Mechanistic Studies and Modeling of Effects of Ingested Lipids on Oral Drug Absorption

Selena Di Maio, Chemical Engineering, Northeastern University

Ingested lipids, typically originating from food and potentially used as delivery agents, can enhance absorption of compounds by several hundred percent, but they can also decrease absorption or have no effect. The influence of lipids on compound absorption originates from colloidal structures they form, compound trafficking between these colloidal structures and aqueous medium, and affects on transport through the intestinal mucosa. However, these effects are typically documented as empirical, compound-specific observations, and not predictable a priori. In addition, quantitative understanding of the fate of ingested lipids is lacking, yet has tremendous implications pertaining to diet-related diseases. Previously, the impact of lipid ingestion on co-administered compound absorption (compound solubility enhancement, change in intestinal permeability) has been studied in isolation. Therefore, the interconnected processes taking place during the lipid digestion, and their dependence on dynamic system colloidal structure and composition, have not been studied in a comprehensive, integrated fashion conducive to enabling quantitative prediction.

The overall goal of this project was to gain quantitative mechanistic insight into and to predict the influence of lipids in the gastrointestinal (GI) tract on compound absorption. The proposed research aimed to thoroughly characterize and model kinetics of parallel processes occurring in the GI tract upon co-dosing a compound with lipids – namely, compound dissolution, lipid digestion, compound partitioning into colloidal phases, absorption – and to relate the kinetics to chemical composition and colloidal
structure of intestinal contents. The result was a systems-based model of the influence of ingested lipids on compound absorption. It is recognized that lipid digestion and absorption are highly complex processes with multiple intricacies not currently possible to capture in mechanistic in vitro studies in a single project, the approach proposed was to start with a simplified system from which an experimental and theoretical framework was developed, feasibility of quantitative prediction was established, and considerable insight into complex effects of lipids on compound absorption was gained. The resulting experimental and theoretical framework is expected to significantly transform study of orally ingested lipids, enabling systems-based consideration of gastrointestinal processes central to nutrition, drug delivery, and diet-related diseases.