

Experiment Number: C96016
Route: Dosed Water, Dosed Water and Gavage Challenge, Gavage, IV
Species/Strain: Rat/Fischer F344

Toxicokinetics Data Summary
Test Compound: Dichloroacetic Acid
CAS Number: 79-43-6

Date Report Requested: 11/09/2016
Time Report Requested: 14:02:25
Lab: Battelle Columbus

Male				
Treatment Groups (mg/kg)				
	2.13 ^a	10 ^b	21.3 ^c	40 ^b
Plasma				
C _{max(pred)} (ug/mL)		0.862 ± 0.090	25.3 ± 2.8	9.58 ± 0.65
T _{max(pred)} (minute)		10.9 ± 0.9	61.3 ± 16.7	29.3 ± 1.4
C _{max(obs)} (ug/mL)	0.135			
T _{max(obs)} (minute)	2.0			
Lambda _z (min ⁻¹)			7.0E-4	
t _{1/2} (minute)			1020.0	
k ₀₁ (min ⁻¹)		0.0916 ± 0.0080	0.0669 ± 0.0294	0.0342 ± 0.0016
t _{1/2(k01)} (minute)		7.57 ± 0.66	10.4 ± 4.6	20.3 ± 0.9
k ₁₀ (min ⁻¹)		0.0916 ± 0.0080	0.00119 ± 0.00213	0.0342 ± 0.0016
t _{1/2(k10)} (minute)		7.57 ± 0.66	581.0 ± 1040.0	20.3 ± 0.9
Cl (mL/min/kg)				
Cl ₁ (mL/min/kg)		391.0 ± 41.0	0.934 ± 1.495	52.5 ± 3.4
V ₁ (mL/kg)				
V _{1(F)} (mL/kg)		4270.0 ± 440.0	783.0 ± 167.0	1540.0 ± 110.0
MRT (minute)				
AUC _{0-t} (ug/mL*min)		22.4	3830.0	700.0
AUC _{inf} (ug/mL*min)		25.6 ± 2.7	36100.0	762.0 ± 50.0

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Male				
	Treatment Groups (mg/kg)			
	42.6 ^d	100 ^b	10 IV ^e	60 IV ^f
Plasma				
C _{max(pred)} (ug/mL)	82.1 ± 4.8	87.3 ± 8.0	31.4 ± 2.0	
T _{max(pred)} (minute)	83.9 ± 9.9	156.0 ± 14.0		
C _{max(obs)} (ug/mL)				
T _{max(obs)} (minute)				
Lambda _z (min ⁻¹)	0.0012			
t _{1/2} (minute)	593.0			
k ₀₁ (min ⁻¹)	0.0494 ± 0.0095	0.00640 ± 5.8E-4		
t _{1/2(k01)} (minute)	14.0 ± 2.7	108.0 ± 10.0		
k ₁₀ (min ⁻¹)	8.42E-4 ± 2.38E-4	0.00640 ± 5.8E-4	0.135 ± 0.005	0.0411
t _{1/2(k10)} (minute)	823.0 ± 232.0	108.0 ± 10.0	5.13 ± 0.21	
Cl (mL/min/kg)			43.0 ± 1.7	
Cl ₁ (mL/min/kg)	0.407 ± 0.090	2.70 ± 0.38		
V ₁ (mL/kg)			318 ± 20	
V _{1(F)} (mL/kg)	484.0 ± 38.0	422.0 ± 39.0		
MRT (minute)			7.40 ± 0.30	
AUC _{0-t} (ug/mL*min)	43200.0	17700.0	229.0	
AUC _{inf} (ug/mL*min)	85700.0	37000.0 ± 5000.0	232 ± 9	

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LEGEND

Data are displayed as mean \pm SEM

MODELING METHOD

- ^a The 2.13 mg/kg group profile was incomplete and, although modeling was possible with WinNonlin Model No. 3, the TK parameters were not considered reliable.
- ^b WinNonlin, Pharsight Corporation, Mountain View, CA; One-compartment model with equal first order absorption and elimination and 1/Yhat2 weighting.
- ^c WinNonlin, Pharsight Corporation, Mountain View, CA; One-compartment model with first order absorption and elimination. Since the terminal linear phases were not fully defined for the 21.3 mg/kg group, elimination parameter estimates using compartmental modeling and non-compartmental analysis (NCA) are reported.
- ^d WinNonlin, Pharsight Corporation, Mountain View, CA; One-compartment model with first order absorption and elimination. Since the terminal linear phases were not fully defined for the 42.6 mg/kg group, elimination parameter estimates using compartmental modeling and non-compartmental analysis (NCA) are reported.
- ^e WinNonlin, Pharsight Corporation, Mountain View, CA; One-compartment model with bolus input, first order output, and 1/Yhat2 weighting.
- ^f TK analysis was not performed on the 60 mg/kg data set because the experimental design only required a partial concentration time profile to be obtained.

ANALYTE

Dichloroacetic acid

TK PARAMETERS

- $C_{\max(\text{pred})}$ = Observed or Predicted Maximum plasma (or tissue) concentration
- $T_{\max(\text{pred})}$ = Time at which C_{\max} predicted or observed occurs
- $C_{\max(\text{obs})}$ = Observed or Predicted Maximum plasma (or tissue) concentration
- $T_{\max(\text{obs})}$ = Time at which C_{\max} predicted or observed occurs
- λ_{z} = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA k_e or k_{elim}
- $t_{1/2}$ = λ_z Half-life, $t_{1/2}$, the terminal elimination half-life based on non-compartmental analysis
- 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 = Clearance of central compartment, Cl_{app} or apparent clearance for intravenous groups
- 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 ****