Tissue plasminogen activator (t-PA) causes bleeding problems in some patients, that did not necessarily correlate with a significant drop of fibrinogen levels. We have therefore evaluated the effect of t-PA on platelet function in vitro.

Incubation of gel-filtered platelets for one hour at 37°C with 180 ng/ml plasminogen and increasing concentrations of t-PA (50–1600 ng/ml) significantly inhibited shape change and aggregation induced by thrombin and the thromboxane mimetic U 46619 in a dose-dependent manner. In an EDTA milieu, which abolishes aggregation, a dual effect of t-PA and plasminogen was observed in the aggregometer: the thrombin- or U 46619-elicited initial decrease in light transmission, reflecting the disc-to-sphere transformation of platelets, was almost completely inhibited from 30 ng/ml t-PA upwards; the subsequent increase in light transmission, reflecting granule secretion, was however enhanced by small amounts of t-PA (up to 200 ng/ml). The latter finding was confirmed by direct measurement of secreted ATP: t-PA at concentrations up to 200 ng/ml enhanced thrombin- or U 46619-induced secretion. The amount of plasmin generated in the gel-filtered platelets-plasminogen-t-PA mixtures was quantified. The same amounts of plasmin, while also inhibiting the disc-to-sphere transformation of the platelets, did not enhance thrombin- or U 46619-induced ATP secretion. When whole blood or platelet-rich plasma or gel-filtered platelets resuspended in rich plasma or gel-filtered platelets resuspended in

The plasma protein inhibitor antithrombin III in its physiological form has been crystallized using standard techniques. The crystals diffract to about 3 Å and belong to space group P4_12_2_1 with cell parameters: a = b = 90.6 Å, c = 380.7 Å. The asymmetric unit contains three molecules of antithrombin III.

The self-rotation function computed with the native data set indicates the presence of a non-crystallographic three-fold axis. Cross rotation function calculations using the model of the cleaved α1-antitrypsin (H. Loebermann et al., J. Mol. Biol. (1985) 17, 531) suggests tertiary structure similarities between the two plasma proteins. This is in agreement with the already described primary sequence homology of these glycoproteins but at variance with the model of active α1-antitrypsin inferred from the previous studies on the cleaved molecule.

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