HEPARIN AND ITS INTERACTION WITH ANTITHROMBIN III. Robert J. Linhardt, R. Erik Edens, H. Reis, Urzidil F. Strobl, James V. Evans, John M. Weiler, Div. of Med. and Prod. Chem., College of Pharmacy and Dept. of Internal Med., College of Medicine, The University of Iowa, Iowa City, IA 52242, USA

Heparin is a polyanion, sulfated linear polysaccharide that has been widely used clinically as an anticoagulant for over a half-century. Heparin's role in anticoagulation involves the regulation of the coagulation cascade, particularly the inhibition of factor Xa and thrombin. This review focuses on the structure and function of heparin, its interaction with antithrombin III (ATIII), and the clinical implications of these interactions.

A COMPARATIVE STUDY OF THREE LOW-MOLECULAR WEIGHT HEPARINS (LMWH) AND UNFRAGMENTED HEPARIN (UH) IN VOLUNTEERS. Beatriz J. Fernandez-Rivera, Juan Carlos Fernandez, Jesus F. Sigala, Juan M. Delgado, and Jose A. Zanuy. Inst. of Internal Medicine and Cardiology, University of Seville, Spain.

The levels of anti-Xa and anti-IIa activity, as reported in laboratory studies and clinical trials of LMWH preparations, show a high degree of variability. The clinical relevance of anti-Xa and anti-IIa activity in vivo is unclear. The incidence of postoperative deep vein thrombosis varies from 8% to 30% in different LMWH studies on comparable populations undergoing elective hip surgery.

The study was conducted with patients undergoing hip joint replacements. LMWH preparations and one UH group (given as a single subcutaneous injection to healthy volunteers). At the dosage level recommended for orthopaedic surgery, the drugs were studied with a standardized blood cross-over technique in 18 healthy volunteers. Intravenous component was added in the design. The following drugs were used: Fragmin (Novo-Nordisk), Xa IIa (IFG), and Fragmin (Kabi Pharmacare) 5000 U, Klexane (Bristol-Myers Squibb) 4000 U, and Heparin (KabiPharmacia) 3000 U. The following variables were assessed: anti-Xa, anti-IIa (Heparin), and anti-Xa and anti-IIa activity.

Blood samples were drawn from antecubital veins 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, and 12 hours after the i.v. injection. All samples were coded and assayed were performed under standardized conditions.

anti-Xa activity (coagulant: aPTT) PFG 100 0.91 1 2 3 4 5 6 7 8 9 10 12

anti-IIa activity (coagulant: pFg I) PFG 100 0.91 1 2 3 4 5 6 7 8 9 10 12

The results were compared to those obtained when free u-Xa (0.4 nM) was added to the samples. The LMWHs showed a lower anti-Xa activity than the UH, while the anti-IIa activity was similar. The LMWHs had a higher inhibitory effect on thrombin than on factor Xa.


Heparin has been used clinically as an anticoagulant for over a half-century. It also has other activities including the ability to regulate gene expression. This angiogenic activity is of particular interest since it is presented that describes the isolation, purification and quantitation of heparin from human hemangiomas. Hemangiomas are vascular tumors that can uncontrollable capillary growth. Most of these lesions are infiltrated by 40-fold higher levels of mast cells than found in the surrounding skin. Although patients with hemangiomas have normal clotting times, the blood coming directly from the lesion usually will not clot. The 1-4 pg of heparin found in each mast cell might be responsible for this localized, procoagulant-anticoagulant anticoagulant effect. Human heparin (649 ng of 2.7-g heparin) was recovered and purified from a large (6.5 g wet wt.) hemangioma. Both its chemical structure and in vitro anticoagulant activity were characterized. Twelve additional smaller heparins, ranging from 0.13 to 24.2 g wet wt., were also examined for total glycosaminoglycan content by carbazole assay and for heparin content by antifactor VII activity. Because of the small size of these tissue samples, the efficiency of glycosaminoglycan extraction and the reproducibility of our analytical method were examined. An average recovery of 67% of the total glycosaminoglycan present was possible by using a single procoagulant process followed by ion-exchange chromatography and methanol precipitation. An average deviation of 14% and a standard deviation of 3% were obtained (n=5). The glycosaminoglycan content ranged from 0 to 5 mg/g-tissue and the heparin content ranged from <1 to 5 mg/g-tissue. The nearly 10-fold difference observed in glycosaminoglycan content in these hemangiomas suggests that high deviations. Neither the mast cell count nor tissue weight correlated with either the glycosaminoglycan or the heparin content of these hemangiomas.