Supplementary Table S1. Physicochemical properties used in the developed PBPK models.
Molecular weight (MW), octanol/water partition coefficient (logP), fraction unbound (Fu), acid dissociation constant (pKa), and water solubility used in the developed PBPK models of APAP and CAF. MWs, logP values and water solubilities are taken from DrugBank (1)and Human Metabolome Database (2). In some cases, logP and Fu values were slightly adjusted to best describe the experimental PK data.

Drug / Metabolite	MW [g/mol]	logP	Water solubility [mg/l]	Fu	Ref.	Compound type	pkA	Ref.
APAP	151.16	0.46	14000.00	0.81	(1)	Acid	9.38	(1)
APAPC	254.31	0.33	337.00	0.60	*	[Acid, base]	[1.93, 9.09]	(1)
APAPG	327.29	-1.04	27700.00	0.98	*	Acid	3.18	(1)
APAPS	231.23	-0.372	1540.00	0.80	*	[Acid, base]	[-2.16,14.65]	(3)
NAPQI	149.15	0.01	987.00	0.02	(4)	Neutral	-	(3)
CAF	194.20	-0.07	21600.00	0.65	(5)	Base	10.40	(1)
PX	180.16	-0.63	9130.00	0.52	(5)	Acid	10.76	(2)
TB	180.16	-0.78	9740.00	0.86	(5)	Acid	9.28	(2)
TP	180.16	-0.02	22900.00	0.58	(5)	Acid	7.82	(2)

* adjusted from parent drug

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