

Experiment Number: NA

Route: Dosed Water, Dosed Water and Gavage Challenge, Gavage, IV

Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary

Test Compound: Dibromoacetic Acid

CAS Number: 631-64-1

Date Report Requested: 12/29/2016

Time Report Requested: 14:38:03

Lab: Battelle Columbus

Male										
Treatment Groups (mg/kg)										
	10 ^a		100 ^a		100 ^b		100 ^c		200 ^a	
Plasma										
C _{max(pred)} (ug/mL)	0.437	± 0.148	94.4	± 8.4	32.4	± 4.0			241	± 16
T _{max(pred)} (minute)	18.5	± 8.4	19.4	± 1.0	19.6	± 2.4			26.3	± 0.8
C _{max(obs)} (ug/mL)							1.89			
T _{max(obs)} (minute)							900			
k ₀₁ (minute ⁻¹)	0.0540	± 0.0246	0.0515	± 0.0026	0.051	± 0.0063			0.0381	± 0.0011
t _{1/2(k01)} (minute)	12.8	± 5.8	13.5	± 0.7	13.6	± 1.7			18.2	± 0.5
k ₁₀ (minute ⁻¹)	0.0540	± 0.0246	0.0515	± 0.0026	0.051	± 0.0063			0.0381	± 0.0011
t _{1/2(k10)} (minute)	12.8	± 5.8	13.5	± 0.7	13.6	± 1.7			18.2	± 0.5
Cl (mL/min/kg)										
Cl _{1(F)} (mL/min/kg)	454	± 233	20.1	± 1.6	57.9	± 9.1			11.6	± 0.6
V ₁ (mL/kg)										
V _{1(F)} (mL/kg)	8420	± 2850	390	± 35	1130	± 140			306	± 21
MRT (minute)										
AUC _{0-t} (ug/mL*min)	38.3		4600		1250				15400	
AUC _{inf} (ug/mL*min)	22.0	± 11.3	4980	± 390	1730	± 270			17200	± 900

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	Male							
	Treatment Groups (mg/kg)							
	200 ^b		200 ^c		400 ^b		100 IV ^d	
	Plasma							
C _{max(pred)} (ug/mL)	100	± 10			253	± 21	162	± 10
T _{max(pred)} (minute)	21.2	± 1.9			29.6	± 2.2		
C _{max(obs)} (ug/mL)			9.73					
T _{max(obs)} (minute)			900					
k ₀₁ (minute ⁻¹)	0.0471	± 0.0043			0.0338	± 0.0025		
t _{1/2(k01)} (minute)	14.7	± 1.3			20.5	± 1.5		
k ₁₀ (minute ⁻¹)	0.0471	± 0.0043			0.0338	± 0.0025	0.0773	± 0.0047
t _{1/2(k10)} (minute)	14.7	± 1.3			20.5	± 1.5	8.96	± 0.54 *
Cl (mL/min/kg)							47.7	± 2.4
Cl _{1(F)} (mL/min/kg)	34.6	± 4.2			19.6	± 2.0		
V ₁ (mL/kg)							617	± 37
V _{1(F)} (mL/kg)	735	± 72			582	± 48		
MRT (minute)							12.9	± 0.8
AUC _{0-t} (ug/mL*min)	5120				17700			
AUC _{inf} (ug/mL*min)	5770	± 710			20400	± 2000	2110	± 100

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LEGEND

Data are displayed as mean \pm SEM

*Data are displayed as mean \pm SD

MODELING METHOD & BEST FIT MODEL

^a WinNonlin, Pharsight Corporation, Mountain View, CA); One-compartment model with equal first order absorption and elimination.

^b WinNonlin, Pharsight Corporation, Mountain View, CA); One-compartment model with equal first order absorption and elimination with 1/Yhat weighting.

^c No TK analysis was performed; DBA values were measurable but all GXA and almost all OXA values were BLOQ or not detected. No TK analysis was performed for the non-challenge group data.

^d WinNonlin, Pharsight Corporation, Mountain View, CA); One-compartment model with bolus input, first order output, and 1/Yhat weighting.

ANALYTE

Dibromoacetic Acid

TK PARAMETERS

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

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

k_{01} = Absorption rate constant, k_a

$t_{1/2(k01)}$ = Half-life of the absorption process to the central compartment

k_{10} = Elimination rate constant from the central compartment also k_e or k_{elim}

$t_{1/2(k10)}$ = Half-life for the elimination process from the central compartment

Cl = Clearance, includes total clearance

$Cl_{1(F)}$ = Apparent clearance of the central compartment, also $Cl_{(F)}$ for gavage groups in non-compartmental model

V_1 = Volume of distribution of the central compartment, includes V_d and V_{volume} of distribution, V_z apparent volume of distribution NCA, V_{app} apparent volume of distribution for intravenous studies

$V_{1(F)}$ = Apparent volume of distribution for the central compartment includes $V_{d(F)}$, $V_{(F)}$ for oral groups, and $V_{c(F)}$

MRT = Mean residence time

AUC_{0-t} = Area under the plasma concentration versus time curve, AUC, from time t_i (initial) to t_f (final), AUC_{last}

AUC_{inf} = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

**** END OF REPORT ****