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INTESTINAL WALL PERMEABILITY STUDY OF RANITIDINE IN DOGS

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Recently a novel *in vivo* approach in dogs, using a regional segmental intestinal perfusion technique, has been developed. The perfusion tube consists of a highly sophisticated multichannel tube with two inflatable occluding balloons, which are placed in 10 cm apart. The tube was introduced orally from the stomach through the upper jejunum under the guidance of solid-state pH meter. In the present study, four healthy dogs were infused in the proximal jejunum on two periods. The two perfusion experiments used the same flow rate, 2 ml/min, and the same perfusion solution to determine the intrasubject variability. The mean (± S.E.) fractions of ranitidine absorbed calculated from the perfusion data were 21.32 ± 2.01 % (n=3) (1st period), 27.88 ± 17.54 % (n=4) (2nd period), respectively. The effective permeabilities (Peffs × 10^4) of ranitidine were 1.51 ± 0.47 cm/sec (n=3) (1st period), 1.50 ± 0.31 cm/sec (n=4) (2nd period), respectively. The pH and osmolarity of perfusion solution were 7.50 ± 0.03 and 300 ± 0.06 mOsm/L. There was no significant intrasubject variation. Mixing equilibrium (steady-state) was reached at about 50 min. *l*-Phenylalanine was absorbed almost completely. Intrinsic intestinal wall permeability of ranitidine showed low permeable characteristics, suggesting permeability-limited absorption. The absorption of *l*-phenylalanine, an actively transported nutrient, was not inhibited by ranitidine. The low intestinal membrane permeability is one of the important factors responsible for the variable oral absorption of ranitidine.

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