Antithrombotic Effect of Chemically Sulfated Citrus Pectin by Direct Inhibition of Thrombin and Factor Xa

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The treatment of venous thrombosis is mainly based on heparin. Although largely effective, it has limitations because its anticoagulant effect is unpredictable, with high risk of bleeding, which requires close laboratory monitoring for its safe use. Moreover, since heparin is obtained from porcine intestines or bovine lungs, contamination by pathogenic agents is a serious concern. Consequently, attempts have been made to develop alternatives to heparin, including research on other naturally sulfated polysaccharides or chemically sulfated derivatives. We now evaluated the anticoagulant, antithrombotic, and bleeding effects of a chemically sulfated polysaccharide (Pec-HWS), obtained from widely available citrus pectin. It had M_w of 12,000 g/mol and consisted of (1? 4)-linked α-D-Gal*p*A units, with almost all its HO-2 and HO-3 groups substituted by sulfate. Pec-HWS had an *in vitro* anticoagulant effect, doubling APTT at a concentration of 8.8 μg/ml. In an *in vivo* venous thrombosis model, it also proved to be an antithrombotic agent, giving rise to total inhibition of thrombosis at a dose of 3.5 mg/kg body weight. Surprisingly, in contrast with heparin, Pec-HWS acted by direct inhibition of α-thrombin and factor Xa by a mechanism independent of AT and/or HCII. Moreover, Pec-HWS provided a lower risk of bleeding than heparin, at a dose of 100% effectiveness against venous thrombosis, indicating it to be a promising antithrombotic agent.

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