Regional In Vivo Dissolution of Immediate Release Ibuprofen in Human Gastrointestinal Tract and Its Relationship to Luminal pH, GI Motility, and Systemic Absorption

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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.

**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**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Number of Subjects</th>
<th>$\text{AUC}_{\text{inf}}$ (µg•hr/ml)</th>
<th>$C_{\text{max}}$ (µg/ml)</th>
<th>$T_{\text{max}}$ (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasted</td>
<td>9</td>
<td>$361.106 \pm 74.788$</td>
<td>$65.630 \pm 15.219$</td>
<td>$3.100 \pm 1.129$</td>
</tr>
<tr>
<td>Fed</td>
<td>11</td>
<td>$257.489 \pm 108.307$</td>
<td>$39.121 \pm 19.067$</td>
<td>$4.965 \pm 1.929$</td>
</tr>
</tbody>
</table>

Average ± Standard Deviation

**Ibuprofen Concentration in Luminal GI Fluid**

**Ibuprofen Concentration in Individual Subjects**

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

**pH of Luminal GI Fluid**

Stomach  Duodenum  Proximal Jejunum  Mid Jejunum

0 1 2 3 4 5 6 7

Time (hr)

0 10 20 30

Concentration (ng/ml)

Fed State

Fasted State