Experiment Number: K08624
Route: IV
Species/Strain: Rats/F344

Toxicokinetics Data Summary
Compound: Thiodiglycolic Acid / **Analyte:** Thiodiglycolic Acid
CAS Number: 123-93-3

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)			
	20 IV Plasma[a]	**20 IV Heart[b]**	**20 IV Thymus[b]**	**20 IV Liver[b]**
Cmax_pred (ug/mL)	32.3 ± 6.4			
Cmax_obs (ug/g)		8.93	8.70	83.0
Tmax_obs (min)		15.5	15.7	25.2
Half-Life (min)		129	109	64.6
Alpha Half-life (min)	22.0 ± 3.0			
Beta Half-life (min)	649 ± 628			
k10 (min^{-1})	0.0227 ± 0.0059			
k10 Half-life (min)	30.6 ± 8.0			
k12 (min^{-1})	0.00849 ± 0.00397			
k21 (min^{-1})	0.00149 ± 0.00119			
Cl (mL/min/kg)	14.0 ± 2.9			
V1 (mL/kg)	619 ± 123			
V2 (mL/kg)	3530 ± 4490			
MRT (min)	296 ± 374			
AUC_0-T (ug/mL*min)	1420 ± 296			

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Female

	Treatment Group (mg/kg)			
	20 IV Plasma[a]	**20 IV Heart[b]**	**20 IV Thymus[b]**	**20 IV Liver[b]**
Cmax_pred (ug/mL)	71.9 ± 19.0			
Cmax_obs (ug/g)		7.78	8.78	183
Tmax_obs (min)		14.7	15.0	44.0
Half-Life (min)		147	149	125
Alpha Half-life (min)	6.35 ± 0.90			
Beta Half-life (min)	129 ± 15			
k10 (min^{-1})	0.0746 ± 0.0125			
k10 Half-life (min)	9.29 ± 1.55			
k12 (min^{-1})	0.0320 ± 0.0046			
k21 (min^{-1})	0.00786 ± 0.00102			
Cl (mL/min/kg)	20.8 ± 2.3			
V1 (mL/kg)	278 ± 74			
V2 (mL/kg)	1130 ± 275			
MRT (min)	67.9 ± 10.4			
AUC_0-T (ug/mL*min)	963 ± 107			

LEGEND

MODELING SOFTWARE

WinNonlin Version 5.0.1

MODELING METHOD & BEST FIT MODEL

[a]WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA, Two-compartment model with bolus input, first order output, and 1/Yhat2 weighting.

[b]WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA, Non-compartment model with bolus input, first order output, and 1/Y2 weighting. Non-compartmental analysis does not calculate a standard error for half-life.

ANALYTE

Thiodiglycolic Acid

TK PARAMETERS

Cmax = Observed or Predicted Maximum plasma (or tissue) concentration
Tmax= Time at which Cmax predicted or observed occurs
Half-Life = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA ke or kelim
Alpha Half-life = Half-life for the alpha phase
Beta Half-life = Half-life for the beta phase
k10 = Elimination rate constant from the central compartment also ke or kelim
k12 = Distribution rate constant from first to second compartment
k21 = Distribution rate constant from second to first compartment
Cl = Clearance, includes total clearance
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
MRT = Mean Residence Time
AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Following blood collection, each animals was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 10, 20, 40, 60, 120, 180, 240, 320, 400, 480, and 600 min. SE is the standard error of the mean. Parameter estimates are reported to three significant figures.

TK_IV PLASMA

20 mg/kg Male and Female

Animals were given a single bolus injection of Thiodiglycolic acid (TDGA) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_IV HEART

20 mg/kg Male and Female

Animals were given a single bolus injection of Thiodiglycolic acid (TDGA) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_IV LIVER

20 mg/kg Male and Female

Animals were given a single bolus injection of Thiodiglycolic acid (TDGA) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK PARAMETERS PROTOCOL (cont'd)

TK_IV THYMUS

20 mg/kg Male and Female

Animals were given a single bolus injection of Thiodiglycolic acid (TDGA) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA