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HIGH CONCENTRATIONS OF HEPARIN ARE MORE INHIBITORY TO PLATE-AGGREGATION IN-VITRO THAN ARE LOW MOLECULAR WEIGHT HEPARINS AND HEPARINOIDS AT THE SAME CONCENTRATION.
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Other investigators have shown that heparin in the usual therapeutic range (0.1-0.5 units/ml) has an enhancing effect on ADP aggregation and an inhibitory effect on collagen and thrombin induced aggregation. The effects of low molecular weight heparin (LMWH) and heparinoids (dermatan sulfate, heparan sulfate) on platelet aggregation have not been as extensively studied.
We have utilized citrated platelet rich plasma (3.2% citrate-whole blood 1:9) drawn in plastic and adjusted to a final platelet count of 250,000/ul. A Bio-Data 4 channel aggregometer was utilized with constant stirring at 37°C. The reaction was allowed to run for 20 minutes. Platelet rich plasma was supplemented 1:9 with saline or heparin and various agonists were then added if no aggregation occurred. ADP, collagen, thrombin, ristocetin and serum from patients with heparin inudced thrombocytopenia (HIT) were utilized as agonists. Heparin was substituted at concentrations of 0.1 to 500 units per ml and various LMWH and heparinoids were substituted in equivalent anti-Xa or gravimetric concentrations.
At low concentrations no inhibitory effect on any of the agonists was observed with any of the heparins or heparinoids. At concentrations of heparin of 100 u/ml or greater, all agonists were inhibited. At equivalent concentrations of five different LMWH (Cy 216, Cy 222, Pk 10169, Kabi 2165 and pentasaccharide) inhibition did not occur at all or at very high concentions only. Dermatan sulfate and heparan sulfate inhibited only at high concentrations. HIT serum could not aggregate platelets with dermatan sulfate or pentasaccharide at any concentrations, but it was a good agonist with the other heparins and heparinoids.

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BINDING AND METABOLISM OF HEPARIN BY ENDOTHELIAL CELLS.
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In this study we show that bovine adrenal capillary endothelial cells (BACE) contain heparin (HP); this HP has been found associated with the cell surface (i. e. trypsin-removable), and intracellularly. However, experiments with [^{35}S]sodium sulfate labelling, demonstrate that BACE cells do not synthesize HP de novo, but they uptake it from serum. We have studied binding, uptake, and metabolism of different molecular weight-HPs: 13 Kd-HP from bovine source, 14 Kd-HP from porcine source, 4.5 Kd, and 2.5-HP fragments. Comparison among different HPs, was carried out by calculating the IC_{50} from competition curves for [^{3}H]-HP. Binding of labelled-HP to BACE cells was specific and saturable. Dextran sulfate and glycosaminoglycans did not compete for binding; only heparan sulfate showed some competition. Binding of different HPs was strictly dependent on their molecular weight; 2.5 Kd-HP was unable to bind to cells, although sulfation degree of this fragment and of unfractionated HP was almost identical. Therefore, we assume that a specific oligosaccharide sequence could be responsible for HP binding to BACE cells; this hypothetical "binding sequence" could then be lost in very low molecular weight-HP fragments. BACE cells are also able to internalize HP, and they release its low molecular weight degradation products into culture medium. Thus we suggest that endothelial cells might represent a site for the metabolism of endogenous and exogenous HP in vivo.

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PRODUCTION AND CHARACTERISATION OF MONOCLONAL ANTIBODIES AGAINST HEPARIN

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To complement the studies using MAbs to AT III and because of the reported ability of heparin to modulate several aspects of the cell-mediated immune response, we have prepared two mouse monoclonal antibodies (MAbs) to porcine mucosal heparin.

MAb 25/15 is an IgG1 and MAb 26/7 is an IgM. Both MAbs have iso-electric points between pH5.85 and 6.55. The MAbs recognise porcine and bovine mucosal heparin and rat mast cell heparin. Heparins with both high and low affinities for antithrombin III (AT III) bound both MAbs but neither MAb altered the binding of heparin to AT III. These antibodies did not recognise other proteoglycans (chondroitin sulphate types A, B and C, keratan sulphate and hyaluronic acid) with the exception of heparan sulphate, (the cellular equivalent of heparin) and Arteparon (Luitpold-Werk, Munchen; a synthetically polysulphated chondriotin sulphate), in competition and solid-phase binding assays. Dextran sulphate (Pharmacia) was also recognised by these MAbs. Cross-reactivity with Arteparon and dextran sulphate indicate that charged sulphate goups on the mucopolysaccharides may be important for MAb binding. The Mabs described may be useful probes for endogenous heparin at the cellular and tissue level and may allow further investigation of the many biological activities of heparin.

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A TRIAL OF SUBCUTANEOUS VERSUS INTRAVENOUS ADMINISTRATION OF LOW MOLECULAR WEIGHT (LMW) HEPARIN AND UNFRACTIONATED (UF) HEPARIN IN THE TREATMENT OF ESTABLISHED DEEP VENOUS THROMBOSIS (DVT).
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In a randomized clinical trial of 100 patients, the in vivo antithrombotic effects of a subcutaneously administered LMW heparin fraction (CY216) used in the treatment of established DVT, was compared with UF heparin administered by either intravenous or subcutaneous routes.

Venograms were used to make the initial diagnosis, and efficacy of treatment was assessed by a repeat venogram done on day 6. Comparison of the venograms were done blind by an expert radiologist.

Patients were randomized to one of three groups: Group 1 received subcutaneous CY216; Group 2 received subcutaneous UF heparin: Group 3 received continuous intravenous UF heparin. Random patients from each group had detailed haematological tests consisting of twice daily KCCT and anti-Xa levels.

Extension of thrombus occurred in significantly more patients receiving intravenous heparin than subcutaneous heparin ($p=0.02$).

There was no difference between the two subcutaneous groups. There were no haematological complications.

We conclude that subcutaneous administratiyon of heparin is the treatment of choice in the treatment of DVT.