Tables

Figures

Supplementary Figure S1

2-compartmental model with first order absorption fit to plasma paracetamol data

Table 1. The results of paracetamol method validation for both plasma and urine

	Plasma		Urine	
	Precision (%)	Accuracy (%)	Precision (%)	Accuracy (%)
QCs	±6.8	±7.4	±7.2	±7.6
Dilution QCs	±8.6	±3.7	±1.2	±12.4

Note: QC = quality control

Table 2. SRM transitions and parameters for the analysis of paracetamol and orthocetamol in urine (SCIEX 4000)

Compound	**Q1 mass (amu, *m/z*)**	**Q3 mass (amu, *m/z*)**	**Dwell (msec)**	**DP**	**CE**	**CXP**
Paracetamol	152.1	110.1	25	71	23	8
		64.9	**25**	**71**	**43**	**4**
		93.0	25	71	33	8
Orthocetamol	152.1	110.0	25	61	40	8
		64.8	25	61	65	4
		91.8	**25**	**61**	**48**	**8**
Paracetamol-d_4	156.2	114.1	25	56	21	6

Note: Quantitative transitions are highlighted in bold. SRM = selected reaction monitoring, Q = quadrupole, DP = declustering potential, CE = collision energy, CXP = cell exit potential

Table 3. Summary of plasma pharmacokinetic parameters for paracetamol following administration of 20 mg/kg BID for nine doses to six exercised Thoroughbred horses.

	Horse 1	**Horse 2**	**Horse 3**	**Horse 4**	**Horse 5**	**Horse 6**
C_{max} (μg/mL)	22.7	16.0	16.7	15.6	20.7	21.4

T_{max} (h)	1.00[1]	1.07[2]	1.92[2]	0.25[1]	1.02[2]	0.25[1]
Cl/F (mL/min/kg)	4.11	3.82	5.54	4.50	5.07	3.77
$t_{1/2\alpha}$ (h)	3.28	3.90	4.12	6.05	4.56	4.25
$t_{1/2\beta}$ (h)	15	115	139	79	113	523

Note: C_{max} = maximal concentration, T_{max} = time the maximal concentration was reached, [1,2] = first/second dose, Cl/F = oral clearance, $t_{1/2\alpha}$ and $t_{1/2\beta}$ = first and second half-lives

Table 4. Summary of modelled parameters for paracetamol following oral administration of 20 mg/kg BID.

Parameter	**Value**
EPC (ng/ml)	7937
Calculated IPC (ng/ml)	16
Nominal IPC (ng/ml)	20
Plasma DT (h)	120
R_{SS}	213
Nominal IUC (ng/ml)	4300
Urine DT (h)	120

Note: EPC = effective plasma concentration (using IV data from Neirinckx et al., 2010), IPC = irrelevant plasma concentration, IUC = irrelevant urine concentration, R_{SS} = steady-state urine to plasma concentration ratio, DT = detection time.

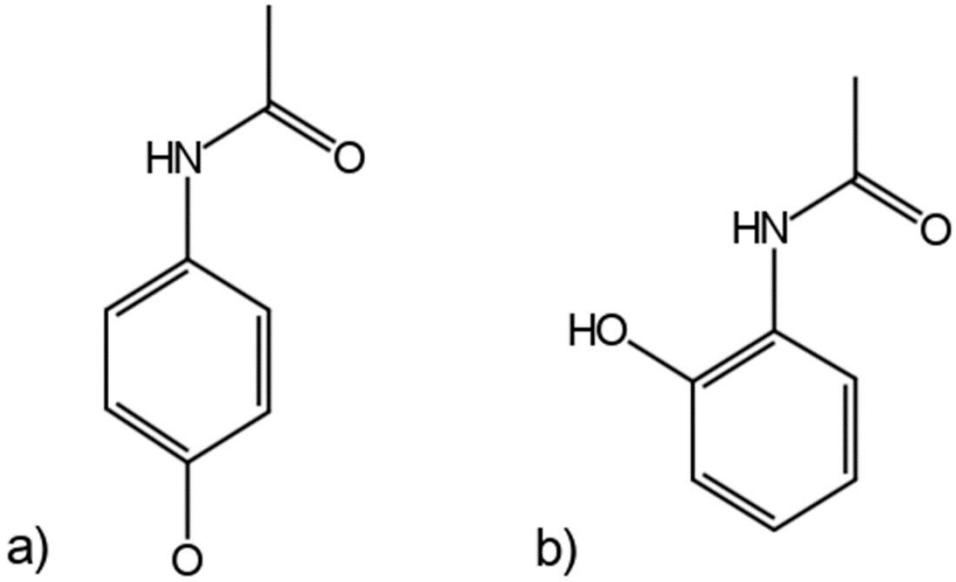

Figure 1. Molecular structure of (a) paracetamol and (b) orthocetamol.

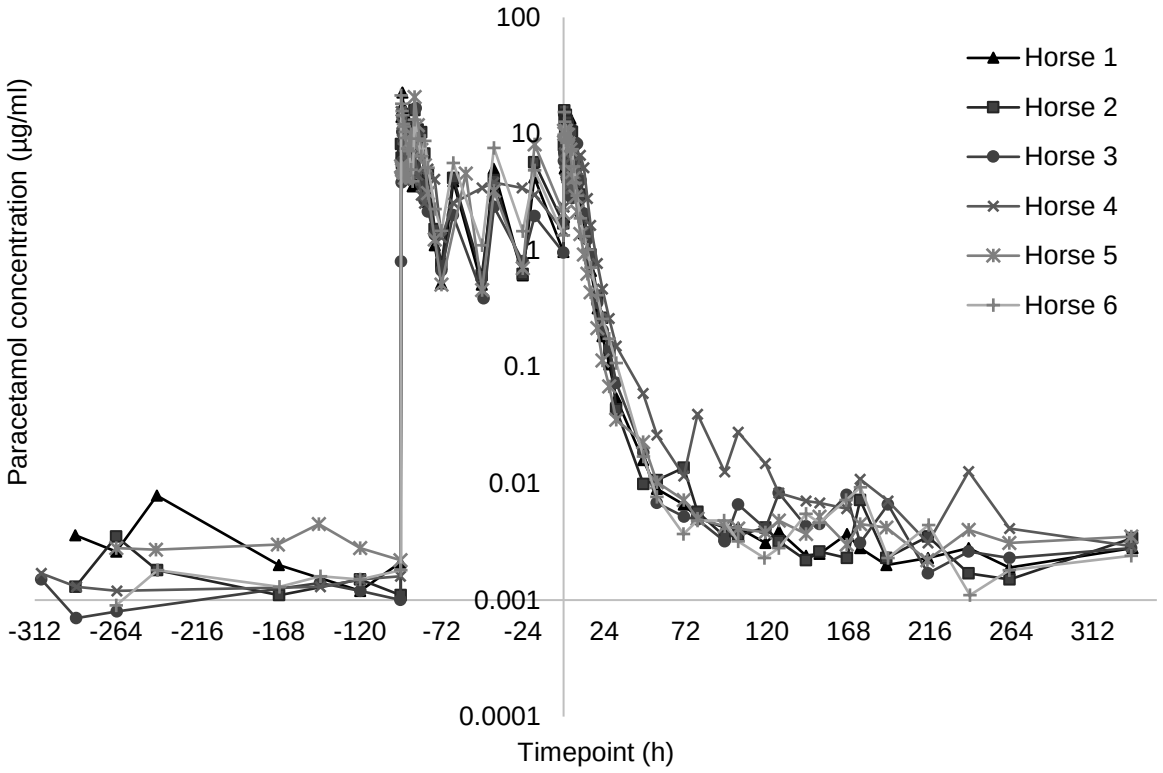

Figure 2. Log plasma paracetamol concentrations versus time in six horses following the administration of nine 20 mg/kg doses of paracetamol over five days

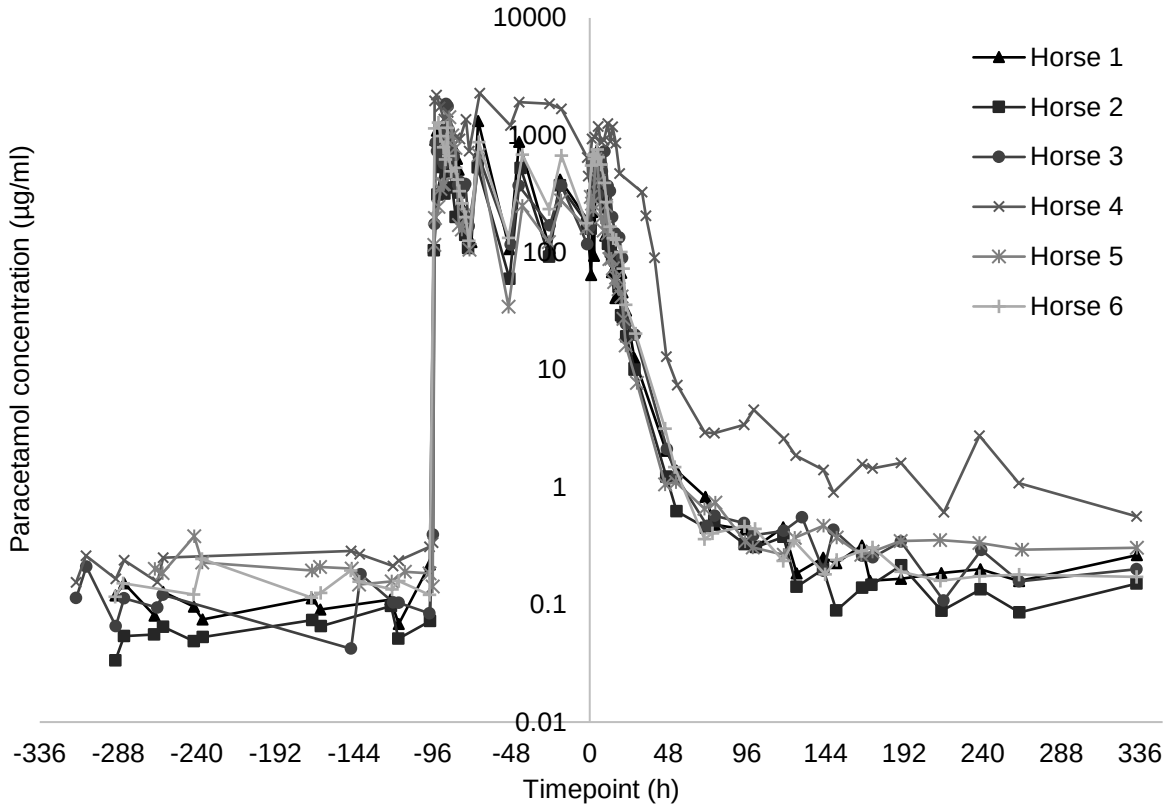

Figure 3. Log urine paracetamol concentrations versus time in six horses following the administration of nine 20 mg/kg doses of paracetamol over five days

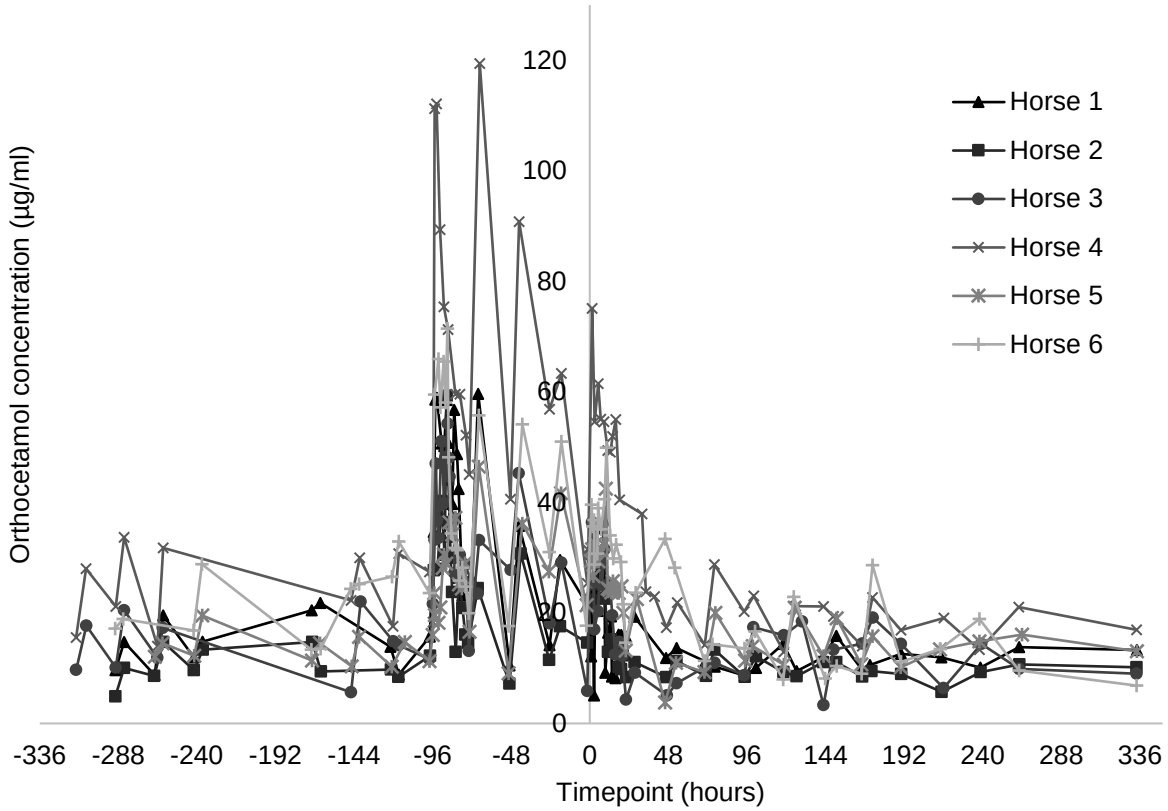

Figure 4. Urine orthocetamol concentrations versus time in six horses participating in the paracetamol administration study (9 doses of 20 mg/kg over 5 days)