Mathematical modeling in pharmacokinetics: a modular, physiological-based approach

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Pharmacokinetic studies have turned into the focus of pharmaceutical companies, after studies manifested that the major reason for attrition is due to poor pharmacokinetics [1]. As a consequence, considerable effort has been put on the development of in silico models to predict and understand the pharmacokinetics of new compounds, in particular in early drug discovery. Meanwhile, considerable progress has been made with the use of physiologically based pharmacokinetic models such that nowadays modeling and simulation is possible prior to any in vivo experiments, solely based on in vitro data [2].

Physiologically based pharmacokinetic modeling approaches offer the advantage of incorporating experimental animal data as well as in vitro and in silico derived data into a coherent framework, from which meaningful and reliable assessments can be made. Many data on physicochemical properties and specific absorption, distribution, metabolism, excretion (ADME) processes are already available at early stages of the drug discovery process. Along the drug discovery process more refined and detailed data are generated, based on which more accurate predictions and analysis can be made.

In the talk, we present the concepts of a hierarchical, modular and physiologically-based approach supporting in silico modeling and simulation in pharmacokinetics/dynamics that is especially tailored to serve the needs in drug discovery. The approach is illustrated in application to the pharmacokinetics of a first-generation sulfonylurea. The different models have been realized in the virtual lab MEDICI-PK [3], a joint cooperation with Computing in Technology (CiT), Rastede/Germany.

References:

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