



Figure S3 Predicted and observed AUC and Cmax ratios of talinolol and quinidine with various dosing regimens of rifampicin.

Closed circles represent observed AUCRs (a and b) and CmaxRs (c and d) of talinolol (a and c) and quinidine (b and d) shown as mean (\pm SD). For talinolol, predicted AUCRs and CmaxRs are shown as mean in symbols of different shapes (squares, diamonds, and triangles for the hepatic β values of 0.2, 0.5, and 0.8, respectively). The closed black squares, diamonds, and triangles of talinolol represent the predicted AUCRs and CmaxRs by incorporating P-gp induction and inhibition effects of rifampicin in the intestine, liver, and kidney. For quinidine, predicted AUCRs and CmaxRs are shown as mean in either closed or open squares. The closed black squares of quinidine represent the predicted AUCRs and CmaxRs by incorporating rifampicin effects for (i) P-gp induction and inhibition in the intestine and kidney, and (ii) CYP3A induction in the intestine and liver. For talinolol and quinidine, the magnitude of P-gp- and/or CYP3A-mediated DDIs in each tissue were estimated. Specifically, predicted DDIs by not considering the intestinal, hepatic, or renal P-gp-mediated DDIs are shown in open orange, red, or gray symbols, respectively. Also, predicted DDIs by not considering the intestinal or hepatic CYP3A induction are shown in open blue or green symbols, respectively. Dosing regimens of talinolol, quinidine, and rifampicin are indicated at the bottom. AUCR, area under the plasma/blood concentration-time curve ratio; CmaxR, maximum plasma/blood concentration ratio; CYP, cytochrome P450; IV, intravenous infusion dose; PO, oral dose; QD, once daily; QUI, quinidine; RIF, rifampicin; TAL, talinolol.