CRATABL, A HEPARIN BINDING LECTIN, INHIBITS FACTOR Xa AND IMPAIRS ARTERIAL THROMBUS FORMATION

Salu, B.R.1; Ferreira, R.S.1; Brito, M.V.1; Ottaiano, T.F.1; Cruz, J.W.M.C.1; Silva, M.C.C.1; Correia, M.T.S.2; Paiva, P.M.G.2; Maffei, F.H.A.3 and Oliva, M.L.V.1

1Departamento de Bioquímica, Universidade Federal de São Paulo, UNIFESP;
2Departamento de Bioquímica, Universidade Federal de Pernambuco, UFPE;
3Departamento de Cirurgia e Ortopedia, Faculdade de Medicina de Botucatu, UNESP.

Introduction: Arterial thrombosis is an important complication of diabetes and cancer, being an important target for therapeutic intervention. Crataeva tapia bark lectin (CrataBL) has been previously shown to have hypoglycemiant effect induced cancer cell apoptosis. It also showed inhibitory activity against Factor Xa (K_{iap}= 8.6 \mu M).

Objective: In the present study we evaluated the anti-thrombotic properties of CrataBL in arterial thrombosis model. Materials and Methods: The in vivo effect of CrataBL in a carotid arterial thrombosis model was evaluated using black, 6 C57 male mice. The right common carotid artery was isolated through a midline cervical incision, and an ultrasonic flow probe was introduced. A 540 nm laser beam was applied and the blood flow was monitored, with laser emission. The aPTT was determined using a semi-automated coagulometer with pool of total plasmas and the fluorescence studies were measured using a Spectra Max Gemini EM microplate fluorometer with Tosyl-Gly-Pro-Arg-AMC as substrate. Discussion and Results: In the photochemically induced thrombosis model in mice, in the groups treated with 1.25, 5.0, or 10 mg/kg CrataBL, prior to the thrombus induction, the time of total artery occlusion was prolonged by 33.38%, 65% and 66.11%, respectively, relative to the time of the control group. Additionally, CrataBL prolongs the activated partial thromboplastin time on human and mouse plasma and it impairs the heparin-induced potentiation of antithrombin III, and heparin-induced platelet activation in the presence of low-dose ADP. It is likely that the dense track of positive charge on CrataBL surface competes with the heparin ability to bind to antithrombin III and to stimulate platelets. In contrast to heparin, the bleeding time in CrataBL-treated mice was no longer than in the control. Conclusion: CrataBL was effective in blocking coagulation, arterial thrombus and interact with heparin.

Keywords: lectin, arterial thrombosis, factor Xa.