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| Title | **A Co-Perfused In Vivo Absorption Model to Probe the Simultaneous Digestion and Drug Absorption process from Lipid-Based Formulations** |
| Keywords (up to 5) | Drug absorption, in vitro-in vivo correlation, poorly water-soluble drugs, lipid-based formulations |
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| Abstract | After oral dosing, a cascade of events in the gastro-intestinal (GI) tract alters the solubilizing capacity of LBFs, often resulting in supersaturation and subsequent drug absorption.1 Drug flux, total absorption and oral bioavailability across the intestinal membrane may be influenced by a delay in digestion perfusate reaching the intestinal segment. The current project is therefore exploring the solubility-digestion-absorption relationship using PWSDs in LBFs when initiating digestion at the site of absorption in the small intestine. This has been examined using an experimental model that combines a traditional *in vitro* digestion experiment with *in situ* intestinal permeability measurements to provide for ‘real time’ assessment of the absorptive drug flux.  The utility of an *in vivo* ‘co-perfused enzyme and dispersed formulation model’ to approximate digestion at the site of absorption is evaluated to reduce lag time between formulation digestion and thereby reducing the drug precipitation potential. Drug flux patterns of fenofibrate and saquinavir obtained with this model are compared with the results from the linear perfusion, in which formulation digestion is initiated in the *in vitro* vessel.  Co-perfusion of bile with a Type IV drug solution of loaded at 85% fenofibrate saturation led to a 3-fold increase in drug flux compared to the linear perfusion. Various parameters were investigated that might have led to this observed difference, such as the dilution by bile (low conc.), slower flow rate, etc. Each parameter tested contributed to a significant higher drug transport across the intestinal wall, with the dilution effect by bile leading to the largest difference.  This work demonstrates the utility of the co-perfused absorption model in developing a better understanding of drug absorption upon concurrent LBF digestion. The data suggest that drug flux might be underestimated when using non-physiological parameters and when introducing an artificial lag-time between formulation digestion and drug absorption. |
| References | 1. Porter, C. J.; Trevaskis, N. L.; Charman, W. N. Lipids and lipid-based formulations: optimizing the oral delivery of lipophilic drugs. *Nature reviews. Drug discovery* **2007,** *6* (3), 231-48. |