Identification of Dominant Parameters in a Drug Absorption Model Using Sensitivity Analysis

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We are investigating a model of drug absorption in human gastrointestinal (GI) tract affected by P-Glycoprotein (Pgp) efflux using two mathematical methods of sensitivity analysis. As first method, the automatic differentiation (AD) technique was used to identify important parameters for further investigation by the second method. In the second method, selected parameters values were taken randomly from plausible values enclosed in specified ranges; average absolute integral of local sensitivity i.e. global sensitivity – was calculated for each parameter. By comparing global sensitivity of each parameter with the average of global sensitivities, we identified 6 (out of 14) most influential parameters for a drug (Imatinib Mesylate) of high dissolution rate and solubility. Excretion rate of drug from body, volume of drug distribution, rate constants of drug from plasma to tissues and vice versa, passive permeability of GI tract cells membrane, surface to volume ratio of GI tract are respectively dominant parameters compared to those related to drug efflux by Pgp and drug metabolism in the cells.