Supplemental Figures

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Effects of β-blockers and tricyclic antidepressants on the activity of human organic anion transporting polypeptide 1A2 (OATP1A2)

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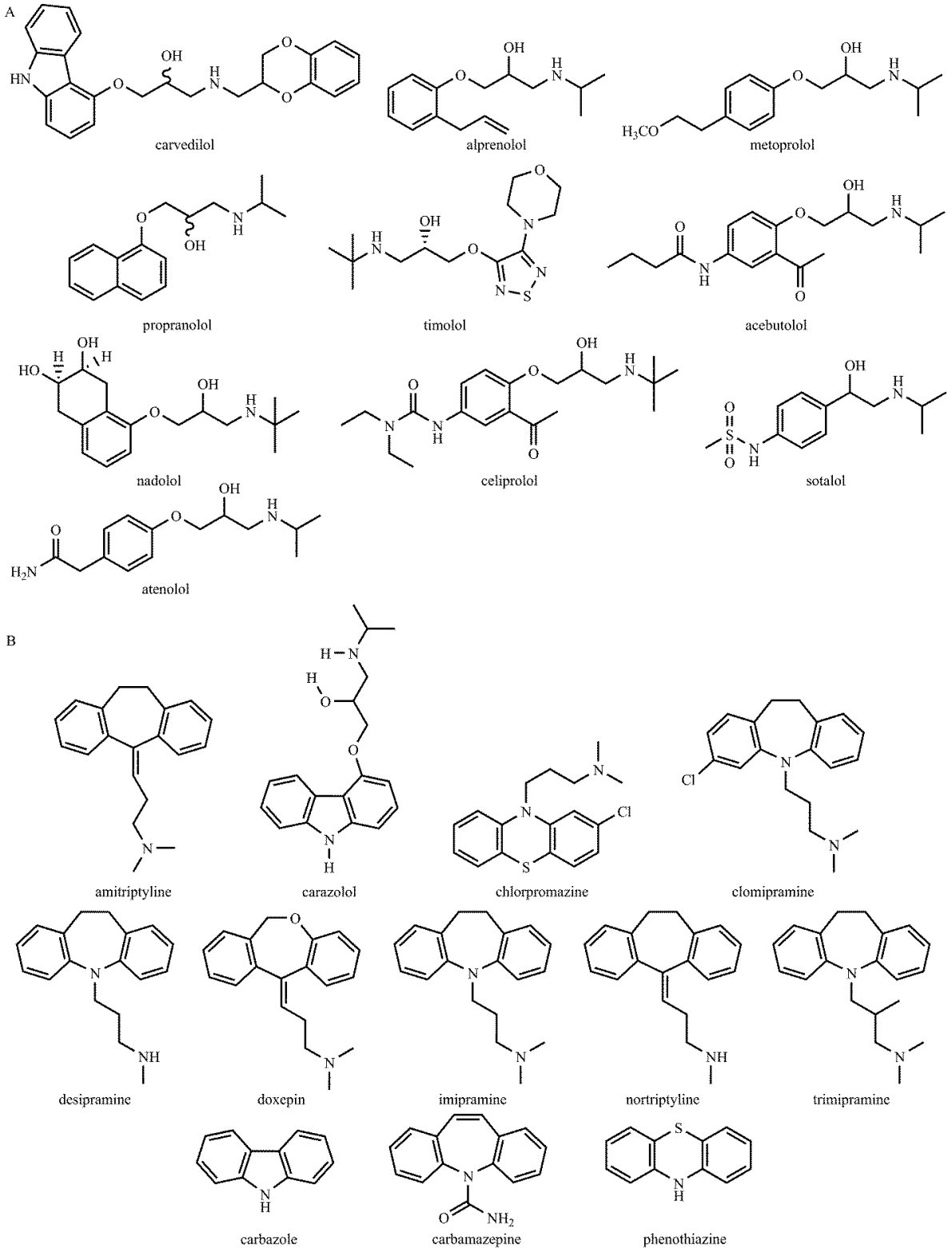
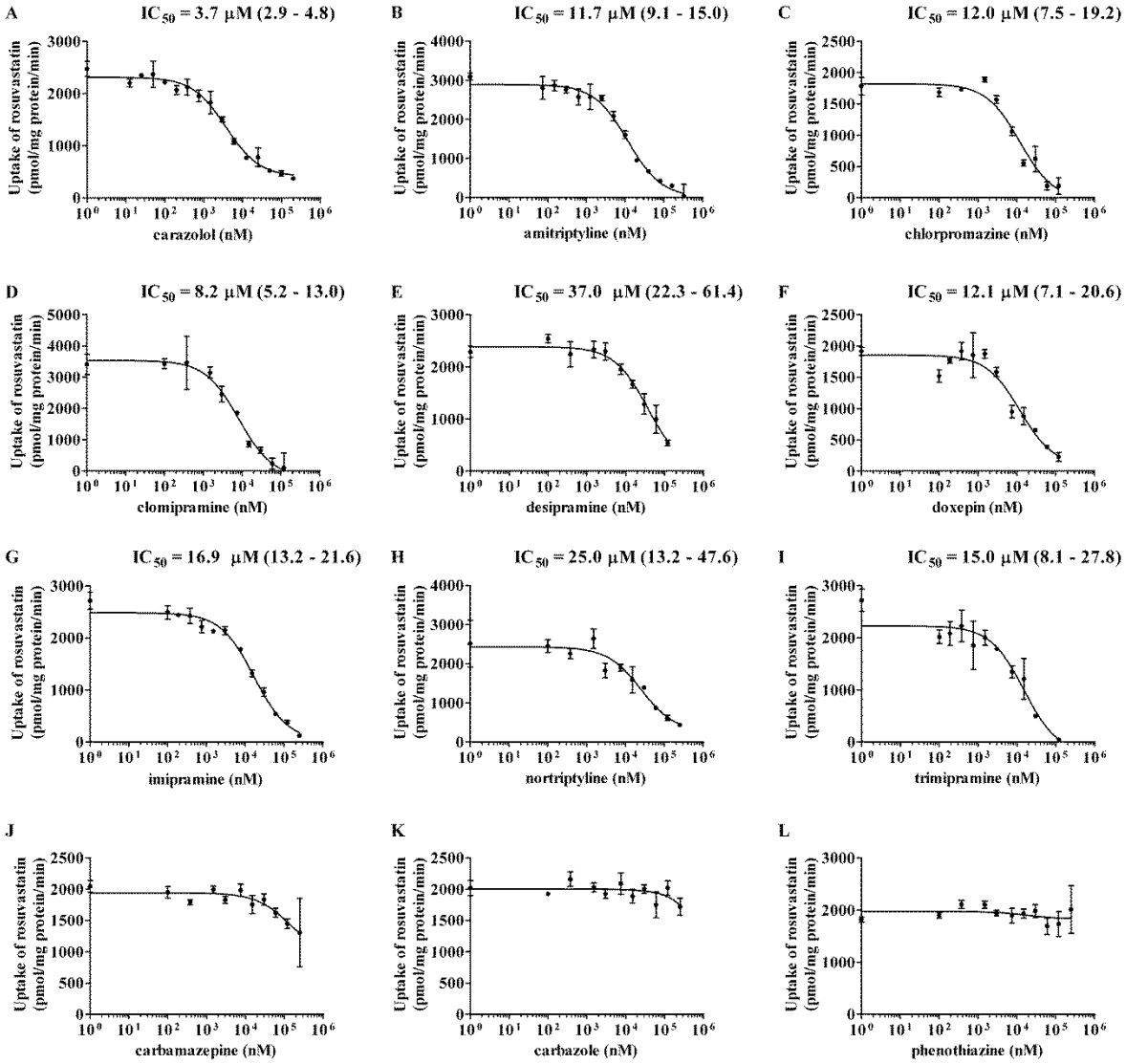
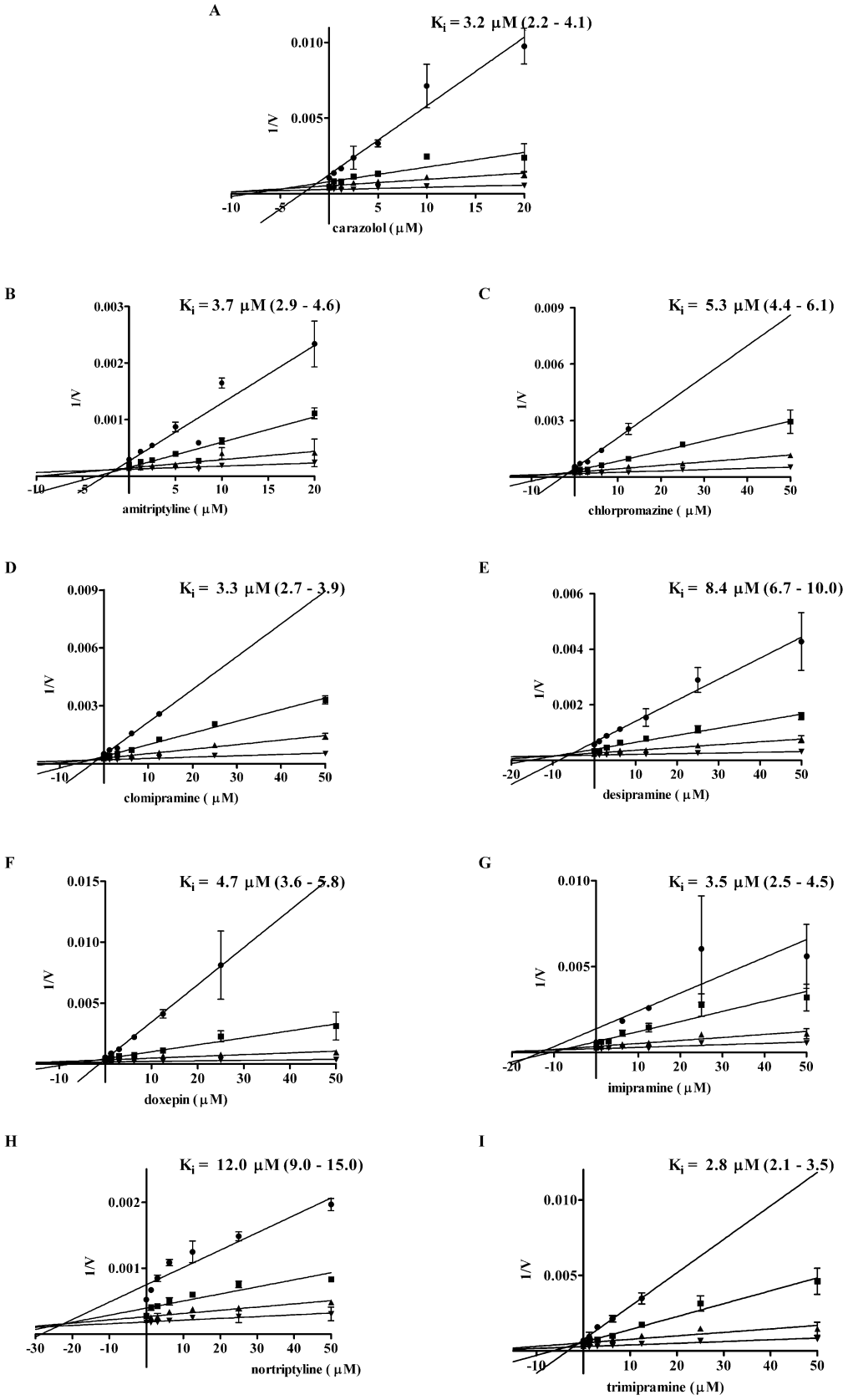


Supplemental Figure 1. Structures of (A) different β-blockers tested and (B) different tricyclic compounds tested.



Supplemental Figure 2. Inhibition of OATP1A2-mediated transport of rosuvastatin by different tricyclic compounds. HEK293-OATP1A2 and HEK293-VC cells were coincubated with rosuvastatin (150 µM) and different tricyclic compounds (12.5 nM – 250 µM) for 2 min at 37°C. The quantity of intracellular rosuvastatin was normalized to protein content. To obtain the net transport, values measured in the VC cells were subtracted from the values measured in OATP1A2-expressed cells. IC_{50} values were calculated by fitting the data to the log(inhibitor)

vs. response equation in GraphPad Prism. (A) carazolol; (B) amitriptyline; (C) chlorpromazine; (D) clomipramine; (E) desipramine; (F) doxepin; (G) imipramine; (H) nortriptyline; (I) trimipramine; (J) carbamazepine; (K) carbazole; and (L) phenothiazine. Each point represents the mean ± S.D. of triplicate from a single experiment. The values in parentheses represent the 95% confidence interval.


A
K_i = 3.2 μM (2.2 - 4.1)
1/V
carazolol (μM)
B
K_i = 3.7 μM (2.9 - 4.6)
amitriptyline (μM)
C
K_i = 5.3 μM (4.4 - 6.1)
chlorpromazine (μM)
D
K_i = 3.3 μM (2.7 - 3.9)
clomipramine (μM)
E
K_i = 8.4 μM (6.7 - 10.0)
desipramine (μM)
F
K_i = 4.7 μM (3.6 - 5.8)
doxepin (μM)
G
K_i = 3.5 μM (2.5 - 4.5)
imipramine (μM)
H
K_i = 12.0 μM (9.0 - 15.0)
nortriptyline (μM)
I
K_i = 2.8 μM (2.1 - 3.5)
trimipramine (μM)

Supplemental Figure 3. Dixon plots of inhibition of OATP1A2-mediated transport of rosuvastatin by different tricyclic compounds. HEK293-OATP1A2 and HEK293-VC cells were coincubated with rosuvastatin (25, 50, 100, 250 µM) and different tricyclic drugs (0.5 – 50 µM) for 2 min at 37°C. The quantity of intracellular rosuvastatin was normalized to protein content. To obtain the net transport, values measured in the VC cells were subtracted from the values measured in OATP1A2-expressed cells. The x-axis represents the concentration of the inhibitor and the y-axis represents the reciprocal velocity (1/V). Linear regression was used to fit each set of data and the intercept of all lines represents the - K_i. The K_i was accurately calculated in GraphPad Prism. (●) 25 µM rosuvastatin; (■) 50 µM rosuvastatin; (▲) 100 µM rosuvastatin; (▼) 250 µM rosuvastatin. (A) carazolol; (B) amitriptyline; (C) chlorpromazine; (D) clomipramine; (E) desipramine; (F) doxepin; (G) imipramine; (H) nortriptyline; and (I) trimipramine. The values in parentheses represent the 95% confidence interval.