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Developing better formulations for oral lipophilic drugs by accounting for both the solubility and the intestinal permeability

Poor aqueous solubility is a major challenge in today's biopharmaceutics. While solubility-enabling formulations can significantly increase the apparent solubility of the drug, the concomitant effect on the drug's apparent permeability has been largely overlooked. The mathematical equation to describe the membrane permeability of a drug comprises the membrane/aqueous partition coefficient, which in turn is dependent on the drug's apparent solubility in the GI milieu, suggesting that the solubility and the permeability are closely related, exhibit a certain interplay between them, and treating the one irrespectively of the other may be insufficient. In this lecture, an overview of this solubility-permeability interplay will be provided, and the available data will be analyzed in the context of the effort to maximize the overall drug exposure. Overall, depending on the type of solubility-permeability interplay, the permeability may decrease, remain unchanged, and even increase, in a way that may critically affect the formulation capability to improve the overall absorption. Therefore, an intelligent design of solubility-enabling formulation needs to consider both the solubility afforded by the formulation and the permeability in the new luminal environment resulting from the formulation.

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, USA. He received his PhD (2007) from the Hebrew University of Jerusalem. From 2007 until 2009, he was a Post-Doctoral Research Fellow at the University of Michigan College of Pharmacy with Professor Gordon Amidon. His research interest is the integration of up-to-date molecular and cellular mechanistic investigations of drug disposition in the context of the human body, in order to enable successful drug delivery and therapy. In implementing this molecular biopharmaceutical approach to ADME research, he is seeking to enable mechanistic-based successful solutions to drug delivery, especially (but not only) oral, in challenging scenarios e.g. low-solubility, low-permeability, efflux transport, extensive metabolism, poor site targeting, various pathophysiological conditions (e.g. obesity, inflammatory bowel disease), and pediatrics patient care. He has authored over 70 top-notch journal papers, and contributed chapters to 7 books.

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