Tables

Table 1. Summary of major parameters in the diclofenac MPS model.

Name	Description	Value	RSE	Unit
$K_{p,PC}$	Partition coefficient of package binding	18.2		-
$K_{p,M}$	Partition coefficient value in the membrane	1.27[1]		-
$K_{puu,EPC}$	Unbound partition coefficient in hepatocytes	1.49	45.3%	-
$CL_{H,int}$	Intrinsic clearance of hepatocytes in the chip	0.0269	41.0%	mL/h
$f_{u,PC}$	Nonspecific binding in the package compartment	0.21[2]	37.6%	-
$f_{u,M}$	Nonspecific binding in the membrane compartment	1[2]	43.4%	-
$f_{u,Media}$	Nonspecific binding in the media (assumed to be same in the basal and apical media)	0.537[2]	56.5%	-
f_{u,EPC_g}	Nonspecific binding in primary cells in the gut insert	1[1]		-
f_{u,EPC_h}	Nonspecific binding in primary cells in the liver insert	0.11[1]		-
f_{u,EPC_r}	Nonspecific binding in primary cells in the kidney insert	0.11[1]		-
P_{app,EPC_g}	Effective permeability in chip membrane	0.00049[2]	39.6%	cm/s
P_{app,EPC_g}	Effective permeability in primary cells in the gut insert	0.00097		cm/s
P_{app,EPC_h}	Effective permeability in primary cells in the liver insert	0.000177	39.1%	cm/s
P_{app,EPC_r}	Effective permeability in primary cells in the kidney insert	0.00097		cm/s

[1]fixed by observed or estimated DMPK parameter

[2]Estimated by blank chip

Table 2. Prediction of human PK parameters for oral diclofenac obtained from the *in silico* model using MPS chip data, compared with clinical values from human studies.

Parameter	***In silico* model (5%–95%)**	**Human[17,37] (clinical data)**	**Ratio**
50 mg diclofenac			
$AUC_{inf}[\mu mol \cdot min/L]$	583.03 (419.58–837.07)	-	-
AUC_{tEnd} $[\mu mol \cdot min/L]$	523.97 (366.37–755.65)	591.33	0.89
C_{max} $[\mu mol/L]$	3.51 (2.50–4.53)	4.74	0.74
T_{max} $[h]$	2.25 (2.0–2.5)	2	1.13
$t_{1/2}[h]$	5.52 (2.51–6.74)	4.04	1.37
100 mg diclofenac			
$AUC_{inf}[\mu mol \cdot min/L]$	1,100.47 (749.56–1,655.70)	971.57	1.13
$AUC_{tEnd}[\mu mol \cdot min/L]$	998.05 (662.88–1,546.35)	912.60	1.09
C_{max} $[\mu mol/L]$	5.38 (3.57–7.44)	4.93	1.09
T_{max} $[h]$	1.8 (1.3–2.0)	1.65	1.09
$t_{1/2}[h]$	5.52 (2.51–6.74)	4.04	1.37

Abbreviation: AUC_{inf}, Area under curve extrapolated to infinity (using the terminal 10% of data points); AUC_{tEnd}, Area under curve from time start to time end of the simulation; C_{max}, Highest drug concentration observed in plasma after administration of an extravascular dose; T_{max}, Time at which the highest drug concentration occurs after administration of an extravascular dose; $t_{1/2}$, Terminal half life time (calculated from the terminal 10% of data points)

Table 3. Gene Ontology analysis of genes correlated with diclofenac exposure Genes are categorized based on biological processes, cellular components, and molecular functions, showing significant correlations with diclofenac exposure. Each entry includes the gene symbol and its functional classification.

Description	**geneID**
Acute inflammatory response	*F3/IL6/PTGES/SAA2*
Acute phase response	*IL6/PTGES/SAA2*
Prostaglandin metabolic process	*PTGES/PTGES2/PTGR1*
Prostanoid metabolic process	*PTGES/PTGES2/PTGR1*
Monocyte chemotaxis	*IL6/DUSP1/CCL20*
Endoplasmic reticulum lumen	*ERO1A/IL6/MINPP1/POGLUT2*
Glutathione binding	*PTGES/PTGES2*
Oligopeptide binding	*PTGES/PTGES2*
Cytokine activity	*INHBA/IL6/CSF3/CCL20*
Heat shock protein binding	*PTGES3L/HSPA6/ZFP36*
Oxidoreductase activity, acting on the CH-CH group of donors, NAD or NADP as acceptor	*PTGES2/PTGR1*
Growth factor activity	*INHBA/IL6/CSF3*
FAD binding	*ERO1A/SQLE*
Intramolecular oxidoreductase activity	*PTGES/PTGES2*
Oxidoreductase activity, acting on the CH-CH group of donors	*PTGES2/PTGR1*