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# Diminazene enhances stability of atherosclerotic plaques in ApoE-deficient mice

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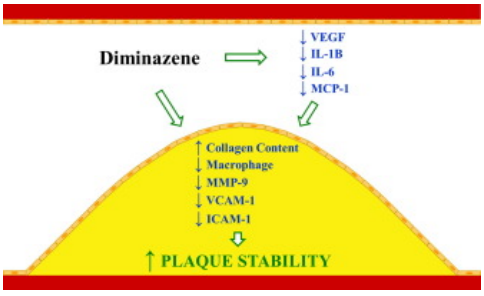
## Abstract

Angiotensin (Ang) II contributes to the development of atherosclerosis, while Ang-(1–7) has atheroprotective actions. Accordingly, angiotensin-converting enzyme 2 (ACE2), which breaks-down Ang II and forms Ang-(1–7), has been suggested as a target against atherosclerosis. Here we investigated the actions of diminazene, a recently developed ACE2 activator compound, in a model of vulnerable atherosclerotic plaque. Atherosclerotic plaque formation was induced in the carotid artery of ApoE-deficient mice by a shear stress (SS) modifier device. The animals were treated with diminazene (15 mg/kg/day) or vehicle. ACE2 was strongly expressed in the aortic root and low SS-induced carotid plaques, but poorly expressed in the oscillatory SS-induced carotid plaques. Diminazene treatment did not change the lesion size, but ameliorated the composition of aortic root and low SS-induced carotid plaques by increasing collagen content and decreasing both MMP-9 expression and macrophage infiltration. Interestingly, these beneficial effects were not observed in the oscillatory SS-induced plaque. Additionally, diminazene treatment decreased intraplaque ICAM-1 and VCAM-1 expression, circulating cytokine and chemokine levels and serum triglycerides. In summary, ACE2 was distinctively expressed in atherosclerotic plaques, which depends on the local pattern of shear stress. Moreover, diminazene treatment enhances the stability of atherosclerotic plaques.

## Graphical abstract



Keywords

Diminazene; Angiotensin-converting enzyme 2; Angiotensin; Atherosclerosis; Inflammation; Plaque stability; Plaque vulnerable

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