Experiment Number: S0577
Route: Intravenous, Gavage
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Compound: Methyleugenol/ **Analyte:** Methyleugenol
CAS Number: 95-15-2

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

Male

	Treatment Group (mg/kg)			
	25 IV Plasma[a,c]	**25 Gavage Plasma[b,d]**	**50 Gavage Plasma[b,d]**	**75 Gavage Plasma[b,d]**
Cmax_obs (ug/mL)	18.2	0.382	1.40	3.10
Tmax_obs (minute)	2	5	5	5
Half-life (minute)	15	30	30	30
AUC_0-T (ug/mL*min)	116.4	4.91	27.4	48.4
F (percent)		4.2	11.8	13.9

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Female

	Treatment Group (mg/kg)			
	25 IV Plasma[a,c]	**25 Gavage Plasma[b,d]**	**50 Gavage Plasma[b,d]**	**75 Gavage Plasma[b,d]**
Cmax_obs (ug/mL)	9.34	0.123	1.01	4.39
Tmax_obs (minute)	2	15	5	5
Half-life (minute)	15	30	30	30
AUC_0-T (ug/mL*min)	106.5	3.27	25.0	605
F (percent)		3.1	11.7	18.9

LEGEND

MODELING SOFTWARE

Sigma Plot Version 5.0

MODELING METHOD & BEST FIT MODEL

[a]AUC was calculated using the trapezoid rule using Sigma Plot Version 5.0. Reported toxicokinetic parameters, ie Cmax, Tmax, and half-life, are observed values only, no attempt was made to model the plasma concentration versus time profiles. Half-life is the half-life of elimination. The concentration time profile appears to be a biphasic curve with a bend occurring at approximately 5 minutes suggesting that these data are best characterized by a two compartment open model, with an initial tissue distribution phase and a terminal linear elimination phase.

[b]AUC was calculated using the trapezoid rule using Sigma Plot Version 5.0. Reported toxicokinetic parameters, ie Cmax, Tmax, and half-life, are observed values only, no attempt was made to model the plasma concentration versus time profiles. Half-life is the half-life of elimination. The concentration time profiles were biphasic with an initial rapid decreasing phase followed by a terminal slower decreasing phase. The initial phase indicates that methyleugenol undergoes distribution to peripheral compartment(s). No absorption phase could be characterized indicating that the rate of absorption was very rapid. Elimination was rapid (half-life is 30 minutes for all oral groups) and there is no evidence of saturation of elimination for methyleugenol..

EXCEPTIONS

[c]The 180 and 300 minute time point values were not used to estimate the half-life of methyleugenol.

[d]The termineal linear phase was sufficiently characterized to determine the elimination kinetics of methyleugenol. However, no absorption phase could be characterized.

ANALYTE

Methyleugenol

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
F = Bioavailability, absolute bioavailability

TK_PARAMETERS PROTOCOL

ANALYSIS METHOD

Plasma samples with 3,4-Dimethoxystyrene as an internal standard were analyzed by reverse phase high performance liquid chromatography (HPLC) with UV detection at 230 nm. Concentrations below the limit of quantitation (LOQ) of 0.050 ug/mL were evaluated and shown to have a high degree of precision and accuracy down to a concentration of 0.025 ug/mL. Values below the LOQ but above 0.025 ug/mL were used to calculate the mean value at each time point for the concentration versus time curves. However, if the value was less than 0.025 ug/mL, then a value of 0.0125 ug/mL (midpoint between 0 and 0.025 ug/mL) was used to calculate the mean. Plasma concentration values have three significant figures down to one thousandth (0.001) of a ug/mL. The toxicokinetic parameters are observed values. There was no attempt made to model the plasma concentration time profile to obtain a best-fit curve.

TK_INTRAVENOUS PLASMA

25 mg/kg Male and Female

Group body weight means shown were probably calculated for the group after replacement animals were substituted. Following a single intravenous or oral gavage dose, 3 mice/sex/dose group were bled by cardiac puncture (under CO2/O2 anesthesia) at each of 8 post-dose time points. The mean plasma concentration at each time point was used to generate semi-logarithmic concentration versus time point curves. Toxicokinetic parameters are observed values. A software program (Sigma Plot Version 5.0) was used to calculate the AUC values using the trapezoidal method

TK_GAVAGE PLASMA

25 mg/kg, 50 mg/kg, 75 mg/kg Male and Female

Group body weight means shown were probably calculated for the group after replacement animals were substituted. Following a single intravenous or oral gavage dose, 3 mice/sex/dose group were bled by cardiac puncture (under CO2/O2 anesthesia) at each of 8 post-dose time points. The mean plasma concentration at each time point was used to generate semi-logarithmic concentration versus time point curves. Toxicokinetic parameters are observed values. A software program (Sigma Plot Version 5.0) was used to calculate the AUC values using the trapezoidal method