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Inhibitory Effect of KR-32558, a Selective Sodium-Hydrogen Exchanger Isoform 1 (NHE-1) Inhibitor, on Rabbit Platelet Aggregation

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This study was designed to examine the effect of KR-32558, [5-(3,5-dichlorophenyl) furan-2-ylcarbonyl]guanidine, selective sodium-hydrogen exchanger isoform 1 (NHE-1) inhibitor, on rabbit platelet aggregation. Rabbit platelets were pretreated with KR-32558, and then platelet aggregations were induced by collagen (3 μg/mL), arachidonic acid (100 μM), U46619 (1 μM), thrombin (0.05 Unit/mL), thapsigargin (0.5 μM) and A23187 (0.3 μM). KR-32558 inhibited the collagen-induced platelet aggregation with the IC_{50} value of 85.9±2.1 μM. KR-32558 inhibited the thapsigargin- and A23187-induced platelet aggregation by 40±1.1 and 24.1±2.6 %, respectively. However, it had little effects on arachidonic acid-, U46619- or thrombin-induced aggregation at the concentration of 100 μM. KR-32558 significantly decreased $[Ca^{2+}]_i$ at a concentration of 100 μM. Taken together, these observations suggest that KR-32558 may be benefit to cardiovascular diseases besides cardio protective effect, and the anti-platelet activity may be partly due to inhibition of Ca^{2+} mobilization.

Key words : NHE-1 inhibitor, platelet aggregation, Ca^{2+} influx