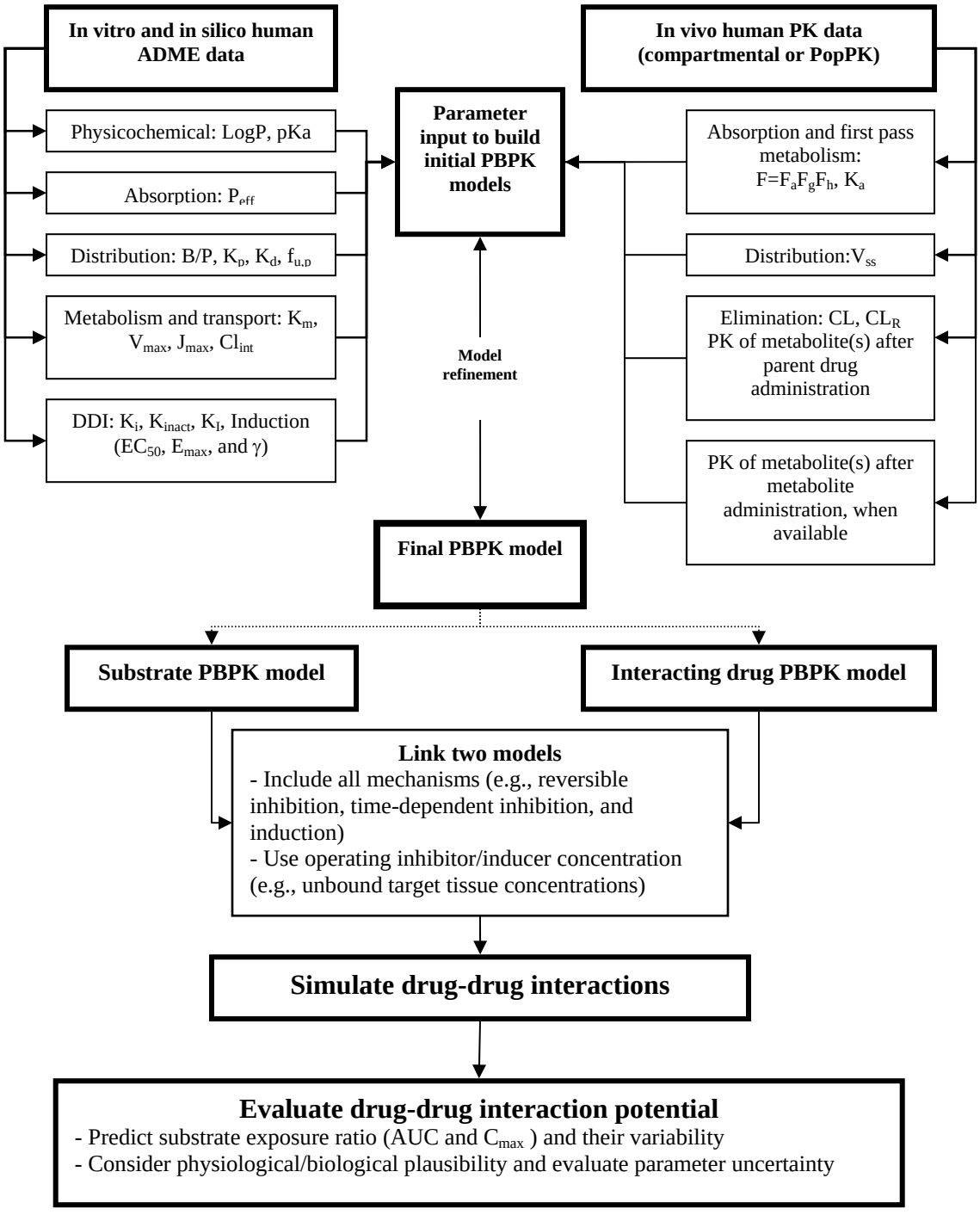
Figure 4. **Using a PBPK Model to Explore Drug-Drug Interaction Potential Between a Substrate Drug and an Interacting Drug (Modified from Zhao et al, *Clin Pharmacol Ther*. 89(2):259-267, 2011).**



Abbreviations: ADME, absorption, distribution, metabolism and excretion; AUC, area under the plasma concentration versus time curve; B/P, blood to plasma ratio; C_{max}, maximum concentration; CL, clearance; CL_r, renal clearance; DDI, drug-drug interactions; EC_{50} or IC_{50}, concentration causing half maximal effect or inhibition; E_{max} or I_{max}, maximum effect or inhibition; F, bioavailability; F_a, fraction absorbed; F_g, bioavailability in the gut; F_h, bioavailability in the liver; $f_{u,p}$, unbound fraction in plasma; γ, Hill coefficient; J_{max}, maximum rate of transporter-mediated efflux/uptake; K_a, first-order absorption rate constant; K_d, dissociation constant of drug-protein complex; K_i, reversible inhibition constant, concentration causing half maximal inhibition; K_I, apparent inactivation constant, concentration causing half maximum inactivation; k_{inact}, apparent maximum inactivation rate constant; K_m, Michaelis-Menten constant, substrate concentration causing half maximal reaction or transport; K_p, tissue-to-plasma partition coefficient; LogP, Logarithm of the octanol-water partition coefficient; P_{eff}, jejunum permeability; PK, pharmacokinetics; PopPK, population pharmacokinetics; V, volume of distribution; V_{max}, maximum rate of metabolite formation.