Experiment Number: S0312
Route: IV, Gavage
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Sulfapyridine/ **Analyte:** Sulfapyridine
CAS Number: 599-79-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: University of Arizona

Male

	Treatment Group (mg/kg)	
	5.0 IV Plasma[a,c]	**1000 Gavage Plasma[a,d]**
Tmax_obs (hour)		1
Half-life (hour)	1.17	0.094
k10 ($hour^{-1}$)	0.590	13470
Cl (L/kg*hr)	0.22	
V1 (L/kg)	0.38	
MRT (hour)	1.66	7.34
AUCinf_pred (M*hour)	90.6	
F (percent)		74.33

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Male

	Treatment Group (mg/kg)	
	5.0 IV Plasma[b,e]	**1000 Gavage Plasma[b,f]**
Tmax_obs (hour)		1
Half-life (hour)	0.629	0.097
k10 ($hour^{-1}$)	7.7	1035
MRT (hour)	0.27	7.11

LEGEND

MODELING METHOD & BEST FIT MODEL

[a]Unknown. Data were computed from the plasma concentration-time curves where each point represents the mean of 5-7 mice. first-order kinetics

[b]Unknown. Data were computed from the plasma concentration-time curves where each point represents the mean of 5-7 mice.
N-acetylsulfapyridine concentrations were low.

EXCEPTION

[c]Tmax value is approximate. Graphed time course 0-8 hours. K is 0.590 hour^-1

[d]Graphed time course 0-24 hours. K is 13470 hour^-1

[e]Graphed time course 0-4 hours.

[f]Graphed time course 0-8 hours. K is 1035 hour^-1

ANALYTE

Sulfapyridine
N-acetylsulfapyridine

TK PARAMETERS

Tmax_obs = Observed or Predicted Maximum plasma (or tissue) concentration
Half-Life = Lambda z Half life, t 1/2, the terminal elimination half-life based on non-compartmental analysis
k10 = Elimination rate constant from the central compartment also ke or kelim
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
MRT = Mean residence time
AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity
F = Bioavailability, absolute bioavailability

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

The supernatant from plasma sample extraction was analyzed by HPLC with UV detection (at 360 nm for SASP because it represents specifically the integrity of azo linkage and at 254 nm for its metabolites). The detection limit in plasma for SASP was 0.32 nmol/mL, for SP, 0.5 nmol/mL, and for N-acetylsulfapyridine (AcSP), 1.0 nmol/mL. Values of Cmax and Tmax were obtained directly from plasma concentration-time profiles. K was estimated by linear least squares regression of the data in the terminal phase. From these values, the half-lives were calculated (t1/2 equals 0.693/K) AUC was calculated using the linear trapezoidal rule and extrapolating to time infinity. For multiple doses, the steady-state AUC (0-24) was used.

TK_INTRAVENOUS PLASMA

5.0 mg/kg

Male mice were administered a single intravenous injection of 5.0 mg/kg of sulfapyridine (SP) in the tail vein. Blood was collected from the interior vena cava following euthanasia. AcSP was detected in plasma and achieved the Cmax one hour after SP dosing. Concentrations of the SP metabolite N-acetyl-5-hydroxy-sulfapyridine (SPOH) after a single intravenous or oral SP dosing was low and no TK parameters were determined for this metabolite.

TK PARAMETERS PROTOCOL (cont'd)

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TK_GAVAGE PLASMA

1000 mg/kg

Male mice were administered a single oral administration of 1000 mg/kg of sulfapyridine (SP) consistent with the dose used in NTP genotoxicity studies. SP reached the Cmax about one hr after dosing and eliminated from the body with a plasma half-life of 7.3 hours. AcSP was found in mouse plasma, but the AUC of N-acetylsulfapyridine (AcSP) was approximately 13 fold less than that of SP. Concentrations of the SP metabolite N-acetyl-5-hydroxy-sulfapyridine (SPOH) after intravenous or oral SP dosing were low and no TK parameters were determined