Sesamol inhibits atherogenic LDL-induced endothelial cell senescence in vivo and in vitro

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OBJECTIVE Highly electronegative L5 low-density lipoprotein (LDL), an atherogenic LDL, induces endothelial cell (EC) senescence and has been implicated in the progression of atherosclerosis. We examine whether sesamol, a natural organic compound and component of sesame oil, prevents EC senescence induced by electronegative LDL (L5) and to investigate the underlying mechanisms. **METHODS** Syrian hamsters, which have a LDL profile similar to that of humans, were fed a normal chow diet (control), a high-fat diet (HFD), or a HFD supplemented with the administration of 50 or 100 mg/ kg sesamol via oral gavage (HFD+sesamol) for 16 weeks (*n*=10 per group). Among these groups, we compared plasma L5 levels and aortic endothelial senescence in the aortic arch. In vitro, we examined the effects of sesamol on human aortic endothelial cell (HAEC) senescence and signaling pathways induced by L5. **RESULTS** Hamsters in the HFD group had higher plasma L5 levels than did the HFD+sesamol groups or control group. Beta-galactosidase (gal) staining showed that aortic endothelial senescence was markedly increased in the aortic arch of the HFD group but not in that of the HFD+sesamol groups when compared with the control group. In vitro, treatment of HAECs with sesamol (1-3 μM) blocked L5-induced EC senescence in a dose-dependent manner. Sesamol also markedly inhibited the L5-induced phosphorylation of p38 MAPK and p53 activation and increased Mdm2 and phosphorylation of Akt. **CONCLUSION** The critical findings of this study suggest that sesamol may provide protection against atherosclerosis and the development of cardiovascular disease in humans.

Key words: sesamol; atherogenic LDL; endothelial cell senescence; Syrian hamsters; p53

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