Effects of polysaccharides enriched in 2,4-disulfated fucose units on coagulation, thrombosis and bleeding: Practical and conceptual implications

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Abstract

Sulfated polysaccharides from marine invertebrates have well-defined structures and constitute a reliable class of molecules for structure-activity relationship studies. We tested the effects of two of these polysaccharides, named a sulfated fucan and a fucosylated chondroitin sulfate, on coagulation, thrombosis and bleeding. The compounds share similar 2,4-disulfated fucose units, which are required for high anticoagulant activity in this class of polymer. These residues occur either as branches in fucosylated chondroitin sulfate or as components of the linear chain in the sulfated fucan. These polysaccharides possess anticoagulant activity but differ significantly in their mechanisms of action. The fucosylated chondroitin sulfate inhibits thrombin by heparin cofactor II, whereas sulfated fucan inhibits thrombin by both antithrombin and heparin cofactor II. In addition, these polysaccharides also have serpin-independent anticoagulant activities. Fucosylated chondroitin sulfate, but not sulfated fucan, activates factor XII. As a result of the complex anticoagulant mechanism, the invertebrate polysaccharides differ in their effects on experimental thrombosis. For instance, the sulfated fucan inhibits venous thrombosis at lower doses than fucosylated chondroitin sulfate. In contrast, fucosylated chondroitin sulfate is significantly more potent than sulfated fucan in arterial thrombosis. Finally, fucosylated chondroitin sulfate increases bleeding, while sulfated fucan has only a discrete effect. In conclusion, the location of 2,4-disulfated fucose units in the polysaccharide chains dictates the effects on coagulation, thrombosis and bleeding.

Key words: sulfated fucans, fucoidan, anticoagulant activity, antithrombotic activity heparin, invertebrate