

# Supplementary Materials: Meta-Analysis of Food Effect on Oral Absorption of Efflux Transporter Substrate Drugs: Does Delayed Gastric Emptying Influence Drug Transport Kinetics?

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**Table S1.** Drugs with reported food-effect (FE) studies and their respective physicochemical and biochemical properties.

Drug	Food-Effect Type	Log Dose Number	Transport Saturation Index	Mechanism of Elimination	C <sub>max</sub> Change (%)	AUC Change (%)	References
5-Aminosalicylic acid	Negative	−0.48	NS	Acetylation (metabolism)	−64.47	−47.75	[1,2]
5-fluorouracil	Negative	−0.86	61.50	BCRP (GI efflux), OAT2	−70.43	−34.92	[3]
6-Mercaptopurine	Negative	−0.09	NS	Aldehyde oxidase (AO), Methyltransferase, xanthine oxidase (XO), Xanthine dehydrogenase (XDH) (metabolism), MRP4, ENBT1	−25	−25	[4]
Abacavir	Negative on C <sub>max</sub>	0.00	41.91	Alcohol dehydrogenase, UGTs (metabolism), P-gp, BCRP (GI efflux)	−26	−3.1	[5,6]
Abiraterone acetate	Positive	2.82	51.08	Esterase, CYP3A4, SULT2A1 (metabolism), P-gp (GI efflux)	630.88	343.29	[7]
ABT-102	None	−0.10	NS	NA	6.98	20.22	[8,9]
ABX-464	Positive	2.10	NS	UGTs (metabolism)	183.67	161.91	[10]
Acetaminophen	None	−0.02	NS	UGT1A1/1A9/2B15, SULT1A1/1A3/1E1/2A1, CYP1A2/2C9/2C19/2D6/2E1/3A4 (metabolism)	21	NA	[11,12]
Acipimox	None	−1.08	NS	Minimal metabolism	NA	NA	[13,14]
Adinazolam	Positive	−0.05	NS	Hepatic metabolism	32.6	9.24	[15]

Afatinib	Negative	0.80	1.65	P-gp/BCRP (GI efflux)	−50	−39	[16–18]
Albendazole	Positive	1.09	10.55	CYP3A4 (metabolism), P-gp (GI efflux)	550	840	[19–21]
Alectinib	Positive	2.06	24.86	CYP3A4, aldehyde dehydrogenases (ADH) (metabolism), P-gp (GI efflux)	164.12	188.42	[22,23]
Alitretinoin	Positive	1.53	NS	CYP3A4 (metabolism)	225.98	295.33	[24]
Alprazolam	None	−0.91	NS	CYP3A4 (extensive metabolism)	23	NA	[25,26]
Amifampridine phosphate	Negative on C <sub>max</sub>	−3.30	NS	N-acetyl transferases (NAT2) (metabolism) (variability due to fast and slow acetylators)	−31.3	−8.85	[27–29]
Amiodarone	Positive	2.70	NS	CYP3A4/2C8 (metabolism)	268.42	135.71	[30,31]
Amitriptyline	None	1.35	NS	UGTs, SULTs (metabolism)	NA	NA	[32]
Amlodipine	None	0.43	0.49	CYP3A4 (metabolism), P-gp (GI efflux)	NA	NA	[33,34]
Amocarzine	Positive	1.84	NS	Extensive hepatic metabolism	170.21	204.55	[35,36]
Amoxycillin	None	0.32	NS	CYPs (metabolism)	NA	5.2	[37]
Ampicillin	Negative	0.52	57.24	MRP2 (GI efflux), PEPT1 (GI uptake), hydrolysis (metabolism)	−25.92	−31.03	[37,38]
Apixaban	None	−0.23	0.87	P-gp (GI efflux) and CYP3A4 (metabolism)	15	21	[39,40]
Aprepitant	Positive	1.79	NS	CYP3A4/1A2/2C19 (extensive metabolism)	314.33	303.45	[41,42]
Artemisinin	None	0.20	NS	CYPs (metabolism)	NA	NA	[43]
Asciminib	Negative	0.88	13.34	UGT2B7, CYP3A4 (metabolism), P-gp/BCRP (GI efflux)	−71.23	−63.55	[44,45]
Atazanavir	Positive	2.69	22.70	CYP3A (extensive metabolism),	57	70	[46], FDA label

				P-gp, MRP1 (GI efflux)			
Atenolol	None	−0.03	15.02	Minimal metabolism, P-gp (GI efflux)	NA	20	[47]
Atorvastatin	Negative	2.71	5.73	P-gp (GI efflux) and CYP3A4 (metabolism)	−47.83	−12.67	[48,49]
Atovaquone	Positive	3.58	81.78	CYP (metabolism), P-gp (GI efflux)	400	200	FDA label
Bendroflumethiazide	None	−0.73	NS	Extensive metabolism	NA	NA	[50,51]
Bevantolol	None	1.47	NS	Extensive metabolism	12.6	7.47	[52]
Bidisomide	Negative	0.13	NS	NA	−52.97	−49.04	[53]
Blonanserine	Positive	−0.65	0.22	P-gp (GI efflux), CYP3A4 (metabolism)	242.32	283.63	[54,55]
BMS-690514	Positive	0.42	NS	CYPs, UGTs (metabolism)	54.96	33	[56,57]
Boceprevir	Positive on AUC	2.14	61.58	Aldoketoreductase-mediated metabolic pathway, CYP3A4/5 (metabolism), P-gp (GI efflux)	NA	60	[58]
Bosentan	None	1.74	9.06	CYP2C9/3A4 (metabolism), OATP2B1 (GI uptake)	22	10	[59,60]
Bosutinib	Positive	2.23	30.16	P-gp (GI efflux), CYP3A4 (metabolism) [B:P =1.2]	80	70	[61], FDA label
Bromazepam	Negative	0.01	NS	CYPs (metabolism)	−34.74	−33.13	2273442, 30115648
Bromfenac	Negative on C <sub>max</sub>	0.90	2.99	OATP1B1, BCRP (GI efflux)	−72	NA	[62,63]
Bromocriptine	None	−0.46	NS	CYP3A/2D6/2C8/2C19 (extensive metabolism)	17.65	8.77	[64,65]
Bumetanide	Negative on C <sub>max</sub>	−0.51	0.22	UGTs (metabolism), OAT1, P-gp (GI efflux)	−62.89	−11.89	[66,67]
Buspirone	Positive	−0.87	NS	CYP3A4 (extensive metabolism)	116	84	FDA label
Cabozantinib	Positive	2.55	13.96	CYP3A4 (extensive metabolism),	48.13	66.14	[68,69]

				MRP2 (GI efflux)			
Canagliflozin	None	2.43	NS	UGT1A9 and UGT2B4 (metabolism)	NA	7.88	[68,70]
Candesartan	Positive on C <sub>max</sub>	0.63	0.73	Intestinal ester hydrolysis, hepatic O-deethylation (metabolism), P-gp (GI efflux)	26.6	NA	[71]
Canertinib (CI-1033)	None	1.81	20.58	OATPs, BCRP (GI efflux)	NA	NA	[72]
Cannabidiol	Positive	1.50	NS	CYP2C19/3A4 enzymes, and UGT1A7, UGT1A9, and UGT2B7 (metabolism)	1400	384.9	[73]
Captopril	Negative	−1.05	18.41	Methyltransferase (metabolism), PEPT1 (GI uptake)	−48.7	−38.95	[74]
Carboxyamidotriazole	Positive	2.75	NS	CYP3A4 (metabolism) [BA and	212	166.09	[75]
Cediranib	Negative on C <sub>max</sub>	1.06	4.00	UGT1A4 (major), FMO1, FMO3, CYPs (minor) (metabolism), P-gp (GI efflux)	−31.74	−19.73	[76,77]
Cefpodoxime proxetil	None	0.64	NS	Esterase (metabolism)	NA	NA	[78]
Cefuroxime axetil	Positive	0.85	39.18	Esterases (metabolism), PEPT1 (GI uptake)	42.85	44.97	[79,80]
Celecoxib	Positive	1.62	5.51	CYP2C9 (metabolism). P-gp (GI efflux)	29.28	11.49	[81]
Ceritinib	Positive	2.95	35.83	CYP3A4 (metabolism), P-gp (GI efflux)	47.79	83.79	[82,83]
Chloroquine	Positive	2.14	46.52	CYP3A4 (metabolism), P-gp (GI efflux)	51.5	41.81	[84,85]
Chlorothiazide	Positive	0.70	67.63	BCRP (GI efflux), limited metabolism	25	25	[86,87]
Cibenzoline	None	2.12	NS	CYP3A/2D6 (metabolism)	16	NA	[88]
Cilazapril	Negative	−1.72	0.48	Hydrolysis (metabolism), PEPT1 (GI	−28.9	−13.82	[89,90]

				uptake), P-gp (GI efflux)			
Cilostazol	Positive	1.09	10.83	CYP3A4/2C19 (metabolism), OATP1B1-, and OATP1B3, MRP2, BCRP, P-gp (GI efflux)	94.56	25.51	[91,92]
Cinnarizine	Positive	1.76	NS	Extensive hepatic metabolism	28.26	57.14	[93]
Ciprofloxacin	Negative on C <sub>max</sub>	0.17	60.36	CYP1A2 (metabolism), BCRP (GI efflux)	−33	NA	[94,95]
Ciramadol	None	−1.17	NS	UGTs (metabolism)	18.8	3.81	[96]
Clodronate	Negative	−0.81	NS	No metabolism	−77.8	−90.2	[97,98]
Clopidogrel	Positive	1.41	9.32	Esterase, CYPs (metabolism), P-gp (GI efflux)	515.6	869.67	[99,100]
Clozapine	None	−0.57	1.53	CYP1A2, 2C, 2D6, 2E1 and 3A3/4 (extensive metabolism), OATPs, P-gp (GI efflux)	20	8.05	[101,102]
Cobicistat	None	2.68	7.73	CYP3A, 2D6 (metabolism), OCT2, P-gp (GI efflux)	NA	6.88	[103]
Cobimetinib	None	0.28	1.51	CYP3A, UGT2B7 (metabolism), P-gp (GI efflux)	7.5	10	[104,105]
Codeine	None	−0.38	NS	UGT2B7/2B4, CYP3A4/2D6 (metabolism), OCT1	NA	NA	[106,107]
Crizotinib	None	2.21	22.21	P-gp (GI efflux) and CYP3A4 (metabolism)	14.07	14.27	[108], FDA label
Cyclandelate	Positive	0.60	NS	Metabolism	25	25	[109]
Cyclosporine	Positive	1.45	NS	CYPs (metabolism)	25	25	[110]
Dabrafenib	Negative	2.26	11.55	CYP2C8, CYP3A4 (metabolism), P-gp, BCRP (GI efflux)	−50.64	−30.08	[111,112]
Danazol	Positive	1.36	NS	CYP3A4 (metabolism)	140	290.83	[113,114]
Darunavir	Positive	1.68	NS	CYP3A4 (metabolism)	62.11	38.57	[115]

Deferasirox	Positive	2.21	NS	UGT1A1/1A3, CYPs (metabolism)	43.55	31.05	[116,117]
Deflazacort	None	0.92	3.26	Esterase (metabolism), P-gp (GI efflux)	17.02	0.78	[118,119], FDA label
Deramciclane	Positive on AUC	2.07	NS	CYP2E1 (Extensive metabolism)	24	31	[120]
Desloratadine	None	0.88	0.97	UGT2B10, CYP2 C8 (metabolism), P-gp (GI efflux)	NA	NA	[121,122]
Desmopressin	Negative	−2.14	NS	Intestinal degradation	−45.91	−40.54	[123,124]
Dextropropoxy phene	None	1.79	NS	CYP3A4 (metabolism)	NA	NA	[107,125]
Diclofenac	Negative on C <sub>max</sub>	1.65	6.75	CYP2C9 (metabolism), OATP1B3, P-gp/BCRP (GI efflux)	−61	−15	[126]
Dicoumarol	Positive on AUC	1.18	NS	CYP2C (metabolism)	NA	242	[127]
Didanosine	Negative	−0.64	63.50	BCRP (GI efflux), Purine nucleoside phosphorylase (PNP)	−53.71	−46.61	[128,129]
Digoxin	Negative	−1.60	0.04	P-gp (GI efflux)	−25	−25	[130]
Diprafenone	Positive on AUC	0.82	NS	CYP2D6 (metabolism)	8.78	36.16	[131,132]
Dixyrazine	Positive	0.49	NS	Degradation	25	25	[133,134]
Dolutegravir	Positive	0.34	4.77	UGT1A1, UGT1A3, UGT1A9 (metabolism), BCRP, and P-gp (GI efflux)	36.89	48.27	[135,136]
Doravirine	None	2.10	NS	CYP3A4/5 (metabolism)	15.53	17.94	[137,138]
Dovitinib	None	1.16	NS	CYP1A1/2, flavin-containing monooxygenase (FMO) (metabolism)	5.89	8.8	[139,140]
Doxycycline	None	0.10	18.00	CYPs (metabolism), P-gp (GI efflux)	20	NA	[141–143]
Dronedarone	Positive	2.90	28.74	CYP3A4 (metabolism), P-gp (GI efflux)	25	25	[144]
Duloxetine	Positive on C <sub>max</sub>	1.91	NS	CYPs 1A2, 2D6 (extensive metabolism)	31.33	4.24	[145,146]

Efavirenz	None	2.45	76.03	CYP2B6 (metabolism), BCRP (GI efflux)	16.81	13.58	[147,148]
Eltrombopag	Negative	1.30	4.52	UGT1A1, UGT1A3, CYP1A2, CYP2C8 (metabolism), BCRP (GI efflux), OATP1B1	−64.71	−59.36	[149,150]
Elvitegravir	Positive	1.96	NS	CYP3A4, UGT1A1/3 (metabolism)	56	87	[58,151]
Enoxacin	None	0.17	NS	CYPs (metabolism), MATE-1	9.6	8.6	[151,152]
Entecavir	Negative on C <sub>max</sub>	−3.22	0.14	BCRP (GI efflux)	−62.97	−22.36	[153,154]
Eprosartan	Negative on C <sub>max</sub>	2.14	23.05	OATP1B1 and MRP2 (GI efflux)	−25.25	−14	[155]
Erlotinib	Positive	1.83	15.25	BCRP (GI efflux)	57.16	100.25	[156,157]
Erythromycin	Negative	0.64	27.25	CYP3A4 (metabolism), P-gp (GI efflux)	−53.78	−56.45	[158,159]
Eslicarbazepine	None	0.76	107.99	Hydrolysis (metabolism), P-gp (GI efflux)	NA	NA	[160–162]
Estramustine	Negative	3.65	38.15	CYPs (metabolism), P-gp (GI efflux)	−72.68	−71.07	[163]
Ethionamide	None	0.38	NS	EthA enzyme (metabolism)	NA	NA	[164,165]
Etoposide	None	−0.39	6.80	CYP3A4/5 (metabolism), P-gp (GI efflux)	22	12.25	[166,167]
Etoricoxib	Negative on C <sub>max</sub>	2.17	NS	CYPs (metabolism), MRP4	−35.8	−2.88	[168,169]
Evacetrapib	Positive	2.21	NS	CYP3A/CYP2C8 (metabolism)	51.05	44.29	[170,171]
Everolimus	Negative on C <sub>max</sub>	0.69	0.08	P-gp (GI efflux) and CYP3A4 (metabolism)	−60.34	−20.49	[172,173]
Fedratinib	Positive on AUC	2.32	38.12	CYP3A4, CYP2C19, and flavin-containing monooxygenase 3 (FMO3) (metabolism), P-gp (GI efflux)	3.57	30.73	[174], FDA label

Fenofibrate	Positive	3.15	NS	Esterase, UGTs, CYPs (metabolism)	282.84	234	[175,176]
Fenoldopam	Negative	0.17	NS	Glucuronidation, sulfation, and methylation (metabolism)	−79.94	−63.25	[177,178]
Fexinidazole	Positive	1.71	NS	CYP1A2, 2B6, 2C19, 3A4, and 3A5 and, to a lesser extent, 2D6 (metabolism)	291.6	247	[179]
Fiduxosin	Positive	1.78	NS	NA	337.32	136.01	[180,181]
Flecainide	None	1.39	19.31	CYP3A4/2D6 (metabolism), P-gp (GI efflux)	4.11	13.08	[182]
Flubendazole	Positive	1.78	NS	Metabolism	25	25	[183]
Fluconazole	None	−0.54	13.06	CYP3A4 (metabolism), P-gp (GI efflux)	5.12	6.19	[184]
Fluvoxamine	None	1.44	4.60	CYPs (metabolism), P-gp (GI efflux)	NA	−7	[185,186]
Fosamprenavir (prodrug)	Negative	0.61	47.81	CYP3A4 (metabolism), P-gp (GI efflux)	−28	−46	[187]
Fosaprepitant	Positive	2.02	NS	CYP3A4 with minor metabolism by CYP1A2 and CYP2C19 (metabolism)	33	47	[188], EMEA label
Fostamatinib (R406 prodrug)	None	0.59	3.45	CYP3A4, UGT1A9 (metabolism), P-gp (GI efflux)	NA	NA	[189,190]
Furosemide	Negative	0.12	4.84	P-gp/BCRP (GI efflux), OATP2B1 (GI uptake)	−44	−33	[66]
Gabapentin	Positive	−1.62	140.16	LAT1/2 (GI uptake)	32	26	[191–193]
Ganciclovir	None	−0.46	156.72	Minimal metabolism, P-gp (GI efflux)	12.94	19.14	[194]
Gatifloxacin	None	0.40	42.62	P-gp (GI efflux)	8.57	7.01	[195]
Gefitinib	None	1.57	22.38	CYP3A4/3A5/2D6 (metabolism), P-gp, BCRP (GI efflux)	NA	NA	[196], monograph
Gemifloxacin	None	0.78	32.87	P-gp, MRP2 (GI efflux)	14	12	[197,198]
Gepirone	Positive on AUC	−1.13	NS	CYP3A4 and CYP2D6 (metabolism)	−9.34	36.97	[199]



Ginkgolide A	Positive	−0.48	NS	CYPs (metabolism)	118.11	85.64	[200,201]
Glasdegib	Negative on C <sub>max</sub>	0.93	10.68	P-gp (GI efflux) and CYP3A4 (metabolism)	−25.68	−10.96	[202,203]
Glyburide	None	0.99	0.40	CYP3A4/2C9/2C19/3A7/3A5 (metabolism), P-gp, BCRP (GI efflux), MRP1	11.03	12.34	[204]
Griseofulvin	Positive	1.60	NS	Desmethylation, UGTs (metabolism)	25	25	[205,206]
GW420867X	None	0.52	6.71	CYPs (metabolism), P-gp (GI efflux)	NA	NA	[207]
Halofantrine	Positive	3.95	19.98	CYP3A4 (metabolism), P-gp (GI efflux)	561.95	189.74	[208,209]
Hydralazine	Positive	−1.12	NS	Extensive–first pass metabolism by acetylation	143.67	254	[210,211]
Hydrocodone	Positive on C <sub>max</sub>	−0.35	NS	CYP3A4, 2D6 (metabolism)	42.07	11.18	[212–214]
Ibrutinib	Positive	1.92	38.14	CYP3A, and to a minor extent by CYP2D6 (extensive metabolism), P-gp (GI efflux)	281.82	158.9	[215,216], FDA label
Icotinib	Positive	2.10	NS	CYP3A4, CYP3A5, and CYP1A2 (metabolism)	59	79	[217,218]
Imipramine	None	0.48	7.13	CYP2C19/1A2/3A4 (extensive metabolism), P-gp (GI efflux)	NA	NA	[219,220]
Imiquimod	None	0.21	NS	NA	NA	NA	[221,222]
Indinavir	Negative	1.51	26.07	CYP3A4 (metabolism), P-gp (GI efflux)	−86	−78	[223,224]
Indomethacin	Negative on C <sub>max</sub>	1.62	2.79	CYP2C9, 2C19, 2D6 (metabolism), P-gp (GI efflux)	−29	1.5	[225,226]
Ipriflavone	Positive	1.66	NS	Extensive metabolism	25	25	[227]
Isoniazid	Negative on C <sub>max</sub>	−1.46	NS	NAT2, CYP2E1 (metabolism)	−56.04	−11.94	[228]
Isosorbide–5–mononitrate	None	−2.55	NS	Hepatic metabolism	−20	16.45	[229,230]
Isotretinoin	Positive	1.83	NS	2C8, 2C9, 3A4, and 2B6 (metabolism)	144.44	86.03	[231]

Itraconazole	Positive	1.62	NS	CYP3A4 (metabolism)	109	69.75	[232,233]
Ivermectin	Positive	1.78	NS	Extensive metabolism	207.19	164.72	[234,235]
Ixazomib	Negative	−0.05	0.44	CYPs (metabolism), P-gp (GI efflux)	−70.39	−32.04	[236–238]
Ketoconazole	Negative	1.90	15.05	CYP3A4 (metabolism), P-gp (GI efflux)	−43.21	−39.15	[239]
Labetalol	None	2.14	21.92	UGTs (metabolism), P-gp (GI efflux)	−21.64	19.29	[240]
Lacosamide	None	0.24	31.96	CYP2C9, CY2C19, and CYP3A4 (metabolism), P-gp (GI efflux)	NA	NA	[241]
Lanopepden (GSK1322322)	Positive on AUC	1.12	NS	UGTs (metabolism)	NA	27.22	[242]
Lapatinib	Positive	2.43	103.26	CYP3A4 and CYP3A5 (extensive metabolism), P-gp, BCRP (GI efflux)	203	325	[243,244]
Lenalidomide	Negative on C <sub>max</sub>	−1.07	7.71	P-gp (GI efflux), minimal metabolism	−50	−20	[245]
Lenvatinib	None	0.81	0.94	CYP3A and aldehyde oxidase (metabolism), P-gp, BCRP (GI efflux)	−5	6	[246], FDA label
Lesinurad	None	2.31	39.57	CYP2C9 (metabolism), BCRP (GI efflux)	16.19	10.35	[247,248]
Lesogaberan	None	−2.52	NS	Hepatic metabolism	24	NA	[249,250]
Levetiracetam	None	−1.87	235.01	Enzymatic hydrolysis and hydroxylation (metabolism), P-gp (GI efflux)	NA	NA	[251]
Levofloxacin	None	−0.08	33.21	Limited metabolism, OATP1A2 (GI uptake), BCRP (GI efflux)	13.55	9.7	[252–254]
Linezolid	None	0.02	44.46	P-gp (GI efflux) and CYP3A4 (metabolism)	18.42	3.29	[255,256]

Linifanib	Negative on C <sub>max</sub>	−0.11	2.05	CYP3A4 (metabolism), P-gp (GI efflux)	−37.11	−15.16	[255,257]
Lisinopril	None	−0.43	1.97	Limited metabolism, P-gp (GI efflux)	NA	NA	[258,259]
Lonafarnib	Negative on C <sub>max</sub>	2.68	NS	CYP3A4, CYP3A5, CYP2C8 (extensive metabolism)	−52	−23	[260,261]
Lopinavir	Positive on AUC	2.92	25.44	P-gp, MRP2 (GI efflux), CYP3A4 (metabolism)	18	27	[262,263]
Loratadine	Positive	0.47	1.04	CYP3A4 (metabolism), P-gp (GI efflux)	52.87	75.77	[264,265]
Losartan	None	1.93	9.46	CYPs (metabolism), P-gp (GI efflux)	−16.16	14.83	[266]
Lumefantrine	Positive on C <sub>max</sub>	4.19	9.07	CYP3A4 (extensive metabolism), P-gp (GI efflux)	100	NA	[267]
Lurasidone	Positive	1.01	NS	CYP3A4 (extensive metabolism)	97	103.25	[268,269]
Manidipine	Positive	1.91	NS	CYP3A4 (extensive metabolism)	25.81	42.4	[270,271]
Maraviroc	Negative	1.05	2.34	P-gp (GI efflux) and CYP3A4 (metabolism)	−33	−33	[272], FDA label
Mavoglurant	Positive	1.21	NS	CYP2C8, CYP2C9, CYP2C19 with minor to negligible contributions of CYP2D6, CYP3A4, and CYP1A1 (extensive metabolism)	25	25	[273]
Mebendazole	Positive	2.19	NS	Extensive metabolism	25	25	[274,275]
Mefloquine	Positive	1.90	79.30	CYP3A4 (metabolism), P-gp (GI efflux)	72.8	39.91	[276]
Megestrol	Positive	2.28	NS	CYP3A4, UGT2B17 (metabolism)	629.41	139	[277,278]
Melphalan	Negative	−0.95	NS	Hydrolysis to mono and dihydroxy	−42.2	−31.8	[279]

				products (metabolism)			
Menatetrenone (Vit K2)	Positive	2.09	NS	NA	25	25	[280]
Metformin	None	0.16	NS	OCTs, MATEs (mainly renal)	15.55	3.79	[281,282]
Methotrexate	None	−0.76	0.66	BCRP (GI efflux)	19.31	NA	[283]
Methylphenidate	None	−0.06	6.86	CES1A1 (metabolism), P-gp (GI efflux) (variability due to d and l enantiomers)	22.75	15.42	[284,285]
Metoclopramide	None	−0.41	4.00	CYP2D6/3A/1A 2 (metabolism), P-gp and BCRP (GI efflux)	NA	NA	[286,287]
Metoprolol	Positive	0.00	NS	CYP2D6 (extensive metabolism)	123.53	132	[288,289]
Migalastat	Negative	−3.11	NS	O-glucuronidation (metabolism), SGLT-1 (minor)	−40.93	−37.93	[290,291]
Mirabegron	Negative	1.69	58.72	P-gp (GI efflux), OATP1A2 (GI uptake) and CYP (metabolism)	−72.84	−47.73	[292,293]
Mirtazapine	None	−1.26	NS	CYP1A2, CYP2D6, CYP3A4 (metabolism)	5.26	12.5	[294,295]
MMI270B	Negative on C <sub>max</sub>	0.05	NS	Metabolism	−55.5	−17.34	[296]
Momelotinib	None	1.39	19.30	CYPs (metabolism), Pgp, BCRP (GI efflux)	24.17	22.44	[297,298]
Nadolol	Negative on C <sub>max</sub>	−0.85	10.34	Renal excretion mainly, P-gp (GI efflux)	−34.4	−23.76	[299,300]
Nalidixic acid	Positive	−0.36	NS	CYPs, UGTs (metabolism)	91.3	87.78	[301,302]
Naloxegol	Positive	0.25	1.53	P-gp (GI efflux), CYP3A4 (metabolism)	30	45	[303], EMEA label
Nateglinide	Negative on C <sub>max</sub>	1.45	NS	CYP2C9, CYP3A (metabolism), OATs, Monocarboxylate transporter (MCT) 6	−33.66	−5.63	[304,305]

Nelfinavir	Positive	3.42	NS	CYP2C19 and CYP3A (metabolism)	420	230	[306], FDA label
Nifedipine	None	1.13	6.93	CYP3A4 (metabolism), BCRP (GI efflux)	22.85	9.32	[307,308]
Niflumic acid (given as talniflumate–Prodrug)	Positive	1.53	NS	UGTs (metabolism)	417.41	386.38	[309]
Nilotinib	Positive	2.90	30.22	CYP3A4 (metabolism), P-gp/BCRP (GI efflux)	112	82	[310]
Nilvadipine	None	0.29	NS	Extensive first pass metabolism	NA	NA	[311,312]
Nitrofurantoin	Positive	−0.02	16.80	Extensive metabolism, BCRP (GI efflux)	25	25	[313]
Norfloxacin	None	0.20	50.10	CYP1A2 (limited metabolism), BCRP (GI efflux)	NA	NA	[314,315]
Omadacycline	Negative	0.75	20.20	P-gp (GI efflux)	−50	−61.11	[316,317]
Orteronel	Negative	1.17	52.07	P-gp, BCRP (GI efflux), CYP (minor) (metabolism)	−50.62	−40.18	[318], FDA monograph
Ospemifene	Positive	2.66	NS	CYP3A4, CYP2C9, CYP2C19, and CYP2B6 (metabolism)	260	180	[319]
Oxaprozin	None	2.17	NS	CYPs, UGTs (metabolism)	NA	NA	[320,321]
Oxfendazole	Positive	0.56	NS	Extensive metabolism	238.46	673.86	[322–324]
Oxybutynin	Positive on C <sub>max</sub>	0.60	1.12	CYP3A4 (extensive metabolism), P-gp (GI efflux)	121.43	6.06	[325–327]
Palbociclib	Positive on C <sub>max</sub>	1.46	NS	CYP3A, SULT2A1 (metabolism)	36.84	18.75	[328,329]
Panobinostat	Negative on C <sub>max</sub>	1.98	2.29	P-gp (GI efflux) and CYP3A4 (metabolism)	−47.82	−18.18	[330,331], FDA label
Penicillin	Negative	0.55	29.90	PEPT1 (GI uptake)	−25	−25	[332]
Pexmetinib	Positive on C <sub>max</sub>	4.51	NS	NA	49.04	20.51	[333]

PF-04449913 (Glasdegib maleate B)	None	0.93	10.68	CYP3A4/5 (metabolism), P-gp, BCRP (GI efflux)	16.56	18.66	[334]
Phenytoin	Positive	1.23	NS	CYPs (metabolism)	45.45	109	[335,336]
Pictilisib (GDC-0941)	None	0.38	3.12	P-gp and BCRP (GI efflux)	−23.08	17.6	[337]
Piperaquine	Positive	2.49	NS	CYP3A4 (metabolism)	217	172.66	[338]
Pitavastatin	Negative on C <sub>max</sub>	0.61	0.38	UGT1A3, UGT2B7, CYP2C9, CYP2C8 (metabolism), P-gp/MRP2/BC RP (GI efflux), OATP1B1/1B3/2 B1/NTCP	−43.1	−11	[339], FDA label
Pleconaril	Positive	1.56	NS	Extensive metabolism	147.83	122.55	[340,341]
Ponatinib	None	1.79	3.38	CYP3A (metabolism), P-gp, BCRP (GI efflux)	NA	NA	[342,343], FDA label
Posaconazole	Positive	1.82	11.42	UGTs (metabolism), P-gp (GI efflux)	287.88	290.8	[344–346]
Pradigastat	Positive	2.20	NS	NA	36.02	30.87	[347,348]
Prazosin	None	−2.24	0.10	CYPs (metabolism), BCRP (GI efflux)	NA	NA	[107]
Pregabalin	Negative on C <sub>max</sub>	−1.73	37.68	LAT1/2 (GI uptake)	−25	NA	[192]
Preladenant	Negative on C <sub>max</sub>	−0.34	NS	O-desmethy lati on, carboxylation (metabolism)	−38.16	−4.47	[349,350]
Pretomanid (PA 824)	Positive	1.23	NS	CYP3A4 (metabolism)	38.01	43.23	[351]
Primaquine	Positive on C <sub>max</sub>	0.33	NS	CYP2D6, UGTs (Extensive metabolism)	26	14	[352–354]
Procainamide	None	0.00	NS	OCT3, CYP2D6 (metabolism)	NA	NA	[355]
Propafenone	Positive on C <sub>max</sub>	2.20	NS	CYP2D6 (Extensive metabolism)	50.31	7.37	[356,357]
Propranolol	Positive	0.61	NS	CYP2D6, 1A2, and 2C19 (metabolism)	87.5	127.13	[288]
Pseudoephedri ne	None	−0.93	NS	Extensive hepatic metabolism	7.31	−1.57	[358,359]

R1663	None	1.90	NS	CYP3A4 (extensive metabolism)	NA	NA	[360]
Raltegravir	Positive	0.31	NS	UGTs (metabolism), OAT1	96.31	112	[361,362]
Ravuconazole	Positive	−0.60	NS	NA	25	25	[363]
Repirinast	Positive on C <sub>max</sub>	2.48	NS	NA	220	NA	[364]
Ribavirine	Positive	−1.62	32.76	CNT2 and ENT1 (GI uptake),	66	42	[365], FDA label
Riboflavin (Vitamin B2)	Positive	−2.61	0.04	hRFT-1, hRFT-2 and hRFT-3 (GI uptake)	25	25	[366,367]
Rifabutin	None	1.55	NS	Hepatic metabolism	16.87	NA	[368]
Rifalazil	Positive	0.94	NS	Esterase, CYP3A4 (metabolism)	101.22	44.66	[369]
Rifampicin	Negative on C <sub>max</sub>	1.76	NS	Desacetylation (metabolism), Degradation, ET (P-gp)	−35.77	−6.4	[370,371]
Rilpivirine	Positive	1.41	NS	CYP3A (metabolism)	74.12	65.97	[372,373], FDA label
Riociguat	Negative on C <sub>max</sub>	−0.83	0.24	CYP1A1, 2J2, 3A4 and 3A5, UGT1A1, UGT1A9 (metabolism), P-gp, BCRP (GI efflux), OCT2	−34.91	−11.63	[374]
Ritonavir	Negative on C <sub>max</sub>	2.50	5.55	P-gp (GI efflux) and CYP3A4 (metabolism)	−26.67	−23.4	[375–377]
Rivaroxaban	Positive	0.90	1.84	CYP3A4/5, CYP2J2 (metabolism), P-gp, BCRP (GI efflux)	25	25	[378,379]
Rosuvastatin	Negative	−0.40	0.83	BCRP (GI efflux)	−31.03	−37.16	[380]
Rufinamide	Positive	0.57	NS	CES (metabolism)	95.89	42.83	[381,382]
Rupatadine	None	1.17	NS	CYP3A4/2C9/2 C19/2D6 (High first pass metabolism)	−5.9	23.03	[383]
Sacubitril (Prodrug)	Negative on C <sub>max</sub>	2.93	19.44	UGT2B17, CES1 (metabolism), P-gp (GI efflux)	−73.12	−21	[384,385]
Sacubitrilat (sacubitril metabolite)	Negative on C <sub>max</sub>	2.35	20.87	OATP1B1 and OATP1B3, P-gp (GI efflux)	−27.13	−7.89	[384,385]

Safinamide	None	1.31	6.62	Cytosolic amidases, MAO-A, ALDH, CYP3A4 (metabolism), OAT3, BCRP (GI efflux)	NA	NA	[386]
Sapropterin	Positive	−0.86	11.61	P-gp (GI efflux), CYP3A4, and CYP2D1 (metabolism)	25	34.52	[387]
Saquinavir	Positive on AUC	2.99	35.78	CYP3A4 (metabolism), P-gp, MRP1/2 (GI efflux)	NA	570.83	[388]
Saroglitazar	Negative on C <sub>max</sub>	1.03	0.36	P-gp (GI efflux) and CYP3A4 (metabolism)	−33.46	−3.82	[389,390]
Selegiline Hydrochloride	Positive	0.20	NS	CYP2B6 and CYP3A4, 2A6 (metabolism)	228.13	305.36	[391,392]
Selexipag (ACT-333679)	Negative on C <sub>max</sub>	−0.43	0.03	CES1, CYP2C8, CYP3A4, UGT1A3, UGT2B7 (metabolism), OATP1B1, OATP1B3, P-gp/BCRP (GI efflux)	−35	1.1	[393]
Selumetinib	Negative on C <sub>max</sub>	0.85	6.55	CYP2C19, UGT1A1 (metabolism), BCRP (GI efflux)	−50.28	−16.11	[394,395]
Sertindole	None	0.22	NS	CYP2D6/3A4 (metabolism)	NA	NA	[396,397]
Sildenafil	Negative on C <sub>max</sub>	−0.94	NS	CYPs	−29.18	−11.27	[398]
Sofosbuvir (GS-331007)	Negative on C <sub>max</sub>	0.29	30.22	CES1 (metabolism), P-gp and/or BCRP (GI efflux)	−25	NA	[399], FDA label
Solithromycin	None	1.98	18.93	CYP3A4 (metabolism), P-gp (GI efflux)	NA	NA	[400,401]
Sotalol	Negative	−0.09	NS	No metabolism	−25	−25	[402]
SRT-2104	Positive	2.48	NS	NA	249	273.53	[403]
Sulpiride	Positive	−0.13	11.72	PEPT1 (GI uptake), OCT1, OCT2, MATE1, and MATE2-K	25	25	[404]
Sunitinib maleate	None	0.81	3.76	CYP3A4 (metabolism),	9.96	18.63	[405,406]



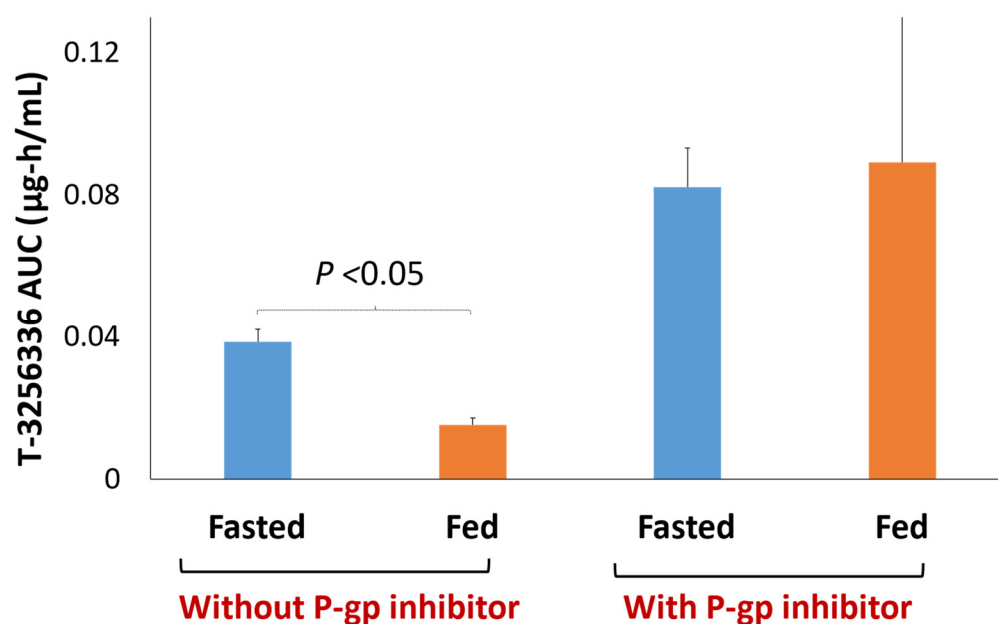
				P-gp, BCRP (GI efflux)			
Tacrolimus	Negative	0.70	0.25	CYP3A4 (metabolism), P-gp/BCRP (GI efflux)	−77.03	−33.45	[407,408]
Tadalafil	None	−0.49	2.05	CYP3A4 (metabolism), P-gp (GI efflux)	16.16	8.16	16487221
Talazoparib	Negative on C <sub>max</sub>	−1.70	0.05	Minimal metabolism, P-gp, BCRP (GI efflux)	−46	NA	[409]
Tedizolid	Negative on C <sub>max</sub>	0.80	NS	SULT1A1, SULT1A2, SULT2A1 (metabolism)	−26.56	2.38	[410,411]
Tegafur/Ftorafur	Negative on C <sub>max</sub>	−1.24	NS	CYP2A6 (metabolism), dihydropyrimidine dehydrogenase (DPD) (catabolic pathway), MRP8 (pepsinogen secretion)	−33.23	−8.76	[3]
Telaprevir	Positive on AUC	1.93	44.13	CYP3A4 (extensive metabolism), P-gp (GI efflux)	NA	330	[58,412]
Telithromycin	None	2.05	39.41	CYP3A4 (metabolism), P-gp, MRP2 (GI efflux)	NA	NA	[413,414]
Tenoxicam	None	−0.51	NS	CYP2C9/3A4 (metabolism)	NA	NA	[415]
Terbinafine	None	3.13	34.31	CYP2C9/1A2/3A4/2C8/2C19 (metabolism), P-gp (GI efflux)	21.29	22.09	[416–418]
Terfenadine	Positive	2.72	NS	CYP3A4 (metabolism)	25	25	[419]
Testosterone undecanoate	Positive	3.64	NS	Extensive metabolism, lymphatic transport	34960.24	27842.58	[420,421]
Tetracycline	Negative on C <sub>max</sub>	0.18	45.00	P-gp (GI efflux)	−50	NA	[422]
Tetrahydrocannabinol	Positive	1.18	NS	CYPs 2C9, 3A4, UGTs (metabolism)	25	25	[423]
Theophylline	Negative	−0.80	199.82	CYP1A2 (extensive metabolism),	−59	−47	[424,425]

				PEPT1 (GI uptake), P-gp (GI efflux)			
Ticlopidine hydrochloride	None	1.66	NS	CYP3A4, CYP2C19, and CYP2B6 (metabolism)	21.29	20	[426–428]
Tipranavir	Positive on AUC	3.59	NS	CYP3A (extensive metabolism)	16	31	[58]
Tocotrienols (Vitamin E)	Positive	3.18	NS	CYP-mediated omega oxidation (CYP4F2) (metabolism), cholesterol transporter Niemann–Pick C1-like 1 (NPC1L1)	216	175.86	[429–431]
Tofacitinib	None	−0.83	1.41	CYP3A4/2C19 (metabolism), P-gp (GI efflux)	24.16	0.5	[432,433]64803, FDA label
Tolterodine	Positive	0.18	NS	CYP2D6 (extensive metabolism)	43	33.33	[434,435]
Topiramate	None	−1.23	11.79	CYP3A4 (metabolism), P-gp (GI efflux)	10.43	4.18	
Topotecan	None	−1.69	0.41	Hydrolysis (metabolism), P-gp/BCRP (GI efflux)	15.8	13.92	[436–438]
Torsemide	Negative on C <sub>max</sub>	0.83	NS	CYP2C9 (extensive metabolism), OATP	−33	−2	[439]
Trametinib	Negative on C <sub>max</sub>	−0.58	0.13	CES (metabolism), P-gp/BCRP (GI efflux)	−68.42	−15.26	[440,441], FDA label
Treprostinil	Positive on AUC	−0.26	NS	CYP2C8, UGTs (metabolism)	13	49	[442,443]
Troglitazone	Positive	3.12	36.24	Sulfation, glucuronidation (extensive metabolism), BCRP (GI efflux)	100	58.33	[444,445]
Trovaflaxacin	None	1.06	19.21	UGT, CYP, SULT (metabolism), P-gp (GI efflux)	11.53	3.29	[446,447]
Tyramine	Negative	−0.85	NS	MAO-A, FMO3, PNMT, DBH,	−78.16	−68.92	[448,449]

				and CYP2D6 (metabolism)			
Udenafil	None	1.00	15.48	CYP3A4 (metabolism) and P-gp (GI efflux)	20.26	3.9	[450,451]
Uracil	Negative	−1.52	NS	CYP2A6 (metabolism), sodium-depend ent nucleobase transporter (rSNBT1)	−75.84	−34.92	[3,452]
Valsartan	Negative	1.14	7.35	OAT1, OAT3, OATP1B1, OATP1B3, MRP2 (GI efflux)	−40	−50	26225262
Vardenafil	None	−0.91	0.82	CYP3A4/3A5/2 C (metabolism), P-gp, BCRP and MRP2 (GI efflux)	NA	NA	[453–455]
Veliparib	None	−0.24	6.55	CYPs (metabolism), P-gp (GI efflux)	17.64	4.08	[456–459]
Vemurafenib	Positive	4.03	78.38	CYP3A4 (metabolism), P-gp, BCRP (GI efflux)	114.28	184.48	[460,461]
Venetoclax	Positive	2.33	NS	CYP3A4 (extensive metabolism)	300	352	[462], FDA label
Venlafaxine	None	−0.06	7.21	CYP2D6 (metabolism), P-gp (GI efflux)	NA	NA	[463]
Verinurad	Negative on C <sub>max</sub>	1.23	2.30	UGT2B17 (metabolism), CYP3A, P-gp (GI efflux)	−52.86	−23.14	[464–466]
Vinorelbine	Negative	1.59	6.16	CYP3A4 (extensive metabolism), MRP2 (GI efflux)	−34.99	−33.64	[467,468]
Voriconazole	Negative	0.20	45.80	CYP2C19, CYP3A4, CYP2C9 (metabolism), P-gp (GI efflux)	−60.56	−43.1	[469–471]
Zafirlukast	Negative	2.32	NS	CYP3A4, CYP2C9 (extensive metabolism)	−25	−25	[472,473]
Zalcitabine	Negative on C <sub>max</sub>	−3.07	NS	Metabolism, OAT1	−38.49	−13.89	[474–476]

Zileuton	Positive on C <sub>max</sub>	1.65	NS	CYP1A2, CYP2C9 and CYP3A4 (metabolism)	27	1.4	[477,478]
Zimelidine	None	−0.78	NS	Extensive first pass metabolism	NA	NA	[107,479]
Ziprasidone	Positive	1.65	NS	CYP3A4, CYP1A2 (metabolism)	84	104	[480,481]
Zolmitriptan	None	−1.28	0.35	CYP1A2 (metabolism), P-gp (GI efflux)	15.85	12	[482,483]
Zolpidem	Negative on C <sub>max</sub>	−0.35	0.46	CYP3A4, CYP2C9, CYP1A2, CYP2D6, CYP2C19 (metabolism), P-gp (GI efflux)	−44.15	12.02	[484–486]
Zuclopenthixol	Positive on AUC	1.79	NS	Sulfoxidation, side chain N-dealkylation and glucuronic acid conjugation, CYP2D6 (metabolism)	NA	26	[487,488]
Olanzapine	None	−0.67	7.71	Metabolism, P-gp (GI efflux)	−19.75	−3.49	[489–491]
Warfarin	Negative on C <sub>max</sub>	−0.23	NS	CYP2C9, 1A2, 2C19, 3A4, 2C8, 2C18 (metabolism)	−47.61	−7.12	[492]
Acebutolol	None	0.79	18.72	P-gp (GI efflux)	−20.73	−5.65	[493]
Pantoprazole	Negative on AUC	−0.49	4.17	Metabolism, P-gp (GI efflux)	−4.78	−33.34	[494]
Rabeprazole	None	−0.62	NS	Metabolism	21.46	7.76	[494]
Omeprazole	Negative on C <sub>max</sub>	−0.35	4.63	P-gp	−26.67	−11.98	[494]
Peficitinib	Positive	0.58	NS	Metabolism	56.05	34.77	[495]

NA: not available; NS: non-substrate.



**Figure S1.** P-gp-dependent food-effect due to prolonged gastric emptying time and increased efficiency of P-gp efflux in the fed state. This mechanism is exemplified in the literature [496].

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