Glycosaminoglycan Anticoagulant Properties from Atherosclerotic Lesions

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In order to investigate if the concentration and/or the anticoagulant activity of arterial wall glycosaminoglycans (GAG) are affected in atherosclerosis we compared normal segments from human aorta (78-year-old woman) with segments exhibiting different grades of atherosclerotic lesions, fibrous plaque (atheroma) or calcified ulcerated lesions. Atheroma and complicated lesions presented significant lower glycosaminoglycan concentrations, 1.52 ± 1.60 (n=15) and 0.97 ± 0.53 (n=18), respectively, when compared with normal segments, 2.41 ± 1.08 µg hexuronic acid / mg tissue dry weight (n=11). The anticoagulant activity of aortic GAGs was evaluated by a thrombin amidolytic assay using plasma as a source of thrombin inhibitors or purified antihrombin (AT) or heparin cofactor II (HCII). As indicated by the concentration of GAG necessary to inhibit by 50% the thrombin activity (IC_{50}), no significant difference was observed in the anticoagulant properties of the GAGs from normal and lesionated areas. Thus, the IC_{50} was 1.40±0.83, 1.11±0.83 and 1.83±0.86 µg/ mL for normal, atheroma and complicated lesions areas, respectively. Similar results was observed when purified AT or HCII was used instead of plasma. Fractions enriched in heparan sulfate (HS) or condroitin sulfate plus dermatan sulfate (CS+DS) from the three groups were obtained by anion exchange chromatography. All HS fractions exhibit the same anticoagulant properties. Surprisingly, CS+DS fractions from lesionated areas present a higher anticoagulant potential in the presence of AT. This activity was not altered by chondroitinase ABC treatment, indicating the presence of heparin-like chains. Our results show that atherosclerotic lesions present lower GAG content, however this anticoagulant property is not affected.

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