Supplementary Table S3. ADME processes implemented in the PBPK models.
Metabolizing reactions, active transport processes (influx, efflux), and clearance processes (renal, biliary, hepatic) that were implemented in the PBPK models to represent specific ADME behavior. In case of CEL and ZLT, renal clearance is represented by glomerular filtration (GFR), and GFR and tubular secretion, respectively. Diclofenac, DFN; hydroxy, OH; acyl glucuronide, AGLU; celecoxib, CEL; carboxy, COOH; glucuronide, GLU; zileuton, ZLT; sulfoxide, SO; licofelone, LCF; rifampicin, RIF; desacetyl, DA.

ID	Drug / Metabolite	Metabolite / transporter type / clearance process	Metabolic enzyme / transporter / clearance type	Km [µmol/l]	kcat / specific clearance [1/min]*
1	CEL	OH-CEL	CYP2C9 (zero 2C9*3)[1]	5.1[1]	9.4
1	CEL	OH-CEL	CYP2C9 (one 2C9*3)[1]	5.9[1]	7.1
1	CEL	OH-CEL	CYP2C9 (two 2C9*3)[1]	11.0[1]	4.0
1	OH-CEL	COOH-CEL	ADH2[1]	10.0[1]	54.7
1	COOH-CEL	Hepatic	UGT1A1[2]	100.5*	326.4
1	CEL	Renal[2]	Glomerular filtration[3]	/	8.00**
2	DFN	3'-OH-DFN	CYP2C9[4]	9.0[5]	1.5
2	DFN	4'-OH-DFN	CYP2C9[4]	9.0[5]	67.7
2	DFN	5-OH-DFN	CYP3A4[6]	43.0[5]	6.8
2	DFN	DFN-AGLU	UGT2B7[6]	105.9*	14232.1
2	DFN	Influx	OAT2[7]	48.8[7]	19482.5
2	DFN-AGLU	Influx	OAT2[7]	8.6[7]	3696.3
2	DFN	Renal[2]	Plasma clearance	/	0.008
2	DFN-AGLU	Renal[7]	Plasma clearance	/	315.8
2	3'-OH-DFN	Hepatic[6,2]	Plasma clearance	/	2.8
2	4'-OH-DFN	Hepatic[6,2]	Plasma clearance	/	25.6
2	5-OH-DFN	Hepatic[6,2]	Plasma clearance	/	15.3
3	LCF	LCF-AGLU	UGT2B7[6,8,9]	10.0	340.6
3	LCF	OH-LCF	CYP2J2[6,8,9]	10.0	49.0
3	LCF	Renal[10]	Plasma clearance	/	15.8
3	LCF-AGLU	Hepatic[6]	Plasma clearance	/	4905.0
3	OH-LCF	Hepatic[6]	Plasma clearance	/	4922.4
4	RIF	Influx	OATP-C[11]	1.21[11]	0.08
4	RIF	Efflux	ABCB1[12]	68.5*	21.5
4	RIF	DA-RIF	CES2[13]	53.0*	1.2
4	RIF	Renal[14]	Plasma clearance	/	0.05
4	DA-RIF	Biliary[15]	Plasma clearance	/	0.2
4	DA-RIF	Renal[15]	Plasma clearance	/	3.8
5	ZLT	ZLT-SO	CYP3A4[2]	0.8*	0.4
5	ZLT	OH-ZLT	CYP1A2[2]	0.4*	0.2
5	ZLT	ZLT-GLU	UGT1A9[2]	0.9*	10056.9
5	ZLT-SO	Renal[16]	Tubular secretion[16]	/	6.2
5	OH-ZLT	Renal[16]	Tubular secretion[16]	/	6.2
5	ZLT-GLU	Renal[16]	Tubular secretion[16]	/	2.5
5	ZLT-SO	Renal[16]	Glomerular filtration[16]	/	1.3**
5	OH-ZLT	Renal[16]	Glomerular filtration[16]	/	1.3**
5	ZLT-GLU	Renal[16]	Glomerular filtration[16]	/	1.3**

* fitted to experimental data

** [GFR fraction]

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