HEPARIN STABILITY IN DEXTROSE SOLUTIONS

W. Anderson, J.E. Harthill, I.A. Couper*, and S. Stafford, Department of Pharmaceutical Technology, University of Strathclyde and *Glasgow Royal Infirmary

The anticoagulant activity of heparin in dextrose solution has been claimed to be stable (Mitchell & others, 1976), unstable (Jacobs & others, 1973) and temporarily unstable (Okuno & Nelson, 1975); its apparently erratic behaviour in such solutions requires elucidation.

An activated factor X assay (Yin & others, 1973) was used to determine the anticoagulant activity of heparin (from pig mucosa, 161 (BP) units mg^{-1}; given by Dr. H.G. Hind, Evans Biological Institute, Runcorn) after its addition (30 u ml^{-1}) to 5% dextrose solution (Baxter Labs.), which was kept sterile at constant temperature of 15°, 25° and 35° and sampled at time intervals.

Table 1. Loss and recovery of heparin anticoagulant activity in dextrose solutions

Solution in which heparin was dissolved (30 u ml^{-1})	Fall in activity† within 5 h, %	Time for recovery of activity† , h
Dextrose 5%	65	24 - 48
" + NaCl 0.9%	40	5 - 7
" + NaCl 2%	0	-

†calculated as percentage of zero-time anticoagulant activity.

The decline in activity frequently occurred by 1 h. Addition of 0.9% NaCl to the dextrose solution clearly modified the pattern of activity change which was abolished altogether by addition of 2% NaCl. The eventual recovery of full anticoagulant activity showed that heparin had not been destroyed. Also, the acceleration of recovery when 0.9% NaCl had been added together with abolition of the effect when 2% NaCl was present, suggest that a reversible salt-sensitive rearrangement or interaction of the heparin molecule took place in presence of a certain dextrose concentration. When 5% dextrose solution was replaced by 4.5% dextrose solution, the only change observed was a ± 15% variation in activity over 5 h; lower concentrations of dextrose caused no change. The pattern of activity change in 5% dextrose was independent of temperature for the temperatures used, supporting the view that degradative change was not occurring.

Concurrent chemical determination of heparin using toluidine blue, which measures macroanion activity (McIntosh, 1941) showed no variation in heparin concentration throughout 72 h, indicating no change in available ester sulphate and confirming belief about the integrity of the heparin molecule in such conditions.

Whether, in use, the temporary modification of anticoagulant activity in 5% dextrose solution is rapidly restored on injection into the completely different *in vivo* environment has still to be determined. Meanwhile, doubt about the complete suitability of 5% dextrose solution as a vehicle for heparin infusion persists and the need for vigilance and improvement in the laboratory control of heparin therapy is underlined.

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