

Experiment Number: K10214

Toxicokinetics Data Summary

Request Date: 7/11/2023

Route: IV, Gavage

Compound: Perfluorodecanoic acid/ Analyte: Perfluorodecanoic acid

Request Time: 10:03:16

Species/Strain: Rats/Harlan Sprague Dawley

CAS Number: 335-76-2

Lab: Battelle Columbus

Male

Treatment Group (mg/kg)

2 IV Plasma^a

2 Gavage Plasma^b

10 Gavage Plasma^b

20 Gavage Plasma^b

Cmax_pred (ng/mL)	7300 ± 740	7520 ± 360	42400 ± 2700	81300 ± 3600
Tmax_pred (hour)		8.27 ± 0.63	9.06 ± 0.85	10.0 ± 0.6
Cmax_obs (ng/mL)		8020	45400	81000
Tmax_obs (hour)		12.0	12.0	6.0
Alpha Half-life (hour)	27.0 ± 17.0	175 ± 31	123 ± 40	111 ± 24
Beta Half-life (hour)	854 ± 61	1620 ± 220	995 ± 80	1070 ± 60
k01 (hour ⁻¹)		0.656 ± 0.066	0.562 ± 0.072	0.482 ± 0.042
k01 Half-life (hour)		1.06 ± 0.11	1.23 ± 0.16	1.44 ± 0.13
K10 (hour ⁻¹)	0.00195 ± 0.00024	0.00120 ± 0.00008	0.00145 ± 0.00011	0.00143 ± 0.00008
k10 Half-life (hour)	356 ± 44	579 ± 40	478 ± 38	485 ± 27
k12 (hour ⁻¹)	0.0138 ± 0.0100	0.00178 ± 0.00039	0.00217 ± 0.00093	0.00264 ± 0.00073
k21 (hour ⁻¹)	0.0107 ± 0.0062	0.00141 ± 0.00034	0.00271 ± 0.00091	0.00283 ± 0.00062
Cl1 (mL/hr/kg)	0.534 ± 0.031			
Cl1_F (mL/hr/kg)		0.310 ± 0.014	0.331 ± 0.013	0.338 ± 0.009
V1 (mL/kg)	274 ± 28			
V2 (mL/kg)	355 ± 69			
V1_F (mL/kg)		259 ± 13	228 ± 16	236 ± 12
V2_F (mL/kg)		327 ± 44	183 ± 30	220 ± 23
MRT (hour)	1180 ± 80			
AUC_0-T (ng/mL*hr)	3500000	5410000	28500000	55000000
AUCinf_pred (ng/mL*hr)	3750000 ± 220000	6440000 ± 290000	30200000 ± 1200000	59200000 ± 1600000
F (percent)		172	161	158

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Female

Treatment Group (mg/kg)

2 IV Plasma^a

2 Gavage Plasma^b

10 Gavage Plasma^b

20 Gavage Plasma^b

	2 IV Plasma ^a	2 Gavage Plasma ^b	10 Gavage Plasma ^b	20 Gavage Plasma ^b
Cmax_pred (ng/mL)	8400 ± 1240	10400 ± 600	55200 ± 3200	124000 ± 10000
Tmax_pred (hour)		9.01 ± 0.8	9.29 ± 0.88	10.8 ± 1.2
Cmax_obs (ng/mL)		10500	57500	145000
Tmax_obs (hour)		24.0	24.0	24.0
Alpha Half-life (hour)	5.92 ± 4.64	295 ± 110	298 ± 116	226 ± 81
Beta Half-life (hour)	904 ± 83	1240 ± 290	1260 ± 330	1240 ± 270
k01 (hour ⁻¹)		0.672 ± 0.078	0.646 ± 0.080	0.508 ± 0.078
k01 Half-life (hour)		1.03 ± 0.12	1.07 ± 0.13	1.37 ± 0.21
K10 (hour ⁻¹)	0.00137 ± 0.00022	0.00101 ± 0.00007	0.00102 ± 0.00008	0.00122 ± 0.00012
k10 Half-life (hour)	506 ± 81	685 ± 50	681 ± 55	569 ± 55
k12 (hour ⁻¹)	0.0510 ± 0.0432	0.000599 ± 0.000274	0.000603 ± 0.000286	0.00100 ± 0.00047
k21 (hour ⁻¹)	0.0655 ± 0.0515	0.00129 ± 0.00069	0.00125 ± 0.00071	0.00141 ± 0.00068
Cl1 (mL/hr/kg)	0.327 ± 0.024			
Cl1_F (mL/hr/kg)		0.192 ± 0.009	0.182 ± 0.010	0.192 ± 0.011
V1 (mL/kg)	238 ± 35			
V2 (mL/kg)	186 ± 57			
V1_F (mL/kg)		189 ± 11	178 ± 11	158 ± 13
V2_F (mL/kg)		87.9 ± 23.9	85.8 ± 25.3	112 ± 27
MRT (hour)	1300 ± 120			
AUC_0-T (ng/mL*hr)	5760000	9740000	50800000	100000000
AUCinf_pred (ng/mL*hr)	6130000 ± 450000	10400000 ± 500000	55000000 ± 2900000	104000000 ± 6000000
F (percent)		170	179	170

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Male

Treatment Group (mg/kg)

10 Gavage Brain^{c,d}

Cmax_obs (ng/g)	2590
Tmax_obs (hour)	24.0
Half-life (hour)	865

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Female

Treatment Group (mg/kg)

10 Gavage Brain^{c,d}

Cmax_obs (ng/g)	2380
Tmax_obs (hour)	24.0
Half-life (hour)	987

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Male

Treatment Group (mg/kg)

10 Gavage Kidney^{c,d}

Cmax_obs (ng/g)	27800
Tmax_obs (hour)	24.0
Half-life (hour)	832

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Treatment Group (mg/kg)

10 Gavage Kidney^{c,d}

Cmax_obs (ng/g)	57300
Tmax_obs (hour)	24.0
Half-life (hour)	918

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Treatment Group (mg/kg)

10 Gavage Liver^{c,d}

Cmax_obs (ng/g)	112000
Tmax_obs (hour)	24.0
Half-life (hour)	983

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Female

Treatment Group (mg/kg)

10 Gavage Liver^{c,d}

Cmax_obs (ng/g)	126000
Tmax_obs (hour)	24.0
Half-life (hour)	900

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LEGEND

MODELING SOFTWARE

WinNonlin, Version 5.0.1

MODELING METHOD & BEST FIT MODEL

^aWinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA, Two-compartment model with bolus input, first order output, and $1/Y_{hat}^2$ weighting

^bWinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA Two-compartment model with first order input and first order output $1/Y_{hat}^2$ weighting

^cWinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA Non-compartmental (NCA) model with first order input, first order output, and uniform weighting.

EXCEPTION

^dGroup mean of actual time points at 1 hour was outside acceptance criteria and used for NCA.

ANALYTE

Perfluorodecanoic acid

TK PARAMETERS

C_{max} = Observed or Predicted Maximum plasma (or tissue) concentration

T_{max} = Time at which C_{max} predicted or observed occurs

Half-Life = λ_z Half life, $t_{1/2}$, the terminal elimination half-life based on non-compartmental analysis

Alpha Half-life = Half-life for the alpha phase

Beta Half-life = Half-life for the beta phase

k₀₁ = Absorption rate constant, k_a

k₀₁ Half-life = Half-life of the absorption process to the central compartment

k₁₀ = Elimination rate constant from the central compartment also k_e or k_{elim}

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TK PARAMETERS (cont'd)

k10 Half-life = Half-life of the absorption process to the central compartment

k12 = Distribution rate constant from first to second compartment

k21 = Distribution rate constant from second to first compartment

Cl1 = Clearance of central compartment, Clapp or apparent clearance for intravenous groups

CL1_F = Apparent clearance of the central compartment, also Cl_F for gavage groups in non-compartmental model

V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution, Vz apparent volume of distribution NCA,
Vapp apparent volume of distribution for intravenous studies

V2 = Volume of distribution for the peripheral compartment

V1_F = Apparent volume of distribution for the central compartment includes Vd_F, V_F for oral groups, and Vc_F

V2_F = Apparent volume of distribution for the peripheral compartment

MRT = Mean residence time

AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast

AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

F = Bioavailability, absolute bioavailability

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Plasma and tissue concentrations of perfluorodecanoic acid (PFDA) were measured using liquid chromatography with mass spectroscopy (LC-MS/MS). Parameter estimates are reported to three significant figures. Associated with study C20615.

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TK PARAMETERS PROTOCOL (cont'd)

TK_INTRAVENTOUS PLASMA

2 mg/kg Male and Female

For both the IV and gavage routes, samples from three rats per sex were provided for analysis at each time point. Plasma samples were collected at 12 time points post-administration and analyzed for PFDA concentrations. Plasma Time points for the IV dosed animals were 0.0833, 1, 6, 12, 24, 192, 528, 864, 1200, 1848, 2520, and 3360 hours. Limit of quantitation LOQ is 25 ng/mL.

TK_GAVAGE PLASMA (cont'd)

2 mg/kg, 10 mg/kg, 20 mg/kg Male and Female

For both the IV and gavage routes, samples from three rats per sex were provided for analysis at each time point. Plasma samples were collected at 13 time points post-administration and analyzed for PFDA concentrations. Plasma Time points for the gavage dosed animals were 0.50, 1, 2, 6, 12, 24, 192, 528, 864, 1200, 1848, 2520, and 3360 hours. Limit of quantitation LOQ is 25 ng/mL.

TK_GAVAGE BRAIN

10 mg/kg Male and Female

Rats were given a single gavage administration of 10 mg/kg PFDA. Tissue samples were collected at 5 time points post-administration and analyzed for PFDA concentrations. Three samples were collected per time point. Time points were 1, 24, 864, 1848, and 3360 hours.

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TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE KIDNEY

10 mg/kg Male and Female

Rats were given a single gavage administration of 10 mg/kg PFDA. Tissue samples were collected at 5 time points post-administration and analyzed for PFDA concentrations. Three samples were collected per time point. Time points were 1, 24, 864, 1848, and 3360 hours

TK_GAVAGE LIVER

10 mg/kg Male and Female

Rats were given a single gavage administration of 10 mg/kg PFDA. Tissue samples were collected at 5 time points post-administration and analyzed for PFDA concentrations. Three samples were collected per time point. Time points were 1, 24, 864, 1848, and 3360 hours.