Salvianolic acid B attenuates MMP-2 and MMP-9 expression in vivo in apolipoprotein-E-deficient mouse aorta and in vitro in LPS-treated human aortic smooth muscle cells.

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摘要

Abstract

Salvianolic acid B (Sal B), a water-soluble antioxidant derived from a Chinese medicinal herb, is believed to have multiple therapeutic and preventive against human vascular diseases, including atherosclerosis and restenosis. To elucidate the underlying cellular mechanisms, we produced hypercholesterolemia by feeding apo-E-deficient mice a 0.15% cholesterol diet and inflammation in human aortic smooth muscle cells (HASMCs) with the endotoxin lipopolysaccharide(LPS), focusing on the metallopreteinases MMP-2 and MMP-9, the relevant signal transduction pathways and the effects of Sal B. Immunohistochemical analyses indicated apo-E- deficient mice fed a 0.15% cholesterol diet for 12 weeks exhibited thickened intima and elevated levels of MMP-2 and MMP-9 in aortic sections, both of which were attenuated by 0 .3% Sal B dietary supplement. Western blotting and zymography analyses indicated that unstimulated HASMCs exhibited basal levels of protein and activity levels for MMP-2 and barely detectable levels for MMP-9, both of which were markedly upregulated by LPS, which also induced cell migration. Sal B significantly attenuated upregulations of both MMPs as well as the LPS-induced cell migration through the inactivation of MMP-2 and MMP-9 protein synthesis as well as the downregulation of the extracellular-signal- regulated kinase 1/2 (ERK1/2) and c-Jun NH2-terminal kinase(JNK). These results demonstrate that Sal B has anti-migration properties on smooth muscle cells and may explain its anti-atherosclerotic

properties. This novel mechanism of action of Sal B, in addition to its previously reported inhibition of LDL oxidation, may help explain its efficacy in the treatment of atherosclerosis.