Involvement of p38 MAPK Phosphorylation and Nitrate Formation in Aristolochic Acid-Mediated Antiplatelet Activity

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摘要

Abstract

Aristolochic acid (AsA) is produced from Aristolochia fangchi, and has been used as a Chinese herbal medicine. AsA possesses various biological activities including antiplatelet, antifungal, and anti-inflammatory properties. The aim of this study was to examine the mechanisms of AsA in inhibiting platelet aggregation. AsA (75 - 150 microM) exhibited more-potent activity of inhibiting platelet aggregation stimulated by collagen (1 microg/mL) than other agonists. AsA (115 and 150 microM) inhibited collagen-induced platelet activation accompanied by [Ca+2)]i mobilization, thromboxane A2 (TxA2) formation and phosphoinositide breakdown. On the other hand, AsA also markedly increased levels of NO/cyclic GMP, and cyclic GMP-induced vasodilator-stimulated phosphoprotein phosphorylation. AsA inhibited p38 MAPK but not ERK1/2 phosphorylation in washed platelets. In conclusion, the most important findings of this study suggest that the inhibitory effects of AsA possibly involve the (1) inhibition of the p38 MAPK-cytosolic phospholipase A2-arachidonic acid-TxA2-[Ca+2)]i cascade, and (2) activation of NO/cyclic GMP, resulting in inhibition of phospholipase C. These results imply that Aristolochia fangchi treatment alone or in combination with other antiplatelet drugs, may result in alteration of hemostasis in vivo.