STUDIES ON THE MECHANISM OF THE RATE ENHANCING EFFECT OF HEPARIN ON THE THROMBIN - ANTI-THROMBIN III REACTION. L-O. Andersson and E. Holmer. Research Department, Biochemistry, AB Kabi, Stockholm, Sweden.

The rate of the reaction between thrombin and antithrombin III is greatly increased in the presence of heparin. Several different mechanisms has been suggested to explain this effect. Published online: 2019-04-16 is that the binding of heparin to antithrombin III transforms it to a much more rapidly acting inhibitor. Another possible mechanism is that the heparin is bound to thrombin and that this complex then reacts with antithrombin III. This study was performed to clarify how heparin actually works. A commercial heparin preparation was fractionated by affinity chromatography on matrixbound antithrombin III into a high and a low affinity fraction. The high affinity fraction had strong anti-coagulant activity both when assayed by activated partial thromboplastin time and in purified thrombin-antithrombin III system. The low affinity heparin fraction had very low activity in both test systems. The strength of the binding of the two heparin fractions to antithrombin III and thrombin, respectively, was determined by a crossed immunoelectrophoresis technique. The results obtained showed that the high affinity heparin was strongly bound to antithrombin III as expected. The low affinity heparin was also bound but with a much lower strength. In contrast thrombin had essentially the same affinity for both heparin fractions indicating that the mechanism suggested first is the correct one. Competition experiments using both heparin fractions and the thrombin-antithrombin III system also yielded results in good agreement with that. Thus heparin acts as anti-coagulant by forming complex with antithrombin III making it a rapidly acting inhibitor.

POSTER SYMPOSIUM XIX

Thrombosis: Artificial Surfaces.

SYNTHETIC POLYMERS ARE MADE NON THROMBOGENIC BY STABLE COUPLING WITH AN ANTIPLATELET AGENT. D. Mari, M. Cattaneo, G. A. Gattinoni, N. Dioguardi. Institute of Clinical Medicine, Univ. Milano, Italy

A number of porous fibres made of synthetic polymers (cellulose triacetate) entrap enzymatic systems without altering their biological activity. Such fibres inserted in extracorporeal circuits have a potential clinical applicability to remove toxic substances involved in the pathogenesis of acute liver failure. Since platelets (pl) adhere extensively when fibres are exposed in vitro to human blood, the possibility was evaluated to affect thrombogenicity by coating the fibres with antithrombotic substances. A preliminary screening carried out in vitro by means of a model of pl adhesiveness to plastic columns filled with fibres showed that the antiplatelet agent ditazol (D) was the most effective compound in reducing pl adhesion. D was further evaluated with more sensitive experimental models involving ^{51}Cr labelled pl. Fibres were wrapped around a bob rotating in blood for different periods. Pl adhered massively within the first minutes to the uncoated fibres whereas both the rate and extent of adhesion decreased when fibres were coated with D. Heparinized blood flowing in a circuit by means of a pump insuring a constant flow rate of 500 ml/min was filtered through a cartridge inserted in the circuit and filled with coated fibres. Adhesion of ^{51}Cr pl to coated fibres was significantly lower than to uncoated fibres. Scanning EM showed scattered individual pl adhering to coated fibres whereas large aggregates formed on the uncoated fibres. These findings show that stable coupling of an antiplatelet agent to synthetic polymers markedly reduce their thrombogenicity.