A novel drug SP-8356 attenuated neointimal hyperplasia and with its related arterial stiffness via affecting CD147/MMP-9 pathway in a rat atherosclerotic carotid artery

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Background and Aims

Neointimal hyperplasia and with its related arterial stiffness are the crucial pathophysiological features in atherosclerosis and in-stent restenosis. CD147 plays important roles in neointimal hyperplasia through matrix metalloproteinase-9 (MMP-9) expression. Thus, CD147 can emerge as an effective therapeutic target for treatment of neointimal hyperplasia. We identified that a novel drug SP-8356 ((1S,5R)-4-(3,4-dihydroxy-5-methoxystyryl)-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-one) could bind to CD147 which was involved in MMP-9 expression. We investigated the suppressive effects of a novel drug SP-8356 on neointimal hyperplasia and arterial stiffness using an atherosclerotic rat model.

Methods

Atherosclerosis was induced in Sprague-Dawley rats by partial ligation of the right carotid artery coupled with atherogenic diet and vitamin D injection. The elasticity of blood vessels was assessed by measuring pulse wave velocity using Doppler ultrasonography. After sacrifice, the blood vessels were stained with hematoxylin/eosin or antibodies against α -smooth muscle-actin (α -SMA), smooth muscle myosin heavy chain (SM-MHC), collagen type III, and MMP-9.

Results

Fig. 1

Fig. 2

Fig. 3

Conclusions

SP-8356 exhibited anti-atherosclerotic effect by suppressing CD147/MMP-9 pathway. Therefore, SP-8356 could be a promising therapeutic drug for vascular remodeling disorders involving neointimal hyperplasia and arterial stiffness.