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CORRELATION BETWEEN RAT, DOG AND HAMAN SMALL INTESTINAL PERMEABILITIES OF RANITIDINE

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While ranitidine is well known to be absorbed rapidly, the underlying cause of variable bioavailability in intra- and inter-subjects has not been clarified yet. Intestinal permeability is a key controlling factor for oral absorption of highly soluble drugs. In the present study, intestinal perfusions have been conducted to determine the intestinal permeabilities (Peffs) of ranitidine in the rats, dogs and humans and compared to the estimated fractions of dose absorbed (FAs) in humans. A new *in vivo* methodology, using a regional segmental perfusion technique, has been used in the dogs and humans. *In situ* single-pass perfusion experiments have been performed in the rats. In the dog and human studies, perfusion experiments have been conducted on two periods to determine the intrasubject variability. There was low significant intrasubject variation as compared to intersubject variation. The Peffs of ranitidine were 33%, 51%, and 45% inthe rats, dogs and humans, respectively. The FAs were approximately the same for all three species models, suggesting rats and dogs are good animal models for estimating the oral absorption of ranitidine in humans. In addition, the estimated extent of absorption of this drug is consistent with the average bioavailability, indicating that ranitidine has permeability-limited absorption characteristics.

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