



## New derivative of staphylokinase SAK-RGD-K2-Hirul exerts thrombolytic effects in the arterial thrombosis model in rats

Janusz Szemraj<sup>1</sup>, Agnieszka Zakrzewska<sup>2</sup>, George Brown<sup>1</sup>, Adrian Stankiewicz<sup>2</sup>, Anna Gromotowicz<sup>2</sup>, Tomasz Grędziński<sup>2</sup>, Ewa Chabielska<sup>2</sup>

<sup>1</sup>Department of Medical Biochemistry, Medical University of Łódź, Mazowiecka 6/8, PL 92-215 Łódź, Poland

<sup>2</sup>Department of Biopharmacy, Medical University of Białystok, Mickiewicza 2c, PL 15-222 Białystok, Poland

**Correspondence:** Janusz Szemraj, e-mail: jszemraj@csk.am.lodz.pl

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### Abstract:

SAK-RGD-K2-Hir and SAK-RGD-K2-Hirul are recombinant proteins that are derivatives of r-SAK (recombinant staphylokinase). They are characterized by their fibrin-specific plasminogen activation properties and their antithrombin and antiplatelet activities. The difference between these proteins is the presence of the antithrombotic fragment (hirudin or hirulog) in the C-terminal portion of the r-SAK.

The aim of the present study was to examine the thrombolytic potentials of SAK-RGD-K2-Hir and SAK-RGD-K2-Hirul in an electrically induced carotid artery thrombosis model in rats and to compare the potentials to that of r-SAK.

We determined that a bolus injection of SAK-RGD-K2-Hirul was more effective than one of r-SAK in the improvement and maintenance of carotid patency and in arterial thrombus weight reduction; however, it had the same potency as SAK-RGD-K2-Hir. The bleeding time, prothrombin time and activated partial thromboplastin time were significantly prolonged in the animals that were treated with either dose (1.5 or 3.0 mg/kg) of SAK-RGD-K2-Hir or SAK-RGD-K2-Hirul, whereas no changes were observed in the plasma fibrinogen concentration or the  $\alpha_2$  plasmin inhibitor level. r-SAK alone did not change the bleeding time or coagulation parameters.

In conclusion, our findings demonstrate the thrombolytic activity of intravenous bolus injection of the novel thrombolytic agent SAK-RGD-K2-Hirul in rats. Although this protein compares favorably with r-SAK, we were unable to show the presence of any beneficial effects of SAK-RGD-K2-Hirul over those of SAK-RGD-K2-Hir. Furthermore, our results suggest that high doses of SAK-RGD-K2-Hirul bear the risk of bleeding.

### Key words:

recombinant protein, antiplatelet activity, thrombolytic agent, anticoagulant agent, arterial thrombosis

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