ALGAL SULFATED GALACTANS AS NEW ANTITHROMBOTIC COMPOUNDS

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Heparin remains the cornerstone treatment of venous thromboembolism. However the heparin source is limited and there is a great need of new compounds from natural sources. Marine algae are abundant source of sulfated galactans with anticoagulant and antithrombotic activities. But, the search for these compounds cannot be restricted to common coagulation assays. It demands a detailed and extensive study on their effects that could affect the hemostatic system. We isolated a variety of sulfated galactans from several species of marine alga. These polysaccharides have an identical saccharide structure and the same size chain, but with differences in their sulfation patterns. The anticoagulant activity of the algal galactans is due to inhibition of factor Xa and/or thrombin by activation of their specific serpins. The galactans have also a serpin-independent anticoagulant activity due to inactivation of intrinsic tenase and prothrombinase complexes. Furthermore, some sulfated galactans have a procoagulant effect due to activation of factor XII. This last effect depends on the sulfation pattern of the polysaccharide. As a consequence of their anti- and procoagulant actions the algal galactans differ in their venous antithrombotic activities. Thus, a sulfated galactan from *G. crinale* exhibits procoagulant and prothrombotic effects in low doses, but in high doses this polysaccharide inhibits venous thrombosis and prolongs *ex vivo* recalcification time. In contrast, a sulfated galactan from *B. occidentalis* is a very potent anticoagulant and antithrombotic compound in low doses, inhibiting venous experimental thrombosis and prolonging *ex vivo* recalcification time, but these effects are reverted in high doses. Both sulfated galactans do not modify bleeding time in rats. These results indicate that slight differences in the proportions and/or distribution of sulfated residues along the galactan chain is critical for the interaction between proteases, inhibitors and activators of the coagulation system, resulting in a distinct pattern in anti- and procoagulant activities and in the antithrombotic action. These studies may help to find a specific and potent antithrombotic devoid of undesirable effects.