BOVINE INTESTINAL HEPARIN AND THERAPEUTIC USE BEYOND ANTICOAGULANT ACTIVITY

Santos, R.P. 1; Kropf, F. 1; Lordelo, C.V.M. 1; Koslowski, E.O. 1; Pereira, M.S. 1; Tovar, A.M.F. 1; Mourão, P.A.S. 1

1 Universidade Federal do Rio de Janeiro Instituto de Bioquímica Médica Leopoldo de Meis (Rio de Janeiro Brasil)

The therapeutic application of heparin (UFH) is not restricted to its anticoagulant activity since anti-inflammatory and anti-tumor effects are associated with its administration. However, the anticoagulant action limits the use of UFH as an anti-inflammatory or anti-tumorigenic agent, mainly due to bleeding complications. This study aimed to evaluate the therapeutic potential of UFH chains that exhibit low anticoagulant activity, obtained by ion exchange chromatography fractionation of bovine mucosal UFH (Bovine UFH). We fractionated bovine UFH into structurally distinct polysaccharide chains, here referred to as F1 and F2, which showed differences in their anticoagulant activities. Anti-inflammatory effect was performed in a model of inflammation induced by intraperitoneal injection of 4 % thioglycolate in C57BL/6 mice, analyzing leukocyte specific counting in the peritoneal fluid 3 hours after. Anti-metastatic effect (short term): murine tumor cells (MC38-GFP) were injected directly into the bloodstream, the animals were sacrificed 30 min after and the percentage of tumor cells associated with platelets present in the lungs determined. We tested F1 fraction, which displayed a lower degree of sulfation and reduced anticoagulant activity, for its anti-inflammatory and anti-tumorigenic potential. The results point to a slight or no inhibition of migration of polymorphonuclear leukocytes to the peritoneal fluid, in a peritonitis model induced by thioglycolate. However, in a tumor metastasis inhibition assay the results were slightly different. Bovine UFH and F1 exhibited an intermediary potential when compared with porcine UFH and F2. The models tested in both, the anti-inflammatory and anti-tumor activities, are very dependent on the interaction with P-selectin. The initial data point to a borderline competitive capacity of the F1 fraction with ligands of P-selectin.

Financial support: CNPq, CAPES, FAPERJ

Key words: anti-inflammatory effect, anti-tumorigenic effect, heparin