

SERPIN-INDEPENDENT ANTICOAGULANT ACTIVITY OF SULFATED POLYSACCHARIDES FROM MARINE ORGANISMS

Glauser, B.F.^{1,5}; Monteiro, R.Q.^{2,3}; Mourão, P.A.S.^{1,3}; Pereira, M.S.^{1,4}

¹Laboratório de Tecido Conjuntivo, HUCFF; ²Laboratório de Hemostase e Venenos, ³IBqM, CCS; ⁴ICB; ⁵IQ, CT, UFRJ

Sulfated Galactan (SG) from the red alga *Botryocladia occidentalis* and Fucosylated Chondroitin Sulfate (FucCS) from the sea cucumber *Ludwigothurea grisea* are sulfated polysaccharides with novel structures and a wide range of biological properties, including anticoagulant and antithrombotic activity. These polysaccharides catalyze factor Xa and/or thrombin inhibition by activation of antithrombin (AT) and/or heparin cofactor II (HCII). We now demonstrate that these polysaccharides have an additional anticoagulant mechanism independent of the serpins. Thus, both FucCS and SG prolongs APTT assay using AT and HCII depleted plasma. We also showed the effects of FucCS and SG on specific assays of the intrinsic tenase and prothrombinase complexes, which are serpin-independent coagulation steps. Standard heparin had no effect on prothrombinase assay up to 1ug/mL while FucCS and SG are inhibitors of this pathway, reaching maximum effect at 1ug/mL and 10ug/mL, respectively. The intrinsic tenase complex was also inhibited by FucCS and SG. FucCS also prevents *in vitro* platelet aggregation induced by thrombin and collagen but not by ADP. In addition, FucCS and SG are antithrombotic agents on a venous arterial shunt and on a model of thrombosis based on laser induced endothelial lesion. We now intend to determine the relative contribution of the serpin-independent effect of FucCs and SG on coagulation as well as the contribution of their effect on platelet aggregation for their antithrombotic activity.