ADME NTP Study S0845 Isoeugenol Toxicokinetics

Sex/Species: male F344 rats.
Vehicle: intravenous, ethanol:Emulphor:saline (10:10:80).

CASRN 97-54-1

Radiolabeled with carbon-14 (position not specified); [^{14}C]Isoeugenol

Studies Performed:

Single 15.6 mg/kg intravenous dose to rats with sampling at 1, 3, 5, 7, 10, 12, 15, 20, 30, 45,and 60 minutes as well as 6, 12, 24, and 48 hours postdose. (n = 3 with indwelling catheters)

Toxicokinetics:

Pharmacokinetic parameters for parent isoeugenol were calculated using Winnonlin software (Scientific Consulting, Inc., Apex, NC). Data were best fitted as a two compartment model (intravenous bolus dose). Parent isoeugenol was not detected in blood by HPLC within 60 minutes after administration.

Whole blood was counted for total radioactivity at each time point. At 48 hours, 12 % of the total radioactivity was recovered; after 60 minutes, less than 1 % of the total dose was recovered. For both parent and total radioactivity, the means for each time point to 60 minutes were plotted in a figure and are not shown here.

Table 1 Pharmacokinetic Parameters of Intravenously Administered [^{14}C]-Isoeugenol (15.6 mg/kg, 120 uCi/kg).

Parameter (units)	V_{ss} L/kg	$t_{1/2}$ min	MRT Min	V_D L/kg	AUC ug/min/ml	CLs L/min/kg
Mean ± sem	22.41 ± 1.24	12.13 ± 1.17	11.6 ± 0.51	13.96 ± 1.14	8.13 ± 0.22	1.92 ± 0.05

Where:

V_{ss} is the steady-state apparent volume of distribution, the apparent volume into which the compound is distributed at steady state.

$t_{1/2}$ is the terminal half-life, the time it takes half the concentration of parent to be removed from the blood.

MRT is the mean residence time, the average time the drug resides in the body.

V_D is the volume of distribution, the apparent volume into which the compound is distributed.

AUC is the area under the curve, an expression of the amount of compound in the blood over time.

CL_s is the systemic body clearance, describes the elimination of drug from the body by all processes.