The HMG-CoA reductase inhibitor rosvastatin inhibits plasminogen activator inhibitor-1 expression and secretion in human adipocytes.

Abstract:
Human preadipocytes and adipocytes are known to produce the proatherogenic factor PAI-1 and proinflammatory cytokines, and obesity was found to be state of increased adipose production of these factors. In the present study, we investigated the effect of rosvastatin on the regulation of PAI-1 gene expression in human adipocytes. Human preadipocytes, adipocytes in primary culture and the SGBS cell line were used as cell models. Cells were transfected using various constructs and promoter activity was measured as luciferase activity. PAI-1 expression was measured by quantitative RT-PCR and ELISA. Rosuvastatin inhibited PAI-1 mRNA expression and secretion of the protein in a concentration-dependent manner. This effect was reversed by isoprenoids. Addition of MEK-inhibitors and NFkappaB inhibitors also reduced PAI-1 expression and PAI-1 promoter luciferase activity. Further experiments revealed that rosvastatin down-regulated the MEKK-1 mediated activation of the PAI-1 promoter. In conclusion our data suggest that rosvastatin inhibits PAI-1 expression and release from human adipocytes via a MEKK-1-dependent but not a NFkappaB-dependent mechanism.