Experiment Number: K99050
Route: Gavage
Species/Strain: Rat/F344/NCrl

Toxicokinetics Data Summary
Compound/Analyte: Ginkgo Biloba Extract/Isorhamnetin
CAS Number: 90045-36-6

Request Date: 11/27/2019
Request Time: 2:30:16
Lab: Battelle

Male

	Treatment Group (mg/kg)		
	30 Gav[a]	**100 Gav[a]**	**300 Gav[a]**
	Plasma		
Cmax_obs (ng/mL)	5.92	6.81	24.6
Tmax_obs (minute)	15.0	720	480
Half-life (minute)	3320	ND	ND
AUC_0-T (ng/mL•min)	6710	8430	18000
AUCinf_pred (ng/mL•min)	25700	ND	ND

LEGEND

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin (Version 7.0, Certara, L.P., Princeton, NJ) non-compartmental library models with no weighting factors, Non-compartmental model, parameter estimates are reported to three significant figures. ND = Not determined. The 100 and 300 mg/kg groups did not have enough measurable concentrations of ISR after the Tmax_obs necessary to characterize the terminal phase. In addition, the 30 mg/kg group had a poorly characterized terminal elimination phase, without even one half-life before the Tlast and 73.9 percent of the AUCinf_pred extrapolated.

ANALYTE
Isorhamnetin

TK PARAMETERS
Cmax = Observed or Predicted Maximum plasma (or tissue) concentration
Tmax = 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
AUCinf = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

TK PARAMETERS PROTOCOL

TK PARAMETERS

TK analysis was performed on Ginkgolide A (GLA), Ginkgolide B (GLB), Ginkgolide C (GLC), Ginkgolide J (GLJ), Bilobalide (BLL), Isorhamnetin (ISR), Quercetin (QCT), and Kaempferol (KMF) after a single gavage administration of ginkgo biloba extract (GBE) batch 1 (Lot 020703) in corn oil at doses of 30, 100, and 300 mg/kg. Blood samples were collected prior to dose administration and at 11 time points post dose administration from typically three animals/time point/group. Time points were Pre-dose, 5, 10, 15, 30, 60, 90, 120, 240, 480, 720, and 1440 minutes. The LLOQ was 4 ng/mL for GLA, 1 ng/mL for GLC and GLB, 5 ng/mL for BLL and ISR, 3 ng/mL for QCT, 10 ng/mL for GLJ, and 40 ng/mL for KMF. The LOD is 3 ng/mL for GLA, 0.3 ng/mL for GLC, 2 ng/mL for BLL and ISR, 1 ng/mL for QCT, 0.4 ng/mL for GLB, 5 ng/mL for GLJ, and 40 ng/mL for KMF. Body weight ranges are 111.8-187.5 g, 114.5-187.7 g, and 111.8-186.6 g for 30, 100, and 300 mg/kg dosed male rats, respectively.

TK PARAMETERS (cont'd)

The plasma samples were hydrolyzed, heated, cooled, then extracted with ethyl acetate and centrifuged. The organic layer for each sample was removed, concentrated to dryness under nitrogen gas and reconstituted in methanol for analysis. The samples were hydrolyzed to convert the flavonol glycosides to corresponding aglycones which are the compounds quantified. A liquid chromatography coupled with tandem mass spectrometric (LC-MS/MS) method was used to quantitate known GBE constituents, terpene trilactones (Ginkgolide A [GLA], Ginkgolide B [GLB], Ginkgolide C [GLC], Ginkgolide J [GLJ], and Bilobalide [BLL]) and aglycones (Isorhamnetin [ISR], Kaempferol [KMF], and Quercetin [QCT]) of flavonol glycosides.