Experiment Number: S0577
Route: Intravenous
Species/Strain: Rats/Fischer 344

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)			
	37 IV Plasma[a]	**37 Gavage Plasma[b]**	**75 Gavage Plasma[b]**	**150 Gavage Plasma[b]**
Cmax_obs (ug/mL)	45.7	0.656	1.52	3.84
Tmax_obs (minute)	2	5	5	5
Half-life (minute)	75	60	75	115
AUC_0-T (ug/mL*min)	581.4	33.5	155.6	459.5
F (percent)		5.8	13.2	19.5

Experiment Number: S0577
Route: Intravenous
Species/Strain: Rats/Fischer 344

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

Female

	Treatment Group (mg/kg)			
	37 IV Plasma[a]	**37 Gavage Plasma[b]**	**75 Gavage Plasma[b]**	**150 Gavage Plasma[b]**
Cmax_obs (ug/mL)	49.5	1.14	3.22	8.25
Tmax_obs (minute)	2	5	5	5
Half-life (minute)	75	95	80	105
AUC_0-T (ug/mL*min)	495.4	27.0	133.1	307.9
F (percent)		5.5	13.3	15.3

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 best fit for the data points appears to be a biphasic curve suggesting a two compartment open model with well defined distribution (time points 2 through 15 minutes) and elimination phases (time points 30 minutes through 6 hours).

[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. Results were characteristic of a two compartment open model with first-order absorption and elimination with a biphasic curve having no initial upward phase that would indicate absorption but an initial fast decreasing phase followed by a later slow decreasing phase. The fast decreasing phase describes the distribution phase and the later slow decreasing phase, or terminal linear portion, describes the elimination phase .

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

37 mg/kg Male and Female

Group body weight means shown were probably calculated for the group after replacement animals were substituted. Following single administration IV and oral dosing three rats/sex/dose group were bled at eight post-dose time points. Each rat was bled twice (at two separate post-dose time points) by retroorbital puncture (under CO2/O2 anesthesia) yielding three data points/sex/dose and route/time point. 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

37 mg/kg, 75 mg/kg, 150 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.