

Experiment Number: K07378
Route: IV, Gavage, Dosed Water
Gavage Challenge, Dosed Water
Species/Strain: Rats/F344

Toxicokinetics Data Summary
Compound: Bromochloroacetic acid/ **Analyte:** Bromochloroacetic acid

Request Date: 7/11/2023
Request Time: 10:03:16

CAS Number: 5589-96-8

Lab: Battelle Columbus

Male

Treatment Group (mg/kg)

10 IV Plasma^{a,m}

80 IV Plasma^b

Cmax_pred (ug/mL)	20.2 ± 2.1	
k01 Half-life (min)	5.86 ± 0.25	
k10 (min ⁻¹)	0.118 ± 0.005	0.0260
Cl (mL/min/kg)	58.5 ± 4.6	
V1 (mL/kg)	494 ± 52	
MRT (min)	8.46 ± 0.36	
AUCinf_pred (ug/mL*min)	171 ± 13	

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CAS Number: 5589-96-8

Lab: Battelle Columbus

Female

Treatment Group (mg/kg)

10 IV Plasma^{a,m}

80 IV Plasma^b

Cmax_pred (ug/mL)	25.6 ± 3.2	
k01 Half-life (min)	5.54 ± 0.27	
k10 (min ⁻¹)	0.125 ± 0.006	0.0279
Cl (mL/min/kg)	48.7 ± 4.7	
V1 (mL/kg)	390 ± 49	
MRT (min)	8.00 ± 0.39	
AUCinf_pred (ug/mL*min)	205 ± 20	

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Male

Treatment Group (mg/kg)

10 Gavage Plasma^c

40 Gavage Plasma^d

100 Gavage Plasma^e

Cmax_pred (ug/mL)	0.475 ± 0.031	6.74 ± 0.33	28.1 ± 1.9
Tmax_pred (min)	21.9 ± 1.9	53.2 ± 2.6	61.4 ± 3.4
Cmax_obs (ug/mL)	0.532 ± 0.029	7.91 ± 0.73	38.5 ± 2.1
Tmax_obs (min)	15.0	60.0	45.0
k01 (min ⁻¹)	0.0457 ± 0.0039	0.0188 ± 0.0009	0.0163 ± 0.0009
k01 Half-life (min)	15.2 ± 1.3	36.9 ± 1.8	42.5 ± 2.3
k10 (min ⁻¹)	0.0457 ± 0.0039	0.0188 ± 0.0009	0.0163 ± 0.0009
k10 Half-life (min)	15.2 ± 1.3	36.9 ± 1.8	42.5 ± 2.3
Cl _{1_F} (mL/min/kg)	354 ± 37	41.0 ± 2.5	21.3 ± 1.8
V _{1_F} (mL/kg)	7750 ± 510	2180 ± 110	1310 ± 90
AUC _{0-T} (ug/ml*min)	25.5	1090	4920
AUC _{inf_pred} (ug/mL*min)	28.2 ± 3.0	976 ± 61	4690 ± 390

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Female

Treatment Group (mg/kg)

10 Gavage Plasma^c

40 Gavage Plasma^d

100 Gavage Plasma^e

Cmax_pred (ug/mL)	0.599 ± 0.026	11.6 ± 0.7	44.7 ± 3.0
Tmax_pred (min)	17.8 ± 1.1	45.4 ± 2.6	58.0 ± 3.3
Cmax_obs (ug/mL)	0.638 ± 0.052	11.1 ± 0.7	54.0 ± 4.4
Tmax_obs (min)	15.0	20.0	45.0
k01 (min ⁻¹)	0.0560 ± 0.0035	0.0220 ± 0.0013	0.0172 ± 0.0010
k01 Half-life (min)	12.4 ± 0.8	31.5 ± 1.8	40.2 ± 2.3
k10 (min ⁻¹)	0.0560 ± 0.0035	0.0220 ± 0.0013	0.0172 ± 0.0010
k10 Half-life (min)	12.4 ± 0.8	31.5 ± 1.8	40.2 ± 2.3
Cl1_F (mL/min/kg)	344 ± 26	27.9 ± 2.1	14.2 ± 1.2
V1_F (mL/kg)	6140 ± 270	1270 ± 80	822 ± 56
AUC_0-T (ug/ml*min)	33.0	1290	5600
AUCinf_pred (ug/mL*min)	29.1 ± 2.2	1430 ± 110	7050 ± 600

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CAS Number: 5589-96-8

Lab: Battelle Columbus

Male

Treatment Group (mg/kg)

**2.88 Dosed Water and
Gavage Challenge Plasma^f**

**28.8 Dosed Water and
Gavage Challenge Plasma^f**

**57.6 Dosed Water and
Gavage Challenge Plasma^f**

Cmax_pred (ug/mL)	0.248 ± 0.025	10.7 ± 0.7	25.4 ± 5.7
Tmax_pred (min)	14.2 ± 4.0	29.4 ± 3.0	21.0 ± 11.1
Cmax_obs (ug/mL)	0.352 ± 0.036	10.9 ± 0.6	43.8 ± 25.7
Tmax_obs (min)	15.0	15.0	15.0
k01 (min ⁻¹)	0.224 ± 0.115	0.0709 ± 0.0138	0.145 ± 0.114
k01 Half-life (min)	3.09 ± 1.58	9.78 ± 1.90	4.78 ± 3.76
k10 (min ⁻¹)	0.0107 ± 0.0058	0.0128 ± 0.0010	0.00814 ± 0.00170
k10 Half-life (min)	64.8 ± 35.3	54.1 ± 4.3	85.2 ± 17.7
Cl1_F (mL/min/kg)	107 ± 41	23.6 ± 1.4	15.6 ± 2.9
V1_F (mL/kg)	9990 ± 1890	1840 ± 210	1910 ± 570
AUC_0-T (ug/mL*min)	9.56	1200	3770
AUCinf_pred (ug/mL*min)	26.9 ± 3.58	1220 ± 2.4	3700 ± 12.2

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Request Date: 7/11/2023
Request Time: 10:03:16

CAS Number: 5589-96-8

Lab: Battelle Columbus

Female

Treatment Group (mg/kg)

**2.7 Dosed Water and
Gavage Challenge Plasma^f**

**27.4 Dosed Water and
Gavage Challenge Plasma^f**

**54.9 Dosed Water and
Gavage Challenge Plasma^f**

Cmax_pred (ug/mL)	0.412 ± 0.026	12.9 ± 1.5	31.5 ± 3.4
Tmax_pred (min)	15.4 ± 1.6	23.5 ± 4.8	23.7 ± 4.9
Cmax_obs (ug/mL)	0.410 ± 0.050	15.0 ± 5.9	44.3 ± 8.6
Tmax_obs (min)	20.0	15.0	30.0
k01 (min ⁻¹)	0.154 ± 0.038	0.102 ± 0.036	0.111 ± 0.036
k01 Half-life (min)	4.49 ± 1.10	6.82 ± 2.40	6.27 ± 2.06
k10 (min ⁻¹)	0.0193 ± 0.0047	0.0125 ± 0.0015	0.0103 ± 0.0009
k10 Half-life (min)	36.0 ± 8.8	55.5 ± 6.7	67.3 ± 5.7
Cl1_F (mL/min/kg)	95.3 ± 11.9	19.8 ± 1.9	14.1 ± 1.4
V1_F (mL/kg)	4940 ± 710	1590 ± 280	1370 ± 200
AUC_0-T (ug/mL*min)	17.5	1260	3660
AUCinf_pred (ug/mL*min)	28.7 ± 1.3	1380 ± 4.7	3900 ± 6.9

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CAS Number: 5589-96-8

Lab: Battelle Columbus

Male

Treatment Group (mg/kg)

2.88 Dosed Water Plasma^g 28.8 Dosed Water Plasma^h 57.6 Dosed Water Plasma^h

Cmax_obs (ug/mL)	0.0801	2.66	5.17
Tmax_obs (hour)	24	24	24

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CAS Number: 5589-96-8

Lab: Battelle Columbus

Female

Treatment Group (mg/kg)

2.7 Dosed Water Plasma^g

27.4 Dosed Water Plasma^h

54.9 Dosed Water Plasma^h

Cmax_obs (ug/mL)	0.189	3.84	7.36
Tmax_obs (hour)	24	15	24

Experiment Number: K07378

Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Bromochloroacetic acid/ Analyte: Bromochloroacetic acid minus Isomer

Request Time: 10:03:16

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

Male

Treatment Group (mg/kg)

10 IV Plasma^{i,n}

80 IV Plasmaⁱ

NO DATA RECORDED

Lambda_z (min ⁻¹)	0.236	
Half-life (min)	2.94	
Cl (mL/min/kg)	126	
V1 (mL/kg)	534	
MRT (min)	3.10	
AUC_0-T (ug/mL*min)	79.0	
AUCinf_pred (ug/mL*min)	79.4	

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Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Bromochloroacetic acid/ Analyte: Bromochloroacetic acid minus Isomer

Request Time: 10:03:16

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

Female

Treatment Group (mg/kg)

10 IV Plasma^{i,n}

80 IV Plasma^j

NO DATA RECORDED

Lambda_z (min ⁻¹)	0.314	
Half-life (min)	2.21	
Cl (mL/min/kg)	206	
V1 (mL/kg)	656	
MRT (min)	2.57	
AUC_0-T (ug/mL*min)	46.7	
AUCinf_pred (ug/mL*min)	48.5	

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Toxicokinetics Data Summary

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Gavage Challenge, Dosed Water

Compound: Bromochloroacetic acid/ Analyte: Bromochloroacetic acid plus Isomer

Request Time: 10:03:16

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

Male

Treatment Group (mg/kg)

10 IV Plasma^k

80 IV Plasma^{lo}

NO DATA RECORDED

Cmax_pred (ug/mL)	21.6 ± 5.4	
Alpha Half-life (min)	1.96 ± 0.76	
Beta Half-life (min)	9.48 ± 0.51	
k10 (min ⁻¹)	0.156 ± 0.033	
k10 Half-life (min)	4.46 ± 0.96	
K12 (min ⁻¹)	0.105 ± 0.072	
K21 (min ⁻¹)	0.166 ± 0.044	
Cl1 (mL/min/kg)	71.9 ± 4.3	
V1 (mL/kg)	462 ± 116	
V2 (mL/kg)	291 ± 75	
MRT (min)	10.5 ± 0.5	
AUC_0-T (ug/mL*min)	143	
AUCinf_pred	139 ± 8	

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Toxicokinetics Data Summary

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CAS Number: 5589-96-8

Request Date: 7/11/2023

Request Time: 10:03:16

Lab: Battelle Columbus

Female

Treatment Group (mg/kg)

10 IV Plasma^k

80 IV Plasma^{l,o}

NO DATA RECORDED

Cmax_pred (ug/mL)	13.5 ± 1.0	
Alpha Half-life (min)	4.99 ± 0.50	
Beta Half-life (min)	13.7 ± 3.9	
k10 (min ⁻¹)	0.126 ± 0.007	
k10 Half-life (min)	5.52 ± 0.30	
k12 (min ⁻¹)	0.00795 ± 0.00352	
K21 (min ⁻¹)	0.0562 ± 0.0189	
Cl1 (mL/min/kg)	92.9 ± 3.4	
V1 (mL/kg)	739 ± 54	
V2 (mL/kg)	105 ± 16	
MRT (min)	9.08 ± 0.35	
AUCinf_pred	108 ± 4	

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Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

LEGEND

MODELING SOFTWARE

WinNonlin, Version 4.0, 5.0, 5.0.1

WinNonlin Pharsight Corp.

Graphical Analysis

MODELING METHOD & BEST FIT MODEL

^aWinNonlin, Pharsight Corp., One-compartment model with bolus input, first order output, and 1/Y^{hat} weighting. Parameter estimates are reported to three significant figures.

^bGraphical Analysis, For the 80 mg/kg IV male and female rat groups, the partial BCA plasma concentration time data was evaluated using graphical analysis.

^cWinNonlin Pharsight Corp., One-compartment model with equal first order absorption and elimination no weighting. Model 5 where k_a equals k_e (a one-compartment model with equal first order absorption and elimination). Parameter estimates and SEM are reported to three significant figures. GXA and OXA plasma concentration time point data were not presented because all values were BLOQ (4.209 ug/mL GXA and 4.192 ug/mL OXA).

^dWinNonlin Pharsight Corporation, One-compartment model with equal first order absorption and elimination 1/Y weighting. Model 5 where k_a equals k_e (a one-compartment model with equal first order absorption and elimination). Parameter estimates and SEM are reported to three significant figures. GXA and OXA plasma concentration time point data were not presented because all values were BLOQ (4.209 ug/mL GXA and 4.192 ug/mL OXA).

^eWinNonlin Pharsight Corporation, One-compartment model with equal first order absorption and elimination 1/Y^{hat} weighting. Model 5 where k_a equals k_e (a one-compartment model with equal first order absorption and elimination). Parameter estimates and SEM are reported to three significant figures. GXA and OXA plasma concentration time point data were not presented because all values were BLOQ (4.209 ug/mL GXA and 4.192 ug/mL OXA).

^fWinNonlin, version 4.0, 5.0, or 5.0.1, Pharsight Corporation, Mountain View, CA, One-compartment model with first order absorption and elimination. Parameter estimates and SEM are reported to three significant figures.

^gWinNonlin, version 4.0, 5.0, or 5.0.1, Pharsight Corporation, Mountain View, CA, No kinetic modeling was possible for the non-challenge group animals. Almost all the BCA plasma concentration values were BLOQ of 0.0750 ug/mL. GXA and OXA plasma concentrations were BLOQ or not detected.

Experiment Number: K07378

Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

MODELING METHOD & BEST FIT MODEL

^hWinNonlin, version 4.0, 5.0, or 5.0.1, Pharsight Corporation, Mountain View, CA, No extensive TK analysis was performed for the non-challenge group data, however, non-compartmental analysis was used to determine C_{max} and AUC values for the mid and high dose BCA groups for the purpose of examining dose proportionality. No kinetic modeling was possible for the non-challenge group animals for GXA and OXA. The plasma concentrations of GXA and OXA were either BLOQ (4.349 and 4.169 µg/mL, respectively), or not detected, for all dosage groups.

ⁱWinNonlin Pharsight Corp., Noncompartmental analysis using the mean plasma concentration time. The BCA minus isomer was eliminated much faster than BCA plus isomer for rats and mice.

^jWinNonlin Pharsight Corp., The half-life values for the BCA minus isomer could not be determined because the test chemical was eliminated very quickly from the systemic circulation which only allowed detection of the BCA minus isomer concentration in plasma at the first time point.

^kWinNonlin Pharsight Corp., Two-compartment model with bolus input, first order output, and 1/Y² weighting. The BCA minus isomer was eliminated much faster than BCA plus isomer for rats and mice.

^lWinNonlin Pharsight Corp., Noncompartmental analysis BCA (+) terminal decay phase half-life is 26.9 min (male rat)

EXCEPTIONS

^mV₁ represents V_d

ⁿCl represents Cl_{app}, V₁ represents V_z. Noncompartmental TK analysis was performed on the 10 mg/kg data sets for the BCA (-) isomer because the data were not sufficient for compartmental modeling.

^oNoncompartmental TK analysis was performed on the 80 mg/kg data set because the experimental design only required a partial concentration time profile to be determined. Only half-life values for the terminal linear phases were presented in this report for the high dosage group data sets.

ANALYTE

Bromochloroacetic acid

Bromochloroacetic acid minus Isomer

Bromochloroacetic acid plus Isomer

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Dosed Water

Compound: Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

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TK PARAMETERS

Cmax_pred = Observed or Predicted Maximum plasma (or tissue) concentration

Tmax_pred = Time at which Cmax predicted or observed occurs

Cmax_obs = Observed or Predicted Maximum plasma (or tissue) concentration

Tmax_obs = Time at which Cmax 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}

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

Cl = Clearance, includes total clearance

Cl1 = Clearance of central compartment, Cl_{app} 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 V_d and V volume of distribution, V_z apparent volume of distribution NCA,
 V_{app} 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 $V_{d,F}$, 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}

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

λ_z = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA k_e or k_{elim}

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Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. Three animals/sex/species were bled at each time point. Blood collection times are 0, 2, 5, 10, 20, 40, 75, 90, and 120 minutes. The plasma samples were analyzed by gas chromatography-flame ionization detection (GC-FID) system. The level of detection for Bromochloroacetic acid in plasma from the IV groups was 0.07445 ug/mL. Plasma and urine concentration time point values were reported to at least three significant figures.

TK_INTRAVENTOUS PLASMA

10 mg/kg Male and Female (Analyte: Bromochloroacetic acid)

Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were administered a single IV dose through an implanted jugular catheter.

ANALYSIS METHOD

Blood was collected for BCA analysis at 60, 120, and 180 minutes from 5 animals (3 animals per time point). Blood was collected twice from same animal. Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. The plasma samples were analyzed by gas chromatography-flame ionization detection (GC-FID) system. The level of detection for Bromochloroacetic acid in plasma from the IV groups was 0.07445 ug/mL. Plasma and urine concentration time point values were reported to at least three significant figures.

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Compound: Bromochloroacetic acid

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Species/Strain: Rats/F344

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

CAS Number: 5589-96-8

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TK PARAMETERS PROTOCOL (cont'd)

80 mg/kg Male (Analyte: Bromochloroacetic acid)

Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were administered a single IV dose through an implanted jugular catheter.

ANALYSIS METHOD

Blood was collected for BCA analysis at 60, 120, and 180 minutes from 5 animals (3 animals per time point). Blood was collected twice from same animal. Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. The plasma samples were analyzed by gas chromatography-flame ionization detection (GC-FID) system.

80 mg/kg Female (Analyte: Bromochloroacetic acid)

Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were administered a single IV dose through an implanted jugular catheter.

ANALYSIS METHOD

Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. Three animals/sex/species were bled at each time point. Blood collection times are 0, 2, 5, 10, 15, 20, 45, 60, 90, 120, and 180 minutes. The plasma samples were analyzed by high performance liquid chromatography- ultraviolet detection, HPLC-UVD. The LOQ for BCA in plasma for the rat gavage group samples was 0.07316 ug/mL. Plasma and urine concentration time point values were reported to at least three significant figures.

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Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Bromochloroacetic acid

Request Time: 10:03:16

Species/Strain: Rats/F344

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

CAS Number: 5589-96-8

Lab: Battelle Columbus

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE PLASMA

10mg/kg Male and Female (Analyte: Bromochloroacetic acid)

Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were administered a single gavage dose.

ANALYSIS METHOD

Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. Three animals/sex/species were bled at each time point. Blood collection times are 0, 2, 5, 10, 15, 20, 45, 60, 90, 120, 180, 240, and 360 minutes. The plasma samples were analyzed by high performance liquid chromatography- ultraviolet detection, HPLC-UVD. The LOQ for BCA in plasma for the rat gavage group samples was 0.07316 ug/mL. Plasma and urine concentration time point values were reported to at least three significant figures.

TK_GAVAGE PLASMA

40 mg/kg Male and Female (ANALYTE: Bromochloroacetic acid)

Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were administered a single gavage dose. There was no TK analysis for the urine mid-level dose gavage groups because no plasma samples were taken from the separate group of animals from which urine samples were collected.

Experiment Number: K07378

Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Bromochloroacetic acid

Request Time: 10:03:16

Species/Strain: Rats/F344

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

CAS Number: 5589-96-8

Lab: Battelle Columbus

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. Three animals/sex/species were bled at each time point. Blood collection times are 0, 2, 5, 10, 15, 20, 45, 90, 180, 270, 360, and 420 minutes. The plasma samples were analyzed by high performance liquid chromatography- ultraviolet detection, HPLC-UVD. The LOQ for BCA in plasma for the rat gavage group samples was 0.07316 ug/mL. Plasma and urine concentration time point values were reported to at least three significant figures.

TK_GAVAGE PLASMA

100 mg/kg Male and Female (ANALYTE: Bromochloroacetic acid)

Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were administered a single gavage dose. There was no TK analysis for the urine high-level dose gavage groups because no plasma samples were taken from the separate group of animals from which urine samples were collected.

ANALYSIS METHOD

For the challenge Drinking Water Study groups, exposure continued up through the fourteenth day of exposure and, on the 14th day of exposure (Study Day 14), the BCA treated drinking water was replaced by untreated water (control tap water), which the animals were exposed to overnight prior to being given a single gavage administration on Day 15. Three animals/sex/species were bled at each time point. Blood collection times are 2, 5, 10, 15, 20, 30, 45, and 60 minutes. Samples were analyzed using a validated capillary gas chromatography (GC) method with electron capture detection (ECD) for BCA. LOQ for BCA in plasma and urine was 0.0750 µg/mL.

Experiment Number: K07378

Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Sodium Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

TK PARAMETERS PROTOCOL (cont'd)

TK_DOSED WATER AND GAVAGE CHALLENGE PLASMA

2.88 mg/kg Male, 2.7 mg/kg Female (ANALYTE: Bromochloroacetic acid)

Listed date of first exposure is Day 15 gavage dose date. Day 1 Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were dosed for two weeks from dosed drinking water available ad libitum. These animals were also challenged with a gavage dose on study day 15.

ANALYSIS METHOD

For the challenge Drinking Water Study groups, exposure continued up through the fourteenth day of exposure and, on the 14th day of exposure (Study Day 14), the BCA treated drinking water was replaced by untreated water (control tap water), which the animals were exposed to overnight prior to being given a single gavage administration on Day 15. Three animals/sex/species were bled at each time point. Blood collection times are 5, 10, 15, 30, 60, 120, 180, and 240 minutes. Samples were analyzed using a validated capillary gas chromatography (GC) method with electron capture detection (ECD) for BCA. LOQ for BCA in plasma and urine was 0.0750 µg/mL.

TK_DOSED WATER AND GAVAGE CHALLENGE PLASMA

28.8 mg/kg Male and 27.4 mg/kg Female (ANALYTE: Bromochloroacetic acid)

Listed date of first exposure is Day 15 gavage dose date. Day 1 Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were dosed for two weeks from dosed drinking water available ad libitum. These animals were also challenged with a gavage dose on study day 15.

Experiment Number: K07378

Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Sodium Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

For the challenge Drinking Water Study groups, exposure continued up through the fourteenth day of exposure and, on the 14th day of exposure (Study Day 14), the BCA treated drinking water was replaced by untreated water (control tap water), which the animals were exposed to overnight prior to being given a single gavage administration on Day 15. Three animals/sex/species were bled at each time point. Blood collection times are 5, 10, 15, 30, 60, 120, 240, and 360 minutes. Samples were analyzed using a validated capillary gas chromatography (GC) method with electron capture detection (ECD) for BCA. LOQ for BCA in plasma and urine was 0.0750 µg/mL.

TK_DOSED WATER AND GAVAGE CHALLENGE PLASMA

57.6 mg/kg Male and 54.9 mg/kg Female (ANALYTE: Bromochloroacetic acid)

Listed date of first exposure is Day 15 gavage dose date. Day 1 Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were dosed for two weeks from dosed drinking water available ad libitum. These animals were also challenged with a gavage dose on study day 15.

ANALYSIS METHOD

For the non-challenge Drinking Water Study groups, Bromochloroacetic acid (BCA) exposure continued through the fourteenth day of exposure and into the fifteenth day of exposure, so that beginning on the fourteenth day of exposure (Study Day 14), this group of rats and mice had blood samples collected over a 21-hour period beginning at 9:00 am on Day 14. Plasma was collected at 8 time points every 3 hours (180 minutes) Collection times were 9 AM (Day 14), 12 PM, 3 PM, 6 PM, 9 PM, 12 AM (Day 15), 3 AM, 6 AM. For the rats the glyoxylic acid (GXA) and oxalic acid (OXA) plasma concentrations were either below the level of quantitation (BLOQ) or not detected at all dosing concentrations.

Experiment Number: K07378

Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Sodium Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

TK PARAMETERS PROTOCOL (cont'd)

TK_DOSED WATER

2.88 mg/kg, 28.8 mg/kg, 57.6 mg/kg Male and 2.7 mg/kg, 27.4, 54.9 mg/kg Female (ANALYTE: Bromochloroacetic acid)

Day 1 Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were dosed for two weeks from dosed drinking water available ad libitum.

ANALYSIS METHOD

Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. Three animals/sex/species were bled at each time point. Blood collection times are 0, 2, 5, 10, 20, 40, 60, 75, 90, and 120 minutes. The plasma samples were analyzed by gas chromatography-electron capture detection (GC-ECD) system. The target LOQ for plus and minus bromochloroacetic acid isomers in rat and mouse plasma samples was 0.03750 ug/mL. The actual LOQ ranged from 0.03620 to 0.03924 ug/mL. Plasma and urine concentration time point values were reported to at least three significant figures.

TK_INTRAVENTOUS PLASMA

10 mg/kg Male and Female (ANALYTE: Bromochloroacetic acid_plus_isomer & Bromochloroacetic acid_minus_isomer)

Day 1 Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were given a single bolus intravenous injection through an indwelling jugular catheter.

Experiment Number: K07378

Toxicokinetics Data Summary

Request Date: 7/11/2023

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

Compound: Sodium Bromochloroacetic acid

Request Time: 10:03:16

Analyte: Bromochloroacetic acid, Bromochloroacetic acid plus Isomer, Bromochloroacetic acid minus Isomer

Species/Strain: Rats/F344

CAS Number: 5589-96-8

Lab: Battelle Columbus

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

Rat blood samples were collected using the retro-orbital method. Animals were anesthetized with CO₂/O₂ prior to bleeding. Three animals/sex/species were bled at each time point. Four out of five animals were bled twice (n equals 5 animals). Blood collection times are 60, 120, and 180 minutes. The plasma samples were analyzed by gas chromatography-electron capture detection (GC-ECD) system. The target LOQ for plus and minus bromochloroacetic acid isomers in rat and mouse plasma samples was 0.03750 ug/mL. The actual LOQ ranged from 0.03620 to 0.03924 ug/mL. Plasma and urine concentration time point values were reported to at least three significant figures.

TK_INTRAVENOUS PLASMA

80 mg/kg Male and Female (ANALYTE: Bromochloroacetic acid_plus_isomer & Bromochloroacetic_acid_minus_isomer)

Day 1 Mean weights are based on animals available for use prior to dosing and does not take into account substituted animals. Animals were given a single bolus intravenous injection through an indwelling jugular catheter.