

32g Novel Measurement and Modeling of in Vivo Oral Drug Absorption Rate in Rats

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A novel method for determining drug dissolution and/or absorption rate in live rats is described. A drug tablet was immobilized at a designated point in the digestive tract using a pharyngostomy procedure. The tablet was attached to the end of a fine surgical thread and administered to the anesthetized animal through an esophageal feeding tube. The thread was secured by affixing the attached thread to the neck. Blood samples were taken periodically following surgery. The animal was then euthanized, an autopsy was done, and the recovered tablet was examined and weighed. The usefulness and reproducibility of the method is shown in data from seven rats where naproxen tablets were immobilized in the stomach. Because the drug used in this study (naproxen) is poorly water soluble in low pH medium, it was assumed the rate of appearance in the bloodstream is the rate of dissolution in the stomach. This assumption was tested by comparing blood concentrations over time with a mathematical model. Absorption and metabolism rate constants used in the model were taken from the literature. Results show that care must be taken to insure tablet placement in the desired location in the GI. The tablet and thread must be compressed and coated adequately to maintain their connection and to keep the tablet intact in the esophagus. Eight hours sampling time is adequate to determine a steady-state concentration. Blood concentrations calculated by the model were found to be within one standard deviation of the averaged experimental values, giving validity to the novel dissolution method developed in this study.