Angipur is a new blocker of platelet receptors IIb/IIIa

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A preclinical study of a new derivative of xanthine angipur (3-methyl-8-piperiazinyl-7-thietanyl-1-ethylpurinedione hydrochloride) was carried out.

In studies on the effect on the functional activity of platelets *in vivo*, with a single intravenous administration to rats, the studied compound significantly inhibited platelet aggregation and was comparable in terms of antiplatelet activity with the comparison drug tirofiban (ED_{50} 0.89 vs. 0.9 mg/kg, respectively).

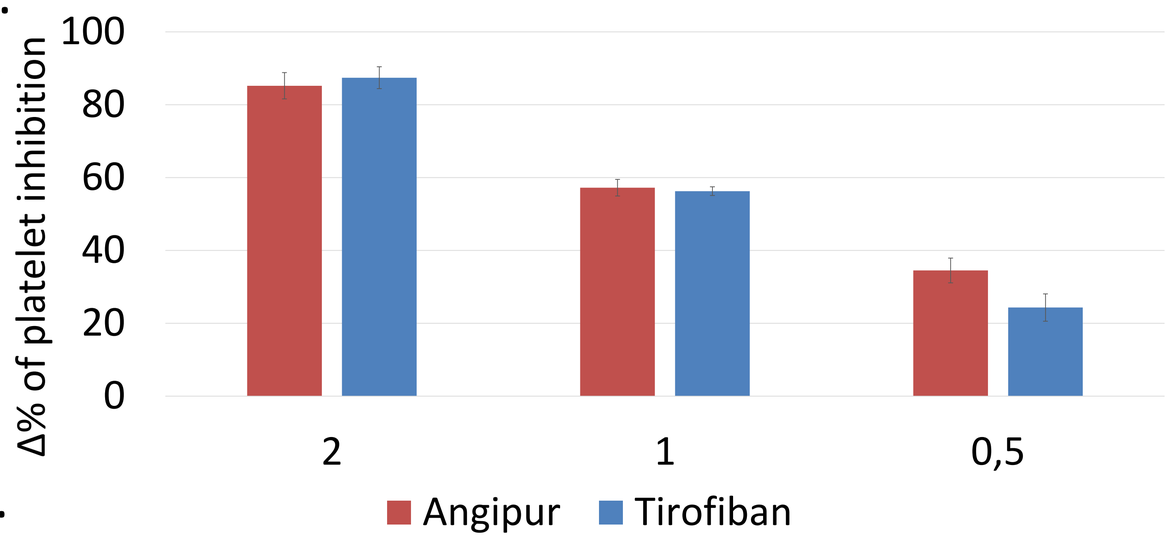

Fig. 1. Antiplatelet activity of angipur and tirofiban on the model of ADP-induced platelet aggregation *in vivo*

Figure 2 shows the results of studying the antithrombotic activity of angipur and tirofiban. As follows from the graphs, the level of antithrombotic activity of angipur was comparable to tirofiban. The value of ED_{50} for the studied samples was 0.26 and 0.3 mg/kg, respectively.

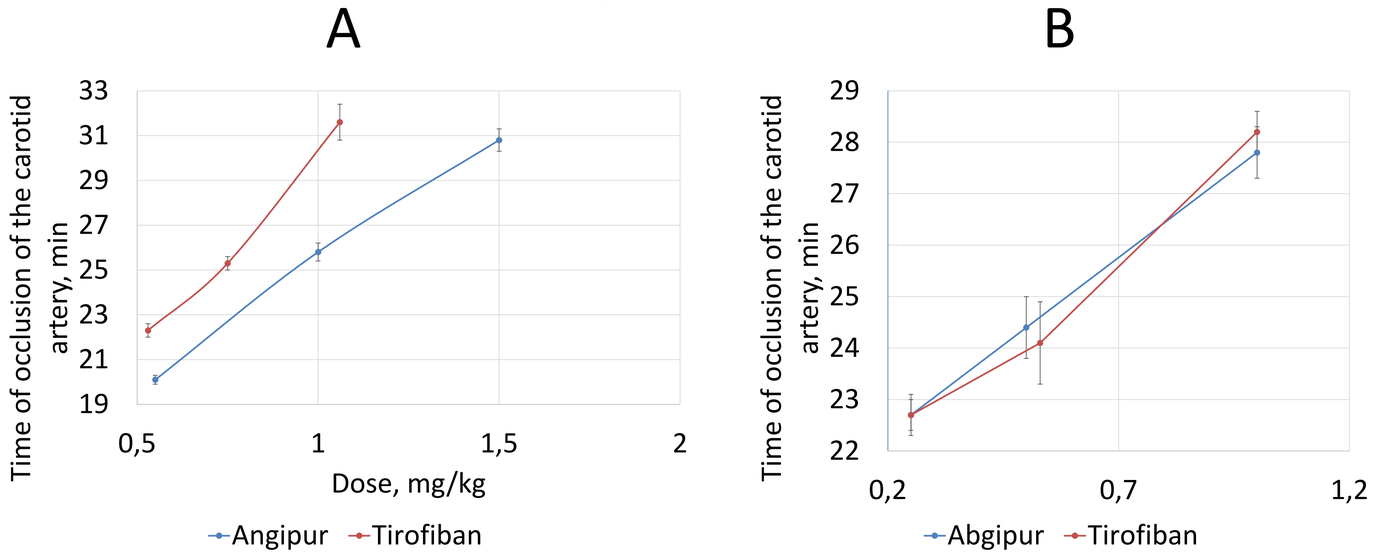

Fig. 2. Antithrombotic activity of angipur and tirofiban on models of carotid artery thrombosis induced by iron chloride (A) and electric current (B) *in vivo*

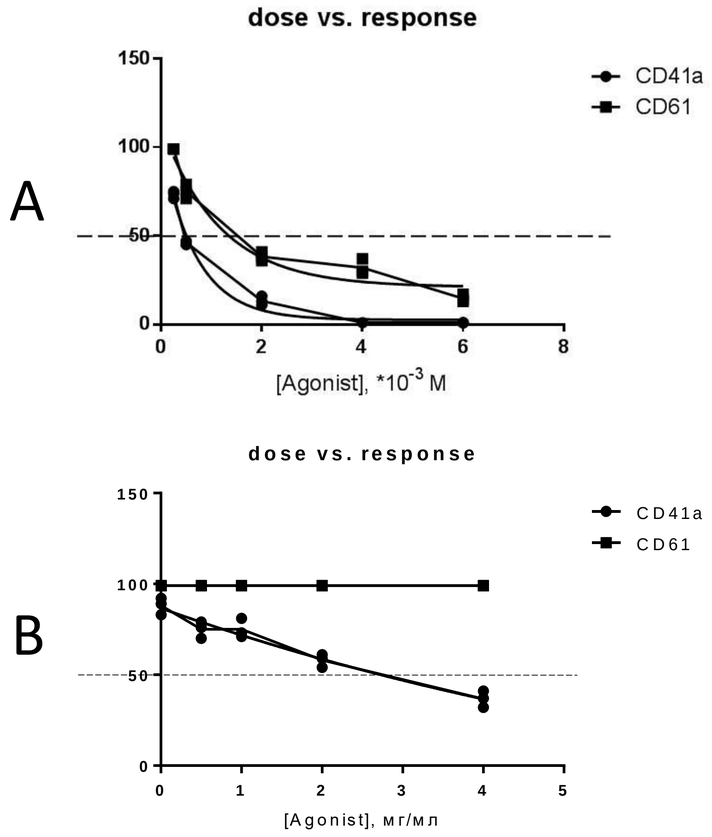

Fig. 3. Binding of angipur and tirofiban to platelet integrins CD61 and CD41a by flow cytometry.

In conditions of generalized epinephrine-collagen thrombosis in mice, the angipur contributed to 80% survival of experimental animals and exceeded the antithrombotic activity of the comparison drug by 1.2 times. The study of the mechanism of the antiplatelet effect of angipur by flow cytometry and ELISA, as well as under conditions of platelet stimulation by various agonists, allowed us to conclude that this agent has a blocking effect on glycoprotein IIb/IIIa platelet receptors. The study of the effect on the bleeding time allowed us to conclude that angipur contributed to the prolongation of the studied indicator, but to a lesser extent than the comparison drug. The therapeutic index, as the LD_{50}/ED_{50} ratio, for angipur was 35.5, which is 6.3 times higher than the values of tirofiban. This parameter indicates a higher level of safety of angipur compared to the reference. Based on the conducted preclinical studies, taking into account the data on the study of chronic toxicity and pharmacokinetics, the starting dose for phase I clinical trials was established. Currently, phases I and II of clinical trials have been successfully completed.

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