

α_2 -PLASMIN INHIBITOR: A NOVEL INHIBITOR OF BLOOD COAGULATION AND KININ GENERATION. H. Saito, G. Goldsmith, M. Moroi and N. Aoki. Case Western Reserve University School of Medicine, Cleveland, Ohio, U.S.A. and Jichi Medical School, Tochigi, Japan.

A novel α_2 -plasmin inhibitor (α_2 PI), chemically and immunologically distinct from any known inhibitors, has recently been isolated and characterized from human plasma (Moroi and Aoki, J. Biol. Chem. 251:5956, 1976). We have studied the effect of purified α_2 PI upon various proteases participating in human blood coagulation and kinin generation. At physiological concentrations, (50 μ g/ml), α_2 PI inhibited the clot-promoting and prekallikrein-activating activity of Hageman factor fragments (HF_f, MW= 30,000), the amidolytic, kininogenase and clot-promoting activities of plasma kallikrein, and the clot-promoting activity of activated plasma thromboplastin antecedent (activated PTA, XI_a). For example, activated PTA was inhibited to 50% and 12% of original activity after incubation with α_2 PI for 10 and 30 min at 37°C respectively. At higher concentrations (200 μ g/ml), activated Stuart factor (X_a) was also inhibited. Heparin (1.5 units/ml) did not enhance the inhibitory function of α_2 PI against HF_f, plasma kallikrein or activated PTA. These results suggest that α_2 PI is an inhibitor of broad specificity that may play an important role in regulation of blood coagulation, fibrinolysis and kinin generation.

THE IMMUNOSUPPRESSIVE ACTIVITY OF PLASMIC DEGRADATION PRODUCTS OF HUMAN FIBRINOGEN. T.S. Edgington, L.K. Curtiss and E.F. Plow. Scripps Clinic and Research Foundation, La Jolla, California, U.S.A.

Plasmic cleavage of human fibrinogen leads to generation of immunosuppressive activity not expressed by the intact molecule, and which is demonstrable *in vitro* and *in vivo*. This activity is not associated with the high molecular weight derivatives X, Y, D and E, but is present in the small dialyzable peptide fraction obtained from plasmic digestion. The peptides inhibit in a non-toxic fashion, the stimulation of ³H-thymidine uptake and blastogenesis of lymphocytes by phytohemagglutinin (PHA) and allogeneic cells (MLC) under conditions of both macrophage dependence and macrophage independence. The peptides also suppress the plaque-forming cell response of mice to sheep red blood cells *in vivo*. Approximately 30 μ g peptides/culture leads to a 50% inhibition of the PHA and MLC systems, and approximately 400 μ g/mouse produces a 50% suppression of the plaque-forming cell response. Intact fibrinogen chains exhibit negligible activity, but plasmic digests of A α chain are suppressive. Consistent with derivation from the A α chain was the demonstration that the activity was generated from limited plasmic digest of fibrinogen which produced fragment X, and this activity was soluble at 80°C for 10 minutes. The release of the active peptide by limited plasmic degradation, and the activity of these peptides at physiologic concentrations suggests that this system may be of importance *in vivo* in association with local fibrinogenolysis or fibrinolysis at sites of thrombosis. This has been in part substantiated by the experimental initiation of fibrinogenolysis *in vivo* with streptokinase.