Kitaguchi et al.:

In Vitro-Based Prediction of Human Plasma Concentrations of Food-Related Compounds

Supplementary Data

Tab. S1: *In vitro* experimental values used in this study

Compound	P_{app} Caco-2 cells (10^{-6} cm/s)	P_{app} hiPSC-SIECs (10^{-6} cm/s)	$CL_{h, int}$ HepaRG (mL/min/kg)	$P_{app, AtoB}$ LLC-PK1 (10^{-5} cm/min)	$P_{app, BtoA}$ LLC-PK1 (10^{-5} cm/min)	f_{up} RED device (%)
Daidzin (as daidzein)*	0.0574 ± 0.00854	0.0150	(22.3) *	(66.1 ± 1.79) *	(148 ± 20.8) *	(2.32 ± 0.324) *
Daidzein	36.8 ± 1.55	1.59	22.3	66.1 ± 1.79	148 ± 20.8	2.32 ± 0.324
Genistin (as genistein)*	0.0910 ± 0.0275	0.00925	(31.1) *	(94.8 ± 4.30) *	(113 ± 7.50) *	(0.503 ± 0.0942) *
Genistein	33.7 ± 1.02	2.68	31.1	94.8 ± 4.30	113 ± 7.50	0.503 ± 0.0942
Quercetin	9.49 ± 0.636	0.463	16.2	3.69 ± 1.85	75.1 ± 11.6	0.131 ± 0.0458
Gallic acid	0.235 ± 0.0470	0.409	0.179	37.1 ± 23.4	10.6 ± 0.527	64.1 ± 2.33
Caffeic acid	0.183 ± 0.0530	1.03	1.12	5.09 ± 1.77	16.0 ± 2.34	39.5 ± 3.24
Ferulic acid	24.6 ± 2.03	7.86	0.733	48.9 ± 2.64	46.9 ± 7.72	29.1 ± 3.20
Cyanidin 3-glucoside	0.0128 ± 0.00621	0.0985	0.979	10.6 ± 3.62	2.70 ± 1.14	17.6 ± 0.962
Curcumin	3.50 ± 0.805	0.0666	24.8	N.T.	N.T.	0.0821 ± 0.0520
Caffeine	32.9 ± 1.81	43.5	N.C.	248 ± 10.5	197 ± 21.8	100
Acrylamide	32.8 ± 0.834	23.3	0.168	256 ± 5.52	172 ± 27.2	100
Butylated hydroxyanisole	40.9 ± 2.45	41.6	6.25	264 ± 13.5	192 ± 30.8	3.82 ± 0.166
Butylated hydroxytoluene	1.71 ± 0.128	2.19	3.40	N.T.	N.T.	12.0 ± 3.61
Aflatoxin B1	31.7 ± 0.996	32.5	N.C.	182 ± 4.99	139 ± 7.88	12.7 ± 1.07
Ochratoxin A	4.94 ± 0.425	2.48	N.C.	10.1 ± 3.68	3.56 ± 0.669	0.00596 ± 0.00121
Bisphenol A	29.7 ± 2.23	4.29	70.0	206 ± 15.5	124 ± 19.5	3.16 ± 0.242
Bisphenol S	23.4 ± 0.742	5.85	3.76	121 ± 4.49	77.0 ± 11.6	5.78 ± 0.138
Chlorpyrifos	4.56 ± 2.05	1.77	26.4	36.5 ± 0.218	32.8 ± 6.80	0.0117 ± 0.00186
Picloram	2.98 ± 0.151	3.88	N.C.	22.2 ± 2.05	15.9 ± 1.50	5.96 ± 1.23

N.C., not calculated; N.T., not tested
*: These values represent aglycones (daidzein or genistein).

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Tab. S2: ***In silico*-predicted and *in vitro*-derived physiology-based kinetic parameters**

Compound	k_a (10^{-3} min^{-1})		k_e (10^{-3} min^{-1})		First pass (%)		V_d (L)		pKa		Log P	
	Percepta	*In vitro*	Percepta	*In vitro*	Percepta	*In vitro*	Percepta	*In vitro*	Percepta	Reported	Percepta	Reported
Daidzin (Daidzein)*	59	2.65	1.3	3.24	45	86.1	133	38.0	8.06	7.51	2.91	2.51
Daidzein	59	69.1	1.3	3.24	45	98.0	133	38.0	8.06	7.51	2.91	2.51
Genistin (Genistein)*	56	3.36	1.4	2.21	49	94.9	60.2	32.9	7.8	7.25	2.63	3.04
Genistein	56	66.1	1.4	2.21	49	96.1	60.2	32.9	7.8	7.25	2.63	3.04
Quercetin	26	35.0	6.2	0.488	0.1	97.5	32.9	18.2	7.67	8.45	1.95	1.82
Gallic acid	0.29	5.41	6.9	10.3	7	2.93	15.4	16.2	4.3	4.21	0.69	0.7
Caffeic acid	1.8	4.77	6.3	15.9	0.3	10.5	43.4	16.8	4.48	4.62	1.35	1.15
Ferulic acid	6.7	56.4	3.3	8.79	0.2	82.0	49.7	16.9	4.48	4.58	1.68	1.51
Cyanidin 3-glucoside	0.038	1.25	9.5	5.09	5	2.43	35.7	11.2	4.4	5.88	−1.35	N.R.
Curcumin	51	21.1	1.2	0.190	16	99.0	154	29.4	8.94	8.38	2.56	3.28
Caffeine	55	65.4	2.6	2.80	18	0	98.0	35.4	-	-	0.28	−0.07
Acrylamide	12	65.3	2.3	4.34	26	46.3	56.0	29.0	-	-	−0.67	−0.67
Butylated hydroxyanisole	63	72.9	1.4	1.10	45	3.81	574	55.5	10.1	N.R.	3.14	2.82
Butylated hydroxytoluene	57	16.7	1.4	2.21	58	27.0	5390	248	12.1	12.2	5.07	5.1
Aflatoxin B1	55	64.1	2.2	0.390	40	0	64.4	35.0	-	-	1.08	1.25
Ochratoxin A	33	25.2	3.8	0.00110	10	66.6	16.1	11.7	3.13	4.3	4.42	4.74
Bisphenol A	59	62.0	1.2	8.85	50	94.5	560	68.3	9.7	9.87	3.63	3.32
Bisphenol S	55	55.1	1.9	2.63	33	86.6	62.3	38.0	7.7	7.02	1.81	2.36
Chlorpyrifos	56	24.1	1.2	0.0773	46	76.0	1680	42.6	-	-	4.78	4.96
Picloram	4.3	19.4	2.5	1.38	15	0	23.8	9.41	2.28	2.3	2.59	1.9

N.R., not reported; *, These values represent aglycones (daidzein or genistein).

Tab. S3: The C_{max} values of 20 food-related compounds

Compound	C_{max} (µg/mL)			
	Reported	*In silico*-predicted	*In vitro*-based (without F_g)	*In vitro*-based (with F_g)
Daidzin (Daidzein)*	0.004[a]	0.11	0.11	0.028
Daidzein	0.005 [a]	0.18	0.17	0.021
Genistin (Genistein)*	0.004 [a]	0.23	0.091	0.0091
Genistein	0.005 [a]	0.36	0.59	0.045
Quercetin	0.0108[b]	0.19	0.51	0.013
Gallic acid	0.356[c]	0.084	0.73	0.76
Caffeic acid	0.00323[d]	0.0063	0.019	0.017
Ferulic acid	0.0109[e]	0.023	0.10	0.019
Cyanidin 3-glucoside	0.0130[f]	0.00022	0.029	0.030
Curcumin	0.006[g]	1.1	2.0	0.023
Caffeine	3.36[h]	1.4	4.0	4.9
Acrylamide	0.00208[i]	0.012	0.030	0.021
Butylated hydroxyanisole	0.117[j]	0.031	0.33	0.57
Butylated hydroxytoluene	0.09[k]	0.0016	0.017	0.030
Aflatoxin B1	0.000000941[l]	0.00000024	0.00000050	0.00000083
Ochratoxin A	0.000119[m]	0.000017	0.000030	0.000011
Bisphenol A	0.00152[n]	0.0057	0.036	0.0040
Bisphenol S	0.00257[o]	0.0058	0.0093	0.0019
Chlorpyrifos	0.030[p]	0.0078	0.27	0.12
Picloram	3.6[q]	5.2	26	30.2

C_{max}, peak plasma concentration
*: These values represent the deglycosylated forms (daidzein or genistein).
The reported kinetic parameters were obtained from previously reported literature:

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