Some observations on the pharmacokinetics of trimethoprim in the horse

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Although the pharmacokinetics of trimethoprim have been studied in a number of species (Kaplan, Weinfeld, Cotler, Abruzzo & Alexander, 1970; Meshi & Sato, 1972), no similar work has yet been published for the horse.

Five Shetland type ponies, mean weight 179 kg (±8.4 s.d.), were used in these experiments. Trimethoprim powder (170 mesh B.S.S., Burroughs Wellcome) was dissolved in 10% v/v aqueous lactic acid to give a solution containing 150 mg/ml. In three experiments, 6.5 ml of this solution was injected into the pectoral muscle. In five experiments, the trimethoprim solution was diluted with water to give a concentration of 50 mg/ml, and 20 ml was administered intravenously into the left jugular vein. Blood samples were collected from the right jugular vein at intervals after dosing. Total 24 h urine collections were taken for 48 h after injection (Warwick, 1966). Trimethoprim was assayed in blood and urine by a fluorimetric technique (Kaplan *et al.*, 1970).

After intravenous injection, the fall in trimethoprim blood concentrations followed a biexponential decay curve. The mean disposition rates were 1.4/h (±0.20 s.d.) and 0.18/h (±0.05 s.d.) corresponding to half-lives of 0.5 and 3.8 hours. Peak blood levels of trimethoprim were found 3 h after i.m. injection in all three experiments. Figure 1 shows the results obtained with one pony. During the first 24 h after i.v. injection, 9.1% (±2.9 s.d.) of the dose was excreted unchanged in the urine. A further 1.0% (±0.6 s.d.) was excreted during the second 24 hours. Thin-layer chromatography of chloroform extracts of urine (Meshi & Sato, 1972) showed the major ultraviolet light absorbing spot to correspond to trimethoprim. Spots corresponding to 3′- and 4′-*O*-demethylated trimethoprim were detectable.

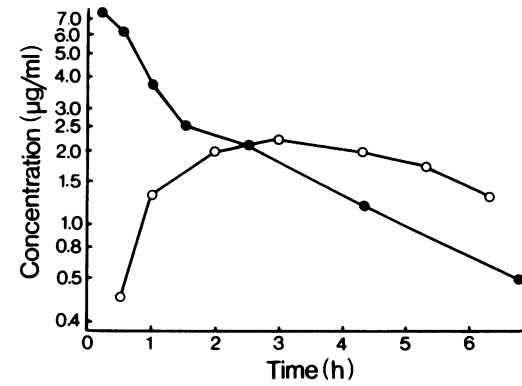

Fig. 1 Blood concentrations of trimethoprim after i.v. (●) and i.m. (○) injection. Pony 6, 178 kg weight.

The rapid clearance of trimethoprim in ponies resembles that found in dogs (Kaplan *et al.*, 1970). *O*--demethylation appears to occur in ponies as in other species (Schwartz, Vetter & Englert, 1970).

The authors acknowledge gifts of metabolites from Dr L.A. Nielson, Burroughs Wellcome, and Dr J. Reider, Hoffman-La Roche, and the technical assistance of Miss F. Anderson and Miss McKenzie, A.I.A.T.

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