PLASMA CLEARANCE OF TRITIATED-TUNICAMYCIN IN SHEEP

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Annual ryegrass toxicity (ARGT) is caused by ingestion of corynetoxins for which there are oral and subcutaneous toxicity data for purified toxin (Jago and Culvenor 1987). However there are no data concerning the fate of ingested ARGT toxin in a live animal. We recently prepared tritiated-tunicamycin which is a mixture of compounds almost identical in structure and biological properties (including toxicologic properties) to ARGT toxin. In this study we investigate the loss of tritiated-toxin from the plasma pool of two first cross ewes fed on a maintenance ration.

Tritiated-toxin ($4x10^5$ dpms/ug) was purified by HPLC and the plasma infusate was prepared as described by Lindsay and Leat (1977). In the first study (Ewe 27, 28.7 kg), a single injection ($7.5x10^6$ dpms/kg liveweight) of labelled toxin was administered and venous blood samples (5 ml) were taken at increasing intervals over 10 hrs after toxin injection; a further sample was taken after 24 hrs. This procedure was repeated in the second study (Ewe 145, 25.3 kg), except that blood samples were taken over the 24 hr period. Total plasma radioactivity curves for both studies are presented in Figure 1. The clearance of tritiated-label from the plasma pool was similar in both studies, following an exponential rate for approximately 10 hrs after which it reached an apparent equilibrium accounting for 3% of the original activity. HPLC purification of this plateau material indicated that it was a hydrophillic derivative of the labelled toxin. The rapid partitioning of label from plasma to the red blood cell pool during the first hr after toxin injection in Ewe 145 is presented in Figure 2. Disappearance of 95% of infused activity from both the plasma and red blood cell pool cannot be accounted for by simple dilution of toxin in the extracellular fluid and urine and it is estimated that 80% of the toxin is tissue associated.

This study clearly demonstrates the rapid clearance from plasma and presumably, incorporation of label into body tissues. However further experiments with individually purified and labelled toxin components are needed to adequately interpret the in vivo kinetic behaviour and possible metabolism of ARGT.

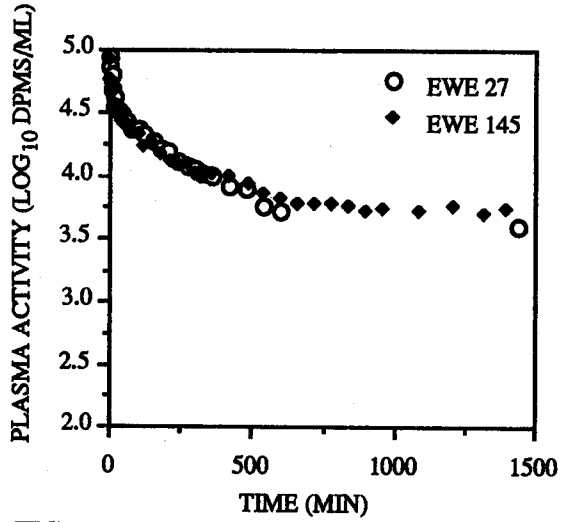

FIGURE 1. Plasma clearance of tritiated-tunicamycin.

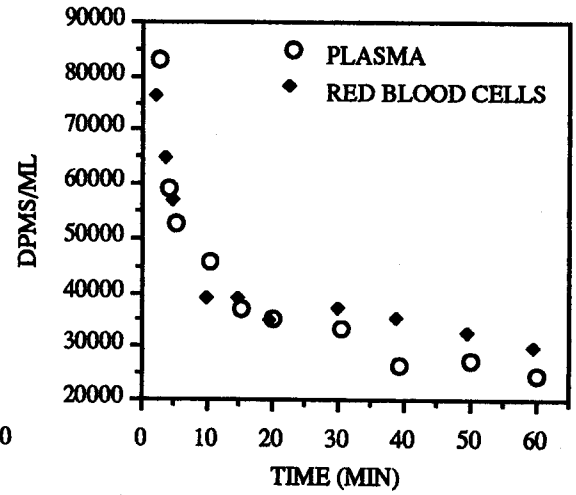

FIGURE 2.Partitioning of tunicamycin from plasma to red blood cells.

JAGO, M.V. and CULVENOR,C.C.J. (1987). Aust. Vet. J. 64: 232.
LINDSAY, J.L. and LEAT, W.M.F. (1977). J. Agric. Sci. 89: 215.

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