

is less readily dissipated from the paws causing a greater rise in paw temperature and consequently greater injury.

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Some observations on blood level data following oral administration of aspirin as tablets and capsules

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Experimentally prepared capsules and commercially available tablets of aspirin, each of 500 mg, were tested and were shown to conform to the British Pharmacopia tests for uniformity of weight, uniformity of active ingredient and five single-capsule assays yielded results of 97.7% (S.D.=0.62%) active ingredient. From single-tablet assays they contained 100.6% of aspirin (S.D.=1.72%).

Two capsules or two tablets, were administered in a randomized cross-over experiment, to 9 healthy volunteers, two weeks being allowed before the second test was commenced. Venous blood was withdrawn before and at various times after administration, and plasma salicylate levels determined after alkaline hydrolysis.

In every subject, the tablet preparation produced a higher concentration of salicylate in the plasma 0.5 and 1 h after administration than did the capsule formulation, and the peak levels occurred earlier and more consistently for the tablet at about 2 h.

The time to reach maximum blood level varied from about 2 to 4 h for the capsules. Average peak salicylate levels between the two groups were virtually identical (66.2 µg/ml and 64.1 µg/ml; S.D., 10.8 and 10.3).

Extrapolation of the log concentration vs. time graph, after peak levels to a common time scale, showed similar elimination rates for the two formulations, and confirms that the individual peak levels obtained differed little between the formulations.

A polynomial regression of the first few points up to the maximum indicated a lag time in the appearance of salicylate in the plasma, and this was significantly higher for the capsule which averaged 0.23 h and 0.07 h for the tablet. The disintegration time in water of the experimental formulation was 519-524 s, and that of the commercial preparation only 14-18 s, but, whereas the tablet almost immediately became dispersed in water, it was approximately 45 s before the edges of the capsule broke open to release some of the contents. Thus, the delayed and less consistent maxima plasma salicylate levels of the capsule formulation may be due to the slow release of the drug from the dosage form. Quantitative pharmacokinetic data and dissolution rate profiles are being evaluated.

Hepatic clearance of propranolol in dogs

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Studies in which ¹⁴C-propranolol was given to man indicate that this drug is almost totally absorbed after oral dosing (Paterson *et al.*, 1970). However, peak plasma con-