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Virtual assessment to provide insights into drug-excipient-intestinal fluid interactions and support virtual formulation design

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This presentation will focus on oral drug delivery of compounds in the small –to - intermediate sized space (drug-like and beyond-rule-of-5 space). A majority of the discovered drug candidates are problematic to deliver to the site of action. In the small molecular space (Mw<500 Da) a large fraction is poorly soluble in water and compounds having aqueous solubility less than that of marble are not uncommon. In the new modality space the delivery problem is related to poor permeability across cell membranes. For both categories, extensive formulation efforts are demanded to bring them into the clinic. The molecular reasons behind the poor solubility (typically simplified into solid-state effects versus solvation effects) may guide the selection of suitable formulation strategies, whereas size, polarity and hydrogen bond patterns are crucial determinants for poor permeability. In this talk I will focus on describing how methods commonly used in computational chemistry and computational (cell) biology (*e.g.* Multivariate Data Analysis, Molecular Dynamics simulations and Computational Fluid Dynamics) are useful tools for prediction of formulation strategies and formulation performance of poorly solubles and poorly permeables. These computational tools also enable us to better understand molecular interactions taking place during release, dissolution and permeation. I will provide examples on how these techniques now can be used to guide which formulation strategy to select, but also how they can be used to evaluate formulation performance and in vivo processing of enabling formulations. These tools enable computational pharmaceutics and can be used to educate and train computational formulators making use of a similar tool box as the computational chemists.