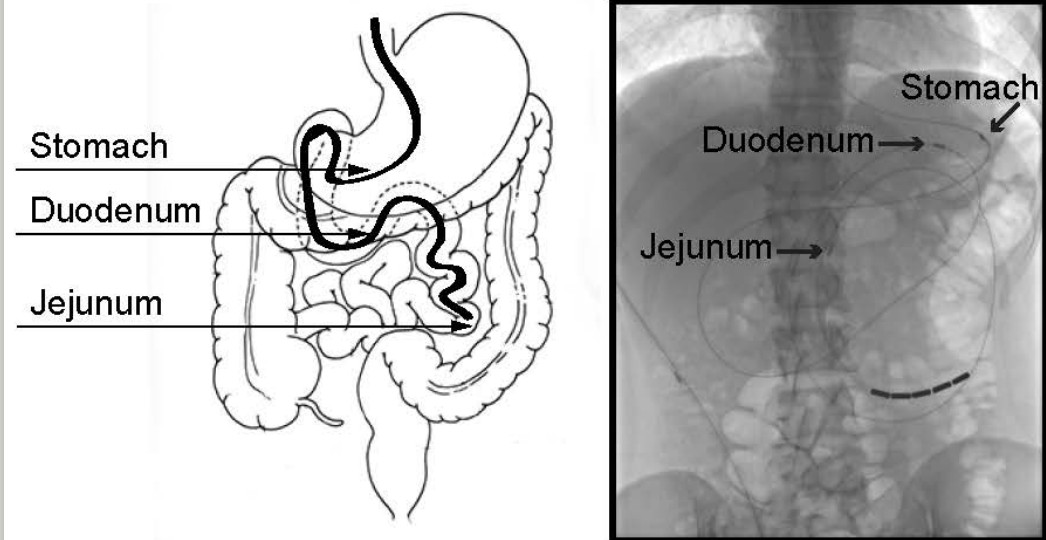


Purpose

Drug dose, dissolution, gastric emptying, gastrointestinal (GI) motility, solubility, and intestinal content influence systemic drug absorption. Regional GI tract *in vivo* drug dissolution must be better understood to refine *in vitro* methodologies to predict drug bioavailability. We aimed to quantify plasma and GI luminal concentrations of the highly absorbable drug ibuprofen in different regions of the stomach and small bowel in relation to fasting vs. fed status and to luminal pH, GI motility, and fluid dynamics using a novel multi-lumen aspiration catheter.

Methods

Specialized manometry catheters with 4 aspiration ports were orally inserted with fluoroscopic positioning of collection sites in the stomach, duodenum, and jejunum (N=20 procedures in 14 healthy humans).

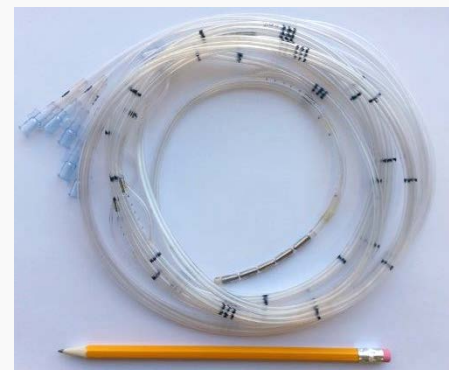


Subjects were randomized to fasting or fed conditions (Pulmocare, Abbott Nutrition, 710 cal before drug dosing).

Subjects ingested immediate release ibuprofen 800 mg tablet in 250 mL of water.

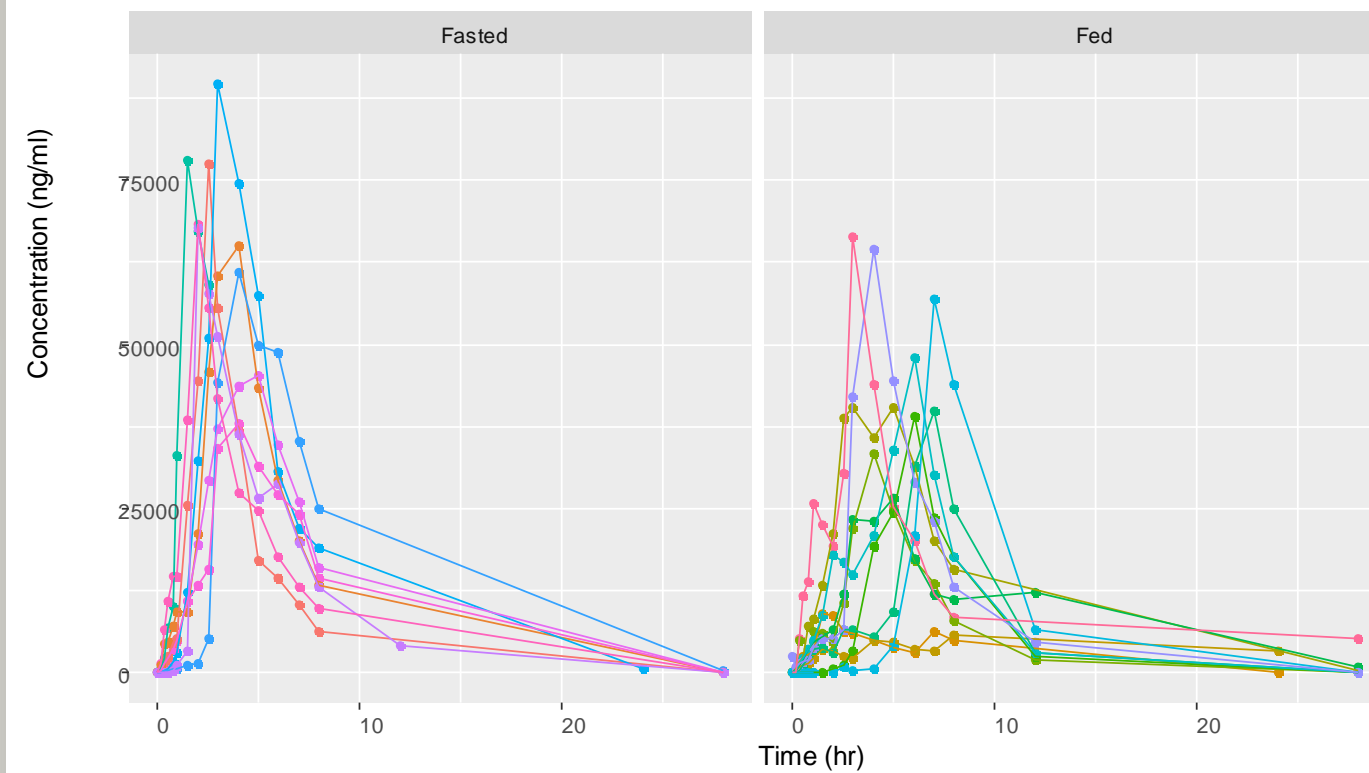
GI fluid samples were collected x 7 h and venous blood was obtained x 28 h post dosing.

GI fluid and plasma ibuprofen concentrations were measured by LC-MS/MS and were related to GI fluid pH levels.



Results

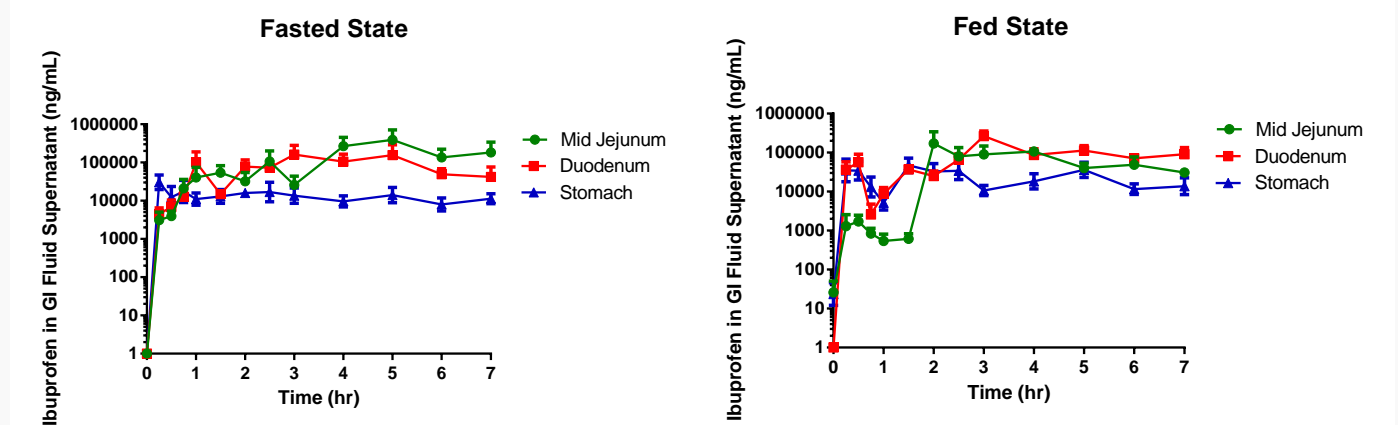
Ibuprofen Concentration in Plasma



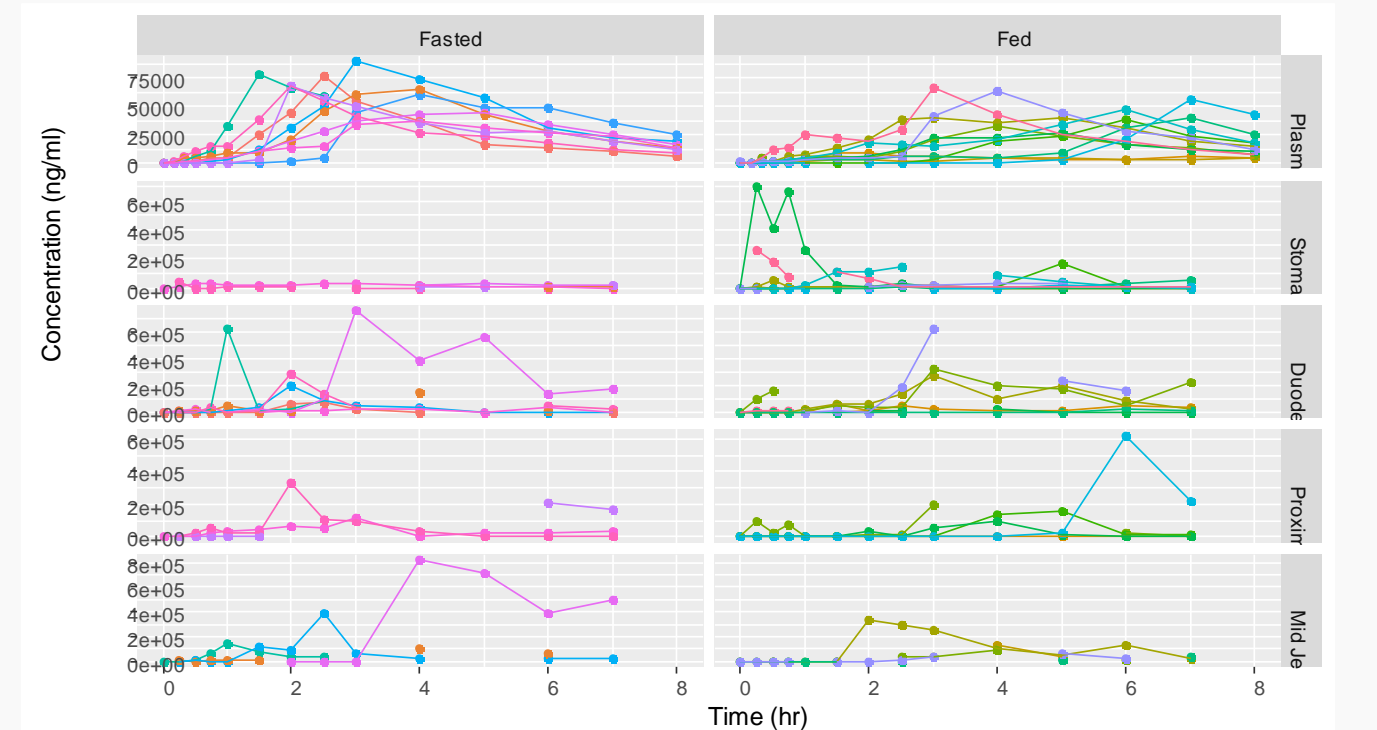
Phase	Number of Subjects	AUC _{inf} (µg•hr/ml)	C _{max} (µg/ml)	T _{max} (hr)
Fasted	9	361.106 ± 74.788	65.630 ± 15.219	3.100 ± 1.129
Fed	11	257.489 ± 108.307	39.121 ± 19.067	4.965 ± 1.929

Average ± Standard Deviation

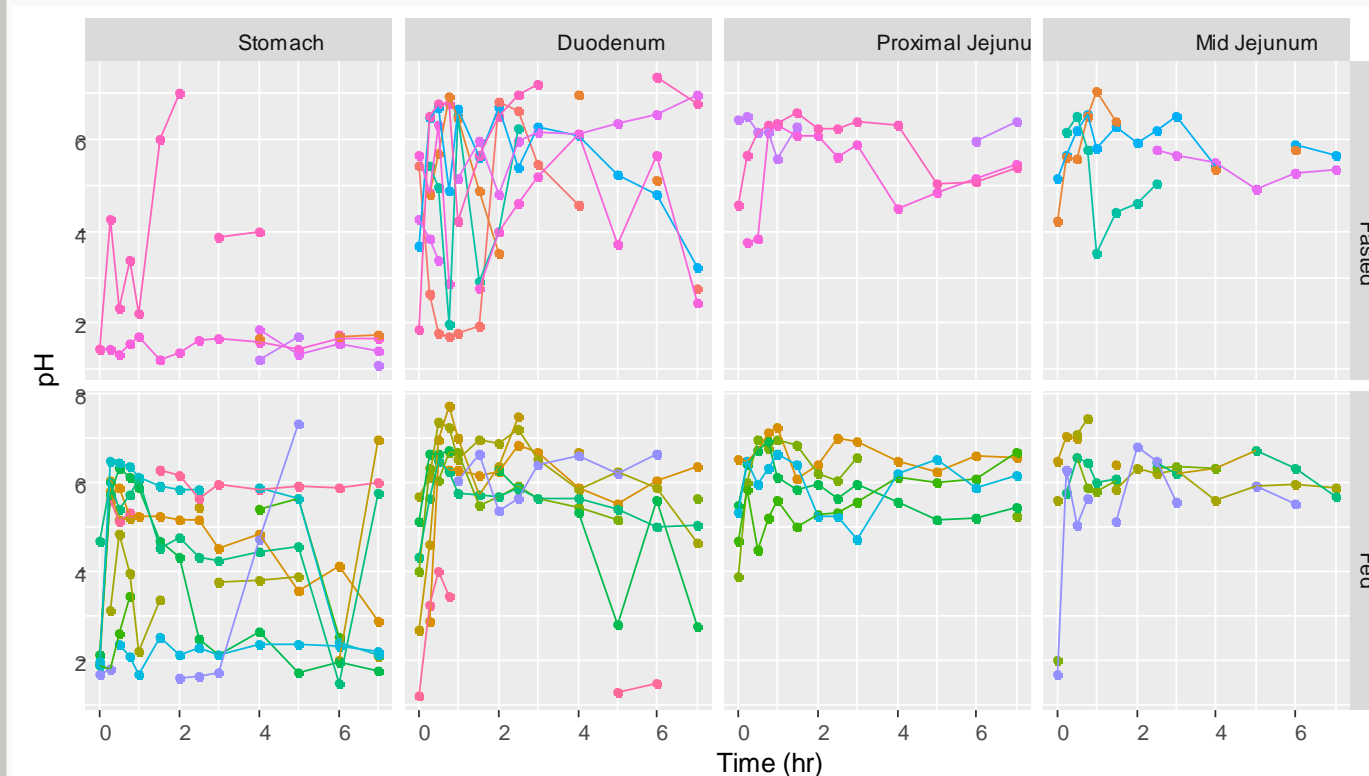
Ibuprofen Concentration in Luminal GI Fluid



Ibuprofen Concentration in Individual Subjects



pH of Luminal GI Fluid



C_{max} Correlates with Phase III Motility (Fasted)

