Physiologically-based pharmacokinetics modelling of Semaglutide in children and adolescents with healthy and obese body weights

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Abstract

Aim: Develop PBPK models of semaglutide to estimate the pharmacokinetic profile for subcutaneous (SC) injections in children and adolescents with healthy and obese body weights. Methods: Pharmacokinetic modeling and simulations of semaglutide SC injections were performed using the Transdermal Compartmental Absorption & Transit (TCAT) model implemented in GastroPlus v.9.5 modules. A PBPK model of semaglutide was developed and verified in the adult population, by comparing the simulated plasma exposure with the observed data, and further scaled to the pediatric populations with normal and obese body weight. Results: The Semaglutide PBPK model was successfully developed in adults and scaled to the pediatric population. Our P-PBPK simulations indicated a significant increase in Cmax values for the 10-14 years pediatric population with healthy body weights, which was higher than the observed values in adults at the reference dose. Since gastrointestinal adverse events are related to increased semaglutide exposure, peak concentrations outside the target range may represent a safety risk for this pediatric age group. Besides, PBPK models indicated that body weight was inversely related to semaglutide exposure in children and adolescents, which is in line with the results observed in population pharmacokinetic studies in adults. Conclusion: Due to the absence of semaglutide pharmacokinetic data for the pediatric population, these PBPK models will aid in the development of dosing regimens and sampling times. Thus, increasing the efficiency of future pediatric clinical trial studies which can be replaced or improved by PBPK models.

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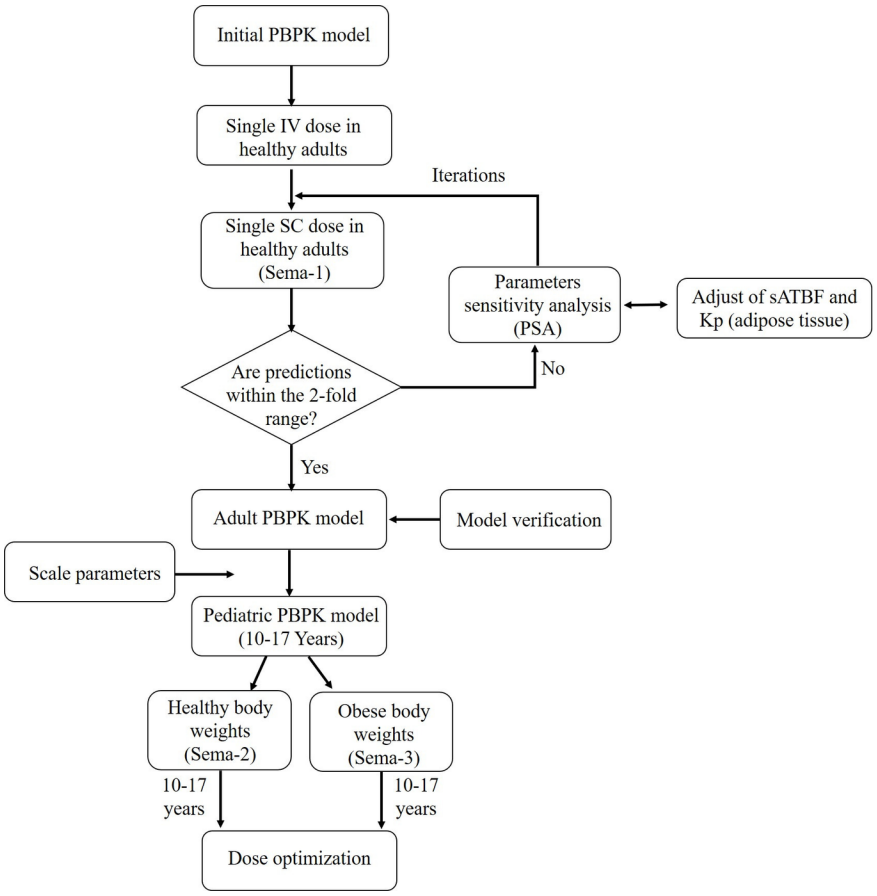

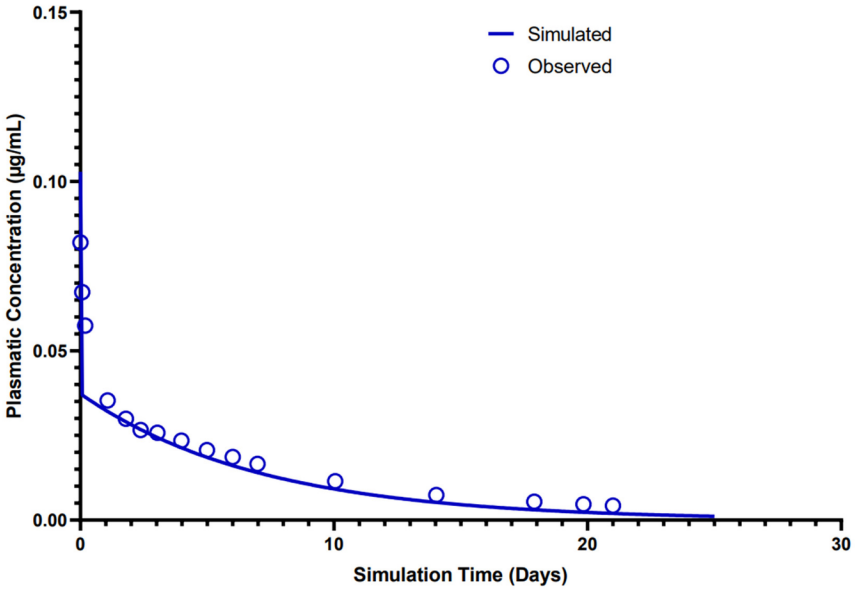

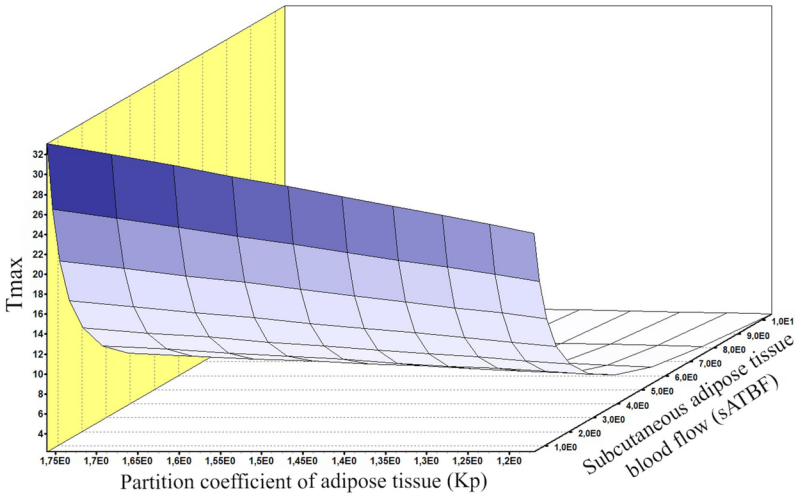

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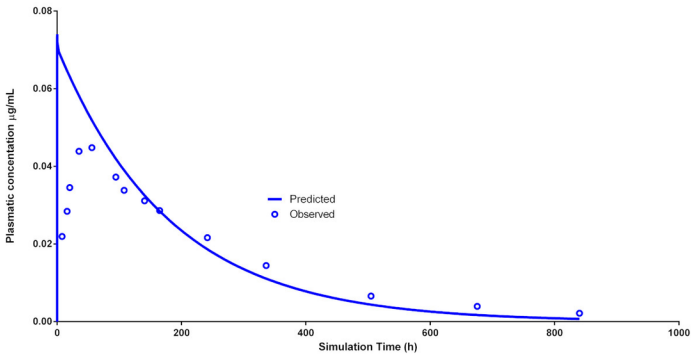

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