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ON THE ANTICOAGULATORY ACTIVITY OF DIFFERENT HEPARINS. B. Angelkort, A. Petrick. Department of Internal Medicine, Technical University Aachen, Fed. Rep. W-Germany.

The anticoagulatory effectivity of different heparins is seen as to be equal. The study aims for proving the anticoagulatory effects of two sodium heparins with comparable molecular weights (heparin-Na(Thr^R.), Na-heparin (Liq^R.) made by two different manufacturers and one heparin (Calc^R.) in patients undergoing chronic hemodialysis (N=10) in crossover trial. Antithrombin III-activity, fibrinogen, hematocrit, platelets, blood lipids were of comparable levels in the three patient groups. 20 and 60 min. after application of heparin-Na (Thr^R.) the average plasma levels are constant: 1,46 ± 0,28 and 1,45 ± 0,38 U/ml, after application of Na-heparin (Liq^R.) plasma levels and anticoagulatory effect tends to be lower. Ca-heparin has a significant meaner anticoagulatory effect as the two sodium-heparins. Between heparin-Na (Thr^R.) and Ca-heparin there is a significant difference, whereas the differences between Na-heparin (Liq^R.) and Ca-heparin is not performed to be significant. There endures no dominance for the measurement of heparin in plasma with chromogenic substrate instead of the plasma-thrombin-time in supervising an anticoagulation therapy.

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PLATELET FACTOR 4 (PF4) AND PROTAMINE SULFATE (PS) NEUTRALIZATION OF HEPARIN FRACTIONATED ACCORDING TO CHARGE DENSITY. M-C. POON AND R.E. HURST. Departments of Medicine, Public Health and Biochemistry, University of Alabama in Birmingham and Birmingham VA Medical Center, Birmingham, Alabama, USA.

Both PF4 and PS have been postulated to neutralize heparin by electrostatic complex formation. The present study examined the role of charge density (Z) of the heparin in neutralization reactions with PF4 and PS. Fractions varying systematically in charge density were isolated from 3 hog mucosal (HM) heparins (2 decolorized and 1 undecolorized) using 2 phase sequential extraction system. Fractions were similarly isolated from a decolorized beef lung (BL) heparin. Thrombin inhibition (ThI) assays were performed in the absence and presence of a constant amount of PF4 or PS for each fraction and for a series of dilutions of a standard heparin. The potencies of fractionated heparins varied systematically in a non-linear manner with Z^2. However, in all heparins studied, potency curves generated in the presence of PF4 and PS paralleled each other closely. With the 2 decolorized heparins, these curves also closely paralleled the potency curves generated in the ThI assay in the absence of PF4 or PS (ThI-buffer curves), but for the undecolorized heparin, the ThI-buffer curve was distinctly of steeper slope with greater potency. In contrast, with BL heparin , the ThI-buffer curve was of shallower slope and of lower potency.

The parallel behavior of PF4 and PS curves supports a similarity in the mechanism of neutralization. The potency of heparin fractions is related to their charge density. With decolorized HM heparins, PF4 and PS do not selectively neutralize a subfraction with different potency, but with the undecolorized heparin, PF4 and PS is somewhat selective towards neutralizing more potent heparin species. In contrast, with BL heparin, a less active heparin species is apparently preferentially inactivated by PF4 and PS, and moreover, the activity is less subject to neutralization.

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INFLUENCE OF VARIATIONS IN THE CHEMICAL STRUCTURE OF HEPARIN ON ITS ANTICOAGULANT AND ANTI Xa ACTIVITIES. A.S. Perlin and L. Ayotte, Department of Chemistry, McGill University, Montreal, Quebec, Canada, and J.C. Lormeau, Institut Choay, Paris, France.

Fractions of hog mucosal heparin, prepared by graded sedimentation as barium salts, are distinguished by large differences in chemical composition and relatively small differences in molecular weight. These fractions were found to vary widely in anticoagulant activity and in their ability to potentiate the inhibition of Factor Xa. Anticoagulant activity was highest for fractions that consisted mainly of L-iduronic acid 2-sulfate and 2-deoxy-2-sulfamino-D-glucose 6-sulfate, and decreased overall by a factor of 3 (from 145 to 56 USP units) as the proportion of residues of 2-acetamido-2-deoxy-D-glucose, D-glucuronic acid and L-iduronic acid became progressively more prominent. Conversely, a 10-fold increment in anti Xa activity (from 59 to 639 units/mg) accompanied the increase in the relative proportions of the minor, non-sulfated, heparin constituents. These findings suggest that individual steps of the coagulation process are subject to selective catalytic effects on reaction rate by differently constituted molecules within a heparin preparation.

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LOW MOLECULAR WEIGHT HEPARINS: ANTI-X_a/APTT AND PLATELET AGGREGATION. F.Fussi, M.R.Smith, A.Girolami, L.Visentini, F.Fabris. Hepar Ind., Franklin, Ohio, USA and Istituto di Semeiotica Medica, University of Padova, Italy.

Porcine mucosal Heparin (mean molecular weight= 15.000 Dalton) has been chemically depolymerized in presence of peroxides and N-sulphate groups have been re-introduced by reaction with sulphotrioxides of amines. The depolymerization has been stopped at different times and the products are essayed for Anti-X_a, APTT and their ratio. A rise in the ratio Anti-X_a/APTT has been observed.

In order to check for an activity on the platelet aggregation, two sets of experiments have been carried out: in a first model, the 5-hydroxytriptamine (5-HT) release has been measured after addition of different quantities of products to washed platelets. One commercil Heparin gave a significant rise in 5-HT release whereas a normal porcine mucosal Heparin did not show any modification in basal values, nor significant modifications have been observed for low molecular weight heparins (10.000 to 7.000 D). Heparansulphate (HS) and Dermatansulphate (DS) show a slight anti-aggregating activity in this test.

In a second model, the percentage inhibition in collagen induced platelet release has been measured in a platelet rich plasma (PRP). All the tested heparins show a very significant inhibition, whereas HS and DS have no inhibiting activity in this test.