The antiplatelet activity of rutaecarpine, an alkaloid isolated from evodia rutaecarpa, is mediated through inhibition of phospholipase C

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摘要

Abstract

In this study, the mechanism involved in the antiplatelet activity of rutaecarpine in human platelet suspensions was investigated. In platelet suspensions (4.5 x 10(8)/ml), rutaecarpine (100 and 200 microM) did not influence the binding of FITC-triflavin to platelet glycoprotein IIb/IIIa complex. Additionally, rutaecarpine (200 microM) did not significantly change the fluorescence of platelet membrane labeled with diphenylhexatriene (DPH). On the other hand, rutaecarpine (50 and 100 microM) dose-dependently inhibited the increase in intracellular free Ca2+ of Fura 2-AM loaded platelets stimulated by collagen. Moreover, rutaecarpine (100 and 200 microM) did not significantly affect the thromboxane synthetase activity of aspirin-treated platelet microsomes. Furthermore, retaecarpine (100 and 200 microM) significantly inhibited [3H]arachidonic acid released in collagen-activated platelets but not in unactivated-platelets. Nitric oxide (NO) production in human platelets was measured by a chemiluminesence detection method in this study. Rutaecarpine (100 and 200 microM) did not significantly affect nitrate production in collagen (10 microg/ml)-induced human platelet aggregation. On the other hand, various concentrations of rutaecarpine (50, 100, and 200 microM) dose-dependently inhibited [3H]inositol monophosphate formation stimulated by collagen (10 microg/ml) in [3H]myoinositol-loaded platelets at different incubation times (1, 2, 3, and 5 minutes). It is concluded that the antiplatelet activity of rutaecarpine may possibly be due to the inhibition of phospholipase C activity, leading to reduce phosphoinositide breakdown, followed by the inhibition of thromboxane A2 formation, and then inhibition of [Ca2+]i mobilization of platelet aggregation stimulated by agonists.