The antiplatelet activity of PMC, a potent a-tocopherol analogue, is mediated through inhibition of cyclooxygenase. Br.

林建煌;許準榕

Sheu JR;Lee CR;Lin CC;Kan YC;Lin CH;Hung WC;Lee YM and Yen MH

Abstract

PMC, a potent α-tocopherol derivative, dose-dependently (5–25μM) inhibited the ATP-release reaction and platelet aggregation in washed human platelets stimulated by agonists (collagen and ADP).PMC also dose-dependently inhibited the intracellular Ca2+ mobilization, whereas it did not inhibit phosphoinositide breakdown in human platelets stimulated by collagen.PMC (10 and 25μM) significantly inhibited collagen-stimulated thromboxane A2 (TxA2) formation in human platelets. On the other hand, PMC (25 and 100μM) did not increase the formation of cyclic AMP or cyclic GMP in platelets. Moreover, PMC (25, 100, and 200 μM) did not affect the thromboxane synthetase activity of aspirin-treated platelet microsomes.PMC (10 and 25μM) markedly inhibited the exogenous arachidonic acid (100μM)-induced prostaglandin E2 (PGE2) formation in the presence of imidazole (600μM) in washed human platelets, indicating that PMC inhibits cyclo-oxygenase activity.We conclude that PMC may exert its anti-platelet aggregation activity by inhibiting cyclo-oxygenase activity, which leads to reduced prostaglandin formation; this, in turn, is followed by a reduction of TxA2 formation, and finally inhibition of [Ca2+]i mobilization and ATP-release.