

# The Effect of Liver and Kidney Disease on the Pharmacokinetics of Clozapine and Sildenafil: A Physiologically Based Pharmacokinetic Modeling

Suzan Mansour ,Amira M Ghoneim

## Abstract

Background and Objectives: Physiologically based pharmacokinetic (PBPK) modeling permits clinical scientists to reduce practical constraints for clinical trials on patients with special diseases. In this study, simulations were carried out to validate the pharmacokinetic parameters of clozapine and sildenafil. Also, the effect of age on pharmacokinetic parameters of both drugs was investigated in healthy population and in patients with renal and hepatic impairment. Methods: A full PBPK model was built in the simulator for clozapine and sildenafil based on physicochemical properties and observed clinical results. The model used was Advanced, Dissolution, Absorption and Metabolism (ADAM) for both drugs. Results: The PBPK model adequately predicted the pharmacokinetic parameters of clozapine and sildenafil for the healthy adult population. In the simulation results, the bioavailability of both drugs was remarkably raised in both renal and hepatic impairment in young and elderly populations. Conclusion: PBPK modeling could be helpful in the investigation and comparison of the pharmacokinetics in populations with specific disease conditions. Keywords: physiologically based pharmacokinetic, clozapine, sildenafil, liver, kidney, impairment

*Drug Design, Development and Therapy* 2020, April