

Experiment Number: NA

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

Species/Strain: Rat/Fischer 344

Toxicokinetics Data Summary

Test Compound: Dibromoacetic Acid

CAS Number: 631-64-1

Date Report Requested: 12/29/2016

Time Report Requested: 14:38:12

Lab: Battelle Columbus

	Female											
	Treatment Groups (mg/kg)											
	3.4 ^a		3.4 ^b		10 ^c		34.3 ^d		34.3 ^b		40 ^c	
Plasma												
C _{max(pred)} (ug/mL)	2.12	± 0.15			1.99	± 0.23	31.4	± 1.3			26.7	± 2.2
T _{max(pred)} (minute)	29.9	± 1.6			37.4	± 3.8	26.1	± 2.4			31.2	± 2.4
C _{max(obs)} (ug/mL) *			0.393						8.02			
T _{max(obs)} (minute)			1260						1260			
k ₀₁ (minute ⁻¹)	0.0335	± 0.0018			0.0267	± 0.0027	0.0708	± 0.0143			0.0320	± 0.0024
t _{1/2(k01)} (minute)	20.7	± 1.1			25.9	± 2.6	9.78	± 1.98			21.6	± 1.6
k ₁₀ (minute ⁻¹)	0.0335	± 0.0018			0.0267	± 0.0027	0.0177	± 0.0022			0.0320	± 0.0024
t _{1/2(k10)} (minute)	20.7	± 1.1			25.9	± 2.6	39.1	± 4.8			21.6	± 1.6
k ₁₂ (minute ⁻¹)												
k ₂₁ (minute ⁻¹)												
Cl ₁ (mL/min/kg)												
Cl _{1(F)} (mL/min/kg)	19.8	± 1.4			49.5	± 6.8	12.2	± 0.7			17.7	± 1.8
V ₁ (mL/kg)												
V ₂ (mL/kg)												
V _{ss} (mL/kg)												
V _{1(F)} (mL/kg)	591	± 43			1850	± 220	687	± 70			552	± 46
MRT (minute)												
AUC _{0-t} (ug/mL*min)	150				196		2710				2130	
AUC _{inf} (ug/mL*min)	172	± 12			202	± 28	2810	± 160			2260	± 230

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	Female				
	Treatment Groups (mg/kg)				
	68.6 ^d	68.6 ^b	100 ^e	10 IV ^f	110 IV ^g
	Plasma				
C _{max(pred)} (ug/mL)	67.2 ± 2.9		101 ± 9	58.3 ± 5.9	
T _{max(pred)} (minute)	30.0 ± 3.1		54.6 ± 2.2		
C _{max(obs)} (ug/mL) *		18.6			
T _{max(obs)} (minute)		0			
k ₀₁ (minute ⁻¹)	0.0712 ± 0.0138		0.0183 ± 7.0E-4		
t _{1/2(k01)} (minute)	9.74 ± 1.89		37.8 ± 1.5		
k ₁₀ (minute ⁻¹)	0.0121 ± 0.0013		0.0183 ± 7.0E-4	0.226 ± 0.020	0.0420
t _{1/2(k10)} (minute)	57.2 ± 6.0		37.8 ± 1.5	3.06 ± 0.27 *	
k ₁₂ (minute ⁻¹)				0.142 ± 0.032	
k ₂₁ (minute ⁻¹)				0.133 ± 0.021	
Cl ₁ (mL/min/kg)				38.8 ± 1.3	
Cl _{1(F)} (mL/min/kg)	8.61 ± 0.53		6.68 ± 0.59		
V ₁ (mL/kg)				172 ± 17	
V ₂ (mL/kg)				183 ± 19	
V _{ss} (mL/kg)				354 ± 24	
V _{1(F)} (mL/kg)	710 ± 61		365 ± 34		
MRT (minute)				9.13 ± 0.63	
AUC _{0-t} (ug/mL*min)	7810		9440		
AUC _{inf} (ug/mL*min)	7970 ± 490		15000 ± 1300	258 ± 8	

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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 No TK analysis was performed; Most DBA values were below the limit of quantitation (BLOQ) and all GXA and almost all OXA values were BLOQ or not detected so no TK analysis was performed for the non-challenge group data.

^c WinNonlin, Pharsight Corporation, Mountain View, CA; One-compartment model with equal first order absorption and elimination and $1/Y_{hat}$.

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

^e WinNonlin, Pharsight Corporation, Mountain View, CA; One-compartment model with equal first order absorption and elimination and $1/Y_{hat}^2$.

^f WinNonlin, Pharsight Corporation, Mountain View, CA; Two-compartment model with bolus input, first order output, and $1/Y$ weighting.

^g WinNonlin, Pharsight Corporation, Mountain View, CA; Non-compartmental analysis.

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

k_{12} = Distribution rate constant from first to second compartment etc.

k_{21} = Distribution rate constant from second to first compartment etc.

Cl_1 = Clearance of central compartment, Cl_{app} or apparent clearance for intravenous groups

$Cl_{1(F)}$ = 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_2 = Volume of distribution for the peripheral compartment

V_{ss} = Volume of distribution at steady state

$V_{1(F)}$ = 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 ****