

($12.5\pm 0.8\%$, $7.6\pm 0.3\%$ vs $34.2\pm 1.1\%$, respectively, p both < 0.01). In addition, resveratrol also in a concentration-dependent manner decreased the levels of ROS and phosphorylated ERK1/2 in both VSMC and balloon-injured carotid arteries. No differences in blood tests of liver and kidney functions among these different groups.

Conclusion Resveratrol attenuates neointimal formation after balloon injury and VSMC proliferation via inactivation of ERK1/2 pathway. Resveratrol has no adverse effects on liver and kidney functions in the effective ranges.

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RESVERATROL ATTENUATES NEOINTIMAL FORMATION AFTER BALLOON INJURY AND VASCULAR SMOOTH MUSCLE CELLS PROLIFERATION VIA INACTIVATION OF ERK1/2 PATHWAY

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Background Proliferation of vascular smooth muscle cells (VSMC) and subsequently neointimal formation play major roles in the pathogenesis of atherosclerosis and restenosis.

Aim To determine the possible mechanism of resveratrol in the inhibition of neointimal formation and VSMC proliferation.

Methods The cultured rat VSMC were incubated with resveratrol (0, 1, 10 and 100 $\mu\text{mol/l}$) for 72 h and VSMC proliferation was detected using the bromodeoxyuridine (BrdU) assay. The level of intracellular reactive oxygen species (ROS) was measured using the ROS assay kit. The activity of extracellular signal-regulated kinase (ERK1/2) was determined by western blot analysis. The rat carotid arteries were injured by balloon catheter, followed by oral administration of resveratrol with dosages of 0, 2.5, 5 and 10 mg/kg per day in different groups. The rats were euthanised for morphometric and immunohistochemical analysis, western blot, detection of ROS and biological safety at 14 days after balloon injury.

Results VSMC proliferation was inhibited by resveratrol in a concentration-dependent manner. Compared with the untreated control group, 10 and 100 $\mu\text{mol/l}$ resveratrol caused a significant reduction in VSMC proliferation (0.627 ± 0.03 , 0.390 ± 0.002 vs 0.942 ± 0.03 , respectively, p both < 0.01). The neointimal formation after balloon injury was inhibited by resveratrol in a concentration-dependent manner. Oral administration of resveratrol with dosages of 5 and 10 mg/kg per day caused a significant reduction in the percentage of anti-proliferating cell nuclear antigen (PCNA) positive cells in the neointima compared with the untreated control group