

Derivation of equation 3; $F = Q/(Q+Cl_o)$

From equation ; $F = 1-ER$

ER is the extraction ratio of the elimination rate to the input rate of a drug.

ER is $= CL_h/Q$

then, $F = 1- CL_h/Q$

Where, CL_h is hepatic clearance and Q is the liver blood flow.

By substituting oral CL ($F \times CL_o$) for CL_h one will get

$F = 1- (F \times CL_o)/Q$ solving this equation for F one will get

$F = Q/(Q+Cl_o)$

Table S1. Predicted and observed F in adults predicted from oral clearance and liver blood flow (LBF) or liver plasma flow (LPF) (drugs metabolized only in the liver)

Drugs/age	Oral CL	Observed	Observed	Predicted	Predicted	Ratio	Ratio	References
	mL/min	Mean %F	%F Range	LBF	LPF	LBF	LPF	
Diclofenac	499	54 ± 2	NA	76	63	1.41	1.17	S1
Voriconazole (EM)	572	75 ± NA	63-87	74	60	0.98	0.80	S2
Voriconazole (PM)	157	94 ± NA	79-110	91	84	0.97	0.90	S2
Azithromycin	1910	43 ± 13	NA	46	31	1.06	0.72	S3
Busulfan	240	80 ± 19	47-103	87	78	1.09	0.97	S4
Clonidine	292	88 ± 9	NA	85	74	0.96	0.85	S5
R-ketoprofen	163	85 ± 21	NA	91	84	1.07	0.99	S6
S-ketoprofen	173	81 ± 18	NA	90	83	1.11	1.03	S6
Oxycodone	1334	60 ± 20	NA	55	39	0.91	0.65	S7
Theophylline	50	100 ± 10	86-111	97	94	0.97	0.94	S8
Amiodarone	758	65 ± 22	22-104	68	53	1.04	0.81	S9
Bosutinib	3128	34 ± 9	NA	34	21	1.00	0.63	S10
Oseltamivir	438	79 ± 12	NA	79	66	0.99	0.84	S11
Glasdegib	231	79 ± 13	72-83	87	79	1.11	1.00	S12
Letermovir	64	100 ± NA	NA	96	93	0.94	0.91	S13
Melatonin	8403	14 ± 7	NA	16	9	1.14	0.66	S14
Fimasartan	3440	19 ± 7	NA	32	20	1.68	1.05	S15
Selegiline	32450	4 ± NA	NA	5	3	1.17	0.75	S16
Ibuprofen	53	103 ± 12	88-120	97	94	0.94	0.91	S17
Imatinib	249	98 ± NA	NA	87	77	0.88	0.79	S18
Nintedanib	29656	5 ± NA	NA	5	3	1.00	0.60	S19
Venlafaxine	2217	40 ± 14	NA	42	28	1.05	0.69	S20
Propranolol	5270	22 ± 3	10-30	23	14	1.06	0.63	S21
Lignocaine	920	37 ± 9	NA	63	48	1.72	1.30	S22

EM = extensive metabolizer, PM = poor metabolizer, NA = not available

Table S1 continues

Drugs/age	Oral CL	Observed	Observed	Predicted	Predicted	Ratio	Ratio	References
	mL/min	Mean %F	%F Range	LBF	LPF	LBF	LPF	
Hydrocortisone	305	96 ± 20	NA	84	74	0.87	0.77	S23
Morphine	7577	24 ± 5	11-45	17	10	0.73	0.42	S24
Metoprolol	800	50 ± NA	NA	67	52	1.33	1.03	S25
Fentanyl	2315	31 ± NA	NA	41	27	1.32	0.87	S26
Hydromorphone	766	62 ± 33	35-125	68	53	1.09	0.85	S27
Telmisartan	1358	43 ± NA	NA	54	38	1.26	0.90	S28
Ciprofloxacin	695	69 ± 7	NA	70	55	1.01	0.80	S29
Diazepam	34	98 ± 6	79-140	98	96	1.00	0.98	S30
Divalproex Sodium	8	90 ± NA	NA	100	99	1.11	1.10	S31
Trimipramine	650	41 ± 4	18-63	71	57	1.73	1.38	S32

NA = not available

Table S2. Predicted and observed F in adults predicted from oral clearance and liver blood flow (LBF) or liver plasma flow (LPF) (drugs metabolized in the liver and the gut)

Drugs/age	Oral CL mL/min	Observed Mean %F	Observed %F Range	Predicted LBF	Predicted LPF	Ratio LBF	Ratio LPF	References
Midazolam	763	48 ± 0.12	32-64	68	53	1.41	1.10	S33
Simvastatin	19440	5 ± NA	NA	7	4	1.42	0.80	S34
Methadone	163	86 ± NA	NA	91	84	1.06	0.98	S35
Saquinavir	33250	4 ± NA	NA	4.6	2.5	1.15	0.62	S36, S37
Acalabrutinib	2651	25 ± NA	NA	38	24	1.50	0.97	S37
Crizotinib	1670	43 ± NA	32-66	49	34	1.14	0.78	S37
Abemaciclib	434	45 ± NA	NA	79	66	1.75	1.47	S37
Buspirone	39667	4 ± NA	NA	3.9	2.1	0.97	0.53	S38
Nisoldipine	16670	6 ± NA	5-8	8.8	4.9	1.45	0.82	S36, S39
Atorvastatin	4464	14 ± NA	NA	26	16	1.88	1.14	S40
Felodipine	6461	14 ± NA	15-20	20	12	1.42	0.83	S36, S41
Verapamil	5017	20 ± 15	20-30	24	14	1.21	0.72	S42
Cyclosporine	2609	21 ± 6	11-30	38	25	1.81	1.17	S43
Sildenafil	683	41 ± NA	25-63	70	55	1.71	1.34	S44
Nifedipine	873	63 ± 18	NA	65	49	1.03	0.78	S45
Alfentanil	742	43 ± 19	NA	68	53	1.59	1.25	S46
Triazolam	563	55 ± NA	NA	74	60	1.34	1.09	S36, S47
Zolpidem	422	72 ± NA	NA	79	67	1.10	0.93	S36, S48
Quinidine	605	72 ± 17	44-89	73	58	1.01	0.81	S49
Alprazolam	630	84 ± NA	80-100	72	57	0.85	0.68	S36, S50

Table S3. Predicted and observed F in adults predicted from oral clearance and liver blood flow (LBF) or liver plasma flow (LPF) (Extensively renally excreted medicines)

Drugs/age	Oral CL	Observed	Observed	Predicted	Predicted	Ratio	Ratio	References
	mL/min	Mean %F	%F Range	LBF	LPF	LBF	LPF	
Famotidine	1030	45 ± 12	38-51	61	45	1.35	1.00	S51
Cefetamet	399	41 ± 12	24-64	80	68	1.95	1.66	S52
Cefixime	147	52 ± 32	NA	92	85	1.76	1.64	S53
Cimetidine	840	60 ± 38	30-100	66	50	1.09	0.84	S54
Digoxin	262	74 ± 9	63-84	86	76	1.16	1.03	S55
Ranitidine	1485	51 ± 10	35-65	52	36	1.02	0.71	S56
Apixaban	87	68 ± 15	51-86	95	91	1.39	1.33	S57
Atenolol	293	58 ± 16	32-81	85	74	1.46	1.28	S58
Edoxaban	595	62 ± 15	NA	73	59	1.18	0.95	S59
Safinamide	83	95 ± 9	84-119	95	91	1.00	0.96	S60
Recainam	733	73 ± 16	48-105	69	54	0.94	0.74	S61
Cefprozil	265	89 ± 7	NA	86	76	0.96	0.86	S62
Levofloxacin	163	100 ± NA	NA	91	84	0.91	0.84	S63
Gatifloxacin	190	96 ± NA	NA	89	82	0.93	0.85	S64
Moxifloxacin	185	92 ± NA	NA	90	82	0.97	0.89	S65
Actisomide*	1466	30 ± NA	NA	51	37	1.70	1.22	S66
Actisomide**	922	43 ± NA	NA	63	48	1.48	1.12	S66
Candoxatrilat	4053	25 ± NA	NA	28	17	0.88	0.54	S67
Sulopenem	1719	40 ± NA	NA	48	34	1.20	0.85	S68
Gemifloxacin	556	65 ± NA	NA	74	60	1.14	0.93	S69
Doxycycline	43	75 ± NA	NA	97	95	1.30	1.27	S70
Tigecycline	583	56 ± NA	NA	73	59	1.31	1.06	S70

*400 mg dose, **500 mg dose

Table S4. Predicted and observed F in children predicted from oral clearance and liver blood flow (LBF) or liver plasma flow (LPF)

Drugs/age	Oral CL	Observed	Observed	Predicted	Predicted	Ratio	Ratio	References
	mL/min	Mean %F	%F Range	LBF	LPF	LBF	LPF	
Midazolam								
Preterm	2.9	49 ± NA	12-100	97	94	1.98	1.10	S71
0.5-2 y	286	37 ± 21	NA	57	40	1.53	1.44	S72
5.5-6 y	585	27 ± NA	NA	53	37	1.97	1.07	S73
Cyclosporine								
1.1-2.5 years	518	22 ± NA	11-35	48	34	2.16	1.52	S74
0.8-6.9 years	265	42 ± 11	NA	68	54	1.62	1.29	S75
7.1-15.6 years	510	43 ± 17	NA	66	52	1.53	1.21	S75
Cefetamet								
3-7 years	230	47 ± 14	29-70	74	59	1.57	1.26	S76
8-12 years	393	42 ± 5	36-47	74	59	1.76	1.06	S76
3.5-17.3 months	100	38 ± 19	25-72	81	71	2.13	1.87	S77
Zidovudine								
Term <14 days)	32	89 ± 19	NA	82	72	0.92	0.81	S78
Term >14 days)	85	61 ± 19	NA	74	61	1.20	1.00	S78
Term (55 days)	100	52 ± NA	NA	73	60	1.40	1.15	S78
Famotidine								
Children (11-15 y)	718	51 ± NA	NA	66	52	1.32	1.04	S79
0-1 y	131	42 ± NA	NA	77	66	1.84	1.56	S80

Table S4 continues

Drugs/age	Oral CL mL/min	Observed Mean %F	Observed %F Range	Predicted LBF	Predicted LPF	Ratio LBF	Ratio LPF	References
Voriconazole								
2-<6 years	252	63 ± 55	NA	75	62	1.19	0.99	S81
6-<12	279	67 ± 42	NA	78	66	1.16	0.99	S81
Busulfan								
1.4-6 y	99	68 ± 31	22-120	86	78	1.27	1.15	S4
Digoxin								
2-33 days	55	72 ± 13	52-79	81	71	1.12	0.98	S82
Clonidine								
3-10 y	195	55 ± NA	NA	81	71	1.48	1.29	S83
Ranitidine								
3.5-16 y	1183	48 ± 20	22-96	54	40	1.12	0.82	S84
Theophylline								
5-13 y	51	68 ± 26	35-113	95	91	1.40	1.34	S85
Itraconazole								
0.5-2 years	541	32 ± NA	NA	44	30	1.37	0.92	S86-87
2-5 years	553	35 ± NA	NA	60	42	1.75	1.24	S86-87
5-12 years	991	30 ± NA	NA	49	32	1.63	1.06	S86-87
Pantoprazole								
11 (6-16) years	191	77 ± NA	NA	85	79	1.10	1.03	S88

Table S4 continues

Drugs/age	Oral CL mL/min	Observed Mean %F	Observed %F Range	Predicted LBF	Predicted LPF	Ratio LBF	Ratio LPF	References
Oxycodone 6-93 months	656	37 ± 17	10-58	49	35	1.32	0.94	S89
Ibuprofen 27 weeks	0.52	77 ± NA	NA	100	99	1.29	1.29	S90-S91
Levofloxacin 0.5-<2 years	49	100 ± NA	NA	90	83	0.90	0.83	S63
2-<5 years	64	100 ± NA	NA	90	83	0.90	0.83	S63
5-<10 years	108	96 ± NA	NA	89	81	0.92	0.85	S63
10-<12 years	150	95 ± NA	NA	90	83	0.94	0.87	S63
12-16 years	163	100 ± NA	NA	90	84	0.90	0.84	S63
Digitoxin 5.9-9.2 years	2.0	100 ± NA	NA	99	99	0.99	0.99	S92
Doxycycline >2-<8 years	24	92 ± NA	NA	97	84	1.05	0.92	S93
>8	51	80 ± NA	NA	97	94	1.21	1.18	S93

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