

WHAT SNAKE VENOMS COMPONENTS CAN DO FOR THE TREATMENT OF THROMBOTIC DISEASES?

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Thrombotic disorders are the major cause of morbidity and mortality in Western societies. Clinical regulation of thrombosis involves drugs that affect the activity and generation of thrombin. A number of proteins from bothropic venoms interfere with the hemostatic system and have been characterized as procoagulant or anticoagulant factors. Bothrojaracin (BJC), a 27 kDa C-type lectin-like protein from *Bothrops jararaca* venom is a selective and potent thrombin and prothrombin inhibitor ($KD = 0.6$ nM and $KD = 75$ nM, respectively). This ability would confer to BJC a new mechanism of action for an antithrombotic drug, therefore we further analyzed its effect *in vivo*. It was observed that administration of 1 mg/kg of BJC decreased thrombus weight by 95% (to 0.5 ± 0.1 mg). in an animal model that combines hypercoagulability with stasis. This effect was maintained at least for 48 hrs after drug administration. Using another animal model, BJC (1mg/kg) administered 60 min prior to thromboembolism induced by thrombin, protected 100% of the mice group from dead. Western blotting assays using *ex vivo* plasma showed an interaction between BJC and prothrombin detectable up to 12 h. Altogether, our data show that BJC is a potent antithrombotic agent that could further help the development of new dual mechanistic drugs directed to prothrombin and thrombin inhibition.

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