Experiment Number: S0558
Route: Gavage, IV
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Compound: Anthraquinone/ **Analyte:** Anthraquinone
CAS Number: 84-65-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)			
	4 IV Plasma[a,c]	**80 Gavage Plasma[b,d]**	**200 Gavage Plasma[b,d]**	**800 Gavage Plasma[b,d]**
Cmax_obs (ug/mL)	2.73 ± 1.16	0.68 ± 0.17	2.11 ± 0.58	3.47 ± 1.07
Tmax_obs (minute)	2			
Tmax_obs (hour)		4	4	4
Half-life (hour)	4	4-6	4-6	4-6
AUC_0-T (ug/mL*min)	3.45	3.67	9.98	21.9

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Female

	Treatment Group (mg/kg)			
	4 IV Plasma[a,c]	**80 Gavage Plasma[b,e]**	**200 Gavage Plasma[b,d]**	**800 Gavage Plasma[b,d]**
Cmax_obs (ug/mL)	3.44 ± 0.54	0.71 ± 0.06	1.59 ± 0.15	2.63 ± 1.23
Tmax_obs (minute)	2			
Tmax_obs (hour)		4	4	4
Half-life (hour)	4		4-6	4-6
AUC_0-T (ug/mL*min)	2.16	3.37	7.91	15.7

LEGEND

MODELING SOFTWARE

SIGMA PLOT, Version 5.0

MODELING METHOD & BEST FIT MODEL

[a] Sigma Plot, Version 5.0, was used to calculate the AUC 0-T values by the trapezoidal method. Other reported toxicokinetic parameters are observed values only. Half-life of elimination was "eye-balled" (Half-life). As requested by the NTP, no attempt was made to model the plasma concentration versus time profiles. The plasma concentration time profile was a biphasic curve suggesting that anthraquinone is best described by a two-compartment open model with an initial tissue distribution phase (the initial portion of the biphasic curve), and an elimination phase (the terminal linear portion of the biphasic curve).

[b] Sigma Plot, Version 5.0, was used to calculate the AUC 0-T values by the trapezoidal method. Other reported toxicokinetic parameters are observed values only. Half-life of elimination was "eye-balled" (Half-life). As requested by the NTP, no attempt was made to model the plasma concentration versus time profiles. The plasma concentration time profile was characteristic of a two-compartment open model with first order absorption and elimination with initial upward phase (absorption) and later slow decreasing phase (elimination).

EXCEPTIONS

[c] AUC from 0-10 hours, Cmax variation unclear could be SD or SEM

[d] Cmax variation unclear could be SD or SEM

[e] The elimination phase was unclear for this dose group. Cmax variation unclear could be SD or SEM.

ANALYTE

Anthraquinone

TK PARAMETERS

Cmax_obs = Observed or Predicted Maximum plasma (or tissue) concentration
Tmax_obs = Time at which Cmax predicted or observed occurs
Half-Life = Lambda z Half-life, t 1/2, the terminal elimination half-life based on non-compartmental analysis
AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Plasma was analysed for anthraquinone concentration by high performance liquid chromatography (HPLC) using an internal standard, a methanol-water mobile phase, and UV detection at 253 nm. The Limit of Quantitation (LOQ) was 0.025 ug/mL.

TK_INTRAVENOUS PLASMA

4 mg/kg

Mice and Fischer 344 rats were administered a single intravenous or gavage dose. Blood was collected post-dosing from 3 animals/species/route/dose/timepoint for up to 8 timepoints (gavage) or 9 timepoints (intravenous). Mortality was observed in a few mice administered anthraquinone intravenously attributed to rapid rate of delivery and sensitivity to the DMSO formulation. Other rats and mice administered anthraquinone intravenously exhibited clinical signs of toxicity. Group mean and minimum and maximum body weights are for the original group animals before substitutions. Associated with C88036 report date is 10/18/ 1994.

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE PLASMA

80 mg/kg, 200 mg/kg, 800 mg/kg

Mice and Fischer 344 rats were administered a single intravenous or gavage dose. Blood was collected post-dosing from 3 animals/species/route/dose/timepoint for up to 8 timepoints (gavage) or 9 timepoints (intravenous). Mortality was observed in a few mice administered anthraquinone intravenously attributed to rapid rate of delivery and sensitivity to the DMSO formulation. Other rats and mice administered anthraquinone intravenously exhibited clinical signs of toxicity. Group mean and minimum and maximum body weights are for the original group animals before substitutions. Associated with C88036 report date is 10/18/ 1994.