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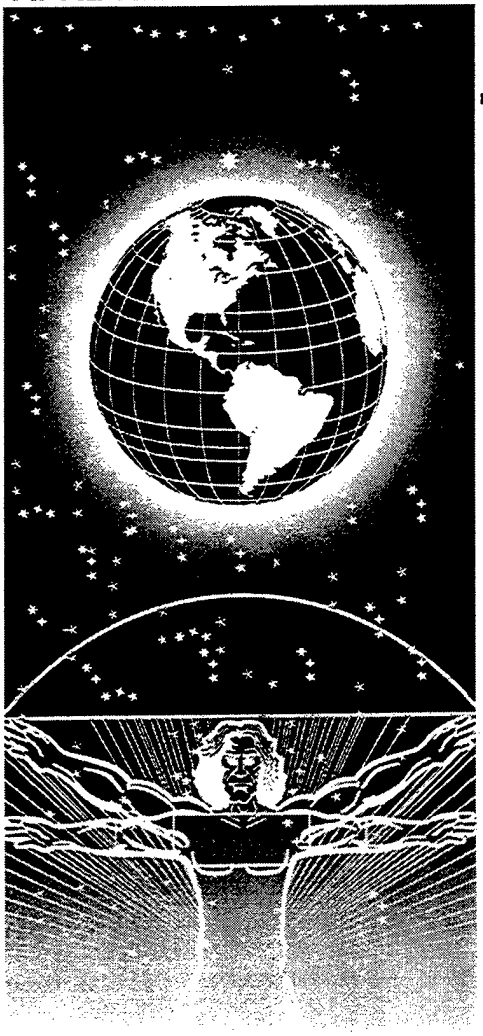

UNITED STATES AIR FORCE
RESEARCH LABORATORY

DERMAL ABSORPTION OF JP-8 JET FUEL AND ITS COMPONENTS

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The animal use described in this study was conducted in accordance with the principles stated in the "Guide for the Care and Use of Laboratory Animals", National Research Council, 1996, and the Animal Welfare Act of 1966, as amended.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

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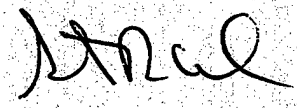

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The dermal absorption of jet fuels in general and JP-8 in particular is not well understood, even though the use by government and industry, worldwide, is over 59 billion gallons per year. JP-8, which is similar to kerosene, is composed of hundreds and perhaps thousands of hydrocarbon chemicals and their isomers. Exposures to JP-8 can occur from vapor, liquid or aerosol. Inhalation and dermal are the most prevalent routes of exposure. It is recognized that JP-8 may cause irritation when the skin is exposed repeatedly or for prolonged periods, but whether systemic toxicity from dermal absorption of fuels may occur is unknown. The purpose of this investigation was to measure the flux of JP-8 and its major constituents through rodent skin to assess the potential for systemic effects with human exposures. The composition of a specific test sample (POSF-3509) of JP-8 was analyzed. Static diffusion cells containing dermatomed rodent skin were used to determine the flux of JP-8 and it's components. Thirteen individual components of JP-8 were identified in the receptor solution. The flux from this JP-8 fuel ranged from a high of 82.4 nanograms/cm2/hr (the additive DIEGME) to a low of 0.5 nanograms/cm2/hr (tridecane). Permeability coefficients, which can be used to estimate the absorption of components from other fuels, were also calculated. These fluxes suggest that JP-8 will not cause systemic toxicity.

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PREFACE

This is one of a series of technical reports describing the effects of dermal exposures to JP-8 fuel. This research was accomplished at the Operational Toxicology Branch, Human Effectiveness Directorate of the Air Force Research Laboratory. This research was completed under Man Tech – Geo-Centers Joint Venture Contract (F41624-96-C-9010). Lt. Col. (sel) Stephen L. Channel served as Contract Technical Monitor for the U.S. Air Force, Air Force Research Laboratory. Air Force Medical Operations Agency sponsored this study. This research was supported by the Air Force Office of Scientific Research and the Air Force Medical Operations Agency.

The animal use described in these studies was conducted in accordance with the principles stated in the "Guide for the Care and Use of Laboratory Animals", National Research Council, 1996, and the Animal Welfare Act of 1966, as amended.

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ABSTRACT

The dermal absorption of jet fuels in general and JP-8 in particular is not well understood, even though the use by government and industry, worldwide, is over 59 billion gallons per year. JP-8, which is similar to kerosene, is composed of hundreds and perhaps thousands of hydrocarbon chemicals and their isomers. Exposures to JP-8 can occur from vapor, liquid or aerosol. Inhalation and dermal are the most prevalent routes of exposure. It is recognized that JP-8 may cause irritation when the skin is exposed repeatedly or for prolonged periods, but whether systemic toxicity from dermal absorption of fuels may occur is unknown. The purpose of this investigation was to measure the flux of JP-8 and its major constituents through rodent skin to assess the potential for systemic effects with human exposures. The composition of a specific test sample (POSF-3509) of JP-8 was analyzed. Static diffusion cells containing dermatomed rodent skin were used to determine the flux of JP-8 and it's components. Thirteen individual components of JP-8 were identified in the receptor solution. The flux from this JP-8 fuel ranged from a high of 82.4 nanograms/cm^2/hr (the additive diethylene glycol monomethyl ether) to a low of 0.5 nanograms/cm^2/hr (tridecane). Permeability coefficients, which can be used to estimate the absorption of components from other fuels, were also calculated. These fluxes suggest that JP-8 will not cause systemic toxicity because the low fluxes will not cause body burden that even approach levels which are recognized safe.

INTRODUCTION

Jet fuel use

The U.S. Department of Defense uses over 2 billion gallons of jet fuel per year [Henz, 1998], and civilian jets use over 59 billion gallons per year, worldwide [Armbrust, 1998]. Fuels workers around the world are exposed to this fuel in many different ways. Understanding exposures to jet fuel and the possible health hazards of jet fuel is difficult for several of reasons. First, today's jet fuel is kerosene, a mixture of petroleum compounds that boil within a specified range. Each fuel must meet performance specifications established by the military and the American Society for Testing and Materials (ASTM). Since testing is done on performance, the composition of jet fuel can vary considerably from batch to batch. Second, exposures occur over a wide range of scenarios and locations, making specific exposure guidelines difficult. Finally, the toxicity of a complex mixture such as jet fuel is difficult to describe.

Fuel	1991	1992	1993	1994	1995	1996	Total
JP-4	1355.14	858.81	681.05	203.11	66.88	0.66	3165.65
JP-5	463.35	376.52	327.51	148.92	33.57	350.29	1700.16
JP-8	12.43	12.7	213.51	531.4	995.6	1749.02	3514.66

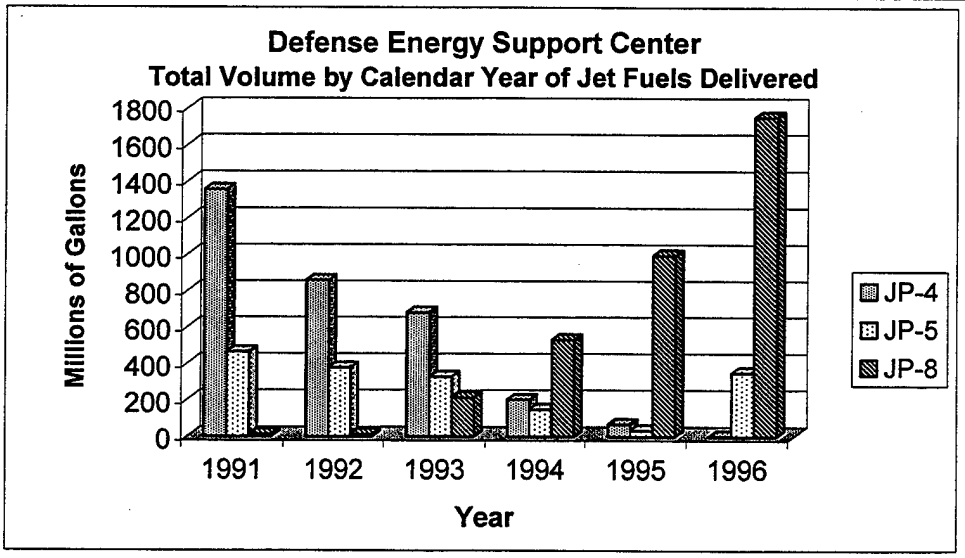

Figure 1. Total Volume by Calendar Year of Jet Fuels Delivered (Defense Energy Support Agency Survey of Jet Fuels). Inset table shows actual values.

Military and civilian turbine engine aircraft are the primary users of jet fuel. The military and civilian designations for this fuel are JP-8 and Jet A, respectively. The North Atlantic Treaty Organization (NATO) countries selected JP-8 (called F-34 in NATO) as the primary jet fuel in 1972. The U.S. military plans to have all battlefield equipment (i.e. tanks, other fighting vehicles, portable heaters, stoves, etc.) using JP-8 in the next ten

years. Figure 1 shows the quantity of jet fuel delivered to DoD from 1991 to 1996. The graph depicts the change from JP-4 to JP-8 over the same time period. While JP-8 is touted as the single battlefield fuel for all U.S. and NATO air and ground forces and will streamline logistics operations, more uses for jet fuel create additional exposures and possible health effects.

JP-8 composition

Over decades of use, safety concerns have directed fuel users toward a less flammable fuel. The kerosene in widespread use around the world today is safer than previous fuels due to its higher flash point. Turbine fuels are made by blending petroleum refinery streams. Refinery streams are blended in certain ratios in order to meet published military and civilian specifications. JP-8 is blended from distilled petroleum streams with boiling points between 150 and 260 °C. JP-4 was a 50/50 mix of gasoline and kerosene [U.S.Air Force, 1996]. Since these fuels are blended from various hydrocarbon streams, they can vary considerably from batch to batch. The fuel must meet performance specifications, but is not constrained to any particular chemical makeup. The petroleum stock used to make fuels is critical to the makeup of the final, blended kerosene.

JP-8 differs from Jet A and straight run kerosene due to additives required by the military specification. These include fuel system icing inhibitor, corrosion inhibitor, and static dissipater. JP-8 is composed of hundreds and perhaps thousands of individual chemicals and their isomers. The chemical composition is not regulated, with a few exceptions. The specification limits aromatics to 25 %, sulfur to 0.3 %, and olefins to 5.0 % [U.S. Air Force, 1992]. On average, JP-8 contains 17.7 % aromatics, 0.05 % sulfur, and 1.1 % olefins [Henz, 1998]. Aliphatic hydrocarbons make up over 80 % of the total. In order to assess the toxicity of jet fuel, a standardized fuel was developed to normalize on-going and future health effects research efforts. The Air Force Research Laboratory, Propulsion Directorate, Fuels Branch (AFRL/PRSF) blended a research fuel (designated POSF-3509) from a variety of refinery streams which represent the petroleum used to make jet fuels around the world. This was the fuel used in this study.

JP-8 exposures

Exposure to JP-8 occurs as a vapor, aerosol and/or liquid. The lower vapor pressure of JP-8 compared to JP-4 decreases inhalation exposure because vapor concentrations under the same atmospheric conditions are lower. However, aerosolized fuel and fuel vapor in confined spaces are still potential inhalation hazards. Prolonged or repeated skin contact to aerosol or liquid JP-8 has the potential to cause local and systemic effects. JP-8 aerosol can be produced when turbine engines are started at low ambient temperatures. The uncombusted fuel/water aerosol mixture may be inhaled, irritate the eyes or soak clothing and come into prolonged contact with the skin of ground personnel. Other JP-8

dermal exposures include splashes during refueling or fuel handling, handling fuel system engine components, direct contact with fuel soaked parts during fuel system maintenance operations, and contact with fuel leaks on the underside of the aircraft or on the ground.

JP-8 toxicity

Human epidemiology data is very limited with respect to jet fuels. JP-8 has been tested with standard toxicity batteries and found to be relatively non-toxic. JP-8 long term toxicity testing was conducted in rats and mice using vapors at 0, 500, and 1,000 mg/m^3 on a continuous basis for 90-days. This exposure was followed by recovery until two years of age. Limited toxicity was evident, with no tumor formation. The male rat-specific α2-microglobulin protein droplet nephropathy was observed as the only toxic effect. This nephropathy in male rats does not occur in humans since humans do not produce α2-microglobulin. As a result, the limited toxicity seen in the 90 day study was not relevant to humans [Mattie, 1991]. In another study, male rats were dosed by gavage with undiluted JP-8 (0, 750, 1500, 3000 mg/kg) daily for 90 days. This study revealed a dose-dependent decrease in body weights due to JP-8 ingestion, as well as the male rat-specific α2-microglobulin nephropathy seen in the previous study. Changes were noted in blood and urine that were neither dose-dependent nor biologically significant, according to the author. Gastritis and perianal dermatitis were significant treatment-related effects. Although there were no histopathological or weight changes in the livers of exposed rats, there was an increase in the liver enzymes AST and ALT. The elevated enzymes did not increase as the JP-8 dose was increased [Mattie, 1995]. An additional study using female rats revealed a dose-dependent decrease in body weights. These rats were dosed orally for a total of 90 days in addition to mating, gestation and lactation (0, 325, 750, 1500 mg/kg JP-8 daily) [Mattie, 1995]. Organ weight ratio (liver:body, liver:brain and kidney:brain) increases were observed. Liver weight increases were noted, but did not show histopathologic changes or increases in liver enzymes (ALT, AST). Stomach cell hyperplasia and perianal dermatitis were other treatment-related effects seen in this study [Mattie, 1995]. One-hour, daily, aerosol inhalation exposures for up to 28 days showed changes in pulmonary function and decreased substance P levels in rats [Pfaff, 1995]. JP-8 with additives (JP-8 +100) was shown to be the same as JP-8 in an acute toxicity battery [Wolfe, 1996]. Genetic toxicity tests showed no evidence for mutagenicity and no evidence for significant genetic risks associated with JP-8 jet fuel [Brusick, 1978]. JP-8 was not a teratogen in a rat model [Cooper and Mattie, 1996]. JP-8, when tested on rabbits and guinea pigs, was slightly irritating to the skin and a weak skin sensitizer [Kinkead, 1992].

Dermal absorption

Although the skin is a good barrier to many chemicals (especially water and water soluble chemicals) some chemicals penetrate through the skin when long exposures or high concentrations occur. Only minimal information is available on the systemic

toxicity of JP-8 after dermal exposure. Hydrodesulfurized kerosene (which is similar to JP-8 without the additives) was shown to be without reproductive or developmental effects when rats were dosed dermally with 494 mg/kg/day for 7 weeks [Schreiner et al., 1997]. Petroleum middle distillate streams, which are similar to JP-8 (except without the additives), have been shown to increase the incidence of skin cancer in mice who were treated for 24 months to a lifetime [Freeman et al., 1993; Broddle et al., 1996]. These studies indicate that the potential for systemic toxicity after dermal exposures is real; however, some of the effects could have been due to inhalation of the volatile components of JP-8 during and after the dermal exposures.

Chemicals penetrate into and through the skin based on their chemical characteristics [Scheuplein and Blank, 1971; Dugard and Scott, 1984a; and Flynn, 1990]. Large molecular weight chemicals tend to move more slowly though the skin. Polarity and lipid solubility also have important effects. Charged chemicals do not passively cross membranes, including the skin, very well and chemicals that have an affinity for lipids can often enter the primary skin barrier – the stratum corneum. The vehicle or the other components that make up a mixture of chemicals also can have a great effect on the rate of penetration. If a chemical is applied to the skin in a vehicle, such as water, the relative affinity of the chemical for the skin versus the affinity of the chemical for the vehicle will determine whether the chemical will have a tendency to stay in the vehicle or be driven into the skin by the thermodynamics of the situation [Barry et al., 1985; Jepson and McDougal, 1997]. Diffusion cells using isolated skin from laboratory animals or humans are often used to measure the rate of absorption of chemicals [Bronaugh, 1982]. These *in vitro* tests have many assumptions but can be useful estimates of potential fluxes in human exposure situations if they are carefully accomplished. The purpose of this investigation was to measure the flux of JP-8 and its major constituents through rodent skin to assess the potential for systemic effects with human exposures.

MATERIALS AND METHODS

JP-8 analysis

JP-8 and Volpo saline samples were analyzed on a Gas Chromatograph with Flame Ionization Detection (FID). They were injected at 140 C with a Tekmar 7000 headspace sampler (Cincinnati OH). They were injected onto a 0.53mm X 30m SPB-1 column in a Varian 3700 (Palo Alto CA) GC with a FID. The column oven temperature program started at 50°C, was held at this temperature for 5 minutes and then heated at 5°C/min to 190°C. JP-8 standards were run in the same manner. The results were processed with Perkin-Elmer Nelson integration software (Norwalk CT). Total integrated peak areas were used to determine total JP-8 absorption. The GC/FID gave the same pattern as the GC/MSD chromatograms.

For the analysis of individual components, major individual peak identities were confirmed by retention time check with known standards. FID gives similar response to unsubstituted hydrocarbons. This was checked with six unsaturated hydrocarbons and confirmed. Diethylene glycol monomethyl ether (DIEGME), the only substituted hydrocarbon, gave 37% of the FID response of JP-8. The DIEGME response was corrected; the others were calibrated directly with JP-8. Isomers of methyl naphthalene and isomers of dimethyl naphthalene were integrated separately and their masses were combined.

JP-8 Composition

Because of the variability in JP-8 fuel batches, part of a specific batch (POSF-3509) has been set aside for research purposes so that data from individual laboratories will be comparable. Table 1 shows the relative proportions of the major hydrocarbon components of the JP-8 that was used in these studies. The larger components that could be identified make up less that 25% of this complex mixture of many hundred chemicals. Figure 2 shows a mass spectrum that illustrates the number of compounds in the JP-8 mixture.

Table 1. Composition of JP-8 (POSF-3509) as analyzed by gas chromatography.

Component	Percent (w/w)
Undecane	6.0
Dodecane	4.5
Decane	3.7
Tridecane	2.7
Tetradecane	1.8
Methyl naphthalene	1.2
Nonane	1.1
Trimethyl benzene	1.0
Pentadecane	1.0
Dimethyl benzene (xylene)	0.59
Naphthalene	0.26
Dimethyl naphthalene	0.21
Ethyl benzene	0.15
Diethylene glycol monomethyl ether	0.08
Methyl benzene (toluene)	0.06

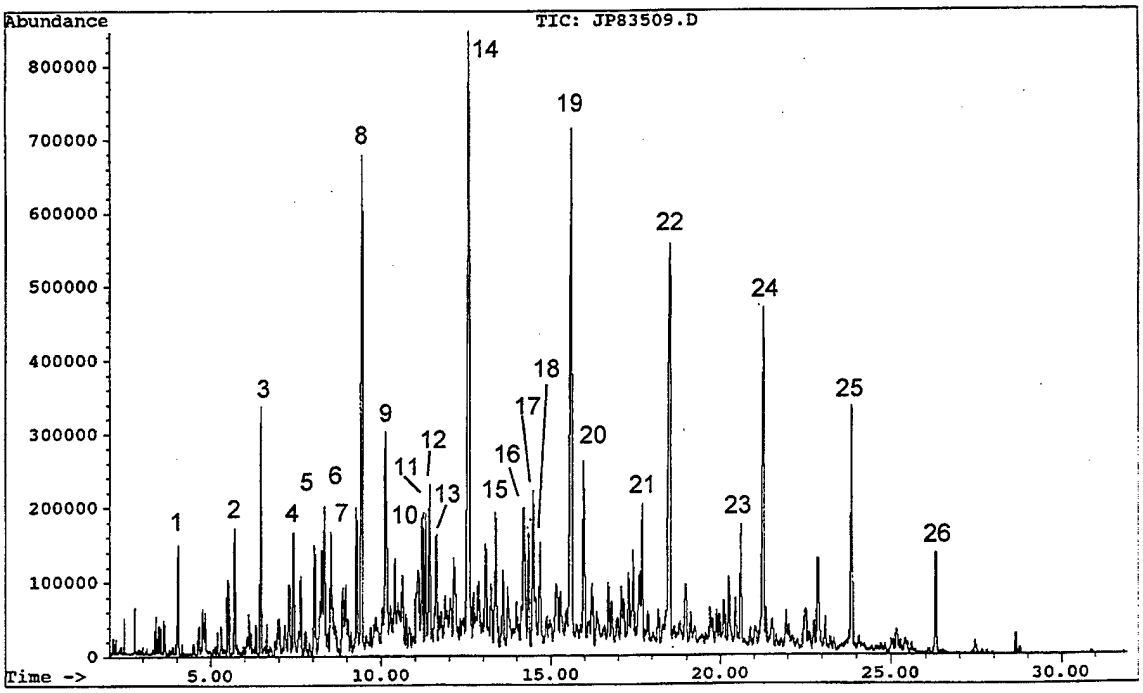

Figure 2. Chromatographic spectrum of JP-8 (POSF-3509) as analyzed by gas chromatography/mass spectrometry (GC/MS).

Skin preparation

Male rats (CDF® F-344/CrlBr, Charles River Breeding Laboratories), weighing 267-363g, were sacrificed using CO_2. The back of the animal was closely clipped of fur with Oster® animal clippers (McMinnville TN) and a #40 blade, taking care not to damage the skin. An Oster® finishing clipper (0.22mm) was used to carefully remove the fur stubble. A thin cardboard circle the diameter of the outside edge of the diffusion cell was used as a template to mark a circle on the midscapular area of the rat's back with a waterproof marker. The marked skin containing the future exposure site was gently excised from the back using scissors and blunt dissection. The skin was placed stratum corneum side up on a 5 x 30 cm oak board and dermatomed to 560 micrometers using a Padgett dermatome (Kansas City MO). The skin was trimmed with scissors to match the size of the circular mark and placed on the glass receptor chamber that was previously filled with receptor solution.

Diffusion cell methods

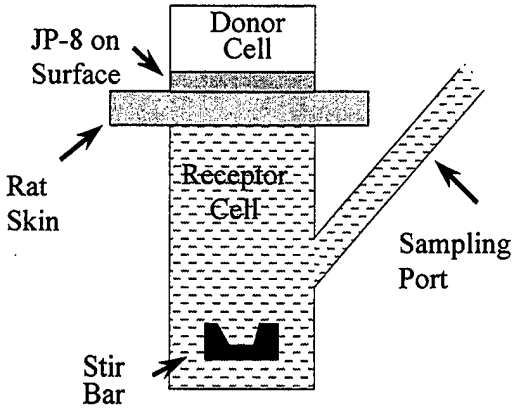

Figure 3. Schematic of static diffusion cell apparatus for measuring absorption of JP-8 through isolated rat skin.

Static Diffusion cells with 4.9 cm^2 skin exposure area (Figure 3) were used to determine flux of JP-8 and its components. These brown glass cells (Crown Glass Company, Somerville NJ) fit 9 to a countertop console which provides magnetic stirring of the receptor solution and fluid flow to the water jackets (not shown in Figure 3) around the receptor cells. These diffusion cells have a 12.5 mL stirred receptor compartment right under the skin with a 7 cm long sampling port. The receptor compartment was filled with a solution of 6% Volpo 20 (polyethylene glycol-20 oleyl ether, Croda, Mill Hill PA) in physiological saline. Skin temperature in the cells was controlled at 32°C with a Haake DC3 circulating water bath (Karlsruhe, Germany). The donor chamber was placed on top of the skin and secured by screw clamps. Two milliliters of JP-8 was placed in the donor chamber. The receptor solution was sampled at half-hour intervals for 4 hours. Chemical concentration in the samples was determined by headspace analysis using gas chromatography with electron capture detection. The experiment was repeated on 2 different days and the results were pooled.

Component Identification

A Hewlett-Packard (Wilmington, DE) 5890 gas chromatograph with a 5971 series mass spectrometric detector (MSD) was used for the separation and identification work. The temperature program used was a 50°C start temperature, then ramped at 2°C per minute to 180°C and held there until the end of the run time. JP-8 and Volpo saline samples were run on the GC/MSD with a 0.20mm X 30m SPB-1 (Supelco, Bellefont PA) column. The Volpo saline samples run contained JP-8 components that had penetrated

the skin. Identities were determined for the materials with the larger concentrations. Identities of the smaller concentration materials were found only if they were well separated.

Flux and permeability determinations

Flux (mass/area-time) was determined from the slope of the plot of cumulative chemical mass in the receptor solution over time. The mass was normalized for surface area. Time points before chemical was detected in the receptor solution were not used. Flux was determined for each diffusion cell and reported with standard deviation. The first two hours of the experiment were used to determine the flux for DIEGME because after two hours the flux was not linear. For the individual components, permeability coefficients (distance/time) were estimated by dividing individual fluxes by the concentration of the JP-8 component [Bond and Barry, 1988].

RESULTS

During a four-hour experiment after JP-8 was placed on the skin in the diffusion cell, many chemical peaks were detected in the receptor solution samples. The majority of the peaks were very small and not resolved from other peaks and therefore could not be identified. The time course of appearance of mass in the receptor solution during four-hour experiments is shown in Figure 4. Total chemical mass absorbed by four hours was 1381 nanograms (data not shown). The sum of all the JP-8 component peak areas was low at half an hour and increased to 282 nanograms per square centimeter of skin at four hours. Flux calculated from the slope of the linear regression through the points in Figure 4 is 67.9 nanograms per centimeter squared per hour.

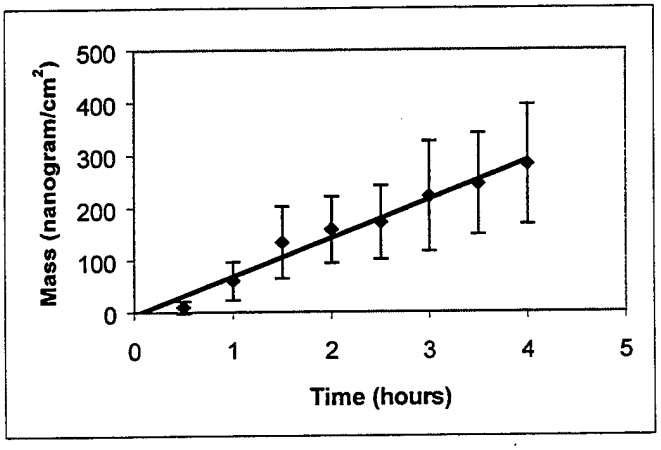

Figure 4. Plot of cumulative chemical absorbed over time when skin in a static diffusion cell was exposed to JP-8. Error bars are standard error of the mean. Line is the linear regression which was used to estimate flux.

Thirteen individual components of JP-8 in the receptor solution had large enough peaks to be identified. Figures 5 and 6 show individual chemical concentrations for eight diffusion cells at half-hour intervals during the exposures. Methyl benzene (Figure 5) was the chemical with the least variability (coefficient of variation at 4 hours was 23%) and dodecane (Figure 6) was the chemical with the most variability (coefficient of variation at 4 hours was 77%). It is important to point out that both Figures 5 & 6 are based on the same 20 uL samples from the same experiments. The difference in variability (best and worst shown here) can therefore only be attributed to the GC integration routine because of size and location of the peaks.

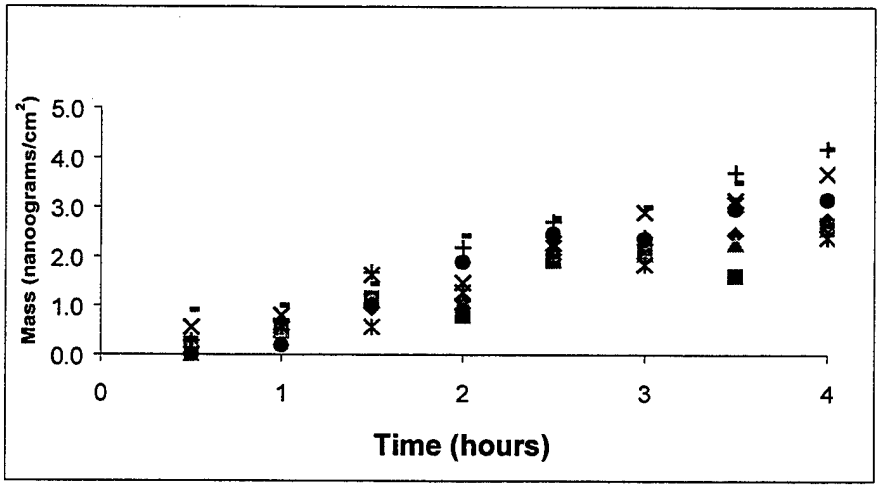

Figure 5. Mass per unit area of methyl benzene appearing in each of the diffusion cells during exposure to JP-8. There are eight individual samples at each sample time.

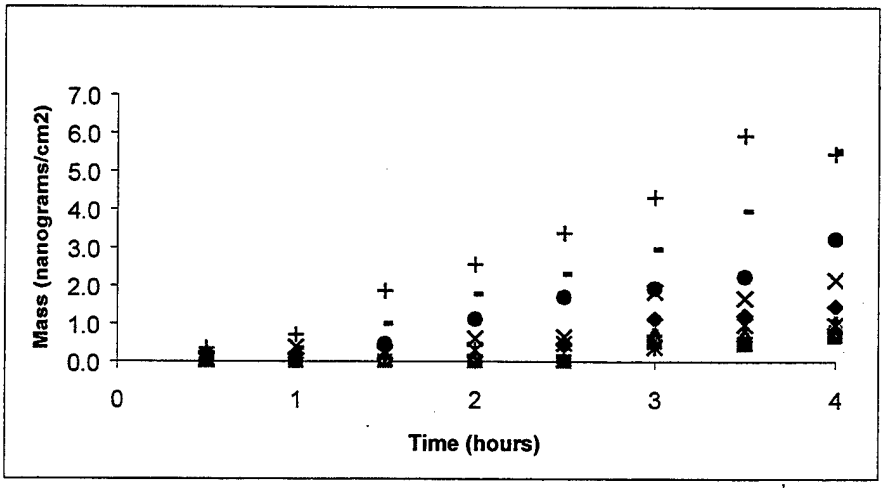

Figure 6. Mass per unit area of dodecane appearing in each of the diffusion cells during exposure to JP-8. There are eight individual samples at each sample time.

Table 2 shows cumulative mass absorbed at four hours for each of the components that were identified. The mass of diethylene glycol monomethyl ether (DIEGME, ice inhibitor additive) was considerably larger the mass of any of the hydrocarbon components which could be identified.

Table 2. Mass of individual chemicals absorbed after four-hour static diffusion cell experiments in which rat skin was exposed to JP-8.

Component	Cumulative absorbed (nanograms ± SE)
Diethylene glycol monomethyl ether	189.8 ± 68.6
Decane	9.3 ± 4.2
Methyl naphthalene	8.5 ± 3.2
Trimethyl benzene	7.6 ± 2.7
Undecane	7.1 ± 4.9
Naphthalene	6.1 ± 2.3
Dimethyl benzene	4.8 ± 1.5
Methyl benzene	3.2 ± 0.7
Dimethyl naphthalene	3.0 ± 1.1
Dodecane	2.6 ± 2.0
Ethyl benzene	2.4 ± 0.8
Nonane	2.1 ± 1.5
Tridecane	1.2 ± 0.7

Table 3 shows fluxes and breakthrough times of JP-8 components that were identified. The component with the greatest flux was DIEGME that had flux more than an order of magnitude greater than the next hydrocarbon component. The flux of DIEGME was approximately 150 times greater than the flux of tridecane, the chemical with the smallest flux. Breakthrough time was also very short for DIEGME but about two hours for tridecane.

Table 3. Fluxes and breakthrough times of JP-8 components across rat skin exposed for four hours in diffusion cells. Flux is calculated from slope of the cumulative absorbed plot and breakthrough time is estimated as the place the flux line intercepts the exposure time.

Component	Flux ± SE (nanograms/cm^2/hour)	Breakthrough time (hours)
Diethylene glycol monomethyl ether*	82.4 ± 24.2	0.5
Decane	2.58 ± 1.08	1.0
Methyl naphthalene	2.48 ± 0.83	1.0
Trimethyl benzene	2.01 ± 0.8.	1.0
Undecane	1.94 ± 1.29	1.0
Naphthalene	1.67 ± 0.61	0.5
Dimethyl benzene (xylene)	1.27 ± 0.38	0.5
Dimethyl naphthalenes	.938 ± .267	1.0
Methyl benzene (toluene)	.856 ± .151	0.5
Dodecane	.816 ± .581	1.0
Nonane	.615 ± .384	1.0
Ethyl benzene	.604 ± .234	0.5
Tridecane	.534 ± .311	2.0

*Flux for DIEGME was calculated from the slope of the first two hours .

Permeability coefficients for the components of JP-8 that were identified in the receptor solution are shown in Table 4. These permeability coefficients were calculated as described in the methods section and reflect the influence of the vehicle (JP-8) and the concentration of chemical in that vehicle.

Table 4. Permeability coefficients for each of the chemical components identified in the receptor solutions from JP-8 exposures.

Component	Permeability Coefficient (cm/hr)
Diethylene glycol monomethyl ether	1.3×10^{-4}
Methyl benzene (toluene)	1.7×10^{-6}
Naphthalene	8.1×10^{-7}
Dimethyl naphthalene	5.5×10^{-7}
Ethyl benzene	5.0×10^{-7}
Dimethyl benzene (xylene)	2.7×10^{-7}
Methyl naphthalene	2.5×10^{-7}
Trimethyl benzene	2.4×10^{-7}
Decane	8.7×10^{-8}
Nonane	6.7×10^{-8}
Undecane	4.0×10^{-8}
Tridecane	2.4×10^{-8}
Dodecane	2.3×10^{-8}

DISCUSSION

JP-8 is a complex mixture of hydrocarbons that have related but different chemical characteristics and therefore a wide-range of potential interactions with a biological system. Prolonged or repeated JP-8 contact with the skin has been shown to cause irritation [Kinkead, et al., 1992; Wolfe et al., 1996; Baker et al., 1999]. It is uncertain whether JP-8 or its components can be absorbed through the skin in sufficient concentration to cause systemic toxicity. No systemic toxicity has been documented from JP-8 dermal exposures in humans or laboratory animals. The purpose of these studies is to measure and express absorption parameters in a way that will allow estimations of systemic toxicity based on the total amount of chemical absorbed and on individual component toxicity.

Total JP-8 absorbed

In our static diffusion cells the flux of JP-8 was measured to be 67.9 ng/cm^2/hr based on the sum of the individual GC integration areas. If we can assume our experimental situation is a reasonable approximation of a human exposure situation, we can then use the principles related to Fick's Law to estimate the total amount of chemical that might be absorbed in any particular human exposure scenario. If we know the flux (J), the surface area exposed (A) and the exposure time (t) we can estimate the total amount of chemical absorbed through human skin according to:

$$Mass = JAt \qquad (1)$$

We are concerned about how much chemical might be absorbed if both hands were constantly wet with JP-8 during an 8 hour shift. The surface area of both hands is 840 cm^2 [USEPA, 1996]. We get the following calculation for mass of JP-8 absorbed.

$$456,288\,(ng) = 67.9\,(ng/cm^2hr) \times 840\,(cm^2) \times 8\,(hr) \qquad (2)$$

This corresponds to 456 micrograms or about 0.5 milligram that would be absorbed systemically through the hands during this scenario.

With this estimate, we can approximate systemic toxicity from dermal exposure based on studies from other exposure routes. The current interim NRC recommended standard equivalent to an occupational exposure limit (OEL) for JP-8 vapor is 350 mg/m^3 [Committee on Toxicology, 1996] and we can assume it to be a safe level in humans. The respiratory volume during an 8-hour workshift is 10 m^3 [Walker et al., 1996]. If we assume that an individual breathes air containing JP-8 at the AFOSH standard for the whole workshift and all of the JP-8 is absorbed, the mass absorbed would be 3,500 milligrams. The systemic dose from dermal absorption through both hands for the entire 8-hours (0.5 mg) would be approximately four orders of magnitude less that the mass absorbed by inhalation at the AFOSH standard.

The surface area of the whole body is approximately 18,000 cm^2 [USEPA Exposure Factors Handbook]. A calculation similar to above for an 8-hour whole body exposure to JP-8 gives the following amount for total absorbed:

$$10{,}538{,}080\,(ng) = 67.9\,(ng/cm^2hr) \times 18000\,cm^2 \times 8\,(hr) \quad (3)$$

If we compare this total body dermal exposure (10.7 mg) with the safe amount according to the OEL (35,000 mg), we can see that it is very unlikely that the dermal route of absorption can be a systemic hazard in any realistic exposure scenario.

Individual component absorption

Table 2 shows the masses of individual components in the receptor solution at the end of the experiments. The sum of all the masses of identified components in Table 2 is 247.7 nanograms. If we compare this mass (determined by adding all the individual chemical peaks together) with the total mass from identified and unidentified peaks (1381 nanograms), we find that we were able to identify only 18 percent of the mass absorbed. The other 82 percent represents area from the gas chromatography analyses which were either too small or too poorly defined to be identified in this mixture of many hundreds of components.

Diethylene glycol monomethyl ether

Dugard and coworkers [1984b] measured the dermal absorption of diethylene glycol monomethyl ether (DIEGME) through heat separated human epidermal membranes. They reported a flux of 206 ± 156 ng/cm^2/hr from the pure chemical. This is about 5 times higher than the flux from JP-8 measured in this study (Table 3). DIEGME flux as a pure chemical would be expected to be higher than DIEGME flux from JP-8 (which acts as a vehicle) because the concentration of pure chemical is several orders of magnitude higher than the concentration of DIEGME in JP-8 (0.1 percent). According to Fick's law, flux is directly proportional to concentration so, all other things equal, flux should be higher from pure liquid. Dugard's study used heat separated epidermis as the membrane and we used dermatomed rat skin, which includes epidermis and some dermis. According to Fick's law the flux is inversely proportional to the thickness of the membrane. Human epidermis is about 30 microns thick [Branchet, 1990] and although Dugard didn't measure their epidermal preparation it is certainly much thinner than our rat preparation which was dermatomed at 560 microns. For these reasons the flux should be greater in Dugard's study. The effect of the JP-8 (as a vehicle) on the absorption of DIEGME is not known. It is possible that the JP-8 either enhances or limits the absorption of DIEGME based on thermodynamic principles. DIEGME does preferentially move (partition) to the water phase of a fuel/water mixture and perhaps the fuel would help DIEGME penetrate the skin.

With our flux measurement we can estimate the potential for systemic toxicity from DIEGME in JP-8. DIEGME is relatively non-toxic; a 13-week vapor inhalation

study in rats showed no treatment related effects at 216 ppm for 6 hours a day and five days a week (Miller et al., 1985). If we also assume that 216 ppm (1,060 mg/M^3) would be a safe level for humans we can compare systemic toxicity from inhalation with dermal absorption. If we assume an individual breathes air containing 1,060 mg/M^3 for the whole workshift and all of the JP-8 is absorbed through the lungs, the mass absorbed would be 10,600 milligrams. Calculating the total chemical absorbed through two hands exposed to JP-8 containing DIEGME (equation 3) gives 0.554 mg or about one 19 thousandth of the daily inhalation dose which caused no effects in rats over a 13-week period of daily administration.

$$553,728\,(ng) = 82.4\,(ng/cm^2 hr) \times 840\,(cm^2) \times 8\,(hr) \qquad (4)$$

This calculation would overestimate absorption through the skin because the DIEGME flux would decrease as the concentration of DIEGME in JP-8 was depleted by absorption into the skin.

Because of the low concentration of DIEGME in JP-8 (0.08%), the volume of JP-8 that would contain 10,600 milligrams of DIEGME is 16.5 liters. Therefore to exceed what appears to be a safe level, an individual would have to be exposed to and completely absorb all of the DIEGME from more than 16 liters of JP-8. This is an unlikely scenario and although DIEGME is the chemical with the largest dermal flux from the fuel, it is unlikely that enough could be absorbed to be a systemic hazard.

In an informal experiment to determine the amount of JP-8 which would completely cover one hand, we immersed one hand in JP-8 for 5 seconds, allowed it to drip for 10 seconds and then determined the mass of chemical which stuck to the skin of the hand by determining the weight of JP-8 remaining in a beaker. The volume of JP-8 that stuck to a large sparsely-haired hand was 2.88 ml and the volume of JP-8 that stuck to a small hairy hand was 2.75 ml. According to the USEPA Draft Exposure Factors Handbook [1996], the average surface area of one hand for a male is 420 ± 12.7 cm^2. Dividing the average volume of JP-8 clinging to one hand (2.82 ml) by this average hand area gives .0067 ml/cm^2. This is the maximum loading of JP-8 on the skin that is achievable without continuous immersion. If the whole body surface area (19,400 cm^2), [USEPA, 1996] is taken into account, it is estimated that 0.13 liters of JP-8 would stick to the whole body. This is much less (2 orders of magnitude) than the more than 13 liters that would have to be exceeded to exceed the safe level for DIEGME. It's safe to assume that based on existing toxicity information and our experimental flux, DIEGME absorption from JP-8 should not cause systemic toxicity.

Hydrocarbon components

Flux of the hydrocarbon components of JP-8 was much less than the DIEGME and ranged from 0.5 to 2.5 ng/cm^2/hr (Table 3). None of these chemicals are very toxic, but naphthalene with a Threshold Limit Value (TLV)™ of 52 mg/m^3 has the lowest threshold

limit value. The flux of naphthalene is 1.67 ng/cm^2/hr and during an exposure to JP-8 on both hands continuously for 8 hours, .011 mg would be absorbed systemically:

$$11,222\,(ng) = 1.67\,(ng/cm^2 hr) \times 840\,(cm^2) \times 8\,(hr) \quad (5)$$

At the TLV™, 520 mg could be absorbed through the respiratory tract during an 8-hour shift if the air concentration was at the limit. It is easy to see that it is impossible to get enough naphthalene through the skin to approach the TLV™. These calculations address acute systemic toxicity of JP-8.

Permeability coefficients

The permeability coefficients estimated in this study and shown in Figure 4 are useful for determining the permeability of a JP-8 component from JP-8 of a different composition. Permeability coefficients are concentration independent and if the concentration of a specific component of JP-8 is known to be much larger or smaller the permeability coefficient can be used to determine the mass of chemical which might be absorbed according to:

$$Mass = PACt \quad (6)$$

where P is the permeability coefficient, A is the surface area exposed, C is the concentration of the component in JP-8 and t is the exposure time.

CONCLUSIONS

It is possible to assess the absorption of JP-8 as a sum of all the integrated peaks that penetrate the skin. The number of identified peaks that penetrate the skin is fewer than the number of peaks which can be identified in the fuel. Based on our flux measurements and theoretical calculations, the amount of fuel that could be absorbed through the skin and available systemically is very small. Contact of the hands with JP-8 for 8-hours would be expected to give a body burden of about four orders of magnitude less than the body burden at the inhalation exposure limit. It is also possible to identify individual components of JP-8 that penetrate the skin. Of these components, diethylene glycol monomethyl ether showed the greatest flux although it is only present in JP-8 at 0.08 %. Other hydrocarbon components exhibited fluxes that were more than one hundred-fold less than the diethylene glycol monomethyl ether. Based on our flux measurements, JP-8 would not be expected to be absorbed through the skin well enough to be a systemic hazard. The additive DIEGME and the hydrocarbon component with the lowest TLV™ would also not be systemic hazards.

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