

Antithrombotic Activity *in vivo* of Sulfated Polysaccharides from *Ulva lactuca* and its Effect in NO Production by Endothelial Cells

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INTRODUCTION: Studies report that anticoagulant/antithrombotic activity of sulfated polysaccharides can be attributed to their different structural characteristics: molecular weight, sulfation teor and structural conformation. In this study, sulfated polysaccharides extracted from *Ulva lactuca*(UI) macroalgae were examined respect to chemical composition, anticoagulant activity and antithrombotic effect *in vivo*. **MATERIAL AND METHODS:** Powdered algae was submitted to proteolytic digestion for 24h, 60°C. After this time, the filtrate was fractionated with ice-cold acetone at 4°C overnight. Chemical composition of fractions was determinate by fluorophore assisted carbohydrate electrophoresis (FACE), paper chromatography and Raman spectroscopy. Sulfate and protein content were determined by gelatin-barium and Bradford methods. Anticoagulant activity was investigated by PT, aPTT, TT coagulation tests and chromogenic assays for IIa and Xa factors. Antithrombotic activity *in vivo* was evaluated by inferior vena cava ligation assay in Wistar rats. Using endothelial cell culture, metalloproteinase activity by zymogram and nitric oxide production by Griess assay were measured. **DISCUSSION AND RESULTS:** Fraction obtained, UI50, composed by ramnose, glucose, galactose and galacturonic acid (1:0.08:0.05:0.33) showed high level of sulfate (~20%). UI50 doubled aPTT with 0.5µg/ul, compared a commercial HMW heparin 0.02ug/ul. Moreover, this fraction was able to prolonging PT with 0.2ug/ul. Chromogenic assay revealed that UI50 (1-1.5µg/ul) was capable to inhibit anti-IIa and anti-Xa. Analysis by endothelial cell culture revealed that UI50 fraction (25-50µg/mL) increased the nitric oxide release to culture medium during 2-24hs and also modified the metalloproteinase activity. *In vivo* model was observed a reduction in thrombi weight on groups treated with 50UI (2-20µg/g) when compared to negative control group. **CONCLUSION:** Alterations in NO production and metalloproteinase activity may be related to antithrombotic activity. These results corroborate with anticoagulant and antithrombotic activities showed by UI50 fraction. However, additional studies about structural features and biological assays are necessary to investigate this polymer as therapeutic agents.

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Keywords: *Ulva lactuca*, antithrombotic activity, nitric oxide