

# Molecular mechanisms governing different pharmacokinetics of ginsenosides and potential for ginsenoside-perpetrated herb-drug interactions on OATP1B3

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## - Supporting Information Appendix S5 - Rat tissue distribution of ginsenosides

**Table 1**

Tissue distribution of ginsenosides after i.v. administration at 2.5  $\mu\text{mol}\cdot\text{kg}^{-1}$  in rats treated with and without rifampin at 20  $\text{mg}\cdot\text{kg}^{-1}$

Parameters	Ppt-type						Ppd-type		
	Ginsenoside Rg <sub>1</sub>		Ginsenoside Re		Notoginsenoside R <sub>1</sub>		Ginsenoside Rb <sub>1</sub>	Ginsenoside Rc	Ginsenoside Rd
	(-) Rif	(+) Rif	(-) Rif	(+) Rif	(-) Rif	(+) Rif	(-) Rif	(-) Rif	(-) Rif
<b>Plasma data</b>									
C <sub>5min</sub> ( $\mu\text{M}$ )	6.30 $\pm$ 0.80	10.7 $\pm$ 1.4*	4.38 $\pm$ 0.48	5.28 $\pm$ 0.30*	6.33 $\pm$ 1.21	8.27 $\pm$ 0.44*	64.8 $\pm$ 6.8	57.0 $\pm$ 1.8	29.0 $\pm$ 1.2
AUC <sub>0-t</sub> (h· $\mu\text{M}$ )	1.29 $\pm$ 0.20	3.65 $\pm$ 0.32*	0.938 $\pm$ 0.210	2.79 $\pm$ 0.17*	2.85 $\pm$ 0.34	4.40 $\pm$ 0.42*	237 $\pm$ 58	221 $\pm$ 4	92.3 $\pm$ 5.9
AUC <sub>0-∞</sub> (h· $\mu\text{M}$ )	1.30 $\pm$ 0.21	3.66 $\pm$ 0.33*	0.942 $\pm$ 0.212	2.80 $\pm$ 0.17*	2.86 $\pm$ 0.34	4.41 $\pm$ 0.43*	590 $\pm$ 215	517 $\pm$ 32	136 $\pm$ 14
t <sub>1/2</sub> (h)	0.121 $\pm$ 0.027	0.412 $\pm$ 0.094*	0.273 $\pm$ 0.154	0.549 $\pm$ 0.031*	0.483 $\pm$ 0.015	0.820 $\pm$ 0.251*	9.00 $\pm$ 4.38	10.3 $\pm$ 0.5	4.88 $\pm$ 0.47
MRT (h)	0.178 $\pm$ 0.040	0.469 $\pm$ 0.112*	0.198 $\pm$ 0.086	0.562 $\pm$ 0.043*	0.455 $\pm$ 0.097	0.686 $\pm$ 0.169*	12.9 $\pm$ 6.2	14.6 $\pm$ 0.8	6.94 $\pm$ 0.71
<b>Heart data</b>									
C <sub>5(15)min</sub> ( $\mu\text{M}$ )	1.02 $\pm$ 0.15	1.24 $\pm$ 0.04	0.723 $\pm$ 0.103	0.667 $\pm$ 0.103	0.824 $\pm$ 0.199	1.32 $\pm$ 0.11*	5.11 $\pm$ 0.47	3.99 $\pm$ 0.37	2.42 $\pm$ 0.36
AUC <sub>0-t</sub> (h· $\mu\text{M}$ )	0.361 $\pm$ 0.019	0.572 $\pm$ 0.143	0.147 $\pm$ 0.010	0.389 $\pm$ 0.029*	0.352 $\pm$ 0.026	0.581 $\pm$ 0.112*	23.6 $\pm$ 2.6	19.0 $\pm$ 0.3	12.4 $\pm$ 0.8
AUC <sub>0-∞</sub> (h· $\mu\text{M}$ )	0.370 $\pm$ 0.013	0.611 $\pm$ 0.129*	0.167 $\pm$ 0.034	0.413 $\pm$ 0.036*	0.391 $\pm$ 0.008	0.670 $\pm$ 0.124*	48.1 $\pm$ 5.5	33.4 $\pm$ 2.9	27.6 $\pm$ 4.9
t <sub>1/2</sub> (h)	0.172 $\pm$ 0.081	0.361 $\pm$ 0.067*	0.172 $\pm$ 0.040	1.017 $\pm$ 0.101*	0.298 $\pm$ 0.064	0.312 $\pm$ 0.119	8.00 $\pm$ 0.90	6.67 $\pm$ 0.80	9.23 $\pm$ 1.48
MRT (h)	0.251 $\pm$ 0.103	0.481 $\pm$ 0.052*	0.216 $\pm$ 0.033	1.112 $\pm$ 0.193*	0.427 $\pm$ 0.094	0.452 $\pm$ 0.183	11.7 $\pm$ 1.1	9.55 $\pm$ 1.09	13.3 $\pm$ 2.1

<b>Liver data</b>									
C <sub>5(15)min</sub> (µM)	8.44 ± 1.40	1.51 ± 0.27*	4.28 ± 0.28	1.12 ± 0.10*	7.38 ± 1.02	1.32 ± 0.09*	5.43 ± 0.46	4.53 ± 0.31	3.48 ± 0.33
AUC <sub>0-t</sub> (h·µM)	2.03 ± 0.15	0.660 ± 0.021*	1.77 ± 0.09	0.675 ± 0.105*	2.60 ± 0.30	0.797 ± 0.062*	24.1 ± 2.1	20.9 ± 1.5	17.2 ± 0.8
AUC <sub>0-∞</sub> (h·µM)	2.08 ± 0.15	0.781 ± 0.039*	1.86 ± 0.08	0.742 ± 0.121*	2.91 ± 0.37	1.10 ± 0.11*	62.6 ± 12.6	70.6 ± 22.2	42.6 ± 13.4
t <sub>1/2</sub> (h)	0.182 ± 0.013	0.339 ± 0.028*	0.225 ± 0.016	0.593 ± 0.057*	0.431 ± 0.213	0.533 ± 0.068	11.9 ± 3.1	16.4 ± 8.0	10.8 ± 5.5
MRT (h)	0.251 ± 0.020	0.491 ± 0.052*	0.325 ± 0.023	0.861 ± 0.089*	0.532 ± 0.195	0.770 ± 0.101	17.1 ± 4.4	23.6 ± 11.4	15.6 ± 7.8
<b>Kidney data</b>									
C <sub>5(15)min</sub> (µM)	7.62 ± 0.32	9.32 ± 0.35*	9.58 ± 1.89	17.0 ± 1.3*	14.6 ± 2.2	23.1 ± 6.1	6.17 ± 0.22	4.88 ± 1.15	4.08 ± 0.48
AUC <sub>0-t</sub> (h·µM)	6.94 ± 0.24	13.2 ± 1.5*	4.98 ± 0.47	14.0 ± 1.4*	13.6 ± 2.0	21.9 ± 2.6*	24.4 ± 2.9	24.2 ± 0.5	16.9 ± 4.1
AUC <sub>0-∞</sub> (h·µM)	10.4 ± 2.3	21.8 ± 3.2*	6.81 ± 1.19	17.7 ± 0.7*	17.2 ± 4.1	26.7 ± 3.2*	69.5 ± 11.3	105 ± 24	39.6 ± 10.6
t <sub>1/2</sub> (h)	5.69 ± 3.41	4.67 ± 3.05	7.14 ± 2.55	4.19 ± 0.53	5.80 ± 2.14	3.69 ± 0.22	16.6 ± 7.8	20.9 ± 5.4	8.14 ± 3.12
MRT (h)	7.01 ± 4.25	6.41 ± 3.16	7.86 ± 3.32	4.69 ± 0.92	6.31 ± 1.91	4.34 ± 0.26	19.3 ± 6.3	30.2 ± 7.7	11.8 ± 4.4
<b>Lung data</b>									
C <sub>5(15)min</sub> (µM)	1.67 ± 0.31	1.92 ± 0.16	1.64 ± 0.53	1.92 ± 0.30	2.01 ± 0.54	2.87 ± 0.15	5.21 ± 0.24	4.57 ± 0.49	3.53 ± 0.44
AUC <sub>0-t</sub> (h·µM)	0.701 ± 0.020	1.12 ± 0.07*	0.417 ± 0.106	1.056 ± 0.268*	1.20 ± 0.24*	1.74 ± 0.14*	30.4 ± 1.8	25.8 ± 0.3	17.5 ± 0.5
AUC <sub>0-∞</sub> (h·µM)	0.712 ± 0.019	1.12 ± 0.07*	0.433 ± 0.105	1.11 ± 0.24*	1.24 ± 0.25*	1.78 ± 0.14*	136 ± 57	81.2 ± 15.3	40.9 ± 10.5
t <sub>1/2</sub> (h)	2.11 ± 0.63	1.09 ± 0.18*	0.386 ± 0.296	0.618 ± 0.274	0.769 ± 0.061	0.763 ± 0.063	21.7 ± 9.7	14.4 ± 3.5	9.90 ± 3.40
MRT (h)	0.897 ± 0.047	0.770 ± 0.061*	0.503 ± 0.397	0.749 ± 0.273	0.807 ± 0.158	0.869 ± 0.085	31.2 ± 14.0	20.9 ± 4.9	14.3 ± 4.8
<b>Brain data</b>									
C <sub>5(15)min</sub> (µM)	0.063 ± 0.017	0.081 ± 0.017*	0.050 ± 0.001	0.113 ± 0.067	0.05 ± 0.01	0.058 ± 0.005	0.345 ± 0.078	0.330 ± 0.014	0.303 ± 0.055
AUC <sub>0-t</sub> (h·µM)	0.025 ± 0.003	0.038 ± 0.010*	0.078 ± 0.012	0.126 ± 0.021*	0.08 ± 0.01	0.108 ± 0.014*	1.17 ± 0.11	1.30 ± 0.17	0.92 ± 0.32
AUC <sub>0-∞</sub> (h·µM)	0.028 ± 0.005	0.047 ± 0.010*	0.132 ± 0.011	0.189 ± 0.020*	0.15 ± 0.01	0.184 ± 0.011*	2.02 ± 0.37	2.47 ± 0.52	1.12 ± 0.55
t <sub>1/2</sub> (h)	0.299 ± 0.080	0.372 ± 0.151	3.007 ± 0.484	3.05 ± 2.79	3.90 ± 0.33	4.01 ± 2.18	6.00 ± 2.45	7.07 ± 1.54	2.95 ± 1.19
MRT (h)	0.430 ± 0.117	0.538 ± 0.223	4.422 ± 0.690	3.93 ± 3.35	5.61 ± 0.54	5.96 ± 3.66	9.10 ± 3.66	10.4 ± 2.47	4.37 ± 1.62

Three rats per group. (-) Rif, rats free of rifampin treatment. (+) Rif, rats treated with Rifampin. \*, P < 0.05.