

Experiment Number: K00284
Route: Intravenous
Species/Strain: Rats/Fischer 344

Toxicokinetics Data Summary
Compound: Carbon disulfide/ **Analyte:** Free Carbon disulfide
CAS Number: 75-15-0

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: NIEHS Midwest
Research Institute

Male

Treatment Group (mg/kg)

10 IV Blood^{a,b}

50 IV Blood^{a,b}

	10 IV Blood ^{a,b}	50 IV Blood ^{a,b}
Cmax (ug/g)	21.4	54.8
Alpha Half-life (minute)	1.2	1.3
Beta Half-life (minute)	32.6	23.6
k10 (minute ⁻¹)	0.21	0.13
k10 Half-life (minute)	3.3	5.3
k12 (minute ⁻¹)	0.32	0.31
k21 (minute ⁻¹)	0.06	0.12
Cl (mL/min)	97.1	119
V1 (mL)	468	912
MRT (minute)	32	27
AUCinf_pred (ug*min/mL)	103	422

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LEGEND

MODELING SOFTWARE
PCNONLIN

MODELING METHOD & BEST FIT MODEL

^a nonlinear regression analysis using PCNONLIN, Statistics Consultants, Inc., Lexington, KY, linear two-compartment model

EXCEPTION

^b V1 represent Vc, Volume of distribution of the central compartment

ANALYTE

Free Carbon disulfide

TK PARAMETERS

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

Alpha Half-Life = Half-life for the alpha phase

Beta Half-Life = Half-life for the beta phase

k10 = Elimination rate constant from the central compartment also ke or kelim

k10 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

Cl = Clearance, includes total clearance

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

Vss = Volume of distribution at steady state

MRT = Mean Residence Time

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

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TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Toxicokinetic analyses were performed using the averaged concentrations (3 rats/timepoint/dose) for the free CS₂ determinations. Blood was collected at 7 timepoints from 3-120 minutes, Compartmental modeling was calculated using nonlinear regression analysis (PCNONLIN, Statistical Consultants, Lexington, KY). A two-compartment model using an unweighted regression was fit to the data. The observed and predicted values showed good correlation (0.999). Toxicokinetic analyses were not performed on the data from assays for total CS₂ because the results of the quality control samples indicated that standards could not be prepared in the water media used for dilution.

TK_INTRAVENTOUS BLOOD

10 mg/kg, 50 mg/kg

Cannulated rats were given carbon disulfide via the lateral tail vein. Blood samples were collected from each of 3 rats via the implanted cannula at 3, 5, 10, 20, 40, 60, 120, and 240 minutes after dosing. The carbon disulfide concentration in samples taken after 120 minutes was below the limit of quantification of the analytical method. Animals were dosed and blood samples were collected at one laboratory and the blood samples were shipped to a second laboratory for analysis. Blood specimens were analyzed for free carbon disulfide with a validated method by analyzing the headspace over the samples using gas chromatography with flame photometric detection with sulfur mode filter using methyl sulfide as the internal standard. Limit of quantitation (LOQ) is 1 ug/g. Limit of detection is equal to LOQ or lower.