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Implications of segmental-dependent intestinal permeability in oral drug delivery

While each of the two key parameters of oral drug absorption, the solubility and the permeability, has been comprehensively studied separately, the relationship and interplay between the two has been largely ignored. For instance, when formulating a low-solubility drug, what are the effects on the apparent permeability? The direct correlation between the intestinal permeability and the membrane/aqueous partitioning, which in turn is dependent on the drug's apparent solubility in the GI milieu, suggests that the solubility and the permeability are closely associated, exhibiting certain interplay between them, and the current view of treating the one irrespectively of the other may not be sufficient. In this lecture, our results on this solubility-permeability interplay will be presented. Decreased apparent permeability accompanied the solubility increase when different solubilization methods are employed; however, increasing the apparent solubility by supersaturation e.g. via amorphous solid dispersions, circumvented the solubility-permeability tradeoff, and the permeability remained steady. Most recently, even increased permeability was discovered, when the supersaturation saturated efflux processes. Overall, the solubility-permeability interplay cannot be ignored when using solubility-enabling formulations; looking solely at the solubility may be misleading with regards to absorption predictions, and hence, the solubility-permeability interplay must be taken into account to strike the optimal solubility–permeability balance, in order to maximize the overall absorption.

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.

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