alpha-Naphthoflavone, a potent antiplatelet flavonoid, is mediated through inhibition of phospholipase C activity and stimulation of cyclic GMP formation.

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摘要

Abstract

The aim of this study was to systematically examine the inhibitory mechanisms of the flavonoid alpha-naphthoflavone (alpha-NF) in platelet activation. In this study, alpha-NF concentration dependently (5-20 microM) inhibited platelet aggregation stimulated by agonists. alpha-NF (5 and 10 microM) inhibited intracellular Ca(2+) mobilization, phosphoinositide breakdown, and thromboxane A(2) formation stimulated by collagen (1 microg/mL) in human platelets. In addition, alpha-NF (5 and 10 microM) markedly increased levels of cyclic GMP and cyclic GMP-induced vasodilator-stimulated phosphoprotein (VASP) Ser(157) phosphorylation. Rapid phosphorylation of a platelet protein of Mr 47,000 (P47), a marker of protein kinase C activation, was triggered by phorbol-12,13-dibutyrate (60 nM). This phosphorylation was markedly inhibited by alpha-NF (5 and 10 microM). However, alpha-NF (5 and 10 microM) did not reduce the electron spin resonance (ESR) signal intensity of hydroxyl radicals in collagen (1 microg/mL)-activated platelets. These results indicate that the antiplatelet activity of alpha-NF may be involved in the following pathways. (1) alpha-NF may inhibit the activation of phospholipase C, followed by inhibition of phosphoinositide breakdown, protein kinase C activation, and thromboxane A(2) formation, thereby leading to inhibition of intracellular Ca(2+) mobilization. (2) alpha-NF also activated the formation of cyclic GMP, resulting in inhibition of platelet aggregation. These results strongly indicate that alpha-NF appears to represent a novel and potent antiplatelet agent for treatment of arterial thromboembolism.