IMPROVING RISK ASSESSMENT OF CONTAMINATED SOIL FROM IQUALIT, NUNAVUT

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By

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Keywords: risk assessment, soil contamination, airborne particulate matter, *in vitro* bioaccessibility

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ABSTRACT

Risk assessment guidelines utilize conservative values when estimating the exposure to humans from contaminated soil. The conservative guidelines include a default bioavailability of 100% and it is assumed that soil inhalation exposure is insignificant compared to the combined exposure from ingestion and dermal absorption. Due to the conservative guidelines, Site Specific Risk Assessments often attempt to determine the relative bioavailability of contaminants, however due to the high cost of *in vivo* models, *in vitro* models for polycyclic aromatic hydrocarbon (PAH) bioaccessibility are being developed. One such development for *in vitro* models is the addition of a lipophilic phase which acts as a sink for organic contaminants such as PAHs. The primary objective of this research project is to determine if exposure to contaminants in soil presents excessive risk to human health specifically to the residents of Iqaluit. I hypothesize that exposure from soil inhalation is a relevant exposure pathway for human health. Furthermore, I hypothesize that *in-vitro* PAH bioaccessibility models require a lipid sink to accurately represent *in-vivo* bioavailability of PAHs.

In this thesis, soil inhalation was a relevant exposure pathway for both carcinogenic and non-carcinogenic risk for residents in Iqaluit, NU. Using enrichment factors it was found that the soil was the primary source for many airborne contaminants. Vehicle traffic on unpaved roads led to a large amount of soil re-suspended into the atmosphere, leading to an airborne particulate matter with an aerodynamic diameter less than 10 μm (PM_{10}) average concentration of 35 ± 17 μg m^{-3}. Once roads were paved the average PM_{10} concentration was significantly ($p < 0.05$) reduced to 6.5 ± 6 μg m^{-3} and as a result both carcinogenic and non-carcinogenic risk from soil inhalation was reduced. The results demonstrate that soil inhalation is likely a relevant exposure pathway under particular environmental conditions and that paving roads is an effective method of reducing this risk.

To better characterize the correlation between *in* vivo bioavailability and *in vitro* bioaccessibility models a case study using eight PAH contaminated soils is performed to determine if the addition of a lipid sink improves this correlation. The addition of a lipid sink significantly increases PAH release for *in vitro* models ($P < 0.05$). In the presence of a lipid sink, results of the *In Vitro* Digestion model (IVD) closely corresponded with a slope of 0.85 ($r^2=0.45$, $P<0.07$) to the *in vivo* results, whereas there was no correspondence in the absence of a lipid sink ($r^2 = 0.03$). The results from the other *in vitro* digestion model, the Relative Bioaccessibility Leaching Procedure (RBALP), did not correspond to the *in vivo* results, with or without the addition of lipid sink, but did tightly reflect total soil PAH concentration. The *in vivo* release and uptake of PAHs is correlated to fugacity capacity, indicating that PAH release and uptake is a function of both matrix and PAH properties.

Environmental conditions play a major role in risk assessment, hence the importance of site specific risk assessments. In Iqaluit, vehicle traffic on unpaved roads is the major source of airborne particulate matter and as a result the soil inhalation pathway is relevant in terms of risk assessment. The correlation between *in vivo* PAH uptake and release to soil fugacity capacity demonstrates environmental conditions, such as soil properties, influencing bioavailability and subsequently risk assessment.

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LIST OF ABBREVIATIONS

ADAF	Age Dependent Adjustment Factor
AF_{GIT}	Gastrointestinal Tract Absorption Factor
AF_{Inh}	Inhalation Absorption factor
Ag	Silver
Al	Aluminum
As	Arsenic
ASE	Accelerated Solvent Extraction
Ba	Barium
BaP	Benzo(a)pyrene
BaP Eq	Benzo(a)pyrene Equivalents
BbF	Benzo(b)fluoranthene
Be	Beryllium
BkF	Benzo(k)fluoranthene
BW	Body weight
Caco-2	Human Colorectal Carcinoma Cell Line
CCME	Canadian Council of Ministers of the Environment
Cd	Cadmium
Co	Cobalt
Cr	Chromium
CRM	Certified Reference Material
CSF	Cancer Slope Factor
Cu	Copper
EDI	Estimated Daily Intake

EF	Enrichment Factor
EVA	Ethylene Vinyl Acetate
Fe	Iron
FOREhST	Fed ORganic Estimation human Simulation Test
GI	Gastro-intestinal
GW	Gas Works
Hg	Mercury
HPLC-FD	High Pressure Liquid Chromatography coupled Fluorescence Detection
HHRA	Human Health Risk Assessment
HQ	Hazard Quotient
IcdP	Indeno(1,2,3-cd)pyrene
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IVBA	*In vitro* bioaccessibility
IVD	*In vitro* digestor
LBR	Lower Base Region
LE	Life expectancy
Mg	Magnesium
Mn	Manganese
Mo	Molybdenum
Nap	Naphthalene
Ni	Nickel
NIST	National Institute of Sciences and Technology
OSU-IVG	Ohio State University In-Vitro Gastrointestinal

PAH	Polycyclic Aromatic Hydrocarbon
Pb	Lead
PBET	Physiological Based Extraction Test
PHC	Petroleum Hydrocarbon Contaminated
PM_{10}	Particulate Matter with an aerodynamic diameter < 10 µm
$PM_{2.5}$	Particulate Matter with an aerodynamic diameter < 2.5 µm
PQRA	Preliminary Quantitative Risk Assessment
RBALP	Relative Bioavailability Leaching Procedure
Sb	Antimony
SBET	Simple Based Extraction Test
Se	Selenium
SHIME	Simulator of the Human Intestinal Microbial Ecosystem
Sn	Tin
Sr	Strontium
SSRA	Site Specific Risk Assessment
TDI	Tolerable Daily Intake
Ti	Titanium
Tl	Thallium
TSP	Total Suspended Particulates
U	Uranium
V	Vanadium
WP	Wood Preservation
Zn	Zinc

Z_{soil}	Fugacity Capacity of Soil
Z_{water}	Fugacity Capacity of Water

1 INTRODUCTION

Human health risk assessments (HHRA) are often performed to identify situations where potential adverse effects to human health may occur due to exposure to environmental contaminants. Exposure to environmental contaminants can occur through media such as soil and standardized equations have been developed with the purpose of estimating the daily intake of hazardous contaminants through a specific medium. These exposure estimates are further differentiated based on the three main human exposure pathways of inhalation, ingestion, and dermal absorption. Frequently in risk assessment the inhalation pathway is ignored as the inhalation pathway is generally considered to be insignificant relative to the ingestion and dermal absorption pathways; however the inhalation pathway can be calculated if deemed appropriate. The early stage in a tiered HHRA is known as Preliminary Quantitative Risk Assessment (PQRA) and during a PQRA the most conservative estimates are utilized to evaluate exposure. If the PQRA gives any indication of excessive human health risk additional research may be conducted to better characterize the site and potential toxicity; this is known as Site Specific Risk Assessment (SSRA). Bioavailability is one of the key concepts in HHRA and in a PQRA the default assumption is that 100% of the contaminant is bioavailable; whereas SSRA involves intensive research to obtain the relative bioavailability of contaminants in a specific medium which leads to more realistic exposure estimates.

1.1 Objectives and Hypotheses

The primary objective of this thesis is to determine if there is any excessive risk to human health from exposure to trace metals and polycyclic aromatic hydrocarbons (PAHs) in soil in Iqaluit, NU. The secondary objective is to examine methods to improve key concepts in risk assessment. During investigation of the stated objectives there are three hypotheses investigated: (1) exposure from soil inhalation is a relevant exposure pathway for human health, (2) paving

roads decreases the human health risk from soil inhalation and (3) *in-vitro* PAH bioaccessibility models require a lipid sink to accurately represent *in-vivo* bioavailability of PAHs.

For the first hypothesis, a human health risk assessment is performed for both soil ingestion and inhalation for both carcinogenic and non-carcinogenic risk and is evaluated and presented in Chapter 3 (Comparison of Human Exposure Pathways in an Urban Brownfield: reduced Risk from Paving Roads). The second hypothesis, the effect of paving roads and the subsequent effect of risk is also presented in Chapter 3. Lastly the third hypothesis is presented in Chapter 4 (Human Exposure Assessment: A Case Study of 8 PAH Contaminated Soils Using *in Vitro* Digestors and the Juvenile Swine Model), where *in-vivo* PAH release is compared against two *in-vitro* models with and without the addition of a lipid sink. The final chapter discusses future directions and implications associated with the current findings.

2 LITERATURE REVIEW

2.1 Human Health Risk Assessment

In Canada, in order to establish consistency among results human health risk assessments are performed utilizing standardized guidelines (Health Canada 2004a). These guidelines help create uniformity between sites and allow risk assessors or risk managers to prioritize between sites when allocating resources. Due to the fact that resources are limited, it is very important to have an accurate risk assessments performed at each specific site to maximize the efficiency of resources. Indeed, Gupta et al. (1996) acknowledges that when there are multiple sites that present the same relative risk, the United States Environmental Protection Agency (US EPA) will remediate the site with the lowest relative cost. The PQRA has the default assumption that 100% of a contaminant is bioaccessible and this is assumption can potentially lead to overestimating the human health risk (Richardson et al. 2006). For assessing the risk from soil inhalation the default assumption for the inhalable airborne concentration is 0.76 µg m^{-3} for paved roads or 250 µg m^{-3} for unpaved roads, a 330% difference (Health Canada 2004a). Obtaining accurate risk assessment information helps organizations, municipalities, and individuals alike to make an efficient use of both time and resources for the betterment of human health.

Risk can be viewed as a function of three components: 1) receptor – e.g., humans, 2) exposure – e.g., ingestion of soil and 3) toxicity –e.g., presence of hazardous compounds within exposure medium. Remove any of these components and risk is eliminated (Figure 2.1).

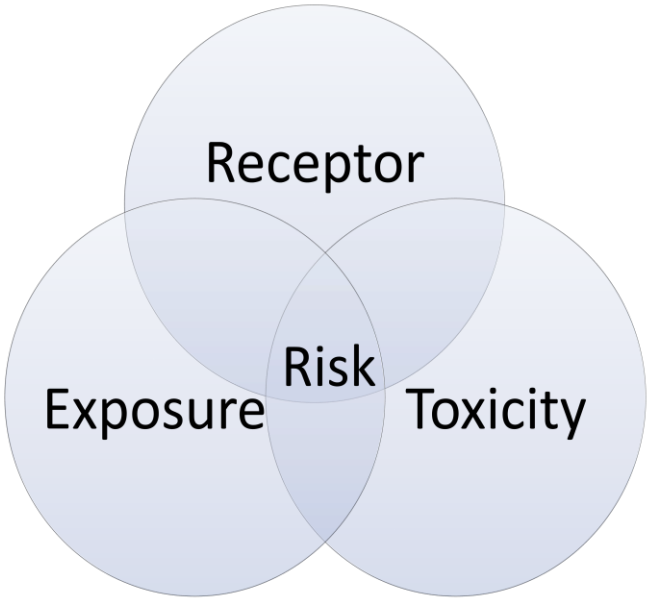

Figure 2.1 Venn diagram illustrating that risk is a function of receptor, exposure and toxicity.

2.1.1 Receptor

In HHRA, the receptor is clearly defined – humans; however there are subclasses within humans and they are represented in **Table 2.1** along with their respective physical and behavioral characteristics. When conducting risk assessments it is essential to determine the most sensitive receptor with the idea being that if the most sensitive receptor is protected then the entire population will be protected (Health Canada 1994). The setting in which a receptor is exposed is an important factor; for example construction workers have their exposure limited to the time they spend on site, whereas residents who live and work in a contaminated area are subjected to constant exposure.

Table 2.1 Health Canada recommended receptors and receptor characteristics for human health risk assessment. Table has been modified from Richardson (1997).

Receptor Characteristic	Infant	Toddler	Child	Teen	Adult	Construction Worker
Age	0 – 6 months	7 months – 4 years	5 – 11 years	12 – 19 years	≥20 years	≥20 years
Body Weight (kg)	8.2	16.5	32.9	59.7	70.7	70.7
Inhalation Rate (m^3 d^{-1})	2.1	9.3	14.5	15.8	15.8	15.8
Inhalation Rate (m^3 h^{-1})	0.088	0.388	0.604	0.658	0.658	0.658
Soil Ingestion Rate (g d^{-1})	0.02	0.08	0.02	0.02	0.02	0.1
Time spent Indoors (h d^{-1})	22.5	22.5	22.5	22.5	22.5	16
Time Spent Outdoors (h d^{-1})	1.5	1.5	1.5	1.5	1.5	8

2.1.2 Exposure

The exposure component of risk assessment simply accounts for the type of exposure from exposure media (air, water, and soil) and the exposure pathway (ingestion, inhalation and dermal absorption). Reducing risk from the exposure component for fugitive dust emissions involves engineering controls such as street sweeping, wet suppression, paving and vegetative stabilization (Watson and Chow 2000).

2.1.3 Toxicity

Toxicity is the third and final component in the risk paradigm. Currently when viewed in terms of risk assessment, toxicity is separated out as either a carcinogenic or non-carcinogenic response. Risk can be reduced through various methods of remediation, in which hazardous contaminants are removed from the exposure medium (Cunningham and Berti 1993; Mulligan et al. 2001)

2.1.3.1 Non-Carcinogenic Risk

For compounds that do not have a carcinogenic mechanism of action, toxicity occurs when exposure exceeds a threshold (Health Canada 1994). For non-carcinogenic risk, hazard quotients (HQ) are used to determine the risk and according to Health Canada (2004a) are calculated as follows:

$$\mathrm{HQ} = EDI \div TDI \qquad \text{(Eqn. 2.1)}$$

Where EDI = estimated daily intake (mg $kg^{-1}d^{-1}$), TDI = tolerable daily intake (mg $kg^{-1}d^{-1}$), and HQ = hazard quotient (unitless). In Canada exposures coupled with a $HQ \leq 0.2$ are deemed negligible if background exposure is not included; however if background exposure is included $HQ \leq 1$ are acceptable (Health Canada 2004a).

2.1.3.2 Carcinogenic Risk

Carcinogenic compounds display non-threshold kinetics. To account for the carcinogenic mechanism of action risk is presented as a probability (i.e. 1 in 1,000,000) and according to Health Canada (2004a) is calculated as:

$$\mathrm{Risk} = EDI \times CSF \qquad \text{(Eqn 2.2)}$$

Where EDI = estimated daily intake (mg $kg^{-1}d^{-1}$), CSF = cancer slope factor (mg $kg^{-1}d^{-1})^{-1}$ and risk = probably of developing cancer over a lifetime. Due to the fact that carcinogenic risk cannot be eliminated, risk assessors view it in terms of acceptable risk and in Canada the current acceptable incremental lifetime carcinogenic risk is 1 in 100,000 (Health Canada 2004a). In early life stages it is likely that humans are more sensitive to carcinogens and therefore, age dependent adjustment factors (ADAFs) have been developed by the US EPA. There is an adjustment factor of 10 for the first 2 years of life and an adjustment factor of 3 for ages between 2 and 16 years (US EPA 2005). Using ADAFs and relative life expectancy from each stage of life, carcinogenic risk is modified to reflect lifetime probability of developing cancer.

2.2 Soil Exposure

For HHRA exposure to soil is an important exposure pathway as anthropogenic activities over recent years have been increasing the concentration of hazardous contaminants in soil (Menzie et al. 1992; Nriagu and Pacyna 1988). Soil quality has been declining despite the research linking soil quality and human quality of life (Abrahams 2002; Kibblewhite et al. 2008; Oliver 1997). Humans are exposed to soil through the three primary pathways: ingestion, inhalation and dermal absorption. Inadvertent soil ingestion occurs via soil particles adhering to hands and subsequent hand-to-mouth activity resulting in the ingestion of soil particles. While the majority of individuals do not intentionally ingest soil, there is a childhood disorder known as pica in which toddlers ingest up to 60 grams of soil per day (Calabrese et al. 1999). Inhalation of soil particles leads to both inhalation and ingestion exposure. Soil particles with an aerodynamic diameter larger than 10 µm do not reach the lower respiratory tract and are removed by muco-ciliary action and ingested, whereas soil particles less than 10 µm in diameter are considered an inhalation hazard as they penetrate deep into the lungs (Bright et al. 2006).

Ingestion of soil particles is generally considered the major route of soil exposure (Bright et al. 2006), while inhalation of soil particles is often not quantified, as soil ingestion generally results in exposures one to two orders of magnitude greater. Conversely, Health Canada (2004b) and US EPA (2011) have both ingestion and inhalation TDIs and/or CSFs for many contaminants, and regularly the inhalation pathway has a TDI that is lower and a CSF that is greater than the corresponding ingestion pathway. Although the exposure may be less from the inhalation pathway, the risk may be relatively similar. Therefore, there appears to be a research gap to identify conditions that make soil inhalation relevant to risk assessment.

2.2.1 Soil Re-suspension

Before soil particles can be inhaled they need to be re-suspended into the atmosphere and both natural and anthropogenic processes facilitate soil re-suspension. Re-suspension of soil is primarily caused by vehicular traffic, wind-erosion, and physical disturbances by heavy equipment or agricultural practices (Bright et al. 2006). Most notably, vehicular traffic on unpaved roads is thought to be the major source of re-suspended soil (Watson and Chow 2000). Wind erosion in areas with low soil moisture content, minimal vegetative cover, high wind velocity, and long stretches of unprotected soil leads to the re-suspension of soil making a significant contribution to the total concentration of airborne particulate matter (Woodruff and Siddoway 1965). For example, Dillner et al. (2006) reported that soil particles comprised over 98% of the total suspended particulate (TSP) mass during dust storms, whereas Chow et al. (1992) reported that 30-62% of the annual average particulate matter was attributed to soil particles.

2.2.2 Exposure Estimates

Humans are exposed to contaminants in soil via ingestion, inhalation, and dermal absorption. Soil ingestion (2.3) and soil inhalation (2.4) exposure algorithms are shown below and are calculated as follows according to Health Canada (2004a):

$$\text{Dose}\,(\text{mg kg}^{-1}d^{-1}) = \frac{C_S \times IR_S \times AF_{GIT} \times D_1 \times D_2 \times D_3}{BW \times LE} \qquad \text{(Eqn 2.3)}$$

$$\text{Dose}\,(\text{mg kg}^{-1}d^{-1}) = \frac{C_S \times P_{Air} \times IR_A \times AF_{Inh} \times D_1 \times D_2 \times D_3 \times D_4}{BW \times LE} \qquad \text{(Eqn 2.4)}$$

Where C_S (mg kg^{-1}) represents contaminant concentration in soil ingested or inhaled. IR_S (kg d^{-1}) and IR_A (m^3 h^{-1}) are the soil ingestion and air inhalation rates, respectively. AF_{GIT} and AF_{Inh} (unitless) are the respective relative absorption from the GI tract and inhalation pathway. P_{Air} (kg

m^{-3}) is the particulate concentration in air. BW (kg) is the body weight and LE is the life expectancy of the receptor. D_1, D_2, D_3, and D_4 are exposure duration modifiers that account for the fraction of time that the receptor is actually exposed, and are in units of days per week, weeks per year, and years per lifetime. An additional duration modifier for inhalation exposure is used to account for hours per day exposed. Exposure to dermal absorption is not shown as there is minimal relevance to research presented below.

The exposure estimates presented offer a degree of plasticity that accompanies the transition from PQRA to SSRA. This plasticity is particularly useful when assessing soil inhalation exposure for a few reasons. Generally it is thought that the soil inhalation pathway is insignificant relative to ingestion and dermal absorption; however soil inhalation should be calculated if the assessor believes it is applicable (Health Canada 2004a). The typical PQRA assumption for P_{Air} is 0.76 µg m^{-3}(based on US EPA 1992) and if vehicular traffic on unpaved roads is a concern the assumption is 250 µg m^{-3} (based on Clairborn et al. 1995). A SSRA allows the use of airborne particulate matter samplers that provide accurate descriptions of site airborne particulate matter concentration. The default assumption for C_S is to use either the average or maximum contaminant concentration in soil, however other values may be used providing that adequate references are supplied and they indicate a more appropriate exposure value. For example, Siciliano et al. (2009) found that there is a higher concentration of contaminants in the < 45 µm size fraction of soil. Furthermore, smaller size fractions of soil are more prone to be re-suspended opposed to bulk soil (Clairborn et al. 1995; Chow et al. 1994), therefore using the average or maximum contaminant concentration in soil may not be ideal for inhalation estimates.

2.3 Airborne Particulate Matter

Inhalation of soil particles occurs through the inhalation of airborne particulate matter. Airborne particulate matter can be viewed as a complex conglomerate of both inorganic and organic substances (Brook et al. 1997). Particulate matter can be divided into categories based on particle size relevant to human exposure. Total suspended particulates (TSP) have no dimensional restrictions and any particles larger than 10 µm will be swept into the esophagus by muco-ciliary action and ingested (Bright et al. 2006). Particulate matter with an aerodynamic diameter less than 10 µm will be deposited in the trachea and bronchioles before being swept into the esophagus, creating both an inhalation and ingestion hazard, and is referred to as PM_{10} or coarse particulate matter (Bright et al. 2006; Brook et al. 2004; Wang et al. 2002). Particulate matter with aerodynamic diameter less than 2.5 µm is capable of penetrating deep into the lung reaching the alveoli and is referred to as $PM_{2.5}$ or fine particulate matter (Bright et al. 2006; Brook et al. 2004; Wang et al. 2002).

2.3.1 Health Effects

In recent years there has been an abundance of research identifying the potential impact of particulate matter on human health (Brook et al. 2004; Dockery et al. 1993; Dominici et al. 2006; Brook et al. 2010; Brunekreef and Forsberg 2005). From epidemiological studies it has been suggested that the majority of the toxicity is dependent upon the airborne concentration of PM_{10} and $PM_{2.5}$ (Brook et al. 2004; Dominici et al. 2006; Brook et al. 2010; Pope et al. 2009; Pope et al. 2002; Suwa et al. 2002). Not surprisingly, the majority of the particulate toxicity occurs on the cardiopulmonary system. Analysis from the National Mortality and Morbidity Air Pollution Study estimated that that the short term cardiopulmonary mortality increases by 0.31 % for each 10 µg m^{-3} increase in PM_{10} (Dominici et al. 2005). Furthermore, it has been estimated that increased annual average $PM_{2.5}$ concentrations leads to increased cardiopulmonary and lung

cancer mortality (Pope et al. 2002). Suwa et al. (2002) found that PM_{10} caused a systemic inflammatory response and was associated with the progression of atherosclerosis within the coronary artery and aorta. A review performed by Pope et al. (1995) conclude that particulate matter pollution can also be responsible for increased respiratory symptoms, decreased lung function, and increased cardiovascular morbidity and mortality.

Although the epidemiological research indicates that airborne particulate matter has a negative effect on human health the toxic mechanism of action is still unclear. Currently it is inconclusive if the toxicity of airborne particulate matter is directly related to the chemical composition or particle size, or if toxicity is simply dependent upon the physical stress created by increased particle mass (Harrison and Yin 2000). Mechanisms of toxicity for particle matter have been proposed, such as oxidative stress in the lung resulting in constant low level inflammation (MacNee and Donaldson 2003), but thus far no mechanism of action has been explicitly confirmed. Nevertheless, for certain contaminants the toxicity from the inhalation pathway differs compared to the combined ingestion and dermal absorption pathways, and therefore inhalation risk is calculated separately from ingestion and dermal absorption (Health Canada 2004b).

2.4 Bioaccessibility in Human Health Risk Assessment

Risk assessors use *in vitro* bioaccessibility models in SSRA to better characterize exposure estimates. *In vitro* bioaccessibility models estimate the contaminant fraction solubilized into simulated gastro-intestinal (GI) fluids that can potentially be absorbed by GI epithelial cells. Before *in vitro* bioaccessibility estimates can be used in risk assessment they must be validated against an acceptable *in vivo* model, however the high costs of *in-vivo* models limits the wide-spread validation of contaminants (Richardson et al. 2006). *In vivo* bioavailability calculates the percentage of ingested contaminant that is absorbed across the GI epithelium and enters systemic

circulation (Ruby et al. 1999) whereas *in vitro* bioaccessibility calculates the percentage of ingested contaminant solubilized into simulated GI fluids (Rodriguez and Basta 1999). Ideally, risk assessments would be performed using the most accurate exposure estimate, *in vivo* bioavailability not *in vitro* bioaccessibility, but there are downsides to *in vivo* models that make them inefficient for use in widespread risk assessment. First and foremost, there is considerable ethical debate for the constant euthanasia of animals solely to better characterize risk to humans. Additionally, animal models require a considerable investment of both time and money (Rees et al. 2009); ergo *in vitro* models have become the preferred methodology. With the validation of an *in vitro* model, risk assessors are allowed the accuracy of *in vivo* research without the unnecessary consumption of substantial resources.

2.4.1 *In vivo* Bioavailability

Currently there are many different animal models utilized for *in vivo* bioavailability estimates. Common animal models used include the rat (Budinsky et al. 2008), mouse (Smith et al. 2011), juvenile swine (Casteel et al. 2006) and monkeys (Roberts et al. 2007). A review performed by Ramesh et al. (2004) indicates that the various rat and mouse models were most frequently used for the bioavailability of PAHs and this may be due to the relative lower cost of housing and maintenance as well as the ease of handling the animals compared to swine and monkeys. Despite the vast number of studies involving mouse and rats there is still ample research conducted with swine (Casteel et al. 2006; Juhasz et al. 2009; Budinsky et al. 2008) and monkeys (Roberts et al. 2007; Freeman et al. 1995). As bioavailability research advances there is growing importance to use animal models that possess GI tracts similar to humans. The GI tract of humans is closely related to that of swine and monkeys, with swine having anatomically similar GI tracts (Patterson et al. 2008) and nutritional requirements (Cooper et al. 1997).

Monkeys are non-human primates that closely resemble human physiology (Kararli 1995; Ikegami et al. 2003).

Not all models use the same methodology when evaluating bioavailability. This disparity is largely due to the unique toxicokinetics of environmental contaminants. To determine arsenic bioavailability, collection of urine and feces is a common strategy as arsenic is primarily eliminated via the urine (Buchet et al. 1981). Conversely, for lead bioavailability blood, kidney, liver and bone samples are routinely collected (US EPA region 8 2005**;** Schroder et al. 2004). Other studies employ the usage of surgical procedures to insert a catheter for continuous blood sampling and they subsequently determine bioavailability using area under the plasma-concentration (AUC) time curve (Rees et al. 2009; Budinsky et al. 2008).

2.4.2 *In vitro* bioaccessibility

There are many *in vitro* bioaccessibility models currently used in risk assessment. The general theme behind *in vitro* models is to mimic the physiological conditions present in the human gastrointestinal tract. Bioaccessibility models are developed to account for the main parameters of human oral digestion such as peristaltic mixing, transit times, body temperature, pH, saliva, and secretions – gastric, pancreatic, and biliary. The peristaltic mixing and transit times can be accounted for by using magnetic stirring (150 rpm for 2 h) - Simulator of the Human Intestinal Microbial Ecosystem (SHIME) (Van de Wiele et al. 2004), end over end rotation (30 rpm for 1 h) - Relative Bioavailability Leaching Procedure (RBALP) (Drexler and Brattin 2007), or directly mixing an inert gas through the simulated fluids (1.0L/min) - Physiological Based Extraction Test (PBET) (Ruby et al. 1996). The pH values used in the gastric compartment for *in vitro* models generally ranges between 1.3 (Ruby et al. 1993) to 2.5 (Ruby et al. 1996), and for the intestinal compartment range between 6.5 (Laird et al. 2007) to 7 (Ruby et al. 1996). Body temperature of 37°C is the only consistent parameter among the

various models (Ruby et al. 1999; Oomen et al. 2003; Drexler and Brattin 2007). Simulated gastric fluids are another area of diversity between *in vitro* models. The RBALP and Simplified Based Extraction Test (SBET) are one compartment models and the simulated fluids consists of an approximately 0.4 M glycine solution acidified to a pH of 1.5(Drexler and Brattin 2007; Juhasz et al. 2008). The gastric phase of the PBET utilizes pepsin, acetate, citrate and lactate and malate in de-ionized (DI) water at pH 1.3 (Ruby et al. 1993) whereas the SHIME simply uses DI water acidified to pH 1.5 (Laird et al. 2007) and both of these models utilize pancreatin and bile in their intestinal compartments. A unique aspect of the SHIME is that it incorporates a microbial community in a colon compartment (Laird et al. 2007). Furthermore, human colorectal carcinoma cell line (Caco-2) and ethylene vinyl acetate (EVA) thin films have been used as a lipophilic component within various models for bioaccessibility estimates of various lipophilic substances (Minhas et al. 2006; Vasiluk et al. 2007; Oomen et al. 2001).

2.4.3 Validation of Bioaccessibility Models

Overall, research on the processes determining *in vivo* release of contaminants found in soil exists in a tiered hierarchy between metals and organics. To date there has been an extensive amount of research performed to validate the usage of *in vitro* models for metals, particularly lead and arsenic (Ruby et al. 1999; Rodriguez and Basta 1999; Schroder et al. 2004; Basta et al. 2007; Juhasz et al. 2007; Van de Wiele et al. 2007) and the processes related to the release of metal contaminants are being elucidated (Schroder et al. 2004; Juhasz et al. 2007; Laird et al. 2011). Conversely, research for the validation of organic contaminants has not been as thoroughly investigated but is developing (Vasiluk et al. 2007; Cave et al. 2010; Cavret et al. 2003). At the center of developing research for organic bioaccessibility is the idea that organic contaminant bioavailability may be driven by chemical potential, also referred to as fugacity (Minhas et al. 2006; Siciliano et al. 2010; Reichenberg and Mayer 2006; Vasiluk et al. 2008).

With the concept of fugacity and the lipophilic nature of many organic contaminants, such as PAHs, lipophilic phases have been added to *in vitro* models in an attempt to clarify *in vivo* absorption (Minhas et al. 2006; Vasiluk et al. 2007; Oomen et al. 2001; Hurdzan et al. 2008).

2.4.4 Fugacity

The concept of fugacity was first introduced over 100 years ago by Lewis (1901) as an alternative to chemical potential when working with chemicals in multiple phases. Fugacity is the thermodynamic quantity equivalent to chemical potential and has also been defined as the escaping tendency of a chemical. In short, Lewis (1901) states that if a chemical present in one phase comes in contact with a second phase the chemical will have a tendency to escape to the second phase. This escaping tendency can be viewed as a pressure exerted by the chemical and therefore fugacity can be measured as a partial pressure. Mackay (1979) generalizes that fugacity calculations are most appropriate for persistent environmental chemicals and that at low concentrations, the concentration of most chemicals are linearly related to fugacity. The relationship between concentration and fugacity is as follows:

$$C_p = F \times Z_p \qquad \text{(Eqn 2.5)}$$

Where C_p = chemical concentration within a phase (mol m^{-3}), F = fugacity or escaping tendency (Pa), and Z_p = fugacity capacity of the phase (mol m^{-3} Pa^{-}). Notably, fugacity acts as a partial pressure and has units of Pa. As a general condition for fugacity, any chemical compound in multiple phases, equilibrium is reached when all phases reach the same fugacity (Lewis 1901). Therefore, a chemical will always move from an area of high fugacity to an area of lower fugacity. The fugacity capacity is akin to solubility as the fugacity capacity refers to the ability of a phase to absorb a chemical. Alternatively, fugacity capacity can be viewed as the potential of a medium to dissolve a chemical.

Modern day use of fugacity can be attributed to the work of MacKay (1979), Mackay and Patterson (1981), and Mackay and Patterson (1982). Despite the popular use of the fugacity concept with environmental fate models (Macleod and Mackay 1999; Kawamoto et al. 2001; Toose et al. 2004), Mackay (2004) states that the greatest value of the fugacity concept lies with its ability to help elucidate the phenomenon of bioconcentration, bioaccumulation, and biomagnification. Mackay (1982) argues that the bioconcentration of polychlorinated biphenyls from water to fish can easily be explained by the large fugacity capacity of fish relative to the fugacity capacity of water. Gobas et al. (1993) illustrates that intestinal absorption and biomagnification of organochlorines can be accurately explained in both fish and humans using fugacity. Conversely, Kelly et al. (2004) indicates that there are multiple factors outside of fugacity that influence the bioaccumulative potential of various commercial chemicals. However, *in vitro* PAH bioaccessibility models using EVA thin films and Caco-2 cells, which create a fugacity gradient based on their relatively higher fugacity capacity, report that the fugacity gradient between the aqueous phase and the EVA thin films or Caco-2 cells is the driving force behind PAH uptake (Minhas et al. 2006; Vasiluk et al. 2007).

PREFACE

The following chapter has been accepted as a peer-reviewed article in the journal Environmental Toxicology and Chemistry (31 (10): 2423-2430). The main focus of the chapter is to perform a risk assessment for a site with contaminated soil and to demonstrate the relevance of soil inhalation.

3 COMPARISON OF HUMAN EXPOSURE PATHWAYS IN AN URBAN BROWNFIELD: REDUCED RISK FROM PAVING ROADS

3.1 Introduction

Declining soil quality is growing concern worldwide because anthropogenic activities result in increasing concentrations of contaminants in soil, most notably trace metals (Nriagu and Pacyna 1988), heavy metals (Nriagu and Pacyna 1988; Grzebisz et al. 2002; Loska et al. 2004) and PAHs (Menzie et al. 1992; Srogi 2007). In recent years, it has been shown that contaminated soil has the potential to adversely affect humans across the globe. Studies from the USA (Filippelli and Laidlaw 2010), Australia (Laidlaw and Taylor 2011), and Tunisia (Ghorbel et al. 2010) have demonstrated that lead in soil poses a risk to human health, particularly children. Studies from Canada (Zhang et al. 2009) and China (Qiao et al. 2011) found that arsenic in soil presents excessive carcinogenic risk. In Taiwan, heavy metal contamination of paddy soils threatens rice production and food safety, prompting the development of risk-based site assessments aimed at protecting agricultural production and minimizing human exposure (Lai et al. 2010).

Humans are exposed to contaminants in soil through various pathways and ingestion of soil particles is commonly considered the major route of exposure (Bright et al. 2006). Inhalation of soil particles, in the form of airborne particulate matter, is often not quantified as soil ingestion generally results in exposures one to two orders of magnitude greater than inhalation (Granero and Domingo 2002; RIVM 2001). As such some risk assessments focus entirely on ingestion exposure and ignore the inhalation pathway (Poggio et al. 2008; Guney et al. 2010). However, in studies that consider inhalation pathways, work shows that inhalation can, in certain situations, be an important exposure pathway. For example, Lai et al (2010) found that inhalation of soil particles contributed 17% to the total heavy metal exposure at a site in southern Taiwan. As well, review

and opinion articles suggest that re-suspended soil is a likely human health concern (Sing and Sing 2010; Skinner 2007).

In northern Canada, within the city of Iqaluit the Lower Base Region (LBR) is the site of a former military base that has been converted to residential use and has a history of soil contamination (Siciliano et al. 2009). This particular site has three factors that contribute to increased inhalation exposure: unpaved roads, a lack of vegetative cover, and contaminant enrichment in the <45 µm size fraction of soil. As of 2007, none of the roads in Iqaluit were paved, which resulted in soils being re-suspended into the air via vehicular traffic (Gillies et al. 2005). Furthermore, in southern California, geological material, such as fugitive dust from unpaved road, paved roads and agricultural operations was found to account for 60% of particulate matter less than 10 µm (PM_{10}) (Magliano et al. 1999). In northern European countries, suspension of road dust is the primary contributor to PM_{10}, and approximately 90% comes from non-exhaust sources (Forsberg et al. 2005; Omstedt et al. 2005). In addition, during residential development, a large majority of the vegetative cover within the city was removed and has not been able to recover. Vegetative cover can reduce wind velocity and increase the surface moisture content, effectively binding soil particles into larger aggregates and reducing the re-suspension of soil (Watson and Chow 2000);this lack of a vegetative cover has also contributed to a greater load of suspended particulate matter in the local atmosphere. Finally, metal concentrations in the <45µm fraction in Iqaluit soil are higher than those in the bulk soil (Siciliano et al. 2009), and smaller size fractions of soil are more likely to be re-suspended opposed to the bulk soil (Chow et al. 1994; Clairborn et al. 1995). Taken together, these conditions suggest that soil inhalation exposure may be an important pathway.

The Iqaluit LBR has been the site of numerous studies (Laird et al. 2011; Siciliano et al. 2009; Siciliano et al. 2010) that have characterized exposure, contaminant concentrations, and contaminant bioaccessibility. Thus, this location is an ideal site for testing the importance of the inhalation exposure pathway in a northern urban setting and evaluate whether simple municipal activities can reduce exposure pathways and thereby mitigate exposure. It should be noted that many northern municipalities have competing public health concerns and risks, so solutions that increase the functionality or aesthetic value of a city and also reduce exposure pathways are particularly prized. During the summer of 2008 and 2009 roads were paved within the city. Thus the purpose of this study was to (1) evaluate the relative magnitude of the inhalation versus ingestion pathway and (2) evaluate if paving roads significantly decreased the risk of adverse effects from chemicals of potential concern in the soils of this municipality.

For this study three size fractions of airborne particulate matter were collected to characterize human exposure to airborne contaminants: total suspended particulates (TSP), particulate matter with an aerodynamic diameter less than 10 μm (PM_{10}), and particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$). For this risk assessment, particulate matter less than PM_{10} is considered representative of inhalation exposure, as it reaches the lower respiratory tract. Particulate matter greater than $PM_{2.5}$ is considered representative of ingestion exposure, as it is eventually removed from the respiratory tract by muco-ciliary action and ingested (Bright et al. 2006), subsequently the PM2.5-PM10 size fraction is quantified for both ingestion and inhalation exposure. Soil ingestion exposure was determined using the reported values from previous studies (Siciliano et al. 2009; Siciliano et al. 2010).

3.2 Materials and Methods

3.2.1 Particulate Matter

Three Ecotech Mirco-Vol 1100 (American Ecotech; Warren, RI) low flow (3 L min^{-1}) air samplers were set up outside a residential home within the Iqaluit LBR to collect TSP, PM_{10} and $PM_{2.5}$ across 47-mm Whatman glass fibre filters. The samplers were set to collect at a height of approximately 0.8 m to reflect the exposure to a toddler—as they have the largest intake rate to body mass ratio (Richardson 1997)—and the filters were replaced once per week for a total of seven weeks. Laboratory and field blanks were collected with each set of filters as a blank correction for both airborne particulate concentration and chemical analysis. Filters were cut into sections using an acetone washed scalpel for analysis. Filters were preconditioned for 24 hours under 50% relative humidity both before and after sampling to determine mass of particulate matter. Samples were re-weighed 1 hour after the initial weighing and the mean was taken to represent the mass.

3.2.2 Metal Analysis

Approximately 30 mg filter samples were microwave digested with an acid mix of $HNO_3/H_2O_2/HF$ following the procedures of Laird et al. (2011) and analyzed for total metal content using inductively coupled plasma-mass spectrometry (ICP-MS). Metals analyzed were beryllium (Be), aluminum (Al), titanium (Ti), vanadium (V), chromium (Cr), manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), copper (Cu), zinc (Zn), arsenic (As), selenium (Se), strontium (Sr), molybdenum (Mo), silver (Ag), cadmium (Cd), tin (Sn), antimony (Sb), barium (Ba), mercury (Hg), thallium (Tl), lead (Pb), and uranium (U). Both Se and Tl had values below their respective detection limits of 3 and 1 µg kg^{-1} and thus were excluded from the risk assessment. The National Institute of Standards and Technology (NIST) certified reference material (CRM)

1640a (trace elements in water) was included in each set of analyses for quality assurance purposes; average recoveries ranged from a low of 93% for As to a high of 105% for Mo.

3.2.3 PAH Analysis

Accelerated solvent extraction (ASE) was used to extract PAHs from approximately 30 mg filter samples following the procedures of James et al. (2011) and analyzed using High Pressure Liquid Chromatography coupled with Fluorescence Detection (HPLC-FD) (Marriott et al. 1993). The PAHs included in the analyses were: naphthalene (Nap), fluorene, pyrene, benzo(a)anthrancene, chrysene, benzo(b)fluoranthene (BbF), benzo(k)fluoranthene, (BbK), benzo(a)pyrene (BaP) dibenzo(a,h)anthrancene, benzo(g,h,i)pyrene, and indeno(1,2,3-c,d)pyrene (IcdP). Recovery of individual PAHs from blank filters spiked with a known amount of PAHs ranged from 67% for BbF to 117% for chrysene, and averaged 83%. Fluorene and pyrene had values below the detection limit of 0.64 pg and were excluded from the risk assessment.

3.2.4 Enrichment Factors

Enrichment factors (EF) are calculated as previously described (Gao et al. 2002).

$$EF = \frac{[X]_{atm}}{[Al]_{atm}} \div \frac{[X]_{soil}}{[Al]_{soil}} \qquad \text{(Eqn 3.1)}$$

Where $[X]_{atm}$ and $[Al]_{atm}$ are the concentrations of the contaminant and Al in the atmosphere and $[X]_{soil}$ and $[Al]_{soil}$ are the mean concentrations of the contaminant and Al in the soil. Aluminum is used as a reference element assuming that its anthropogenic contribution is minimal (Gemenetzis et al. 2006). An EF approaching 1 indicates that the soil is the predominant source for the contaminant. An EF >5 suggests that a significant fraction of the contaminant can be attributed to a non-soil source. An EF >100 suggests that the element comes from an anthropogenic source. Given that the contaminant concentration in the <45 μm size fraction of the soil was more likely to be re-suspended (Chow et al. 1994; Clairborn et al. 1995), and had higher

contaminant concentrations (Siciliano et al. 2009; Siciliano et al. 2010), this fraction was used to calculate enrichment factors. Using bulk soil would have resulted in larger enrichment factors, when in fact the soil is naturally enriched.

3.2.5 Exposure Assessment

The hypothetical receptor of concern in this scenario is an individual who lives (and works) within the lower base region. The primary focus is on the toddler as they have the highest intake rate to body mass ratio (Richardson 1997); therefore if the risk assessment is protective of toddlers it will be protective of the other receptors.

Three pathways were examined for exposure comparison: incidental soil ingestion, particulate matter inhalation, and particulate matter ingestion following tracheal deposition. Soil ingestion represents the fraction of soil that adheres to hands and is subsequently ingested. Dermal exposure has been excluded because the additional pathway does not influence the primary results of the study. Particulate matter inhalation represents inhaled airborne contaminants that reach the respiratory tract and particulate matter ingestion represents larger airborne contaminants that are inhaled but are swept into the esophagus by muco-ciliary action and ingested. Exposure via soil ingestion, particulate matter inhalation and particulate matter ingestion is calculated as:

$$EDI_{\text{ingestion-soil}} = \frac{[X]_{soil} \times IR_{soil} \times AF_{git} \times YE}{BW \times LE} \quad \text{(Eqn 3.2)}$$

$$EDI_{\text{inhalation-PM}} = \frac{([Y]_{air} \times IR_{air} \times AF_{inh} \times t_{outdoor} + [Y]_{air} \times 70\% \times IR_{air} \times AF_{inh} \times t_{indoor})YE}{BW \times LE} \quad \text{(Eqn 3.3)}$$

$$EDI_{\text{ingestion-PM}} = \frac{([Z]_{air} \times IR_{air} \times AF_{git} \times t_{outdoor} + [Z]_{air} \times 70\% \times IR_{air} \times AF_{git} \times t_{indoor})YE}{BW \times LE} \quad \text{(Eqn 3.4)}$$

Where EDI = estimated daily intake (mg kg^{-1} day^{-1}) , $[X]_{soil}$ = concentration of contaminant in soil (mg kg^{-1}); $[Y]_{air}$ = concentration of contaminant in particulate matter less than 10 µm in diameter (mg m^{-3}); $[Z]_{air}$ = concentration of contaminant in particulate matter greater than 2.5 µm in diameter (mg m^{-3}); IR_{soil} = soil ingestion rate (kg day^{-1}); IR_{air} = air inhalation rate (m^3 h^{-1}); AF_{git}

= ingestion absorption factor (unitless); AF_{inh} = inhalation absorption factor (unitless); $t_{outdoor}$ = time spent outdoors (h day^{-1}); t_{indoor} = time spent indoors (h day^{-1}); BW = body weight (kg); YE = years exposed (y); and LE = life expectancy (y). Both YE and LE variables apply only for carcinogenic risk. Soil PAH concentration and relative bioaccessibility was obtained from Siciliano et al. (2010), while soil metal concentration and relative bioaccessibility was obtained from Siciliano et al. (2009) and Laird et al. (2011), respectively. Contaminant concentrations used are displayed in **Table 3.1**. The most conservative values were always used; therefore, in situations where $PM_{2.5}$ concentration were greater than PM_{10} concentration, the $PM_{2.5}$ value was used. The inhalation absorption factor was assumed to be 1. Environmental contaminant concentrations and particulate matter concentrations were determined experimentally. From the Canadian Compendium, it was assumed that a toddler would weigh 16.5 kg, have an inhalation rate of 0.388 $m^3\,h^{-1}$, spend 1.5 h d^{-1} outdoors and 22.5 h d^{-1} indoors (Richardson 1997). Similarly, it was assumed that an adult would weigh 70.7 kg, have an inhalation rate of 0.658 $m^3\,h^{-1}$, and spend 1.5 h d^{-1} outdoors and 22.5 h d^{-1} indoors. It is assumed that toddlers and adults have a soil ingestion rate of 8.0 x 10^{-5} kg d^{-1} and 2.0 x 10^{-5} kg d^{-1}, respectively (Health Canada 2004b). For this risk assessment it is assumed that the indoor concentration of airborne toxicants, in mg m^{-3}, is 70% of the outdoor concentration (Hawley 1985; Abt et al. 2000).

3.2.6 Risk Assessment

Carcinogenic risk was determined using Equation 3.5 and non-carcinogenic risk was calculated using Equation 3.6, utilizing hazard quotients (HQ):

$$\text{Risk} = EDI \times CSF \qquad \text{(Eqn 3.5)}$$

$$\text{HQ} = EDI \div TDI \qquad \text{(Eqn 3.6)}$$

Where Risk = a unitless probability of an individual developing cancer over a lifetime, EDI = estimated daily intake (mg kg^{-1} d^{-1}); CSF = cancer slope factor (mg kg^{-1} $d^{-1})^{-1}$; and TDI = tolerable daily intake (mg kg^{-1} d^{-1}). Values for CSF and TDI were obtained from Health Canada and U.S. Environmental Protection Agency Integrated Risk Information System (Health Canada 2004b; US EPA 2011). Age dependant adjustment factors (ADAFs) were used to account for the susceptible early life stages. An adjustment factor of 10 was used for the first two years of life, an adjustment factor of three was used for ages between two and 16 years and no adjustment was made for ages 16 years and older (US EPA 2005). Potency equivalency factors were used to calculate carcinogenic risk from PAHs and were obtained from Canadian Council of Ministers of the Environment (CCME 2010). Briefly, carcinogenic risk is expressed as the sum total benzo(a)pyrene (BaP) equivalents for PAHs with the same mode of toxic action using their relative potency to BaP.

3.2.7 Statistical Analysis

The Anderson-Darling test was applied to all data to test for normality. Significant difference was determined using student's *t* test.

3.3 Results

Whereas soils in the Iqaluit LBR were the primary source of V, Cr, Mn, Ni, Cu, Hg, and Pb in the airborne particulate matter (**Figure 3.1**), PAHs and the metals Be, Zn, Sb, and Ba were derived primarily from anthropogenic (non-soil) sources. Non-soil sources also contributed to the As, Sr, Mo, Ag, Cd and U found in the airborne particulates (**Figure 3.1**). The EF for PAHs in the TSP was only approximately one; however, because 77% of PAHs present in the TSP originated in the $PM_{2.5}$ fraction—which has an EF for PAHs of approximately 100—it can be concluded that PAHs in airborne particulate matter were most likely of anthropogenic origin.

Table 3.1 Average concentration of metals and polycyclic aromatic hydrocarbons in soil and airborne particulate matter.

Contaminant	Soil Concentration (mg/kg)	TSP Concentration (mg/m3)		PM_{10} Concentration (mg/m3)		$PM_{2.5}$ Concentration (mg/m3)	
		Before Paving	After Paving	Before Paving	After Paving	Before Paving	After Paving
Ag	0.53	$1.1x10^{-7}$	$5.5x10^{-8}$	$1.7x10^{-8}$	$1.0x10^{-8}$	$2.5x10^{-9}$	$1.2x10^{-9}$
As	2.4	$5.1x10^{-7}$	$2.2x10^{-7}$	$1.0x10^{-7}$	$2.5x10^{-8}$	$2.3x10^{-9}$	$4.3x10^{-9}$
Ba	1142	$1.6x10^{-3}$	$6.9x10^{-5}$	$4.0x10^{-4}$	$1.8x10^{-5}$	$1.6x10^{-5}$	$1.4x10^{-5}$
Be	1.5	$4.7x10^{-7}$	$3.5x10^{-7}$	$5.5x10^{-7}$	$1.1x10^{-8}$	$1.5x10^{-8}$	$7.4x10^{-8}$
Cd	4.6	$5.0x10^{-7}$	$3.1x10^{-7}$	$9.8x10^{-8}$	$4.8x10^{-8}$	$1.3x10^{-8}$	$9.6x10^{-9}$
Cr	67	$2.7x10^{6}$	$1.3x10^{-6}$	$3.6x10^{-7}$	$1.7x10^{-7}$	$3.5x10^{-8}$	$7.8x10^{-9}$
Cu	15	$1.4x10^{-7}$	$8.0x10^{-8}$	$2.4x10^{-8}$	$1.0x10^{-8}$	$2.4x10^{-9}$	$3.0x10^{-9}$
Hg	0.97	$9.5x10^{-10}$	$8.3x10^{-10}$	$3.8x10^{-10}$	ND	ND	$1.4x10^{-10}$
Mn	655	$2.2x10^{-6}$	$5.7x10^{-7}$	$2.6x10^{-7}$	$6.5x10^{-8}$	$6.9x10^{-9}$	$1.3x10^{-7}$
Mo	1.9	$1.3x10^{-7}$	$6.1x10^{-8}$	$2.6x10^{-8}$	$5.0x10^{-9}$	$2.0x10^{-9}$	$1.8x10^{-8}$
Ni	16	$4.2x10^{-8}$	$2.3x10^{-8}$	$1.0x10^{-8}$	$4.7x10^{-9}$	$1.3x10^{-9}$	$4.4x10^{-9}$
Pb	29	$3.9x10^{-7}$	$2.4x10^{-7}$	$7.3x10^{-8}$	$7.9x10^{-9}$	$3.3x10^{-9}$	$2.1x10^{-8}$
Sb	0.21	$1.5x10^{-7}$	$8.5x10^{-8}$	$2.5x10^{-8}$	$5.8c10^{-9}$	$3.2x10^{-10}$	$1.0x10^{-8}$
Sr	216	$2.7x10^{-5}$	$1.6x10^{-5}$	$5.0x10^{-6}$	$6.9x10^{-7}$	$1.1x10^{-7}$	$1.4x10^{-7}$
U	1.0	$9.4x10^{-8}$	$4.8x10^{-8}$	$1.3x10^{-8}$	$4.0x10^{-9}$	$6.3x10^{-10}$	$4.1x10^{-10}$
V	73	$7.5x10^{-8}$	$2.9x10^{-8}$	$5.4x10^{-8}$	$2.7x10^{-8}$	ND	$3.1x10^{-8}$
Zn	81	$2.8x10^{-4}$	$2.0x10^{-4}$	$2.8x10^{-4}$	$4.6x10^{-5}$	$2.3x10^{-5}$	$6.8x10^{-6}$
Benzo(a)anthrancene	7.0	$2.8x10^{-7}$	$1.5x10^{-7}$	$5.9x10^{-7}$	$1.0x10^{-7}$	$1.5x10^{-7}$	$3.3x10^{-7}$
Benzo(a)pyrene	6.7	$1.4x10^{-7}$	$7.2x10^{-8}$	$5.0x10^{-7}$	$1.0x10^{-7}$	$1.1x10^{-7}$	$2.0x10^{-7}$
Benzo(b)fluoranthrene	11	$2.6x10^{-7}$	$2.0x10^{-7}$	$3.4x10^{-7}$	$6.2x10^{-8}$	$3.9x10^{-7}$	$2.9x10^{-7}$
Benzo(g,h,i)pyrene	4.3	$7.0x10^{-8}$	ND	$4.0x10^{-7}$	$1.0x10^{-7}$	$1.6x10^{-7}$	$3.7x10^{-7}$
Benzo(k)fluoranthrene	5.3	$2.8x10^{-7}$	$1.4x10^{-7}$	$2.4x10^{-7}$	$2.3x10^{-8}$	$5.7x10^{-8}$	$1.9x10^{-7}$
Chyrsene	14	$5.4x10^{-7}$	$6.7x10^{-7}$	$1.2x10^{-6}$	$8.9x10^{-8}$	$7.0x10^{-7}$	$8.6x10^{-7}$
Dibenzo(a,h)anthrancene	2.0	ND	$2.1x10^{-8}$	ND	$3.3x10^{-8}$	ND	$3.3x10^{-8}$
Indeno(1,2,3-c,d)pyrene	8.5	ND	ND	$3.1x10^{-7}$	ND	ND	$2.7x10^{-7}$
Naphthalene	0.31	$1.2x10^{-8}$	$6.1x10^{-9}$	$6.6x10^{-8}$	$8.5x10^{-9}$	$8.6x10^{-7}$	$5.0x10^{-9}$

ND = not detected; TSP = total suspended particulates; PM_{10} = particulate matter less than 10 µm; $PM_{2.5}$ = particulate matter less than 2.5 µm.

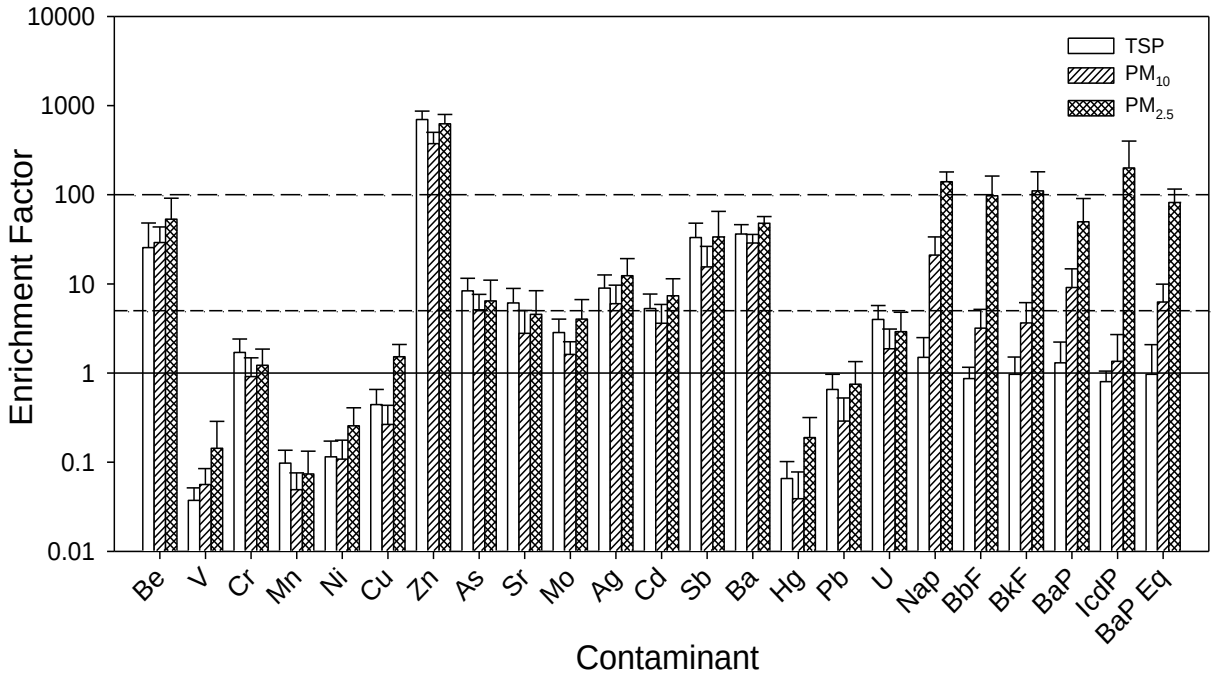

Figure 3.1 Enrichment factors for three size fractions of airborne particulate matter. Each vertical bar is the mean of 3–5 measurements and the error bar is the standard error of the estimate. An enrichment factor of approximately 1 (—) indicates that the soil is the dominant source of the contaminant, an EF greater than 5 (- - -) suggests that a significant fraction can be attributed to a non-soil source, and an EF greater than 100 (– – –) suggests that the element comes from an anthropogenic source. Metals are displayed on the left of the graph and PAHs on the right. PAHs are abbreviated as follows: Nap – naphthalene, BbF – benzo(b)fluoranthrene, BkF – benzo(k)fluoranthrene, BaP – benzo(a)pyrene, IcdP – Indeno(1,2,3-c,d)pyrene and BaP Eq – benzo(a)pyrene equivalents.

When comparing the estimated daily intake from each exposure pathway (**Figure 3.2**), intake from soil ingestion was generally one to two orders of magnitude greater than the combined intake of airborne particulates via both inhalation and ingestion. Indeed, Ag and Zn were the only elements where intake through soil ingestion was less than the combined intake of airborne particulate matter. Exposure to Ag is not a concern as total Ag exposure is 10,000 times lower than the TDI and the enrichment factor for Zn (~500; **Figure 3.1**) indicates that soil was not the primary source of this metal. Likewise, inhalation accounts for a large proportion of the estimated daily intake of Ba (33%) and Be (48%), and again the enrichment factors for these metals (~ 37

and 36, respectively) indicate that these metals derive primarily from anthropogenic sources. With the exception of these metals, the ingestion of airborne particulates contributes ≤1% to the total EDI for most metals and the PAHs, with particulate inhalation contributing 1 to10% and soil ingestion contributing 90 to 99% of the total EDI. For PAHs in particular, the ingestion of airborne particulates represents only a minor exposure pathway (contributing ≤0.2% to the total EDI). Indeed, the majority of the airborne PAHs were found in the $PM_{2.5}$ fraction; thus in terms of the airborne particulates, inhalation is the primary exposure pathway.

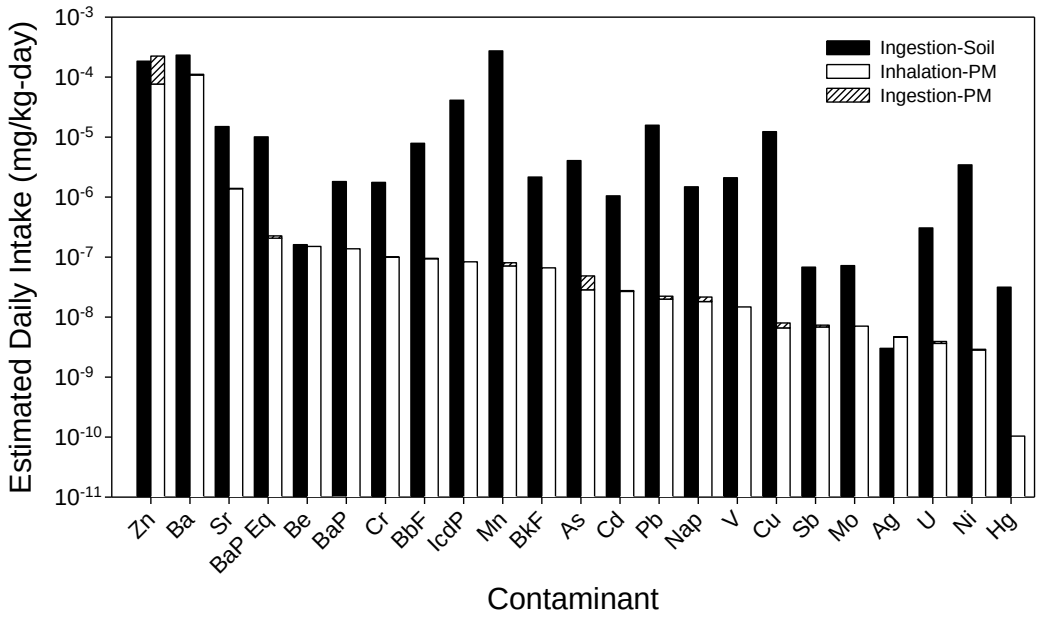

Figure 3.2 Estimated daily intake (EDI, in mg kg^{-1} d^{-1}) for a toddler. Inhalation-PM and ingestion-PM are stacked for comparison against ingestion-soil. Contaminants are ordered from highest to lowest exposure from the combined particulate matter exposure. Nap – naphthalene, BbF – benzo(b)fluoranthrene, BkF – benzo(k)fluoranthrene, BaP – benzo(a)pyrene, IcdP – Indeno(1,2,3-c,d)pyrene and BaP Eq – benzo(a)pyrene equivalents.

The amounts of TSP ($p < 0.1$) and PM_{10} ($p < 0.05$) materials decreased significantly following road paving (**Figure 3.3**). There was a high degree of temporal variability in the amounts of particulate matter collected, which could be partly attributed to the changes in precipitation,

vehicular traffic, and wind velocity (Watson and Chow 2000). Furthermore, the city of Iqaluit sprays the roads with $CaCl_2$ as a dust suppressant when deemed necessary, which in turn complicates comparing airborne particulate matter concentrations with temporal precipitation and wind velocity. Before the roads were paved the average concentrations (mean ± standard deviation) of TSP, PM_{10}, and $PM_{2.5}$were 85 ± 56 µg m^{-3}, 35 ± 17 µg m^{-3}, and 3.8 ± 2.2 µg m^{-3}, respectively. After paving, the average concentrations of TSP, PM_{10}, and $PM_{2.5}$ were 15 ± 14.4 µg m^{-3}, 6.5 ± 6.0 µg m^{-3}, and 2.3 ± 1.9 µg m^{-3}, respectively. In general, paving the roads reduced airborne concentrations of the various contaminants by 25 to 75%, and reduced the amount of particulate matter ingested and inhaled to 16 and 18% of their respective pre-paving values. Whereas Ba exhibited the greatest reduction (96%) in airborne concentration, Hg exhibited the smallest reduction (13%) (**Figure 3.4**).

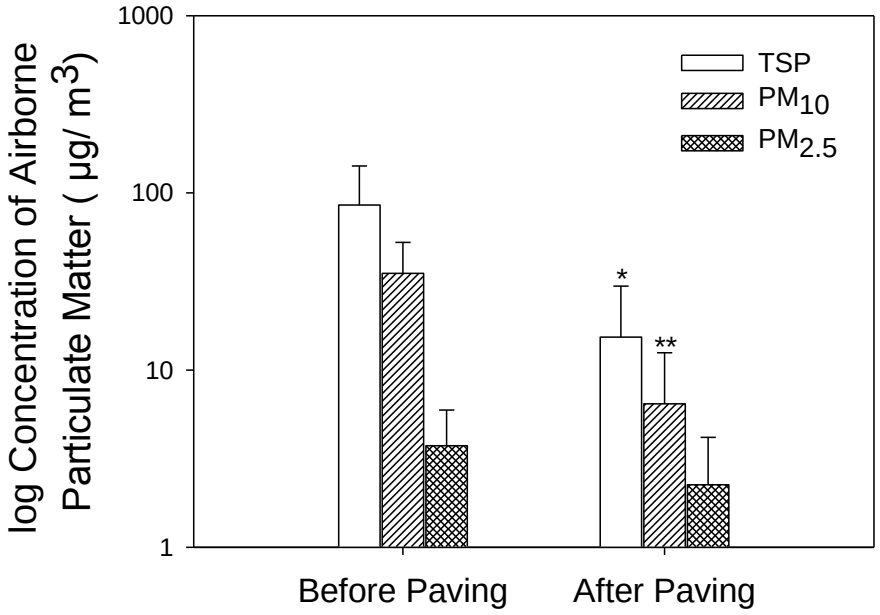

Figure 3.3 Average concentration of airborne particulate matter (n = 3 or 4). Error bars represent the standard deviation of the mean. Using students t-test paving roads significantly reduces the concentration of TSP ($p < 0.1$) and PM_{10} ($p < 0.05$) but not $PM_{2.5}$.

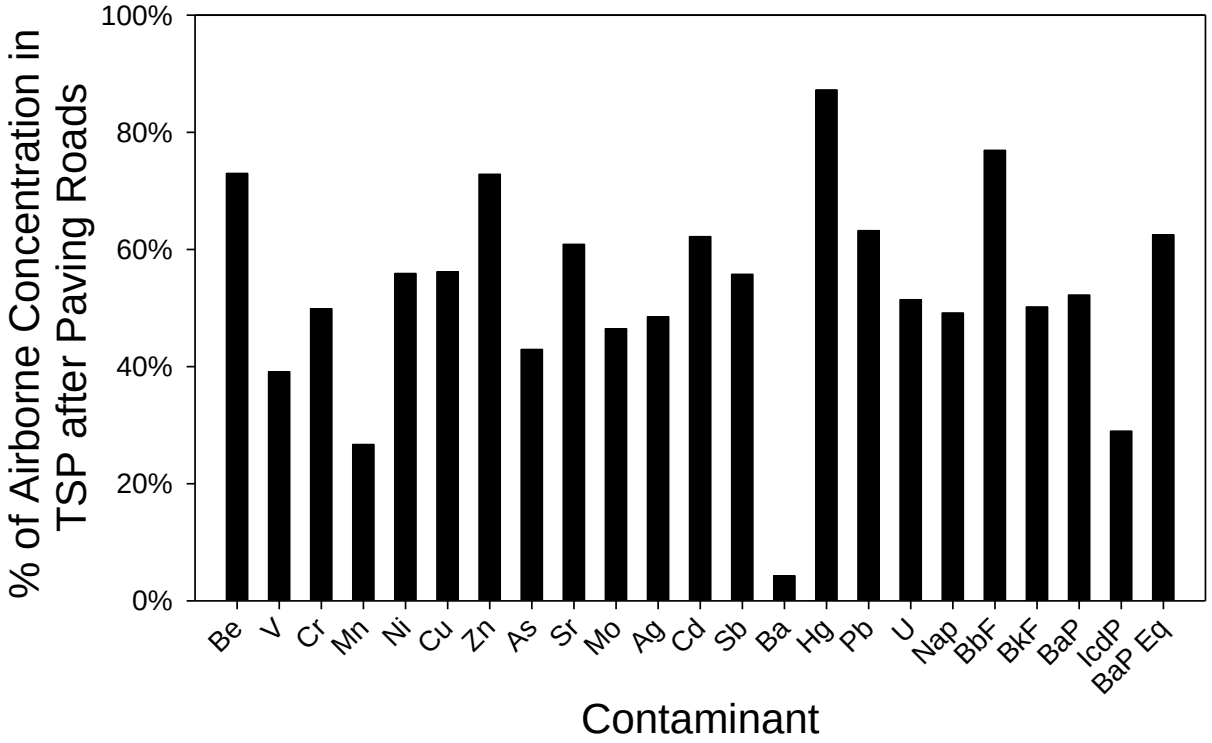

Figure 3.4 Percent of airborne concentration after paving roads compared to pre-paving. Percentages were calculated as the mean post-paving concentrations (n = 3) divided by the mean pre-paving concentrations (n = 4) in µg m^{-3} from TSP. Nap – naphthalene, BbF – benzo(b)fluoranthrene, BkF – benzo(k)fluoranthrene, BaP – benzo(a)pyrene, IcdP – Indeno(1,2,3-c,d)pyrene and BaP Eq – benzo(a)pyrene equivalents.

As a result of road paving, carcinogenic risk from airborne contaminants was reduced (**Figure 3.5**). Moreover, this reduction was generally much greater for toddlers than for adults. Not surprisingly, paving roads was more effective at reducing risk from carcinogens that have only inhalation CSFs (i.e., Cr and Cd) as opposed to carcinogens that have both inhalation and ingestion cancer slope factors (i.e., As and BaP equivalents). Conversely, Be has only an inhalation cancer slope factor and paving roads was not effective at reducing carcinogenic risk, however the soil is not the primary source (**Figure 3.1**). After paving roads incremental lifetime carcinogenic risk to a toddler from Cr is reduced by 46%, Cd by 48%, and Be by only 13%, whereas the carcinogenic risk to a toddler from As and BaP equivalents is reduced by only 12% and 5%, respectively.

Hazard quotients presented negligible risk from all exposure pathways and are displayed in **Table 3.2**. Notably, the hazard quotients from the inhalation pathway for Be, Cr, and Mn are larger than their respective ingestion counterparts.

Table 3.2 Hazard quotients for human exposure at a contaminated brownfield site.

Contaminant	HQ Inhalation- PM		Percent Reduction (%)	HQ Ingestion-PM		Percent Reduction (%)	HQ Ingestion-Soil
	Before Paving	After Paving		Before Paving	After Paving		
Ag	-	-	-	6.3×10^{-6}	3.2×10^{-6}	50	6.0×10^{-7}
As	-	-	-	4.7×10^{-4}	2.0×10^{-5}	57	1.4×10^{-2}
Ba	-	-	-	2.8×10^{-2}	1.2×10^{-3}	96	1.5×10^{-2}
Be	2.0×10^{-2}	1.8×10^{-2}	13	1.0×10^{-5}	7.4×10^{-9}	26	8.1×10^{-5}
Cd	-	-	-	1.7×10^{-4}	1.1×10^{-4}	38	1.3×10^{-3}
Cr	3.2×10^{-2}	1.5×10^{-2}	46	1.0×10^{-4}	4.8×10^{-5}	52	1.8×10^{-3}
Cu	-	-	-	1.3×10^{-6}	7.4×10^{-7}	43	4.1×10^{-4}
Hg	9.1×10^{-7}	4.5×10^{-7}	50	1.0×10^{-7}	8.7×10^{-8}	13	1.1×10^{-4}
Mn	3.7×10^{-3}	9.4×10^{-4}	75	8.0×10^{-7}	2.1×10^{-7}	75	2.0×10^{-3}
Mo	-	-	-	7.2×10^{-6}	3.4×10^{-6}	53	1.5×10^{-5}
Ni	2.1×10^{-3}	1.0×10^{-3}	55	1.3×10^{-6}	7.1×10^{-7}	45	2.7×10^{-3}
Pb	-	-	-	2.9×10^{-5}	1.8×10^{-5}	38	4.4×10^{-3}
Sb	9.0×10^{-5}	2.1×10^{-5}	77	1.8×10^{-5}	1.0×10^{-5}	43	1.7×10^{-4}
Sr	-	-	-	1.2×10^{-5}	7.1×10^{-6}	40	2.5×10^{-5}
U	-	-	-	4.3×10^{-5}	2.2×10^{-5}	49	5.1×10^{-4}
V	-	-	-	2.3×10^{-5}	8.8×10^{-6}	61	2.3×10^{-4}
Zn	-	-	-	1.7×10^{-3}	1.2×10^{-3}	28	6.2×10^{-4}
Nap	6.0×10^{-6}	8×10^{-7}	87	1.7×10^{-7}	8.6×10^{-8}	49	7.4×10^{-5}

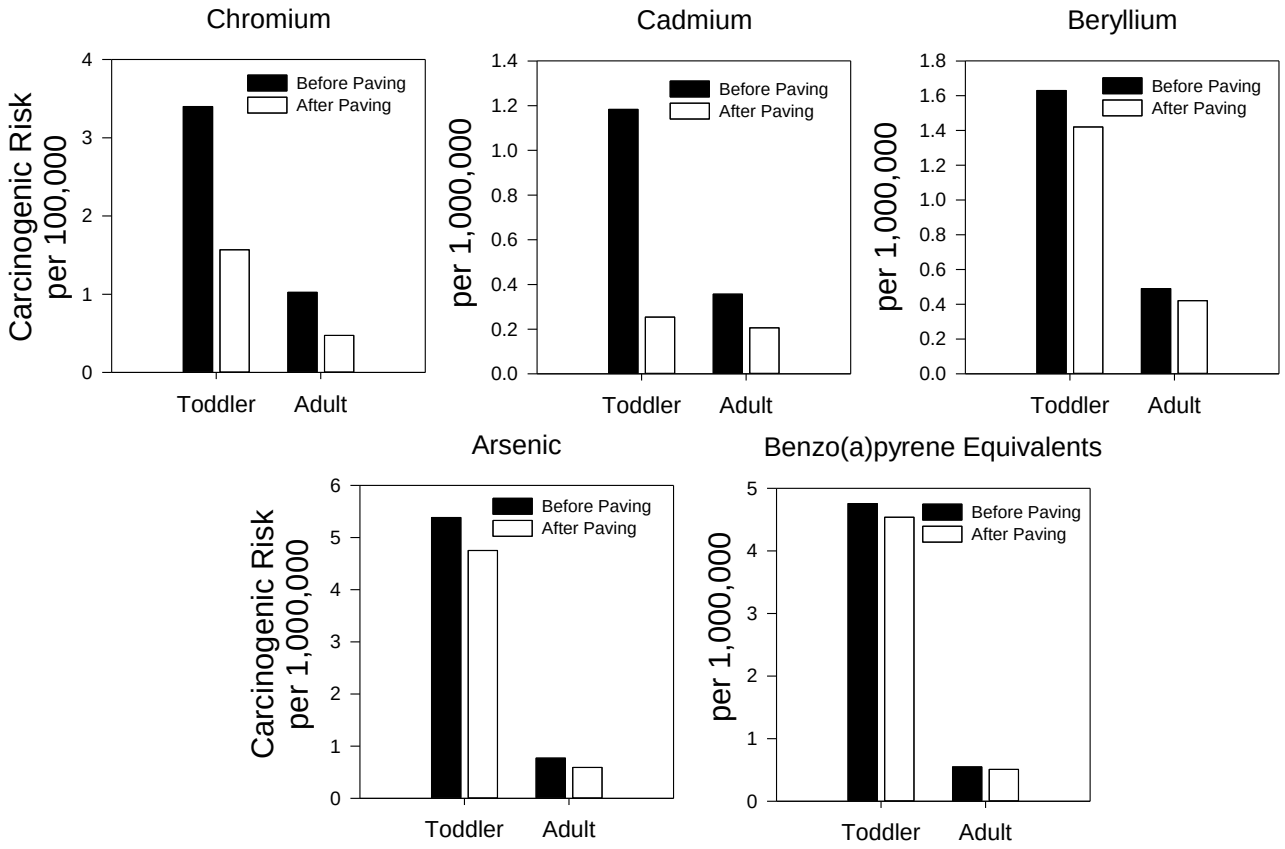

Figure 3.5 Incremental lifetime carcinogenic risk to toddlers and adults before and after paving roads. Carcinogenic risk for Cr exposure is expressed as per 100,000 individuals and all others are expressed as per 1,000,000 individuals. PAH carcinogenicity has been converted to benzo(a)pyrene equivalents using Canadian Council of Ministers of the Environment guidelines. Age Dependant Adjustment Factors (ADAFs) were used to account for the susceptible early life stages.

3.4 Discussion

The results from this risk assessment indicate that paving roads is an effective method of reducing risk from the inhalation of contaminated soil. Paving roads does not eliminate the re-suspension of soil particles from roads; instead the rate of soil re-suspension is limited by the rate at which soil particulates are deposited onto the roads (Hussein et al. 2008). In Iqaluit, mean $PM_{2.5}$ concentrations (3.1 µg m^{-3}) are lower than those reported for a number of other Canadian cities (6.7–11.8 µg m^{-3} (Celo and Dabek-Zlotorzynska 2010); 7.2–20.9 µg m^{-3} (Brook et al. 1997)); but are comparable to the concentrations reported for a rural location in New Brunswick, Canada (4.5

μg m^{-3} (Celo and Dabek-Zlotorzynska 2010)). Additionally, individual airborne PAH concentrations in Iqaluit (ranging from 1–5 × 10^{-4} μg m^{-3}) are similar to those found in rural locations across Canada and lower than the concentrations reported in their respective urban counterparts (Sanderson et al. 2004; Blanchard et al. 2002). Pre-paving PM_{10} (35 ± 17 μg m^{-3}) and TSP (85 ± 56 μg m^{-3}) concentrations in Iqaluit are consistent with those found across Canada (Brook et al. 1997) (i.e., 27 ± 16 μg PM_{10} m^{-3} and 55 ± 38 μg TSP m^{-3}). However, whereas this same study reports that $PM_{2.5}$ contributes an average of 51% of the PM_{10} mass and 30% of the TSP mass, in Iqaluit $PM_{2.5}$ contributes only 11% of the PM_{10} mass and only 4% of the TSP mass—indicating that the airborne particulate matter consists mainly of larger size fractions. Paving roads reduces the TSP and PM_{10} fractions to 15 ± 14 μg m^{-3} and 6.5 ± 6.0 μg m^{-3}, respectively. As a result, concentrations of airborne particulate matter in Iqaluit are amongst the lowest reported values for Canadian cities (Brook et al. 1997). As expected, paving roads did not significantly reduce the concentration of $PM_{2.5}$, because most soil particles are greater than 2.5 μm in diameter (Querol et al. 2001). Based on the low concentration of $PM_{2.5}$ and the reduction of TSP and PM_{10} after paving roads it becomes apparent that vehicular traffic on unpaved roads is the major source of airborne particulate matter for Iqaluit, which supports the findings of Forsberg et al. (2005) and Omsted et al. (2005) indicating that in certain conditions the primary source of particulate matter can be geological material.

In the present case study, soil inhalation is the dominant pathway of carcinogenic risk for Cr and Cd. Despite the fact that inhalation of particulate matter only contributes a maximum of 10% of the EDI, inhalation hazard quotients are comparable to their respective ingestion counterparts; for Be, Cr, and Mn, the inhalation hazard quotient is greater than ingestion. The results generated here show that whereas soil ingestion dominates in terms of total exposure, this is only half of the

equation in terms of risk assessment. The other half is TDI or CSF and for many contaminants there are TDIs and/or CSFs for both the inhalation and ingestion pathways (Health Canada 2004b; US EPA 2011). Thus, whereas exposure from soil ingestion can be one to two orders of magnitude greater than soil inhalation, the inhalation pathway often has a TDI that is much lower, or a CSF that is much greater than the ingestion pathway—thus making soil inhalation relevant for risk assessment. The soil inhalation risk is mainly attributed to exposure from PM_{10}, the inhalable fraction of airborne particulate matter, resulting from the vehicular traffic on unpaved roads. Before paving roads the city of Iqaluit used $CaCl_2$ as a dust suppressant to control soil re-suspension, therefore it is highly probable that the effect of paving roads has a larger capacity of reducing airborne particulate concentrations then what has been displayed here (**Figure 3.3**). The inhalation risk to human health in Iqaluit is a function of unpaved roads providing an infinite reservoir of contaminants to be re-suspended (Gillies et al. 2005) and the lower TDI or greater CSF for the inhalation pathway.

According to Siliciano et al. (Siciliano et al. 2009), Ag, As, and Cd have increasing concentration with decreasing particle size in soil and their enrichment factors may be overestimated due to natural enrichment; however Cr, Ni, Co, Sb, and Hg have decreasing concentration with decreasing particle size and their enrichment factors may be underestimated. Notably, Ba concentration was not linked to particle size and enrichment factors for Ba ranged from 29–48 indicating that there is a significant non-soil source for Ba; yet the reduction in airborne concentration of Ba after paving was greater than that for any other contaminant. Reduction in Ba concentration from paving roads is currently unknown to the authors, but under investigation.

Not explored here is the potential of contaminants to leach into the soil from the pavement. Undoubtedly, chemicals present in concrete or asphalt can leach into the surrounding soil and potentially increase the carcinogenic risk. The contribution of hazardous contaminants leaching into the soil is currently unknown; however other researchers have found that the risk associated with contaminant leaching from concrete and asphalt pavement to be minimal (Sadler et al. 1999; Marion et al. 2005; Kayhanian et al. 2009). In contrast, research by Van Metre et al. (2009) has shown that asphalt and coal tar sealant can provide a significant source of PAHs in dust, water and sediment. Notably, sealant makes the significant contribution, whereas the contribution from asphalt or concrete is negligible in comparison (Simon and Sobieraj 2006)

The risk assessment described herein utilizes various levels of conservatism. The inductively coupled plasma-mass spectrometry method used for metal analysis reports the total metal content within the sample and did not determine speciation. Metal toxicity varies with speciation, thus when multiple TDIs and CSFs were available based on metal speciation, the most conservative value was always used. In the case of chromium, carcinogenic risk could be as low as 2.3 in 1,000,000 opposed to the 1.6 in 100,000 if the primary species present is trivalent chromium and not hexavalent chromium (2004). Comparing the environmental conditions in Iqaluit to published values (Kotas and Stasicka 2000) indicates that hexavalent chromium may be the dominant species and without further analysis it is impossible to rule out hexavalent chromium as the dominant species, therefore the most conservative CSF was used. Further, we used the most conservative exposure factors from the Canadian Compendium which does not explicitly account for changes in human activity occurring during long winter months; in Iqaluit such months range from September until late May. For the exposure assessment we overestimate exposure by quantifying the 2.5-to 10-µm size fraction for both inhalation and ingestion exposures. We justify this overestimation as

the ingestion exposure makes a negligible contribution to the cumulative exposure (≤1% to the total EDI) and although particulate matter is swept into the GI tract it is unknown if individual contaminants are completely absorbed while in the lower respiratory tract.

From the data presented in the present study, vehicular traffic on unpaved roads can be a major source of airborne particulate matter. Although soil ingestion is still the dominant exposure pathway, soil inhalation can result in excessive risk to human health. Paving roads was found to be an effective measure for mitigating risk by reducing the amount of soil particles re-suspended into the atmosphere.

PREFACE

The following chapter has been accepted as a peer-reviewed article in the journal Environmental Science and Technology (45 (10): 4586-4593). The focus of the article is to compare *in vitro* release of PAHs to *in vivo* release of PAHs in swine serum and determine which model parameters best simulate *in vivo* conditions.

4 HUMAN EXPOSURE ASSESSMENT: A CASE STUDY OF 8 PAH CONTAMINATED SOILS USING *IN VITRO* DIGESTORS AND THE JUVENILE SWINE MODEL

4.1 Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a class of hydrophobic organic contaminants produced by the incomplete combustion of organic substances resulting from natural and anthropogenic processes, and are commonly found in soil (Menzie et al. 1992; Blumer 1976). Highly contaminated industrial sites include gasworks, petroleum refineries and wood preservation plants (Wilson and Jones 1993). Typically, at least nine different PAH compounds (benzo[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene, chrysene, dibenzo[a,h]anthracene, benzo[g,h,i]perylene, and indeno[1,2,3-c,d]pyrene) are considered when assessing the cancer risk to people from contaminated soils (CCME 2010; Perera 1997). Many other PAHs, especially the alkyl-substituted PAHs are known or suspected carcinogens, but are not routinely included in cancer risk assessment from contaminated soil. Ingestion of soil is a major route of exposure at most contaminated sites and is particularly relevant to children due to their hand-to-mouth activities and relatively smaller body mass, which increases their risk (Calabrese et al. 1999). Since PAHs are commonly present in complex mixtures that each demonstrate a unique potency, the total carcinogenic risk due to PAHs is frequently expressed as total benzo(a)pyrene (BaP) equivalents, which calculates PAH exposure according to the relative carcinogenic potency to benzo(a)pyrene (Collins et al. 1998).

Accurate estimation of PAH oral exposure (e.g. due to incidental soil ingestion) requires determination of the fraction of ingested PAHs that are absorbed into systemic circulation (i.e., bioavailability). However, intestinal absorption of PAHs appears to vary widely. A review of the bioavailability of various orally ingested PAHs showed PAH bioavailability to range between 6 - 100%, depending on dose, vehicle, and animal species (Ramesh et al. 2004). Additionally,

bioavailability varies among individual PAH compounds. For example, phenanthrene bioavailability (86%), measured using an *in vivo* swine model, is greater than benzo(a)pyrene bioavailability (31%) (Cavret et al. 2003). In this same study, phenanthrene bioaccessibility, an *in vitro* surrogate for bioavailability, was greater than the bioaccessibility of benzo(a)pyrene (Cavret et al. 2003). The intestinal absorption of PAHs is thought to occur via one of two pathways: passive diffusion as was shown using the Caco-2 human colorectal carcinoma cell line (Vasiluk et al. 2007), and bile-dependent absorption (Rahman et al. 1986). The bile-dependent absorption pathway is likely linked to the role of bile constituents in mobilizing PAHs from soil into micelles (Van de Wiele et al. 2004; Khan et al. 2008).

Contaminant bioaccessibility can be used to estimate bioavailability from soils. Bioaccessibility is defined as the fraction of contaminant in soil that can be mobilized from soil particles and is potentially available for uptake into systemic circulation. Thus, bioaccessibility will never be less than bioavailability and as a result can act as a conservative estimate of bioavailability where resources prevent the use of animal models to measure bioavailability. The *in vitro* bioaccessibility of ingested environmental contaminants can be estimated using *in vitro* digestion models. The most studied of these digestors is the Physiological Based Extraction Test (PBET). PAH bioaccessibility determined with this method ranges from: 27-53% (Khan et al. 2008), 9-69% (Tang et al. 2006), and 15-63% (Lu et al. 2010). Studies using other digestors indicate similar ranges, with PAH bioaccessibility ranging from 29% using the Simulator of the Human Intestinal Microbial Ecosystem (SHIME) to 36% using the Fed ORganic Estimation human Simulation Test (FOREhST) (Cave et al. 2010). However, to the authors' knowledge, no such PAH bioaccessibility exists for the Relative Bioaccessibility Leaching Procedure (RBALP) model currently in use by industry (Drexler and Brattin 2007; Smith et al. 2010).

PAHs are a class of lipophilic organic contaminants with relatively high octanol to water partitioning coefficients (K_{ow}), which indicates a tendency to partition into lipophilic phases. Since the lipid membrane of intestinal enterocytes can be viewed as a lipophilic phase, the intestinal epithelium is likely to act as a lipid sink for PAH absorption. However, most *in vitro* bioaccessibility models do not routinely include a lipophilic phase and, therefore, may underestimate PAH bioaccessibility. It has been suggested that *in vitro* models should include a lipophilic membrane for lipophilic compounds, as the driving force for uptake from soils is the fugacity gradient that exists between the gastrointestinal fluid and the lipophilic membrane (Vasiluk et al. 2007). Similarly, *in vitro* work using the SHIME model for PAH bioaccessibility found that individual PAH bioaccessibility was correlated with the fugacity capacity of octanol (Siciliano et al. 2010).

In order to be useful for human health risk assessment, *in vitro* bioaccessibility models must be linked to results obtained using an *in vivo* model. Swine are often used to model human digestion due to the many similarities between the gastrointestinal (GI) tracts of juvenile swine and toddlers (Miller and Ullrey 1987). The GI tract of swine is anatomically similar to that of humans, with analogous intestinal divisions, organ sizes and cell types (Patterson et al. 2008). Swine also have similar nutritional requirements as humans (Cooper et al. 1997). These similarities have made swine an accepted model for assessing the bioavailability of lead and arsenic in soil (Rodriguez and Basta 1999; Juhasz et al. 2008; Casteel et al. 1997; Lavelle et al. 1991). More recently, the swine model has been extended to include organic contaminants including dioxins (Budinsky et al. 2008) and PAHs (Cavret et al. 2003).

In the present study, we compare the bioavailability of PAHs in soils from eight different contaminated sites, measured using juvenile swine, with the bioaccessibility of PAHs from the

same soils according to two *in vitro* gastrointestinal models, to evaluate the use of *in vitro* PAH bioaccessibility for the human health risk assessment of PAH-contaminated soils. Additionally, we compare the PAH bioaccessibility with and without the addition of a C18 membrane to determine if a lipid sink improves the ability of *in vitro* models to predict the bioavailability of PAHs *in vivo*.

4.2 Materials and Methods

4.2.1 Soils

A total of eight contaminated soils were obtained from various sites in Sweden (n=5) and Canada (n=3) (**Table 4.1**). Altogether there were three soils from wood preservation sites (WP), three soils from gas works sites (GW), and two soils from petroleum hydrocarbon contaminated (PHC) sites. All soils were air-dried at room temperature for at least 24 hours and sieved through a 45 µm mesh before subsequent testing. Previous studies evaluating the release of PAHs from soils often used a 250 µm mesh (Cave et al. 2010; Tang et al. 2006; Lu et al. 2010). The <250 µm size fraction is thought to better estimate human exposure than bulk soil (Duggan et al. 1985). However, more recent research indicated that the <45 µm size best approximates the fraction of soil that adheres to hands (Siciliano et al. 2009; Yamamoto et al. 2006). Soil pH, soil organic carbon and particle size were analyzed as previously described (Siciliano et al. 2009).

4.2.2 PAH Extraction

Accelerated Solvent Extraction (ASE) was used to extract PAHs from the soil (Lundstedt et al. 2000). Approximately 1 g of soil was weighed into hexane rinsed ASE cells. The cells were filled with clean Ottawa sand and packed with an acetone-rinsed rod. Samples were extracted using a Dionex® Accelerated Solvent Extractor (ASE 200) which was run with an 80:20 mix of hexane: dichloromethane. The cells were extracted at 2030 psi and 150˚C with a heat up time of 7 min and a static time of 5 min. Cells were purged for 1 min with 2 cycles per cell and a 10%

flush volume. The solvent collected was evaporated to near dryness and re-suspended in 2 mL acetonitrile. Samples were then syringe filtered through Whatman Glass Micro-Fibre (GMF) 0.45 µm filters into labeled 2 mL amber HPLC vials. All soils were extracted five times.

4.2.3 C18 Membrane

Circular octadecyl carbon (C18) solid phase extraction membranes (Empore Line 2215, 3M Company, Minneapolis, MN), as previously used by Hurdzan et al. (2008) as a lipophilic sink for assessing the bioaccessibility of phenanthrene, were chosen to act as the lipid sink in the *in vitro* digestors. The C18 membranes have a diameter of 47 mm and an inner matrix of polytetrafluoroethylene. The C18 membranes were conditioned immediately prior to use following the procedures of Hurdzan et al. (2008).

After incubation of the C18 membranes in the *in vitro* digestors, absorbed PAHs were extracted using vacuum filtration. Membranes were placed in the center of the apparatus with 10 mL of methanol, and vacuum was applied to elute the methanol. The process was repeated with two additional 10-mL aliquots of methanol, and the pooled methanol was evaporated to near dryness and re-suspended in 2 mL of acetonitrile. The extracts were syringed filtered using Whatman GMF 0.45 µm filters into labelled 2-mL amber HPLC vials and stored at -20°C until analysis.

4.2.4 In Vitro Digestion model (IVD)

The IVD used was similar to the OSU-IVG described by Basta et al. (2007), and the protocol followed that of Laird et al. (2007) for the gastric and small intestinal stages, except all equipment and tools used were made out of glass and all glass material was pre-cleaned using methanol followed by acetone. Approximately 0.3 g of soil were transferred into a 125 mL pre-cleaned pre-weighed amber glass jar along with 30 mL of gastric fluid (12 M HCl in DI-water at pH 1.4). The pH was corrected to 1.50 ± 0.02 with drop-wise addition of 0.5M HCl and the

samples were incubated and shaken for two hours at 37°C and 70 rpm. For the small intestinal phase 15 mL of small intestinal solution (containing 12.5g L^{-1} NaHCO3, 6 g L^{-1} Oxgall bile, and 0.9 g L^{-1} porcine pancreatin powder) were added to the samples and the pH was corrected to 6.5 ± 0.15 via drop-wise addition of 0.5M HCl. The final mass of the jar was recorded to calculate the total amount of fluid added. A C18 membrane was added to the samples requiring the addition of a lipid sink, and anaerobic conditions were created by allowing nitrogen gas to flow through the jars for 30 minutes. The samples were incubated and shaken again for two hours at 37°C and 70 rpm. A 15-mL aliquot of the supernatant was filtered using Whatman GMF 0.45 µm filters and stored at -20°C until analysis.

4.2.5 Relative Bioaccessibility Leaching Procedure (RBALP)

The RBALP method was similar to that used by Smith et al. (2010). Approximately 1 g of soil was transferred into a 125 mL pre-cleaned glass bottle along with 100 mL of gastric fluid (0.4 M glycine solution at pH ~ 1.5). The gastric fluid was prepared following the procedures of (Drexler and Brattin 2007). The samples were then added to the RBALP apparatus, which can hold up to ten samples. Inside the apparatus the samples are submerged in a water bath at 37°C while being rotated end over end at 30 rpm for 1 hour. An additional stage has been added to the RBALP to act as an intestinal component where the samples are removed from the apparatus and the pH of each bottle was adjusted to 7.0 ± 0.2 with NaOH (50% w.w., trace metal grade). After the pH adjustment, 175 ± 20 mg of bile (bovine, mixture of 50% free and conjugated bile acids) and 50 ± 10 mg of pancreatin (porcine, activity equivalent to 8 x U.S.P. specifications) were added to each extraction bottle. The C18 membrane was added to the appropriate test units, and bottles were recapped and returned to the extractor for an additional four hours, submerged in water at 37°C and rotated end over end at 30 rpm. The samples were then removed from the

apparatus and a 15-mL aliquot of the supernatant was syringe filtered using 0.45 µm cellulose acetate filters and stored at -20°C until analysis.

4.2.6 Animals and Pilot Study

Swine (female Landrace cross, 7-8 weeks of age) were obtained from the Prairie Swine Centre in Saskatoon, Saskatchewan and housed in the Animal Care Unit of the Western College of Veterinary Medicine, University of Saskatchewan. Swine were randomly allocated to control (n=5) and treatment (n=24) groups, and maintained on ad libitum standard grower ration and water. Animals were allowed to acclimate for one week prior to initiation of the study.

A pilot study was conducted to determine if PAH uptake from soil exhibited dose dependent kinetics. A certified reference soil (CRM140-100 Resource Technology Corporation Lot 010572) was used for this portion of the study. Animals in three treatment groups (n=2 each) were dosed orally with 2, 5, and 10 g of soil in a dough treat, consisting of a mixture of flour, corn syrup, water and flavouring. Previous work in our lab indicated that there is a comparable amount of PAHs found in serum and whole blood throughout the time course study; therefore we found that serum is an acceptable surrogate for whole blood because of the difficulties associated with processing whole blood containing anticoagulants. As well, PAH concentration peaked at 2-3 hours after a single oral dose of contaminated soil in swine, and that serum concentration was correlated with total body parent PAH concentration (unpublished). Therefore, at 2 hours post dosing, pigs were weighed and euthanized with a captive bolt gun. The brachial artery was severed immediately after euthanasia and 50-100 ml of blood was collected into an I-CHEM jar (125 mL straight side, certified clean amber glass jar, VWR). Blood samples were allowed to clot at room temperature overnight, and were centrifuged at 3000 g for 10 minutes to facilitate the separation of serum. Serum was immediately decanted into a new I-CHEM jar following centrifugation. Samples were stored in the dark at 4˚C prior to extraction.

4.2.7 Swine Study

Swine in the treatment groups were dosed orally with 5 g of soil in a dough treat (Casteel et al. 1997), consisting of a mixture of molasses, oats, flour and pig feed. Negative control animals were dosed with dough treats only. Treatment groups (n=3 pigs per group) received one of eight different soils. These soils contained a variety of concentrations of the nine PAHs of interest. Only two pigs were dosed with the PHC2 soil as it had a very strong diesel odour and one of the pigs refused to eat it. Animals were euthanized and serum samples were collected as in the pilot study.

4.2.8 Solid Phase Extraction

In order to remove any impurities, all fluid samples were extracted using Solid Phase Extraction (Hennion 1999) with Waters® Oasis HLB columns (Waters Corporation, Milford MA). Approximately 5 mL of filtered fluid was transferred into a vial and weighed. Acidified deionized water (10 mL of 0.3 M H_2SO_4) was added to the sample and the sample vial was reweighed. The cartridges were conditioned first with 2 mL of Milli-Q water, then with 2 mL of methanol. The sample (10 mL) was run through the column, rinsed with 2 mL of methanol, and eluted with 9 mL of acetonitrile into a new vial. The eluate was evaporated to near dryness, re-suspended in 2 mL of acetonitrile and filtered using Whatman GMF 0.45 µm filters into a 2 mL labelled amber HPLC vials.

4.2.9 High Pressure Liquid Chromatography (HPLC)

Prepared samples were analyzed with High Pressure Liquid Chromatography coupled with Fluorescence Detection (HPLC-FD) to quantify PAH concentration (Marriott et al. 1993). A 10 µL aliquot of each sample was injected onto a Varian PAH Pursuit (3 µm particle size, 100 mm length and 4.6 mm inner diameter) column guarded with a Varian MetaGuard 3 µm C18 4.6 mm column. The column was maintained at 28˚C using a column heater. The runtime was set to 30

minutes and acetonitrile and HPLC grade water were used as solvents. The solvent flow was 1 mL min^{-1} with a starting gradient of 60:40 acetonitrile:water. After 3 minutes, the acetonitrile: water ratio was gradually increased until, 10 minutes later, 100% acetonitrile was flowing through the column. After a further 7 minutes, the solvent ratio was returned to 60:40 acetonitrile:water for the remainder of the run. The HPLC was calibrated with an external standard to estimate the quantity of PAH in each injection.

4.2.10 Fugacity Analysis

The fugacity capacity of soil (Z_{soil}) was calculated as described by Mackay (2001):

$$Z_{soil} = \frac{\text{Solubility}}{\text{Vapour Pressure}} \times \text{Soil organic carbon} \times K_{oc} \times \text{Soil particle density} \quad (1)$$

The solubility, vapour pressure and the organic carbon partitioning coefficient (K_{oc}) of the PAHs were obtained from Shiu and Mackay (1997) and ATSDR (1995). Soil organic carbon was determined following the methods of Siciliano et al. (2009). The soil particle density was assumed to be 2.65. Similarly, the fugacity capacity of water (Z_{water}) was calculated as:

$$Z_{water} = \frac{solubility}{vapour\ pressure} \quad (2)$$

4.2.11 Quality Assurance and Control

Coronene was used as an internal standard for the analysis of soils. Coronene (0.1µg) was added to each ASE vial and recovery averaged 90% with a standard deviation of 13%. Every 10th ASE vial was loaded with clean sand and extracted as a blank. For the *in vitro* digestors, every 5th digestor did not receive soil and acted as a blank. On average, approximately 0.05 µg of PAHs were present in blank digestors with C18 membranes present and 0.2 µg of PAHs were present in blank digestors without C18 membranes. Each soil was extracted by five replicate digestors. Spike recoveries for the digestors averaged 109%. Percent recovery from the C18 membranes was evaluated by spiking PAHs onto the C18 membranes and extracting the

membranes as described above. The recovery of PAHs from C18 membranes averaged 92%. Serum from control swine was also analyzed for background PAHs. Every serum sample and every tenth sample of simulated gastrointestinal fluid were extracted by SPE in duplicate as quality control. Every tenth SPE was run with water to act as a blank. PAH recovery from the SPE averaged 50%. The HPLC was calibrated with an external standard consisting of 10µg/mL of each PAH and the calibration was updated daily. On average, % deviation of analytical system duplicates for soil was 3%, swine was 17.5%, digestors were 7% for the RBALP and 21% for the IVD. The limit of detection for the HPLC analytical system was between 0.07 and 0.64 pg for the various PAHs.

4.2.12 Statistical Analysis

The Anderson-Darling test was applied to all data to test the assumption of normality. Data that were non-normal were log-normally distributed and therefore log-transformed prior to data analysis. Analysis of PAH content has been modified to express total BaP equivalents, which assumes the concentration of the various PAHs to be additive and calculated as one concentration. A list of the relative potency of each compound to benzo[a]pyrene is given in **Table 4.2**. Data were analyzed for significant difference using two-way analysis of variance ($\alpha = 0.05$), followed by the Tukey test.

4.3 Results

The total soil potency equivalency factors of the 8 soils used in the study ranged over three orders of magnitude, from 0.17 to 650 µg BaP equivalents g^{-1} soil. These values are close to the 10^{-6} and 10^{-5} risk based guidelines for Canada of 0.6 and 5.3 µg BaP equivalents g^{-1} soil respectively. Total PAH concentration and individual PAH concentration in soil showed no linear relationship with soil properties: organic carbon content ($r^2 = 0.016$, $p < 0.76$), soil pH (r^2

= 0.12, $p < 0.40$), sand content ($r^2 = 0.087$, $p < 0.48$), silt content ($r^2 = 0.001$, $p < 0.82$), or clay content ($r^2 = 0.03$, $p < 0.74$).

Table 4.1 Physical and chemical properties of bulk soils prior to being sieved to <45 µm.

Soil	Total Carcinogenic [PAHs] (µg BaP Equivalents g^{-1} soil)	Particle Size Composition (%)			Organic Carbon (%)	Soil pH
		Sand	Silt	Clay		
WP1	67	42	54	4	2.5	5.7
WP2	3.7	47	53	0	8.5	5.4
WP3	4.0	49	47	4	3.2	5.9
GW1	650	44	41	15	6.5	6.5
GW2	14	59	31	10	4.6	6.7
GW3	0.17	51	44	5	7.7	4.4
PHC1	0.47	62	30	8	5.5	6.7
PHC2	16	98	1.5	0.5	57	4.8

The addition of a C18 membrane significantly increased ($p < 0.05$) the total amount of BaP equivalents released from soil into simulated GI fluids for both the IVD and RBALP (**Figure 4.1**). PAH release (mean ± standard error of the mean) into the simulated gastrointestinal fluids of the IVD was 6.6×10^{-3} (SE=4.1×10^{-3}) µg BaP equivalents without the addition of C18 membrane. However, PAH release increased to 0.29 (SE=0.16) µg BaP equivalents in the presence of a C18 membrane. Similarly, PAH release using RBALP without a C18 membrane was 0.14 (SE=6.9×10^{-2}) µg BaP equivalents but increased to 0.67 (SE=0.37) µg BaP equivalents when the C18 membrane was added. The large variation observed for mean PAH release among soils was due to the large variation of PAHs found within the eight soils, from 0.17 to 650 µg BaP equivalents g^{-1} soil.

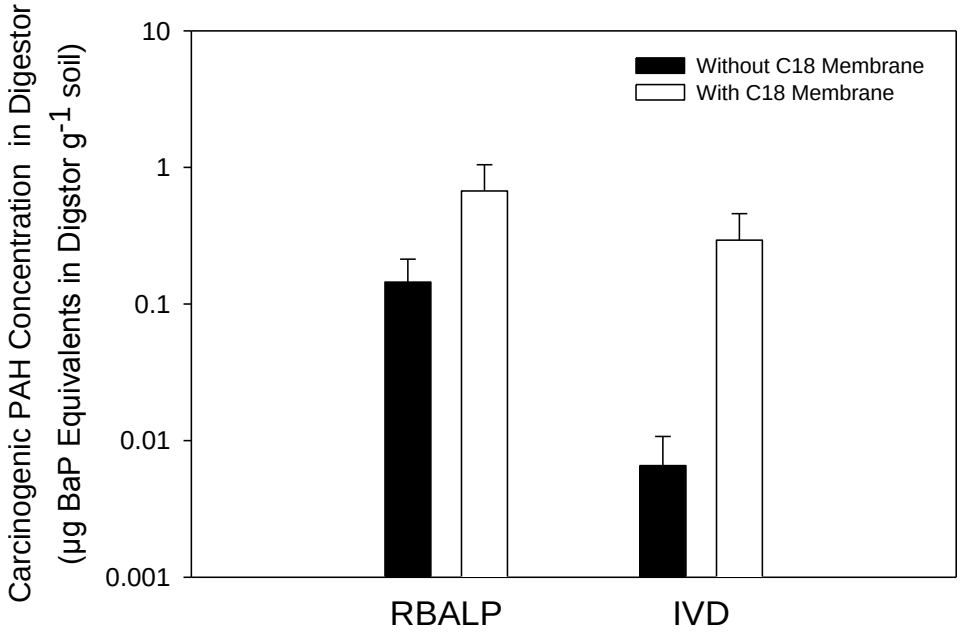

Figure 4.1 Comparison of the bioaccessiblity of PAHs from eight different contaminated sites using the Relative Bioaccessibility Leaching Procedure (RBALP) and the *In vitro* Digestor (IVD) in the presence or absence of a C18 membrane. PAH release was converted to BaP equivalents using Canadian Council of Ministers of the Environment guidelines to estimate the total potential cancer exposure from nine different PAHs. Each soil (n=8) was digested (n=4 or 5) and bars represent the geometric mean of the released PAHs. Error bars are the standard error of this mean.

Results of the pilot pig study using certified reference soil (CRM-140) indicated that the kinetics of PAH absorption from soil are dose-dependent for swine. As the amount of soil given to the pigs increased, (2, 5 and 10 grams of soil) the amount of PAHs found in the serum increased in a linear fashion (Serum Concentration = 4.3 Soil Mass + 1.1, r^2=0.99). With this method, PAH bioavailability of CRM soil was determined to be 20%.

PAH bioaccessibility in the IVD, as calculated by µg BaP equivalent release in the presence of a C18 membrane, increased with increasing PAH bioavailability ($p<0.069$), as measured using a juvenile swine model (**Figure 4.2**). In contrast, no relationship was observed between PAH bioaccessibility measured using the RBALP with a C18 membrane and PAH bioavailability. Neither IVD ($r^2 = 0.03$) nor RBALP ($r^2 = 0.02$) PAH bioaccessibility correlated with PAH

bioavailability without the addition of C18 membrane to the *in vitro* gastrointestinal model. Release of BaP equivalents in the RBALP model was correlated with BaP equivalents found in soil ($r^2 = 0.89$, $p < 0.001$), whereas the IVD had a weaker correlation with BaP equivalents found in soil ($r^2 = 0.42$, $p < 0.053$). As a result of the strong link between the RBALP and BaP equivalents found in soil, the RBALP has a lower PAH bioaccessibility compared to the IVD (**Table 4.3**). The RBALP has higher bioaccessibility for soils with lots of BaP equivalents leading to greater BaP equivalents released on average. The IVD has higher bioaccessibility for soils with less BaP equivalents and when averaging across the eight soils the IVD bioaccessibility (6.0%) is greater than RBALP bioaccessibility (3.8%).

Table 4.2 Carcinogenic potency equivalency factors relative to benzo[a]pyrene according to Canadian Council of Ministers of the Environment (CCME)

PAH	Potency Equivalency Factor
Benzo[a]anthracene	0.1
Benzo[a]pyrene	1
Benzo[b]fluoranthene	0.1
Benzo[ghi]perylene	0.01
Benzo[k]fluoranthene	0.1
Chrysene	0.01
Dibenzo[ah]anthracene	1
Indeno(1,2,3-cd)pyrene	0.1

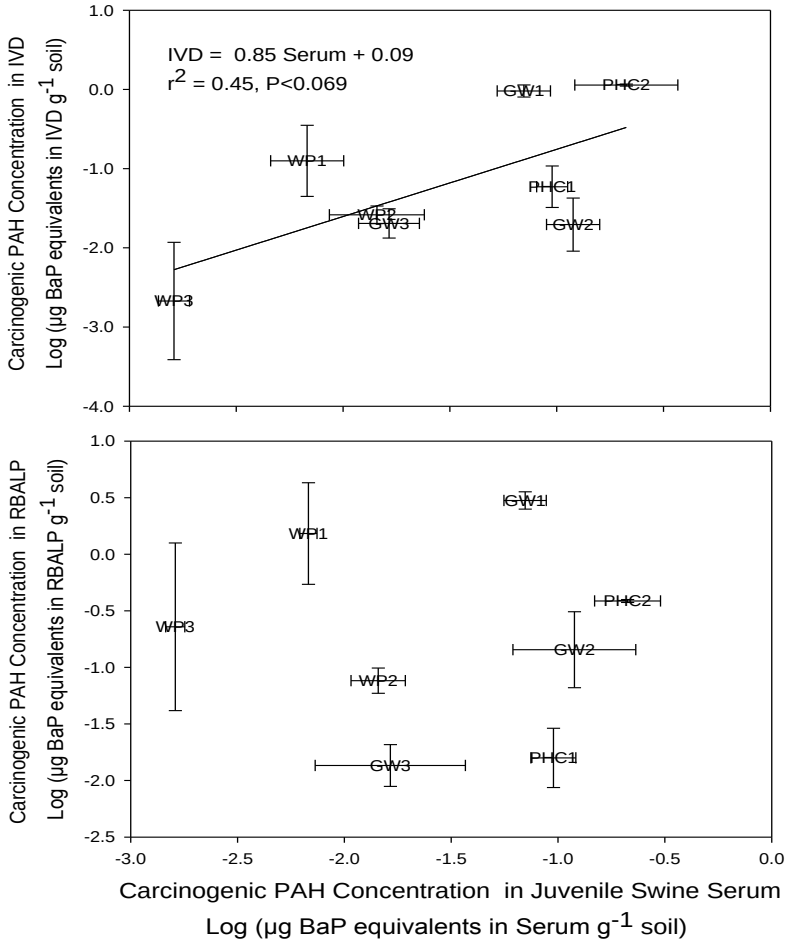

Figure 4.2 Comparison of the PAHs released in the IVD (top) or RBALP (bottom panel) model in the presence of a C18 membrane to PAHs present in swine serum using eight soils. Soils are labelled as to the source of contamination: WP=Wood Preservation Facility, GW=Gas Works Facility, PHC=Inadvertent hydrocarbon release. Comparison of the PAHs released in the swine model to PAHs released in the RBALP model (bottom) using eight soils. PAH release was converted to BaP equivalents using Canadian Council of Ministers of the Environment guidelines to estimate the total potential cancer exposure from nine different PAHs. Each point represents the geometric mean (n= 4 or 5) from each soil for the in-vitro models and n=3 for each soil for the *in vivo* models. Error bars are standard error of this mean.

PAH release in the *in vitro* digestors appeared to plateau for soil from two sites, GW1 and PHC2 (**Figure 4.2**). To investigate whether the C18 membranes were becoming PAH-saturated for soil samples GW1 and PHC2, the release of PAHs in digestors containing two C18 membranes was compared to digestors with one C18 membrane. Samples with two C18 membranes showed no significant difference in PAH content for soils GW1 and PHC2 compared

to samples with one C18 membrane (P<0.90). Samples with one C18 membrane released 1.0 ug BaP equivalents g^{-1} soil (Stdev = 0.63, n=10) compared to 0.97 ug BaP equivalents g^{-1} soil (Stdev = 0.27, n=6) for soil samples incubated with two C18 membranes.

Table 4.3 In vitro bioaccessibility and in vivo bioavailability of the eight soils used in this study. Soils are labeled as to the source of contamination: WP=Wood Preservation Facility, GW=Gas Works Facility, PHC=Inadvertent hydrocarbon release. Value are the average of n=5 digestions for the IVD and RBALP and n=3 for In Vivo.

Soil	IVD - PAH Bioaccessibility (% BaP equivalents) [1]	RBALP - PAH Bioaccessibility (% BaP equivalents) [1]	In Vivo Bioavailability of PAHs (% BaP equivalents) [1]
WP1	0.2 (0.1)	2.3 (0.2)	0.03 (0.03)
WP2	0.7 (0.4)	2.1 (0.3)	0.41 (0.1)
WP3	0.4 (0.1)	5.8 (0.6)	0.29 (0.2)
GW1	0.1 (0.02)	0.5 (0.2)	0.01 (0.002)
GW2	0.1 (0.1)	1.0 (0.6)	1.5 (1.0)
PHC1	13 (2.6)	3.4 (1.0)	29 (16)
PHC2	7.2 (2.3)	2.5 (0.9)	1.3 (0.01)
GW3	12 (3.0)	7.9 (3.6)	10 (2.2)

[1] Standard error in parentheses

Uptake of BaP equivalents in the swine model can be predicted using fugacity capacity of soil (Z_{soil}) but not concentration of PAHs in soil (**Figure 4.3**). As Z_{soil} increases there is an increase of BaP equivalents in the serum ($r^2 = 0.45$, $p<0.06$). However one soil, PHC2, had excessive leverage and when removed from data analysis the relationship is weaker ($r^2 = 0.36$, $p<0.15$). In order to compare Z_{soil} with BaP equivalents absorbed, the Z_{soil} for each individual PAH was multiplied by the appropriate potency equivalency factor given in **Table 4.2** to yield Z_{soil} in units of mol BaP equivalents m^{-3} Pa^{-1}. No single PAH dominated the relationship between fugacity capacity of soil and uptake into swine serum (**Table 4.4**). Sand and silt content in soil is correlated with organic matter content and thus, with fugacity capacity of soil ($r^2 = 0.88$). In this study, we used generic K_{oc} values which may not be representative for each individual PAH coming from the various soils used here. Using 114 historically contaminated sediments, Hawthorne et al. (2006) found that individual PAH K_{oc} values range between 2-3

orders of magnitude. Thus, our use of fugacity capacity here is limited to exploring the basis of PAH partitioning between soils and mammals, and likely should not be used to extrapolate to different soil types not studied here.

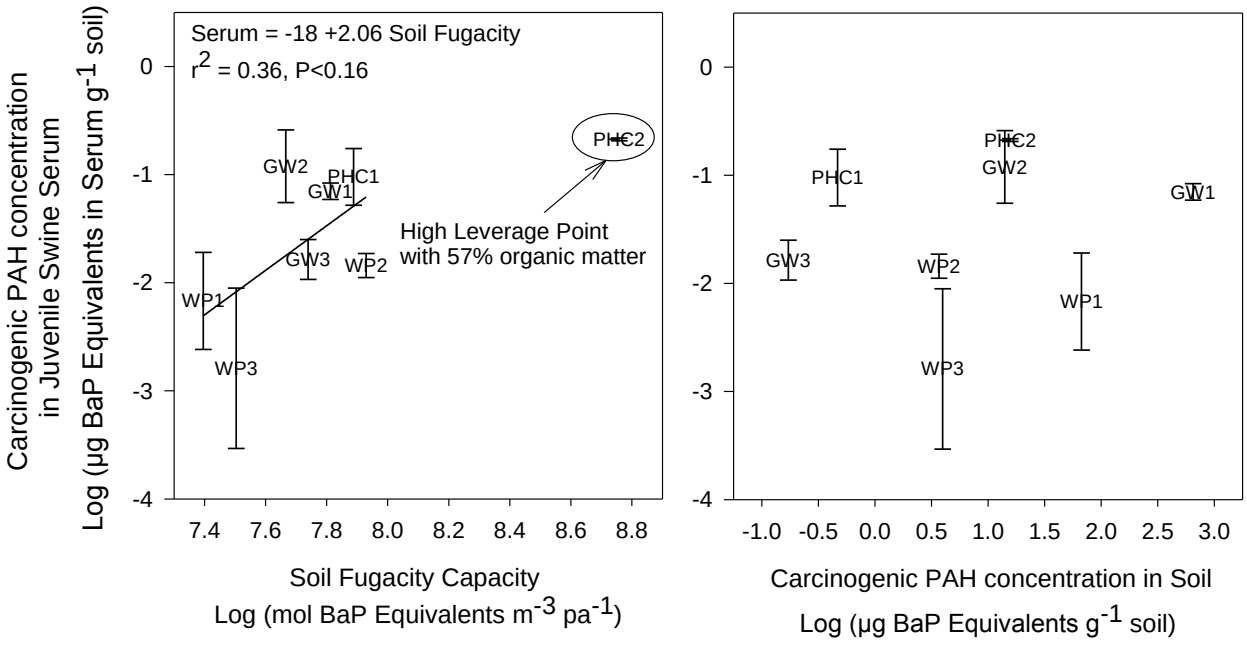

Figure 4.3 Comparison of PAHs released in the swine model to soil fugacity capacity (left) and PAH concentration in soil (right). Soil fugacity capacity was calculated using generic K_{oc} values according to ATSDR [39], rather than soil specific K_{oc} values. PAH release was converted to BaP equivalents using Canadian Council of Ministers of the Environment guidelines to estimate the total potential cancer exposure from nine different PAHs. Each point represents the geometric mean of each soil given to pigs (n=3). Error bars represent the standard error of this mean.

Bioavailability of individual PAHs can be predicted based on the water fugacity capacity of each PAH (**Figure 4.4**). A lower Z_{water} will lead to a lower partitioning into the intestinal fluid. However, the PAHs with low Z_{water} that do reach the intestinal fluid are more likely to be absorbed by the intestinal epithelial cells, as compounds with low Z_{water} tend to be more lipophilic. Supporting this, the octanol fugacity capacity is also linked to PAH bioavailability, although the relationship is not as strong (r^2=0.71, P<0.001). Thus, one can think of the

intestinal fluid as a bridge to the lipid sink of the intestinal epithelial cells. PAHs desorb from soil into the intestinal fluid and then are absorbed into the epithelium.

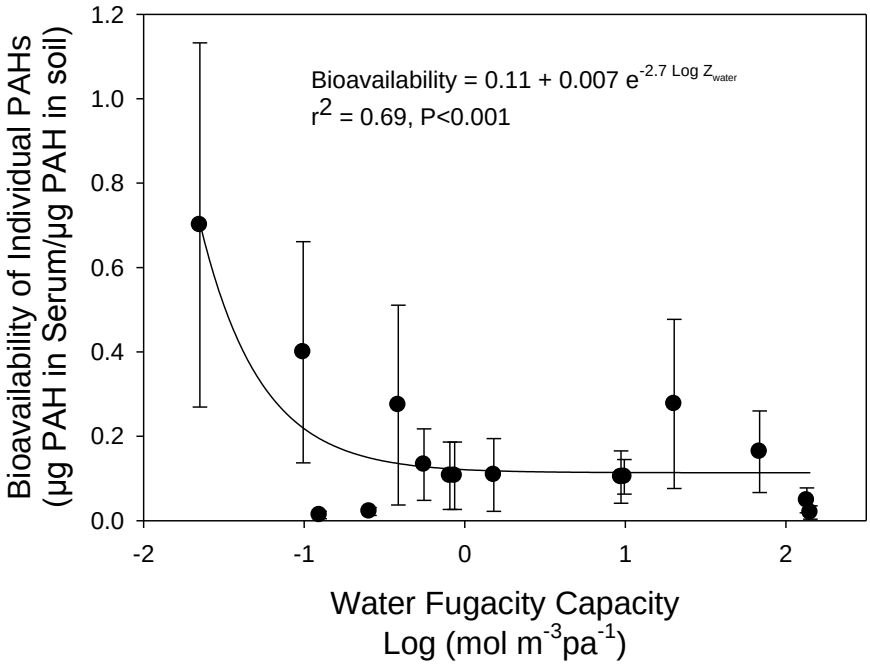

Figure 4.4 The average bioavailability of individual PAHs in pigs dosed with the eight soils compared to their water fugacity capacity. Bioavailability was calculated by dividing the total amount of the compound in the serum by the total dose of the compound given to the swine. Bioavailability values were averaged across the eight different soils and the error bars represent the standard error associated with the bioavailability in these soils.

4.4 Discussion

The results described herein indicate that the inclusion of a lipid sink, such as the C18 membrane used in this study, may be an essential component for GI models to accurately estimate PAH bioaccessibility of contaminated soils. This observation is a function of the hydrophobicity and poor water solubility of PAHs and is likely equally applicable to other high-K_{OW} contaminants such as dioxins and organochlorine pesticides. Additionally, these results are in agreement with research that showed up to 80% of phenanthrene spiked into organic matter became adsorbed onto a C18 Empore membrane when extracted using simulated GI fluids

(Hurdzan et al. 2008). In contrast, Vasiluk et al. (2008) demonstrated that maximal PAH dissolution from skim milk powder was not mediated by the presence of a lipid sink (Ethylene Vinyl Acetate or EVA thin film) but instead by the addition of $NaHCO_3$. It is as of yet unknown whether this discrepancy is due to the differences in lipid sink (i.e., EVA vs C18), exposure matrix (i.e., skim milk vs soil), or both.

Table 4.4 Relationship between bioavailability of PAHs and soil fugacity capacity across eight different soils.

PAH	Intercept[1]	Slope[2]	r^2
Naphthelene	-1.91 (0.83)	2.00 (1.2)	0.31
Acenaphthene	-5.99 (3.6)	1.74 (1.8)	0.13
Fluorene	-6.52 (1.9)	2.23 (0.91)	0.50
Phenanthrene	-6.03 (1.7)	1.39 (0.59)	0.48
Fluoranthene	3.43 (5.3)	-1.58 (1.3)	0.19
Anthrancene	-8.66 (2.7)	1.79 (0.89)	0.40
Pyrene	3.96 (4.9)	-1.60 (1.3)	0.19
Benzo(a)anthracene	-8.85 (5.4)	1.24 (0.98)	0.21
Chrysene	-12.7 (5.2)	2.09 (1.0)	0.40
Benzo(b)fluoranthene	10.1 (7.2)	-2.6 (1.5)	0.33
Benzo(k)fluoranthene	-9.68 (3.4)	1.76 (0.82)	0.44
Benzo(a)pyrene	-16.7 (7.1)	2.32 (1.1)	0.41
Dibenzo(ah)anthracene	-6.42 (14)	0.50 (1.7)	0.01
Benzo(ghi)perylene	-21.0 (11)	2.61 (1.6)	0.30
Indeno(123-cd)pyrene	-6.58 (4.6)	0.77 (0.60)	0.21

[1] Standard error in parentheses
[2] The slope has units of Log µg BaP equivalents in Swine Serum per (Log mole BaP equivalents m^{-3} Pa^{-1}). Standard error of the slope is in parentheses.

The differences in results generated using the IVD and RBALP (**Table 4.3**) reflect the fact that bioaccessibility is operationally defined (Fendorf et al. 2004). Although both *in vitro* models utilized equivalent Liquid:Soil Ratios (100:1 – 150:1), simulated gastric (pH 1.5) and intestinal (pH 6.5 – 7.0) conditions, and used 0.45 µm filtration syringe filtration, substantial differences in shaking procedures and small intestinal residence times affected PAH bioaccessibility. For example, RBALP procedures required each experimental unit (i.e., digestor) to be rotated end over end at 30 rpm. In contrast, the IVD used a far less vigorous horizontal shaking procedure. In addition, the IVD used a considerably shorter small intestinal residence time of 2 hours whereas RBALP used 4 hours. The vigorous shaking in addition to the longer small intestinal residence time used by RBALP were sufficient to result in significant (up to 10-fold) increases in PAH bioaccessibility compared to the IVD. The aggressive RBALP shaking protocol likely led to the strong correlation between BaP equivalents in the soils and BaP equivalents released in RBALP but not the IVD. We interpret this to suggest that PAH dissolution processes may have been closer to their thermodynamic equilibrium for the RBALP but not the IVD extractions. As observed by Vasiluk et al. (2008), differences in PAH solubilization do not necessarily correspond to differences in PAH bioavailability; therefore, reaching equilibrium under simulated GI conditions is only desirable if also reached *in vivo*. Our *in vivo* results suggest that equilibrium is not reached *in vivo*. For example, there was no relationship between *in vivo* PAH bioavailability and BaP equivalents in the studied soils. However, based on our pilot study with a certified reference soil, we assume that all eight soils peak at approximately 2 hours post dosing. This was not confirmed for all eight soils and it may be possible that peak serum PAH concentrations are linked to PAH concentration in soil.

Comparing the RBALP and IVD models with the *in vivo* results suggests that since equilibrium is not reached *in vivo, in vitro* models should not necessarily use the most aggressive approach to extract PAHs from soils. Further research is required to ascertain how to best design *in vitro* GI models to most closely simulate *in vivo* conditions.

Table 4.5 Relationship between individual PAH release from *in-vitro* and *in-vivo* models in eight different soils sieved to 45 µM.

PAH	Swine Serum vs. IVD				Swine Serum vs. RBALP			
	Intercept[1]	Slope[2]	r^2	P	Intercept	Slope	r^2	P
Benzo(a)anthracene	0.08	0.95	0.32	0.14	1.10	-0.99	0.01	0.89
Chrysene	0.01	0.63	0.45	0.07	0.55	4.17	0.07	0.54
Benzo(b)fluoranthene	0.04	1.84	0.10	0.45	0.15	29.44	0.58	0.03
Benzo(k)fluoranthene	0.03	0.77	0.41	0.09	0.10	-0.34	0.01	0.83
Benzo(a)pyrene	0.02	1.31	0.32	0.14	0.47	0.52	0.01	0.95
Dibenzo(ah)anthracene	0.14	1.03	0.02	0.71	0.03	-0.32	0.01	0.91
Benzo(ghi)perylene	0.02	-8.01	0.08	0.50	0.02	-5.24	0.05	0.61
Indeno(123-cd)pyrene	0.01	0.0006	0.01	0.96	0.15	-0.15	0.08	0.49

[1]An intercept is fit because of background PAHs present in serum.
[2]The slope has units of Log [PAH] concentration per gram of soil in digestor per Log [PAH] concentration per gram of soil in swine serum

The bioaccessibility of soil PAHs in this study were comparatively lower than those described by Ramesh et al. (2004), 6 – 100%. The low PAH bioaccessibilities reported herein are likely due to the fact that fasted conditions were employed in both the IVD and RBALP. Previous publications indicated that the use of fed conditions increases measures of PAH bioaccessibility using *in vitro* GI models (Oomen et al. 2000; Hack and Selenka 1996). Additionally, PAH bioaccessibility tends to be lower for the small size fraction (<45 µm) employed in the current study (Siciliano et al. 2010). Thus, the PAH bioaccessibilities reported herein are a function of the fasted conditions of the IVD and RBALP and the use of a small particle size fraction for the contaminated soils. Notably, although the swine were not fasted

prior to PAH exposure, PAH bioaccessibility measured using the fasted IVD model was closely linked to *in vivo* bioavailability with a slope of 0.85.

It is not immediately clear whether PAH bioaccessibility should be expressed in terms of BaP equivalents (as performed in this study), summed according to the total µmol of PAHs released, or left in terms of individual PAHs. The relationship between *in-vitro* and *in-vivo* release of individual carcinogenic PAHs is displayed in **Table 4.5**. BaP equivalents is a convenient manner in which to express the hazards posed by human exposure to a mixture of PAHs since each share the same mode of toxic action with varying potencies (Collins et al. 1998). Thus, BaP equivalents approach integrates an individual's exposure to a chemical mixture by weighting the calculation towards more potent PAHs (e.g., benzo[a]pyrene and dibenzo[ah]anthracene; potency equivalency factor = 1) while putting less weight on less potent PAHs (e.g., phenanthrene and fluoranthene; potency equivalency factor = 0.001). The authors admit, however, that the BaP equivalent approach to the calculation of PAH bioaccessibility is not without its challenges. For example, the use of the BaP equivalent approach blurs the line between the exposure and toxicity characterizations, typically performed separately during human health risk assessment. In addition, the BaP equivalent approach for the calculation of bioaccessibility is inappropriate for PAHs that do not share the same mode of toxic action (e.g., naphthalene). Therefore, naphthalene bioaccessibility should be reported in addition to measures of BaP equivalent bioaccessibility of PAHs. The minimum, mean, 90^{th} percentile, and maximum bioaccessible/bioavailable of each individual PAH is displayed in **Table 4.6**.

From data presented in this study, the addition of a C18 membrane as a lipophilic phase significantly increases the amount of PAHs released in the in-vitro models. In the case of the IVD model, the C18 membrane improves the correlation between BaP equivalents released and

BaP equivalents absorbed in the swine model, suggesting that *in vitro* models may require the addition of a lipophilic phase to improve the accuracy of bioaccessibility estimates of organic contaminants.

Table 4.6 Minimum, mean, 90th percentile, and maximum values of bioaccessibility from the IVD and RBALP models as well as the bioavailability from the juvenile swine model for the PAHs analyzed here.

PAH	µg BaP equivalents[1]	IVD[2]				RBALP[3]				Swine[4]			
		Min	Mean	90th Percentile	Max	Min	Mean	90th Percentile	Max	Min	Mean	90th Percentile	Max
Naphthelene	0	1.4	46.6	82.0	90.8	1.6	12.7	26.7	50.1	0	43.1	77.7	78.4
Acenaphthene	0	10.0	49.9	82.3	86.4	2.4	16.6	43.4	67.2	0	0.3	0.7	0.8
Fluorene	0	0.1	23.9	70.2	115.6	6.5	21.8	41.1	53.1	0	19.8	58.8	96.8
Phenanthrene	0	0	0.4	1.1	2.3	0.8	3.8	9.1	12.5	0	3.2	10.4	11.2
Anthrancene	0	0	14.6	35.7	93.3	0.2	3.7	8.2	12.4	0	7.7	25.4	37.2
Fluoranthene	0	0	4.2	10.4	25.4	0	0.8	2.0	2.0	0	3.7	9.7	27.9
Pyrene	0	0.7	12.4	29.4	35.6	0.3	11.0	26.9	31.8	0	0.5	1.8	3.0
Benzo(a)anthracene	0.1	0	6.8	17.7	40.5	0.5	6.4	12.1	22.1	0	1.0	2.7	3.4
Chrysene	0.01	0	14.7	36.1	111.1	0.6	15.0	32.9	91.1	0	2.2	5.1	13.2
Benzo(b)fluoranthene	0.1	0	1.3	3.2	6.2	0.3	4.5	11.1	17.1	0	0.1	0.2	0.4
Benzo(k)fluoranthene	0.1	0	23.7	87.0	92.1	0.1	5.73	15.7	27.0	0	14.1	44.3	59.4
Benzo(a)pyrene	1	0	5.0	15.1	23.4	0.1	2.8	6.6	8.1	0	10.4	29.8	65.9
Dibenzo(ah)anthracene	1	0	3.4	9.2	15.4	0.2	5.4	12.7	30.8	0	9.3	26.6	50.3
Benzo(ghi)perylene	0.01	0	0.7	1.8	2.5	0	1.1	2.5	4.3	0	0	0.1	0.3
Indeno(123-cd)pyrene	0.1	0	0.1	0.4	0.8	0.1	2.4	5.3	6.2	0	0.2	0.6	1.3

[1] Relative potency equivalency factors according to Canadian Council of Ministers of the Environment.
[2] Bioaccessibility from the IVD was calculated as: (amount recovered in fluid + amount recovered from C18 disk) ÷ total amount in soil
[3] Bioaccessibility from the RBALP was calculated as: (amount recovered in fluid + amount recovered from C18 disk) ÷ total amount in soil
[4] Bioavailability from swine was calculated as: amount found in serum ÷ total amount in soil dosed

5 SYNTHESIS

Human health risk assessments use standardized guidelines to ensure consistency among results between many sites. PQRA utilize conservative exposure estimates as a failsafe to prevent excessive exposure to potentially harmful substances. This conservatism can lead to inaccuracies in exposure and risk assessment and therefore lead to costly yet unnecessary cleanup efforts. Generally speaking, it is believed that the risk associated with soil inhalation exposure is thought to be negligible when comparing to ingestion and dermal absorption (Granero and Domingo 2002; RIVM 2001). However the plasticity of SSRA allows risk assessors to incorporate modifications to exposure estimates if sufficient research warrants such action (Health Canada 2004a). One of the key concepts in SSRA is to use *in vitro* bioaccessibility models to obtain more realistic relative bioavailability estimates when assessing exposure (Richardson et al. 2006). The *in vitro* bioaccessibility models can provide useful information that prevents the inefficient spending of resources. To address these key issues in risk assessment this research project investigates if the inhalation of soil particles is relevant in terms of risk assessment, the effect of paving roads on soil inhalation and if current *in vitro* bioaccessibility models provide accurate estimates of *in vivo* PAH release.

5.1 Principle Findings

The inhalation of soil particles was found to be a relevant exposure pathway, particularly in terms of carcinogenic risk (**Figure 3.5**). Soil inhalation as a relevant pathway is a function of a few contributing factors. Soil particles were the major source of airborne particulate matter in Iqaluit and this is observed with the decrease in particulate matter after paving roads (**Figure 3.3**). After paving roads the TSP concentration in Iqaluit was reduced from 85 ± 56 µg m^{-3} to 15 ± 14.4 µg m^{-3} and the PM_{10} concentration was reduced from 35 ± 17 µg m^{-3} to 6.5 ± 6.0 µg m^{-3}. In Iqaluit there is a higher concentration of contaminants within the fraction of soil that is re-

suspended (Chow et al. 1994; Clairborn et al. 1995; Siciliano et al. 2010; Siciliano et al. 2009). Although the exposure from the combined inhalation pathways was still generally lower than the direct ingestion of soil, the lower TDI and greater CSF values offset the greater exposure from soil ingestion. Thus there was a significant risk from the inhalation pathway.

Paving roads was found to be an effective method of reducing the risk from soil inhalation. Paving roads reduces the airborne concentration of contaminants by 25-75 %, with two outliers, Hg reduction the least at 13% and Ba reduction the greatest at 96% (**Figure 3.4**). As a result of reduced airborne concentrations carcinogenic (**Figure 3.5**) and non-carcinogenic risk is reduced (**Table 3.2**). Although the soil may not be the primary source for all airborne contaminants (**Figure 3.1**), the soil still contributes to the airborne concentration, and by reducing the re-suspension of soil particles, carcinogenic risk from both Cd and Be is reduced (**Figure 3.5**), which suggests that paving roads may be an alternative for reducing exposure even if the soil isn't the primary source.

Current *in vitro* bioaccessibility models are potentially reporting inaccurate estimations of the relative bioavailability for PAHs. Results from **Figure 4.2** show that the inclusion of a C18 membrane improves the correlation between the *in vitro* IVD and *in vivo* swine models for PAH release. Furthermore, the addition of a C18 membrane significantly ($p < 0.05$) increased the amount of BaP equivalents released into the simulated GI fluids (**Figure 4.1**), suggesting that *in vitro* models that do not include a lipophilic phase may be under-estimating the relative bioavailability. The correlation between *in vivo* PAH release and uptake to the fugacity capacity of both soil (**Figure 4.3**) and water (**Figure 4.4**) indicates that the concept of fugacity may play a key role in understanding what drives the bioavailability of PAHs in soil.

5.2 Discussion

The research presented above indicates that there are obvious research gaps in the area of HHRA. In total there are five particular areas that have been addressed here: concentration of respirable particulate matter from soil, relative risk from the inhalation and ingestion of particulate matter, implications of particle size on human exposure, the importance of validating *in vitro* models, and elucidating factors affecting PAH bioavailability/bioaccessibility.

The current risk assessment guidelines for estimating soil inhalation exposure can over-estimate and under-estimate exposure from soil inhalation. The assumption from the guidelines is that vehicle traffic on unpaved roads creates approximately 250 µg PM_{10} m^{-3} from soil particles (Health Canada 2004a) and compared to the 35 µg PM_{10} m^{-3} found in Iqaluit (**Figure 3.3**), the PM_{10} concentration is vastly over-estimated especially considering that there are additional PM_{10} sources in Iqaluit (**Figure 3.1**). Conversely, and of greater concern, if there are no unpaved roads the assumption is that there is approximately 0.76 µg PM_{10} m^{-3} which is much lower than the 6.5 µg PM_{10} m^{-3} reported here, although it is unlikely that this value is comprised entirely of soil particles. According to Brook et al. (1997) soil derived particles across all sites on average in Canada accounts for approximately 50% of the coarse fraction (PM_{10}), and from the same study the average PM_{10} concentration is 27 µg m^{-3}; using these values soil derived particles contribute approximately 13.5 µg m^{-3} (27 µg m^{-3} x 50% = 13.5 µg m^{-3}), which is a 1780% ([13.5 µg m^{-3} / 0.76 µg m^{-3} x 100%] = 1780%) increase compared to the standard guideline (Health Canada 2004a). While it is important for PQRA to be conservative, 250 µg PM_{10} m^{-3} is not a concern, but the 0.76 µg PM_{10} m^{-3} assumption is certainly under-estimating exposure and risk assessors may be forced to re-think the way they evaluate soil inhalation.

While some risk assessments do not include soil inhalation (Poggio et al. 2008; Guney et al. 2010) citing that it is insignificant to the combined soil ingestion and dermal absorption

pathways (Granero and Domingo 2002; RIVM 2001), the research presented here shows that soil inhalation can be a relevant risk pathway (**Figure 3.5**). The ingestion of particulate matter, inhalation of particles larger than 10 µm, contributed ≤ 1% to the total EDI for most metals and PAHs (**Figure 3.2**). For this specific exposure scenario it would appear as if the ingestion of soil as inhaled particulate matter is arguably an insignificant exposure pathway.

According to the standardized guidelines used for risk assessment by Health Canada (2004a) the average or maximum contaminant concentration in soil should be used. Currently, for human exposure to soil ingestion many studies sieve soil through a 250 µm mesh (Cave et al. 2010; Tang et al. 2006; Lu et al. 2010) to better estimate the size fractions humans are exposed to (Duggan et al. 1985). However, more recent research would suggest that humans are exposed to a smaller size fraction of soil (Siciliano et al. 2009; Yamamoto et al. 2006), and it has been suggested that a 45 µm mesh may best approximate human exposure (Siciliano et al. 2009). Unpaved roads provided an infinite reservoir of soil particles to be re-suspended by vehicle traffic (Nicholson et al. 1989) and the grinding of tires against soil particles shifts the size distribution towards smaller particles (Watson and Chow 2000). This is supported by research that shows the majority of the airborne mass is attributed to particles with a median diameter between approximately 6 to 30 µm (Lundgren and Burton 1995). Considering that soil inhalation is likely only relevant for sizes ≤ 10 µm and soil ingestion occurs for sizes ≤ 40 µm (Siciliano et al. 2009; Yamamoto et al. 2006), using soil concentrations after passing through a 45 µm mesh maybe a more accurate exposure estimate.

Risk assessors are continuing to use *in vitro* bioaccessibility estimates without validating against *in vivo* models and this may be due to the high cost of *in vivo* testing (Richardson et al. 2006). Not validating against an *in vivo* model can lead to inaccurate exposure estimations that

result in unnecessary policy decisions. As seen with **Figure 4.2**, the IVD with the addition of a C18 membrane is correlated with *in vivo* PAH release from the swine and without the addition of a C18 membrane the IVD under-estimates bioaccessibility (**Figure 4.1**). In contrast, the RBALP model did not correlate with *in vivo* results with or without a C18 membrane; however that doesn't necessarily imply that the RBALP under-estimates bioaccessibility, but rather, inaccuracies are associated with these estimations. This discrepancy may be a result of PAH release from the RBALP model having a strong correlation to PAH concentration in soil (r^2 = 0.89, $p < 0.001$), whereas the *in vivo* swine model does not show any such correlation (**Figure 4.3**). Due to the RBALPs correlation with soil PAH concentration there is an increasing amount of PAHs being released into GI fluids as soil PAH concentration increases, which results in inaccurate estimations of relative bioavailability.

The concept of fugacity may play a key role in determining factors that control *in vivo* PAH bioaccessibility, such that *in vitro* models can be more accurately designed. As seen in **Figure 4.3**, uptake of BaP equivalents can be predicted using the fugacity capacity of soil. Furthermore, **Figure 4.4** illustrates that the bioavailability of individual PAHs can be predicted based on the fugacity capacity of water. As stated previously, equilibrium is reached when the fugacity between multiple phases is the same for any given chemical (Lewis 1901) and the relationship between chemical concentration and fugacity is simply:

$$C_p = F \times Z_p \qquad \text{(Eqn 2.5)}$$

Therefore, in a model consisting of just soil and simulated intestinal fluids, the bioaccessibility will be limited proportionally to fugacity capacity of the fluids. However, when a lipophilic phase is added to the system, a larger fugacity gradient is created and bioaccessibility is no longer limited by the relatively lower fugacity capacity of the fluids. Although reaching

equilibrium may not actually occur in an *in vivo* setting; the principles remain the same and as PAHs move from a media of high fugacity (soil) to a media with lower fugacity (GI fluids), the PAHs are being also being absorbed from the GI fluids into the epithelial cells, thus creating a fugacity gradient where PAHs are constantly desorbed from the soil. Complicating matters with using fugacity calculations in either *in vivo* or *in vitro* digestion models is that the soil is being digested by GI fluids, altering the composition, and likely altering the fugacity capacity of both the soil and fluid media.

The importance of AF_{GIT} has already been thoroughly discussed and AF_{Inh} is equally important for risk assessment. In this risk assessment there is an overlap of exposure where particles with diameters between 2.5 and 10 µm are considered both an ingestion and inhalation hazard. For the ingestion exposure the AF_{GIT} was used to estimate exposure and for inhalation exposure the AF_{Inh} was assumed to be 1. AF_{Inh} is difficult to determine due to the complex nature of both particulate matter and the respiratory tract. Particle deposition in the respiratory tract is defined by particle characteristics, such as size, shape and diameter (Heyder et al. 1986), and receptor characteristics, including breathing pattern and specific lung structure and geometry (Heyder et al. 1986; Kim and Kang 1997). Clearance of particles from the respiratory tract follows both a fast (muco-ciliary clearance) and slow (alveolar macrophage clearance) phase (Moller et al. 2004; Stahlhofen et al. 1990). It appears as if the fast phase is applicable for particles larger than 6 µm and can be cleared within hours, whereas the slow phase is for smaller particles that penetrate deep into the lung and require months prior to clearance (Moller et al. 2004; Stahlhofen et al. 1990). Considering that the residence time in the lung is variably depending upon particle size it can be difficult to determine meaningful AF_{Inh} without knowing the size distribution of inhaled soil particles.

5.3 Future Directions

The results generated here indicate that soil inhalation is a relevant exposure pathway and that paving roads was an effective method to reduce the re-suspension of soil particles. Many communities and municipalities may need to consider paving roads not only for the aesthetic value but to improve the quality of life by reducing exposure from re-suspended soil particles. Although the soil may not the primary source for every airborne contaminant, the soil can still contribute to the airborne concentration of many contaminants and paving roads may be a notable alternative to reducing exposure when other direct methods are limited in their capacity. For example, current technology for reducing airborne emissions from industrial activities may not be cost effective and therefore not implemented, but if roads are paved the airborne concentration of many contaminants is effectively reduced.

Additional research validating *in vitro* models for organic contaminants is warranted. To expand on the current research it would be interesting to examine PAH bioaccessibility with a colon compartment using microbes. The current weak correlation with *in vivo* swine results suggest that *in vitro* models can be improved. Depending on the significance of PAH metabolism in an *in vivo* setting, which *in vitro* models likely do not account for, the *in vivo* PAH uptake may not be accurately represented. Accounting for metabolites in both *in vitro* and *in vivo* models may help clarify which processes govern PAH bioavailability. The fugacity concept has potential to elucidate factors controlling PAH bioavailability/bioaccessibility. Additional information may be gained by investigating the change in fugacity capacity of soil and GI fluids, during digestion, and how this interaction affects PAH bioavailability/bioaccessibility. To improve the *in vitro* models, a fundamental step is to determine what governs organic contaminant absorption in an *in vivo* setting and then build an *in vitro* model which includes only the essential components. The bioavailability of organic contaminants is undoubtedly related to

the interaction between the physiochemical properties of the contaminant and the physiochemical properties of the exposure matrix and their interaction with the gastro-intestinal properties such as fluids, enzymes, peristaltic mixing, and absorption across epithelial cells.

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