Molecular mechanisms involved in the antithrombotic activity of aegyptin, a novel mosquito-derived collagen-binding protein

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Aegyptin is a 30 kDa mosquito salivary gland protein that binds to collagen and inhibits platelet aggregation. It was previously demonstrated that aegyptin recognizes the von Willebrand Factor binding-site in collagen which could explain at least in part, its biological activity. In this study we aimed to evaluate: 1. whether this protein could prevent in vitro collagen-induced plasma clotting; 2. the in vivo antithrombotic activity of aegyptin. It was observed that aegyptin abolished the collagen-mediated acceleration of human rich platelet plasma clotting. This effect was also observed in the absence of platelets. In accordance with this observation, aegyptin has effect on thrombin generation in plasma. Aegyptin has no antithrombotic activity in vitro by employing an arteriovenous shunt model in rats. This model is independent of collagen-exposure since presents no vascular surface for thrombus formation. On the other hand, aegyptin prevents laser-induced carotid thrombus formation in the presence of Rose Bengal in vivo, a model that is based on vessel injury. Thus, time for thrombus formation in animals treated with 50 µg/kg aegyptin was 54.6 ± 9.4 min, in contrast with controls receiving saline (19.4 ± 2.4 min). Strikingly, antithrombotic doses of aegyptin caused minor bleeding in rats, as assessed by a tail-transection model. Our results demonstrate that aegyptin is an effective antithrombotic agent in vivo. In addition, our data support a platelet and contact phase-dependent antithrombotic activity of aegyptin. This molecule might be regard as an important tool to dissect the hemostatic role of collagen in vivo.

Keywords: Trombosis, Platelets and Aegyptin.

Supported by CNPq, FAPERJ, and FUJB.