Inhibitory mechanisms of resveratrol in platelet activation: pivotal roles of p38 MAPK and NO/cyclic GMP

許準榕
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Abstract

Resveratrol has been reported to have antiplatelet activity; however, the detailed mechanisms have not yet been resolved. This study aimed to systematically examine the detailed mechanisms of resveratrol in the prevention of platelet activation in vitro and in vivo. Resveratrol (0·05–0·25 μmol/l) showed stronger inhibition of platelet aggregation stimulated by collagen (1 μg/ml) than other agonists. Resveratrol (0·15 and 0·25 μmol/l) inhibited collagen-induced platelet activation accompanied by [Ca+2]i mobilization, thromboxane A2 (TxA2) formation, phosphoinositide breakdown, and protein kinase C (PKC) activation. Resveratrol markedly increased levels of NO/cyclic guanosine monophosphate (GMP), and cyclic GMP-induced vasodilator-stimulated phosphoprotein phosphorylation. Resveratrol markedly inhibited p38 mitogen-activated protein kinase (MAPK) but not Jun N-terminal kinase or extracellular signal-regulated kinase-2 phosphorylation in washed platelets. Resveratrol-reduced hydroxyl radical (OH−) formation in the electron spin resonance study. In an in vivo study, resveratrol (5 mg/kg) significantly prolonged platelet plug formation of mice. In conclusion, the main findings of this study suggest that the inhibitory effects of resveratrol possibly involve (i) inhibition of the p38 MAPK-cytosolic phospholipase A2-arachidonic acid-TxA2-[Ca+2]i cascade and (ii) activation of NO/cyclic GMP, resulting in inhibition of phospholipase C and/or PKC activation. Resveratrol is likely to exert significant protective effects in thromboembolic-related disorders by inhibiting platelet aggregation.