

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

Toxicokinetics Data Summary
Compound/Analyte: Ginkgo Biloba Extract/Ginkgolide J
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^b

300 Gav^b

Plasma

Cmax_obs (ng/mL)	ND	9.86	19.9
Tmax_obs (minute)	ND	60.0	120
Half-life (minute)	ND	ND	ND
AUC_0-T (ng/mL•min)	ND	2000	6350
AUCinf_pred (ng/mL•min)	ND	ND	ND

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

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

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

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 30 mg/kg group had samples that were ND or BLOD at all time points.

^b 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.

ANALYTE

Ginkgolide J

TK PARAMETERS

C_{max} = Observed or Predicted Maximum plasma (or tissue) concentration

T_{max} = Time at which C_{max} 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 t_i (initial) to t_f (final), AUC_{last}

AUC_{inf} = 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.

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

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

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

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.