Thrombolysis Using Liposomal-Encapsulated Streptokinase: An *In Vitro* Study

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Abstract

The clot-lysing ability of streptokinase (SK) was examined using membrane-bound thrombi. Encapsulation of SK in large unilamellar phospholipid vesicles (liposomes) resulted in entrapping approximately 30% of its original activity. Measurements of streptokinase activity for liposomal-encapsulated streptokinase (LESK) indicated little loss of activity or leakage in Tris-buffered saline over a 24-hr period at temperatures of 4 and 23°C. However, incubation of free SK and LESK in platelet-poor plasma (PPP) at 37°C resulted in a decrease of SK activity. The retention of SK activity in LESK was considerably higher than that of unentrapped SK. Clot-dissolving time (CDT) was measured by monitoring the pressure drop during slow filtration in plasma through membrane-bound thrombi. The results indicated that both LESK and free SK were able to activate the fibrinolytic system. Without prior incubation in PPP at 37°C, the CDT of a SK and PPP mixture (SK/PPP) was 10.7 ± 1.9 min (n = 12), while that of a LESK and PPP mixture (LESK/PPP) was 12.4 ± 1.7 min (n = 12). The CDT-detected clot-lysing abilities of both SK and LESK were diminished by incubation in PPP, but to different extents. After 15- and 30-min incubations, the CDT of SK/PPP increased significantly to 15.5 ± 1.5 and 24.1 ± 2.4 min (n = 5, $P < 0.05$), respectively. In contrast, the CDT of LESK/PPP increased to 13.3 ± 0.8 min (n = 5) after 15 min of incubation and to 16.0 ± 1.1 min (n = 5, $P < 0.05$) after a 30-min incubation. These results suggest that entrapment of SK in liposomes preserves the thrombolytic potential of the plasminogen activator by limiting its exposure to the components of the plasma.