[Title] Impact of P-glycoprotein-mediated active efflux on drug distribution into lumbar cerebrospinal fluid in nonhuman primates

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Supplemental Table 1. Efflux ratio and % of control in in vitro P-gp inhibition study

The efflux ratio (ER) was calculated for desloratadine and quinidine from the ratio of the apparent permeability (P_{app}) in basal-to-apical direction ($P_{app,B-A}$) to that in apical-to-basal direction ($P_{aap,A-B}$) in the P-gp-expressing cells (ER_{P-gp}) and control cells (ER_{Ctrl}). The percentage of control values for P-gp-mediated transcellular transport ($ER_{P-gp} – ER_{Ctrl}$) of desloratadine and quinidine in the presence of zosuquidar were calculated from the ER values as described in Materials and Methods.

(A) Desloratadine

Zosuquidar (μmol/L)	P-gp-expressing LLC-PK1 cells			Control LLC-PK1 cells			ER_{P-gp}-ER_{Ctrl}	% of control
	$P_{app,A-B}$	$P_{app,B-A}$	ER_{P-gp}	$P_{app,A-B}$	$P_{app,B-A}$	ER_{Ctrol}		
	($\times 10^{-6}$ cm/sec)	*($\times 10^{-6}$ cm/sec)*		*($\times 10^{-6}$ cm/sec)*	*($\times 10^{-6}$ cm/sec)*			
0	2.44 ± 0.01	31.65 ± 0.80	12.97 ± 0.33	10.97 ± 0.40	11.75 ± 0.27	1.07 ± 0.05	11.90 ± 0.39	100.0 ± 4.3
0.0001	2.65 ±0.15	29.12 ± 0.96	10.99 ± 0.71	10.20 ± 0.91	10.66 ± 0.51	1.05 ± 0.11	9.94 ± 0.91	83.5 ± 8.5
0.001	3.03 ± 0.15	28.47 ± 1.04	9.40 ± 0.59	10.65 ± 0.88	10.66 ± 0.52	1.00 ± 0.10	8.40 ± 0.87	70.6 ± 6.8
0.003	4.60 ± 0.58	27.89 ± 0.47	6.06 ± 0.77	12.52 ± 0.38	10.99 ± 0.38	0.88 ± 0.04	5.18 ± 0.38	43.5 ± 2.0
0.01	6.62 ± 0.39	25.52 ± 0.51	3.85 ± 0.24	11.36 ± 0.29	10.41 ± 0.22	0.92 ± 0.03	2.93 ± 0.29	24.6 ± 0.8
0.03	9.99 ± 0.83	18.04 ± 0.38	1.81 ± 0.15	11.15 ± 0.86	10.10 ± 0.59	0.91 ± 0.09	0.90 ± 0.85	7.6 ± 0.7
0.1	12.42 ± 0.57	13.65 ± 0.40	1.10 ± 0.06	11.89 ± 1.11	9.63 ± 0.07	0.81 ± 0.08	0.29 ± 1.11	2.4 ± 0.2
1	16.63 ± 1.50	15.59 ± 0.52	0.94 ± 0.09	12.76 ± 1.13	13.15 ± 0.54	1.03 ± 0.10	–0.09 ± 1.13	–0.8 ± 0.1[a]

a: Handled as zero when estimating the IC_{50} value by least-squares nonlinear regression analysis.

(B) Quinidine

Zosuquidar (μmol/L)	P-gp-expressing LLC-PK1 cells			Control LLC-PK1 cells			$ER_{P\text{-}gp}$-ER_{Ctrl}	% of control
	$P_{app,A\text{-}B}$	$P_{app,B\text{-}A}$	$ER_{P\text{-}gp}$	$P_{app,A\text{-}B}$	$P_{app,B\text{-}A}$	ER_{Ctrol}		
	(×10^{-6} cm/sec)	*(×10^{-6} cm/sec)*		*(×10^{-6} cm/sec)*	*(×10^{-6} cm/sec)*			
0	2.70 ± 0.60	39.52 ± 3.26	14.64 ± 3.26	15.86 ± 0.46	18.05 ± 0.54	1.14 ± 0.05	13.50 ± 0.6	100.0 ± 4.2
0.0001	1.88 ± 0.24	38.04 ± 2.59	20.23 ± 2.59	14.07 ± 1.35	16.91 ± 0.27	1.20 ± 0.12	19.03 ± 1.35	141.0 ± 13.8
0.001	2.18 ± 0.26	36.49 ± 2.01	16.74 ± 2.01	14.92 ± 0.80	16.80 ± 0.14	1.13 ± 0.06	15.61 ± 0.80	115.6 ± 6.3
0.003	2.98 ± 0.32	37.31 ± 1.36	12.52 ± 1.36	17.73 ± 0.75	17.67 ± 0.23	1.00 ± 0.04	11.52 ± 0.75	85.3 ± 3.8
0.01	4.25 ± 0.30	36.98 ± 0.63	8.70 ± 0.63	15.83 ± 0.28	16.39 ± 0.45	1.04 ± 0.03	7.66 ± 0.28	56.7 ± 1.9
0.03	8.23 ± 0.64	31.23 ± 0.30	3.79 ± 0.30	15.87 ± 0.25	16.07 ± 0.56	1.01 ± 0.04	2.78 ± 0.25	20.6 ± 0.8
0.1	16.96 ± 0.44	22.50 ± 0.04	1.33 ± 0.04	16.70 ± 0.45	15.81 ± 0.27	0.95 ± 0.03	0.38 ± 0.45	2.8 ± 0.1
1	23.38 ± 0.30	21.29 ± 0.03	0.91 ± 0.03	19.26 ±0.63	18.39 ± 0.23	0.95 ± 0.03	–0.04 ± 0.63	–0.3 ± 0.0[a]

a: Handled as zero when estimating the IC_{50} value by least-squares nonlinear regression analysis.