Physiologically Based Pharmacokinetic Modeling of Metformin and Prediction of Pharmacokinetics in Geriatric Population

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Objectives: Developing and validating geriatric PBPK models shall enrich our knowledge about their limitations and lead to a better use of the generated data. This study was conducted to investigate how PBPK models describe the pharmacokinetics of metformin in geriatric population.

Methods: A first-order absorption/PBPK model for metformin was built in the Simcyp simulator version 14 release 1 (Certara USA, Inc., Princeton, USA). Full PBPK model was constructed for metformin based on physicochemical properties and clinical observations. The model was refined and validated across several different dose levels using clinical plasma concentration data obtained in healthy adults aged 20-45 years following single oral administrations of metformin. Following appropriate optimization of the metformin PBPK model, geriatric (65-85 years) pharmacokinetics was predicted using Simcyp geriatric module. The predicted $T_{max}$, $C_{max}$, AUC, and CL/F values were within 1.5-fold of the observed data of metformin.

Results: The metformin pharmacokinetic profiles obtained from PBPK model were comparable to the observed clinical plasma concentration data for healthy adults aged 20–45 years. Geriatric PBPK model reasonably predicted the CL/F of metformin in elderly population. The predicted $T_{max}$, $C_{max}$, AUC, and CL/F values were within 1.5-fold of the observed data of metformin.

Conclusions: The geriatric PBPK model of metformin adequately characterized the pharmacokinetics of metformin in elderly population. PBPK modeling and simulation might be used as a powerful tool to guide geriatric clinical trial design.