A Peculiar Heparin/HS-like from Marine Shrimp with Anti-Xa Activity and Negligible Hemorrhagic Potential

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INTRODUCTION: Heparin and heparan sulfate (HS) are sulfated polysaccharides with great therapeutic value. Clinically, heparin has been used as the major drug in treatment of thromboembolic diseases. However, its use is followed by side effects, as hemorrhage. Therefore, there is a great interest by the search for heparin analogues with low bleeding potential. In this work, we report some structural features and anticoagulant activity of a peculiar heparin/HS purified from the heads of the shrimp *Litopenaeus vannamei*, the most commonly farmed shrimp species in Brazil.

MATERIAL AND METHODS: Shrimp heparin/HS compound was purified after acetone fractionation, ion-exchanged chromatography and gel filtration through a Sephadex G-25 column. Its structural analysis was performed by enzymatic depolimerization and NMR spectroscopy. Anticoagulant activity was investigated by the activated partial tromboplastin time (aPTT) and anti-Xa activity, according to the instructions of commercial kits. Finally, the bleeding potential was analyzed by a model of topical scarification in rat tail.

RESULTS AND DISCUSSION: Structural analysis revealed that the shrimp heparin/HS-like compound shares structural features of both heparin and heparan sulfate, such as the high degree of N,6-sulfated glucosamine and minor N-acetylation together with the high content of glucuronic acid. Interestingly, signals corresponding to non-sulfated iduronic acid were not observed, suggesting a particular mode of shrimp heparin/HS biosynthesis. In addition, the occurrence of the rare 3-O sulfo group on N-sulfated glucosamine linked to glucuronic acid can justify the significant anticoagulant activity in aPTT assay and 97% of Factor-Xa inhibition by shrimp compound. In contrast to mammalian heparin, shrimp heparin/HS has a negligible hemorrhagic effect.

CONCLUSIONS: These findings have particular interest since they reveal a novel molecule with a peculiar structure and significant anti-Xa activity. Its low bleeding potential makes of the shrimp heparin/HS-like compound a better alternative than mammalian heparin.

Key Words: Anti-Xa activity, *Litopenaeus vannamei*, heparin, glycosaminoglycan, heparan.

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