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Implications of segmental-dependent intestinal permeability in oral drug delivery

Arik Dahan
Ben-Gurion University of the Negev, Beer-Sheva, Israel

On several levels, the dissolution and the permeability are related and should maintain a certain relationship between them. For instance, Tsume and Amidon (Mol Pharmaceutics 2010) have shown that the higher the permeability is, the more lax the dissolution criterion for granting a biowaiver can be. In this talk, regional-dependent intestinal permeability will be discussed, including dissolution aspects, as well as pathophysiological conditions. Permeability is location dependent, and pertains to each point throughout the gastrointestinal tract. A drug may exhibit significantly different intestinal permeability not only between the small and large intestine, but even within the small intestine, i.e. between the proximal jejunum and the distal ileum. The asymmetrical pH profile throughout the small intestine may be the underling mechanism for such segmental-dependent permeability of certain ionizable drugs. An asymmetrical expression pattern of different transporters throughout the intestinal tract may also cause such regional-dependent permeability. Asymmetrical intestinal enzymes expression may significantly influence the systemic bioavailability of a drug, although not necessarily affect the permeability. In these cases, rapid vs. sustained dissolving drug products may result unexpectedly different systemic drug levels. In conclusion, it is prudent to consider the intestinal permeability pattern when deciding on a certain dissolution profile.

Biography

Arik Dahan is an Associate Professor of Pharmaceutics and Biopharmaceutics at the Department of Clinical Pharmacology and the School of Pharmacy, Ben-Gurion University of the Negev in Beer-Sheva, Israel. He is also an Adjunct Professor of Pharmaceutical Sciences at the College of Pharmacy, University of Michigan. Dr. Dahan received his Ph.D. (2007) from the Hebrew University of Jerusalem. He was a Post-Doctoral Research Fellow at the University of Michigan (2007-2010) with Professor Gordon Amidon. Dr. Dahan's research interest is the integration of up-to-date molecular/cellular mechanistic investigations of drug disposition in the context of the human body. In implementing this molecular biopharmaceutical approach to ADME research, Dr. Dahan is seeking to enable mechanistic-based successful solutions to drug delivery/therapy, in challenging scenarios e.g. low-solubility, low-permeability, extensive metabolism, poor site targeting, various pathophysiological conditions, and pediatrics. He has published over 60 top-notch Journal papers.

arikd@bgu.ac.il

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