ADP-mimic platelet aggregation caused by rugosin E, an ellagitannin isolated from Rosa rugosa Thunb.

Teng CM;Kang YF;Chang YL;Ko FN;Yang SC and Hsu FL

Abstract

Among the nine ellagitannins, rugosin E was the most potent platelet aggregating agent with an EC50 of 1.5 +/- 0.1 microM in rabbit platelets and 3.2 +/- 0.1 microM in human platelets. The aggregations caused by rugosin E and ADP were inhibited by EGTA, PGE1, mepacrine, sodium nitroprusside and neomycin, but not by indomethacin, verapamil, TMB-8, BN52021 and GR32191B. Rugosin E-induced thromboxane formation was suppressed by indomethacin, EGTA, PGE1, verapamil, mepacrine, TMB-8 and neomycin. ADP-scavenging agents, such as CP/CPK and apyrase inhibited concentration-dependently ADP (20 microM)-, but not rugosin E (5 microM)-induced platelet aggregation. In thrombin (0.1 U/ml)-treated and degranulated platelets, rugosin E and ADP still caused 63.5 +/- 3.0% and 61.2 +/- 3.5% of platelet aggregation, respectively. Selective ADP receptor antagonists, ATP and FSBA inhibited rugosin E- and ADP-induced platelet aggregations in a concentration-dependent manner. Both rugosin E and ADP did not induce platelet aggregation in ADP (1 mM)-desensitized platelets. In contrast to ADP, rugosin E did not decrease cAMP formation in washed rabbit platelets. Both rugosin E and ADP did not cause phosphoinositide breakdown in [3H]myo-inositol-labeled rabbit platelets. In fura-2/AM-load platelets, both rugosin E and ADP induced increase in intracellular calcium concentration and these responses were inhibited by ATP and PGE1. All these data suggest that rugosin E may be an ADP receptor agonist in rabbit platelets.