Towards a physiologically relevant \textit{in vitro} system for oral drug product delivery in the gastrointestinal (GI) tract

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**Drug Delivery in GI Tract**

What are the important factors in oral drug delivery?
- Permeability.
- Solubility.
- Dose.
- Dissolution

How the critical parameters for human \textit{in vivo} drug dissolution are measured?
- Gastric emptying rate.
- GI tract content.
- GI tract pH.
- GI tract buffer capacity.
- Motility.
... 

**GI Motility & Hydrodynamics**

\textit{in vivo} Mixing
- Peristaltic Waves: progressive wavelike contractions of longitudinal and circular muscles.
- Segmentation Contractions: movement of circular muscles that moves chyme in two directions.

\textit{in vitro} Mixing
- Stirrer: the rotating domain which generates shear rate. However, in common dissolution apparatuses the \textit{in vitro} shear rates are orders of magnitude greater than the \textit{in vivo} shear rates.

Dissolution Vessel: the stationary domain which its shape has an impact on hydrodynamics and particle suspension.

**Goal and Methodology**

Facts:
- The hydrodynamics conditions influence the convective mass transport.
- Current \textit{in vitro} drug dissolution devices have orders of magnitude higher shear rates than \textit{in vivo} systems.

Goals:
- Design an \textit{in vitro} system for GIS which simulates \textit{in vivo} hydrodynamics conditions.
- Predicting the average shear rate in \textit{in vitro} system by fluid mechanics theories.
- Validating the calculated average shear rates with experiments and mass transport modeling.

**Stirrer and Vessel Design**

What are the main design goals?
- Vessel design: should minimize the dissolution test variability.

- Stirrer design: should maximize the particle suspension and generate shear rate which is \textit{in vivo} shear rate range.

**How to estimate \textit{in vitro} average shear rate?**

The answer is with mass transport modeling.

Factors taken into account in mass transport modeling:
- Shear rate
- Drug properties
- Particle size and distribution
- pH stomach, duodenum, jejunum
- Stomach emptying rate
- Buffer pKa and concentration

**How accurate is the mass transport model?**

**Summary & Conclusion**

- The hydrodynamics are among the critical factors in determining the drug dissolution rate.
- The hydrodynamics are controllable in \textit{in vitro} system with general system design.
- Mass transport modeling can predict the \textit{in vitro} shear rates and validate the average shear rates which was calculated by CFD simulations.

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