Poster Board P3-006

0877 BAY g 6575, AN ANTITHROMBOTIC COMPOUND THAT STIMULATES PROSTACYCLIN RELEASE FROM THE VESSEL WALL

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Oral administration of Bay g 6575 (1-(2-(β-naphtyloxy)ethyl)-3-methyl-2-pyrazolin-5-one) has been shown to reduce or prevent subsequent experimental thrombus formation in arteries or veins of rabbits and rats (1). In these animals, no effect on blood coagulation, fibrinolysis or platelet aggregation could be demonstrated (1). Ingestion of 1.2 g Bay g 6575 daily for one week by six healthy volunteers had no effect on parameters of blood coagulation, fibrinolysis or platelet aggregation "ex vivo", but seemed to inhibit platelet aggregation "in vivo" (less decrease of the platelet aggregate ratio after venous occlusion, ref. (2). Plasma drawn from five volunteers after a single oral dose of 1.2 g of the same compound stimulated prostacyclin release from "exhausted" rat aorta slices, while plasma from the same individuals before intake of the substance did not. Whereas administration of Bay g 6575 or dipyridamole alone had no effect on platelet aggregation "ex vivo", combined administration resulted in a striking and prolonged inhibition of ADP-induced platelet aggregation. It is proposed that the previously described antithrombotic properties of Bay g 6575 in animals (1) are a consequence of stimulation of prostacyclin release from the vessel wall and that this effect is also demonstrable in humans.

(1) Seuter, F. et al. Arzneimittelforschung, 1979, in press.
(2) Chamone, D.A.F. et al. Thrombos.Haemostas., 1977, 38, 132.

Venom and Thrombin-Like Enzymes

Level 5 – Red Side (Waterloo Foyer)

Discussion Group 12.00 – 12.45

P5-025 0878 ISOLATION OF A NEW ENZYME FROM HUMAN PLASMA FRACTIONS AND ITS EFFECTS ON COAGULATION

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A new hydrolase enzyme has been isolated from human plasma fractions. This enzyme has been purified to homogeneity by adsorption to and elution from DEAE-Sephadex, Benzamidine-EACA-Sepharose, and Heparin-Sepharose. The molecular weight, as judged by SDS-polyacrylamide gel electrophoresis, is 70,000 daltons; and there are 2 peptide chains (45,000 and 25,000) after reduction. This enzyme, isolated in an active form, hydrolyzes S-2238 (H-D-Phe-Pip-Arg-PNA), a chromogenic substrate (AB Kabi), at a rapid rate, S-2251 to a slightly lesser extent, and S-2222, S-2302, and S-2160 about equally and much more slowly. $CaCl_2$ greatly enhances its activity. The enzyme is inhibited by antithrombin III especially in the presence of heparin, but poorly by soybean trypsin inhibitor or by diisopropylfluorophosphate. The enzyme binds to and can be eluted from insoluble barium salts. In vitro, the protein will activate and degrade human Factor VIII, will activate human Factor V, and will inhibit epinephrine-induced platelet aggregation; however, the in vivo function is unknown. Comparison with known properties of protein C and other coagulation-related proteins indicates that this enzyme has not been previously described.