International Journal of Soil, Sediment and Water
Documenting the Cutting Edge of Environmental Stewardship

Volume 3 | Issue 1 Article 4

2-6-2010

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Recommended Citation
Abdel-Rahman, Mohamed S. Ph.D. and Turkall, Rita M. Ph.D. (2010) "Determination of Oral or Dermal Benzene Exposure from Contaminated Soils," *International Journal of Soil, Sediment and Water*: Vol. 3: Iss. 1, Article 4.
Available at: http://scholarworks.umass.edu/intljssw/vol3/iss1/4

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DETERMINATION OF ORAL OR DERMAL BENZENE EXPOSURE FROM CONTAIMINATED SOILS

Benzene Bioavailability from Soil

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ABSTRACT

Soil contamination with dangerous, toxic chemicals remains one of the most difficult problems in this era. Health risk assessments often do not consider the amount of chemicals in soil that are absorbed and their disposition (kinetics). The aim of these studies was to compare the extent to which adsorption to either a sand or clay content soil affects the kinetics and manner which benzene is subsequently handled in orally or dermally exposed rats. Dermal exposure increased absorption half-lives ($t_{1/2}$) by 25, 60 and 44-fold compared with oral exposure to benzene alone, or in the presence of sandy or clay soil, respectively. The elimination $t_{1/2}$ following dermal versus oral exposure were increased about 2-fold in benzene alone and sandy soil groups, while in the clay soil group the increase was 13-fold. The area under the blood concentration versus time curve (AUC) of benzene in the presence of either soil was increased after oral and decreased after dermal exposure compared with exposure to benzene alone. The urinary recovery, 48 hours following dermal exposure to benzene alone, was 3-fold greater than following oral exposure. Tissue distribution after all oral exposures resulted in the highest concentrations of radioactivity in gastric contents > stomach > fat > duodenum > adrenal. The highest tissue concentrations of radioactivity after dermal exposure to benzene alone were kidney > liver > treated skin; however, after exposure in the presence of either soil the highest tissue concentrations were treated skin > kidney > liver. The results of these studies reveal that the presence of sand or clay content soil produced qualitative and quantitative differences in the

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disposition of benzene in the body following oral or dermal exposures. These differences will impact the risk assessment of benzene.

Keywords**:** benzene, dermal or oral exposures, soil bioavailability effects

1. INTRODUCTION

Soil contamination with dangerous toxic chemicals remains one of the most difficult problems of this era. The hazardous chemical may persist in the environment; therefore, the potential for long-term health risk exists. The sources of hazardous chemical wastes are numerous. Industry, agriculture, and institutions such as hospitals and universities are all sources of materials that need to be discarded. People living in proximity to hazardous waste disposal sites or workers at these sites are at serious health risk if the sites are poorly managed or improperly designed. Contamination of soil and the leaking of these chemicals to both surface and ground water may lead to long-lasting toxicological problems. As industrial facilities are shut down, all too often they leave behind heavily contaminated soil. Furthermore, transportation of hazardous wastes to disposal sites also poses hazards since accidents are an ever-present possibility. If housing, schools, or office buildings are built over these areas, even in the distant future, exposure is likely to occur. Children who play in and around the soil in these areas will receive direct exposure. Children have been estimated to ingest 50-180 mg of soil per day (Clausing *et al*., 1987; Binder and Sokal, 1986).

Paralleling the growth of hazardous wastes, there has been an increasing interest in the development of procedures for assessing public health risks associated with exposures to hazardous materials. Estimates of health risk following exposure to contaminated soils have largely been based on results of studies performed with pure chemicals. However, the clay, mineral, and organic components of soil form complex, heterogeneous surfaces which are capable of adsorbing organic molecules (Hamaker and Thompson, 1972). The strength of the chemical-soil attractive forces can profoundly affect the reversibility of the adsorptive process. Therefore, the availability and the rate of chemical entering the body, its distribution to tissues, and the rate and amount of excretion may greatly differ from pure chemical investigation. Lucier *et al*. (1986) and McConnell *et al*. (1984) suggest that dioxin in soil from Times Beach and Minker Stout sites in Missouri was biologically available, as measured by microsomal enzyme studies in guinea pigs. Umbreit *et al*. (1986) reported that despite the high concentration of dioxin from two manufacturing sites in New Jersey, this soil was unable to produce toxic effects in orally exposed guinea pigs

compared with similar amounts of pure dioxin. Tight binding of dioxin to the soil matrix of the New Jersey sites correlated directly with its reduced bioavailability.

Widespread exposure to petrochemicals in dumping sites and groundwater has prompted an evaluation of the kinetics of benzene after oral and dermal treatment. Benzene is a common industrial chemical used for the synthesis of aromatic components (Baselt, 1982; Sandmeyer, 1981). It has been identified as the fourth most frequent substance recorded in 818 abandoned dump sites on the U.S. Environmental Protection Agency's 1985 National Priority List for Cleanup.

Frantz (1984) investigated the percutaneous absorption of benzene in animals and men. He reported that less than 0.2% of the applied doses were absorbed in all species studied. Other investigators (Susten *et al*., 1985) suggest that workers in tire plants may absorb 4-8 mg of benzene daily through the skin from a rubber solvent mixture containing 0.5% (v/v) benzene.

This study was conducted to compare the extent to which adsorption to either of two different soils (sandy and clay) affects the manner in which benzene is subsequently handled in orally and dermally exposed adult male rats.

2. MATERIALS AND METHODS

2.1 Chemicals

All studies were conducted using uniformly labeled ^{14}C–benzene 50 mCi/mmole (ICN Pharmaceuticals, Irvine, CA) with radiochemical purity >98%. Prior to use, dilution with HPLC-grade, unlabeled benzene (Aldrich Chemical Co.) was carried out to reduce specific activity to a workable range.

2.2 Soils

Studies were conducted on two different soils that are representative of soil types widely distributed in the United States (USDA, 1972, 1977). The Atsion soil consists of 90% sand, 8% silt, 2% clay, 4.4% organic matter; has a pH of 4.2; and was collected from the Cohansey sand formation near Chatsworth in south central New Jersey. The Keyport soil contains 50% sand, 28% silt, 22% clay, 1.6% organic matter; has a pH of 5; and was collected from the Woodbury formation near Moorestown in southwestern New Jersey. Soil particle size distribution was as follows: Atsion soil = 50-100 µm (22.2%), 100-250 µm

(76.3%), > 250 µm (1.5%); Keyport soil = 50-100 µm (17%), 100-250 µm (65.3%), 250-500 µm (13.6%), > 500 µm (4.1%). Soil analyses were performed by the Soil Testing Laboratory at Rutgers Cooperative Extension Resource Center, Rutgers University, New Brunswick, NJ. Organic matter content was measured by a modified Walkley and Black (1934) dichromate oxidation method. Because of the Atsion soil's higher sand content and the Keyport soil's higher clay content, these soils will be referred to as sandy and clay, respectively.

2.3 Animals

Male Sprague-Dawley rats weighing 250-300 g were purchased from Taconic Farms, Germantown, NY, and were immediately quarantined for one week. Animals were housed three per cage at a temperature of 25 ^{o}C and humidity 50% controlled environment with a 12 hour light/dark cycle. Food and water were provided *ad libitum*.

2.4 Benzene Administration

The oral administration of benzene was performed as follows: 150 µl of ^{14}C–benzene solution (5 µCi) alone or the same volume of radioactivity added to 0.5 g of soil, was combined with 2.85 mL of aqueous 5% gum acacia and a suspension formed by vortexing. This volume of benzene, or benzene soil suspension, was immediately administered by gavage to groups of rats which had been fasted overnight. Heparinized blood samples were collected at 5, 10, 14, 18, 20, 22, 30, 45, 60, 90, and 120 minutes by cardiac puncture of anesthetized rats. Immediately after the collection of the 120 minute blood sample, rats were sacrificed by an overdose of anesthesia and whole organs or samples of kidney, liver, lung, pancreas, spleen, bone marrow, brain, duodenum, adrenal, fat, esophagus, heart, ileum, skin, testes, thymus, thyroid, carcass, stomach, and gastric contents were collected and stored at -75 ^{o}C. Three hundred mg or smaller samples of tissues were used to determine the distribution of radioactivity as previously reported (Turkall *et al*., 1988).

In the dermal application, 30 minutes prior to the administration, five rats/group were shaved on their right costo-abdominal areas. A shallow glass cap (Q Glass Co., Towaco, NJ) circumscribing approximately a 13 cm^2 area was tightly fixed with Lang's jet liquid acrylic and powder (Lang Dental Manufacturing Corp., Inc., Chicago, IL) on the shaved skin of each animal. Rats were anesthetized during the cap attachment procedure. Either 300 mL of ^{14}C–benzene (40 µCi) alone or with 1 g of soil was introduced by syringe through an

opening in the cap, which was immediately sealed. This volume of benzene coated the soil with no excess fluid remaining. Rats were rotated from side to side so that the soil-chemical mixture covered the entire circumscribed area. Volatilization losses during administration of ^{14}C–benzene were determined and dosages were adjusted appropriately. Blood was collected by cardiac puncture under anesthesia at 2, 4, 8, 12, 24, 30, 48 and 72 hours. Blood samples from both routes of administration were processed and radioactivity was measured by liquid scintillation spectrometry, as previously described (Turkall *et al*., 1988; Skowronski *et al*., 1988).

2.5 Excretion and Metabolism Studies

In the excretion studies, groups of six rats each were administered benzene or benzene adsorbed to the soil, as described above. Pairs of animals were housed in all-glass metabolism chambers (Bioserve Inc., Frenchtown, NJ) for the collection of expired air, fecal and urine samples. Expired air was passed through activated charcoal tubes (SKC Inc., eighty-Four, FA) for the collection of ^{14}C–benzene, then bubbled through traps filled with ethanolamine:ethylene glycol monomethyl ether (1:2, v/v) for the collection of $^{14}CO_2$. Charcoal tubes and trap mixtures were collected at 1, 2, 6, 12, 24, and 48 hours, and fecal samples were collected at 24 and 48 hours. Samples were processed and radioactivity was measured as previously described (Turkall *et al*., 1988).

At the conclusion of the dermal excretion studies, rats were sacrificed by an overdose of anesthetic. The glass caps were opened, and 1.0 to 1.2 mL of ethyl alcohol was introduced through the cap opening. The animals were rotated from side to side and 100 µL aliquots of ethanol were removed to determine the percent of benzene dose remaining on the skin application sites (Skowronski *et al*., 1988). Then the glass caps were removed from the rats and tissue specimens were collected to determine the distribution of radioactivity as described above.

To determine benzene metabolism, urine samples were extracted and analyzed by high performance liquid chromatography, as established in our laboratory (Turkall *et al*., 1988).

2.6 Statistical Analysis

Exploratory data analysis was used to summarize replicate data in the plasma time course study. This approach allows a curve to be fitted to all data points, while providing resistance to those points which depart from the primary pattern

(Tukey, 1977; Velleman and Hoaglin, 1981). The curve fitting procedure which was utilized is called smoothing. The curve fitting procedure "4235EH" smoother was utilized for these studies as described by Velleman and Hoaglin (1981). Each replicate was smoothed over all time points, a median value was calculated from all smoothed replicates at each time point, and a second smooth was applied to these median values. The final smoothed data was used to calculate the rate constants and $t_{1/2}$ of absorption and elimination from plasma by regression analysis and the method of residuals (Gibaldi and Perrier, 1975) as well as to determine a maximum concentration was achieved. Plasma concentrations from 0 minutes to the time at which maximum concentration was achieved were used for absorption calculations.

For elimination calculations, 45 through 120 minute time point concentrations were used in oral route studies, while 12 through 72 hours and 24 through 72 hours time point concentrations were used in dermal route studies in the soil and pure groups, respectively. Since the rate constants and the $t_{1/2}$ are calculated from smoothed date, the standard errors (SE) of the rate constants were determined by the bootstrap method (Effron, 1982; Effron and Tibshirani, 1985). AUC was calculated by the trapezoidal rule using individual replicate data, reflects volatilization losses, and is reported as the mean $\pm$ SEM. Statistical differences between the treatment groups, were determined by analysis of variance (ANOVA), F test, and Scheffe's multiple range test. Comparison of slopes were determined using analysis of covariance.

3. RESULTS AND DISCUSSION

Absorption and elimination $t_{1/2}$ data following administration of ^{14}C–benzene orally and dermally to male rats is displayed in Table 1. The $t_{1/2}$ of absorption into plasma in the presence of either soil for oral or dermal treatment was not statistically altered compared to their respective pure group. However, dermal exposure increased absorption $t_{1/2}$ to 25, 60 and 44-fold compared to oral exposure in pure, sandy and clay groups, respectively. In oral treatment, the elimination $t_{1/2}$ of the clay group was significantly decreased ($p < 0.05$) compared to either sandy or pure groups. No significant change in elimination $t_{1/2}$ occurred after dermal exposure. In pure and sandy groups, the elimination $t_{1/2}$ of dermal treatment were increased about 2-fold versus oral treatments, while in the clay group the increase was 13-fold.

Table 1. Absorption and Elimination Half-Lives of Radioactivity in Male Rat Plasma

Treatment	$t_{1/2}$ (hr)[a]			
	Absorption		Elimination	
	Oral	Dermal	Oral	Dermal
Pure [b]	0.12	3.1	13.4	23.0
Sandy [c]	0.06	3.6	10.8	24.5
Clay [d]	0.10	4.4	1.4 [e]	19.4

[a]Values calculated from five or six rats per group.
[b]^{14}C–benzene alone.
[c]^{14}C–benzene adsorbed to sandy soil.
[d]^{14}C–benzene adsorbed to clay soil.
[e] Significantly different from treatment with pure benzene ($p < 0.05$).

The AUC for the 2-hour period following oral administration was increased in both sandy and clay groups; however, only clay soil was significantly different ($p < 0.05$) compared to the pure group. Following dermal administration, both soils significantly ($p < 0.05$) decreased AUC values compared to pure group during the 72 hours studied (Table 2)

Table 2. Area Under Concentration Versus Time Curve of Radioactivity in Male Rat Plasma[a]

Treatment	Percent Initial Dose (mL/min)	
	Oral	Dermal
Pure [b]	1.53 ± 0.06	0.41 ± 0.21
Sandy [c]	2.60 ± 0.19	0.22 ± 0.08[e]
Clay [d]	3.64 ± 0.43[e]	0.17 ± 0.07[e]

[a]Values calculated from five or six rats per group.
[b]^{14}C–benzene alone.
[c]^{14}C–benzene adsorbed to sandy soil.
[d]^{14}C–benzene adsorbed to clay soil.
[e] Significantly different from treatment with pure benzene ($p < 0.05$)

Tables 3 and 4 display the patterns of urinary and expired air excretion of radioactivity following oral and dermal application of ^{14}C–benzene. In oral treatment the expired air represented the primary excretion route of ^{14}C–activity with lesser amounts eliminated in urine during the 48 hours following administration of benzene alone. Expired air and urine represented about equal excretion routes of ^{14}C–activity in the sandy soil treated group, while urine represented the primary route, with lesser amounts eliminated through the expired air in the clay soil group. The percentages of radioactivity in expired air of the clay soil group were significantly lower than those of the pure group at 0-12, 0-24, and 0-48 hours after oral treatment. Unmetabolized ^{14}C–benzene represented 98, 97 and 81% of the total radioactivity collected in the expired air of ^{14}C–benzene, sandy soil, and clay soil groups after oral treatment, respectively, with CO_2 comprising the remainder. With dermal application, the major route of

excretion was the urine, and to a lesser extent, the expired air, in all treatment groups. During the 48-hour collection period, 86.2% of the initial dose was recovered in the urine of the pure benzene group. At the same time period, sandy and clay soil significantly decreased urinary excretion to 64.0% and 45.4%, respectively. The expired air recovery in dermal treatment was significantly decreased in the sandy soil group compared with the pure group, while the clay group was without significant change. Less than 1% of the administered dose was expired as $^{14}CO_2$ in all groups.

Table 3. Urinary Recovery of Radioactivity Following Oral or Dermal Administration of ^{14}C–Benzene[a]

Time (hour)	Oral			Dermal		
	Pure	**Sandy**	**Clay**	**Pure**	**Sandy**	**Clay**
0-12	23.2 ± 6.9	44.7 ± 21.5	37.9 ± 12.6	9.7 ± 3.8	16.2 ± 0.1	7.2 ± 1.7
12-24	2.3 ± 0.8	5.6 ± 1.9	7.2 ± 1.9	58.8 ± 2.8	31.3 ± 2.8[b]	25.1 ± 3.4[b]
0-24	25.5 ± 7.8	51.6 ± 20.7	45.1 ± 13.4	68.4 ± 2.9	47.4 ± 2.2[b]	32.3 ± 4.0[b]
24-48	0.5 ± 0.5	1.3 ± 0.7	0.8 ± 0.1	17.8 ± 1.8	16.6 ± 1.1	13.1 ± 1.9
0-48	26.0 ± 7.9	52.8 ± 21.4	45.9 ± 13.6	86.2 ± 2.1	64.0 ± 2.8[b]	45.4 ± 4.8[b]

[a]Values represent percentage of initial dose (mean ± SEM) of six animals per group.
[b]Significantly different than treatment with benzene alone ($p < 0.05$).

Table 4. Expired Air Recovery of Radioactivity Following Oral or Dermal Administration of ^{14}C–Benzene[a]

Time (hour)	Oral			Dermal		
	Pure	**Sandy**	**Clay**	**Pure**	**Sandy**	**Clay**
0-12	58.2 ± 7.2	50.0 ± 7.6	15.6 ± 10.0[b]	9.4 ± 1.0	3.9 ± 0.8[b]	8.5 ± 1.2
12-24	0.1 ± 0.0	0.2 ± 0.1	0.1 ± 0.0	2.5 ± 0.4	0.4 ± 0.1[b]	1.1 ± 0.2[b]
0-24	58.2 ± 7.2	50.2 ± 7.6	15.7 ± 10.1[b]	12.0 ± 1.4	4.3 ± 0.8[b]	9.6 ± 1.3
24-48	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.0	0.8 ± 0.2	1.6 ± 0.5	0.5 ± 0.2
0-48	58.2 ± 7.2	50.2 ± 7.6	15.0 ± 10.1[b]	12.8 ± 1.1	5.9 ± 1.3	10.1 ± 1.4

[a]Values represent percentage of initial dose (mean ± SEM) of six animals per group.
[b]Significantly different than treatment with benzene alone ($p < 0.05$).

By comparing the excretion routes for the two different routes of administration, it can be seen that the urinary recovery in the dermal pure group after 48 hours from the administration exceeded the value of the oral pure group (86.2% versus 26.0%), but the other two treatments were almost without change. In the oral route, more than 82% of total radioactivity excreted in the urine of all treatment groups appeared during the 0-12 hour period following administration. However, in the dermal route, the highest amount of radioactivity in urine was recovered in the 12-24 hour interval (Table 3). Table 4 reveals that more than 98% of radioactivity excreted in expired air of all oral treatment groups appeared during the first 12-hour period following administration. In dermal application, the highest portion of radioactivity in expired air (approximately 75% of total) was also recovered in the 0-12 hour period following the administration. The

total activity recovered in expired air following oral administration far exceeded the values following dermal administration in the period studied. During the 48-hour period, the radioactivity in the feces of oral treatment was 0.6, 1.3 and 1.4% of initial doe in pure, sandy and clay groups, respectively. In the dermal route < 0.5% fecal recovery occurred in all groups during the same time period.

Tissue distribution of radioactivity after oral administration is displayed in Table 5. Gastric contents contained the highest concentration of radioactivity in all groups, with the mean activity (as percentage of initial dose/g) of the clay group (18.7) being about 6-fold higher than that of either the sandy soil (2.8) and pure benzene (2.1) groups. Stomach contained the highest tissue concentration of radioactivity, with fat the second highest in all treatments, followed by the duodenum an adrenal. No statistically significant differences were detected in the tissue concentrations of radioactivity between the oral treatment groups.

Table 5. Tissue Distribution of Radioactivity in Male Rat Following Oral Administration of ^{14}C–Benzene

Gastric Contents[a]	
Pure Benzene	2.1 ± 1.8
Sandy Soil	2.8 ± 0.7
Clay Soil	18.7 ± 10.8[b]
In All Treatment Groups:	
Gastric Contents > Stomach[c] > Fat > Duodenum > Adrenal	

[a]Values represent percent initial dose per gram (mean ± SEM) from five rats per group, 2 hours following oral administration.
[b]Significantly different than treatment with pure benzene ($p < 0.05$)
[c]No statistical differences between treatment groups.

In the dermal route, soil-related differences were observed in tissue distribution. The distribution patterns of ^{14}C–activity for pure and soil-adsorbed benzene are demonstrated in Table 6. ^{14}C–activity 48 hours post administration of soil-adsorbed benzene was greatest in the treated skin followed by kidney, liver, duodenum, spleen treated fat, and untreated fat, as well as bone marrow in both soil groups. In the pure benzene group, kidney contained the highest amount of radioactivity, followed by liver, treated skin, duodenum, treated fat, and untreated fat as well as bone marrow. Clay soil treatment statistically increased radioactivity (10-fold) in treated skin, while statistically decreasing radioactivity (4-Sfold) in treated fat compared to benzene alone. It is worth noting that at necropsy, ethanol extraction of all dermal application sites contained only 0.1% of the initial dose indicating loose retention of chemical.

Table 6. Tissue Distribution of Radioactivity in Male Rat Following Dermal Administration of ^{14}C–Benzene

Pure Benzene Group:
Kidney > Liver > Treated Skin > Duodenum > Treated Fat > Untreated Fat > Bone Marrow
Sandy and Clay Groups:
Treated Skin[a] > Kidney > Liver > Duodenum > Spleen > Treated Fat[b] > Untreated Fat > Bone Marrow

[a]Significantly increased in the clay group compared to the pure benzene group ($p < 0.05$).
[b]Significantly decreased in the clay group compared to the pure benzene group ($p < 0.05$).

Data showing the urinary metabolites of ^{14}C–benzene in the male rat after oral and dermal application are given in Table 7. Phenol was the major urinary metabolite detected in the 0-12 hour urines of all treated groups in both routes of administration. Smaller quantities of hydroquinone, catechol, and benzenetriol compared to phenol were also detected. The type and percentage of benzene metabolites produced were not altered in the presence of either soil after oral administration, while after dermal administration, hydroquinone was statistically decreased in the 0-12 hour interval in the presence of sandy soil compared to the pure group. Similar metabolite percentages were detected in 12-24 hour urines of all treated groups (data not shown). The parent compound was not detected in the urine of any treatment group. Use of acid hydrolysis in the preparation of urinary extract did not permit identification of conjugation products.

Table 7. Urinary Metabolites of ^{14}C–Benzene in the Male Rat[a]

	Oral			**Dermal**		
Metabolite	**Pure**	**Sandy**	**Clay**	**Pure**	**Sandy**	**Clay**
Phenol	39 ± 1	41 ± 3	34 ± 2	38 ± 3	44 ± 4	46 ± 3
Catechol	14 ± 1	15 ± 3	18 ± 2	13 ± 1	14 ± 5	12 ± 1
Hydroquinone	17 ± 3	25 ± 3	26 ± 1	19 ± 2	10 ± 1	25 ± 1
Benzenetriol	12 ± 3	14 ± 3	20 ± 4	5 ± 2	17 ± 7	13 ± 2

[a]Values represent percent of total radioactivity in the 0-12 hour collection period from 6 animals per group (mean ± SEM).
[b]Statistically different than treatment with benzene alone ($p < 0.05$).

4. CONCLUSIONS

This study revealed that the presence of sandy and clay soil produced qualitative and quantitative differences in the manner of the availability of benzene in the body following oral or dermal treatments. Although the soil group in oral treatment did not significantly alter the rate of benzene absorption ($t_{1/2}$), AUC for 0-2 hour post-administration was increased in both soil groups. Because

the density of benzene is less than water, some gavaged material could be vaporized out of the gastrointestinal tract directly without absorption into the body. Adsorption of benzene to the soil decreased the vaporization of benzene. Detection of the bulk of radioactivity excreted in expired air as unmetabolized benzene during the same time period supports this conclusion. The relatively stronger adsorption of benzene to clay soil is supported by significantly increased AUC, significantly decreased excretion in expired air, as well as relatively high concentration of radioactivity in the gastric contents 2 hours after the oral administration.

Dermal exposure of pure and soil-adsorbed benzene produced plasma concentration of radioactive compound comparable to those generated by oral administration only when rats were exposed to eight times the concentration of ^{14}C–benzene used in the oral route (40 versus 5 μCi). Also, this laboratory reported that peak plasma concentrations after dermal treatments were delayed about 36-fold compared to those which occurred following oral administration (Turkall *et al*., 1988; Skowronski *et al.,* 1988). The absorption and elimination $t_{1/2}$ in all groups after dermal treatment were much longer compared to their respective oral groups. The result of this study is in agreement with those of Frantz (1984) and Susten *et al.* (1985), that indicated benzene was not readily absorbed through the skin. After dermal application, both soil groups demonstrated a significantly lower amount of ^{14}C–activity in urine compared to the pure group, while radioactivity in expired air was decreased significantly after sandy soil administration.

Routes of excretion and amount excreted by the various routes were changed in the presence of the soils in both routes of administration. Expired air recoveries were decreased in all dermal treatments compared to the oral experiments, while the urine was the primary route of excretion in all dermal groups as well as the oral clay group. The fecal route remains a minor excretion route in the presence or absence of soils.

The quantity and quality of benzene metabolites produced were almost without change, except the amount of hydroquinone in the dermal sandy group was significantly decreased. Phenol was the primary urinary metabolite in all the treatments studied.

Malkinson and Gehlmann (1977) reported that the most important factors related to chemical persistence in soil are organic matter and clay content of the soil. In both the dermal and the oral soil-adsorbed benzene studies, altered bioavailability results revealed that a higher percentage of clay rather than organic matter is controlling the retention of benzene in soil. Particle sizes, and thus

surface area of the two soils are essentially equivalent and do not appear to be a factor in this study.

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