34 Dermal Absorption of Chemical Contaminants from Soil

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BACKGROUND

Recently, Spalt et al. (1) critically reviewed the available (English language) literature describing dermal absorption from soil. The earliest entry in that review is a paper by Swiss investigators concerning oral and dermal absorption of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in multiple formulations including soil (2). That investigation was inspired by dioxin contamination events in Germany and Italy in the 1970s. All but one of the subsequent studies identified in the review were conducted in the United States. Given the universality of English as the language of science, this observation presumably reflects research funding priorities stemming from political attention to hazardous waste sites and other contaminated lands, and the relative importance of quantitative risk assessment in the regulatory environment in the United States, rather than mere language bias. Regardless, the total body of research is quite limited [Spalt et al. (1) found fewer than 50 distinct studies] and represents the efforts of a relatively small group of investigators. In addition to its limited scope, significant shortcomings of the extant dermal-absorption-from-soil literature include (*i*) a lack of uniformity of methodology, which greatly hinders systematic comparison across compounds and laboratories, (*ii*) frequently inadequate reporting of experimental details, and (*iii*) obvious flaws in some experimental approaches.

As a consequence, commonly used procedures for estimation of dermal absorption of chemical contaminants from soil are not well developed. Current U.S. Environmental Protection Agency (USEPA) guidance for use in investigations of the worst uncontrolled and abandoned toxic waste sites in the United States, those designated Superfund sites, presents recommendations for estimation of absorption of contaminants from both soil and water (3). The soil protocol is

TABLE 1 Chemicals for Which Fractional Dermal Availabilities from Soil are Specified in Current U.S. Enviromental Protection Agency Guidance

Arsenic
Cadmium
Chlordane
2,4-Dichlorophenoxyacetic acid
DDT
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and other dioxins
Lindane
Benzo(*a*)pyrene and other polyaromatic hydrocarbons
Aroclors 1242/1254 and other polychlorinated biphenyls
Pentachlorophenol
Semivolatile organic compounds
Organic nitro compounds (12 values)

Source: From Ref. 3, as supplemented by Ref. 32.

relatively primitive and depends heavily upon literal acceptance of results, expressed as fraction of initial dose absorbed, for the limited number of chemicals (shown in Table 1) for which experimental results are available. In some cases, measurements made on one chemical were extended to the entire class of chemicals [e.g., benzo(*a*)pyrene as a surrogate for all polyaromatic hydrocarbons, TCDD for all dioxins, and Aroclor 1242 or 1254 for all polychlorinated biphenyls (PCBs)]. For contamination of soil by semivolatile organic compounds (SVOCs) not otherwise listed, a default availability of 10% is recommended. For unlisted chemicals that cannot be characterized as SVOCs, no default is stipulated and a qualitative approach is recommended.

In contrast, a relatively well-founded protocol for estimation of dermal absorption of chemicals from water is described in the same guidance. This disparity reflects the fact that many more studies with much greater uniformity of methodology are available for water. Specifically, data describing absorption from water obtained in vitro using human cadaver skin were available for about 90 organic compounds at the time the USEPA guidance was written,[a] whereas only about one-third as many compounds have been studied in experimental investigations of absorption from soil by all methods. A theoretically more rigorous approach for soil, based on the water permeation data, has been proposed by Bunge and Parks (4,5), but has not been adequately tested due to lack of suitable data and has not been widely adopted. In a limited comparison with results from a set of experiments that were sufficiently described (6), the Bunge and Parks approach (5) over-estimated dermal absorption of lindane and 2,4-dichlorphenoxyacetic acid (2,4-D) from two soils.

All soils have a limited capacity to interact with a given contaminant, which is essentially the saturation limit (7). If the amount of contaminant in soil exceeds this limit, neat chemical will be present. Based on rudimentary chemical and physical principles, an organic chemical sorbed to soil at a concentration less than saturation of the soil would be expected to be less available for dermal absorption than it would be in neat form. Sorption on soil should lower fugacity and hence reduce the thermodynamic driving force for dermal absorption and might also reasonably be expected to increase mass transfer resistance. In concert, these effects should reduce flux into skin. Recent results for two different soils

[a] There are now water data for approximately 150 compounds.

contaminated with methyl paraben (7,8), which included determinations of soil saturation, are consistent with the fugacity argument. The results reported in the early paper by Poiger and Schlatter (2) noted above are also generally in accord with this basic concept. In those experiments, TCDD was apparently less well absorbed from soil than from neat compound and even less well absorbed from activated carbon than from soil. However, the intervening literature is not consistent on even this fundamental point as several investigators have reported that they did not observe reduced availability from soil in the experiments they conducted. A sampling of those reports is described briefly below.

SELECTED EXAMPLES

Case 1

Wester et al. (9–13) have conducted in vivo experiments using rhesus monkeys in which absorption of radiolabeled chemicals [Aroclor 1242, benzo(*a*)pyrene, chlordane, 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (DDT), 2,4-D, and pentachlorophenol] was assessed after application in solvent and in soil to abdominal skin. Availability was assessed by collection of urine for several days to several weeks with adjustment for radiolabel recovery after intravenous administration. In four of six cases, Wester et al. found no statistical difference between availability (expressed as percent of initial dose) from soil and solvent. They summarized these results in the following manner (13):

> Absorption levels of pentachlorophenol, chlordane, PCBs, and ... 2,4-D are the same from acetone and soil.

Note that Wester et al. do not conclude merely that their in vivo results do not show a difference between absorption from their soil and absorption from solvent deposition for the four compounds, a position that would be both accurate and appropriately cautious. Rather they assert that soil (and apparently not just their own rather artificial soil, which is described in more detail below) has no effect on transfer of these lipophilic compounds to skin. Strong empirical evidence exists that soils are sorbents for a broad range of non-ionized organic chemicals [e.g., (14)]. Because the quotation above is inconsistent with fundamental chemical principles, it is reasonable to question the adequacy of the experimental protocol on which it is based.

There are at least two explanations for the observed results. The first is that all four compounds were applied to the soil at concentrations exceeding the saturation limit. This does not appear to be the case in these experiments (1) (but cannot be absolutely ruled out as characteristics of the post-sieved soil were not reported). A second, more plausible explanation is that the methods used in the solvent deposition and soil application protocols were actually much more similar than might be first assumed. Wester et al. did not report the time elapsed between chemical addition to soil and application of amended soil to skin, suggesting that they considered this variable to be unimportant. They did routinely describe mixing under conditions that would permit solvent to dissipate (9–13), but acknowledge that they did not verify dissipation (12). Visual examination of soil is not an adequate test for the presence or absence of solvent residue and cannot provide assessment of whether an added chemical has reached equilibrium with (i.e., dissolved into) soil organic carbon. The Yolo County soil used in all studies by Wester et al. was prepared by sieving a soil with a relatively low organic carbon content (approximately 1% by weight) to exclude particles with diameters less than

180 μm or greater than 300 μm. The resulting soil would have consisted of fine to medium sand with unknown and probably lower organic carbon content than the whole soil. If the time elapsed between chemical amendment of the soil and application of that soil to the monkeys' abdomens was relatively short, the applied chemicals may have still been in solvent or present as neat chemical on the surface of the soil grains at the time of application. Spreading the soil on the skin could then have distributed chemical either alone or in residual solvent to the skin. This would make the initial chemical transfer substantial, and larger than from chemical sorbed to soil. Under those circumstances, similar dermal absorption from solvent and soil applications would be expected.

Direct transfer of chemical to skin, either in solvent or as neat chemical not yet adsorbed by the soil, would also explain why transfer from soil was apparently efficient even though complete coverage of the exposed skin may have lasted for only a brief period. Wester et al. applied their soil to the abdomens of anesthetized monkeys with the animals in a horizontal position. After the application site was covered with a water vapor permeable membrane sandwiched between a pair of concave aluminum eye guards, the monkeys were placed in an upright position in restraint chairs. Given the particle size range used, sloughing of the soil to the bottom of the cover device is likely. The fact that absorption from soil was statistically indistinguishable from absorption from solvent-deposited chemical suggests that transfer from soil to skin had already occurred prior to placement of the monkeys in the restraint chairs.

Case 2

Qiao and Riviere (15) examined absorption of 3,3′,4,4′-tetrachlorobiphenyl (TCB) in an ex vivo pig model. They compared results following deposition in acetone, methylene chloride, a water–acetone mixture, and a soil–water–acetone mixture. Since acetone and methylene chloride would be expected to evaporate quickly (after application at $\mu L/cm^2$ solvent loadings), two of the experiments were actually tests of absorption from solvent-deposited pure compound. Radiolabel was counted in various compartments. Overall "penetration" was assessed as cumulative perfusion plus depot in tissues other than stratum corneum. The highest value was reported for the non-occluded soil–water–acetone mixture. Qiao and Riviere concluded that:

> The data indicate that PCB dermal risk can be much higher with exposure in soil than with exposure in liquid solutions.

The overall mass recovery (i.e., the sum of TCB found ultimately in all compartments expressed as a fraction of the initial mass applied) in the various versions of the study were both highly variable and generally low (mean recoveries ranged from 39% to 80% across vehicles). Under the circumstances, cautious interpretation would seem appropriate. A noticeable difference between the non-occluded soil–water–acetone experiments and the solvent deposition experiments (which provide the basis for the conclusion quoted above) is that in the solvent deposition experiments much larger portions of the initial dose were recovered from the dosing device (an adhesive template). A plausible partial explanation for the observed result is therefore that the soil matrix served to retard loss of TCB to the dosing device. More importantly, the TCB was added at about 3000 ppm of dry soil, an amount probably substantially in excess of its solubility in that phase (1). In addition, the initial "soil" mixture was roughly 55% soil, 30% water, and 15% acetone. The manner in which the TCB was added was not described, but apparently occurred only "several hours" before the start of the experiment. Storage conditions in the interim were also not reported. Under these circumstances, it is unlikely that much of the TCB had partitioned to the soil. Therefore, transfer of TCB to skin during the course of the experiment was probably from phases other than soil, including neat compound. Qiao and Riviere cite the PCB work by Wester et al. (11) noted above as supportive of their finding.

Case 3

Abdel-Rahman and co-workers (16–18) have reported results of in vivo studies in which soils and radiolabeled volatile organic compounds (VOCs) were applied to rats. In these experiments, glass caps were fitted to the backs of the rats. Although the protocol is ambiguously described, it appears that soil was first applied under the cap and then benzene, toluene, or *m*-xylene was added to the soil. Soil–chemical contact time prior to chemical–skin contact in these experiments was therefore negligible. In addition, the chemicals were added to each of two soils at roughly 25% by weight, an amount greatly in excess of the likely sorption capacity of either. Results were assessed by monitoring radiolabel in blood, tissues, and excreta. Interpretation of these experiments is complicated by competition between volatilization and dermal absorption, and by the authors' decision to present results normalized by the non-volatilized fraction. Despite the presence of the glass caps, losses of benzene and toluene were very substantial (roughly 40–70% of initial dose). In the case of *m*-xylene, volatilization losses were apparently very minor, and absorption from soils, as represented by area under the plasma concentration versus time curve, was reported to be statistically indistinguishable from absorption from pure *m*-xylene. Cumulative excretion (urine, feces, and expired air) of radiolabel at 48 hours approached 100% of initial dose with or without soil. Given that the soils were supersaturated, this is not surprising. Application of *m*-xylene alone and *m*-xylene slurried with soil both led to dermal exposure to, and absorption of, *m*-xylene liquid. The value of these experiments with respect to understanding of dermal absorption from contaminated soils is unclear. Opportunity for significant dermal contact with soils saturated with solvents is limited at best. In readily accessible, near-surface soils, VOCs evaporate relatively rapidly, and are unlikely to be found at high concentrations. Solvent contamination of subsurface soils is a common problem, but cleanup of subsurface solvents does not routinely involve manual excavation.

DISCUSSION

The examples presented above are illustrative of the generally poor quality of the existing dermal-absorption-from-soil literature. Use of poorly designed protocols and uncritical acceptance of results are common. Many of the published studies display little understanding of conditions under which exposures to contaminated soils might occur, of relevant properties of soils, or of basic sorption/desorption phenomena. Spalt et al. (1) identified few studies without one or more significant flaws. Key shortcomings include the use of soil supersaturated with the target chemical, failure to appropriately consider the effects of multiple soil layers, and incomplete reporting of experimental details needed for interpretation of results. In at least 10 published studies, soil saturation was likely to have been

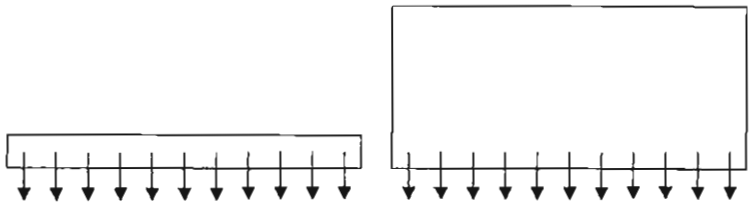

FIGURE 1 Schematic of initial flux from thin and thick soil loads.

exceeded (in some cases greatly exceeded) (1). Experiments in which exposure is to supersaturated soils, which contain free chemical, do not advance understanding of dermal absorption of chemicals sorbed on soil. Saturation should be evaluated in advance. A rough estimate of the saturation limit of a given chemical in soil can be generated from the following two equations:

$$K_d = f_{oc} K_{oc} \tag{1}$$

$$C_{soil,sat} = C_{w,sat} K_d \tag{2}$$

where K_d is the soil:water partition coefficient (mL/g), f_{oc} is the weight fraction of organic carbon in the soil, K_{oc} is the organic carbon:water partition coefficient (mL/g), $C_{soil,sat}$ is the saturation limit of the contaminant in soil (mg/kg), and $C_{w,sat}$ is the saturation limit of the contaminant in water or solubility (mg/L). Implicit in equation (1) is the assumption that sorption occurs in the organic carbon fraction and not on inorganic surfaces. It is therefore not applicable if the potential sorbate is ionized or if the soil has very low organic carbon or substantial clay mineral content. Even in the absence of such conditions, estimates of $C_{soil,sat}$ are uncertain because $C_{w,sat}$ and K_{oc} are uncertain. Estimates of $C_{w,sat}$ and K_{oc} should not be assumed to deviate less than a factor of 10 from actual values (19). Even if experimental values are available, differences in experimental conditions can render a given value substantially uncertain (19). Investigators wishing to examine absorption from soil should therefore conduct their experiments at concentrations well below estimated saturation limits.

Common reliance upon fractional absorption as the primary measure of dermal uptake from soil is an additional problem. Reduced fractional absorption with increased mass of applied soil (i.e., increased number of soil layers) is well documented (6,8,20–22). Arguments to the contrary (13,23–25) are based on demonstrable errors (1). The underlying concept is simple. Consider thin and thick layers of soil (shown schematically in Fig. 1). If coverage is complete in each case, and conditions other than soil loading, such as concentration of the contaminant in the soil (C_{soil}), are equivalent, initial fluxes from the thick and thin layers should also be equivalent, although the chemical load to the skin (mass of chemical/area) will be smaller for the thin layer. That is:

$$J_{thin} = J_{thick} \tag{3}$$

and

$$C_{soil}\left(\frac{M_{soil}}{A}\right)_{thin} < C_{soil}\left(\frac{M_{soil}}{A}\right)_{thick} \tag{4}$$

in which J is flux through skin (mass of chemical/area/time), M_{soil}/A is soil load (mass of soil/area), and C_{soil} (M_{soil}/A) is the chemical load. It follows then that the fractional rate of absorption (time^{-1}), defined as the ratio of the flux of chemical to the chemical load, must be greater for the thin layer as stated in equation (5):

$$\frac{J_{thin}}{C_{soil}\left(\frac{M_{soil}}{A}\right)_{thin}} > \frac{J_{thick}}{C_{soil}\left(\frac{M_{soil}}{A}\right)_{thick}} \tag{5}$$

Fractional absorption can therefore be artificially reduced by applying soil loads well in excess of the minimum required to cover the skin sample with a single layer of soil particles (i.e., the monolayer load). This phenomenon has long been recognized. Early USEPA guidance (26) contains an explicit, if imperfect (6), protocol for adjustment of fractional absorption for layering. Nevertheless, more recent guidance (3) still relies upon fixed values of fractional availabilities for a limited number of compounds.

Nominal estimation of monolayer loading is straightforward. Assuming face-centered packing of solid spherical soil particles of uniform diameter, the mass of soil required to provide monolayer coverage can be estimated (6) as:

$$\left(\frac{M_{soil}}{A}\right)_{monolayer} = \frac{\rho_{particle}(\pi d^3/6)}{d^2} = \rho_{particle}\frac{\pi d}{6} \tag{6}$$

where $(M_{soil}/A)_{monolayer}$ is the soil load (mg/cm^2) representing a monolayer, $\rho_{particle}$ is the particle density of the soil (mg/cm^3), and d is the particle diameter (cm), usually taken as the geometric mean of the range of particle diameters. Assuming a soil particle diameter of 10 μm and specific gravity of 2.65, equation (6) gives a value of 1.4 mg/cm^2 for $(M_{soil}/A)_{monolayer}$. Since soil particles are not actually uniformly sized spheres, the output from equation (6) is approximate.

Actual exposures to soil typically involve average skin loadings less than 1 mg/cm^2 (27–31). That means that normal exposures to most skin surfaces are probably at sub-monolayer loadings (although averages may reflect localized multilayer clumps). The potential therefore does exist for underestimation of dermal absorption if the value of fraction absorbed used in an exposure assessment is taken directly from experiments conducted with multiple soil layers (assuming that other factors, such as duration of exposure, are appropriate). For instance, consider the 3% dermal absorption of TCDD reported in the previously discussed work by Poiger and Schlatter (2), and taken as the current default estimate by the USEPA (3). Poiger and Schlatter's soil was sieved to less than 160 μm and then ground further with mortar and pestle to an unknown final particle size distribution. They applied the soil at a skin load of 13 to 17 mg/cm^2 (dry soil basis), which probably represents at least 5 to 10 layers of soil. Therefore, they could have reduced their soil load without impacting the flux of TCDD into skin in their experiments. Had they done so, they would have found greater apparent fractional uptake.

One way to avoid the layering effect is to conduct experiments at monolayer or lower loading. However, using low loadings may present significant experimental challenges related to achievement of uniform distribution of soil on the skin and/or adequate analytical sensitivity. For these reasons, experiments with multiple layers have advantages over sub-monolayer experiments as long as the results are interpreted appropriately. Data may be extracted as average flux over a specified interval of time. It is reasonable to expect that flux from sub-monolayer

soil loads should not exceed determinations made with multiple soil layers. Given this expectation, an upper limit for the cumulative mass absorbed per unit area of skin $(M_{abs}/A)_{upper\ limit}$ from exposure to a sub-monolayer load of soil $(M_{soil}/A)_{sub}$ over the same time interval (t) as the flux determination in a multiple layer experiment $(J_{multi})_t$ can be estimated as follows:

$$\left(\frac{M_{abs}}{A}\right)_{upper\ limit} = (C_{soil})_{sub}\left(\frac{M_{soil}}{A}\right)_{sub}\left\{1-\exp\left[\frac{-t\,\frac{(J_{multi})_t}{C_{multi}}\,\frac{(C_{soil,sat})_{multi}}{(C_{soil,sat})_{sub}}}{\left(\frac{M_{soil}}{A}\right)_{sub}}\right]\right\} \quad (7)$$

in which $(C_{soil})_{sub}$ and $(C_{soil})_{multi}$ designate the contaminant concentrations on soil for the sub-monolayer and the multiple layer soils, respectively, and $(C_{soil,sat})_{sub}$ and $(C_{soil,sat})_{multi}$ represent the soil saturation concentrations for the sub-monolayer and multiple layer soils. Equation (7) was derived from a differential mass balance of the chemical on the soil with the assumptions that soil concentrations are less than saturation, flux measured in the multiple layer experiments is proportional to concentration, and that maximum flux occurs when the soil is saturated (7). The ratio of soil saturation concentrations is required to adjust the experimental determination from the multiple layer experiment to sub-monolayer coverage of the skin by a different soil. If the sub-monolayer soil in the absorption estimate is the same as the soil used in the multiple layer experiments, then $(C_{soil,sat})_{sub}/(C_{soil,sat})_{multi} = 1$. If the two soils are different, the saturation ratio for an organic compound can be approximated, per equations (1) and (2), by the ratio of the organic carbon mass fraction (f_{oc}) in each soil as given in equation (8):

$$\frac{(C_{soil,sat})_{sub}}{(C_{soil,sat})_{multi}} = \frac{(f_{oc})_{sub}}{(f_{oc})_{multi}} \quad (8)$$

Although equation (7) is based on a plausible assumption of thermodynamic activity as the driving force for mass transfer, additional data of suitable quality are required to test it and, if necessary, to guide development of an improved relationship. In particular, additional data are needed that elucidate the effects of soil load above and below monolayer, exposure time, and soil characteristics such as organic carbon content, particle size distribution, soil hydration, and mineral content. Data describing effects of key chemical properties are also needed, particularly of those properties that could determine soil saturation, soil-to-skin transfer, and transfer between soil layers (e.g., octanol–water partition coefficient, water saturation, and vapor pressure).

Provision of new data will require new experiments. As noted above, prediction of absorption from soil lags prediction of absorption from water, which has benefited from more systematic experimentation using relatively simple in vitro methods. In vivo experiments are frequently considered to be superior to in vitro investigations for physiological reasons, but implementation of in vivo experimentation requires tradeoffs. First, most compounds of interest cannot be tested in vivo in humans. This leads immediately to issues of interspecies extrapolation. In addition, in vivo dermal methodologies using non-human animals typically entail unrealistic exposure conditions, as movements of non-human subjects are not easily controlled. If an air gap develops and/or soil sloughs, mass transfer conditions will be altered from those intended and mathematical description may become very difficult. Experimental procedures should ensure that soil–skin contact is maintained. Because tight wrapping may cause occlusion, which is also undesirable, non-human in vivo studies of absorption from granular material are inherently problematic. Prevention of exposure from routes other than dermal absorption is also often difficult when using animals. A final limitation involving in vivo experimentation with certain animals is the inability to estimate overall recovery. When using humans or other primates in dermal studies, total recovery cannot be measured directly (unless short-term excretion approaches 100%), but must be estimated based on recovery observed following administration by another route.

TABLE 2 Recommendations for Experimental Determination of Absorption from Soil

Particle size range	Fine fractions of soils should not be excluded, and coarse particles should not be included, unless particle size is an experimental variable. The currently most common limit of 150 μm is a reasonable cut point for coarse particles based on precedent, but lower upper limits can also be justified.
Soil load	Potential layering effects should be considered at the design stage. Results should not be reported as percent absorbed if applied loads exceed monolayer unless layering is an experimental variable. Because uniform distribution of soil on skin (especially over small areas) is difficult, experiments conducted above monolayer may be appropriate, or even preferred, but results from layered experiments should be reported in terms of flux only.
Soil saturation	Chemical concentrations in soil should not approach the estimated solubility of the compound of interest in the test soil. This can be demonstrated by measurements at several soil concentrations or by determination of soil saturation.
Soil–chemical contact	At a minimum, thorough blending of the chemical with the soil should be demonstrated. If the target chemical is added to soil by solvent deposition, methods that ensure solvent dissipation prior to application to skin should be employed. Additional time may be necessary to allow the chemical to equilibrate with the soil, which should be the goal. Time of soil–chemical contact prior to skin exposure should be uniform across experiments unless soil–chemical contact time is an experimental variable.
Soil–skin contact	Measurements describing absorption at times less than 24 hours and temporal patterns of absorption are critically lacking in the current literature.
In vitro methodologies	In vitro experiments should be designed such that potential for flux limitation is minimized. Relative capacities of donor and receptor compartments should be evaluated. Design considerations should include modification of experiment duration, soil load, and measurement point.
In vivo methodologies	In vivo experimental protocols should provide continuous contact of the soil with the skin site without occlusion. Assurance that exposure by ingestion or inhalation is negligible should be provided by explicitly substantiated argument or physical means.
Reporting	Complete reporting of methodological parameters should be provided including, but not limited to, characteristics of soil as applied (i.e., the minimum and maximum particle sizes, organic carbon content, level of hydration), soil–chemical and soil–skin contact times, chemical-to-soil and soil-to-skin application methods, postexposure washing methods, and mass recoveries in all compartments before and after any adjustments. If results are corrected for recovery in parallel intravenous or oral studies, parameters derived from those studies, including statistical variability, should be explicitly reported. Mass recovery calculations should be transparent.

Source: From Ref. 1.

In comparison to in vivo experimentation, the in vitro alternative offers several potential benefits including lower cost, greater rapidity, simpler experimentation, routine use of human tissue, and more easily implemented mass accounting. The most commonly mentioned shortcoming involves the potential for flux limitation because the skin is not vascularized. Flux limitation can occur if the rate of transport from the skin to the receptor fluid is slower than the rate of transport from soil to skin. However, studies can be designed in such a way that the layers of the skin beneath the epidermis do not limit flux (i.e., penetration is determined through the epidermis only) and that the capacity for the skin and receptor fluid to absorb contaminant is sufficiently large that the soil-to-skin concentration gradient is not artificially reduced.

RECOMMENDATIONS

The current body of interpretable experimental investigations of dermal absorption of chemical contaminants from soil is inadequate to permit rigorous evaluation of new modeling strategies, to confidently predict uptake of compounds that have not yet been investigated, or even to extend predictions of dermal absorption for contaminants that have been studied (under limited conditions) to alternative conditions. Additional, systematic effort is needed. Recommendations for future investigations have been compiled (1) and are summarized in Table 2.

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Second Edition

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