Inhibitory mechanisms of kinetin, a plant growth-promoting hormone, in platelet aggregation

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摘要

Abstract

Kinetin has been shown to have anti-aging effects on several different systems including plants and human cells. The aim of this study was to examine the detailed inhibitory mechanisms of kinetin in platelet aggregation. In this study, kinetin concentration-dependently (50-150 μM) inhibited platelet aggregation in human platelets stimulated by agonists. Kinetin (70 and 150 μM) also concentration-dependently inhibited intracellular Ca2+ mobilization and phosphoinositide breakdown in platelets stimulated by collagen (1 μg/ml). Kinetin (70 and 150 μM) significantly inhibited thromboxane A2 formation stimulated by collagen (1 μg/ml) and arachidonic acid (60 μM) in human platelets. In addition, kinetin (70 and 150 μM) significantly increased the formation of cyclic AMP. Intracellular pH values were measured spectrofluorometrically using the fluorescent probe BCECF-AM in platelets. The thrombin-evoked increase in pHi was markedly inhibited in the presence of kinetin (70 and 150 μM). Rapid phosphorylation of a platelet protein of molecular weight (Mr) 47 000 (P47), a marker of protein kinase C activation, was triggered by collagen (1 μg/ml). This phosphorylation was inhibited by kinetin (70 and 150 μM). In conclusion, these results indicate that the anti-platelet activity of kinetin may be involved in the following pathways: kinetin's effects may initially be due to inhibition of the activation of phospholipase C and the Na+/H+ exchanger. This leads to lower intracellular Ca2+ mobilization, followed by inhibition of TxA2 formation and then increased cyclic AMP formation, followed by a further inhibition of the Na+/H+ exchanger, ultimately resulting in markedly decreased intracellular Ca2+ mobilization and phosphorylation of P47. These results suggest that kinetin has an effective anti-platelet effect and that it may be a potential therapeutic agent for arterial thrombosis