

# **Triflavin potentiates the antiplatelet activity of platelet activating factor receptor antagonist on activated neutrophil-induced platelet aggregation.**

許準榕;林建煌

Lee LW;Peng HC;Ko WC;Hung WC;Su CH;Lin CH;Huang TF;Yen MH and Sheu JR

## **Abstract**

In this study, specific platelet activating factor (PAF) receptor antagonist ginkgolide B (BN52021) was tested for its antiplatelet activity in zymosan activated polymorphonuclear neutrophil-induced platelet aggregation. Triflavin was also tested for its antiplatelet activity compared with PAF receptor antagonist. Triflavin, an Arg-Gly-Asp-containing disintegrin purified from venom peptide inhibited platelet aggregation by interfering with the interaction of fibrinogen with the glycoprotein IIb/IIIa complex. Furthermore, we also report an efficient high resolution method for quantitative analysis of PAF using high-performance capillary electrophoresis (HPCE). The supernatant of polymorphonuclear neutrophils after their activation by opsonized zymosan induces the aggregation of washed rabbit platelets. In rabbit platelets, BN52021 (100-1000 microM) only partially inhibited activated polymorphonuclear neutrophil-induced platelet aggregation, and its maximal inhibition was estimated to be about 79%. Triflavin also partially inhibited platelet aggregation about 82% induced by activated polymorphonuclear neutrophils. Furthermore, after treatment with a combination of triflavin (0.26 microM) with various concentrations of BN52021 (4-1000 microM), the inhibitory effect of platelet aggregation was almost completely. This inhibition was greater than that produced by the individual drugs alone. These results indicate that a combination of glycoprotein IIb/IIIa complex and PAF receptor antagonist could completely inhibit activated polymorphonuclear neutrophil-induced platelet aggregation. In addition, the amount of PAF released from zymosan (6 mg/ml)-activated polymorphonuclear neutrophils was accurately calculated about  $11.8 \pm 1.5$  ng/10<sup>6</sup> cells, and did not further increase even at a high concentration of zymosan (10 mg/ml). These results suggest that PAF play a major role in the interaction between platelets and polymorphonuclear neutrophils. This interaction may be important in the pathogenesis of thrombosis and inflammatory diseases. Our present findings support the hypothesis that combination therapy with glycoprotein IIb/IIIa complex antagonists and PAF receptor antagonists may

represent a new approach to the treatment of ischemic disorders.