Regional intestinal permeability of drugs in humans and preclinical animal models.

Abstract

For most immediate-release dosage forms, the small intestine is the primary intestinal region for drug absorption. This because it has a large surface area available for drug transport and a more permeable membrane (“leaky”) compared to the colon. However, colonic drug absorption can be quantitatively important for drugs incompletely absorbed in the small intestine (i.e. BCS class II, III and IV), or for BCS class I drugs formulated into oral modified-release dosage forms. An oral modified-release dosage form is used to optimize pharmacokinetics, pharmacodynamics, and dosage regimens, which can reduce side effects, improve therapeutic effect, enable once per day drug administration, and increase patient compliance. Given that the solubility and dissolution are sufficient, development of a modified-release dosage form is feasible, but only as long as the drug is absorbed in all parts of the intestines. This is because drug release needs to be substantially longer than the typical human small intestinal transit time of 3-5 h.

In development of modified-release formulations, it is thus important to have a good understanding at an early stage of colonic drug permeability. However, there is currently a gap in the understanding of the accuracy of preclinical in vitro and in vivo models for the prediction of human colonic drug permeability. There is also uncertainty as to which molecular characteristics determine regional intestinal absorption rate, regardless of the compound's BCS classification.

This presentation will focus on the importance of the colon in drug absorption and drug product development. It will give a summary of available human colonic drug permeability data as well as predictive preclinical models.

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