O 02

In vitro evaluation of drug presence in the micellar pHase of contents of upper small intestine: Rationale, challenges, opportunities

Christos Reppas

Department of pH*armacy, National and Kapodistrian University of Athens, Greece*

After oral administration of enabling drug products or conventional products of lipo pHilic drugs with weakly alkaline characteristics, drug concentrations in the micellar pHase of contents of upper small intestine can be crucial for the overall luminal product performance. Drug concentrations in the micellar pHase of contents of upper small intestine are highly sensitive to the total drug presence in the lumen of upper small intestine, i.e., the total drug arrival and elimination (intestinal transit and epithelial transport) rates, and to the pHysical state of the drug that enters the upper small intestine from the stomach, *i.e.* solid state, aqueous solution, and/or non-aqueous solution.

The in vitro evaluation of drug presence in the micellar pHase of contents of upper small intestine requires prior understanding of the complex in vivo situation.

In vitro evaluations under conditions simulating the drug administration in the fasted state are possible, after considering the appropriate level of simulation of the system and after confirming the usefulness of in vitro data against luminal data in humans. Micellar drug concentrations in the duodenal compartment of the BioGIT system are in line with micellar drug concentrations in the upper small intestine. The BioGIT system has been shown to be useful for evaluating the impact of formulation and/or dose on early exposure, after oral administration of conventional or enabling drug products with a glass of water to fasted adults.

Significant gaps in understanding key luminal drug/drug product related processes do not allow yet for in vitro evaluations of drug presence in the micellar pHase of contents of upper small intestine under non-fasting conditions. Current investigations focus to the identification of gastric contents characteristics which are related to the frequently delayed disintegration of drug products, to the characterization of drug gastrointestinal transfer process and to the evaluation of the importance of drug presence in the micellar vs. the colloidal (non-droplet) pHase of contents of upper small intestine.