesterol from atherosclerotic plaques in the reverse cholesterol transport pathway. It has been reported that efflux activity is mainly dependent on the configuration of apoA-I. Therefore, the current finding shows that policosanols enhanced cholesterol efflux synergistically with apoA-I. It has been suggested that the apoA-I configuration in discoidal HDL may be important for the recognition of cellular proteins as well as for interactions with specific lipid domains of the cell membrane. Our group previously reported that encapsulation of policosanols in rHDL caused a reduction in α -helix content in apoA-I along with an increased exposure of Trp residues. These configurational changes might increase the affinity between apoA-I and the lipid domain of ABCA-1 for enhancement of cholesterol efflux.

Native apoA-I and HDL can stimulate insulin secretion and exert antidiabetic activity, whereas modified apoA-I/HDL cannot. Native reconstituted HDL also displayed insulin secretion activity along with a wound-healing effect. Many studies on patients have reported that policosanols has efficacy in the treatment of hyperlipidemia, diabetes, and hypertension, although the detailed molecular mechanism has not been elucidated. As there has been almost no study on the effects of policosanols on healthy subjects with hyperlipidemia and hypertension, this study investigated the efficacy of policosanols in ordinary and healthy subjects with prehypertension. A recent paper reported that hexacosanol reduces plasma and hepatic cholesterol by activation of adenosine 5'-monophosphate-(AMP-) activated protein kinase (AMPK) and suppression of sterol regulatory element-binding protein-2 in HepG2 and C57BL/6J mice. It has been well known that AMPK activation activities were correlated with increased export of cholesterol and excretion of cholesterol. Recently, AMPK activation enhances antiatherogenic effects of HDL with slightly lowering serum total cholesterol and body weight in apoE^{-/-} mice. Taken together, these papers make agreement that policosanols can enhance HDL functionality via AMPK activation and CETP inhibition.

Keywords: Policosanols, blood pressure, high-density lipoproteins, low-density lipoproteins