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[Inhibition of platelet aggregation by a protease inhibitor, Plasminogen Dipeptidyl Peptidase-4 (Pepstatins)]. Platelets are activated by various platelet agonists and induce vasoconstriction, thrombosis, and inflammation in vivo. We discovered that recombinant urokinase-type plasminogen activator (uPA) and plasmin are involved in platelet aggregation. In this study, the effect of peptidyl dipeptidase 4 (Pepstatins), a serine peptidase inhibitor, on uPA- and plasmin-induced aggregation was examined. Consistent with the previous reports, plasmin enhanced platelet aggregation induced by collagen, thrombin, adenosine diphosphate (ADP), and arachidonic acid. However, Pepstatins strongly inhibited the enhanced platelet aggregation induced by plasmin. Similarly, Pepstatins inhibited the aggregation induced by uPA and plasmin. Next, we investigated the inhibition mechanism of Pepstatins on the function of platelets in vitro. To the one side, Pepstatins inhibited the activation of plasminogen to plasmin by uPA. On the other side, Pepstatins directly inhibited the function of plasmin. These findings suggest that Pepstatins can regulate the function of platelets by inhibiting the activation of plasminogen to plasmin by uPA.

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