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Inhibition of Atherosclerotic Lesion by KR-31378 in LDL Receptor Null Mice

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The recruitment and infiltration of monocytes into the artery wall is a crucial early step in atherogenesis. KR-31378 has been shown to be a neuroprotective agent in rat brain via its potent antioxidant and antiapoptotic actions. Here, we report the effects of this compound on atherogenesis, and some possible mechanisms of action. In Ldlr knock-out mice, treatment with KR-31378 inhibited fatty streak lesion formation and macrophage accumulation. In the test to address the possibility that KR-31378 may influence the initial stages of atherogenesis, KR-31378 decreased the adhesion and migration of monocytes to endothelial cells. The observed decreases in cell adhesion and migration correlated with KR-31378-mediated down-regulation of VCAM-1 and IL-8. Transent transfection assay, electrophoretic mobility shift assay, and IκB degradation assay showed that KR-31378 decreased NF-κB activation.These results indicate that KR-31378 potently reduces lesion formation by inhibiting NF-κB-dependent cellular adhesion and chemotatic molecule expression, which is crucial to monocyte infiltration into the arterial wall.

Keyword : Inflammation, Nuclear factor kappa B, Adhesion molecules