Experiment Number: S0312
Route: IV, Gavage
Species/Strain: Rats/Fischer 344

Toxicokinetics Data Summary
Compound: Salicylazosulfapyridine/ **Analyte:** Salicylazosulfapyridine
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 Group Plasma[a,e]	**5.0 IV Rat A Plasma[b,f]**	**5.0 IV Rat B Plasma[b,g]**	**5.0 IV Rat C Plasma[b,h]**
Half-life (hour)	0.528 ± 0.105	0.445	0.326	0.820
K10 (hour^{-1})	1.465 ± 0.266	1.558	2.126	0.845
Cl (L/hr*kg)	0.65 ± 0.08	0.82	0.70	0.63
V1 (l/kg)	0.48 ± 0.099	0.52	0.33	0.75
MRT (hour)	0.35 ± 0.02	0.37	0.29	0.36
AUCinf_pred (uM*hour)	20.32 ± 2.78	15.36	17.85	19.88

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Male

	Treatment Group (mg/kg)		
	5.0 IV Rat D Plasma[b,i]	**67.5 Gavage Plasma[c,j]**	**675 Gavage Plasma[d,k]**
Half-life (hour)	0.521		
K10 (hour^{-1})	1.329		
Cl (L/hr*kg)	0.45		
V1 (L/kg)	0.33		
MRT (hour)	0.37		
AUCinf_pred (uM*hour)	28.19		

LEGEND

MODELING METHOD & BEST FIT MODEL

[a]Unknown. Data were computed from the plasma concentration-time curves where each point represents the mean of 4 rats. first-order kinetics, Following iv injection, plasma clearance of SASP was consistent with a two-compartment model .

[b]Unknown Data were computed from the plasma concentration-time curves where each point represents data from an individual rat. first-order kinetics, Following iv injection, plasma clearance of SASP was consistent with a two-compartment model.

[c]No modeling. SASP and its metabolites were below detectable limits following low dose oral administration of SASP

[d]No modeling: timpoints at 1,3,6 and 12 hours. The parent compound (SASP) at 1, 3, and 6 hour time points but not at 12 hr (3 out of 4 time points). Metabolites SP and AcSP were detected at 6 and 12 hours.

EXCEPTION

[e]Sulfapyridine (SP) and N-acetyl-sulfapyridine (AcSP), the major metabolites of SASP were not detected in the plasma at this dose level. Cl is systemic clearance, V1 is apparent volume of distribution was calculated by Vd equals systemic Clearance over K. Graphed time course 0-3 hours. K is 1.465 hour^-1 standard error 2.66

[f]Sulfapyridine (SP) and N-acetyl-sulfapyridine (AcSP), the major metabolites of SASP were not detected in the plasma at this dose level. Cl is systemic clearance, V1 is apparent volume of distribution was calculated by Vd equals systemic Clearance over K. K is 1.558 hour^-1

[g]Sulfapyridine (SP) and N-acetyl-sulfapyridine (AcSP), the major metabolites of SASP were not detected in the plasma at this dose level. Cl is systemic clearance, V1 is apparent volume of distribution was calculated by Vd equals systemic Clearance over K. K is 2.126 hour^-1

[h]Sulfapyridine (SP) and N-acetyl-sulfapyridine (AcSP), the major metabolites of SASP were not detected in the plasma at this dose level. Cl is systemic clearance, V1 is apparent volume of distribution was calculated by Vd equals systemic Clearance over K. K is 0.845 hour^-1

[i]Sulfapyridine (SP) and N-acetyl-sulfapyridine (AcSP), the major metabolites of SASP were not detected in the plasma at this dose level. Cl is systemic clearance, V1 is apparent volume of distribution was calculated by Vd equals systemic Clearance over K. K is 1.329 hour^-1

[j]Sulfapyridine (SP) and N-acetyl-sulfapyridine (AcSP), the major metabolites of SASP were not detected in the plasma at this dose level. Cl is systemic clearance, V1 is apparent volume of distribution was calculated by Vd equals systemic Clearance over K. K is 1.329 hour^-2

[k]uM concentration values for 1, 3 and 6 hours; Sulfapyridine and N-acetylsulfapyridine were detected in plasma at 6 and 12 hour time points. Sulfapyridine declined from 6 to 12 hours while N-acetylsulfapyridine increased from 6 to 12 hours.

ANALYTE

Salicylazosulfapyridine

TK PARAMETERS

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

TK PARAMETERS PROTOCOL

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. The apparent K (Lambda_Z) 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 PARAMETERS PROTOCOL (cont'd)

TK_INTRAVENOUS PLASMA

5.0 mg/kg Group, 5.0 mg/kg Rat A-D

Blood samples were collected, via the cannulated jugular vein, at 0.03, 0 .08, 0 .17, 0.25, 0.5, 1.0, 1 .5, 2.0, 3.0, 4.0, 6.0, 12.0, and 24.0 hour following single intravenous administration of Salicylazosulfapyridine (SASP). Parent SASP was below detectable limits in the plasma at 4 hours. Plasma SASP concentration declined rapidly during the first 30 minutes followed by a slower elimination phase. A group parameter and four individual animal parameters are shown. Sulfapyridine (SP) and N-acetyl-sulfapyridine (AcSP), the major metabolites of SASP were not detected in the plasma at this dose level.

TK_GAVAGE PLASMA

67.5 mg/kg, 657 mg/kg

Blood samples were collected, via the cannulated jugular vein, at 0.25, 0.5, 1, 1 .5, 2, 3, 4, 6, 12, and 24 hr following a single low dose oral administration (67.5 mg/kg) of Salicylazosulfapyridine (SASP). Blood was collected, via the inferior vena cava, after euthanization at four time points (1, 3, 6, and 12 hr) following a single oral gavage administration (675 mg/kg) of SASP. SASP and its metabolites were below detectable limits following low dose oral administration of SASP (67.5 mg/kg). SASP, parent compound, was detected in the plasma of rats administered the higher oral dose (675 mg/kg) at 1, 3, and 6 hour time points but was below detectable limits at 12 hours. Plasma sulfapyridine (SP) concentration declined from 6 to 12 hr while N-acetylsulfapyridine (AcSP) increased from 6 to 12 hours.