EPITHEORESE KLINIKES FARMAKOLOGIAS
KAI FARMAKOKINETIKES, INTERNATIONAL
EDITION 16: 71 (2002)

Plasmin Inhibitors and Angiogenesis

M. Hatjiapostolou[1,2], P. Katsoris[1] and E. Papadimitriou[2]

[1]Division of Genetics, Cell & Developmental Biology, Department of Biology and [2]Lab. of Molecular Pharmacology, Department of Pharmacy, University of Patras, Patras, Greece

AIM

Plasmin plays a significant role in basement membrane and extracellular matrix degradation, thus facilitating new vessel formation. The purpose of the present work was to study the effect of two plasmin inhibitors, ε-aminocaproic acid and α_2-antiplasmin, on angiogenesis.

METHODS

We used in vitro cultures of human umbilical vein endothelial cell (HUVEC), the matrigel tube forming assay, the Boyden chamber assay and the in vivo chicken embryo chorioallantoic membrane (CAM) model of angiogenesis.

RESULTS

α_2-Antiplasmin stimulated, while ε-aminocaproic acid inhibited proliferation and migration of HUVEC, as well as tube formation on matrigel. In line with the above, ε-aminocaproic acid inhibited and α_2-antiplasmin stimulated angiogenesis in vivo. The effect in both cases was dose-dependent. Moreover, ε-aminocaproic acid increased and α_2-antiplasmin decreased angiostatin protein amounts in the chicken embryo CAM.

CONCLUSIONS

Plasmin inhibition is expected to inhibit angiogenesis, which is in line with the effects of ε-aminocaproic acid in vivo και in vitro. In contrast, however, α_2-antiplasmin induces angiogenesis. The differential effect of the two plasmin inhibitors on angiostatin production may be the reason for their opposite effects on angiogenesis and should be considered during their experimental or clinical use.