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Percutaneous absorption and metabolic fate of [14C]hydroquinone in the dog

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PERCUTANEOUS ABSORPTION AND METABOLIC FATE OF [^{14}C]HYDROQUINONE IN THE DOG

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OF [^{14}C] HYDROQUINONE IN THE DOG

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ABSTRACT

Hydroquinone is used extensively as a photographic developer. The metabolic fate and percutaneous absorption of [U-^{14}C]HQ was determined in male Beagle dogs. The excretion of ^{14}C was determined after dermal exposure, intravenous (iv) and gavage administrations. For iv studies, 1 or 10 mg/kg of [^{14}C]HQ was injected and blood, urine and breath were collected for 8-12 hours in anesthetized dogs. After recovery from the anesthetic, dogs were housed in metabolism cages for 6 to 7 days for collection of blood, urine and feces. Blood ^{14}C concentrations declined slowly, with 2 apparent phases. Half-life values for the α and β phases were 1.3 and 7.2 hours for the 1 mg/kg dose and 1.0 and 8.0 hours for the 10 mg/kg dose, respectively. Excretion of ^{14}C was rapid initially, with 14.6% and 42.4% of the ^{14}C being excreted in 4 hours for the 1 and 10 mg/kg doses, respectively. Values for urine, feces and total recovery of ^{14}C at 4 to 7 days were 34.5%, 7.1%, and 41.6% for a 1 mg/kg dose and 65.7%, 6.1%, and 71.8% for a 10 mg/kg dose. No ^{14}C was detected in the expired air. The concentration of ^{14}C in the skin 24 hours after iv dosing of 1 mg/kg [^{14}C]HQ was about 10.4% of the dose. The other tissues showed low concentrations of ^{14}C. After the oral administration of 50 mg/kg [^{14}C]HQ to dogs, blood ^{14}C concentrations declined slowly. Half-life values for the α and β phases were 0.85 and 12.5 hr, respectively. The urinary excretion pattern was similar to that seen after iv administration, with 62.5% of the dose being excreted after 4 hours. Values for urine, feces, blood, tissue, and total recovery of ^{14}C at 5 to 7 days were 80.4%, 3.7%, 0.15%, 2.2%, and 86.5%. Analysis for urinary metabolites indicated that the urine of iv and orally-treated dogs did not contain sulfates or glucuronides of HQ as was reported elsewhere for rats dosed orally with [^{14}C]HQ. After dermal application of [^{14}C]HQ, no ^{14}C was detected in the blood. Urinary excretion of ^{14}C accounted for only 0.03% of the applied radioactivity at 2 days and 0.04% at 5 days. Urinary ^{14}C was still detectable at 5 days. The percutaneous absorption rate was about 0.16 nmol/cm^2/min (1.1 μg/cm^2/hr). Using these data to estimate human uptake, assuming immersion of both hands into a photographic developer solution containing HQ for 1 hour, about 0.8 mg of HQ would be absorbed through the skin.

These studies compare the metabolic fate of HQ by different routes of administration and show that HQ is poorly absorbed through the skin.

INTRODUCTION

Hydroquinone (1,4-dihydroxybenzene), is a six carbon aromatic compound with phenolic hydroxyl groups in the para-position. It is a white crystalline solid at room temperature and is soluble in water, ethanol, acetone, ether and chloroform.

Hydroquinone is an effective antioxidant for non-food industrial fats and oils and is used as an intermediate in the production of dyes and in the manufacture of other antioxidants such as butylated hydroxyanisole (BHA) and monotertiary butyl hydroquinone (TBHQ) (Mathtech, 1983). Because of its oxidation potential, hydroquinone is widely used in industry as a developing agent for black and white photographic film. Hydroquinone chemically reduces silver nitrate in a photographic emulsion to metallic silver, and forms colored reaction products with strong alkali and with concentrated sulfuric acid (Mansville Chem. Prod., 1978). Hydroquinone is also used in dermatologic products as a bleach for hyperpigmented skin and has also been used to prevent oxidative degradation of vitamin A in medicinal and biological preparations (Raff and Ettling, 1966).

Hydroquinone and quinone are chemically interconvertible and form a reversible redox system. In the dry, crystalline form, pure hydroquinone is quite stable, and darkens slowly upon prolonged exposure to air. In the presence of moisture (at temperatures not exceeding 37°C) it readily undergoes oxidation via an intermediate

semiquinone radical to form quinone (Carmichael and Mander, 1967). In aqueous solution, hydroquinone reacts with oxygen and undergoes autoxidation. The initial products are quinone and hydrogen peroxide (Raff and Ettling, 1966).

Regarding its environmental effects, quinone and hydroquinone are known to be toxic to unicellular and multicellular aquatic plants. Toxicity to aquatic plants has been reported to include inhibition of respiration, abnormalities in photosynthesis and mortality. The effects of hydroquinone and quinone on terrestrial higher plants include chromosome aberrations, inhibition of growth, interference with seed germination and inhibition of enzyme activity (Dynamac Corp. 1982). Both quinone and hydroquinone are toxic to fish. Hydroquinone altered tyrosinase activity in skin homogenates of the black gold fish, Carassius auratus (Chen and Chavin, 1976).

Oral or parenteral administration of large doses of hydroquinone to mammals rapidly produced nausea, salivation, tremors of the voluntary muscles, convulsions and finally death by respiratory failure (Woodard, 1951). In dogs and cats given large sublethal doses (100 mg/kg of body weight), swelling of the mucous membrane of the lips and eyes was observed within a few hours and lasted for 24-72 hours. Rats dosed with up to 1% hydroquinone in the diet were without apparent toxic effects. However, adult rats given 5% hydroquinone in the diet for 9 weeks showed significant weight loss and developed aplastic anemia (Carlson and Brewer, 1953).

Repeated topical application of (1 and 3%) hydroquinone caused a localized depigmentation of mammalian skin and hair. Denton et al., (1952) reported depigmentation in adult black male mice given hydroquinone by subcutaneous injection.

Several investigators have studied the metabolism of hydroquinone in humans and experimental animals. Hydroquinone, administered by gavage to 50 male rats at doses of 7.5 and 15 mg/kg, 6 days/week for 40 days had no effect on the weight gain, but hematological effects such as anisocytosis, polychromatophilia and erythroblastosis were observed (Delcambre et al., 1962).

Studies by Garton and Williams (1949) showed that hydroquinone was readily absorbed from the gastrointestinal tract in the rat and was eliminated in the urine as conjugates with sulfuric or glucuronic acid. In the rabbit, 43% of an administered oral dose was excreted in the urine as the monoglucuronide and 30% as the sulfate ester.

DiVincenzo et al., (1984), found that rats given a single dose of 200 mg/kg of [^{14}C]hydroquinone orally, excreted 91.9% of the dose in the urine within 2-4 days. The feces contained 3.8% of the dose and about 0.4% was excreted in the expired air. Radioactivity was widely distributed throughout the tissues with the highest concentrations found in the liver and kidneys. About 25-42% of the dose was excreted as hydroquinone monosulfate and 56-66% of the dose as hydroquinone monoglucuronide.

Estimates of absorption of oral doses of hydroquinone in man, dog and rabbit based on urinary excretion data were considerably lower than dose values reported for the rat (Dynamac Corp., 1982).

In view of the limited information concerning the dermal exposure of hydroquinone and because of the potential for dermal contact with photographic processing solutions, the percutaneous absorption of [^{14}C]hydroquinone and its disposition and metabolic fate following an oral and intravenous administration was investigated in dogs. This paper describes such studies.

PHYSICO-CHEMICAL DATA

Chemical Name:	1,4-benzenediol
Molecular weight:	110.11
Molecular Formula:	$C_6 H_6 O_2$
Structure:	
Solubility:	5.8 g/100 g of water at 15°C 9.4 g/100 g of water at 28.5°C Highly soluble in alcohol and ether and only slightly soluble in cold benzene and other nonpolar solvents.
Melting point:	173-174°C
Boiling point:	285°C at 730 mm Hg.
Vapor pressure:	1 mm Hg @ 132.4°C (.000018 mm Hg at 25°C)
Absorption (UV):	288 nm
λmax (log):	
Density:	1.328^{20}_{4}

MATERIALS AND METHODS

Materials

[U-^{14}C]Hydroquinone was purchased from Wizard Laboratories (Davis, CA) with a specific radioactivity of 5.0 mCi/mmol. Its radiochemical purity was greater than 99% as determined by high performance liquid chromatography (hplc). [U-^{14}C]Hydroquinone was dissolved in degassed, distilled water and diluted to a concentration of 100 µCi/mL, placed in amber vials and stored at approximately - 20°C. Unlabeled hydroquinone was obtained from Eastman Kodak Co., Rochester, NY. No impurities were detected by gas chromatography/mass spectrometry (GC/MS).

Animals

Male Beagle dogs weighing 9-15 kg, were purchased from Marshall Research Animals, Inc. (North Rose, NY). They were identified by ear tattoo. Dogs were held in quarantine for at least one week prior to use. Prior to dosing, dogs were fasted for 16 hours and water was provided ad libitum.

Methods

Intravenous Administration

Radiolabeled hydroquinone was dissolved in a degassed saline solution containing unlabeled hydroquinone and about 3 or 4 mL of the solution was administered through an indwelling foreleg intravenous catheter at dose levels of 1 mg/kg (10 or 100 μCi) and 10 mg/kg of body weight (30 μCi). A total of eight dogs was studied at the lower dose, and three dogs at the high dose.

Expired air was collected continuously for 8 hours (from two sets of dogs, at the lower dose) into a polytetrafluoroethylene bag by means of an oral endotracheal tube connected to a two-way valve. The contents of the bag were pumped through a silica gel trap to collect volatile organic materials and through a sodium hydroxide trap (200 mL of 2.5N sodium hydroxide) to collect respiratory carbon dioxide. Traps were changed at 4 and 8 hours. Urine samples were collected at 4, 8 and 12 hours by means of a urethral catheter and blood samples were collected periodically for the first 8 or 12 hours by means of an indwelling forelimb catheter. A continuous saline drip was maintained throughout each experiment to replace lost body fluids. After recovery from the anesthetic, urine, feces and blood samples were collected daily for up to 6 or 7 days from conscious dogs housed in metabolism cages. Samples were either analyzed immediately after collection or preserved with ascorbic acid and stored frozen until analysis.

Major organs and tissues were excised from two dogs at time of sacrifice and assayed for residual radioactivity.

Administration by Gavage

The disposition and excretion of hydroquinone was studied in dogs after oral gavage administration of [^{14}C]hydroquinone. Each dog was strapped separately in a large sling (Harvard Apparatus Co., Inc., South Matick, MA), designed to restrain the animal in an upright position with a minimum of fatigue. The sling was equipped with zippers to give access to the front or the rear of the animal, and to facilitate the removal of the catheters. Ace-Promazine® was administered as a tranquilizer. Approximately 125 µCi of [^{14}C]hydroquinone was dissolved in 25 mL of degassed water containing unlabeled hydroquinone. Twenty milliliters of this preparation (50 mg/Kg, 100 µCi) was given by gastric intubation to each dog, followed by 20 mL of water. The dog remained in the sling for about 8 hours, during which time the total volume of urine was collected by means of a urethral catheter, and blood samples collected in heparinized tubes at various intervals from an indwelling forelimb catheter. Subsequently, urine and blood samples were collected from dogs housed in metabolism cages for up to 7 days. Feces were collected up to 6 days. The dog was sacrificed and all major organs and tissues were removed for the determination of residual radioactivity. A total of two dogs was studied.

Skin Exposures

A suitable area of skin on the dog's thorax was shaved 24 hours prior to a skin absorption study. Atropine sulfate and Ace-Promazine® were administered as pre-anesthetics. Dogs were anesthetized with sodium pentobarbital for an initial collection period of 8 or 12 hours.

[^{14}C]Hydroquinone was added to 25 mL of a saline solution containing unlabeled hydroquinone, to give a final hydroquinone concentration of approximately 4.5 g/L (a concentration equivalent to that found in commercial "black-and-white" developers). A portion of this solution (approx. 40 µCi, 15 mL) was added to a sealed glass absorption cell which was secured to the dog's thorax with surgical adhesive (Skin Bond®, Howmedica, Inc., Largo, FL) and tape. The absorption cell adapted from the design of Würster and Munies (1965) was 15 cm long, 3 cm wide at one end, 4 cm wide at the other end and 1.5 cm deep. Cotton gauze was placed inside the cell to facilitate the uniform distribution of the solution over the surface of the skin. The surface area of the skin exposed to hydroquinone was 55.6 cm^2. Exposures were carried out for 60 minutes, after which the skin was washed thoroughly with soap and water. Blood samples and urine were collected at intervals up to 48 hours and 120 hours respectively. and were analyzed for radioactivity. A total of six dogs was studied.

The skin absorption rates were calculated as nanomoles (nmoles) of [^{14}C]hydroquinone absorbed through the skin per cm^2 of skin surface area per unit of time. The method was based on the procedure known as excretion analysis. The urinary excretion of radioactivity after skin exposure and intravenous administration was measured. The dermal absorption rate was then calculated after correction for incomplete excretion of radioactivity using the data obtained from intravenous experiments.

Radioactivity Measurements

All radioactivity measurements were carried out either with a Packard Model 2660 Tri-Carb (Packard Instrument Co., Downers Grove, IL) or with a LKB Model 1217 Rack Beta (LKB Instruments, Inc., Gaithersburg, MD) liquid scintillation spectrometer. Efficiency corrections were made by external standardization. Radioactive samples were dissolved in Eastman Ready-to-Use II® scintillation fluid (Eastman Kodak Company, Rochester, NY). Sodium hydroxide trap solutions were counted directly in a scintillation fluid composed of 500 mL p-dioxane, 60 g naphthalene, 2.0 g PPO, 0.25 g POPOP and 22.5 g Cab-O Sil®. Blood, feces and tissues were combusted using a Packard Sample Oxidizer (Model 306), and counted in a scintillation fluid containing Permaflour® and Carbosorb®.

Determination of Radioactivity in Excreta, Blood and Tissues

Urine was counted directly in scintillation fluid. Fecal samples were homogenized with water, and transferred to flasks that were manually rotated in a freezing bath containing acetone and dry ice. Samples were then lyophilized using a Virtis, Freezemobile II (Model 10-145V). The dried residues were combusted directly.

Blood samples were combusted directly. All tissues except bone, fat and skin, were homogenized with water, using a homogenizer or a blender. Portions of this homogenate were combusted directly. Fat and representative areas of skin were combusted directly. Cleaned, chopped femoral bone was placed in a flask with an equivalent volume of 70% perchloric acid and heated in a water bath at 60-70°C overnight, until solubilization was complete. Digested samples were then combusted directly.

Characterization of Metabolites in Urine

Processing of Urine

All urine from the iv administration and from the gavage dosing were thawed and filtered by passage through a 0.45 μm Millipore filter. Untreated whole urine from four-hour collections was analyzed directly by hplc. The hplc radioactive peaks were collected according to retention time. Fractions collected from 24

analyses of whole urine were pooled. Total radioactivity in each fraction was determined by liquid scintillation counting (200 µL). Subsequently the pooled fractions were evaporated to dryness using a Büchi Rotovapor (Model R110) at 40°C. The residue was dissolved in 3.0 mL of methanol, assayed for radioactivity and re-analyzed by hplc. A control urine was treated similarly. Samples were also submitted for analysis by gas chromatography/mass spectrometry.

Urine was also extracted prior to hplc analysis. Four-hour urine collections from three dogs (10 mg/kg dose) were pooled. Prior to analysis, duplicate 1.0 mL aliquots of urine, adjusted each to 3.0 mL with distilled water, were passed through two separate Bond Elut® C18 cartridges (Analytichem International, Inc., Harbor City, CA). The cartridge was previously activated by rinsing first with 5.0 mL of methanol followed by 5.0 mL of water. Urine was washed from the column with triplicate 1.0 mL portions of 20% methanol/80% formic acid (0.09%). Radioactivity was quantitatively removed by this procedure. The pooled extract was evaporated under reduced pressure at 40°C to approximately 1.0 mL, assayed for radioactivity and analyzed by hplc. A control urine was treated similarly. Radioactive peaks detected on hplc analysis of unhydrolyzed urine extracts were collected according to retention time. The fractions were evaporated under reduced pressure at 40°C and the residue dissolved in 2.0 mL of methanol. Samples (100 µL) were reanalyzed by hplc and submitted for analysis by gas chromatography/mass spectrometry.

Portions of the untreated whole urine or urine extracts were treated with β-glucuronidase to hydrolyze conjugates. Urine extracts (0.5 mL) was diluted to 1.5 mL with distilled water. A portion of this extract (0.5 mL) was placed in an amber vial and was treated with 0.125 mL of a working solution of β-glucuronidase (from bovine liver, approximately 5000 Fishman units/mL, type B-10, Sigma Chemical Co., St. Louis, MO), prepared in a sodium acetate buffer (0.1 - 0.5M), pH 5.5. The capped vial was incubated at 37°C in a water bath (4-24 hours).

Portions of urine or urine extracts were incubated with sulfatase to hydrolyze the sulfate conjugates. Five tenths (0.5) mL of sample (whole urine or extracted urine) were incubated with aryl sulfatase/β-glucuronidase (1800 Fishman units/mL, Calbiochem, La Jolla, CA or Sigma Chemical Co., St. Louis, MO). Saccharolactone (10-50 mM) in sodium acetate buffer was added to inhibit the activity of the β-glucuronidase. The samples were incubated as above.

Urine from oral and iv dosing were also treated with hydrochloric acid to hydrolyze sulfuric acid esters. A portion of the ^{14}C urine (0.5 mL) was treated with an equal volume of 3N HCl in a 3.5 mL amber vial, heated in boiling water for 1 hour, cooled and neutralized with 1.0 mL of 1M NaOH. Samples were subsequently analyzed by hplc.

HPLC Analysis

A hplc reverse phase method was used to analyze the [^{14}C] hydroquinone and the urine samples. The method was adapted from Greenlee et al., (1981). A Waters high performance liquid chromatograph equipped with a WISP 710 injection system, a 720 System Controller and Data Module was used (Waters Associates, Milford, MA). A Spectroflow absorbence detector (Model 773) at 295 nm was used (Kratos, Westwood NJ). The radioactivity in the column eluate was detected with a ^{14}C Berthold LB 504 detector, fitted with a 400 µL glass cell. The eluant from the column was collected using a SuperRac fraction collector, Model 2211 (LKB, Washington, DC). Columns used were two 10 cm x 4.6 mm Spheri-10 RP-18 MPLC® cartridges, with a 3 cm guard column (Browlee Labs, Santa Clara, CA). The mobile phase was methanol/0.09% formic acid with the following gradient.

Time	Flow (mL/min)	% Formic Acid	% Methanol
Initial	0.7	100	0
20.0	0.7	10	90
25.0	0.7	10	90
30.0	1.5	100	0
35.0	0.7	100	0

All solvents were degassed before use.

Disposition of Radioactivity

The recovery of radioactivity from male Beagle dogs dosed with [^{14}C]HQ is presented in Table 1. After iv administration of 1 mg/kg or 10 mg/kg [^{14}C]HQ, urinary excretion of ^{14}C was rapid initially (Figure 1). The 8 hour and 24 hour cumulative excretion totals were 20% and 26% for the 1 mg/kg dose and 53% and 60% for the 10 mg/kg dose. The majority of the urinary radioactivity (14.6% and 42.4% of the dose for 1 mg/kg and 10 mg/kg, respectively) was eliminated within the first 4 hours. For each dose level, only an additional 6 to 7% of the dose was excreted from day 2 to day 5. At 7 days after a 1 mg/kg dose, about 34.5% of the dose was accounted for in the urine. Total urine radioactivity for a 10 mg/kg dose was 65.7% of the dose at 5 days. Fecal radioactivity accounted for about 4.6% and 2.5% of the dose at 48 hours for the 1 mg/kg and 10 mg/kg doses, respectively. Total fecal radioactivity was 7.1% and 6.1% for 1 mg/kg and 10 mg/kg, respectively by 4 to 5 days. Elimination of radioactivity in the expired air after a 1 mg/kg dose was below the limit of detection (less than 0.05% of the dose).

The overall recovery of radioactivity at 4 to 7 days was 41.6% and 71.8% for 1 mg/kg dose and 10 mg/kg dose, respectively. Blood radioactivity comprised between 7 to 8% of the administered dose at 4 hours and declined to about 1% by 24 hours at both dose levels.

TABLE 1

Excretion of Radioactivity by Dogs Following Intravenous Administration of [U-^{14}C]Hydroquinone[a]

Dose/Collections	Cumulative % of Administered Dose at Various Collection Periods				
	4 hr.	8 hr.	24 hr.	48 hr.	Total[b]
1 mg/kg[c]					
Urine	14.6 ± 0.8	19.6 ± 0.8	26.4 ± 1.1	28.8 ± 1.6	33.2 (33.8, 32.6)
Feces	(d)	(d)	(d)	4.6 ± 0.7	7.1 (6.4, 7.9)
Expired Air	(e)	(e)	(d)	(d)	(d)
Blood	7.8 ± 0.8	4.7 ± 0.7	1.1 ± 0.2	0.3(0.3, 0.3)	< 0.14
Tissues[f]	(d)	(d)	12.0(9.2, 14.8)	(d)	(d)
10 mg/kg[g]					
Urine	42.4 ± 5.6	52.6 ± 5.4	60.0 ± 4.5	63.5 ± 4.4	65.7 ± 4.6
Feces	(d)	(d)	0.52	2.5 ± 0.11	4.8 ± 0.5
Blood[h]	6.6 ± 0.5	4.2 ± 0.5	1.2 ± 0.3	0.5 ± 0.1	(d)

(a) Male Beagle dogs were anesthetized for 8 or 12 hours. [^{14}C]Hydroquinone dissolved in saline was administered as a single dose of 1 mg/kg (10 µCi and 100 µCi) or 10 mg/kg (30 µCi). The overall recovery of ^{14}C at 4 to 7 days was 41.6% and 71.8% for a 1 mg/kg and 10 mg/kg doses, respectively.

(b) Totals are based on 120 hours for urine samples, 96 hours for feces and blood samples.

(c) Four to eight dogs per group ± S.E. except where only two values were determined.

(d) Not measured.

(e) Radioactivity detected was < 0.05% of dose.

(f) Tissues include, brain, heart, intestine, kidney, liver, lungs, pancreas, skin, spleen, stomach and testes. Total skin surface area calculated using the formula:

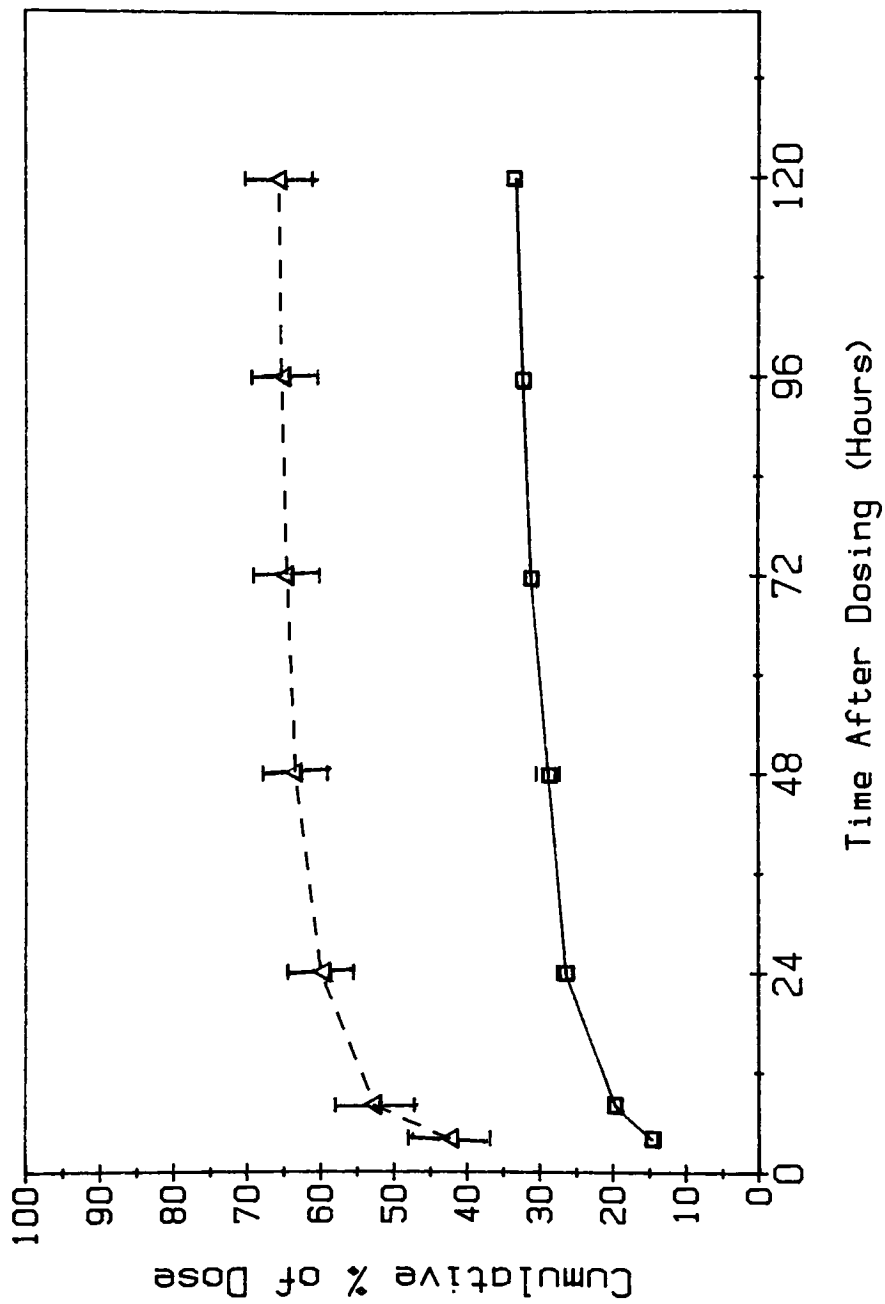
$$\text{Area (sq. cm)} = 11.6 \times \text{weight}^{2/3}.$$ See Reference 1

(g) Three dogs per group ± S.E., except for 24 hour feces where only one sample was available.

(h) Blood volume assumed to be 9.41% of body weight. See Reference 1. See Appendix for details.

Figure 1. The cumulative urinary excretion of radioactivity by dogs after a single intravenous administration of [U-^{14}C]hydroquinone (1 mg/kg, □; 10 mg/kg, Δ). Values represent the mean from 3 to 8 dogs with standard errors shown as vertical bars, except where only two values were determined. Urine was treated with ascorbate and was subsequently counted directly in scintillation fluid (0.5 to 1.0 mL).

FIGURE 1


Cumulative % of Dose
100
90
80
70
60
50
40
30
20
10
0
0
24
48
72
96
120
Time After Dosing (Hours)

The blood concentration of radioactivity, expressed as nmole equiv./mL after iv administration of [^{14}C]HQ is shown in Figures 2 and 3. After iv administration of 1 mg/kg or 10 mg/kg, blood ^{14}C concentration declined slowly from 19.0 nmole equiv./mL at 5 minutes to 1.1 nmole equiv./mL by 24 hours for 1 mg/kg; and from 133.2 nmole equiv./mL at 5 minutes to 11.4 nmole equiv./mL by 24 hours for 10 mg/kg. Elimination kinetics for the first 24 hours revealed evidence of an apparent absorption and elimination phases. The estimated half life values for the 1 mg/kg studies were 1.3 and 7.2 hr for the α and β phases, respectively (Figure 2). For the 10 mg/kg studies, half-life values for the α and β phases were 1.0 and 8.0 hr, respectively (Figure 3).

Concentrations of radioactivity in excised tissues 24 hours after iv dosing with [^{14}C]HQ (1 mg/kg) are presented in Table 2. The highest concentration of ^{14}C was detected in the skin and was equivalent to about 10.4% of the dose. The liver and the intestines contained about 0.6% and 0.5% of the dose, respectively. The other tissues examined showed low concentrations of ^{14}C.

Figure 2. Concentration of radioactivity in the blood following intravenous administration of [U-^{14}C]hydroquinone (1 mg/kg) to male Beagle dogs. Blood samples (0.3 mL) were combusted directly, using a Packard Sample Oxidizer and counted in a scintillation fluid containing Permaflour® and Carbosorb®. ^{14}C disintegrations per minute (dpm) was converted to nmol equivalents hydroquinone/mL blood. Calculated half-life values (hr): α = 1.3, β = 7.2. Data represent mean values from 4 to 8 dogs.

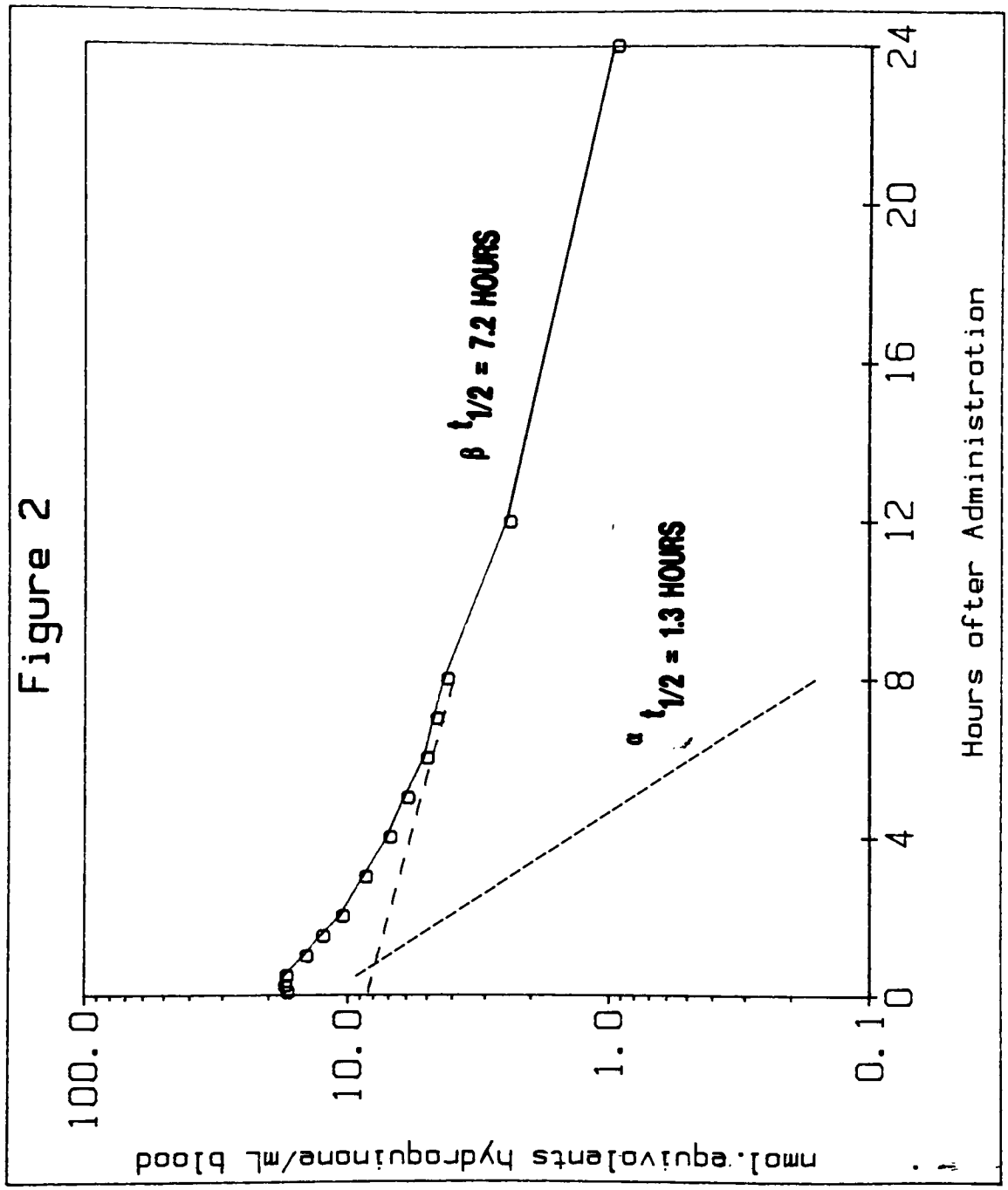


Figure 2
nmol.equivolents hydroquinone/mL blood
100.0
10.0
1.0
0.1
0
4
8
12
16
20
24
Hours after Administration
β t1/2 = 7.2 HOURS
α t1/2 = 1.3 HOURS

Figure 3. Concentration of radioactivity in the blood following intravenous administration of [U-^{14}C]hydroquinone (10 mg/kg) to male Beagle dogs. Blood samples (0.3 mL) were combusted directly, using a Packard Sample Oxidizer and counted in a scintillation fluid containing Permaflour® and Carbosorb®. ^{14}C disintegrations per minute (dpm) was converted to nmol equivalents hydroquinone/mL blood. Calculated half-life values (hr): α = 1.0, β = 8.0. Data represent mean values from 3 dogs.

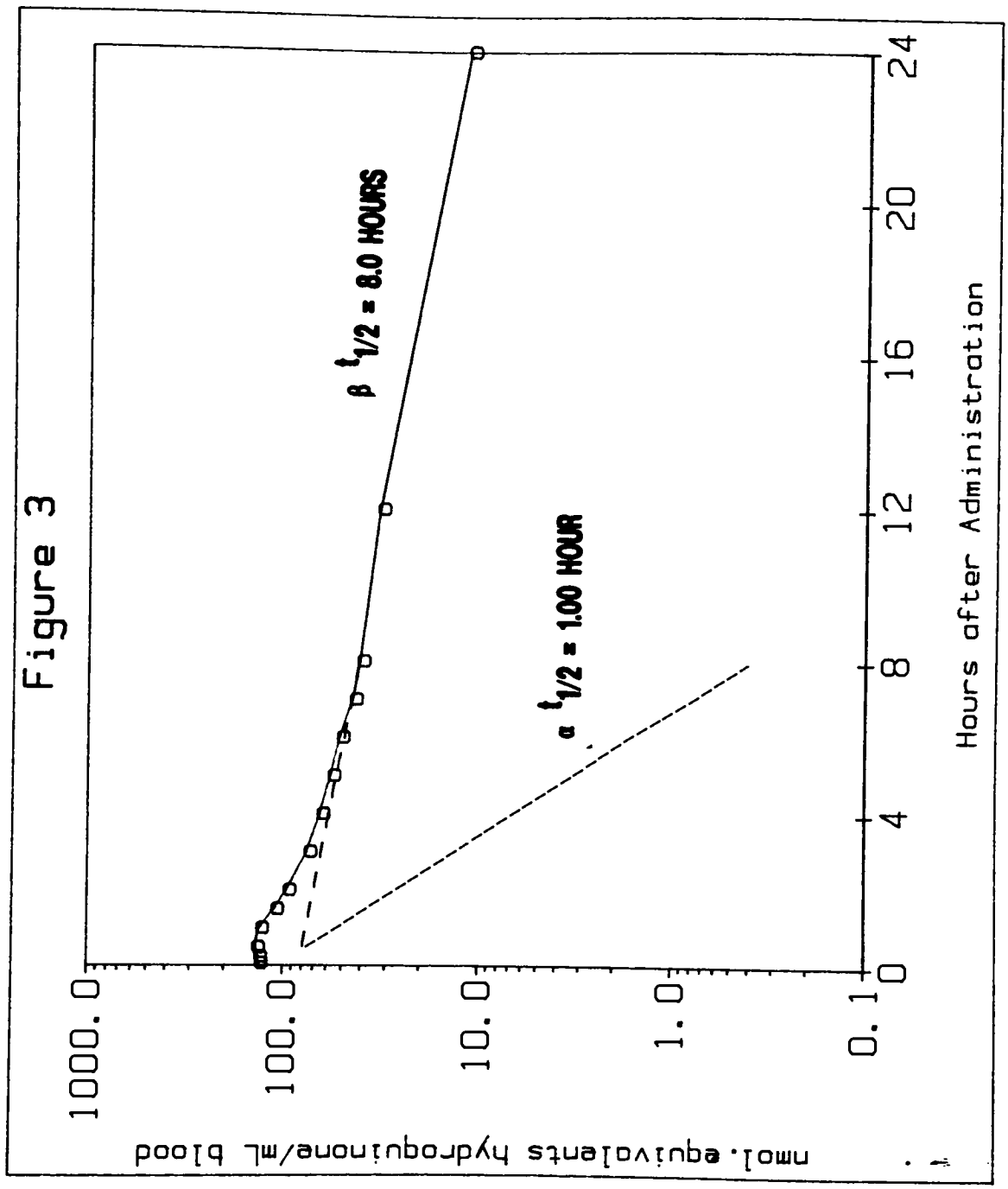


Figure 3
nmol. equivalents hydroquinone/mL blood
1000.0
100.0
10.0
1.0
0.1
0
4
8
12
16
20
24
Hours after Administration
β t1/2 = 8.0 HOURS
α t1/2 = 1.00 HOUR

TABLE 2

Tissue Distribution of Radioactivity in Dogs Dosed Intravenously with 1 mg/kg of [U-^{14}C]Hydroquinone[a]

Tissue	dpm x 10^3/g Wet Weight [b]	% Dose
Brain	1.0	0.03
Bone	1.7	--
Bone Marrow	0.4	--
Fat	1.5	--
Heart	1.4	0.05
Intestine	4.1	0.50
Kidney	3.6	0.09
Liver	4.5	0.58
Lungs	4.5	0.19
Muscle	1.2	--
Pancreas	1.6	0.005
Skin[c]	9.4	10.40
Spleen	3.6	0.11
Stomach	1.8	0.08
Testes	2.2	0.02

(a) Dogs were sacrificed at 24 hours.

(b) Values are expressed as average for two dogs.

(c) Assuming 0.61 m^2 for 11.5 kg. dog. Surface area calculated using the formula: Area (sq. cm.) = 11.6 x weight $^{2/3}$.

Table 3 shows the percentage of the administered dose recovered in the urine, feces, blood and tissues after an oral administration of 50 mg/kg [^{14}C]HQ. About 63% of the dose was excreted in the urine by 4 hours. The excretion pattern was similar to that seen after iv administration (Figure 4). After an initial rapid excretion, radioactivity declined slowly. The 24 hour cumulative excretion of ^{14}C was 78.1% of the dose, and an additional 2% of the dose was excreted during the following 4 days. At 7 days about 80.4% of the dose was accounted for in the urine. The total excretion of radioactivity in the feces was 2.3% and 3.2% of the dose at 24 and 48 hours, respectively. Only an additional 0.6% of the dose was eliminated by 5 days. The concentration of radioactivity in the blood accounted for 2.5% of the dose at 4 hours and declined to about 0.15% by 7 days. Tissue distribution of radioactivity 7 days after oral administration with [^{14}C]HQ is shown in Table 4. The concentration of radioactivity in the tissues other than skin was low. The liver contained 0.3% of the dose. Values for other tissues were less than 0.1% of the dose. The skin contained approximately 1.8% of the dose.

The blood concentration of radioactivity after oral administration of [^{14}C]HQ expressed as nmole equiv./mL is shown in Figure 5. The blood concentration of ^{14}C declined from 309 nmole equiv./mL at 30 minutes to 21.5 nmole equiv./mL by 24 hours. At 7

TABLE 3

Percentage of Total Radioactivity Recovered From Dogs
Dosed by Gavage with [^{14}C]Hydroquinone[a]

	Cumulative % of Administered Dose at Various Collection Periods[b]				
Dose/Collections	4 hr.	8 hr.	24 hr.	48 hr.	Total
50 mg/kg[c]					
Urine	62.5	74.5	78.1	79.2	80.1
	(60.0, 65.0)	(73.3, 75.7)	(76.5, 79.7)	(77.6, 80.7)	(78.5, 81.7)
Feces	(d)	(d)	2.33	3.15	3.71
			(2.40, 2.26)	(3.68, 2.62)	(4.46, 2.95)
Blood[e]	2.51	0.97	0.44	0.30	0.19
	(3.16, 1.87)	(0.92, 1.02)	(0.31, 0.58)	(0.19, 0.40)	(0.11, 0.27)
Tissue[f]	(d)	(d)	(d)	(d)	2.24
					(2.01, 2.46)

(a) Male Beagle dogs were administered Ace-Promazine® as a tranquilizer for 8 hours. [^{14}C]Hydroquinone dissolved in degassed water was given orally as a single dose of 50 mg/kg (20 mL, 100 µCi). Urine and blood were collected for up to 7 days. Fecal samples were collected for 5 days.

(b) Totals are based on 120 hours for urine, feces and blood, 168 hours for tissues. The overall recovery of ^{14}C at 168 hours was 80.4% for urine. The overall recovery of ^{14}C in urine, feces, blood and tissues at 7 days was 86.5% of the dose.

(c) Two dogs per group.

(d) Not measured.

(e) Blood volume assumed to be 9.41% of body weight. See Reference 1

(f) Tissues include brain, heart, intestine, kidney, liver, lungs, pancreas, skin, spleen, stomach and testes.

Figure 4. The cumulative urinary excretion of radioactivity by dogs after a single dose by gavage with [U-^{14}C]hydroquinone (50 mg/kg). Values represent the mean from 2 dogs. Urine was treated with ascorbate and was subsequently counted directly in scintillation fluid (0.5 to 1.0 mL).

FIGURE 4

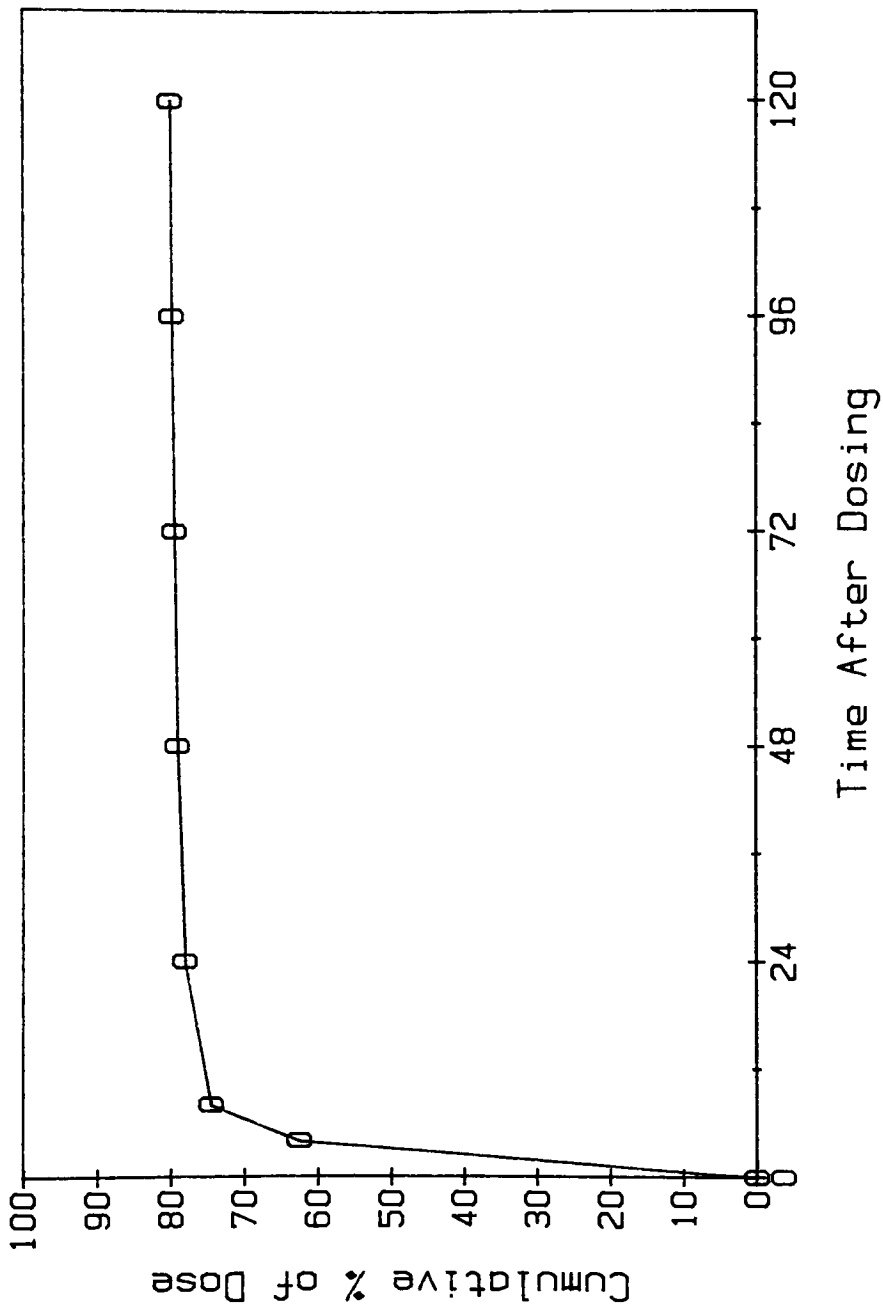

Cumulative % of Dose
100
90
80
70
60
50
40
30
20
10
0
0
24
48
72
96
120
Time After Dosing

TABLE 4

Tissue Distribution of Radioactivity in Dogs Dosed By Gavage with 50 mg/kg of [U-^{14}C]Hydroquinone[a]

Tissue	dpm x 10^3/g Wet Weight [b]	% Dose
Brain	0.121	0.002
Bone	< 0.07	--
Bone Marrow	< 0.025	--
Fat	0.461	--
Heart	0.181	0.007
Intestine	0.33	0.06
Kidney	0.595	0.019
Liver	1.75	0.30
Lungs	0.259	0.012
Muscle	0.141	--
Pancreas	7.17	0.003
Skin (Thorasic)	0.226	1.80[c]
(Dorsal)	1.035	
Spleen	0.361	0.007
Stomach	0.245	0.013
Testes	0.190	0.0017

(a) Dogs were sacrificed at 168 hours.

(b) Values are expressed as an average for two dogs.

(c) Average, assuming 0.64 m^2 for 12.3 kg dog. The surface area was calculated using the formula: Area (sq. cm.) = 11.6 x weight $^{2/3}$.

Figure 5. Concentration of radioactivity in the blood following oral administration of [U-^{14}C]hydroquinone (50 mg/kg) to male Beagle dogs. Blood samples (0.3 mL) were combusted directly using a Packard Sample Oxidizer and counted in a scintillation fluid containing Permaflour® and Carbosorb®. ^{14}C disintegrations per minute (dpm) was converted to nmol equivalents hydroquinone/mL blood. Calculated half-life values (hr): α = 0.85, β = 12.5. Data represent mean values from 2 dogs.

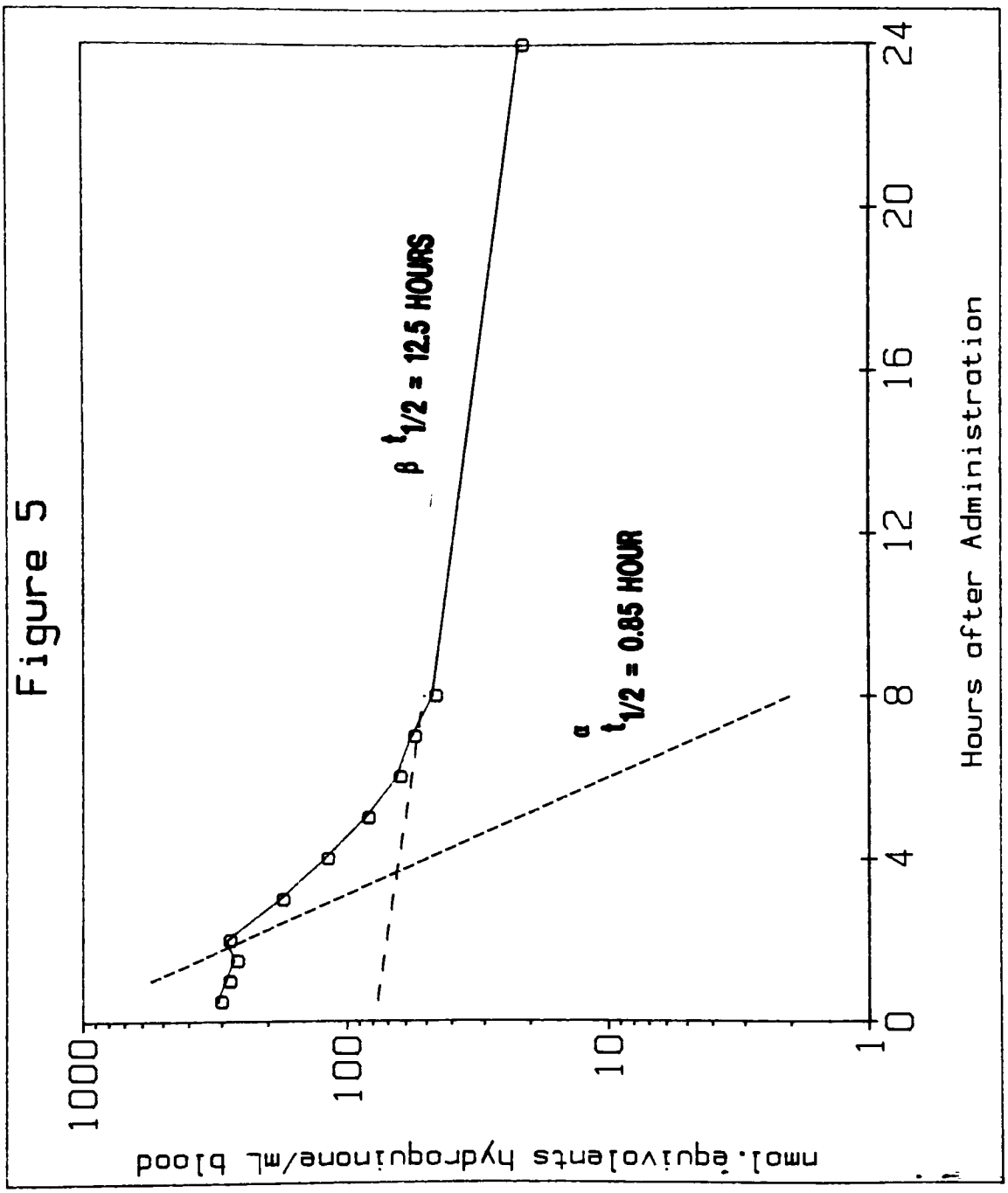


Figure 5
nmol. equivolents hydroquinone/mL blood
1000
100
10
1
0
4
8
12
16
20
24
Hours after Administration
β t1/2 = 12.5 HOURS
α t1/2 = 0.85 HOUR

days, the concentration was 7.1 nmole equiv./mL. The elimination profile was similar to that seen after the iv administration. After an initial rapid distribution phase, the radioactivity declined slowly. The half life values for the distribution and elimination phases were estimated to be 0.85 and 12.5 hr, respectively.

The rate of percutaneous absorption and the elimination of radioactivity following a 60 minute skin exposure to [^{14}C]HQ (4.5 g/L) are summarized in Table 5. The assumption is made that the metabolic fate and disposition of [^{14}C]HQ is similar after iv or skin administration. After dermal application of [^{14}C]HQ, urinary excretion of radioactivity was low. The highest concentrations of ^{14}C were generally detected in the 24 to 48 hour collections (Figure 6). The total amount of ^{14}C excreted by 48 hours was equivalent to about 149 nmoles of HQ and by 120 hours was about 171 nmole of HQ. The average percutaneous absorption rate, calculated using the 48 hour excretion data for the dermal and iv experiments, was approximately 0.16 nmoles/cm^2/minute (1.1/µg/cm^{2}hr). No measurable concentration of radioactivity (< 0.025 µg/mL) was detected in the blood of dogs exposed dermally for 60 minutes to [^{14}C]HQ.

TABLE 5

Percutaneous Absorption and Urinary Elimination of Radioactivity by Dogs Exposed to [U-^{14}C]Hydroquinone[a]

Radioactivity in Urine, nmol. Equivalents[b]					
4 hr.	8 hr.	24 hr.	48 hr.	Total[c]	Percutaneous[d] Absorption Rate nmol/cm^2/min.
2.8 ± 1.5	4.4 ± 2.6	55.1 ± 37.6	149.0 ± 43.9	171.3 (247.6, 94.7)	0.16 ± 0.05

(a) [U-^{14}C]Hydroquinone (15 mL) applied in a 55.6 cm^2 skin absorption cell, approximately 40 µCi per experiment (4.5 g/L). Exposure was carried out for 60 minutes.

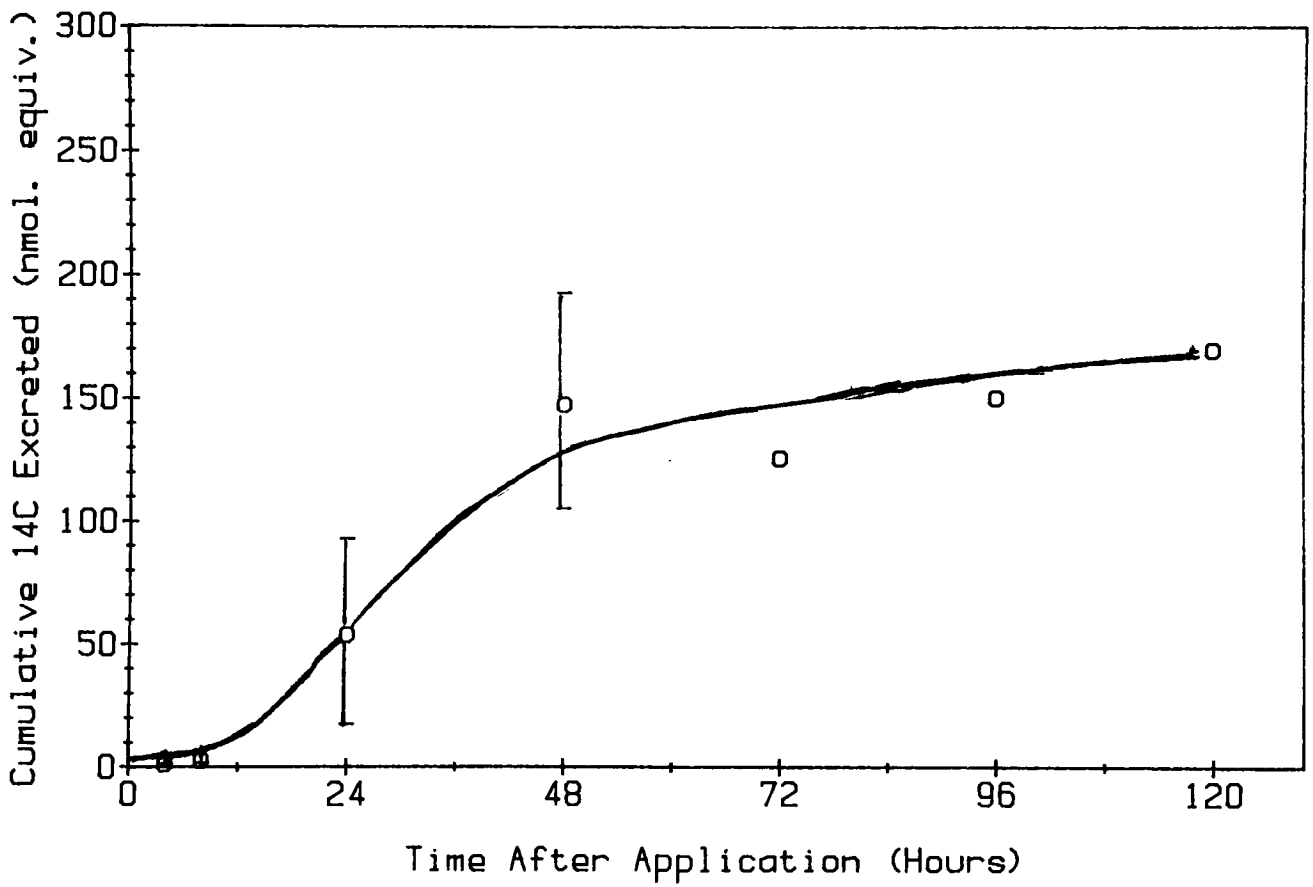
(b) Values presented are mean ± S.E. (where n=5) or average, individual values (where n=2).

(c) Total is based on urine collection for 120 hours.

(d) Calculated after correcting for appropriate % excretion after i.v. administration (28.8% at 48 hours).

Figure 6. The cumulative urinary excretion of radioactivity by dogs after dermal application of [U-^{14}C]hydroquinone (4.5 g/L) for 60 minutes. Values represent the mean from 2 to 5 dogs with standard error shown as vertical bars. Urine was treated with ascorbate and was subsequently counted directly in scintillation fluid (1.0 mL). ^{14}C disintegrations per minute (dpm) was converted to nmole equivalents.

FIGURE 6


Cumulative 14C Excreted (nmol. equiv.)
300
250
200
150
100
50
0
0
24
48
72
96
120
Time After Application (Hours)

HPLC Analysis

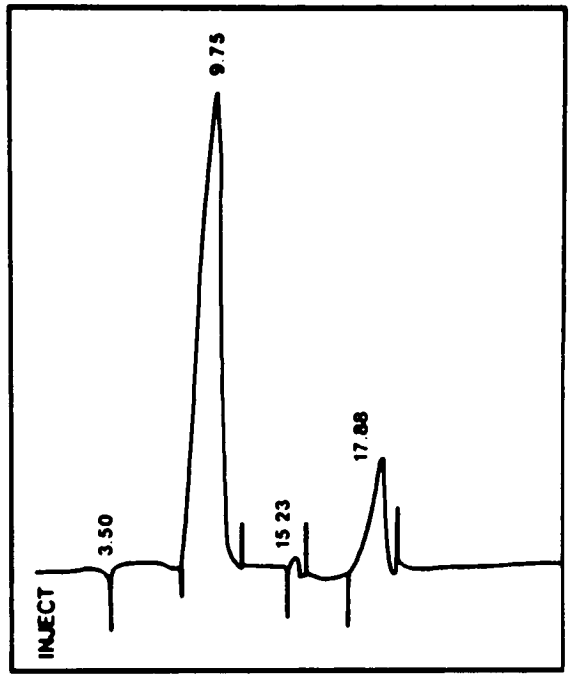
All dose solutions were analyzed by hplc. Radiochemical detection was done to verify the radiochemical purity of the [U-^{14}C]hydroquinone. Figure 7 (a-b) shows a representative chromatogram from the analysis of a 1 mg/kg iv dose solution. Ascorbic acid was added to inhibit oxidation. One uv and radioactive peak was seen. The retention time (9.75 min) was compared to that of an authentic sample of hydroquinone, Figure 7 (c-d).

Unhydrolyzed urine (whole and extracted, collected 4 hours after an iv dosing), contained at least 4 to 5 major and 2 to 3 small radioactive components as detected by hplc analysis. Figure 8 (a-c) shows representative chromatograms of whole unhydrolyzed urine from the iv administration (1 mg/kg and 10 mg/kg) and oral dosing (50 mg/kg). The figures revealed that there is no significant amount of free hydroquinone in the urine (retention time was compared to that of an authentic sample of hydroquinone).

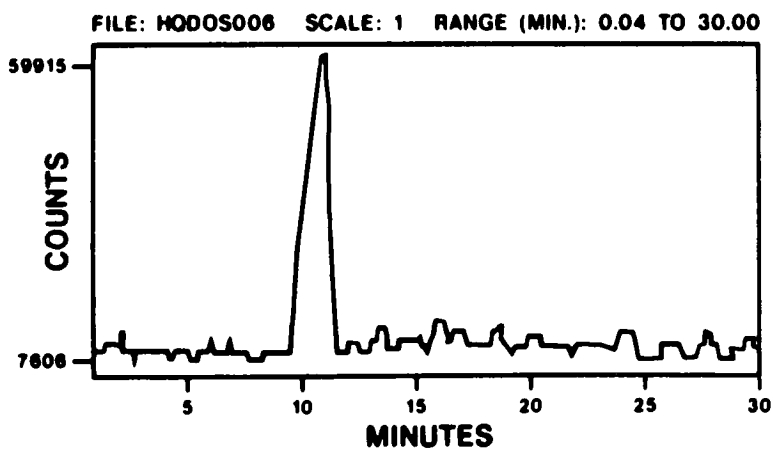
Figure 9 shows a bar graph depicting 4 of the fractions collected from extracts of unhydrolyzed 4-hour urine collections. The first collection and largest component contained about 66.4% of the total ^{14}C injected and represented a collection time of 0 to 12 minutes. The second collection accounted for about 16.1% of the

Figure 7 (a-b). U.V. (top) and radioactive (bottom) hplc chromatograms of a 1 mg/kg dose of [^{14}C]hydroquinone. A dose containing approximately 3.3 µCi/mL was diluted 50x with degassed water. A 50 µL injection was made. Mobile phase: formic acid (0.09%) /methanol. A single U.V. and radioactive peak was seen. The retention time (9.75 minutes) was compared to that of an authentic sample of hydroquinone.

FIGURE 7


9.75
3.50
15.23
17.88
INJECT

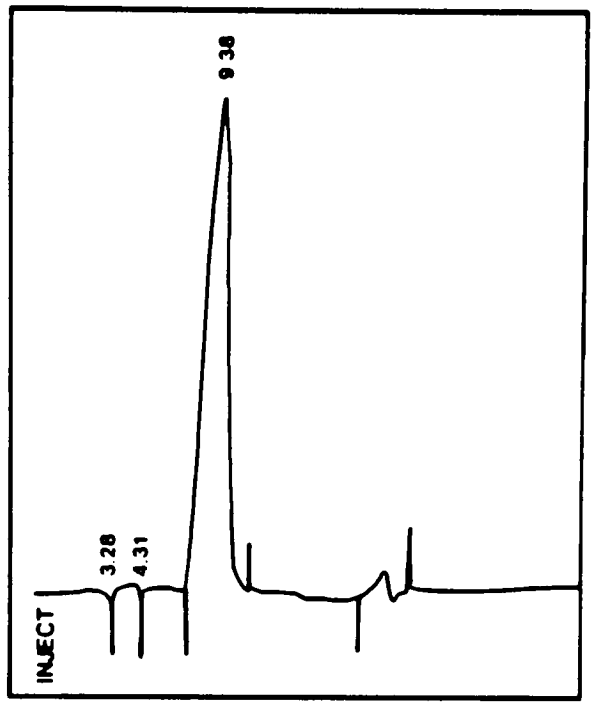
(a)


FILE: HQDOS006 SCALE: 1 RANGE (MIN.): 0.04 TO 30.00
59915
7606
COUNTS
5
10
15
20
25
30
MINUTES

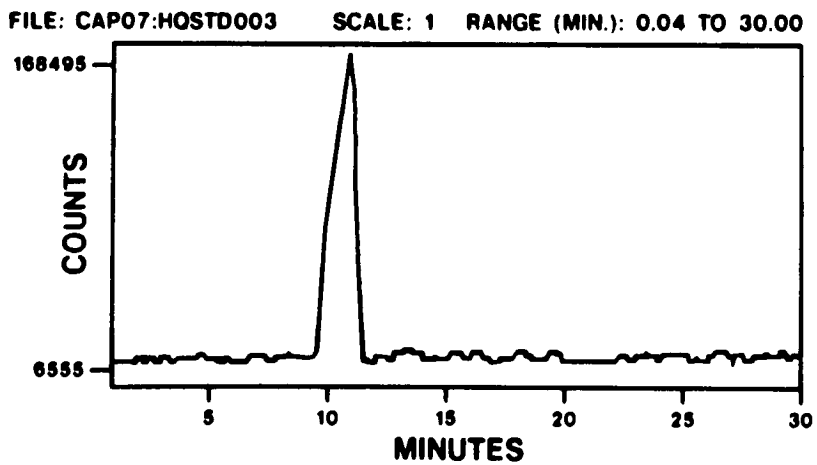
(b)

Figure 7 (c-d). High performance liquid chromatogram of an authentic sample of hydroquinone compound. Fifty milligrams of HQ and 500 mg of ascorbic acid were diluted to 25 mL with degassed water (boiled, then sonicated under reduced pressure), to give a 2 mg/mL stock solution. One hundred microliters of this stock solution was diluted to 10 mL with degassed water to make a 20 µg/mL standard. [U-^{14}C]Hydroquinone was added to make a final solution of 270 µg/mL, containing approximately 0.47 µCi/mL. Volume injected was 25 µL. Mobile phase: formic acid (0.09%)/methanol. A single U.V. (top) and radioactive (bottom) peak was seen. U.V. retention time was 9.38 minutes.

FIGURE 7


9.38
3.28
4.31
INJECT

(c)


FILE: CAP07:HOSTD003 SCALE: 1 RANGE (MIN.): 0.04 TO 30.00
168495
6555
COUNTS
5
10
15
20
25
30
MINUTES

(d)

Figure 8 (a-c). U.V. (left) and radioactive (right) chromatograms from hplc analysis of unhydrolyzed whole urine. Urine was collected 4 hours after the dog received either an iv administration (1 mg/kg or 10 mg/kg) or an oral dose of [U-^{14}C]hydroquinone. U.V. absorption was monitored at 295 nm.

Volume of sample injected was 75, 100 and 25 µL for an iv dose of 1 and 10 mg/kg and an oral dose of 50 mg/kg, respectively. The hydroquinone peak was compared to that of an authentic sample of hydroquinone.

FIGURE 8

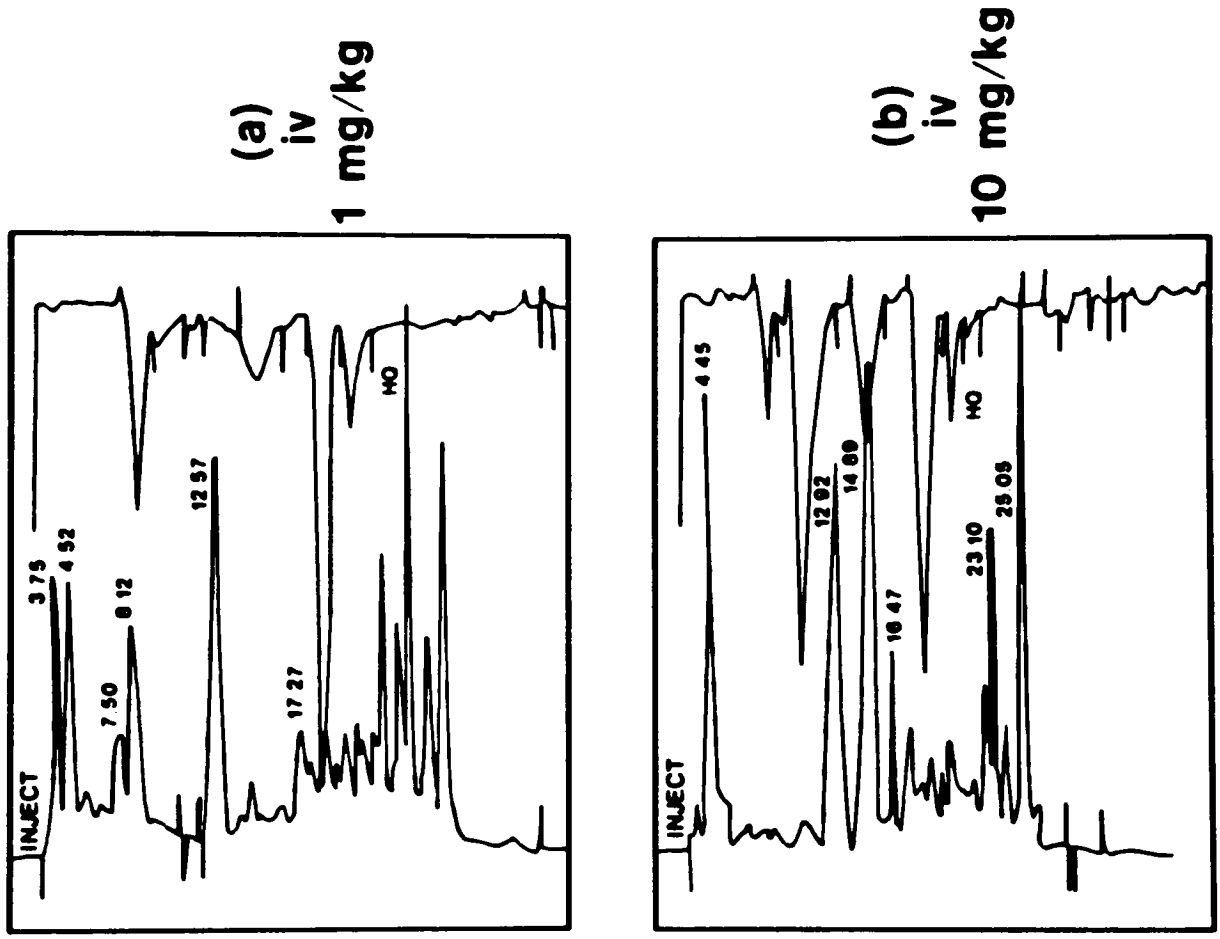
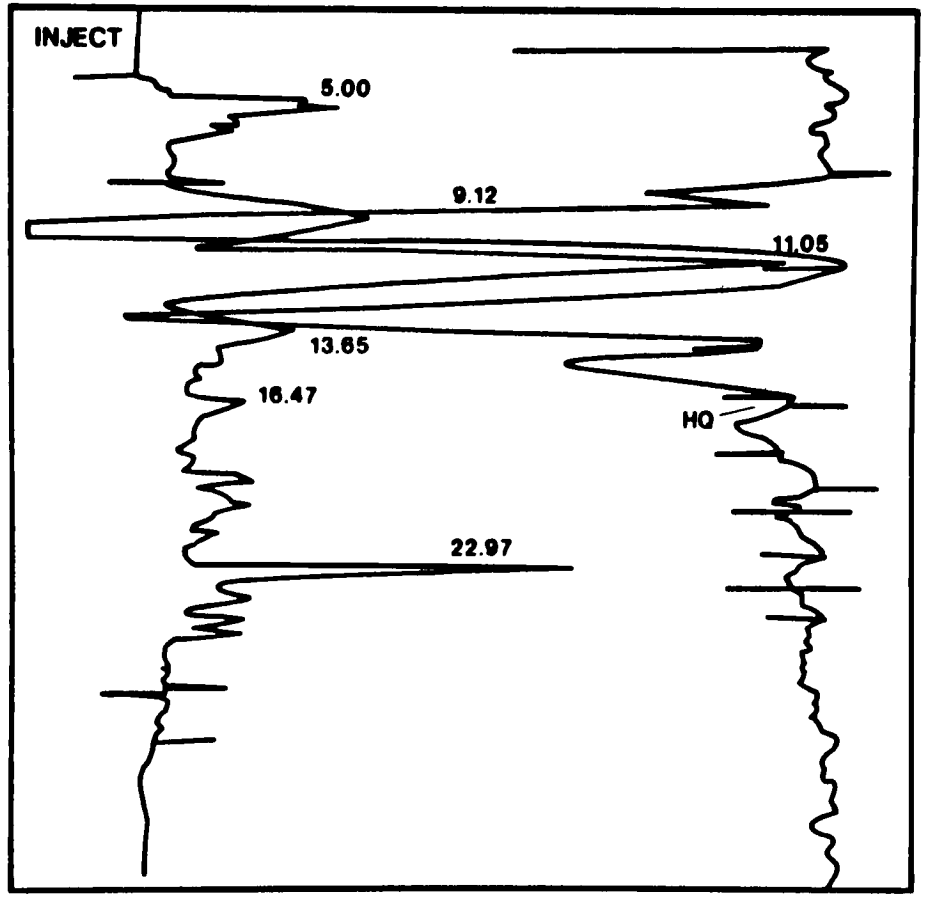

(a)
iv
1 mg/kg
INJECT
3.75
4.52
7.50
8.12
12.57
17.27
HO
(b)
iv
10 mg/kg
INJECT
4.45
12.02
14.00
16.47
23.10
25.05
HO

FIGURE 8

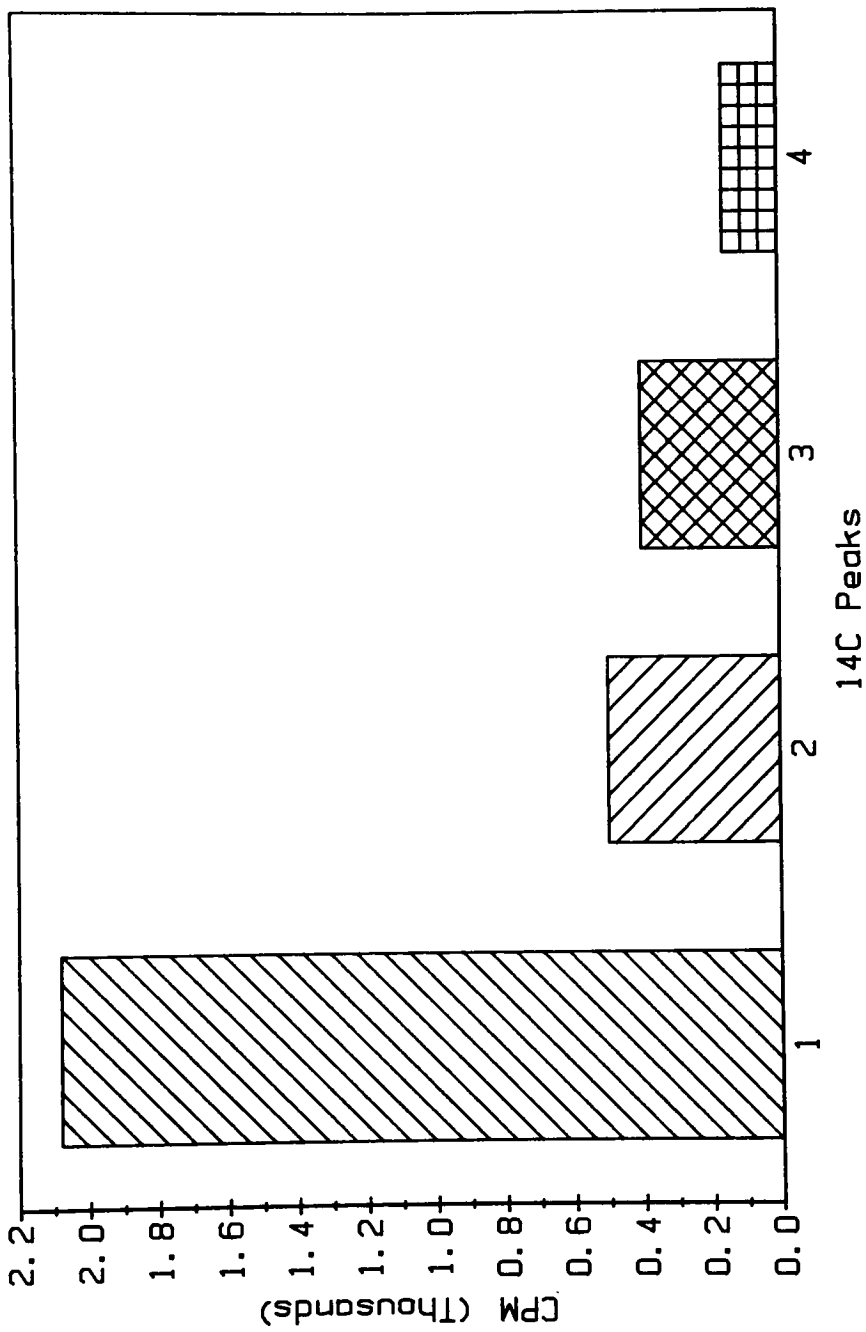


(c)
ORAL
50 mg/kg

Figure 9. Bar graph of radioactive fractions collected from an hplc analysis of extracts from unhydrolyzed urine (20 µL). Urine was collected 4 hours after dogs received an iv administration of 10 mg/kg [U-^{14}C]hydroquinone. The radioactivity, monitored at 295 nm, is reported as ^{14}C counts per minute (cpm) as determined by liquid scintillation spectrometry.

Peaks 1, 2, 3, and 4 contained about 66.4%, 16.1%, 12.8% and 4.7% of the total ^{14}C injected, respectively.

FIGURE 9



injected ^{14}C and was collected from 12 to 17 minutes. The third peak collected from 17 to 20.4 minutes, contained 12.8% of the total ^{14}C. The fourth radioactive peak collected had 4.7% of the injected ^{14}C. The collection time was 20.4 to 30 minutes. An authentic sample of hydroquinone had a retention time of 12.4 minutes.

Because of interfering substances in the concentrated fractions collected from unhydrolyzed whole and extracted urine and the apparent instability of the metabolites, identification of these peaks could not be determined by gas chromatographic/mass spectroscopic analysis.

Treatment of urine with β-glucuronidase, aryl sulfatase or HCl for identification of urinary conjugates, indicated that the urine of iv and orally-treated dogs did not contain glucuronides of hydroquinone. Preliminary evidence suggests the presence of a sulfuric acid conjugate, but does not appear to be hydroquinone monosulfate.

DISCUSSION

These studies accessed quantitatively the percutaneous absorption of hydroquinone in a solution equivalent to that found in commercial black and white photographic developer and investigated the metabolic fate of hydroquinone after iv or oral administration in the dog.

Of interest in these studies was the relatively low recoveries of ^{14}C in the iv studies. Recoveries of 35% and 66% in the iv studies (1 mg/kg and 10 mg/kg) and 80.4% of the dose with oral dosing were seen in the urine. About 7.1, 6.1, and 4.0% of the dose was found in the feces for iv dosing of 1 or 10 mg/kg and oral dosing, respectively. suggesting that biliary excretion of hydroquinone and/or its metabolites was occurring. The concentration of ^{14}C in the blood declined slowly after iv or oral dosing. This may suggest that there is a compartment in the dog acting as a "depot" where the radioactivity is retained. The elimination half-life values were 7.2, 8.0, and 12.5 hrs for the iv 1 mg/kg, 10 mg/kg, and the oral doses, respectively. The concentration of radioactivity in the tissues other than skin was low. The liver contained 0.3 to 0.6% of the dose after iv or oral administration. The low concentration seen in the bone marrow was interesting, since Irons et al. (1979) reported that in rats administered benzene, HQ was formed in the bone marrow and the HQ persisted long after blood levels had declined.

An explanation of the relatively low recovery of radioactivity from [^{14}C]HQ is unclear at this time. The assumption was made that the skin samples tested were representative of the total skin area. The possibility remains that the sample may not be representative, and that the skin area may contain a considerable larger proportion of the remaining radioactivity than estimated by this method.

Based on our findings of the lower dose iv studies, one can speculate that the majority of the unaccounted radioactivity may reside in the skin. These findings were unexpected and had not been reported previously.

Our findings indicate that the metabolism of hydroquinone in the rat was different from the dog. Lockhart, et al., (1984), found that HQ administered orally to rats, was rapidly absorbed from the gastrointestinal tract and was rapidly excreted in the urine. Within 8 hours, over 90% of the dose was excreted in the urine, in contrast to only 20% of the dose seen in the dog after a 1 mg/kg iv administration and 74% after an oral dose. Woodard (1951) also reported low urinary recoveries in dogs dosed orally with 50 mg/kg HQ. The metabolites of [^{14}C]HQ in the urine of iv or orally dosed dogs were also different from those in the urine of orally dosed rats (Figure 10). Apparently the route of metabolism is different for the 2 species. Reverse phase

hplc analysis of radioactivity in the urine showed that the dog urine contained more radioactive components than were found in rat urine. Only 2 major components were seen in the rat urine. A small amount of free hydroquinone was seen in the urine of both species. Garton and Williams (1949a) reported similar findings in rabbits dosed with 100 to 400 mg/kg HQ.

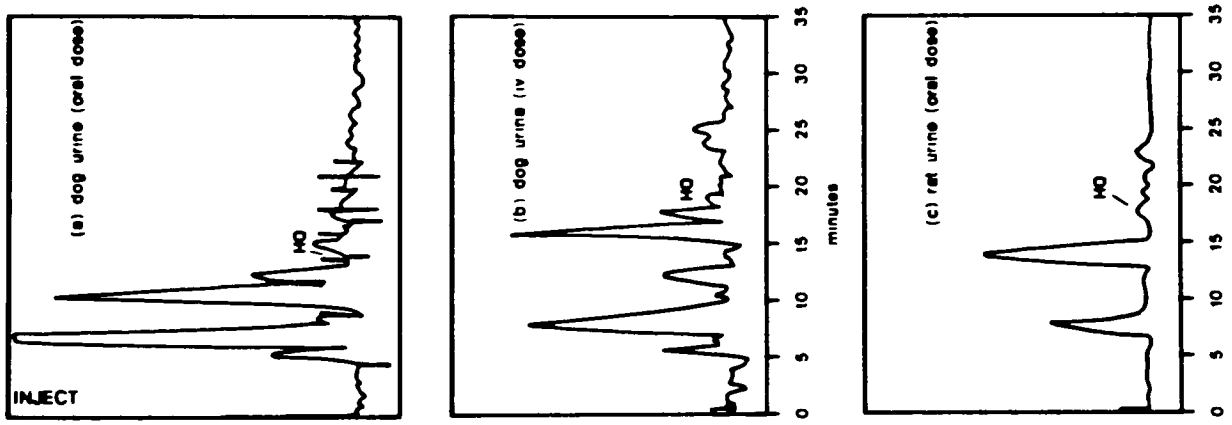
After the treatment of the urine with hydrolytic enzymes, preliminary evidence indicated that neither the sulfate nor the glucuronide of HQ was present in any appreciable quantity in dog urine. The metabolites in the dog urine may be conjugation products with glutathione or with other amino acids. Hydroquinone has been shown to be metabolized to benzoquinone in vitro and the benzoquinone has been known to react rapidly with glutathione and cysteine (Lunte and Kissinger, 1983). Enzyme treatment of rat urine (Figure 11) shows that the 2 major components in the rat urine were HQ monosulfate and HQ monoglucuronide with retention times of approximately 6.5 and 13.5 minutes, Figure 11 (a), respectively. On hydrolysis these moieties gave rise to a peak at approximately 16.4 minutes, corresponding to HQ Figure 11 (b,c). A small peak with retention time of 22 minutes was present in all samples and the retention time of this peak was unchanged by enzyme treatment. The sulfate hydrolysis was not

Figure 10 (a-c). Radioactive chromatograms from the hplc analysis of unhydrolyzed whole dog and rat urine. Dog urine, Figure 10 (a-b), was collected 4 hours after an iv administration (10 mg/kg) or an oral dose (50 mg/kg) of [U-^{14}C]hydroquinone. Rat urine, Figure 10 (c), was collected 8 hours after an oral dose of 50 mg/kg [U-^{14}C]hydroquinone. Urine was filtered by passage through a 0.45 μm Millipore filter and analyzed directly.

Volume of sample injected was 25, 100, and 50 μL for a dog, iv and oral dose, and for a rat orally dosed, respectively.

U.V. absorption was monitored at 295 nm. Mobile phase: formic acid (0.09%)/methanol. The hydroquinone peak was compared to that of an authentic sample of hydroquinone.

FIGURE 10


(a) dog urine (oral dose)
INJECT
HO
(b) dog urine (iv dose)
HO
(c) rat urine (oral dose)
HO
0
5
10
15
20
25
30
35
minutes

complete by 4 hours Figure 11 (c). Lockhart et al., (1984) reported that hydroquinone glucuronide accounted for 61.3 to 63.9% of the dose, after 8 hours and hydroquinone sulfate accounted for 19.1 to 26.2% of the dose in the urine of rats dosed orally with 50 mg/kg [^{14}C]HQ. These findings are in agreement with those of DiVincenzo et al., (1984) in which rats dosed orally with 200 mg/kg of [^{14}C]HQ, excreted 91.9% of the dose in the urine within 2-4 days, and the only radiolabeled compounds in the urine were HQ monoglucuronide and HQ monosulfate.

Percutaneous absorption studies indicated that the extent of absorption of hydroquinone from a 60 minute dermal exposure was very low. The absorption rate of 0.16 nmole/cm^2/min was much slower than those of lipid soluble compounds such as aliphatic ketones and glycol ethers, using the same animal model system. The absorption rates from methyl n-butyl ketone (Di Vincenzo et al., 1978), 2-propoxyethyl acetate and 2-ethoxyethyl acetate (Guest et al., 1985). were 240, 219, and 179 nmole/cm^2/min, respectively. Further evidence that the extent of absorption of hydroquinone is low is seen in published in vitro studies with rat skin (Marty et al., 1981). The percutaneous absorption rate was similar to that seen in vivo in the dog. For human skin, the rate of absorption was slower by a factor of 7 than that seen in the rat.

Figure 11 (a-c). Radioactive chromatograms from the hplc analysis of untreated (11-a) and hydrolyzed (11-b,c) rat urine. Urine was collected 8 hours after the test animal received an oral dose of 50 mg/kg [U-^{14}C]hydroquinone. Urine sample was prepared as follows:

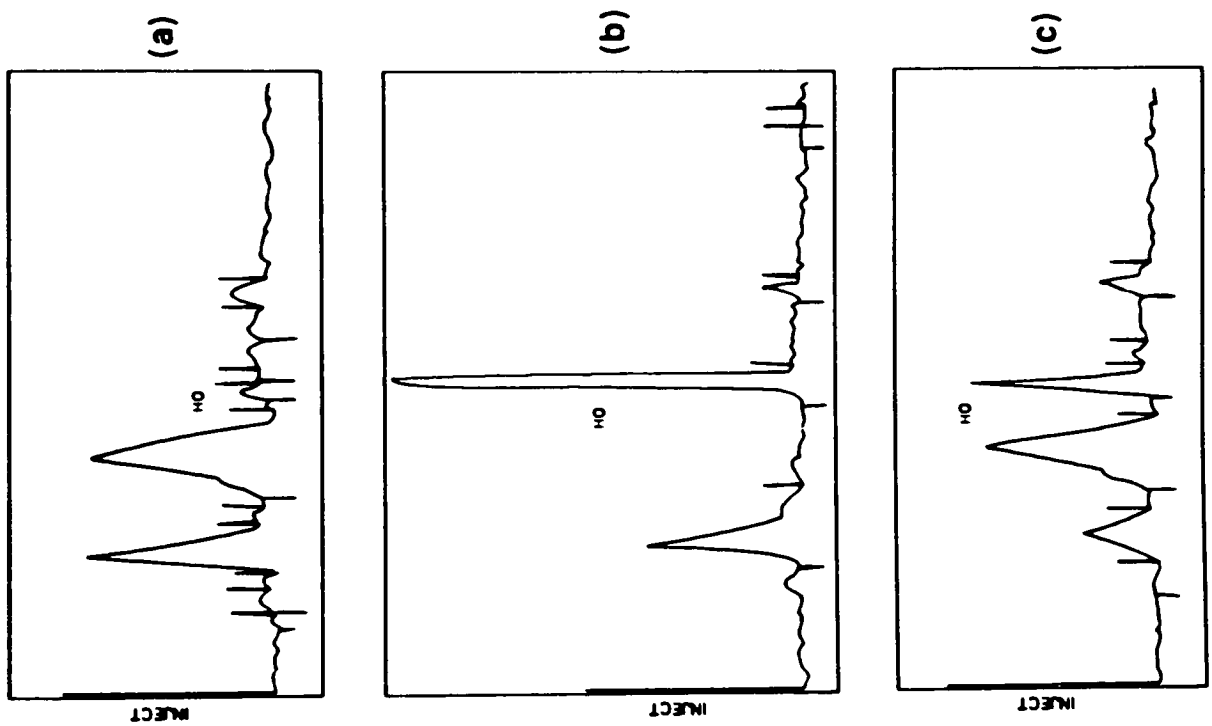
Urine	β-glucuronidase	Sulfatase/Saccharolactone	Buffer	Code
0.5 mL	0	0	1.0 mL	11(a)
0.5 mL	1.0 mL	0	0	11(b)
0.5 mL	0	1.0	0	11(c)

A 10 mM saccharolactone solution was added to inhibit the β-glucuronidase activity in the sulfatase preparation. The enzymes were prepared in a 0.1M sodium acetate buffer, pH 5.5. The final incubation mixture contained 1,800 and 5,000 Fishman units/mL of aryl sulfatase and β-glucuronidase, respectively.

Samples were incubated at 37°C for 4 hours, filtered through a 0.45 µm centrifugal filter (using a Whatman #1 pre-filter) and analyzed directly by hplc (100 µL), using a 23 cm RP-18 MPLC column. U.V. absorption was monitored at 295 nm.

The hydroquinone peak was compared to that of an authentic sample of hydroquinone.

FIGURE 11



The percutaneous absorption rate found in dogs may be used to estimate the dermal uptake of hydroquinone by humans. Assuming a total surface area of 1.85 m^2 for an average adult (of which the hands comprise 4% of the total), immersion of both hands for 60 minutes in a photographic developer solution containing HQ would result in the absorption of about 0.8 mg of hydroquinone (i.e. 11.2 µg/kg for a 70 kg man). These findings suggest that skin contact is unlikely to be a significant route of HQ absorption by humans.

ACKNOWLEDGMENTS

This project is presently on-going at Eastman Kodak Company, Health and Environment Laboratories, Toxicological Sciences Section.

I am grateful to my advisors, Dr. Derek Guest (Study Director) and Dr. George DiVincenzo (Group Leader, Metabolism Group), for their support and guidance throughout my graduate work.

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APPENDIX I

INDEX

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Analyses of radioactive solutions

Molecular weight of Test Compound: 110.11 g/mole
Specific activity of [14C] Test Compound Stock: 5.000 mCi/mmole

DOSE PREPARATION (NOMINAL):	1	2	3	4	5	6	7	8
a) Total uCi of [14C] test compound added	16.67	16.67	16.67	16.67	16.67	16.67	250.00	250.00
b) Test compound (gm) in addition a)	0.00037	0.00037	0.00037	0.00037	0.00037	0.00037	0.00551	0.00551
c) Unlabelled test compound added (gm)	0.01630	0.01550	0.01480	0.01547	0.01705	0.01705	0.02325	0.02325
d) Final total volume (mL) including vehicle	5.00	5.00	5.00	5.00	5.00	5.00	10.00	10.00
e) Test compound per mL of dose	0.00333	0.00317	0.00303	0.00317	0.00348	0.00348	0.00288	0.00288
f) uCi per mL of dose	3.334	3.334	3.334	3.334	3.334	3.334	25.000	25.000

INTRAVENOUS DOSE - SUMMARY

	Dog # 1 (# 412899)	Dog # 2 (# 420280)	Dog # 3 (# 415090)	Dog # 4 (# 418315)	Dog # 5 (# 420255)	Dog # 6 (# 422011)	Dog # 7 (# 455482)	Dog # 8 (# 456730)
mL dose injected	3.00	3.00	3.00	3.00	3.00	3.00	4.00	4.00
mg test cpd inject	10.00	9.53	9.10	9.50	10.46	10.45	11.51	11.51
kg body wt	10.0	9.5	9.5	9.1	10.5	10.5	11.6	11.4
mg/kg body weight	1.0	1.0	0.96	1.04	1.00	1.00	0.99	1.01
uCi per animal	10.14	10.31	10.01	10.09	10.24	10.14	100.57	100.57

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SUMMARY OF: Analyses of radioactive solutions

ASSAY: Dog #1 (# 412899)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	37920	3.416
2	"	37220	3.353
3	"	37544	3.382
4	"	37789	3.404
5	"	37823	3.407
6	"	37093	3.342
7	"	37358	3.366
mean		37535	3.382

ASSAY: Dog #2 (# 420280)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	38067	3.429
2	"	37882	3.413
3	"	38404	3.460
4	"	37969	3.421
5	"	38308	3.451
6	"	37593	3.387
7	"	38763	3.492
mean		38141	3.436

ASSAY: Dog #3 (# 415090)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	37719	3.398
2	"	36544	3.292
3	"	37018	3.335
4	"	37011	3.334
5	"	37157	3.347
6	"	36708	3.307
7	"	37112	3.343
mean		37038	3.337

ASSAY: Dog #4 (# 418315)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	37181	3.350
2	"	37510	3.379
3	"	37466	3.375
4	"	37156	3.347
5	"	37750	3.401
6	"	36922	3.326
7	"	37355	3.365
mean		37334	3.363

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Analyses of radioactive solutions

ASSAY: Dog #5 (# 420255)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	38409	3.460
2	"	38808	3.496
3	"	38005	3.424
4	"	37539	3.382
5	"	38158	3.438
6	"	36051	3.248
7	"	38127	3.435
mean		37871	3.412

ASSAY: Dog #6 (# 422011)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	37418	3.371
2	"	37167	3.348
3	"	38176	3.439
4	"	37529	3.381
5	"	37564	3.384
6	"	37532	3.381
7	"	37270	3.358
mean		37522	3.380

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Analyses of radioactive solutions

ASSAY: Dog #7 (# 455482) and Dog #8 (# 456730)

Sample	mL dose sampled	Diluted to (mL)	Vol diluted sample (mL)	DPM observed	uCi/mL soln
A	0.020	25.00	1.000	44885	25.051
			1.000	43677	
			1.000	44218	
			1.000	45179	
B	0.020	25.00	1.000	44261	24.843
			1.000	45063	
			1.000	44432	
			1.000	42726	
C	0.020	25.00	1.000	43318	25.532
			1.000	45776	
			1.000	45805	
			1.000	46482	
Mean uCi/mL dose:					25.142

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Urinary Radioactivity

Collection Period		1	2	3	4	5	6	7	8	Mean	SD
0-4hr	uCi	1.70	1.41	1.26	1.84	1.58	1.05	13.99	16.18		
	% of dose	16.77	13.63	12.57	18.22	15.42	10.34	13.91	16.09	14.62	2.36
4-8hr	uCi	0.44	0.57	0.27	0.37	0.73	0.94	3.40	3.78		
	% of dose	4.29	5.56	2.71	3.65	7.10	9.24	3.38	3.75	4.96	2.08
8-12hr	uCi	ND	ND	0.13	0.18	0.14	0.12	ND	ND		
	% of dose	ND	ND	1.29	1.82	1.33	1.16	ND	ND	1.40	0.25
8-24hr	uCi	0.78	0.84	ND	ND	ND	ND	10.13	7.58		
	% of dose	7.74	8.17	ND	ND	ND	ND	10.07	7.54	8.38	1.00
12-24hr	uCi	ND	ND	0.26	0.58	0.31	0.42	ND	ND		
	% of dose	ND	ND	2.64	5.75	2.99	4.11	ND	ND	3.87	1.21
24-48hr	uCi	ND	ND	0.30	0.53	0.32	0.34	ND	ND		
	% of dose	ND	ND	2.97	5.22	3.16	3.32	ND	ND	3.67	0.91

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Urinary Radioactivity

Collection Period		1	2	3	4	5	6	7	8	Mean	SD
48-72 hr	uCi	ND	ND	ND	ND	0.22	0.20	ND	ND		
	% of dose	ND	ND	ND	ND	2.18	1.96	ND	ND	2.07	
72-96hr	uCi	ND	ND	ND	ND	0.10	0.15	ND	ND		
	% of dose	ND	ND	ND	ND	0.95	1.45	ND	ND	1.20	
96-120hr	uCi	ND	ND	ND	ND	0.07	0.10	ND	ND		
	% of dose	ND	ND	ND	ND	0.64	0.96	ND	ND	0.80	
120-144hr	uCi	ND	ND	ND	ND	0.10	0.11	ND	ND		
	% of dose	ND	ND	ND	ND	0.95	1.13	ND	ND	1.04	
144-168hr	uCi	ND	ND	ND	ND	0.03	0.02	ND	ND		
	% of dose	ND	ND	ND	ND	0.28	0.22	ND	ND	0.25	
Total 0-168hr	uCi	ND	ND	ND	ND	3.36	3.24	ND	ND		
	% of dose	ND	ND	ND	ND	34.99	33.89	ND	ND		

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (0-4hr)	121.0	1.00	31684	3775684
			1.00	31203	
			1.00	31416	
			1.00	30513	
2	urine (0-4hr)	114.4	1.00	27442	3120403
			1.00	27036	
			1.00	27221	
			1.00	27406	
3	urine (0-4hr)	363.0	1.00	7693	2793739
			1.00	7624	
			1.00	7637	
			1.00	7831	
4	urine (0-4hr)	726.0	1.00	5710	4081391
			1.00	5668	
			1.00	5365	
			1.00	5744	
5	urine (0-4hr)	60.5	1.00	57617	3505975
			1.00	58324	
			1.00	57953	
			1.00	57906	
6	urine (0-4hr)	31.9	1.00	71024	2327081
			1.00	74504	
			1.00	74078	
			1.00	72191	
7	urine (0-4hr)	41.8	0.50	379757	31054976
			0.50	369489	
			0.50	369751	
			0.50	366887	
8	urine (0-4hr)	50.6	1.00	712187	35926430
			1.00	709293	
			1.00	700232	
			1.00	718322	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (4-8hr)	567.1	1.00	1682	966622
			1.00	1712	
			1.00	1685	
			1.00	1741	
2	urine (4-8hr)	473.0	1.00	2691	1273671
			1.00	2700	
			1.00	2668	
			1.00	2712	
3	urine (4-8hr)	550.0	1.00	1105	601838
			1.00	1076	
			1.00	1109	
			1.00	1087	
4	urine (4-8hr)	550.0	1.00	1505	817163
			1.00	1496	
			1.00	1501	
			1.00	1441	
5	urine (4-8hr)	189.2	1.00	8422	1613072
			1.00	8588	
			1.00	8462	
			1.00	8631	
6	urine (4-8hr)	189.2	1.00	10975	2081105
			1.00	11004	
			1.00	10941	
			1.00	11078	
7	urine (4-8hr)	82.5	1.00	91115	7537221
			1.00	92251	
			1.00	90298	
			1.00	91777	
8	urine (4-8hr)	206.8	1.00	40752	8382845
			1.00	40359	
			1.00	40667	
			1.00	40366	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (8-24hr) (a)	638.0	1.00	1832	1175994
			1.00	1828	
			1.00	1861	
			1.00	1852	
1	urine (8-24hr) (b)	310.0	1.00	1822	566680
			1.00	1842	
			1.00	1848	
			1.00	1800	
2	urine (8-24hr) (a)	264.0	1.00	1303	349206
			1.00	1329	
			1.00	1325	
			1.00	1334	
2	urine (8-24hr) (b)	700.0	1.00	2160	1521800
			1.00	2186	
			1.00	2206	
			1.00	2144	
3	urine (8-24hr)	ND	ND	ND	ND
4	urine (8-24hr)	ND	ND	ND	ND
5	urine (8-24hr)	ND	ND	ND	ND
6	urine (8-24hr)	ND	ND	ND	ND
7	urine (8-24hr)	664.0	1.00	33263	22489680
			1.00	34980	
			1.00	33775	
			1.00	33462	
8	urine (8-24hr)	600.0	1.00	27338	16827750
			1.00	28438	
			1.00	28169	
			1.00	28240	

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (8-12hr)	ND	ND	ND	ND
2	urine (8-12hr)	ND	ND	ND	ND
3	urine (8-12hr)	346.5	1.00	822	286296
			1.00	813	
			1.00	838	
			1.00	832	
4	urine (8-12hr)	495.0	1.00	835	407014
			1.00	820	
			1.00	820	
			1.00	814	
5	urine (8-12hr)	385.0	1.00	779	302129
			1.00	798	
			1.00	769	
			1.00	793	
6	urine (8-12hr)	225.5	1.00	1172	261693
			1.00	1172	
			1.00	1135	
			1.00	1163	
7	urine (8-12hr)	ND	ND	ND	ND
8	urine (8-12hr)	ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (12-24hr)	ND	ND	ND	ND
2	urine (12-24hr)	ND	ND	ND	ND
3	urine (12-24hr)	808.5	1.00	725	586365
			1.00	712	
			1.00	712	
			1.00	752	
4	urine (12-24hr)	462.0	1.00	2782	1288980
			1.00	2826	
			1.00	2771	
			1.00	2781	
5	urine (12-24hr)	748.0	1.00	923	680680
			1.00	920	
			1.00	902	
			1.00	895	
6	urine (12-24hr)	572.0	1.00	1613	925353
			1.00	1631	
			1.00	1613	
			1.00	1614	
7	urine (12-24hr)	ND	ND	ND	ND
8	urine (12-24hr)	ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (24-48hr)	ND	ND	ND	ND
2	urine (24-48hr)	ND	ND	ND	ND
3	urine (24-48hr)	1230.0	1.00	541	658973
			1.00	540	
			1.00	527	
			1.00	535	
4	urine (24-48hr)	1250.0	1.00	942	1169688
			1.00	967	
			1.00	892	
			1.00	942	
5	urine (24-48hr)	302.5	1.00	2380	718059
			1.00	2361	
			1.00	2361	
			1.00	2393	
6	urine (24-48hr)	363.0	1.00	2039	748325
			1.00	2037	
			1.00	2089	
			1.00	2081	
7	urine (24-48hr)	ND	ND	ND	ND
8	urine (24-48hr)	ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description		Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (48-72hr)		ND	ND	ND	ND
2	urine (48-72hr)		ND	ND	ND	ND
3	urine (48-72hr)		ND	ND	ND	ND
4	urine (48-72hr)		ND	ND	ND	ND
5	urine (48-72hr)	(a)	1358.3	1.00	329	432619
				1.00	323	
				1.00	316	
				1.00	306	
5	urine (48-72hr)	(b)	572.0	1.00	107	62348
				1.00	111	
				1.00	107	
				1.00	111	
6	urine (48-72hr)		401.5	1.00	1089	440747
				1.00	1101	
				1.00	1100	
				1.00	1101	
7	urine (48-72hr)		ND	ND	ND	ND
8	urine (48-72hr)		ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (72-96hr)	ND	ND	ND	ND
2	urine (72-96hr)	ND	ND	ND	ND
3	urine (72-96hr)	ND	ND	ND	ND
4	urine (72-96hr)	ND	ND	ND	ND
5	urine (72-96hr)	525.0	1.00	420	214856
			1.00	409	
			1.00	406	
			1.00	402	
6	urine (72-96hr)	350	1.00	914	326113
			1.00	960	
			1.00	934	
			1.00	919	
7	urine (72-96hr)	ND	ND	ND	ND
8	urine (72-96hr)	ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (96-120hr)	ND	ND	ND	ND
2	urine (96-120hr)	ND	ND	ND	ND
3	urine (96-120hr)	ND	ND	ND	ND
4	urine (96-120hr)	ND	ND	ND	ND
5	urine (96-120hr)	375.0	1.00	380	146531
			1.00	383	
			1.00	393	
			1.00	407	
6	urine (96-120hr)	470.0	1.00	446	215730
			1.00	466	
			1.00	467	
			1.00	457	
7	urine (96-120hr)	ND	ND	ND	ND
8	urine (96-120hr)	ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (120-144hr)	ND	ND	ND	ND
2	urine (120-144hr)	ND	ND	ND	ND
3	urine (120-144hr)	ND	ND	ND	ND
4	urine (120-144hr)	ND	ND	ND	ND
5	urine (120-144hr)	425.0	1.00	498	215688
			1.00	554	
			1.00	499	
			1.00	479	
6	urine (120-144hr)	485.0	1.00	515	253291
			1.00	521	
			1.00	524	
			1.00	529	
7	urine (120-144hr)	ND	ND	ND	ND
8	urine (120-144hr)	ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (144-168hr)	ND	ND	ND	ND
2	urine (144-168hr)	ND	ND	ND	ND
3	urine (144-168hr)	ND	ND	ND	ND
4	urine (144-168hr)	ND	ND	ND	ND
5	urine (144-168hr)	470.0	1.00	132	62628
			1.00	132	
			1.00	133	
			1.00	136	
6	urine (144-168hr)	300.0	1.00	169	50400
			1.00	166	
			1.00	166	
			1.00	171	
7	urine (144-168hr)	ND	ND	ND	ND
8	urine (144-168hr)	ND	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Fecal Radioactivity

Collection Period		3	4	5	6	Mean
0-48hr	uCi	0.44	0.62	0.35	ND	
	% of dose	4.42	6.10	3.39	ND	4.64
0-72hr	uCi	ND	ND	0.49	0.58	
	% of dose	ND	ND	4.82	5.71	5.27
0-96hr	uCi	ND	ND	0.66	0.80	
	% of dose	ND	ND	6.42	7.87	7.14

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF AOMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
3	feces (0-32hr)	674.30	317.03	20.30	0.116	1322	11464	494964
					0.117	1335		
					0.111	1301		
					0.110	1246		
		674.30	343.50	21.80	0.103	1314	12011	514011
					0.113	1314		
					0.105	1233		
					0.108	1287		
3	feces (32-48hr)	588.70	255.10	39.85	0.119	583	4860	446949
					0.116	568		
					0.130	622		
		588.70	292.11	45.03	0.129	613	4867	441726
					0.113	557		
					0.127	625		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
4	feces (0-48hr)	776.30	361.70	62.70	0.121	1243	10080	1356427
					0.119	1170		
					0.119	1206		
		776.30	387.30	71.60	0.121	1171	9595	1376987
					0.125	1166		
					0.131	1281		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
5	feces (0-48hr)	524.00	254.90	40.78	0.125	1136	9136	765921
					0.137	1242		
					0.133	1232		
					0.132	1205		
		524.00	237.00	38.08	0.127	1166	9221	776337
					0.138	1276		
					0.139	1289		
					0.137	1258		
5	feces (48-72hr)	657.60	225.80	36.52	0.108	318	3036	322892
					0.105	320		
					0.102	311		
					0.117	363		
		657.60	197.70	32.94	0.134	398	2929	320881
					0.132	389		
					0.123	354		
					0.124	362		
		657.60	209.40	36.54	0.127	369	2889	331495
					0.127	363		
					0.127	368		
					0.132	382		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
5	feces (72-96hr)(a)	599.30	185.40	29.56	0.113	255	2254	215332
					0.132	290		
					0.132	303		
					0.131	297		
		599.30	169.00	26.81	0.124	274	2215	210631
					0.124	273		
					0.122	274		
					0.127	280		
		599.30	205.10	33.18	0.118	267	2264	219459
					0.125	282		
					0.120	271		
					0.119	271		
	feces (72-96hr)(b)	337.20	158.70	20.10	0.112	374	3393	144911
					0.131	446		
					0.113	378		
					0.120	418		
		337.20	139.10	17.70	0.116	434	3478	149241
					0.112	391		
					0.111	382		
					0.113	366		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
6	feces (0-72hr)	658.00	218.72	36.61	0.124	1453	11483	1264696
					0.120	1373		
					0.114	1288		
					0.114	1308		
		658.00	230.91	37.92	0.106	1226	11864	1281980
					0.122	1426		
					0.112	1354		
					0.125	1514		
		658.00	179.33	30.37	0.124	1423	11770	1311609
					0.123	1435		
					0.115	1385		
					0.124	1475		
6	feces (72-96hr)	567.30	167.70	21.73	0.100	672	6638	487943
					0.101	671		
					0.114	700		
					0.105	740		
		567.30	192.60	26.70	0.104	627	5916	465284
					0.104	652		
					0.103	652		
					0.108	544		
		567.30	170.90	22.84	0.111	729	6671	505747
					0.107	746		
					0.103	670		
					0.105	697		

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Radioactivity in sodium hydroxide traps

Dog #	Sample Description	Sample size (mL)	Aliquot size (mL)	DPM per aliquot	Mean Total DPM	% of Dose
4	NaOH (0-4hr)	210.0	1.00	26	5460	0.024
			1.00	27		
			1.00	27		
			1.00	26		
5	NaOH (0-4hr)	210.0	1.00	13	3255	0.014
			1.00	17		
			1.00	18		
			1.00	14		
4	NaOH (4-8hr)	216.0	1.00	18	3780	0.017
			1.00	18		
			1.00	19		
			1.00	17		
5	NaOH (4-8hr)	216.0	1.00	16	3132	0.014
			1.00	12		
			1.00	17		
			1.00	13		

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Radioactivity in water traps

Dog #	Sample Description	Sample size (mL)	Aliquot size (mL)	DPM per aliquot	Mean Total DPM	% of Dose*
4	Water Trap	222.0	1.00	2	777	<0.010
			1.00	2		
			1.00	6		
			1.00	6		
5	Water Trap	210.0	1.00	3	788	<0.009
			1.00	2		
			1.00	8		
			1.00	2		

* limit of detection based on 10 DPM greater than background count

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Radioactivity in silica gel traps

Dog #	Sample Description	Sample size (mL)	Aliquot size (mL)	DPM per aliquot	Mean Total DPM	% of Dose*
4	Silica (0-4hr)	30.0	1.00	1	11	<0.001
			1.00	1		
			1.00	1		
			1.00	0		
5	Silica (0-4hr)	30.0	1.00	1	53	<0.001
			1.00	3		
			1.00	3		
			1.00	2		
4	Silica (4-8hr)	30.0	1.00	0	4	<0.001
			1.00	1		
			1.00	0		
			1.00	0		
5	Silica (4-8hr)	30.0	1.00	4	30	<0.001
			1.00	1		
			1.00	0		
			1.00	0		

* limit of detection based on 10 DPM greater than background count

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	3	4	5	6	7	8	Mean	SD
5 min	uCi/mL	0.0019	0.0022	0.0017	0.0022	0.0017	0.0019	0.0228	0.0204	0.0068	0.0085
	nmol./mL	17.24	18.21	13.93	18.53	16.05	18.01	19.60	17.53	17.39	1.62
	total % dose*	17.92	18.79	15.05	18.40	16.65	18.68	24.75	21.74	19.00	2.81
15 min	uCi/mL	0.0021	0.0023	0.0018	0.0021	0.0018	0.0019	0.0213	0.0213	0.0068	0.0084
	nmol./mL	18.88	18.97	14.92	18.30	16.95	17.48	18.32	18.29	17.76	1.24
	total % dose*	19.62	19.57	16.13	18.17	17.58	18.14	23.12	22.69	19.38	2.29
30 min	uCi/mL	0.0021	0.0023	0.0017	0.0022	0.0018	0.0018	0.0219	0.0200	0.0067	0.0082
	nmol./mL	18.81	19.64	14.08	18.40	16.83	16.76	18.87	17.20	17.57	1.65
	total % dose*	19.55	20.27	15.21	18.27	17.46	17.39	23.82	21.34	19.16	2.50
1 hr	uCi/mL	0.0017	0.0020	0.0014	0.0018	0.0015	0.0015	0.0189	0.0171	0.0058	0.0071
	nmol./mL	15.45	16.85	11.80	15.29	14.19	13.61	16.29	14.72	14.78	1.50
	total % dose*	16.06	17.38	12.75	15.18	14.72	14.12	20.56	18.26	16.13	2.35
90 min	uCi/mL	0.0015	0.0017	0.0012	0.0015	0.0013	0.0013	0.0176	0.0139	0.0050	0.0063
	nmol./mL	13.67	14.39	10.14	12.56	11.92	12.26	15.11	11.93	12.75	1.48
	total % dose*	14.21	14.85	10.95	12.47	12.37	12.72	19.08	14.80	13.93	2.32
2 hr	uCi/mL	0.0013	0.0015	0.0010	0.0013	0.0010	0.0009	0.0155	0.0120	0.0043	0.0055
	nmol./mL	11.95	12.89	8.63	10.77	9.08	8.83	13.34	10.31	10.72	1.73
	total % dose*	12.42	13.30	9.32	10.69	9.42	9.16	16.83	12.78	11.74	2.47

* assuming blood volume of 9.41%;

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	3	4	5	6	7	8	Mean	SD
3 hr	uCi/mL	0.0011	0.0013	0.0008	0.0010	0.0009	0.0007	0.0126	0.0103	0.0036	0.0046
	nmol./mL	10.17	11.06	6.44	8.28	7.88	6.52	10.84	8.83	8.75	1.70
	total % dose*	10.57	11.41	6.96	8.22	8.18	6.76	13.69	10.95	9.59	2.28
4 hr	uCi/mL	0.0010	0.0011	0.0006	0.0008	0.0006	0.0005	0.0111	0.0080	0.0030	0.0039
	nmol./mL	8.60	9.61	4.94	6.60	5.73	4.66	9.53	6.90	7.07	1.85
	total % dose*	8.94	9.92	5.34	6.55	5.94	4.84	12.03	8.56	7.76	2.35
5 hr	uCi/mL	0.0008	0.0010	0.0005	0.0006	0.0005	0.0004	0.0105	0.0069	0.0026	0.0036
	nmol./mL	7.30	8.29	4.25	5.34	4.74	3.75	8.99	5.90	6.07	1.80
	total % dose*	7.59	8.56	4.59	5.30	4.92	3.89	11.35	7.31	6.69	2.34
6 hr	uCi/mL	0.0007	0.0008	0.0004	0.0006	0.0004	0.0003	0.0093	0.0056	0.0023	0.0031
	nmol./mL	6.28	6.65	3.54	4.82	3.92	2.88	8.02	4.80	5.11	1.63
	total % dose*	6.53	6.86	3.83	4.78	4.06	2.98	10.13	5.95	5.64	2.12
7 hr	uCi/mL	0.0006	0.0008	0.0004	0.0005	0.0004	0.0002	0.0085	0.0052	0.0021	0.0029
	nmol./mL	5.68	6.82	3.34	4.35	3.34	2.22	7.32	4.48	4.69	1.67
	total % dose*	5.91	7.03	3.61	4.32	3.46	2.30	9.24	5.55	5.18	2.09
8 hr	uCi/mL	0.0006	0.0007	0.0004	0.0005	0.0003	0.0002	0.0077	0.0045	0.0019	0.0026
	nmol./mL	5.73	6.07	2.99	4.06	2.88	1.93	6.60	3.87	4.26	1.58
	total % dose*	5.95	6.26	3.23	4.03	2.98	2.00	8.33	4.80	4.70	1.94

* assuming blood volume of 9.41%;

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	3	4	5	6	7	8	Mean	SD
12 hr	uCi/mL	ND	NO	0.0003	0.0005	0.0002	0.0001	ND	NO	0.0003	0.0001
	nmol./mL	ND	NO	2.14	4.29	2.12	1.28	ND	NO	2.46	1.11
	total % dose*	ND	NO	2.31	4.26	2.20	1.33	NO	NO	2.52	1.07
24 hr	uCi/mL	ND	NO	0.0001	0.0001	0.0001	0.0001	0.0022	0.0010	0.0006	0.0008
	nmol./mL	NO	NO	0.60	0.82	0.89	0.62	1.92	0.83	0.95	0.45
	total % dose*	NO	ND	0.64	0.81	0.93	0.64	2.42	1.03	1.08	0.62
48 hr	uCi/mL	ND	NO	NO	NO	0.00003	0.00003	NO	ND	0.00003	
	nmol./mL	ND	ND	NO	NO	0.25	0.26	NO	NO	0.26	
	total % dose*	ND	NO	ND	ND	0.26	0.27	NO	NO	0.27	
72 hr	uCi/mL	NO	ND	NO	NO	0.00002	<0.00002	NO	ND	0.00002	
	nmol./mL	NO	ND	NO	NO	0.14	<0.14	NO	NO	0.14	
	total % dose*	NO	NO	NO	ND	0.15	<0.14	ND	NO	0.15	
96 hr	uCi/mL	NO	ND	NO	NO	<0.00002	<0.00002	NO	NO		
	nmol./mL	ND	ND	NO	ND	<0.14	<0.14	NO	NO		
	total % dose*	ND	ND	NO	ND	<0.14	<0.15	NO	ND		

* assuming blood volume of 9.41%; NO - not determined; limit of detection based on 10 DPM greater than background count

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (5 min)	0.30	1281	4286
		0.30	1283	
		0.30	1293	
2	Blood (5 min)	0.30	1479	4810
		0.30	1395	
		0.30	1455	
3	Blood (5 min)	0.30	1151	3742
		0.30	1106	
		0.30	1111	
4	Blood (5 min)	0.30	1467	4813
		0.30	1488	
		0.30	1377	
5	Blood (5 min)	0.30	1149	3849
		0.30	1181	
		0.30	1134	
6	Blood (5 min)	0.30	1324	4277
		0.30	1302	
		0.30	1223	
7	Blood (5 min)	0.30	15254	50613
		0.30	14658	
		0.30	15640	
8	Blood (5 min)	0.30	13289	45251
		0.30	12949	
		0.30	14488	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (15 min)	0.30	1405	4694
		0.30	1334	
		0.30	1486	
2	Blood (15 min)	0.30	1488	5011
		0.30	1504	
		0.30	1518	
3	Blood (15 min)	0.30	1230	4009
		0.30	1205	
		0.30	1173	
4	Blood (15 min)	0.30	1429	4754
		0.30	1394	
		0.30	1456	
5	Blood (15 min)	0.30	1251	4064
		0.30	1198	
		0.30	1209	
6	Blood (15 min)	0.30	1286	4152
		0.30	1209	
		0.30	1242	
7	Blood (15 min)	0.30	13774	47292
		0.30	14099	
		0.30	14690	
8	Blood (15 min)	0.30	13794	47231
		0.30	14563	
		0.30	14151	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (30 min)	0.30	1407	4676
		0.30	1388	
		0.30	1413	
2	Blood (30 min)	0.30	1542	5189
		0.30	1511	
		0.30	1617	
3	Blood (30 min)	0.30	1144	3782
		0.30	1117	
		0.30	1143	
4	Blood (30 min)	0.30	1399	4779
		0.30	1453	
		0.30	1449	
5	Blood (30 min)	0.30	1220	4036
		0.30	1231	
		0.30	1181	
6	Blood (30 min)	0.30	1214	3981
		0.30	1099	
		0.30	1270	
7	Blood (30 min)	0.30	14413	48713
		0.30	14157	
		0.30	15272	
8	Blood (30 min)	0.30	13117	44406
		0.30	12986	
		0.30	13862	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (60 min)	0.30	1160	3842
		0.30	1141	
		0.30	1157	
2	Blood (60 min)	0.30	1296	4451
		0.30	1410	
		0.30	1300	
3	Blood (60 min)	0.30	955	3169
		0.30	948	
		0.30	949	
4	Blood (60 min)	0.30	1224	3972
		0.30	1158	
		0.30	1193	
5	Blood (60 min)	0.30	1045	3403
		0.30	990	
		0.30	1028	
6	Blood (60 min)	0.30	917	3232
		0.30	973	
		0.30	1019	
7	Blood (60 min)	0.30	13132	42062
		0.30	11710	
		0.30	13014	
8	Blood (60 min)	0.30	11566	38011
		0.30	11530	
		0.30	11114	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (90 min)	0.30	1023	3400
		0.30	1032	
		0.30	1005	
2	Blood (90 min)	0.30	1101	3802
		0.30	1186	
		0.30	1135	
3	Blood (90 min)	0.30	826	2723
		0.30	766	
		0.30	859	
4	Blood (90 min)	0.30	1001	3262
		0.30	962	
		0.30	973	
5	Blood (90 min)	0.30	872	2859
		0.30	846	
		0.30	855	
6	Blood (90 min)	0.30	753	2912
		0.30	*492	
		0.30	994	
7	Blood (90 min)	0.30	12002	39021
		0.30	12121	
		0.30	10996	
8	Blood (90 min)	0.30	9283	30807
		0.30	9052	
		0.30	9391	

* vial leakage-value not incorporated

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (2 hours)	0.30	880	2972
		0.30	843	
		0.30	952	
2	Blood (2 hours)	0.30	919	3404
		0.30	1136	
		0.30	1009	
3	Blood (2 hours)	0.30	700	2318
		0.30	675	
		0.30	711	
4	Blood (2 hours)	0.30	832	2797
		0.30	838	
		0.30	847	
5	Blood (2 hours)	0.30	739	2177
		0.30	719	
		0.30	501	
6	Blood (2 hours)	0.30	687	2097
		0.30	595	
		0.30	605	
7	Blood (2 hours)	0.30	10562	34432
		0.30	9663	
		0.30	10764	
8	Blood (2 hours)	0.30	8017	26608
		0.30	7985	
		0.30	7945	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (3 hours)	0.30	754	2528
		0.30	756	
		0.30	765	
2	Blood (3 hours)	0.30	890	2921
		0.30	834	
		0.30	905	
3	Blood (3 hours)	0.30	515	1731
		0.30	533	
		0.30	510	
4	Blood (3 hours)	0.30	669	2150
		0.30	630	
		0.30	636	
5	Blood (3 hours)	0.30	571	1890
		0.30	548	
		0.30	582	
6	Blood (3 hours)	0.30	472	1548
		0.30	449	
		0.30	472	
7	Blood (3 hours)	0.30	7325	27998
		0.30	8829	
		0.30	9044	
8	Blood (3 hours)	0.30	6703	22789
		0.30	6791	
		0.30	7016	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (4 hours)	0.30	631	2138
		0.30	648	
		0.30	645	
2	Blood (4 hours)	0.30	740	2540
		0.30	767	
		0.30	779	
3	Blood (4 hours)	0.30	399	1327
		0.30	409	
		0.30	386	
4	Blood (4 hours)	0.30	509	1713
		0.30	518	
		0.30	515	
5	Blood (4 hours)	0.30	422	1374
		0.30	409	
		0.30	406	
6	Blood (4 hours)	0.30	337	1107
		0.30	336	
		0.30	323	
7	Blood (4 hours)	0.30	7405	24607
		0.30	7475	
		0.30	7266	
8	Blood (4 hours)	0.30	5304	17807
		0.30	5360	
		0.30	5362	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (5 hours)	0.30	555	1816
		0.30	544	
		0.30	535	
2	Blood (5 hours)	0.30	660	2191
		0.30	606	
		0.30	706	
3	Blood (5 hours)	0.30	351	1144
		0.30	343	
		0.30	336	
4	Blood (5 hours)	0.30	430	1387
		0.30	434	
		0.30	384	
5	Blood (5 hours)	0.30	356	1137
		0.30	333	
		0.30	334	
6	Blood (5 hours)	0.30	278	891
		0.30	268	
		0.30	256	
7	Blood (5 hours)	0.30	6933	23219
		0.30	6833	
		0.30	7131	
8	Blood (5 hours)	0.30	4393	15224
		0.30	4820	
		0.30	4489	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (6 hours)	0.30	477	1562
		0.30	460	
		0.30	*842	
2	Blood (6 hours)	0.30	557	1756
		0.30	530	
		0.30	493	
3	Blood (6 hours)	0.30	287	951
		0.30	289	
		0.30	280	
4	Blood (6 hours)	0.30	335	1251
		0.30	397	
		0.30	394	
5	Blood (6 hours)	0.30	282	939
		0.30	279	
		0.30	284	
6	Blood (6 hours)	0.30	203	683
		0.30	211	
		0.30	201	
7	Blood (6 hours)	0.30	6225	20718
		0.30	5340	
		0.30	7081	
8	Blood (6 hours)	0.30	3763	12387
		0.30	3685	
		0.30	3700	

* value not incorporated - contamination suspected

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (7 hours)	0.30	424	1413
		0.30	413	
		0.30	435	
2	Blood (7 hours)	0.30	542	1801
		0.30	520	
		0.30	559	
3	Blood (7 hours)	0.30	275	898
		0.30	270	
		0.30	263	
4	Blood (7 hours)	0.30	314	1130
		0.30	360	
		0.30	343	
5	Blood (7 hours)	0.30	241	800
		0.30	236	
		0.30	243	
7	Blood (7 hours)	0.30	5665	18906
		0.30	5588	
		0.30	5762	
8	Blood (7 hours)	0.30	3414	11556
		0.30	3453	
		0.30	3533	
6*	Blood (7 hours)	0.439	123	527
		0.421	104	
		0.421	105	
		0.424	118	

* 4.842g of clotted blood digested to give 9.684g of solution

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (8 hours)	0.30	414	1424
		0.30	438	
		0.30	430	
2	Blood (8 hours)	0.30	473	1603
		0.30	499	
		0.30	471	
3	Blood (8 hours)	0.30	249	804
		0.30	241	
		0.30	234	
4	Blood (8 hours)	0.30	305	1054
		0.30	325	
		0.30	319	
5	Blood (8 hours)	0.30	199	690
		0.30	218	
		0.30	204	
6	Blood (8 hours)	0.30	150	458
		0.30	130	
		0.30	132	
7	Blood (8 hours)	0.30	5171	17033
		0.30	5142	
		0.30	5017	
8	Blood (8 hours)	0.30	2956	9984
		0.30	2981	
		0.30	3049	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (12 hours)	ND	ND	ND
2	Blood (12 hours)	ND	ND	ND
3	Blood (12 hours)	0.30	165	574
		0.30	194	
		0.30	158	
4	Blood (12 hours)	0.30	330	1114
		0.30	326	
		0.30	347	
5	Blood (12 hours)	0.30	157	508
		0.30	153	
		0.30	147	
6	Blood (12 hours)	0.30	92	304
		0.30	91	
		0.30	91	
7	Blood (12 hours)	ND	ND	ND
8	Blood (12 hours)	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (24 hours)	ND	ND	ND
2	Blood (24 hours)	ND	ND	ND
3	Blood (24 hours)	0.30	48	160
		0.30	49	
		0.30	47	
4	Blood (24 hours)	0.30	66	212
		0.30	62	
		0.30	63	
6	Blood (24 hours)	0.30	46	147
		0.30	40	
		0.30	46	
7	Blood (24 hours)	0.30	1480	4953
		0.30	1427	
		0.30	1551	
8	Blood (24 hours)	0.30	673	2149
		0.30	641	
		0.30	620	
5*	Blood (24 hours)	0.412	44	214
		0.412	40	
		0.414	49	
		0.413	45	
		0.416	43	

* 3.828g of clotted blood digested to give 7.667g of solution
ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (48 hours)	ND	ND	ND
2	Blood (48 hours)	ND	ND	ND
3	Blood (48 hours)	ND	ND	ND
4	Blood (48 hours)	ND	ND	ND
5	Blood (48 hours)	0.30 0.30 0.30	20 16 18	60
6	Blood (48 hours)	0.30 0.30 0.30	21 17 18	62
7	Blood (48 hours)	ND	ND	ND
8	Blood (48 hours)	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (72 hours)	ND	ND	ND
2	Blood (72 hours)	ND	ND	ND
3	Blood (72 hours)	ND	ND	ND
4	Blood (72 hours)	ND	ND	ND
5	Blood (72 hours)	0.30 0.30 0.30	10 11 10	34
6	Blood (72 hours)	0.30 0.30 0.30	5 5 7	19
7	Blood (72 hours)	ND	ND	ND
8	Blood (72 hours)	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (96 hours)	ND	ND	ND
2	Blood (96 hours)	ND	ND	ND
3	Blood (96 hours)	ND	ND	ND
4	Blood (96 hours)	ND	ND	ND
5	Blood (96 hours)	0.30	6	21
		0.30	4	
		0.30	9	
6	Blood (96 hours)	0.30	1	9
		0.30	2	
		0.30	5	
7	Blood (96 hours)	ND	ND	ND
8	Blood (96 hours)	ND	ND	ND

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Organ/Tissue Radioactivity at 24 hours

Sample		Average Radioactivity (per Organ/Tissue) Dog #7	Dog #8	Average
Brain	uCi	0.028	0.024	0.026
	% of Dose	0.028	0.024	0.026
Heart	uCi	0.079	0.029	0.054
	% of Dose	0.078	0.029	0.053
Intestines	uCi	0.000	0.000	0.000
	% of Dose	0.000	0.000	0.000
Kidney	uCi	0.107	0.072	0.089
	% of Dose	0.106	0.071	0.089
Liver	uCi	0.592	0.564	0.578
	% of Dose	0.589	0.561	0.575
Lungs	uCi	0.226	0.160	0.193
	% of Dose	0.225	0.159	0.192
Pancreas	uCi	0.000	0.000	0.000
	% of Dose	0.000	0.000	0.000
Skin*	uCi	7.488	13.371	10.429
	% of Dose	7.446	13.295	10.370
Spleen	uCi	0.165	0.061	0.113
	% of Dose	0.165	0.061	0.113
Stomach	uCi	0.077	0.074	0.076
	% of Dose	0.077	0.074	0.075
Testes	uCi	0.020	0.011	0.015
	% of Dose	0.020	0.010	0.015

* surface area calculated using the following formula;
area (sq.cm) = 11.6 x weight^2/3 (g) , see Calculations

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Organ/Tissue (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total mL homogenate	Aliquot size(mL)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
7	Liver	297.76	1109.00	0.50	566	1315274	4417
				0.50	595		
				0.50	563		
				0.50	648		
8	Liver	272.36	1000.00	0.50	603	1252500	4599
				0.50	640		
				0.50	634		
				0.50	628		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Organ/Tissue (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot size(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
7	Kidney	52.35	208.0	0.371	419	236941	4526
				0.302	343		
				0.352	389		
				0.365	433		
8	Kidney	58.99	235.9	0.333	229	159256	2700
				0.353	219		
				0.322	220		
				0.330	234		
7	Brain	62.22	247.6	0.305	75	62050	997
				0.317	84		
				0.325	79		
				0.326	81		
8	Brain	57.70	236.9	0.309	70	54160	939
				0.309	72		
				0.306	71		
				0.323	72		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Organ/Tissue (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot size(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM p g tissue
7	Heart	84.09	343.8	0.421	219	174404	207
				0.463	212		
				0.476	266		
				0.451	222		
8	Heart	79.30	306.1	0.403	78	64340	811
				0.525	111		
				0.412	93		
				0.457	96		
7	Stomach	100.50	394.3	0.489	235	171782	1709
				0.555	280		
				0.532	205		
				0.497	185		
8	Stomach	89.64	354.7	0.496	232	164929	1840
				0.471	211		
				0.581	277		
				0.522	244		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Organ/Tissue (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot size(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
7	Testes	16.00	74.5	0.331	197	44493	2781
				0.322	193		
				0.350	204		
				0.314	192		
8	Testes	14.60	71.4	0.323	105	23382	1601
				0.355	114		
				0.338	112		
				0.331	110		
7	Lungs	96.25	365.4	0.344	467	502358	5219
				0.366	517		
				0.501	646		
				0.423	609		
8	Lungs	95.24	375.0	0.494	491	355505	3733
				0.456	437		
				0.528	494		
				0.501	453		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Organ/Tissue (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot size(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM pe g tissue
7	Spleen	109.63	441.5	0.331	269	367274	335(
				0.321	*125		
				0.314	261		
				0.317	270		
8	Spleen	34.78	136.9	0.329	341	135120	3885
				0.309	300		
				0.328	317		
				0.310	302		

* phase separation in vial - value not included in calculations

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Organ/Tissue (homogenized and combusted)

Dog #	Sample Description	Portion wet weight(g)	Total g homogenate	Aliquot size(g)	DPM per aliquot	Mean DPM per g tissue
7	Muscle (abdominal)	18.64	90.3	0.317	161	2259
				0.325	148	
				0.316	144	
				0.307	137	
8	Muscle (abdominal)	7.73	47.0	0.330	39	741
				0.318	40	
				0.328	40	
				0.329	40	
7	Muscle (femoral)	18.86	95.2	0.317	79	1215
				0.304	73	
				0.353	82	
				0.323	78	
8	Muscle (femoral)	68.40	260.3	0.311	32	403
				0.314	34	
				0.321	35	
				0.357	37	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fat (combusted)

Dog #	Sample Description	Aliquot size(g)	DPM per aliquot	Mean DPM per g tissue
7	Fat (subcutaneous)	0.324	916	2898
		0.308	1148	
		0.378	1048	
		0.353	799	
8	Fat (subcutaneous)	0.323	641	1236
		0.314	383	
		0.324	222	
		0.309	326	
7	Fat (abdominal)	0.354	359	1219
		0.333	319	
		0.307	419	
		0.329	506	
8	Fat (abdominal)	0.367	213	504
		0.317	169	
		0.375	188	
		0.321	129	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fat (combusted)

Dog #	Sample Description	Aliquot size(g)	DPM per aliquot	Mean DPM per g tissue
7	Fat (mesenteric)	0.335	592	1753
		0.306	490	
		0.371	750	
		0.364	591	
8	Fat (mesenteric)	0.370	395	1167
		0.344	447	
		0.316	409	
		0.328	330	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Bone (digested and combusted)

Dog #	Sample Description	Portion wet weight(g)	Total Digest (mL)	Aliquot size(mL)	DPM per aliquot	Mean DPM per g
7	Bone (femoral)	30.60	99.00	0.300	250	2304
				0.300	187	
				0.300	204	
8	Bone (femoral)	30.90	99.00	0.300	129	1143
				0.300	104	
				0.300	88	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Bone marrow (homogenized and combusted)

Dog #	Sample Description	Total (g) homogenate	Aliquot size (g)	DPM per aliquot	Mean DPM per g
7	Bone marrow (femoral)	6.70	0.321	151	479
			0.304	145	
			0.304	149	
8	Bone marrow (femoral)	9.02	0.303	101	339
			0.307	102	
			0.300	105	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 1 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Skin (combusted)

Dog #	Sample Description	Portion wet weight(g)	Surface area(sq.cm)	Aliquot size(g)	DPM per aliquot	Mean DPM per g	Mean DPM per sq.cm
7	skin (thoracic)	17.46	38.50	0.466	3042	6166	2797
				0.466	2523		
				0.455	2271		
				0.426	2352		
				0.456	*29189		
				0.410	3435		
8	skin (thoracic)	9.33	24.00	0.473	6360	12700	4937
				0.452	7151		
				0.430	5387		
				0.448	9477		
				0.404	3022		
				0.469	2706		

* value not included in calculations - contamination suspected

EXPERIMENT:	Dermal absorption of 14C-hydroquinone
TEST COMPOUND:	[U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION:	10 mg/kg
ROUTE OF ADMINISTRATION:	Intravenous
SOURCE:	LN-450,452,466 and File
SUMMARY OF:	Analyses of radioactive solutions

DOSE PREPARATION (NOMINAL):

	1	2	3
a) Total uCi of [14C] test compound added	37.50	75.00	75.00
b) Test compound (gm) in addition a)	0.00083	0.00165	0.00165
c) Unlabelled test compound added (gm)	0.138	0.353	0.353
d) Final total volume (mL) including vehicle	5.00	10.00	10.00
e) Test compound per mL of dose	0.02777	0.03547	0.03547
f) uCi per mL of dose	7.500	7.500	7.500

INTRAVENOUS DOSE - SUMMARY

	Dog # 1 (# 447064)	Dog # 2 (# 456829)	Dog # 3 (# 454923)
mL dose injected	4.00	4.00	4.00
mg test cpd injected	111.14	142.00	142.00
kg body wt	10.9	14.1	14.3
mg/kg body weight	10.19	10.07	9.93
uCi per animal	33.76	30.18	30.18

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SUMMARY OF: Analyses of radioactive solutions

ASSAY: Dog #1 (# 447064)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.002	*33606	
2	"	35869	8.079
3	"	38734	8.724
4	"	35824	8.068
5	"	38057	8.571
6	"	39430	8.881
7	"	36941	8.320
mean		37476	8.441

ASSAY: Dog #2 (# 456829) and Dog #3 (# 454923)

Sample	Vol of dos counted (m	DPM per aliquot	uCi/mL dose
1	0.002	33808	7.614
2	"	33217	7.481
3	"	33499	7.545
4	"	33941	7.644
5	"	33116	7.459
6	"	33455	7.535
7	"	33435	7.530
mean		33496	7.544

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Urinary Radioactivity

Collection Period		1	2	3	Mean	SD
0-4hr	uCi	10.87	16.71	11.94		
	% of dose	32.21	55.36	39.55	42.37	9.66
4-8hr	uCi	3.29	2.77	3.51		
	% of dose	9.73	9.17	11.63	10.18	1.05
8-12hr	uCi	0.88	ND	ND		
	% of dose	2.62	ND	ND		
8-24hr	uCi	ND	1.74	2.43		
	% of dose	ND	5.77	8.05	6.91	3.39
12-24hr	uCi	2.00	ND	ND		
	% of dose	5.91	ND	ND		
24-48hr	uCi	1.23	0.79	1.25		
	% of dose	3.66	2.63	4.13	3.47	0.63
48-72 hr	uCi	0.33	0.50	0.32		
	% of dose	0.98	1.66	1.05	1.23	0.30
72-96hr	uCi	0.24	0.19	0.16		
	% of dose	0.70	0.62	0.52	0.61	0.07
96-120hr	uCi	0.12	0.10	0.10		
	% of dose	0.35	0.34	0.33	0.34	0.01
Total	uCi	18.96	22.80	19.69	20.49	1.66
0-120 hr	% of dose	56.16	75.54	65.26	65.66	7.92

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (0-4hr)	64.0	1.00	381381	24140688
			1.00	377255	
			1.00	373187	
			1.00	376970	
2	urine (0-4hr)	45.1	0.10	83655	37091931
			0.10	80215	
			0.10	81688	
			0.10	83417	
3	urine (0-4hr)	45.1	0.10	58409	26498505
			0.10	58907	
			0.10	60062	
			0.10	57642	
1	urine (4-8hr)	489.0	1.00	15176	7295636
			1.00	14968	
			1.00	15052	
			1.00	14482	
2	urine (4-8hr)	244.2	1.00	25501	6143095
			1.00	25263	
			1.00	24704	
3	urine (4-8hr)	222.2	1.00	34858	7794998
			1.00	35917	
			1.00	34577	
			1.00	34972	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (8-12hr)	480.0	1.00	4031	1963560
			1.00	4046	
			1.00	4202	
			1.00	4084	
2	urine (8-12hr)	ND	ND	ND	ND
3	urine (8-12hr)	ND	ND	ND	ND
1	urine (12-24hr)	690.0	1.00	6447	4430490
			1.00	6293	
			1.00	6491	
			1.00	6453	
2	urine (12-24hr)	ND	ND	ND	ND
3	urine (12-24hr)	ND	ND	ND	ND
1	urine (8-24hr)	ND	ND	ND	ND
2	urine (8-24hr)	674.0	1.00	5747	3865390
			1.00	5744	
			1.00	5740	
			1.00	5709	
3	urine (8-24hr)	559.0	1.00	9749	5392114
			1.00	9579	
			1.00	9567	
			1.00	9689	

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (24-48hr)	820.0	1.00	3324	2740235
			1.00	3333	
			1.00	3351	
			1.00	3359	
2	urine (24-48hr)	310.0	1.00	5706	1758785
			1.00	5727	
			1.00	5516	
			1.00	5745	
3	urine (24-48hr)	550.0	1.00	5187	2769250
			1.00	4981	
			1.00	5049	
			1.00	4923	
1	urine (48-72hr)	840.0	1.00	885	736050
			1.00	884	
			1.00	869	
			1.00	867	
2	urine (48-72hr)	470	1.00	2351	1109553
			1.00	2375	
			1.00	2334	
			1.00	2383	
3	urine (48-72hr)	325.0	1.00	2061	700213
			1.00	2166	
			1.00	2258	
			1.00	2133	

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (72-96hr)	470.0	1.00	1122	522405
			1.00	1126	
			1.00	1103	
			1.00	1095	
2	urine (72-96hr)	607.0	1.00	689	416250
			1.00	693	
			1.00	708	
			1.00	653	
3	urine (72-96hr)	675.0	1.00	507	346950
			1.00	522	
			1.00	514	
			1.00	513	
1	urine (96-120hr)	312.0	1.00	839	264576
			1.00	854	
			1.00	863	
			1.00	836	
2	urine (96-120hr)	450.0	1.00	516	229838
			1.00	501	
			1.00	520	
			1.00	506	
3	urine (96-120hr)	295.0	1.00	735	220070
			1.00	765	
			1.00	720	
			1.00	764	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Fecal Radioactivity

Collection Period		1	2	3	mean	SD
0-24hr	uCi	ND	0.155	ND		
	% of dose	ND	0.51	ND	0.51	
0-48hr	uCi	0.824	ND	0.696		
	% of dose	2.44	ND	2.31	2.37	
24-48hr	uCi	ND	0.679	ND		
	% of dose	ND	2.25	ND	2.25	
48-72hr	uCi	0.273	0.424	0.822		
	% of dose	0.81	1.40	2.72	1.65	0.80
72-96hr	uCi	0.163	0.147	0.257		
	% of dose	0.48	0.49	0.85	0.61	0.17
96-120hr	uCi	1.068	0.095	0.140		
	% of dose	3.16	0.31	0.46	1.31	1.31
Total % of dose (0-120hr)		6.89	4.97	6.35	6.07	0.81

ND - not determined

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
1	feces (0-24hr)	NS	NS	NS	NS	NS	NS	NS
2	feces (0-24hr)	185.2	171.60	14.47	0.111	2436	22079	344801
					0.120	2590		
					0.105	2299		
					0.119	2724		
3	feces (0-24hr)	NS	NS	NS	NS	NS	NS	NS
1	feces (0-48hr)	845.2	191.00	29.26	0.103	1358	13691	1772699
					0.109	1501		
					0.107	1463		
					0.103	1456		
			277.70	35.62	0.120	1644	13962	1513602
					0.112	1525		
					0.106	1550		
					0.119	1655		
			222.50	34.81	0.124	2887	16262	2150367
					0.111	1547		
					0.108	1479		
					0.111	1569		
			164.50	25.80	0.122	1765	14168	1878175
					0.113	1558		
					0.114	1640		
					0.121	1698		

NS - no sample available

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
2	feces (0-48hr)	NS	NS	NS	NS	NS	NS	NS
3	feces (0-48hr)	496.8	236.00	29.31	0.126	3284	25188	1554111
					0.117	2975		
					0.129	3176		
					0.120	2957		
			243.20	30.34	0.110	2642	24786	1536149
					0.117	2904		
					0.122	3028		
					0.126	3211		
1	feces (24-48hr)	NS	NS	NS	NS	NS	NS	NS
2	feces (24-48hr)	480.8	246.43	23.28	0.112	3716	33969	1542910
					0.113	3949		
					0.103	3398		
					0.109	3789		
			224.70	21.98	0.111	3457	31283	1471301
					0.122	3797		
					0.112	3593		
					0.126	3879		
3	feces (24-48hr)	NS	NS	NS	NS	NS	NS	NS

NS - no sample available

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
1	feces (48-72hr)	776.9	235.80	33.48	0.127	684	5368	592126
					0.117	635		
					0.127	644		
					0.114	637		
			268.70	38.49	0.114	614	5515	613706
					0.123	737		
					0.123	651		
					0.116	625		
			230.70	32.95	0.125	653	5500	610336
					0.108	601		
					0.125	696		
					0.107	604		
2	feces (48-72hr)	902.8	388.50	69.32	0.134	743	5698	917895
					0.129	747		
					0.138	787		
					0.118	679		
			424.00	74.60	0.115	701	6066	963583
					0.111	720		
					0.130	742		
					0.122	729		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
3	feces (48-72hr)	722.0	340.80	58.40	0.118	1661	14452	1788000
					0.137	1982		
					0.137	2022		
					0.125	1813		
			351.20	60.68	0.137	2000	14919	1861142
					0.109	1627		
					0.125	1895		
					0.132	1979		
1	feces (72-96hr)	725.8	236.76	33.12	0.132	516	3603	365827
					0.117	423		
					0.116	408		
					0.116	391		
			212.32	28.81	0.107	401	3637	358195
					0.103	388		
					0.102	383		
					0.122	400		
			231.98	31.47	0.107	371	3683	362649
					0.109	377		
					0.110	465		
					0.107	383		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
2	feces (72-96hr)	777.9	364.70	61.30	0.132	327	2474	323415
					0.125	319		
					0.123	303		
					0.152	365		
			375.28	67.50	0.110	272	2363	330661
					0.140	336		
					0.118	271		
					0.141	322		
3	feces (72-96hr)	915.6	302.90	55.51	0.134	475	3331	558915
					0.128	423		
					0.135	437		
					0.118	382		
			310.80	58.79	0.134	459	3379	585155
					0.111	390		
					0.119	390		
					0.124	409		
			270.80	48.45	0.128	462	3478	569753
					0.116	382		
					0.133	464		
					0.119	419		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
1	feces (96-120hr)(a)	537.7	163.80	9.96	0.111	1197	10195	333338
					0.111	1124		
					0.132	1314		
					0.132	1309		
			199.60	11.88	0.137	1373	10261	328391
					0.106	1118		
					0.132	1328		
					0.135	1406		
			164.38	9.85	0.118	1177	9924	319751
					0.118	1159		
					0.119	1178		
					0.118	1180		
1	feces (96-120hr)(b)	579.6	184.82	10.42	0.126	1351	10657	348256
					0.138	1473		
					0.128	1340		
					0.136	1464		
			200.28	11.34	0.124	1312	10560	346568
					0.135	1422		
					0.120	1285		
					0.112	1167		
			185.97	10.37	0.122	1306	10424	336887
					0.113	1187		
					0.120	1297		
					0.130	1258		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
1	feces (96-120hr)(c)	678.8	222.12	12.85	0.113	1162	10420	409207
					0.111	1158		
					0.124	1273		
					0.120	1284		
			231.10	13.34	0.106	1064	10092	395421
					0.127	1310		
					0.106	1058		
					0.122	1224		
			217.00	12.50	0.121	1243	10112	395396
					0.130	1304		
					0.129	1289		
					0.118	1198		
1	feces (96-120hr)(d)	696.7	228.42	14.82	0.119	1101	9311	420900
					0.108	1008		
					0.118	1049		
					0.109	1065		
			225.60	14.83	0.114	1071	9871	452065
					0.120	1118		
					0.123	1200		
					0.127	1399		
			233.30	15.10	0.116	1240	11956	539134
					0.119	1385		
					0.123	1572		
					0.116	1475		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
1	feces (96-120hr)(e)	670.5	224.90	16.96	0.112	1038	9060	458101
					0.105	944		
					0.113	1017		
					0.108	970		
			213.10	16.22	0.107	964	8806	449437
					0.106	925		
					0.119	1042		
					0.124	1083		
			219.30	16.74	0.110	963	8685	444530
					0.107	919		
					0.102	890		
					0.116	1006		
1	feces (96-120hr)(f)	415.9	183.30	22.95	0.114	782	6444	335548
					0.114	694		
					0.106	673		
					0.119	771		
			202.80	26.36	0.111	894	7801	421713
					0.103	781		
					0.110	843		
					0.104	822		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
2	feces (96-120hr)	623.5	278.80	41.78	0.133	310	2242	209503
					0.139	310		
					0.127	280		
					0.128	282		
			304.80	46.29	0.124	273	2232	211324
					0.139	316		
					0.137	286		
					0.140	331		
3	feces (96-120hr)	636.5	295.20	45.26	0.12	363	3184	310763
					0.11	379		
					0.12	357		
					0.13	428		
			311.00	49.49	0.11	349	3076	311538
					0.10	327		
					0.14	403		
					0.11	328		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	3	Mean	SD
5 min	uCi/mL	0.0040	0.0033	0.0033	0.0035	0.0003
	nmol./mL	119.50	139.31	140.85	133.22	9.72
	total % dose*	12.14	14.33	14.70	13.72	1.13
15 min	uCi/mL	0.0041	0.0031	0.0034	0.0035	0.0004
	nmol./mL	121.63	133.63	146.34	133.87	10.09
	total % dose*	12.36	13.75	15.27	13.79	1.19
30 min	uCi/mL	0.0042	0.0031	0.0036	0.0036	0.0005
	nmol./mL	126.54	132.11	154.73	137.80	12.19
	total % dose*	12.86	13.59	16.14	14.20	1.41
1 hr	uCi/mL	0.0044	0.0028	0.0033	0.0035	0.0006
	nmol./mL	130.57	121.28	142.37	131.41	8.63
	total % dose*	13.27	12.48	14.85	13.53	0.99
90 min	uCi/mL	0.0037	0.0023	0.0029	0.0030	0.0006
	nmol./mL	110.06	98.60	122.45	110.37	9.74
	total % dose*	11.19	10.14	12.78	11.37	1.08
2 hr	uCi/mL	0.0032	0.0020	0.0025	0.0026	0.0005
	nmol./mL	94.88	83.72	107.65	95.42	9.78
	total % dose*	9.64	8.61	11.23	9.83	1.08

* assuming blood volume of 9.41%;

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	3	Mean	SD
3 hr	uCi/mL	0.0026	0.0014	0.0020	0.0020	0.0005
	nmol./mL	76.92	61.45	86.74	75.04	10.41
	total % dose*	7.82	6.32	9.05	7.73	1.12
4 hr	uCi/mL	0.0021	0.0013	0.0018	0.0017	0.0003
	nmol./mL	61.60	55.83	75.83	64.42	8.41
	total % dose*	6.26	5.74	7.91	6.64	0.92
5 hr	uCi/mL	0.0018	0.0011	0.0016	0.0015	0.0003
	nmol./mL	55.09	48.74	67.01	56.95	7.57
	total % dose*	5.60	5.01	6.99	5.87	0.83
6 hr	uCi/mL	0.0017	0.0010	0.0014	0.0014	0.0003
	nmol./mL	51.25	41.41	61.27	51.31	8.11
	total % dose*	5.21	4.26	6.39	5.29	0.87
7 hr	uCi/mL	0.0015	0.0008	0.0013	0.0012	0.0003
	nmol./mL	43.60	34.19	54.55	44.12	8.32
	total % dose*	4.43	3.52	5.69	4.55	0.89
8 hr	uCi/mL	0.0013	0.0008	0.0012	0.0011	0.0002
	nmol./mL	37.95	32.71	50.94	40.53	7.66
	total % dose*	3.86	3.36	5.31	4.18	0.83

* assuming blood volume of 9.41%;

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	3	Mean	SD
12 hr	uCi/mL	0.0011	ND	ND		
	nmol./mL	32.21	ND	ND		
	total % dose*	3.27	ND	ND		
24 hr	uCi/mL	0.0002	0.0003	0.0004	0.0003	0.0001
	nmol./mL	5.35	11.92	16.90	11.39	4.73
	total % dose*	0.54	1.23	1.76	1.18	0.50
48 hr	uCi/mL	0.0001	0.0001	0.0001	0.0001	0.0000
	nmol./mL	3.46	5.51	5.83	4.93	1.05
	total % dose*	0.35	0.57	0.61	0.51	0.11

* assuming blood volume of 9.41%; ND - not determined;

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (5 min)	0.30	2881	8874
		0.30	2409	
		0.30	2697	
2	Blood (5 min)	0.30	2173	7237
		0.30	2142	
		0.30	2198	
3	Blood (5 min)	0.30	2100	7317
		0.30	*1246	
		0.30	2290	
1	Blood (15 min)	0.30	2721	9032
		0.30	2755	
		0.30	2653	
2	Blood (15 min)	0.30	2143	6942
		0.30	2062	
		0.30	2043	
3	Blood (15 min)	0.30	2229	7602
		0.30	2312	
		0.30	2301	

* vial leakage - not included in calculations

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (30 min)	0.30	2782	9397
		0.30	2828	
		0.30	2847	
2	Blood (30 min)	0.30	2043	6863
		0.30	1916	
		0.30	2218	
3	Blood (30 min)	0.30	2521	8038
		0.30	2397	
		0.30	2316	
1	Blood (60 min)	0.30	2918	9696
		0.30	2800	
		0.30	3008	
2	Blood (60 min)	0.30	1920	6300
		0.30	1930	
		0.30	1820	
3	Blood (60 min)	0.30	2260	7396
		0.30	2291	
		0.30	2105	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (90 min)	0.30	2397	8173
		0.30	2466	
		0.30	2493	
2	Blood (90 min)	0.30	1581	5122
		0.30	1468	
		0.30	1561	
3	Blood (90 min)	0.30	1847	6361
		0.30	2048	
		0.30	1830	
1	Blood (2 hours)	0.30	2071	7046
		0.30	2106	
		0.30	2164	
2	Blood (2 hours)	0.30	1281	4349
		0.30	1325	
		0.30	1308	
3	Blood (2 hours)	0.30	1665	5592
		0.30	1677	
		0.30	1691	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (3 hours)	0.30	1716	5712
		0.30	1670	
		0.30	1755	
2	Blood (3 hours)	0.30	911	3192
		0.30	952	
		0.30	1010	
3	Blood (3 hours)	0.30	1361	4506
		0.30	1389	
		0.30	1305	
1	Blood (4 hours)	0.30	1374	4574
		0.30	1231	
		0.30	1512	
2	Blood (4 hours)	0.30	896	2900
		0.30	862	
		0.30	852	
3	Blood (4 hours)	0.30	1173	3939
		0.30	1180	
		0.30	1192	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (5 hours)	0.30	1279	4091
		0.30	1234	
		0.30	1169	
2	Blood (5 hours)	0.30	751	2532
		0.30	742	
		0.30	786	
3	Blood (5 hours)	0.30	1074	3481
		0.30	1011	
		0.30	1048	
1	Blood (6 hours)	0.30	1165	3806
		0.30	1086	
		0.30	1174	
2	Blood (6 hours)	0.30	677	2151
		0.30	601	
		0.30	658	
3	Blood (6 hours)	0.30	1014	3183
		0.30	918	
		0.30	933	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (7 hours)	0.30	957	3238
		0.30	897	
		0.30	1060	
2	Blood (7 hours)	0.30	579	1776
		0.30	465	
		0.30	554	
3	Blood (7 hours)	0.30	873	2834
		0.30	841	
		0.30	837	
1	Blood (8 hours)	0.30	819	2818
		0.30	810	
		0.30	907	
2	Blood (8 hours)	0.30	539	1699
		0.30	491	
		0.30	499	
3	Blood (8 hours)	0.30	830	2646
		0.30	798	
		0.30	753	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 10 mg/kg
ROUTE OF ADMINISTRATION: Intravenous
SOURCE: LN-450,452,466 and File

SAMPLING TYPE: Analyses of whole blood (combusted)

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (12 hours)	0.30	719	2392
		0.30	715	
		0.30	719	
2	Blood (12 hours)	ND	ND	ND
3	Blood (12 hours)	ND	ND	ND
2	Blood (24 hours)	0.30	196	619
		0.30	182	
		0.30	179	
3	Blood (24 hours)	0.30	266	878
		0.30	259	
		0.30	265	
1*	Blood (24 hours)	0.330	134	397
		0.324	134	
		0.324	120	
1	Blood (48 hours)	0.30	77	257
		0.30	64	
		0.30	90	
2	Blood (48 hours)	0.30	87	286
		0.30	84	
		0.30	86	
3	Blood (48 hours)	0.30	95	303
		0.30	93	
		0.30	85	

ND - not determined
* 5.924g of clotted blood digested to give 11.848g of solution

EXPERIMENT NAME:	Dermal absorption of 14C-hydroquinone
TEST COMPOUND:	[U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL:	4.5 g/L
ROUTE OF ADMINISTRATION:	Dermal
SOURCE:	LN-450,452,466 and File
SUMMARY OF:	Analyses of radioactive solutions

Molecular weight of Test Compound: 110.11 g/mole

Specific activity of [14C] Test Compound Stock: 5.000 mCi/mmole

SOLUTION PREPARATION (NOMINAL):	1	2*	3	4	5	6
a) Total uCi of [14C] test compound added	66.667	66.667	66.667	66.667	66.667	66.667
b) Test compound (gm) in addition a)	0.00147	0.00147	0.00147	0.00147	0.00147	0.00147
c) Unlabelled test compound added (gm)	0.1125	0.1125	0.1125	0.1125	0.1125	0.1125
d) Final total volume (mL) including vehicle	25.00	25.00	25.00	25.00	25.00	25.00
e) Test compound per mL of solution	0.00456	0.00456	0.00456	0.00456	0.00456	0.00456
f) uCi per mL of solution	2.667	2.667	2.667	2.667	2.667	2.667
Mean uCi/mL of solution		2.667				

DERMALLY APPLIED SOLUTION - SUMMARY:

	Dog # 1 (# 423254)	Dog # 2* (# 424235)	Dog # 3 (# 424331)	Dog # 4 (# 419915)	Dog # 5 (# 457922)	Dog # 6 (# 458872)	Average
mL soln applied	15.00	15.00	15.00	15.00	15.00	15.00	
mg test cpd applied	68.39	68.39	68.40	68.40	68.41	68.41	68.40
kg body wt	10.7	10.9	10.1	10.9	11.1	10.9	10.7
uCi applied/animal	40.24	40.47	40.83	40.91	41.46	41.39	40.97

* Data from Dog #2 not included in averages -see 'Statistics'

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File

SUMMARY OF: Analyses of radioactive solutions

ASSAY: Dog #1 (# 423254)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	30387	2.738
2	"	29407	2.649
3	"	29842	2.688
4	"	28901	2.604
5	"	30196	2.720
6	"	29594	2.666
7	"	30116	2.713
mean		29778	2.683

ASSAY: Dog #2 (# 424235)

Sample	mL dose sampled	Diluted to (mL)	Vol diluted sample (mL)	DPM observe	uCi/mL soln
A	0.100	10.00	0.100	6050	2.714
			0.100	5997	
			0.100	6027	
B	0.100	10.00	0.100	6000	2.682
			0.100	5876	
			0.100	5987	
Mean uCi/mL dose:					2.698

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SUMMARY OF: Analyses of radioactive solutions

ASSAY: Dog #3 (# 424331)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	30160	2.717
2	"	29897	2.693
3	"	30051	2.707
4	"	29964	2.699
5	"	30704	2.766
6	"	30646	2.761
7	"	30078	2.710
mean		30214	2.722

ASSAY: Dog #4 (# 419915)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.002	11776	2.652
2	"	12230	2.755
3	"	12104	2.726
4	"	12129	2.732
5	"	12088	2.723
6	"	12061	2.716
7	"	12385	2.789
mean		12110	2.728

ASSAY: Dog #5 (# 457922)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	30213	2.722
2	"	30729	2.768
3	"	*19230	*
4	"	*25420	*
5	"	31045	2.797
6	"	30667	2.763
7	"	30741	2.769
mean		30679	2.764

ASSAY: Dog #6 (# 458872)

Sample	Vol of dose counted (mL)	DPM per aliquot	uCi/mL dose
1	0.005	31004	2.793
2	"	30875	2.782
3	"	30126	2.714
4	"	31384	2.827
5	"	30195	2.720
6	"	30435	2.742
7	"	30384	2.737
mean		30629	2.759

* sample leakage- replicates not included in calculations

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity
SUMMARY OF: Analyses of radioactive solutions

Collection Period		Average radioactivity* 1	2**	3	4	5	6	mean*
0-4 hr	uCi	<0.00013	0.00079	<0.00050	0.00039	0.00053	<0.00090	0.00018
	nmol.equiv.	<2.065	12.083	<7.542	5.962	7.874	<13.541	2.767
4-8 hr	uCi	<0.00070	0.00119	<0.00159	0.00054	<0.00111	<0.00099	0.00011
	nmol.equiv.	<10.858	18.296	<24.134	8.211	<16.640	<14.880	1.642
8-24 hr	uCi	<0.00252	0.03748	0.00315	0.01354	<0.00315	<0.00255	0.00334
	nmol.equiv.	<38.928	574.912	47.993	205.471	<47.274	<38.282	50.693
24-48 hr	uCi	0.00561	0.06628	0.00280	0.00949	0.00679	0.00615	0.00617
	nmol.equiv.	86.580	1016.540	42.663	143.953	101.740	92.322	93.451
48-72 hr	uCi	nd	nd	nd	nd	0.00332	<0.00293	0.00166
	nmol.equiv.	nd	nd	nd	nd	49.764	<43.963	24.882
72-96 hr	uCi	nd	nd	nd	nd	0.00331	<0.00119	0.00166
	nmol.equiv.	nd	nd	nd	nd	49.637	<17.923	24.819
96-120 hr	uCi	nd	nd	nd	nd	0.00259	<0.00485	0.00130
	nmol.equiv.	nd	nd	nd	nd	38.832	<72.775	19.416
Total	uCi	0.00561	0.10574	0.00596	0.02396	0.01653	0.00615	
	nmol.equiv.	86.58	1621.83	90.66	363.60	247.85	92.32	

* limit of detection based on 10 DPM greater than background count; nd - not determined
** Data from Dog #2 not included in averages- see 'Statistics'

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

SUMMARY OF: Analyses of radioactive solutions

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (0-4 hr)	29.7	1.000	5	149
			1.000	5	
			1.000	7	
			1.000	3	
2	urine (0-4 hr)	66.0	1.000	26	1749
			1.000	29	
			1.000	27	
			1.000	24	
3	urine (0-4 hr)	110.0	1.000	4	413
			1.000	1	
			1.000	4	
			1.000	6	
4	urine (0-4 hr)	28.6	1.000	30	872
			1.000	31	
			1.000	32	
			1.000	29	
5	urine (0-4 hr)	116.6	1.000	9	1166
			1.000	10	
			1.000	10	
			1.000	11	
6	urine (0-4 hr)	200.2	1.000	0	551
			1.000	11	
			1.000	0	
			1.000	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

SUMMARY OF: Analyses of radioactive solutions

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (4-8 hr)	156.2	1.000	1	39
			1.000	0	
			1.000	0	
			1.000	0	
2	urine (4-8 hr)	99.0	1.000	26	2648
			1.000	28	
			1.000	26	
			1.000	27	
3	urine (4-8 hr)	352.0	1.000	7	1848
			1.000	4	
			1.000	4	
			1.000	6	
4	urine (4-8 hr)	52.8	1.000	23	1201
			1.000	23	
			1.000	25	
			1.000	20	
5	urine (4-8 hr)	246.4	1.000	10	2094
			1.000	1	
			1.000	21	
			1.000	2	
6	urine (4-8 hr)	220.0	1.000	8	440
			1.000	0	
			1.000	0	
			1.000	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

SUMMARY OF: Analyses of radioactive solutions

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (8-24 hr)	560.0	1.000	7	4340
			1.000	7	
			1.000	8	
			1.000	9	
2	urine (8-24 hr)	340.0	1.000	236	83215
			1.000	240	
			1.000	254	
			1.000	249	
3	urine (8-24 hr)	700.0	1.000	10	7000
			1.000	11	
			1.000	11	
			1.000	8	
4	urine (8-24 hr)	720.0	1.000	42	30060
			1.000	43	
			1.000	41	
			1.000	41	
5	urine (8-24 hr)	700.0	1.000	3	6300
			1.000	12	
			1.000	12	
			1.000	9	
6	urine (8-24 hr)	566.0	1.000	6	2547
			1.000	6	
			1.000	0	
			1.000	6	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

SUMMARY OF: Analyses of radioactive solutions

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
1	urine (24-48 hr)	940.0	1.000	14	12455
			1.000	16	
			1.000	13	
			1.000	10	
2	urine (24-48 hr)	1096.0	1.000	131	147138
			1.000	137	
			1.000	135	
			1.000	134	
3	urine (24-48 hr)	190.0	1.000	33	6223
			1.000	32	
			1.000	34	
			1.000	32	
4	urine (24-48 hr)	405.0	1.000	53	21060
			1.000	52	
			1.000	50	
			1.000	53	
5	urine (24-48 hr)	460.0	1.000	29	15065
			1.000	34	
			1.000	39	
			1.000	29	
6	urine (24-48 hr)	700.0	1.000	23	13650
			1.000	18	
			1.000	17	
			1.000	20	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

SUMMARY OF: Analyses of radioactive solutions

Dog #	Sample Description	Sample size(mL)	Aliquot size(mL)	DPM per aliquot	Mean total DPM
5	urine (48-72 hr)	655.0	1.000	10	7369
			1.000	10	
			1.000	19	
			1.000	6	
6	urine (48-72 hr)	650.0	1.000	7	4225
			1.000	4	
			1.000	11	
			1.000	4	
5	urine (72-96 hr)	700.0	1.000	6	7350
			1.000	15	
			1.000	18	
			1.000	3	
6	urine (72-96 hr)	265.0	1.000	2	2518
			1.000	20	
			1.000	9	
			1.000	7	
5	urine (96-120 hr)	500.0	1.000	17	5750
			1.000	10	
			1.000	8	
			1.000	11	
6	urine (96-120 hr)	1076.0	1.000	2	2959
			1.000	7	
			1.000	2	
			1.000	0	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		Average radioactivity* 1	2	3	4
5 min	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
15 min	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
30 min	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
60 min	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
90 min	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
2 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
3 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
4 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228

* limit of detection based on 10 DPM greater than background count

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		Average radioactivity* 1	2	3	4
5 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
6 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
7 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
8 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228
24 hr	uCi/mL	<0.00002	<0.00002	0.00002	<0.00002
	nmol./mL	<0.232	<0.230	0.236	<0.228
48 hr	uCi/mL	<0.00002	<0.00002	<0.00002	<0.00002
	nmol./mL	<0.232	<0.230	<0.229	<0.228

* limit of detection based on 10 DPM greater than background count

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Blood radioactivity

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (5 min)	0.30	3	7
		0.30	3	
		0.30	0	
2	Blood (5 min)	0.30	0	0
		0.30	0	
		0.30	0	
3	Blood (5 min)	0.30	13	18
		0.30	2	
		0.30	1	
4	Blood (5 min)	0.30	0	0
		0.30	0	
		0.30	0	
1	Blood (15 min)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (15 min)	0.30	0	0
		0.30	0	
		0.30	0	
3	Blood (15 min)	0.30	0	19
		0.30	10	
		0.30	7	
4	Blood (15 min)	0.30	0	0
		0.30	0	
		0.30	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Blood radioactivity

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (30 min)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (30 min)	0.30	0	0
		0.30	0	
		0.30	0	
3	Blood (30 min)	0.30	10	32
		0.30	10	
		0.30	9	
4	Blood (30 min)	0.30	0	0
		0.30	0	
		0.30	0	
1	Blood (60 min)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (60 min)	0.30	0	0
		0.30	0	
		0.30	0	
3	Blood (60 min)	0.30	5	21
		0.30	9	
		0.30	5	
4	Blood (60 min)	0.30	0	0
		0.30	0	
		0.30	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Blood radioactivity

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (90 min)	0.30	5	7
		0.30	0	
		0.30	1	
2	Blood (90 min)	0.30	10	19
		0.30	7	
		0.30	0	
3	Blood (90 min)	0.30	2	10
		0.30	7	
		0.30	0	
4	Blood (90 min)	0.30	0	0
		0.30	0	
		0.30	0	
1	Blood (2 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (2 hr)	0.30	5	6
		0.30	0	
		0.30	0	
3	Blood (2 hr)	0.30	2	13
		0.30	7	
		0.30	3	
4	Blood (2 hr)	0.30	0	0
		0.30	0	
		0.30	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Blood radioactivity

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (3 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (3 hr)	0.30	7	8
		0.30	0	
		0.30	0	
3	Blood (3 hr)	0.30	6	26
		0.30	7	
		0.30	10	
4	Blood (3 hr)	0.30	0	0
		0.30	0	
		0.30	0	
1	Blood (4 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (4 hr)	0.30	5	8
		0.30	0	
		0.30	2	
3	Blood (4 hr)	0.30	6	14
		0.30	2	
		0.30	5	
4	Blood (4 hr)	0.30	0	0
		0.30	0	
		0.30	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Blood radioactivity

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (5 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (5 hr)	0.30	6	7
		0.30	0	
		0.30	0	
3	Blood (5 hr)	0.30	11	12
		0.30	0	
		0.30	0	
4	Blood (5 hr)	0.30	0	0
		0.30	0	
		0.30	0	
1	Blood (6 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (6 hr)	0.30	0	7
		0.30	3	
		0.30	3	
3	Blood (6 hr)	0.30	12	28
		0.30	7	
		0.30	6	
4	Blood (6 hr)	0.30	0	0
		0.30	0	
		0.30	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Blood radioactivity

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (7 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (7 hr)	0.30	3	3
		0.30	0	
		0.30	0	
3	Blood (7 hr)	0.30	7	16
		0.30	1	
		0.30	6	
4	Blood (7 hr)	0.30	0	0
		0.30	0	
		0.30	0	
1	Blood (8 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (8 hr)	0.30	0	4
		0.30	3	
		0.30	1	
3	Blood (8 hr)	0.30	0	16
		0.30	11	
		0.30	3	
4	Blood (8 hr)	0.30	0	0
		0.30	0	
		0.30	0	

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 4.5 g/L
ROUTE OF ADMINISTRATION: Dermal
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Blood radioactivity

Dog #	Sample Description	Aliquot volume(mL)	DPM per aliquot	Mean DPM/mL
1	Blood (24 hr)	0.30	0	6
		0.30	3	
		0.30	2	
2	Blood (24 hr)	0.30	10	16
		0.30	0	
		0.30	4	
3	Blood (24 hr)	0.30	9	34
		0.30	13	
		0.30	9	
4	Blood (24 hr)	0.30	0	0
		0.30	0	
		0.30	0	
1	Blood (48 hr)	0.30	0	0
		0.30	0	
		0.30	0	
2	Blood (48 hr)	0.30	3	17
		0.30	5	
		0.30	7	
3	Blood (48 hr)	0.30	2	19
		0.30	9	
		0.30	6	
4	Blood (48 hr)	0.30	0	0
		0.30	0	
		0.30	0	

EXPERIMENT:	Dermal absorption of 14C-hydroquinone
TEST COMPOUND:	[U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION:	50 mg/kg
ROUTE OF ADMINISTRATION:	Oral gavage
SOURCE:	LN-450,452,466 and File
SUMMARY OF:	Analyses of radioactive solutions

DOSE PREPARATION (NOMINAL):	1	2
a) Total uCi of [14C] test compound added	125.00	125.00
b) Test compound (gm) in addition a)	0.00275	0.00275
c) Unlabelled test compound added (gm)	0.750	0.780
d) Final total volume (mL) including vehicle	25.00	25.00
e) Test compound per mL of dose	0.03011	0.03131
f) uCi per mL of dose	5.000	5.000

INTRAVENOUS DOSE - SUMMARY

	Dog # 1 (# 498513)	Dog # 2 (# 506443)
mL dose administered	20.00	20.00
mg test cpd in dose	602.24	626.22
kg body wt	12.0	12.5
mg/kg body weight	50.02	50.10
uCi per animal	101.82	101.06

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File

SUMMARY OF: Analyses of radioactive solutions

Dose Assay Dog #1 (# 498513)

Sample	mL dose sampled	diluted to (mL)	Vol. diluted sample (mL)	DPM per aliquot	Mean uCi/mL dose
A	0.010	10.00	0.100	1180	5.167
				1140	
				1137	
				1137	
				1141	
B	0.010	10.00	0.100	1114	4.969
				1104	
				1099	
				1093	
				1106	
C	0.010	10.00	0.100	1136	5.137
				1163	
				1109	
				1154	
				*1036	
Mean uCi/mL of dose					5.091

* this replicate not included in calculations - broken vial

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File

SUMMARY OF: Analyses of radioactive solutions

Dose Assay Dog #2 (# 506443)

Sample	mL dose sampled	diluted to Vol. (mL)	diluted sample (mL)	DPM per aliquot	Mean uCi/mL dose
A	0.010	10.00	0.100	1134 1093 1119 1148	5.061
B	0.010	10.00	0.100	1139 1106 1136	5.077
C	0.010	10.00	0.100	1093 1129 1108 1129	5.021
Mean uCi/mL of dose					5.053

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File

SUMMARY OF: Urinary radioactivity

Collection period		1	2	Average
0-4 hr	uCi:	61.054	65.721	63.387
	% of dose:	59.96	65.03	62.50
4-8 hr	uCi:	13.543	10.788	12.166
	% of dose:	13.30	10.68	11.99
8-24 hr	uCi:	3.242	4.041	3.642
	% of dose:	3.18	4.00	3.59
24-48 hr	uCi:	1.210	0.984	1.097
	% of dose:	1.19	0.97	1.08
48-72 hr	uCi:	0.453	0.500	0.477
	% of dose:	0.44	0.50	0.47
72-96 hr	uCi:	0.262	0.324	0.293
	% of dose:	0.26	0.32	0.29
96-120 hr	uCi:	0.182	0.210	0.196
	% of dose:	0.18	0.21	0.19
120-144 hr	uCi:	0.150	0.168	0.159
	% of dose:	0.15	0.17	0.16
144-168 hr	uCi:	0.093	0.146	0.119
	% of dose:	0.09	0.14	0.12

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample description	Sample size (mL)	Aliquot vol. (mL)	DPM per aliquot	Mean total DPM
1	Urine (0-4 hr)	55.0	1.00	2484688 2469958 2503634 2398956	1.3554E+08
2	Urine (0-4 hr)	37.4	0.50	1945266 1942475 1931697 1984870	1.4594E+08
1	Urine (4-8 hr)	374.0	1.00	80687 81440 79776 79643	3.0065E+07
2	Urine (4-8 hr)	71.5	0.50	168433 168719 165926 166850	2.3950E+07
1	Urine (8-24 hr)	401.5	1.00	17924 18034 17640 18108	7.1975E+06
2	Urine (8-24 hr)	765.0	1.00	11707 11718 11703 11782	8.9715E+06
1	Urine (24-48 hr)	885.0	1.00	3019 3064 3054 3000	2.6853E+06
2	Urine (24-48 hr)	810.0	1.00	2620 2698 2728 2743	2.1848E+06

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample description	Sample size (mL)	Aliquot vol. (mL)	DPM per aliquot	Mean total DPM
1	Urine (48-72 hr)	370.0	1.00	2735 2760 2718 2659	1.0057E+06
2	Urine (48-72 hr)	490.0	1.00	2240 2305 2283 2242	1.1111E+06
1	Urine (72-96 hr)	320.0	1.00	1789 1814 1845 1818	5.8128E+05
2	Urine (72-96 hr)	395.0	1.00	1828 1823 1822 1807	7.1890E+05
1	Urine (96-120 hr)	330.0	1.00	1258 1262 1117 1257	4.0376E+05
2	Urine (96-120 hr)	805.0	1.00	573 583 583 576	4.6589E+05
1	Urine (120-144 hr)	674.0	1.00	503 495 487 494	3.3346E+05
2	Urine (120-144 hr)	566.0	1.00	658 670 646 655	3.7200E+05

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Urinary radioactivity

Dog #	Sample description	Sample size (mL)	Aliquot vol. (mL)	DPM per aliquot	Mean total DPM
1	Urine (144-168 hr)	415.0	1.00	511 492 494 499	2.0709E+05
2	Urine (144-168 hr)	650.0	1.00	495 499 502 493	3.2321E+05

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File

SUMMARY OF: Fecal radioactivity

Collection period		1	2	Average
0-24 hr	uCi:	2.443	2.285	2.364
	% of dose:	2.40	2.26	2.33
24-48 hr	uCi:	1.308	0.363	0.835
	% of dose:	1.28	0.36	0.82
48-72 hr	uCi:	0.702	0.170	0.436
	% of dose:	0.69	0.17	0.43
72-96 hr	uCi:	0.022	0.098	0.060
	% of dose:	0.02	0.10	0.06
96-120 hr	uCi:	0.065	0.071	0.068
	% of dose:	0.06	0.07	0.07
Total 0-120 hr	uCi:	4.54	2.99	3.76
	% of dose:	4.46	2.96	3.71

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
1	Feces (0-24 hr)	151.9	145.9	6.33	0.108	88365	822798	5422496
					0.111	88652		
					0.106	88975		
					0.105	87669		
2	Feces (0-24 hr)	416.6	401.9	47.80	0.120	12667	102388	5073178
					0.100	8811		
					0.100	11434		
					0.110	11170		
1	Feces (24-48 hr)	404.3	210.4	19.10	0.157	12124	77955	2861103
					0.125	9912		
					0.144	11458		
					0.152	11511		
			186.4	16.70	0.129	10720	81351	2946712
					0.132	11068		
					0.143	11285		
					0.141	11215		
2	Feces (24-48 hr)	778.00	277.80	44.40	0.11	691	6079	755958
					0.10	604		
					0.12	710		
					0.14	*402		
			232.60	33.60	0.11	858	7374	828717
					0.13	993		
					0.14	991		
					0.14	977		

* vial leakage - not included in calculations

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
2	Feces (24-48 hr) (continued)	778.0	247.0	40.60	0.121	793	6509	832436
					0.129	834		
					0.130	*378		
					0.130	**		
1	Feces (48-72 hr)(a)	545.0	269.0	33.06	0.173	2170	12368	828423
					0.153	1836		
					0.185	2301		
					0.175	2186		
			250.5	30.76	0.184	2129	12215	817310
					0.163	1986		
					0.154	1941		
					0.140	1750		
1	Feces (48-72 hr)(b)	539.7	274.6	33.00	0.150	1785	11563	749987
					0.169	1925		
					0.147	1696		
					0.162	1851		
			240.9	29.00	0.148	1698	11107	721618
					0.153	1702		
					0.135	1479		
					0.168	1827		

* vial leakage - not included in calculations
** vial not counted

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
2	Feces (48-72 hr)	881.1	290.6	39.10	0.14	404	3034	359676
					0.16	448		
					0.13	455		
					0.14	413		
			250.3	34.47	0.17	548	3097	375839
					0.17	512		
					0.15	471		
					0.14	422		
			318.9	46.80	0.16	481	3065	396358
					0.18	570		
					0.17	522		
					0.17	513		
1	Feces (72-96 hr)	177.6	172.1	10.90	0.111	481	4416	49670
					0.104	448		
					0.107	471		
					0.100	462		
2	Feces (72-96 hr)	929.00	243.7	31.30	0.13	203	1614	192566
					0.12	194		
					0.14	215		
					0.12	209		
			211.4	29.50	0.12	217	1649	213710
					0.14	229		
					0.12	188		
					0.12	190		

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fecal samples (homogenized, lyophilized and combusted)

Dog #	Sample Description	Total wet weight(g)	Portion wet weight(g)	Portion dry weight(g)	Aliquot dry weight(g)	DPM per aliquot	Mean DPM/g dry weight	Mean total DPM
2	Feces (72-96 hr) (continued)	929.00	199.9	29.00	0.12	212	1711	230615
					0.11	183		
					0.14	237		
					0.14	241		
			247.4	35.80	0.13	251	1722	231447
					0.14	210		
					0.12	203		
					0.14	247		
1	Feces (96-120 hr)	249.00	234.9	19.40	0.119	858	7026	144487
					0.102	708		
					0.111	800		
					0.114	769		
2	Feces (96-120 hr)	625.9	319.2	48.47	0.14	249	1677	159381
					0.15	265		
					0.13	204		
					0.15	239		
			275.4	38.63	0.14	246	1773	155634
					0.15	249		
					0.13	236		
					0.12	223		

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	Average
30 min	uci/mL:	0.00319	0.00794	0.00557
	nmol/mL:	171.73	445.92	308.82
	% of dose:	3.54	9.24	6.39
60 min	uci/mL:	0.00390	0.00649	0.00519
	nmol/mL:	209.41	364.81	287.11
	% of dose:	4.32	7.56	5.94
90 min	uci/mL:	0.00488	0.00488	0.00488
	nmol/mL:	262.30	274.07	268.18
	% of dose:	5.41	5.68	5.54
2 hours	uci/mL:	0.00682	0.00368	0.00525
	nmol/mL:	366.66	206.57	286.62
	% of dose:	7.56	4.28	5.92
3 hours	uci/mL:	0.00430	0.00229	0.00329
	nmol/mL:	231.21	128.58	179.89
	% of dose:	4.77	2.66	3.72
4 hours	uci/mL:	0.00284	0.00161	0.00222
	nmol/mL:	152.57	90.19	121.38
	% of dose:	3.15	1.87	2.51
5 hours	uci/mL:	0.00187	0.00124	0.00155
	nmol/mL:	100.55	69.41	84.98
	% of dose:	2.07	1.44	1.76
6 hours	uci/mL:	0.00126	0.00108	0.00117
	nmol/mL:	67.66	60.73	64.20
	% of dose:	1.40	1.26	1.33
7 hours	uci/mL:	0.00104	0.00101	0.00103
	nmol/mL:	55.87	56.89	56.38
	% of dose:	1.15	1.18	1.17

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File

SUMMARY OF: Blood radioactivity

Collection period		1	2	Average
8 hours	uci/mL:	0.00083	0.00088	0.00085
	nmol/mL:	44.54	49.35	46.94
	% of dose:	0.92	1.02	0.97
24 hours	uci/mL:	0.00028	0.00050	0.00039
	nmol/mL:	14.97	27.99	21.48
	% of dose:	0.31	0.58	0.44
48 hours	uci/mL:	0.00017	0.00034	0.00026
	nmol/mL:	9.20	19.28	14.24
	% of dose:	0.19	0.40	0.29
72 hours	uci/mL:	0.00013	0.00029	0.00021
	nmol/mL:	7.19	16.30	11.74
	% of dose:	0.15	0.34	0.24
96 hours	uci/mL:	0.00011	0.00025	0.00018
	nmol/mL:	5.98	13.97	9.98
	% of dose:	0.12	0.29	0.21
120 hours	uci/mL:	0.00010	0.00023	0.00017
	nmol/mL:	5.33	13.08	9.21
	% of dose:	0.11	0.27	0.19
144 hours	uci/mL:	0.00009	0.00020	0.00015
	nmol/mL:	4.80	11.49	8.14
	% of dose:	0.10	0.24	0.17
168 hours	uci/mL:	0.00008	0.00017	0.00013
	nmol/mL:	4.41	9.77	7.09
	% of dose:	0.09	0.20	0.15

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Whole blood (combusted)

Dog #	Sample description	Aliquot volume (mL)	DPM per aliquot	Mean DPM per mL
1	Blood (30 min)	0.30	2187 2051 2144	7091
2	Blood (30 min)	0.30	5486 5415 4958	17621
1	Blood (60 min)	0.30	2609 *1422 2579	8647
2	Blood (60 min)	0.30	4478 4218 4278	14416
1	Blood (90 min)	0.30	3267 3215 3266	10831
2	Blood (90 min)	0.30	3217 3223 3307	10830
1	Blood (2 hours)	0.30	4718 4366 *2150	15140
2	Blood (2 hours)	0.30	2368 2464 2515	8163
1	Blood (3 hours)	0.30	2890 2927 2775	9547
2	Blood (3 hours)	0.30	1533 1529 1511	5081

* vial leakage - not included in calculations

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Whole blood (combusted)

Dog #	Sample description	Aliquot volume (mL)	DPM per aliquot	Mean DPM per mL
1	Blood (4 hours)	0.30	1949 1810 1911	6300
2	Blood (4 hours)	0.30	1068 1101 1039	3564
1	Blood (5 hours)	0.30	1294 *425 1197	4152
2	Blood (5 hours)	0.30	807 821 841	2743
1	Blood (6 hours)	0.30	858 820 837	2794
2	Blood (6 hours)	0.30	734 728 698	2400
1	Blood (7 hours)	0.30	662 *271 722	2307
2	Blood (7 hours)	0.30	686 687 650	2248
1	Blood (8 hours)	0.30	571 522 562	1839
2	Blood (8 hours)	0.30	583 620 552	1950

* vial leakage - not included in calculations

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Whole blood (combusted)

Dog #	Sample description	Aliquot volume (mL)	DPM per aliquot	Mean DPM per mL
1	Blood (24 hours)	0.30	183 196 177	618
2	Blood (24 hours)	0.30	334 319 342	1106
1	Blood (48 hours)	0.30	114 116 114	380
2	Blood (48 hours)	0.30	234 224 228	762
1	Blood (72 hours)	0.30	94 84 89	297
2	Blood (72 hours)	0.30	190 191 199	644
1	Blood (96 hours)	0.30	72 70 76	247
2	Blood (96 hours)	0.30	163 159 175	552

EXPERIMENT: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL CONCENTRATION: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Whole blood (combusted)

Dog #	Sample description	Aliquot volume (mL)	DPM per aliquot	Mean DPM per mL
1	Blood (120 hours)	0.30	67 61 70	220
2	Blood (120 hours)	0.30	140 170 *	517
1	Blood (144 hours)	0.30	58 60 61	198
2	Blood (144 hours)	0.30	141 136 132	454
1	Blood (168 hours)	0.30	55 54 52 57	182
2	Blood (168 hours)	0.30	116 119 112	386

* vial not counted

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File

SUMMARY OF: Tissue/Organ radioactivity at 7 days

Sample		1	2	Average
Liver	uCi:	0.418	0.197	0.307
	% of dose:	0.411	0.195	0.303
Kidney	uCi:	0.015	0.023	0.019
	% of dose:	0.014	0.023	0.019
Brain	uCi:	*<0.004	0.004	<0.004
	% of dose:	*<0.004	0.004	<0.004
Testes	uCi:	0.002	0.002	0.002
	% of dose:	0.002	0.002	0.002
Lung	uCi:	0.011	0.013	0.012
	% of dose:	0.011	0.013	0.012
Heart	uCi:	0.007	0.008	0.007
	% of dose:	0.007	0.008	0.007
Stomach	uCi:	0.012	0.013	0.012
	% of dose:	0.011	0.013	0.012
Intestine	uCi:	0.033	0.091	0.062
	% of dose:	0.032	0.090	0.061
Spleen	uCi:	0.003	0.012	0.007
	% of dose:	0.003	0.012	0.007
Pancreas	uCi:	0.001	0.005	0.003
	% of dose:	0.001	0.005	0.003
Skin** (thoracic)	uCi:	0.299	0.329	0.314
	% of dose:	0.293	0.326	0.309
Skin** (dorsal)	uCi:	1.420	1.499	1.460
	% of dose:	1.395	1.483	1.439

* limit of detection based on 10 DPM above background
** skin surface area calculated usin g the following formula; area (sq.cm) = 11.6 x weight^2/3 (g), see Calculations

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Tissues/Organs (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot weight(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
1	Liver	362.70	1424.49	0.330	214	928110	2559
				0.358	233		
				0.309	199		
				0.303	201		
2	*Liver	463.70	1700	0.50	141	436900	942
				0.50	119		
				0.50	126		
				0.50	128		
1	Kidney	59.57	239.10	0.329	42	32486	545
				0.311	43		
				0.318	43		
				0.330	47		
2	Kidney	79.33	315.30	0.54	109	51181	645
				0.54	70		
				0.53	93		
				0.54	77		
1	Brain	73.68	293.00	0.318	5	6679	91
				0.335	9		
				0.325	9		
				0.338	7		
2	Brain	64.18	250.60	0.58	25	9816	153
				0.54	22		
				0.52	18		
				0.53	20		

* for these tissues, total homogenate and aliquot size values are given in mL

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Tissues/Organs (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot weight(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
1	testes	16.59	108.40	0.55	16	3613	218
				0.54	16		
				0.54	18		
				0.53	22		
2	testes	24.80	125	0.55	17	4008	162
				0.54	16		
				0.55	20		
				0.55	17		
1	*lung	91.12	400	0.53	34	24860	273
				0.52	31		
				0.53	37		
				0.56	31		
2	*lung	123.41	620	0.54	26	29414	238
				0.54	24		
				0.53	29		
				0.54	23		

* for these tissues, total homogenate and/or aliquot size values are given in mL

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Tissues/Organs (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot weight(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
1	heart	85.17	375.70	0.53	21	14816	174
				0.52	20		
				0.53	20		
				0.55	23		
2	heart	97.78	392.50	0.54	25	18365	188
				0.56	33		
				0.54	27		
				0.54	17		
1	*stomach	96.24	465	0.59	37	25833	268
				0.58	34		
				0.54	24		
				0.54	30		
2	*stomach	142.05	563	0.52	22	28787	203
				0.55	36		
				0.59	33		
				0.55	22		

* for these tissues, total homogenate and/or aliquot size values are given in mL

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Tissues/Organs (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot weight(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
1	*intestine	357.60	1500	0.51	32	72917	204
				0.53	21		
				0.58	25		
				0.54	27		
2	*intestine	444.79	1700	0.51	27	202227	455
				0.54	81		
				0.52	78		
				0.54	65		
1	spleen	23.56	97.60	0.338	23	6304	268
				0.315	22		
				0.344	21		
				0.319	19		
2	spleen	58.22	234.20	0.54	63	26470	455
				0.55	66		
				0.52	55		
				0.54	59		

* for these tissues, total homogenate and/or aliquot size values are given in mL

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Tissues/Organs (homogenized and combusted)

Dog #	Sample Description	Total wet weight(g)	Total g homogenate	Aliquot weight(g)	DPM per aliquot	Mean DPM per tissue	Mean DPM per g tissue
1	muscle	82.92	346.10	0.55	22	-	108
				0.55	11		
				0.53	15		
				0.54	8		
2	*muscle	130.00	500	0.52	20	-	176
				0.55	17		
				0.56	49		
				0.53	13		
1	pancreas	12.00	53.00	0.372	21	2562	214
				0.345	15		
				0.350	17		
				0.381	17		
2	pancreas	18.01	73.40	0.57	94	11764	653
				0.53	108		
				0.55	70		
				0.54	79		

* for these tissues, total homogenate and/or aliquot size values are given in mL

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Fat (combusted directly)

Dog #	Sample Description	Portion wet weight(g)	Aliquot weight(g)	DPM per aliquot	Mean DPM per g tissue
1	fat (body)	34.37	0.11	34	283
			0.12	29	
			0.10	31	
			0.15	42	
	fat (intestinal)	45.05	0.11	24	249
			0.12	32	
			0.11	25	
			0.11	31	
2	fat (body)	61.78	0.11	74	651
			0.11	74	
			0.10	77	
			0.11	55	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Bone (digested and combusted)

Dog #	Sample Description	Portion wet weight(g)	Total digest (g)	Aliquot weight(g)	DPM per aliquot	Mean DPM per g tissue
1	bone (femoral)	38.30	94.70	0.383	5	27
				0.366	4	
				0.387	7	
				0.328	0	
2	bone (femoral)	43.50	108.08	0.346	1	38
				0.370	6	
				0.385	11	
				0.319	4	

EXPERIMENT NAME: Dermal absorption of 14C-hydroquinone
TEST COMPOUND: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL DOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Bone marrow (homogenized and combusted)

Dog #	Sample Description	Total digest (g)	Aliquot weight(g)	DPM per aliquot	Mean DPM per g tissue
1	bone marrow	13.95	0.388	2	12
			0.388	5	
			0.428	7	
			0.383	5	
2	bone marrow	15.58	0.393	9	29
			0.369	10	
			0.372	12	
			0.362	13	

EXPERIMENT NAME: Oermal absorption of 14C-hydroquinone
TEST COMPOUNO: [U-14C-Phenyl]1,4-dihydroxybenzene
NOMINAL OOSE LEVEL: 50 mg/kg
ROUTE OF ADMINISTRATION: Oral gavage
SOURCE: LN-450,452,466 and File
SAMPLING TYPE: Skin (combusted directly)

Oog #	Sample Oescription	Portion wet weight (g)	Surface area (sq.cm)	Aliquot weight(g)	OPM per aliquot	Mean OPM per g	Mean OPM per sq.cm
1	skin (left side thorax)	98.59	215.80	0.54	379	576	263
				0.54	299		
				0.50	213		
				0.50	307		
	skin (right side thorax)	72.70	157.60	0.45	202	373	172
				0.43	168		
				0.44	*75		
				0.41	111		
	skin (dorsal)	110.36	167.10	0.43	867	1566	1035
				0.45	1202		
				0.44	344		
				0.44	344		
2	skin (thoracic)	69.29	231.00	0.48	651	781	234
				0.45	370		
				0.47	226		
				0.53	260		
	skin (dorsal)	119.16	255.00	0.46	1088	2280	1065
				0.45	1078		
				0.50	1049		

* incomplete combustion · sample not included in calculations

Calculations

Intravenous and Oral Administration

A: $\%\ ^{14}C$ in blood $= \dfrac{(\mu Ci/mL \times \text{weight of dog (kg)} \times 94.1\ mL/kg)^{(a)}}{\mu Ci \text{ of dose}}$

B: $\%\ ^{14}C$ in skin $= \dfrac{(\mu Ci/g \text{ skin}) \times g/cm^2 \text{ skin}^{(b)} \times \text{surface area } (cm^2)^{(a)}}{\mu Ci \text{ of dose}}$

Surface area $= K \times (\text{weighting})^{2/3}$, $K = 11.6$ for dog[a]

Dermal Application

A: percutaneous absorption rate $(nmole/cm^2/minute) = \dfrac{\text{nmoles absorbed}}{(\text{surface area exposed} \times \text{exposure time})}$

$= \dfrac{\text{nmoles excreted in urine}/\%\ ^{14}C \text{ in urine after iv dose}^{(c)}}{55.6\ cm^2 \times 60 \text{ minutes}}$

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[a]See reference 1; [b]determined empirically for each dog

[c]At same time period