A PECULIAR SHRIMP DERMATAN SULFATE INHIBITS ANGIOGENESIS, THROMBOSIS AND COAGULATION in vitro


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Introduction: Studies suggests that thrombin, a clotting protease, is involved in tumor mechanisms, such as metastasis and angiogenesis, as well in hypercoagulability events tumor-related. Thus, antagonist molecules of these events have been explored. Among them, an important glycosaminoglycan, Dermatan Sulfate (DS) it has been highlighted due its ability to inhibit thrombin. For this reason, this study aimed to characterize and evaluate the potential antithrombotic, anticoagulant and antiangiogenic of dermatan sulfate like polysaccharide (DSL) isolated from the shrimp Litopenaeus vannamei.

Materials and methods: DSL was purified by acetone fractionation and ion-exchange chromatography. The structural characterization was performed by enzymatic depolimerization with chondroitin ABC and AC lyases. Anticoagulant activity was described using chromogenic assays for IIa e Xa factors, as well by the test of the activated partial thromboplastin time (aPTT), while antithrombotic activity was verified by FeCl$_3$-induced carotid artery lesion model. To check the residual hemorrhagic effect of DSL, a modified model of topical scarification in rat tail was performed. Lastly, the antiangiogenic activity was mensured by a capillary formation assay in reconstituted basement membrane (matrigel).

Discussion and Results: DSL was digested only by chondroitinase ABC, presenting one main disaccharide constituted by α-ΔUA(2SO$_4$)→3-GalNAc(4SO$_4$), suggesting a peculiar DS structure, described in crustaceans for the first time. The compound
showed reduced anticoagulant effect by aPTT test and minimum anti-Xa activity, but showed high anti-IIa activity. In thrombotic activity DSL, it was efficient in prolonging significantly, the carotid occlusion time. Significant inhibitory effect on neovascularization was demonstrated, being such effect dose dependent. Regarding antihemostatic activity, the polysaccharide induced non significant hemorrhagic effect. **Conclusion:** The properties submitted by DSL compound obtained from shrimp such as antiangiogenic, antithrombotic and thrombin inhibition potential, along with its insignificant hemorrhagic effect, pointing this glycosaminoglycan as a potential agent for further therapy development.

**Keywords:** Neovascularization. Thrombin. Dermatan sulfate.