Kunitz Family Inhibitors from *Delonix regia* (DrTI) and *Acacia schweinfurthii* (AsTI) Decrease Thrombus Formation Without Increasing Bleeding Time in Mice Through Inhibition of Clotting Contact System

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INTRODUCTION. Treatment of thrombosis in a patient without the risk of bleeding is a major purpose of modern anticoagulant therapy. Plant protease inhibitors have been reported to block a variety of proteolytic processes. DrTI and AsTI from *Delonix regia* and *Acacia schweinfurthii* respectively, are members of the Kunitz family of inhibitors and block trypsin, in 21.9 nM and 3.45 nM range, respectively, but differ in the inhibition of human plasma kallikrein and factor XIa indicating the dynamic nature of its reactive site. **OBJECTIVES**. To study in *vivo* and *ex vivo* effect of those protein inhibitors in haemostasis tests and thrombus formation. **MATERIAL AND METHODS.** Black 6 C57 male mice were used in all models. In arterial thrombosis the right common carotid artery was isolated, an ultrasonic flow probe placed around the artery and a laser beam applied on in this site, after IV injection of rose Bengal dye. Bleeding time was measured in transacted mouse tail, placed in a tube with saline solution at 37ºC. Platelet aggregation was performed using whole blood; aggregometer and was measured in presence of ADP. The activated partial thromboplastin time was performed with poor platelet plasm and measured in a semi-automatic coagulometer. The studied substances were compared with saline and heparin. **RESULTS AND DISCUSSION**. DrTI and AsTI increased human and mouse activated partial thromboplastin time, inhibited *ex vivo* mice platelet aggregation induced by ADP and significantly prolonged the time of total occlusion of mice carotid artery, in comparison to NaCl solution. In contrast to heparin, the bleeding time of the inhibitors treated mice did not differ from that of the NaCl group. **CONCLUSION**. Both inhibitors effectively prevented arterial thrombus formation in mice, without increasing bleeding time, by interfering with the activity of blood coagulation contact factors, huPK and Factor XIa.

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