BioGIT summary

BioGIT is an open in vitro set-up for estimating apparent drug concentrations and % solid fraction in upper small intestine, after co-administration of a solution/suspension/disintegrating/dispersing dosage form with a glass of water to fasted adults. In case of solution formulation, the % precipitated in upper small intestine is estimated. Using part of the sample collected for measuring apparent drug concentration, apparent equilibrium solubility can further be measured and, therefore, apparent supersaturation in upper small intestine can also be estimated.

Experience with BioGIT, to date, is summarized in References 1-4.

Experimental set-up (see Figure 1 and Reference 2)

- BioGIT system simulates the continuous gastrointestinal transfer process in vivo. The in vitro set-up consists of three compartments, the gastric, the duodenal, and the reservoir compartment. It is implemented by using commercially available equipment.
- The in vitro testing conditions were decided, after modelling luminal data collected after administration of highly permeable active pharmaceutical ingredients to healthy adults. The volume of contents in the duodenal compartments is maintained at 40 mL during the entire experiment. The emptying of contents of gastric compartment (on a volume basis) follows first-order kinetics with a half-life of 15 min.
- Initially, 250ml Level III FaSSGF is brought in the gastric compartment and 40ml Level II FaSSIF is brought in the duodenal compartment. A series of phosphate buffer solutions containing sodium chloride, bile salt and lecithin are brought in the reservoir compartment so that the composition of contents of the duodenal contents (pH, buffer capacity, osmolality, bile salt and lecithin concentration) remains unaltered during an experiment.

Figure 1: Graphical representation of the biorelevant gastrointestinal transfer (BioGIT) system. F=F₁+F₂.

Usefulness
BioGIT is useful for evaluating
- formulations for their performance in the upper small intestine
- the impact of dose on concentrations in the upper small intestine
- differences in early exposure, after administration of an immediate release or an enabling product of a highly permeable drug

Limitation
To date, the usefulness of BioGIT has not been evaluated when a non-disintegrating dosage form is employed.
Information to facilitate implementation of BioGIT in practice

Technical details on BioGIT

Data are collected using a dissolution water bath and a mini-vessel with 500 ml capacity with the corresponding mini-paddle (e.g. Erweka, Heusenstamm, Germany) for the gastric compartment and a mini-vessel with 100 ml capacity with the corresponding mini-paddle (e.g. Distek, New Brunswick NJ, USA) for the duodenal compartment (Figure 1). Positioning of the 100-ml capacity mini-vessel in the available dissolution water bath may require appropriate adjusters. In all cases, the temperature in the mini-vessels is set at 37 °C and the mini-paddles rotate at 75 rpm.

Transfer is performed via a three channel peristaltic pump (Reglo ICC pump, part ISM 4308, Ismatec®). In each channel, a Tygon R3607 tube (internal diameter, id, 1.65 mm for the inlet and 2.06 mm for the outlet, Ismatec, Germany) is positioned. One Tygon tube is connected at one end with a stainless steel tube for transferring contents out of the gastric compartment (id 3.0 mm) and at the other end with a stainless steel tube for transferring contents into the duodenal compartment (id 1.0mm). The second Tygon tube is connected at one end with a stainless steel tube for transferring contents out of the reservoir compartment (id 1.0mm) and at the other end with a stainless steel tube for transferring contents into the duodenal compartment (id 1.0mm). The third Tygon tube is connected at one end with a stainless steel tube for transferring contents out of the duodenal compartment (id 1.0mm).

The lower ends of the mini-paddle and the stainless tube in the gastric compartment are 11mm and 17mm from the bottom of the mini-vessel, respectively. In the duodenal compartment, the lower ends of the mini-paddle and of the stainless tubes that transfer contents of gastric and reservoir compartment into the duodenal compartment are 5mm and 15mm from the bottom of the mini-vessel, respectively. The lower end of the stainless tube via which contents of the duodenal compartment are transferred out of the mini-vessel is 25mm from the bottom of the mini-vessel.

For practical reasons, incoming flow rates in the duodenal compartment are changing every 10 minutes so that sampling is possible at midpoint (Table 1).

### Table 1: Incoming flow rates to the duodenal compartment from the gastric compartment (F₁) and the reservoir compartment (F₂) and outcoming flow rate (F) from the duodenal compartment applied in the in vitro experiments.

<table>
<thead>
<tr>
<th>Time Interval (min)</th>
<th>F₁ (ml/min)</th>
<th>F₂ (ml/min)</th>
<th>F (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>9.3</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>10-20</td>
<td>5.9</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>20-30</td>
<td>3.7</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>30-40</td>
<td>2.3</td>
<td>9.3</td>
<td></td>
</tr>
<tr>
<td>40-50</td>
<td>1.4</td>
<td>10.2</td>
<td>11.6</td>
</tr>
<tr>
<td>50-60</td>
<td>0.9</td>
<td>10.7</td>
<td></td>
</tr>
</tbody>
</table>

Information gained from a BioGIT experiment

BioGIT data provide information on the impact of gastrointestinal transfer on concentrations in the upper intestinal lumen during the first hour, after oral administration of solution/suspension/disintegrating/dispersing dosage forms. Specifically, total amount per volume and drug concentration in the duodenal compartment is measured (Figure 2) and, therefore, % solid fraction or, in case of a solution dosage form, % precipitated fraction can be estimated using the following equation:

\[
\text{% Solid fraction (or % Precipitated fraction)} = (1 - \frac{\text{Concentration}}{\text{Total amount per volume}}) \times 100
\]
By adding solid drug in excess in samples collected from the duodenal compartment, equilibrium solubility is measured (Figure 2), and therefore, supersaturation of contents of the duodenal compartment during the experiment can be evaluated using the following equation:

$$Degree \ of \ Supersaturation = \frac{Concentration}{Equilibrium \ solubility}$$

![Figure 2](image)

**Figure 2:** A hypothetical example. Estimated total amount per volume assuming homogenous emptying of contents in the gastric compartment (----) (see Reference 2), measured total drug amount per volume (■), measured concentrations (○), and measured equilibrium solubility of drug in the sample collected from the duodenal compartment (★).

References


