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INTERACTION OF RECOMBINANT PROTEIN – A NEW THROMBOLYTIC, ANTIPLATELET AGENT SAK-RGD-K2-HIR WITH FIBRIN

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The incidence of thromboembolic disorders has been increasing for several years now. Effective treatment in myocardial infarction, pulmonary embolism or deep vein thrombosis is associated with early thrombolytic therapy. The most common strategy of the thrombolytic therapy involves the activation of fibrinolytic system with intravenous plasminogen activators. Aggregation of blood platelets constitutes an important part of the thrombus, and therefore antiplatelet agents have been used in the treatment and prevention of arterial thrombosis. The RGD peptide is a well known component of ligands recognizing platelet integrins. A chimeric proteins, consisting of the staphylokinase and the Kringle 2 domain (K2) of t-PA for activation of fibrinolysis, the Arg-Gly-Asp sequence for the prevention of platelet aggregation were constructed.

The current study was aimed to assess the thrombolytic activity of recombinant staphylokinase (rSAK) variants with antithrombotic and antiplatelet properties in a rat model of arterial and venous thrombolysis.

We have shown that the addition of the RGD sequence to r-SAK resulted in acquisition of the ability to prevent platelet aggregation. The insignificant inhibitory influence of r-SAK on the aggregation of washed platelets *in vitro* was also demonstrated. It may result from accidental plasmin formation (lack of α_2 anti-plasmin) causing degradation of fibrinogen and other proteins involved in the aggregation process. This phenomenon has not been observed in platelet-rich plasma. The efficiency of platelet-platelet interaction blocking by SAK-RGD-K2 was comparable with that of the RGD sequence alone. These results showed that the recombinant protein SAK-RGD-K2 containing the RGD sequence possesses the ability to block platelet aggregation and hence should be more effective in clot lysis than r-SAK. In the arterial and venous thrombolysis animal model we have observed reperfusion, without reocclusion, in all animals treated with SAK-RGD-K2 – protein containing antiplatelet RGD sequence and specific to fibrin Kringle 2 domain (K2) of t-PA.

In conclusion, we have shown that recombinant SAK-RGD-K2, SAK-RGD proteins are strong thrombolytic agents in rat model of arterial and venous thrombolysis.

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