

Table 1: Pharmacokinetic parameters of therapeutic drugs that interact with oraganic anion transporters (OATs) and their possibilities to cause drug-drug interactions

	Bioavailability	CLtot [mL□min ⁻¹ □kg ⁻¹]	Urinary excretion [% of dose]	Protein unbound fraction [%]	Cmax [mg□L ⁻¹]	[μM]	Cu,max [mg□L ⁻¹]	[μM]		Transporter	Ki or Km [μM]	Substrate	R [%]	Reference
Antiinflamatry drugs														
Acetylsalicylate	0.68	9.3	1.4	51	24	133	12.2	67.9	1200 mg po	Rat Oat1	428	PAH	86.2	166
Diclofenac	0.54	4.2	0	0.5	2	6.29	0.01	0.031	50 mg po	Human OAT3	N.D.	E1S		25
Ibuprofen	0.8	0.75	0	1	61.1	296	0.611	2.96	800 mg po	Human OAT1	N.D.	MTX, E1S		25, 26
										Human OAT3	1170	MTX	100	26
										Human OAT3	N.D.	E1S		25
										Human OAT4	N.D.	MTX, E1S		25, 26
										Rat Oat1	3.5	PAH	54.1	166
										Rat Oat1	N.D.	MTX		167
Indomethacin	0.98	1.4	15	10	2.4	6.71	0.24	0.671	50 mg po	Human OAT1	N.D.	PAH, OTA, MTX		21, 26, 168
										Human OAT3	5.95	MTX	90.0	26
										Human OAT3	N.D.	E1S, OTA		25, 26
										Human OAT4	N.D.	E1S, OTA, MTX		24, 26, 28
										Rat Oat1	10	PAH	93.5	166
										Rat Oat1	4.2	E1S	86.2	167
										Rat Oat2	0.366	*	35.3	166
Ketoprofen				5	4.8	18.9	0.24	0.944	50 mg po	Human OAT1	N.D.	MTX		26
										Human OAT3	1180	MTX	90.1	26
										Human OAT4	N.D.	MTX		26
										Rat Oat1	N.D.	PAH, MTX		26, 166
										Rat Oat2	1.84	Salicylate		167
										Rat Oat3	N.D.	Indoxyl sulfate		168
Salicylate (a metabolite of acetylsalicylate)					40	290			650 mg acetylsalicylate po	Human OAT1	N.D.	PAH, MTX		23, 26
										Human OAT3	1020	MTX		26
										Human OAT3	N.D.	E1S		25
										Rat Oat1	341	PAH		166
										Rat Oat1	1000	MTX		167
										Rat Oat2	81.2-88.8	*		170, 171
Antiviral drugs														
Acyclovir	0.3	7.15	75	85	1.21	5.4	1.03	4.59	400 mg po	Human OAT1	342.3	*	86.2	27
										Human OAT3	N.D.	E1S		27
Ganciclovir	0.05	4.6	73	98	1.2	4.7	1.18	4.61	1000 mg po	Human OAT1	N.D.	PAH		27
										Human OAT2	N.D.	PGF2α		27
										Human OAT3	N.D.	E1S		27
Zidovudine	0.63	26	18	0.75	1.6	5.99	1.2	4.49	5 mg□kg ⁻¹ po	Human OAT1	N.D.	PAH		27
										Human OAT2	N.D.	PGF2α		27
										Human OAT3	N.D.	E1S		27
										Human OAT4	N.D.	E1S		27
										Rat Oat3	N.D.	E1S		172
Antibiotics														
Amoxicillin	0.93	2.6	86	82	5	13.7	4.1	11.2	500 mg po	Rat Oat1	N.D.	PAH		173
Carbenicillin										Rat Oat1	500	PAH		173
Cefadroxil			84		12.4	32.5			500 mg po	Human OAT1	6.14	PAH		174
										Human OAT3	8.62	E1S		174
										Rat Oat1	N.D.	PAH		173
										Rat Oat1	>2000	PAH		175
										Rat Oat3	1780	E1S		175
Cefamandole			71		20.4	44.1			1000 mg im	Human OAT1	0.03	PAH		174
										Human OAT3	0.046	E1S		174
										Human OAT4	1.14	E1S		174
										Rat Oat1	450	PAH		173
										Rat Oat3	90	E1S		173

Cefazolin		0.95	80	11	237	521	26.1	57.4	1000 mg iv	Human OAT1 Human OAT3 Human OAT4 Rat Oat1 Rat Oat3 Rat Oat3	0.18 0.55 1.74 450-560 780 N.D.	PAH E1S E1S PAH E1S Indoxyl sulfate	0.3 1.0 2.9 88.5 93.5	174 174 174 175, 176 175 169
Cefoperazone										Human OAT1 Human OAT3 Human OAT4 Rat Oat1 Rat Oat2 Rat Oat3	0.21 1.89 2.8 298-450 N.D. 670	PAH E1S PAH Salicylate E1S		174 174 174 175, 176 170 172
Cefotaxime		3.7	55	64	150	329	96	211	30 mg/kg iv	Human OAT1 Human OAT3 Human OAT4 Rat Oat1 Rat Oat3	3.13 0.29 6.15 >2000 800	PAH E1S E1S PAH E1S		174 174 174 173 173
Ceftriaxone		0.24	49	10	168	303	16.8	30.3	1000 mg iv	Human OAT1 Human OAT3 Human OAT4 Rat Oat1 Rat Oat3	0.23 4.39 2.38 840 >2000	PAH E1S E1S PAH E1S	7.6 12.7 7.3 96.2 -	174 174 174 174 175
Cephalexin	0.9	4.3	91	86	28	80.6	24.1	69.3	500 mg po	Rat Oat1 Rat Oat3	2310 630	PAH E1S	97.1 90.1	173 175
Cephaloridine										Human OAT1 Human OAT3 Human OAT4 Rat Oat1 Rat Oat3	0.74 2.46 3.63 1320-2330 1140	PAH E1S E1S PAH E1S		174 174 174 173 175
Cephalothin										Human OAT1 Human OAT3 Human OAT4	0.22 0.04 0.2	PAH E1S E1S		174 174 174
Minocycline	0.95	1	11	23	3.5	7.65	0.23	0.805	100 mg po	Human OAT1 Human OAT2	N.D. N.D.	PAH PGF2 α		177 177
Penicillin G			15	60						Human OAT1 Human OAT3 Human OAT3 Human OAT4 Rat Oat1 Rat Oat3 Rat Oat3	N.D. N.D. 97.6 N.D. N.D. 418-1680 52.8 N.D.	PAH, OTA MTX E1S, OTA OTA, MTX PAH Pravastatin E1S		21, 28 26 25, 28 24, 169 93, 173 93 172
Tetracycline	0.77	1.67	58	35	2.3	5.18	0.805	1.81	250 mg po	Human OAT1 Human OAT2 Human OAT4	N.D. N.D. N.D.	PAH PGF2 α E1S		178 178 178
Diuretics														
Bumetanide	0.81	2.6	62	1	0.106	0.291	0.001	0.003	3 mg po	Human OAT1 Human OAT3 Human OAT4 Rat Oat1 Rat Oat2 Rat Oat3	N.D. N.D. N.D. 5.5 N.D. N.D.	PAH E1S E1S PAH Salicylate E1S	100	23 25 24 179 175 172
Furosemide	0.71	1.66	71	14	1.7	5.14	0.024	0.072	40 mg po	Human OAT1 Human OAT3 Human OAT4 Rat Oat1 Rat Oat3	N.D. N.D. N.D. 9.5 N.D.	PAH E1S E1S PAH E1S	99.0	21, 168 25 24 179 172
ACE inhibitors														
Enalapril	0.41	4.9	88	50	0.000069	0.00018	0.00003	0.011	10 mg po	Rat Oat2	N.D.	Salicylate		170
Sulphonylureas														
Chlorpropamide	0.32	8.6	0	5	0.15	0.542	0.008	0.027	100 mg po	Rat Oat1	39.5	PAH	100	185
Glibenclamide			23		0.000082	0.000166				Rat Oat1 Rat Oat2	1.6 12.3	PAH Salicylate		185 171
Tolbutamide	0.77	0.22	0.1	9	53	196	4.77	17.6	500 mg po	Rat Oat1	55.5	PAH	75.8	180

<u>H₂ blockers</u>														
Cimetidine	0.6	8.3	62	81	3	11.9	2.43	9.63	400 mg po	Human OAT1 Human OAT3 Rat Oat1 Rat Oat3	N.D. 54.3 >1000 46.8	OTA * PAH Penicillin G	85.5 - 82.6	28 25 181 181
<u>Angiotensin II receptor antagonist</u>														
Losartan	0.358	8.1	15	1.3	0.296	0.7	0.004	0.009	50 mg po	Human OAT1	N.D.	PAH		23
<u>Uricosic drugs</u>														
Probenecid			11	17	22.5	78.8	3.83	13.4	500 mg po	Human OAT1 Human OAT1 Human OAT1 Human OAT2 Human OAT3 Human OAT3 Human OAT3 Human OAT3 Human OAT4 Human OAT4 Human OAT4	12.1 4.41 N.D. 786 9 4.41 29.8 54.9 44.4 N.D.	PAH OTA MTX PGF2 α E1S OTA MTX E1S OTA MTX	47.4 24.8 - 98.0 40.2 24.8 69.0 80.7 76.9 -	182 28 26 183 183 28 183 184 169 182