



Application of measured *in vitro* dermal bioavailability of polycyclic aromatic hydrocarbons (PAH) in soil in detailed quantitative human health risk assessment

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ABSTRACT

Our study shows that site-specific estimates of dermal exposure to selected polycyclic aromatic hydrocarbons contained in contaminated gasworks soil result in lower average daily exposure and risk to human health when compared to the generic assumptions used in risk assessment software. We use site specific *in vitro* dermal bioavailability flux ($\mu\text{g}/\text{cm}^2/\text{h}$) for benzo[a]pyrene measured by earlier research published by the authors, where dermal flux provides an analogue of diffusion through the skin and into systemic circulation. We used measured *in vitro* dermal flux for gasworks contaminated soil containing 150 mg/kg of benzo[a]pyrene to estimate average daily exposure and risk using the Contaminated Land Exposure Assessment (CLEA) framework. Site-specific flux ($0.00237 \text{ ng}/\text{cm}^2/\text{hour}$) was used to calculate an uptake of $23.7 \text{ ng benzo[a]pyrene}/\text{m}^2 \text{ skin}/\text{hour}$, resulting in an average daily exposure (ADE) ranging from 20.7 to $37.3 \text{ ng benzo[a]pyrene}/\text{kg bw}/\text{day}$ for the first six years of a female child's life. The average ratio of average daily exposure to the Health Criteria Value (Index Dose) was 0.54, where a soil concentration of 278.4 mg/kg is equivalent to a ratio of ADE to Index Dose of one. The results show that for the dermal pathway only, the risk to human health calculated using site-specific dermal flux is lower than using default values used in CLEA. In our discussion we highlight that dermal bioavailability varies between sites and PAH and that differences are likely to be influenced by the source of contamination and the physico-chemical properties of soil. Our findings support an evidence-based shift toward sample-specific parameters in regulatory risk assessment frameworks, but the scalability, inter-laboratory reproducibility, range and contaminants tested and the cost-effectiveness of *in vitro* flux testing need to be researched further before broader regulatory adoption.

1. Introduction

1.1. Soil contamination and polycyclic aromatic hydrocarbons

Soil contamination from industrial activities has occurred globally from the deposit of waste, surplus materials and spills and poses long-term risks to human health. In particular, the use of coal as a raw material in processes such as coke and coal gas manufacture has resulted in chemical by-products containing hazardous concentrations of polycyclic aromatic hydrocarbons (PAH) much higher than the raw materials (Nathanail et al., 2002). PAHs are a group of 1000s of compounds with varying physico-chemical properties (Environment Agency, 2008). Some PAH have been well studied and shown to be carcinogenic (Straif et al., 2005, International Agency for Research on Cancer, 2012). PAH are also released from natural sources including eroded coal formations,

hydrothermal vents, volcanoes and wildfires (Richards et al., 2024), the latter a more frequent and exacerbated under global climate change (Canadell et al., 2021; Jones et al., 2022). One of the most studied PAH is benzo[a]pyrene. However, there are many parent PAH and derivative compounds with alkyl groups, oxygen, nitrogen or sulphur incorporated into the ring structure that are not routinely investigated which pose similar health risks to their parent compounds (Williams-Clayson et al., 2023). The importance of the health impacts of contaminated soil has been long recognised by the United Nations and the Sustainable Development Goal (SDG3) (United Nations, 2015). The critical health effects from BaP include a range of cancers and it is protection from these that drove the selection of the health criterion value used in this study (Nathanail et al., 2014).

PAH-contaminated soil is particularly widespread in urban areas because of burning of fossil fuels and deposition of soot and combustion

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products in urban soils, resulting in people being exposed daily to potentially harmful concentrations (background concentrations around 50 mg/kg (mean $\Sigma 16$ PAH) (Vane et al., 2014). PAH and associated health risks are also a concern due to point source releases and spills with post-clean up ranges reported around 50 mg/kg (mean $\Sigma 12$ PAH) (Apiratikul et al., 2020) but also due to elevated background levels pristine environments where such releases are typically absent (Pongpiachan et al., 2017). One of the most recognised sources of PAH include former gasworks (also referred to as manufactured gas plants). Although gasworks are no longer operational, there will be some direct relevance to the by-product coke ovens which operates similar to a gasworks. These still operate in many countries worldwide.

Understanding the spatial distribution and concentration of PAH in soil is crucial to quantifying site-specific daily exposure and health risks. Soil contaminants can enter the human body via three exposure routes: ingestion, inhalation and dermal absorption (Environment Agency, 2009b). Common daily activities such as using green spaces such as gardens, parks, and allotments for recreation and food production result in quantifiable daily exposure to and associated intake of soil. For example, human health risk assessment models assume that intake of soil by a female child over the first six years of her life will be equivalent to approximately 177 mg day⁻¹ over each seven-day period of exposure (Environment Agency, 2009b).

The total concentration of PAH or indeed other soil contaminants is not always equal to the mass of contaminant released from the soil and absorbed by the human body. Soil contamination uptake and its relationship with the total mass in soil is referred to as bioavailability and plays an important part in risk assessments (Nathanail and Smith, 2007; Environment Agency, 2009b). The concept of bioavailability originates in therapeutic drug design and pharmacology, which necessarily involves optimising the release and absorption of pharmaceutical ingredients. Measuring the bioavailability of a substance, in soil or otherwise, is traditionally done by *in vivo* experiments where live animals or organisms are exposed to chemicals in that matrix and the bioavailability quantified as a proportion of the dose applied. Mainly due to ethical concerns with *in vivo* experiments, there is a long term global policy to replace, reduce, and refine their use (e.g. Bolan et al., 2021). This has led to a need for non-animal, commonly known as *in vitro*, methods.

1.2. The skin system and dermal bioavailability

The skin is the largest organ of the human body, typically weighing approximately 5 % of total body mass with an area of approximately 1.8 m² (Pannatier et al., 1978). Skin comprises two layers: the epidermis and the dermis. The outer layer of the epidermis, the stratum corneum, provide the first line of defence against the absorption of chemicals into systemic circulation from skin contact (Chilcott, 2008).

The stratum corneum is highly lipophilic due to extensive secretions of a natural oil complex (sebum) (Stefaniak et al., 2010), supported by a range of living basal cells forming the remainder of the epidermis. It forms the body's primary defence against dehydration, water ingress, ultraviolet radiation from the sun and protects against exogenic substances entering the body. Below the epidermis is the dermis which hosts sebaceous glands which produce and release sebum, host hair follicles, and support blood capillaries. The dermis is largely hydrophilic. The third and deepest layer is the hypodermis, this is where the body's fatty tissue is stored and where the blood and lymphatic vessels are found.

Uncertainties exist about the extent to which potentially harmful chemicals in soil are absorbed through the skin (Hoang, 1992; Environment Agency, 2009b). The absorbed fraction (uptake) of the total dose applied during an exposure event provides a simple estimate of the bioavailability. However, the assumptions required to accurately estimate this fraction are hard to replicate in the laboratory. Beriro et al., 2016 Most notably is the creation of a soil monolayer on the skin. A monolayer refers to a theoretical situation where the surface of the skin

is covered exactly by a single layer of particles (Environment Agency, 2009b). In reality, soil loading on the skin is based on overlapping particles packed on top of one and other, especially if the soils are wet or fine grained (Spalt et al., 2009). Calculating exposure based on a fraction of the dose applied can underestimate the mass of a contaminant in soil absorbed by the body (Wester et al., 1996). For this reason, this paper and previous research by the current authors focuses on using flux as an estimate of the mass absorbed measured by *in vitro* dermal bioavailability experiments (Beriro et al., 2016, 2020; Williams-Clayson et al., 2024).

The absorption of exogenic substances into and through skin into systemic circulation takes place by dissolution and molecular diffusion processes controlled by a two-phase protein-lipid interaction (Michaels et al., 1975). The rate of diffusion through the skin described as flux by Fick's law was first proposed by Adolf Fick in 1855. Flux is proportional to surface area and concentration gradient, and inversely proportional to membrane thickness expressed over time (Equation (1)).

$$J = \frac{\Delta C}{\Delta T} A \quad (1)$$

Where Flux (J) is the penetration rate and calculated using Fick's First Law; ΔC is the change in concentration (concentration gradient), ΔT is the change in time and A is the surface area. Flux is typically expressed as the maximum concentration absorbed into the skin and systemic circulation over time, providing an estimate of the dermal bioavailability.

Dermal bioavailability studies require the use of skin or substitute membrane in experimental models, either *in vivo*, *ex vivo*, or *in vitro*. As stated, there are ethical considerations with the use of *in vivo* models due to the use of live animals in experiments. *Ex vivo* studies, usually based on cadaver skin, can create challenges around the repeatability of experimental data and are expensive technically demanding to replicate. *In vitro* models can use artificial skin to overcome these challenges and have been shown to produce data that are directly comparable to bioavailability measurements derived using human and animal skin (Beriro et al., 2016).

Research by Williams-Clayson et al. (2024) uses Strat-M® (EMD Millipore corp., Burlington, MA, USA), which is an artificial physiologically-based membrane that mimics the epidermis of the skin. Strat-M consists of one layer of polyethersulfone which contains artificial synthetic lipids, and one layer of polyolefin (Kunita et al., 2022). Studies comparing the chemical flux through Strat-M® and human skin (Haq et al., 2018) and pig skin (Simon et al., 2016) report strong *in vivo-in vitro* correlations, supporting its use as a skin substitute. Strat-M® has been used to estimate the *in vitro* dermal bioavailability of metals (Ghislain and Zagury, 2023; Villegas and Zagury, 2021, 2023), phthalates (Pan et al., 2014), and more recently, PAH (Williams-Clayson et al., 2024) in soils.

1.3. Human health risk assessment

The risk to human health from a contaminant in soil is represented by the ratio of exposure to the safe dose, referred to as the Health Criteria Value (HCV). Recognising and modelling differences between contaminant intake and uptake can reduce uncertainty in risk assessments.

"Intake is the amount of a substance ingested or inhaled by an individual ... expressed in terms of a mass of chemical per kilogram body weight per day (for example, mg kg⁻¹ bw day⁻¹)."

"Uptake is the amount of a substance that enters the body following absorption by the gastrointestinal and/or pulmonary systems, or through the skin."

(Environment Agency, 2009b)

The Environment Agency in England recognises that it can be challenging to measure uptake by the body directly resulting in limitations

over its use in risk assessments and the associated evaluation of dose response relationships in experimental or epidemiological studies of chemical toxicity (Environment Agency, 2009b).

In most cases oral and inhalation exposure is parameterised in risk assessment models as intake rather than uptake. Dermal exposure on the other hand is estimated as uptake. This necessitates generic assumptions in risk assessment because there is often very little or no information on chemical toxicity via skin absorption. The Environment Agency consider it more meaningful to use estimates of dermal uptake and comparing this with toxicological health based criteria which are based on intake from other exposure routes (Environment Agency, 2009b).

Average daily exposure, whether intake or uptake, is compared with an exposure representing no appreciable or minimal risk to human health for threshold and non-threshold behaviour respectively. The daily dose of a chemical demonstrating non-threshold carcinogenicity that can be experienced over a lifetime with minimal excess lifetime cancer risk is called the Index Dose (Environment Agency, 2009a).

Where the HCV, the index dose in the case of benzo[a]pyrene, is equal to exposure this represents a level of risk that requires no further consideration. It is this value, expressed as the chemical concentration in soil that is the assessment criterion used to compare to site-specific concentrations as part of a risk-based approach to land contamination risk assessment (Environment Agency, 2025).

The critical adverse human health effects that, as society, we are seeking to prevent are a series of cancers (International Agency for Research on Cancer, 1998). In the absence of a dermal specific health criterion value, dermal exposure is assessed by comparison with the oral health criterion value. When deriving generic assessment criteria for BaP for scenarios involving exposure by various pathways, combined exposure via oral and dermal pathways are compared against the oral HCV, in the case of the UK, it is the index dose that represents minimal risk to health (Nathanail et al., 2014).

1.4. Dermal bioavailability of PAH in soil

Some scientific progress in the advancement of science on the dermal bioavailability of PAH in soil has been made since historical systematic reviews (Beriro et al., 2016; Ruby et al., 2016). For this study, we conducted a rapid review of research published to bring these reviews up to date (Supporting Information). In summary, research on the dermal bioavailability of PAH we identified covered: human biomonitoring (Keir et al., 2023; Sousa et al., 2022; Wang et al., 2021); *in vivo* using mice (Alalaiwe et al., 2020); *in vitro* using porcine and/or human cadaver skin (Simon et al., 2023, 2024; Alalaiwe et al., 2020; Bourgart et al., 2019; Peckham et al., 2017; Xia et al., 2016; Haney et al., 2020; Forsberg et al., 2021; Probert et al., 2024); *in vitro* using artificial skin (Williams-Clayson et al., 2024); and *in vitro* using artificial sebum (Beriro et al., 2020; Luo et al., 2020); and consumer products (Bockers et al., 2016; Barrero-Moreno et al., 2018). Of these studies, five focused on PAH in soil (Williams-Clayson et al., 2024; Forsberg et al., 2021; Haney et al., 2020; Peckham et al., 2017; Xia et al., 2016). None of these studies used flux or similar measures of site specific dermal bioavailability to refine generic exposure assumptions in human health risk assessment. The novelty of our study is the application of dermal flux, measured and reported by Williams-Clayson et al., (2024), to refine generic dermal exposure assumptions in the CLEA framework, to demonstrating how this can be applied to risk assessment of chronic exposure to chemicals in soils.

1.5. Purpose of this study

The aim of our research is to use site-specific dermal flux recorded in artificial receptor solution (proxy for systemic circulation) and generic exposure settings for dermal absorption and compare these with the recommended HCV to estimate potential risk from benzo[a]pyrene in soil. We used Williams-Clayson et al. (2024) flux data in a worked

example of human health risk assessment using the Environment Agency's Contaminated Land Exposure Assessment (CLEA) framework (Environment Agency, 2009b). We discuss the result in the context of the latest literature on the dermal bioavailability of PAH in soil, building on earlier work published by the authors (Beriro et al., 2016, 2020; Williams-Clayson et al., 2023, 2024).

2. Materials and methods

2.1. Measurements of *in vitro* dermal bioavailability of PAH in soils

Williams-Clayson et al. (2024) flux values for benzo[a]pyrene in gasworks contaminated soils were applied to a worked example of human health risk assessment using the CLEA model. The Williams-Clayson et al. (2024) study measured dermal flux of twenty parent and seven alkylated high molecular weight (HMW) PAH at 1 h, 10 h and 24 h timesteps to both receptor solutions and the artificial membrane. The Williams-Clayson et al. (2024) experiment design was consistent with published international guidance on dermal absorption experiments and/or data (OECD, 2004; Kielhorn et al., 2006; Environment Agency, 2009b). Differences between the OECD method and the Clayson-Williams study included: application of a super monolayer of soil on the membrane to create an infinite dose of PAH; and use of the 24 h timestep to represent steady state flux.

Williams-Clayson et al. (2024) flux data for two gasworks soil samples and one reference material were summarised to show the variation of flux between samples for receptor solution and membrane matrices using samples E1.5, H16, and BCR-524 (Table 1). It is noted that membrane flux is much higher than receptor flux, however, our paper is focused on exposure parameters associated with the receptor solution. Our discussion picks up on the significance of the high membrane flux. Our soil samples come from sites with contrasting site use histories which influence the composition and physical form of the PAH and coal

Table 1
Benzo[a]pyrene membrane and receptor solution flux at 24 h.

Sample	Sample description	Soil concentration (mg/kg)	Membrane flux (ng/cm ² /h)	Receptor solution flux (ng/cm ² /h)
H16	Typical small sized town gasworks in the UK using lower temperature horizontal retorts. PAH present would be in the form of the by-product coal tar, and fragments of the bituminous coal feedstock, another source PAH.	150	8.98979 5.30400 0.76944	0.00237 0.00145 0.00157
E1.5	Former chemical works that processed tar from an adjacent gasworks which operated vertical retorts. PAH present likely to be based on pitch and possibly coal.	161	Not analysed	0.00700 0.00580 0.01393
BCR-524	BCR ®Certified Reference Material (milled industrial soil from a wood treatment facility in the U.S). PAH sources principally from creosote oil.	7	1.27242 0.45327 0.19329	0 0.00929 0

tar (Table 1). The remaining samples from the Williams-Clayson study included soils with lower concentrations of PAH and benzo[a]pyrene flux that were not consistently detected at concentrations above the laboratory limit of quantification. This is also true of the shorter time steps for all samples, which necessitated the selection of 24 h. The location of the sites where samples were taken were anonymized due to commercial sensitivities from ongoing remediation and development activities.

2.2. Human health risk assessment

Measured *in vitro* dermal flux was expressed as the mass of contaminant absorbed per unit area of skin per unit time (ng/cm²/h) in the receptor solution. The units were converted into the same units as the HCV, which is mass per unit bodyweight per unit time (mg/kg BW/day). All human health risk assessment parameters except for flux were generic values and were selected based on those published in Nathanail et al. (2014) and the Environment Agency (2009b). These sources include full parameterisation information including exposure durations for skin contact areas different age classes associated with a young female receptor.

The area of skin on a human body varies with age from birth to age sixteen. Exposure takes place indoors and outdoors where skin exposure is lower indoors than it is outdoors. Dermal flux was converted to total hourly exposure using the generic exposed skin areas indoors and outdoors for different ages used in the CLEA model (Environment Agency, 2009b) and reported in the supporting technical documentation (Environment Agency, 2009b).

Hourly exposure (mg/hour) was converted to daily exposure (mg/day) and finally corrected for annual days of exposure to give a daily dose per unit body mass expressed as the mass of contaminant per kilogram bodyweight per day (mg/kg BW/day).

The dermal exposure estimated by the flux was compared to the HCV. This is consistent with the current approach to contaminant human health risk assessment (Environment Agency, 2009b), albeit for only one exposure pathway as oral and inhalation pathways were not considered in this worked example.

The HCV used for this worked example was the Index Dose which represents a minimal level of risk for non-threshold effects of dermal exposure to benzo[a]pyrene. Substances can exhibit different toxicological behaviours by different routes of entry. In such cases it would be appropriate to derive pathway specific HCV but there is currently little or no dose-response information for dermal exposure. It is usual therefore to compare dermal exposures with the HCV for oral exposure.

It should be noted that for risk evaluation the significance of the ratio of exposure to HCV should reflect the specific in-country legal context under which the risk assessment is being carried out and an evaluation of the inherent uncertainties in both estimated exposure and HCV.

The current approach in the CLEA model for estimating average daily exposure through dermal contact with soils and dust indoors and outdoors involves multiplying uptake (mg/day) by exposure frequency (days/year) and exposure duration (years) and dividing by body weight (kg) and averaging time (days).

The CLEA model was used to derive generic assessment criteria and adopts a generic dermal absorption factor (ABSd) of 0.13 to determine the proportion of soil contamination that is absorbed through the skin system by a typical soil exposure event. The use of ABSd is chosen on a contaminant-by-contaminant basis, based on a review of scientific literature. The USEPA (United States Environmental Protection Agency, 2024) recommends an ABSd value for only a limited number of substances based on a review of experimental data. This reflects a wider paucity of data for many organic and inorganic chemicals. In the absence of a literature value, the CLEA model uses a generic default ABSd value of 0.13 for all organic chemicals and of zero for inorganic chemicals. This approach is broadly consistent with the USEPA view, although it applies to both volatile and semi-volatile compounds (United

States Environmental Protection Agency, 2024).

The approach to estimating human dermal exposure to contaminants in soil using the ABSd does not explicitly use contact time. However, contact time is clearly important in establishing the ABSd according to the reported experimental conditions. Ideally, there should be close agreement between the contact time used in the exposure assessment scenario and in the experimental work. If good time-dependent data are available, the ABSd value for a contact time of 12 h is chosen as the default for that chemical. For our study, the most reliable time-dependent flux data was 24 h.

The CLEA model considers several standard exposure scenarios that include dermal exposure indoors and outdoors. The most sensitive land use is the residential with consumption of home grown produce (plant uptake) with the critical receptor being a female child in her first six years of life. The relative contribution of different exposure pathways to exposure to benzo[a]pyrene shows that most exposure (57 %) is from direct soil ingestion followed by outdoor dermal (36 %), consumption of home grown produce (5 %), dermal indoors (1 %) and inhalation of indoor dust (0.2 %) (CLAIRE, 2013; Nathanail et al., 2014).

Generic assessment criteria for residential land use with plant uptake (growing and eating vegetables) have been published for use in human health risk assessment; the Suitable for Use Level (S4UL) is 3.0 mg/kg (Nathanail et al., 2014) and the Category 4 Screening Level (C4SL) is 5.0 mg/kg (CLAIRE, 2013).

3. Results

The highest 24 h benzo[a]pyrene dermal flux for sample H16 (Table 1) was applied to a bespoke human health risk assessment calculator created using the CLEA algorithms (Environment Agency, 2009b). The assessment was used to estimate risks to human health from systemic effects of dermal exposure to benzo[a]pyrene.

Dermal exposure to benzo[a]pyrene for a residential land use was compared against the Index Dose HCV published by the Environment Agency (Environment Agency, 2009b) and used to derive the S4UL (Nathanail et al., 2014).

CLEA was used to derive a generic assessment criterion (GAC) for dermal exposure only. We ignored all pathways other than dermal (indoor and outdoor), resulting in a benzo[a]pyrene GAC of 47 mg/kg. This GAC is equal to the soil concentration that results in exposure equal to 100 % of the HCV and was calculated using CLEA's default dermal absorption factor (0.13) (Table 3).

When we used the highest Williams-Clayson site-specific flux for sample H16 (0.00237 ng/cm²/hour) (Table 1), uptake was calculated to be 23.7 ng benzo[a]pyrene/m² skin/hour, resulting in an ADE ranging from 20.7 to 37.3 ng benzo[a]pyrene/kg bw/day for the first six years

Table 2
Exposure parameters used to calculate the contribution of flux to the index dose.

Age class	BW	Time	Exposed skin area	Flux	ADE	Risk
		Indoors/ garden	Indoor/ outdoor	Indoor/ outdoor		(ADE/ ID)
	kg	Hours per day	m2	mg/day	mg/kg BW/day	
1	5.6	23/1	0.037/0.03	2.0E-05/ 7.1E-07	3.7E-06	1.2E-01
2	9.8	23/1	0.053/0.042	2.9E-05/ 1.0E-06	3.0E-06	9.8E-02
3	12.7	23/1	0.061/0.048	3.3E-05/ 1.1E-06	2.7E-06	8.7E-02
4	15.1	23/1	0.076/0.061	4.1E-05/ 1.4E-06	2.8E-06	9.2E-02
5	16.9	19/1	0.083/0.066	3.7E-05/ 1.6E-06	2.3E-06	7.4E-02
6	19.7	19/1	0.087/0.068	3.9E-05/ 1.6E-06	2.1E-06	6.7E-02
Average						5.4E-01

Notes: BW body weight; ADE average daily exposure; ID index dose.

Table 3

Assessment criteria for dermal uptake pathways using CLEA (SR3) algorithms and estimates based on default ABSd and flux based.

Soil	Soil concentration (mg/kg)	Dermal uptake value	Contribution to the Index dose (%)
Generic assessment criteria	47	ABSd = 0.13	100 %
Sample H16 (Table 1)	150	Flux = 0.00237 ng/cm ² /hour	54 %
Dermal only site-specific assessment criteria	278.4	Flux = 0.00237 ng/cm ² /hour	100 %

(age classes 1 to 6) of a female child's life (Table 2). The daily flux through the skin reflects the different areas of exposed skin indoor and outdoor. The average daily exposure (ADE) is calculated by CLEA.

Table 2 shows that for the first six years of life of a female a flux of 0.0023 ng/cm²/hour measured from soil containing 150 mg/kg benzo[a]pyrene the average ratio of ADE to the Index Dose HCV is 0.54. A soil concentration of 278.4 mg/kg is equivalent to a ratio of ADE to Index Dose of one.

In contrast to the default dermal absorption factor, our peak steady state flux value of 0.00237 ng/cm²/hour resulted in a site-specific assessment criterion for dermal only exposure of 278.4 mg/kg (Table 3). This demonstrates that the refinement offered by the flux-based test would help derive a site-specific assessment criterion for sample H16 of over five times higher than the dermal only GAC. If only 5 % of the HCV is assigned to dermal exposure, the SSAC included all pathways would be 13.9 mg/kg, as opposed to the lower GAC.

We tested the sensitivity of the CLEA model to uptake measured by flux, rather than a proportion of total concentration (ABSd). The test showed that a flux of 0.0237 ng/cm²/hour (10 times higher than the measure value) would result in an exposure of 540 % of the Index Dose whilst a flux of 0.000237 ng/cm²/hour (10 times lower than the measured value) would result in an exposure of 5.4 % of the Index Dose. This demonstrates that CLEA presents a linear relationship between the estimated flux and the predicted average daily exposure through dermal contact. This important because where the relationship between PAH flux and soil concentration is non-linear or stochastic it is likely to be due to complex PAH-soil matrix relationships which are attributable to PAH and soil properties.

4. Discussion

The UK default approach to taking account of dermal exposure in human health risk assessment is that 13 % of the contaminant in soil in contact with skin will form the effective uptake (CLAIRE, 2013; Nathanail et al., 2014). We have shown in the current research that calculating a site-specific assessment criterion using flux data for the dermal exposure routes only would present a lower risk than using a generic dermal absorption factor. The results in assessment criteria higher than published UK-based GAC for a residential land use with plant uptake where the critical receptor is a female in the first six years of life (CLAIRE, 2013; Nathanail et al., 2014). Similar findings from other studies also report that using site or sample specific ABSd from *in vitro* diffusion bioavailability tests result in increased human health assessment criteria in comparison to using an ABSd of 0.13 (Forsberg et al., 2021; Haney et al., 2020). However, questions remain regarding whether generic or sample specific approaches provide a more reasonable, pragmatic and protective approach to informed detailed quantitative human health risk assessment. This is perhaps in part because other studies using human biomonitoring in occupational exposure from firefighting, recognise the large contribution made by other pathways to

measured internal dose (Keir et al., 2023).

Even though for most contaminants the concentration in body tissue is very low following exposure, the rate of dermal absorption is suggested as broadly proportional to the soil concentrations (Hoang, 1992; Paustenbach, 2000). This is reflected by the CLEA model which represents the soil concentration and dermal daily exposure as linear. In reality, the relationship between soil concentration and uptake is more complex and related to molecular and soil properties. For example, previous work illustrates that dermal flux for pyrene appears correlated to soil pyrene concentrations (Williams-Clayson et al., 2024). Conversely, in the same study the relationship between flux and soil concentration for higher molecular weight PAH was shown to be weak.

The cause of potential non-linear or stochastic relationships between dermal flux and soil PAH concentrations is most likely due to PAH and/or soil properties. Simon et al. (2024) showed that molecule size influences absorption, where larger parent PAH (molecular mass >252 g/mol) failed to penetrate human or porcine skin *in vitro* after 48 h. Other studies have reported where alkylated PAH (Williams-Clayson et al., 2024) and larger parent PAH (Probert et al., 2024; Williams-Clayson et al., 2024) showed reduced absorption. Peckham et al. (2017) suggested the transfer to the receptor fluid was not controlled by soil PAH concentrations but instead by their fugacity. They hypothesised that there is a sorption capacity limit for benzo[a]pyrene in soils where in many cases the soil may become saturated at relatively low concentrations that present potentially unacceptable human health risks. This may be compounded by complex PAH mixtures such as contaminated gasworks soils but could be investigated by adapting experimental methods. For example, an infinite sink (e.g. tenax sorbent) could be used to overcome potential diffusion limiting processes and used to evaluate whether fast and slow desorption processes are operating (Posada-Baquero et al., 2022). Fugacity and process modelling could help understanding partitioning along with PAH fate and transport in complex media.

The worked example in this current research used receptor solution flux to compare to an Index Dose based on an oral systematic HCV rather than localised toxicological data. The original Williams-Clayson study showed that membrane flux was much higher than receptor solution flux (Table 1), suggesting that receptor solution flux could be underestimating daily exposure. This is important because some studies have identified PAH as skin carcinogens which meaning that the presence of PAH remaining in the membrane presents health risks (Kennaway, 1955; Siddens et al., 2012; Cavalieri and Rogan, 2014). More recently, Alalaiwe et al. (2020) showed that PAH caused cutaneous inflammation in the skin, with benzo[a]pyrene disrupting skin barriers and causing inflammation. Localised exposure could be compounded by the skin acting as both a sink and source for contaminants. Forsberg et al. (2021) showed continued diffusion of benzo[a]pyrene through skin after soil removal.

Metabolism of PAH while in skin also has the potential to affect exposure. Sousa et al. (2022) highlighted that the stratum corneum represented a key barrier to effective uptake, with epidermal cells metabolising PAHs into hydrosoluble compounds via cytochrome P450. Metabolism of PAH in skin, assuming non-toxic derivatives, may contribute to conservatism in using measured flux. However, Bourgart et al. (2019) reported PAH metabolites (3-hydroxybenzo[a]pyrene (3-OHB[a]P) and 7,8,9,10-tetrahydroxy-7,8,9,10-tetrahydrobenzo[a]pyrene) in the receptor solution of their *ex vivo* human skin diffusion cell experiment.

Xia et al. (2016) highlighted that the industrial process that originally created the PAH contamination mixture can affect solubility and dermal absorption. Their study, and another by Peckham et al. (2017), created their own soils using radiolabelled ¹⁴C-benzo[a]pyrene or PAH from different sources rather than real-world soils. Artificial soils are not considered as representative of natural conditions as real-world soils such as those used by others so findings may not be directly applicable (Forsberg et al., 2021; Haney et al., 2020). Given the different forms of

PAH in the three samples we report here, this is likely to impact the dissolution of PAH from creosote (BCR-524), pitch fragments (E1.5) and crude tar (H16) and hence their dermal bioavailability. This is supported by our evaluation of receptor solution flux data for these three samples. We see that for H16 and E1.5 where benzo[a]pyrene is at similar concentrations (~ 155 mg/kg) maximum flux for H16 ($0.0024 \mu\text{g}/\text{cm}^2/\text{h}$) is lower than E1.5 ($0.139 \mu\text{g}/\text{cm}^2/\text{h}$). Receptor solution flux for BCR-524 (0.0093) is similar to H16 driven by a much lower benzo[a]pyrene concentrations (6 mg/kg).

Our study reports several important findings and raises a range of questions about broader applicability of the results to risk assessment. However, one practical point to consider in relation to the wider use of *in vitro* testing is the financial and technical viability of these methods for commercial laboratories. Some factors that should be considered in future studies include: minimum batch size, selection and use of a suitable certified reference material, minimum quality control requirements, costs per sample, availability and pre-treatment of materials, timescales to deliver flux data, flux timesteps measures, compliance with dermal absorption protocols, and the replicability of test results between laboratories.

Bioavailability testing is not only important for common legacy soil pollution such as PAH but also for emerging contaminants such as pharmaceuticals, pesticides, fluorinated substances such as per- or poly-fluorinated substances (PFAS) and microplastics (Bolan et al., 2021). Modern industrialised society, being by far the main contributor to soil contamination, hold the responsibility to understand the intake and uptake of a wide range of hazardous compounds in soils, so that risks can be better estimated and managed. Measuring site-specific bioavailability testing, irrespective of the contaminant investigated, provides a more realistic estimate of daily exposure and associated risk in comparison to using total concentrations present in soils.

4.1. Limitations of the research

One limitation of this study is that it focussed on the types of PAH associated with coal carbonisation at a gasworks or a site handling coal tar produced at a gasworks. The samples described in Table 1, provide a good representation of the type of PAH contamination found on former British gasworks. They do not cover high temperature horizontal retorts, coking ovens, chamber ovens, carburetted water gas plants or oil gas plants, which could be studied in future. Sample BCR-524, was taken from a former wood treatment site in the USA and would contain a specific fraction of coal tar called creosote oil likely obtained from a gasworks.

We recognise that the data we have used to model human health risks is based on a single measurement, and while this satisfies the research aim it does not reflect the lines of evidence needed for regulatory acceptance. This is arguably mainly due to limited sample numbers and time points (which we have highlighted were less than the limit of quantification). In addition, these samples would not necessarily be representative of PAH derived from vehicle emissions, wood burning or forest fires, industrial combustion plants, oil refineries or other non-gasworks sources.

The risk estimation scenarios reflect UK policy and as such estimates would need to be produced using locally compliant approaches. However, the principles demonstrated here are equally relevant across other jurisdictions and using risk assessment tools other than CLEA that also consider dermal exposure.

In common with the approach used for selecting site specific estimates of contaminant bioavailability for other exposure pathways, a precautionary value from the set available was selected. Site specific data would need to be collected for use in site specific quantitative risk assessments.

4.2. Recommendations for further work

Our study has identified a number of areas of which would benefit from further research and development. These areas include.

- Measurement of dermal flux for a larger range of soil types and contamination sources including other types of gas making process and non-gasworks sources such as those highlighted in the Limitations section.
- Investigation of the causes of the non-linear relationships between original concentration and flux for PAH, including the role of fast and slow sorption and the implications on risk assessment (Posada-Baquerio et al., 2022).
- Evaluate the significance of membrane flux being higher than receptor solution flux (Table 1). This would involve systematically reviewing toxicological data and associated health end points and comparing these to membrane flux.
- Process modelling of flux to understand the kinetics (mechanisms and rates over time) of permeation through the membrane to the receptor solution, which would help to understand the impact of exposure times and durations on health risks.
- Investigate the relevance of this research on other exposure scenarios including relevant acute exposure situations.
- Demonstrate the application of dermal flux-based estimates of dermal bioavailability in various legal contexts – such as land use planning to demonstrate sites are safe for their future use or environmental protection to demonstrate sites pose an unacceptably high risk (Nathanail et al., 2014).

Our study demonstrates how to use dermal flux in estimates of risk to human health from dermal exposure. The dermal only assessment criteria could be combined with oral and inhalation exposure to benzo[a]pyrene to inform an overall estimate of risks from chronic exposure to benzo[a]pyrene in soil. This approach to risk assessment is the same as that envisaged by national guidance such as the UK's land contamination risk management (Environment Agency, 2025).

5. Conclusions

Measurements of benzo[a]pyrene *in vitro* dermal flux reported by Williams-Clayson et al. (2024) across an artificial membrane were used as surrogates of effective dermal exposure uptake. Dermal flux was used to calculate average daily exposure that was compared against a health based criteria value (Index Dose) using a bespoke risk calculator based on CLEA algorithms.

Our research findings have implications for the adoption of dermal flux and similar bioavailability tests by laboratories as part of risk-based land management and associated regulatory framework. Our work demonstrates proof-of-concept for research on the bioavailability and role of such tests in risk assessment and risk management of a wider range of chemicals in soil, including emerging contaminants such as per- and polyfluoroalkyl substances and microplastics. This supports an evidence-based shift toward sample and site specific parameters in regulatory risk assessment frameworks, however, the scalability, inter-laboratory reproducibility, and cost-effectiveness of *in vitro* flux testing need greater emphasis before broader regulatory adoption.

CRediT authorship contribution statement

Darren Beriro: Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Paul Nathanail:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Russell Thomas:** Writing – review & editing, Writing – original draft, Supervision, Funding acquisition, Conceptualization. **Tatiana Cocerva:** Writing – review & editing, Writing – original

draft, Investigation, Formal analysis. **Christopher Taylor:** Writing – review & editing, Supervision, Project administration, Funding acquisition. **Joanna Wragg:** Writing – review & editing, Supervision, Conceptualization. **Jack Lort:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Alison Williams-Clayson:** Writing – review & editing, Investigation, Formal analysis, Data curation, Conceptualization. **Christopher Vane:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2025.123176>.

Data availability

Data will be made available on request.

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