Experiment Number: S0548   **Toxicokinetics Data Summary**   **Request Date:** 7/11/2023
Route: IV, Gavage   **Compound:** Sodium Nitrite / **Analyte:** Nitrite   **Request Time:** 10:03:16
Species/Strain: Rats/Fischer 344   **CAS Number:** 7632-00-0   **Lab:** Midwest Research Institute

Male

Treatment Group (mg/kg)

	20 IV Plasma[b]	40 Gavage Plasma[a]	80 Gavage Plasma[a]
Cmax_pred (ug/mL)	2.5	11	35
Tmax_pred (min)		8.8	17
Alpha Half-life (min)	1.5	NA	NA
Beta Half-life (min)	52	NA	NA
k01 Half-life (min)		79	2.9
k10 Half-life (min)	9.1	1.5	144
k12 (min^{-1})	0.32		
K21 (min^{-1})	0.081		
V1 (mL)	91	15	1400
AUCinf_pred (ug min/mL)	454	308	2550
F (percent)		34	140

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Female

Treatment Group (mg/kg)

	20 IV Plasma[a]	40 Gavage Plasma[a]	80 Gavage Plasma[a]
Cmax_pred (ug/mL)	11	12	32
Tmax_pred (min)		13	28
k01 Half-life (min)		3.7	8.4
k10 Half-life (min)	49	35	60
V1 (mL)	200	140	250
AUCinf_pred (ug min/mL)	796	770	3840
F (percent)		52	130

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LEGEND
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MODELING SOFTWARE
  PCNONLIN

MODELING METHOD & BEST FIT MODEL
  [a]PCNONLIN Statistical Consultants, Inc., Lexington, KY, One compartment model
  [b]PCNONLIN Statistical Consultants, Inc., Lexington, KY, Two compartmental model

ANALYTE
  Nitrite

TK PARAMETERS

  C_{max_pred} = Observed or Predicted Maximum plasma (or tissue) concentration
  T_{max_pred} = Time at which Cmax predicted or observed occurs
  Alpha Half-life = Half-life for the alpha phase
  Beta Half-life = Half-life for the beta phase
  k01 Half-life = Half-life of the absorption process to the central compartment
  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
  V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution, Vz apparent volume of distribution NCA,
      Vapp apparent volume of distribution for intravenous studies
  AUC_{inf_pred} = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity
  F = Bioavailability, absolute bioavailability

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TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Blood collection time points for this group are 2, 5, 10, 20, 30, 45, 60, 75, 90, and 120 minutes post-dose.

TK_INTRAVENOUS PLASMA

20 mg/kg Male and Female

A single intravenous dose of 20 mg/kg was given per study via lateral tail vein. Toxicokinetic analyses were performed using the average concentration for each time point. The data were modeled using nonlinear regression analysis (PCNONLIN, Statistical Consultants, Inc., Lexington, KY). The nitrite data was modeled using compartmental models.

ANALYSIS METHOD

Blood collection time points for this group are 2, 5, 10, and 30 minutes, 1, 2, 4, 6, 8, and 10 hours post-dose.

TK_GAVAGE PLASMA

40 mg/kg, Male and Female

A single oral gavage dose of 40 mg/kg was given per study. Toxicokinetic analyses were performed using the average concentration for each time point. The data were modeled using nonlinear regression analysis (PCNONLIN, Statistical Consultants, Inc., Lexington, KY). The nitrite data was modeled using compartmental models.

Experiment Number: S0548
Route: IV, Gavage
Species/Strain: Rats/Fischer 344

Toxicokinetics Data Summary
Compound: Sodium Nitrite / **Analyte:** Nitrite
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Request Date: 7/11/2023
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Lab: Midwest Research Institute

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

Blood collection time points for this group are 2, 5, 10, and 30 minutes, 1, 2, 4, 6, 8, and 10 hours post-dose.

TK_GAVAGE PLASMA

<u>80 mg/kg, Male and Female</u>

A single oral gavage dose of 80 mg/kg was given per study. Toxicokinetic analyses were performed using the average concentration for each time point. The data were modeled using nonlinear regression analysis (PCNONLIN, Statistical Consultants, Inc., Lexington, KY). The nitrite data was modeled using compartmental models.