



ZLJ-6, a Novel COX/5-LOX Inhibitor, Ameliorates Atherosclerosis by Reducing Macrophage Infiltration in ApoE^{-/-} Mice

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SUMMARY. Atherosclerosis is a chronic inflammatory process involving the recruitment and accumulation of monocytes, macrophages, and dendritic cells in artery walls. Cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX), two major inflammatory pathways, which play pivotal roles in leukocyte recruitment and infiltration, have been reported to be involved in atherogenesis. We therefore investigated the anti-atherogenic effect of ZLJ-6 [(Z)-2-amino-1,5-dihydro-1-methyl-5-[4-(mesyl)benzylidene]-4H-imidazol-4-one mesilate]. ZLJ-6, as a potent COX/5-LOX inhibitor, reduced the overall plasma concentrations of prostanoids and LTB₄. Within these lesions, ZLJ-6 decreased aortic plaque with a striking reduction in plaque macrophages and raise in collagen content in ApoE^{-/-} mice. Aortic expression of proatherogenic molecules including MCP-1, TNF- α , VCAM-1, IL-6, and MMP-2 was also lower in the ZLJ-6 group than the control group. ZLJ-6 also inhibited lipopolysaccharide (LPS) induced peripheral blood monocytes (PBMs) migration *in vitro* by reducing COX-2 and 5-LOX expression in PBMs. These data imply that the anti-atherogenic effect of ZLJ-6 might be associated with its inhibition on macrophages. In conclusion, ZLJ-6 effectively attenuated atherosclerosis in mouse model, suggesting its therapeutic potential for atherosclerosis.

KEY WORDS: Atherosclerosis, Cyclooxygenase/5-lipoxygenase inhibitor, Inflammation, ZLJ-6

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