

Experiment Number: K13111
Route: Intravenous, Oral Gavage
Species/Strain: Rat/Harlan Sprague-Dawley

Toxicokinetics Data Summary
Compound & Analyte: 2-(2H-Benzotriazol-2-yl) phenol
CAS Number: 10096-91-0

Request Date: 3/12/2021
Request Time: 2:30:16
Lab: BAT

Male

Treatment Group (mg/kg)

	2.25 IV ^a Blood	30 Gav ^b Blood	300 Gav ^b Blood
C ₀ min_pred (ng/mL)	866 ± 46		
C _{max} _pred (ng/mL)		69.7 ± 12.7	237 ± 56
T _{max} _pred (hour)		0.862 ± 0.300	1.49 ± 0.36
C _{max} _obs (ng/mL)	790	77.1	273
T _{max} _obs (hour)		0.750	0.750
Alpha_Half-life (hour)	0.117 ± 0.006	0.407 ± 25.7	1.15 ± 2.40
Beta_Half-life (hour)	0.964 ± 0.074	1.57 ± 0.78	192 ± 562
Gamma_Half-life (hour)	22.4 ± 4.4		
k ₀₁ (hour ⁻¹)		2.02 ± 64.9	0.794 ± 1.77
k ₀₁ _Half-life (hour)		0.344 ± 11.1	0.872 ± 1.94
k ₁₀ (hour ⁻¹)	3.12 ± 0.17	0.527 ± 16.9	0.0820 ± 0.288
k ₁₀ _Half-life (hour)	0.222 ± 0.012	1.32 ± 42.1	8.46 ± 29.6
k ₁₂ (hour ⁻¹)	1.38 ± 0.12	0.188 ± 45.7	0.496 ± 1.03
k ₂₁ (hour ⁻¹)	0.995 ± 0.085	1.43 ± 45.7	0.0264 ± 0.0227
k ₁₃ (hour ⁻¹)	1.12 ± 0.09		
k ₃₁ (hour ⁻¹)	0.0423 ± 0.0073		
Cl ₁ (mL/hr/kg)	7920 ± 290		
Cl ₂ (mL/hr/kg)	3510 ± 270		
Cl ₃ (mL/hr/kg)	2850 ± 240		
Cl ₁ _F (mL/hr/kg)		133000 ± 20000	44600 ± 99200
Cl ₂ _F (mL/hr/kg)		47400 ± 9990000	270000 ± 112000
V ₁ (mL/kg)	2540 ± 130		
V ₂ (mL/kg)	3530 ± 310		
V ₃ (mL/kg)	67400 ± 16300		
V ₁ _F (mL/kg)		252000 ± 8040000	544000 ± 1150000
V ₂ _F (mL/kg)		33100 ± 5940000	1020000 ± 10900000

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Treatment Group (mg/kg)

	2.25 IV^a Blood	30 Gav^b Blood	300 Gav^b Blood
MRT (hour)	9.27 ± 2.35		
AUC _{0-T} (ng/mL·hr)	258	216	2160
AUC _{inf} (ng/mL·hr)	284 ± 10	226 ± 34	6720 ± 14900

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LEGEND

MODELING METHOD & BEST FIT MODEL

^a WinNonlin three-compartment model with bolus input, first order output, and $1/Y_{\text{hat}}^2$ weighting (model #18); Cmax_pred based on the model prediction at 0 minutes.

^b WinNonlin two-compartment model with first order input, first order output, and $1/Y_{\text{hat}}^2$ weighting (model #13).

ANALYTE

2-(2H-Benzotriazol-2-yl)phenol

TK PARAMETERS

C_{0min_pred} = Fitted plasma concentration at time zero (IV only)

C_{max_obs} = Observed maximum plasma concentration

C_{max_pred} = Predicted maximum plasma concentration

T_{max_obs} = Time at which observed C_{max} occurs

T_{max_pred} = Time at which predicted C_{max} occurs

Alpha_Half-life = Half-life for the alpha phase

Beta_Half-life = Half-life for the beta phase

Gamma Half-life = Half-life for the gamma phase

k₀₁ = Absorption rate constant, k_a

k_{01_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}

k_{10_Half-life} = Half-life for the elimination process from the central compartment

k₁₂ = Distribution rate constant from first to second compartment

k₂₁ = Distribution rate constant from second to first compartment

k₁₃ = Distribution rate constant from first to third compartment

k₃₁ = Distribution rate constant from third to first compartment

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TK PARAMETERS (cont'd)

Cl1 = Clearance of central compartment

Cl2 = Clearance of the secondary compartment

Cl3 = Clearance of the tertiary compartment

Cl1_F = Apparent clearance of the central compartment, also Cl_F for gavage groups in non-compartmental model

Cl2_F = Apparent clearance of the secondary compartment

V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution

V2 = Volume of distribution for the peripheral compartment

V3 = Volume of distribution for the peripheral compartment

V1_F = Apparent volume of distribution for the central compartment includes Vd_F, V_F for oral groups, and Vc_F

V2_F = Apparent 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

AUC_inf = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

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TK PARAMETERS PROTOCOL

BLOOD

IV 2.25 Rat Male

Harlan Sprague Dawley male rats were intravenously administered a single 2.25 mg/kg dose of 2-(2H-benzotriazol-2-yl)phenol (PBZT). An automated blood sampling system (Culex) was used for this study. Whole blood samples were taken from n=3 animals/timepoint/per group at pre-dose and 16 timepoints at 0.0333, 0.0833, 0.167, 0.25, 0.333, 0.5, 0.75, 1, 2, 4, 8, 12, 18, 24, 48, and 72 hrs. Parent (free) was analyzed by LC-MS/MS with a lower limit of quantitation (LLOQ) of 2.0 ng/mL. Parameter estimates are reported to three significant figures with standard error (SE). Observed values do not have a reported SE.

BLOOD

Gavage 30 Rat Male, 300 Rat Male

Harlan Sprague Dawley male rats were administered a single gavage dose of 30 or 300 mg/kg 2-(2H-benzotriazol-2-yl)phenol (PBZT). An automated blood sampling system (Culex) was used for this study. Whole blood samples were taken from n=3 animals/timepoint/per group at pre-dose and 16 timepoints at 0.0333, 0.0833, 0.167, 0.25, 0.333, 0.5, 0.75, 1, 2, 4, 8, 12, 18, 24, 48, and 72 hrs. Parent (free) was analyzed by LC-MS/MS with a lower limit of quantitation (LLOQ) of 2.0 ng/mL. Parameter estimates are reported to three significant figures with standard error (SE). Observed values do not have a reported SE.