Oral bioaccessibility of semi-volatile organic compounds (SVOCs) in settled dust A review of measurement methods, data and influencing factors

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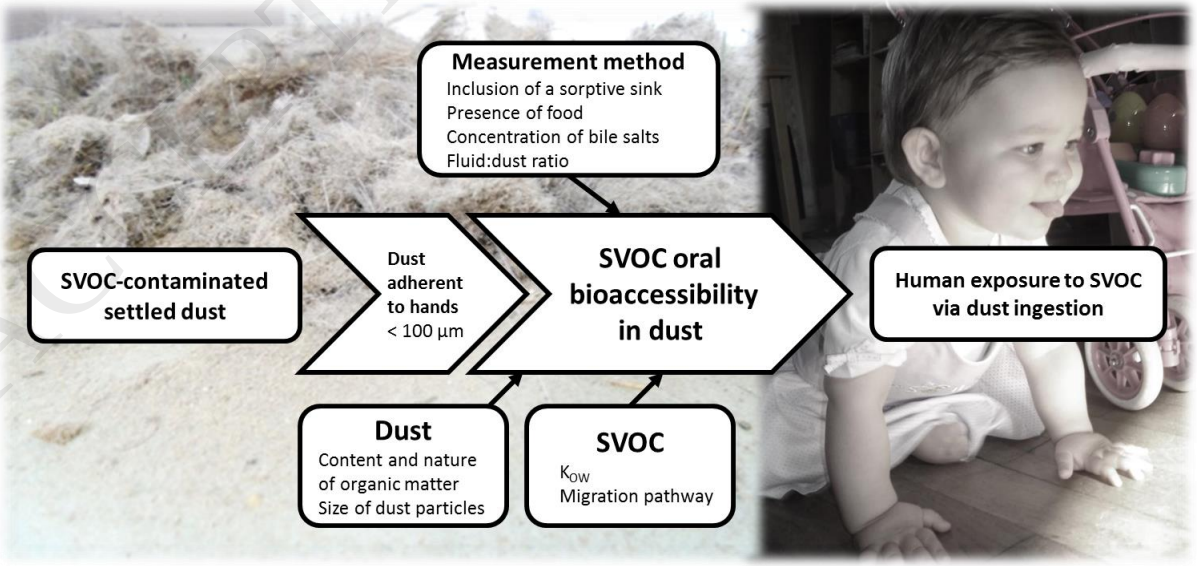
Graphical Abstract :



Highlights :

- Importance of considering bioaccessibility when assessing the exposure dose to SVOCs in dust
- Need for simplification and harmonization of measurement methods
- Main method parameters are inclusion of sorptive sink, bile concentration and fluid to dust ratio
- Need for in-vivo validation of bioaccessibility data

Abstract

Many semi-volatile organic compounds (SVOCs), suspected of reprotoxic, neurotoxic or carcinogenic effects, were measured in indoor settled dust. Dust ingestion is a non-negligible pathway of exposure to some of these SVOCs, and an accurate knowledge of the real exposure is necessary for a better evaluation of health risks. To this end, the bioaccessibility of SVOCs in dust needs to be considered. In the present work, bioaccessibility measurement methods, SVOCs' oral bioaccessibility data and influencing factors were reviewed. SVOC bioaccessibilities (%) ranged from 11 to 94, 8 to 100, 3 to 92, 1 to 81, 6 to 52, and 2 to 17, for brominated flame retardants, organophosphorus flame retardants, polychlorobiphenyls, phthalates, pesticides and polycyclic aromatic hydrocarbons, respectively. Measurements method produced varying results depending on the inclusion of food and/or sink in the model. Characteristics of dust, e.g., organic matter content and particle size, also influenced bioaccessibility data. Last, results were influenced by SVOC properties, such as octanol/water partition coefficient and migration pathway into dust. Factors related to dust and SVOCs could be used in prediction models. To this end, more bioaccessibility studies covering more substances should be performed, using methods that are harmonized and validated by comparison to in-vivo studies.

Keywords

Human exposure; Indoor environment; Dust ingestion; Bioavailability; Pollutant.

1. Introduction

The last decade has seen raising awareness about the presence of semi-volatile organic compounds (SVOCs) in indoor environments [1]. SVOCs are defined by their volatility (boiling point between 240 °C and 400 °C) and vapor pressure (from $1/10^{14}$ to $1/10^{4}$ atm) [1,2]. They include many different chemical families such as phthalates, polycyclic aromatic hydrocarbons (PAHs), polychlorobiphenyls (PCBs), polybromodiphenylethers (PBDEs), organophosphorus flame retardants (OPFRs), organophosphorus (OPs) and organochlorine (OCs) pesticides, pyrethroids, perfluorinated compounds (PFCs), synthetic musks, chlorinated paraffins (CPs), phenols, parabens, etc. [1,3]. Their presence in indoor environment is a matter of concern because many of these SVOCs are suspected of being toxic and/or endocrine disruptors, with effects on the reproductive tract development, the thyroid function, the nervous system and the development of metabolic diseases such as obesity and diabetes [3–6]. In indoor environments, human exposure to SVOCs occurs through different pathways including air inhalation, ingestion of settled dust and dermal contact with surfaces, indoor air and settled dust. Dust ingestion is considered a major pathway of human exposure to several of these SVOCs including PBDEs [7–9], phthalates [9,10], OPFRs [11] and tetrabromobisphenol A (TBBP-A) [12]. Children are particularly concerned because their specific behavior, i.e., crawling on the floor, hand-to-mouth and object-to-mouth contacts, may contribute to a higher ingestion of dust. Moreover, they are more vulnerable to the harmful effects of pollutants because major systems of their organism are still immature [13].

To assess this risk, the SVOC intake by dust ingestion can be calculated according to the following equation [14]:

$$SVOC\ daily\ intake\ by\ dust\ ingestion = \frac{SVOC\ content\ in\ dust * mass\ of\ daily\ ingested\ dust}{body\ weight}$$

The SVOC content in indoor settled dust has already been described in the scientific literature at an international level [15–20]. However, for human exposure assessment, analyses have to be performed on the dust particle size that is adherent to human's hands and likely to be ingested. Previous studies have shown that <100 µm are relevant to human exposure [21,22]. Along with the dust particle size, exposure assessment studies must also consider the bioavailability of chemicals. The evaluation of the human risks associated with SVOC in dust often considers 100% of the SVOC content as the exposure concentration, potentially leading to an overestimated risk. Actually, only a fraction may effectively be absorbed by the body, and this fraction may differ between dust and the matrix that was used in the toxicity tests used for health risk assessment. To refine the exposure dose and establish the link between dust contamination and human exposure via dust ingestion, the oral bioavailability of a SVOC, defined as the fraction of a contaminant reaching the digestive system and absorbed into the systemic circulation should be known. However bioavailability is difficult to assess, mainly because of ethical reasons, as it needs to be measured in vivo. In this context, the notion of bioaccessibility was then considered. Oral bioaccessibility was defined in 2011 as the fraction of a compound that is soluble in the gastrointestinal tract and is therefore available for absorption [23]. It was further defined in 2015 as "the maximal amount of contaminant released from the test matrix in a synthetic gastrointestinal system" [24] thus implying two additional conditions to the original definition: (i) bioaccessibility is assessed by synthetic systems and (ii) the bioaccessibility should be measured in a conservative way ("maximal amount"). Oral bioaccessibility is equal or greater than bioavailability as it does not include losses due to the passage across the intestinal wall and

liver metabolism. It is therefore a conservative measurement of bioavailability that can be measured with ethically friendly synthetic systems. For substances where the major pathway of exposure is dust ingestion, taking oral bioaccessibility into account is important to refine risk assessment and to improve epidemiological studies. Actually the inclusion of oral bioaccessibility allows a better characterization of the participants' exposure to the SVOCs contained in the dust they are exposed to, which is beneficial for the establishment of epidemiological associations between environmental exposures and health outcomes.

The present work is a review of the existing literature related to the in vitro assessment of SVOC oral bioaccessibility in indoor dust. It includes (i) the measurement methods used, (ii) the existing bioaccessibility data, which cover 96 substances from 6 chemical families, i.e. organophosphorus and brominated flame retardants, PCBs, phthalates, pesticides, and HAPs, and (iii) a discussion on the factors influencing oral bioaccessibility.

2. Materials and Methods

A review of the literature was performed using the key words « dust » and « *accessib*» in the title and abstract fields of Science Direct, Pub Med and Web of Science search engines. All years were included. To ensure that no hit was missed, no mention of chemical substance was made in the search because SVOCs cover many individual substances and families of substances, which in addition can be spelt in different ways. The search then resulted in 142, 95, and 156 hits for Science Direct, Pub Med and Web of Science respectively and included many articles related to the bioaccessibility of inorganic elements which has been more studied so far [25].

After all irrelevant hits were removed, 20 relevant articles, published from 2011 to automn 2017, were considered for the purpose of this review.

3. Results & Discussion

3.1. Measurements methods

The ingestion and digestion of food through the human digestive tract follow four main processes (Figure 1): (i) in the mouth, thanks to mastication, food particles are reduced in size and mixed with saliva to produce a bolus; (ii) in the stomach, this bolus is subject to the gastric process which mainly consists in acidic and enzymatic hydrolysis; (iii) in the small intestine further enzymatic hydrolysis and absorption of the nutrients take place; and (iv) in the colon, occurs the large intestine process, which is mainly fermentation and water removal [26].

In vitro methods have been developed for simulating human digestion in three different fields, related to the ingestion of food, soil and dust, respectively. They can be highly sophisticated, like the gastrointestinal dynamic digestion systems, which include stomach and intestinal compartments, equipped with temperature, pH and redox sensors, variable speed pumps to control the flow of meal and digestive secretions and the possibility to work under anaerobic conditions, within a software controlled environment [27,28]. A 5-step multi-chamber reactor was developed to simulate the human intestinal microbial ecosystem in the small and large intestines [29]. On line coupling was implemented between a physiologically relevant bioaccessibility system and inductively coupled plasma spectrometry [30]. A bioaccessibility test was developed by the BioAccessibility Research Group of Europe (BARGE) for the measurement of metals and metalloids in soils and is known as the Unified BARGE Method (UBM) [31]. Less

sophisticated methods have also been developed, such as the physiologically-based extraction test (PBET), the simulator of the human intestinal microbial ecosystem (SHIME), the method from the Dutch National Institute for Public Health and the environment (RIVM), the Fed ORganic estimation human Simulation Test (FOREhST), and the in vitro gastrointestinal (IVG) method [32]. Three standards were documented for soils: the German guideline DIN 19738 [33], the ISO 17402 [34], and the ISO 16751 [35].

Among these existing methods, three were used for measuring SVOC bioaccessibility in dust: the PBET, the FOREhST and the DIN 19738. These methods often come from the experiences gained on soil [36,37] and replicate part or all of the four processes involved in human digestion through in vitro simulations.

Mouth in vitro process. The simulation of the action of saliva is implemented in the BARGE protocol [38], the German standard DIN 19738 [39,40], and the FOREhST [41]. It consists in extracting the dust in a pH neutral aqueous solution containing salts (NaCl, NaSCN or KSCN, Na_2SO_4, $NaHCO_3$, NaOH, KCl, KH_2PO_4 or NaH_2PO_4, $CaCl_2$), proteins (mucin, α-amylase), urea and uric acid, and food (whole milk, skimmed milk and denatured skimmed milk [39] or organic creamy infant food, baby milk powder, and sunflower oil [41]). The solution is stirred for up to 30 minutes at 37 °C. This first process is sometimes considered of limited interest because the extraction time, which should not exceed 2 minutes to be physiological relevant, and the neutral pH do not have much impact on the dissolution of SVOCs, compared to the following processes [24,37].

Stomach in vitro process. The gastric process is present in all models reported in the literature. The dust is introduced in an acidic (pH < 2.5) synthetic gastric fluid containing pepsin, the

enzyme for the degradation of proteins. Salts (NaCl, KCl, KH_2PO_4 or NaH_2PO_4, $CaCl_2$, NH_4Cl) are added in the BARGE and DIN 19737 methods. The authors applying PBET methods add different types of salts (sodium malate and tri-sodium citrate) and acids (lactic and acetic) [42–46], or mucin (protein responsible for the gel texture) [47]. At this stage, food components (starch, yeast extract, casein, pectin, xylan, arabinogalactan, etc.) can be added to simulate the fed state [45,48]. The solutions are then stirred for 1 to 2 hours at 37 °C.

Small intestine in vitro process is also present in all the models reported in the literature. In physiological terms, this process is of a particular importance for bioaccessibility because of the long incubation time and because it is where the absorption through the intestinal wall takes place. In this process, the dust is brought into contact with the intestinal juice at a neutral pH (between 6.5 and 8), either following neutralization of the pH of the preceding gastric solution or after centrifugation, recovery of the dust and introduction in a freshly prepared intestinal solution. In most models, neutralization of the solution is obtained via the addition of bicarbonate, as bicarbonate is the ion secreted in the human body to neutralize gastric secretion in the lumen [49]. Intestinal solutions always include pancreatin (a mixture of digestive enzymes produced by the pancreas) and bile salts (produced by the liver, intended for lipid digestion and promoting absorption in the small intestine). Various other salts are also added, as well as urea and albumin [38] and lipase [38,45]. Again at this stage, dietary components can be added [45,48]. Some authors also add an adsorbent to capture the compounds as they are released in the digestive fluids, thus mimicking the passage of compounds through the intestinal wall [42,45,50]. The solutions are stirred 4 to 7 hours at 37 °C. After incubation, dust is separated from the digestive fluid by centrifugation. However, if foam

particles, originating from product weathering, are present in dust, separation is achieved by filtering the digestive fluid through glass wool [45].

Because of the presence of bile, which promotes the solubilization of hydrophobic organic compounds through the formation of micelles, the fraction of intestinal bioaccessibility is often greater than the fraction of gastric bioaccessibility [51,52]. This was experimentally demonstrated, as shown in Figure 2, where the distribution of bioaccessible SVOC is on average 35% in the gastric fluid and 65 % in the small intestine fluid.

Colon in vitro process. The inclusion of the large intestine process (colon extended PBET) was reported by Abdallah et al. [46], Fang and Stapleton [45], and Kademoglou et al. [48]. Indeed, according to Tilston et al. [53], there could be absorption at the level of the colon, along with water removal. The inclusion of this process is above all a conservative approach because the prolonged incubation time and the presence of carbohydrates in the colon could increase the bioaccessibility of persistent organic pollutants [46], although this was not always confirmed [54]. The synthetic solution, at a nearly neutral pH, contains salts, mucin, cysteine hydrochloride (a reducing agent used to promote anaerobic conditions [53]), bile salts, haemin and food components. The solutions are kept at 37 °C for 8 to 16 hours. For flame retardants, the additional bioaccessibility provided by the colon incubation ranged from 11 to 32% of the total bioaccessibility [46], as shown in Figure 3.

Microbial activity. The SHIME (Simulator of Human Intestinal Microbial Ecosystem) simulates the GI tract form stomach to colon including enzymatic and microbial activities and has mostly been used for studying the interactions between food and microbiota [55]. Siciliano et al. used both the SHIME and a sterile in vitro digestion method to assess the bioaccessibility of PAHs in

soils. They concluded that the release of PAHs in digestive fluids was not influenced by microbial activities [56], which can explain why SHIME was never further used with dust samples.

Physiological parameters. Authors always seek to produce physiologically relevant methods. The temperature of the human body, 37 °C, is respected by all authors. The pH values, close to 6.5 for saliva, close to neutrality in the small intestine and colon compartments, and acidic (pH <2.5) in the gastric medium are physiologically relevant [55]. Authors used relevant incubation times, except for the mouth compartment with long incubation times of up to 30 minutes [39,40]. All authors also apply shaking to their system to simulate the peristaltic movements of human digestion.

Specific human populations. Models used for the analysis of dust aim towards physiological relevance, but they did not consider specific conditions relative to some human populations. In the field of food studies, however, where more sophisticated in vitro digestion models are applied, specific gastro-intestinal conditions of the infants and elderly can be simulated [57]. For infants' gastric conditions, a limited stomach capacity, a relatively high gradient pH (3.2-6.5), and a reduced pepsin secretion are considered, as well as a lower bile salt concentration in the intestinal phase [57]. These specific models could be applied for the evaluation of SVOC bioaccessibility in studies where the population of interest is mainly children.

A step towards the in vitro evaluation of bioavailability. Bioaccessible SVOCs are released in the GI tract while bioavailable SVOCs are those who reached the systemic circulation (Figure 1). Bioaccessible SVOCs become bioavailable once they have crossed the intestinal wall and undergone presystemic metabolisms (both intestinal and hepatic) [58]. A step towards the evaluation of bioavailability can be reached in vitro using Caco-2 cells to mimic the transport

across the intestinal epithelium. Indeed, Caco-2 cells can be cultivated as monolayers on semipermeable membrane where they develop the morphologic characteristics of epithelium cells, possessing a brush border and tight junctions between adjacent cells [59,60]. In their review, Cui et al. mentioned that HT29-MTX goblet cells are sometimes cultured with Caco-2 cells, because they can produce the mucus that otherwise lacks to Caco-2 cells monolayers. They also emphasized the need to evaluate the toxicity of the investigated substance towards Caco-2 cells, before using them, because if the behavior of the Caco-2 cells is compromised, the transmembrane passage could be affected [32]. Kang et al. attempted to measure the uptake by Caco-2 cells of BDE-28, -47, -99 and -153, respectively, and reported absorption rates of 30%, 26%, 41% and 59% respectively [51]. Likewise, Pan et al. measured an absorption rate of 42% for BDE-209 [52]. In both studies, authors only considered the cell uptake, ignoring the transfer between cells. They may therefore have underestimated the overall transfer across the Caco-2 cells monolayer. Still, using Caco-2 cells can help for a better assessment of a SVOC human internal dose.

Method validation. The validation of a SVOC bioaccessibility assessment method involves two major steps. From an analytical point of view, the extraction of the digestive fluids and of any adsorbent included to the model, and the instrumental analysis of the extracted SVOCs, must be performed using quality control steps, as proposed by Rodríguez-Navas et al [61]. Once this analytical validation is achieved, then the bioaccessibility data produced by the method should be validated by comparison to bioavailability data measured in vivo, taking into account the metabolism and the fate of the substance in the body. However, in vivo data related to the bioavailability in dust are really scarce. Huwe et al. produced data for the bioavailability of

PBDEs, measured in rats that had ingested a reference dust material, the SRM 2585, with known SVOC contents [62]. Pan et al. found a correlation between the bioaccessibility of BDE-209 in dust, measured with a PBET method and its relative bioavailability measured in rats' blood (slope 0.63; r^2 0.73, $p = 0.031$) [52]. Plichta and Fromme produced bioavailability data for phthalates by measuring the urine concentrations of piglets that had ingested contaminated dust [63].

This lack of data on SVOC bioavailability in dust led us to extend our review to soil studies, where more bioavailability tests were conducted. In 2004, Pu et al. measured the absolute bioavailability of phenanthrene in the blood of rats that had ingested contaminated soils, and its bioaccessibility in the same soils using a PBET method. Depending on the type of soil investigated, bioavailability varied between 15% and 49%, whereas bioaccessibilities varied between 18% and 89%. The authors found a linear relationship between bioaccessibility and bioavailability ($r^2 = 0.53$, $p < 0.05$), thus encouraging the use of bioaccessibility to predict bioavailability but also emphasizing the need for more studies, covering more chemicals and more types of soils [64]. More recently, James et al. assessed the PAH bioavailability in juvenile swines, by measuring their blood concentrations after the ingestion of contaminated soils. Bioavailability varied from 0 to 40% according to the PAH and the soil. In this study, however, no relationship could be established between partition coefficients into simulated intestinal fluids and bioavailability [65]. However in a previous study, James et al. had added a C18 membranes to simulate lipid sinks and had then found a linear relationship between the bioaccessibility of PAHs in soils, measured with an in vitro digestion model (IVD) in the presence of a C18

membrane, and their bioavailability, measured in swines' blood serum (slope = 0.85, r^2 = 0.42, $p < 0.07$) [66].

The relative bioavailability of PCBs (101, 138, 153 and 180) in soil was assessed by measuring concentrations found in swines' adipose tissue: values were all greater than 45%, independently of the investigated soil or PCB congener [67]. For PCBs 52 and 118 in soil, the relative bioavailability measured in rats' blood was greater than 87% and could not be linked to their bioaccessibility measured by PBET, which produced underestimated results (40% to 80%) [68].

Li et al. estimated the soil bioavailability of DDT and its metabolites (DDTr) by measuring their concentration in mice's adipose tissues after soil ingestion: values varied from 18% to 65% depending on the type of soil. They compared it to DDTr bioaccessibility using a PBET model with and without Tenax® TA as a sorptive sink. When adding Tenax® TA in the model, DDTr bioaccessibility increased up to 22 fold, and could then be linked by a linear regression to bioavailability (slope = 1.2, r^2 = 0.62, p=0.065) [69].

An in vivo/in vitro validation study was also undertaken for PFOA in food, and showed a good correlation ($r=0.76$, $p<0.01$) between PFOA bioaccessibility, assessed with the UBM method, and its bioavailability measured in rats' liver [70].

Lack of data for bioavailability validation in dust studies are not only due to ethical concerns, but also practical difficulties. Actually, it can be difficult to have enough dust with a sufficient SVOC content so that consequent bioavailable concentrations measured after ingestion are meaningful. However, before bioaccessibility values can be relied upon in risk assessment and epidemiological studies, they must be validated versus in vivo studies and so more of these studies should be performed taking into account the metabolism and the fate of the substance

in the body. Moreover, due caution should be applied when choosing the animal species for in vivo validation: Duan et al. showed that swine's and rat's bioavailability measurements of benzo[a]pyrene in soils were correlated, but bioavailability was underestimated by about a quarter in the rat study, which should be taken into account [71]. While rats are more often considered for in vivo measurements, swines are recommended because their digestive system is comparable to that of children in terms of body size, gut physiology and genetic profile, and because they produce more conservative bioavailability estimates.

For optimal dust bioaccessibility measurements, advantage should be taken from the experience and feedback from validation studies performed in the field of outdoor soils. In addition, efforts should be made towards method simplification, so they can be applied on numerous samples with a minimal cost and be eventually used in epidemiological studies to establish refined associations between the presence of SVOCs indoor and health outcome in populations.

3.2. SVOC bioaccessibilities in dust reported in the literature

Bioaccessibility data related to SVOC in dust reported in the literature were compiled and are shown as percentages in Figure 4. Data comparison was limited by the differences in measurement methods, the nature of the dust (settled dust or dust collected from air conditioning filter) and its particle size (sieving fraction from 20-60 µm to < 250 µm). Some of these limitations (inclusion of food or adsorbent in the measurement method) are visually shown in Figure 4.

Brominated flame retardants (BFRs). The bioaccessibility of BFRs has been the most widely documented with 162 results (143 for PBDEs [45–47,50–52,72] and 19 for alternative BFRs (2-

ethylhexyl-tetrabromo-benzoate (EH-TBB), bis(2-ethylhexyl) tetrabromophthalate (BEH-TEBP), tetrabromobisphenol A (TBBP-A) and hexabromocyclododecanes (HBCDs) [45,46,73]). For PBDEs, valued ranged from 11 to 71% (median 37%) with the lowest bioaccessibilities observed for BDE-209 (11-63%, median 19%). For alternative BFRs, bioaccessibilities ranged from 12% to 94% (median 37%). Highest bioaccessibilities were observed for alternative BFRs, as determined by Abdallah, when using Tenax® TA in their CE-PBET model (72-94%) [46]. Data are reported in Table **1** and graphically displayed in Figure 4.

Organophosphorus flame retardants. OPFR bioaccessibilities were only recently reported with 22 results published in 3 articles in 2014 [45], 2015 [42], and 2016 [41] for tris(2-chloroethyl) phosphate (TCEP), tris(1-chloro-2-propyl) phosphate (TCPP), tris(1,3-dichloro-2-propyl) phosphate (TDCPP), and triphenyl phosphate (TPHP). Reported bioaccessibilities, shown in Table 2 and in Figure 4, ranged from 8% to 103%, depending on the compound and the measurement method.

PCBs. Fifty-two values documenting the bioaccessibility of PCBs were published in three articles in 2012 [39] and 2013 [74,75]. Overall, values ranged from 3% to 92% (median 22%), depending on the congener and the measurement method used (data shown in Table 3 and Figure 4). In the presence of food, valued ranged from 41 to 92% (median 74%, n=5) [39]. Without food, bioaccessibility values, ranging from 3 to 46% (median 20%, n=42) [74,75], might have been underestimated.

Phthalates. The bioaccessibility of phthalates in dust was published in three articles in 2012 [43], 2013 [76], and 2015 [42]. Thirteen values were reported that ranged from 1% to 81% with a median of 13% (Table 4 and Figure 4). However, these values were obtained using a PBET

method without sorbent and might have been underestimated (see discussion below). A right evaluation of the bioaccessibility of phthalates is nevertheless crucial, with respect to the high contamination levels found in indoor dust.

Pesticides. The bioaccessibility of pesticides in dust was assessed in three articles published in 2012, 2013, and 2016. Investigated substances were mainly organochlorine pesticides [39,44], fipronil [40], piperonyl butoxide [39] and permethrine [39]. Reported bioaccessibilities, shown in Table 5 and Figure 4, ranged from 6 to 52% (median 14%). In the absence of food they ranged from 6 to 40% (median 12%, n=14). They increased in the presence of food, from 29% to 52% (median 41%, n=5), thus showing again the conservative aspect of adding food to the model, as not to underestimate oral bioaccessibility.

PAHs. The bioaccessibility of PAHS was only reported in one article from 2011 on air conditioning filter dust [77], and ranged from 2% to 17% (median 7%). Reported values for PAHs are the lowest, compared to all other chemical families. These in vitro tests were performed without sorptive sink. In soil studies, the addition of a sorptive sink to the in vitro model caused an increase of PAHs bioaccessibility, by a factor of 1.2 to 2.8 [78], or from 4-7 % to 16-31% [79]. Even taking this increase into account, PAHs would remain among the less bioaccessible substances, and it is therefore even more important to take their bioaccessibility into account for a more accurate estimate of the exposure dose.

3.3. Discussion on the factors influencing oral bioaccessibility

The oral bioaccessibility of SVOCs in dust is influenced by different factors that can be classified in three categories: (i) factors related to the measurement method, (ii) factors related to the dust as a matrix and (iii) factors related to the SVOC chemical properties (Table 7).

3.3.1. Influence of the measurement method

The results from the literature showed variations that could be attributed to the measurement method used for measuring bioaccessibility. A good understanding of the factors influencing SVOC bioaccessibility is necessary to progress towards a relevant and unified measurement method. These factors are listed below.

Presence of sorptive sink. Human digestion is a dynamic process where the equilibrium of the compounds' distribution between the matrix and the digestive fluids is constantly displaced because of the dilution created by fluids secretion and the passage of the compounds across the intestinal wall. To mimic this phenomena some authors used an adsorbent, i.e., Tenax® TA, for capturing the compounds as they are released in the digestive fluids [42,45,48,50]. By doing so, He et al. observed an increase of approximately 30% of the bioaccessibility of OPFRs after adding 2.5 g of Tenax® TA in their method [42]. Similarly, the addition of 0.5 g of Tenax® TA increases the bioaccessibility of OPFR (+ 37% on average) and PBDE (+ 86% on average), which are thus close to the in vivo data measured in the rat after ingestion of SRM 2585 [45]. The use of an adsorbent is therefore important for a more accurate measurement of SVOC bioaccessibility, and at least for avoiding underestimating its value. However, there are some practical difficulties with its use, and authors struggle to find easy to implement solutions for retrieving the adsorbent from the fluids and separating it from the dust. A novel method using dialysis membranes was proposed by Kademoglou et al. to solve this problem [48]. In soil or fuel

soot applications, authors attempted to use silicon cords [80,81] or silicon sheets [54]: these are easier to manipulate since the silicon can simply be removed from the fluids and rinsed. However, substances do not adsorb on silicon; they are absorbed in the material, according to equilibrium equations between fluids and silicon that need to be assessed. Authors also attempted to use adsorption on activated carbon as a sink: while in this case there is no risk of the compounds being back-released in the fluids, SVOC can be hard to desorb from the activated carbon and it might only be possible to measure the non-bioaccessible content left in the dust [78].

Presence of food. An increase of about 30% of pesticides' and PCBs' bioaccessibility was measured in the presence of milk in the in vitro system. This increase was attributed to the presence of proteins, which are known to increase the solubility of organic substances [39]. Such an increase was also observed for PAHs in soils in the presence of lyophilized milk and in fuel soot in the presence of soybean oil [82]. However this increase was not confirmed for OPFRs with the FOREhST method. Quintana et al. even observed that the release of OPFRs in the intestinal fluid was higher in the absence of food. They hypothesized that it might be due to the binding of OPFRs to food components, that would then bind to dust particles, thus reducing OPFRs bioaccessibility [41].

Concentration of bile salts. The biliary concentration of 1.78 g / L usually reported [42,45,46,48] has not been optimized since before 1993 [83]. However Yu et al. optimized the biliary concentration and concluded that it should be between 4.0 and 7.0 g/ L so as not to underestimate the bioaccessibility, but without physiological reference [47]. The median concentration of bile salts in the intestines, as reported by Mudie et al. in their review of human

physiological parameters, was 2.7 mM in the fasted state and ranged from 3.6 to 11.9 mM in the fed state [49]. Considering a bile molecular weight of 408.6 g/mol, these concentrations are equivalent to 1.1 g/L for the fasted state and from 1.5 to 4.9 g/L in the fed state. Bile concentration is an important parameter to consider because it determines the formation of micelles. Indeed, micelles have a positive impact on bioaccessibility because they mobilized apolar substances thus enhancing their solubilization and making them bioaccessible. The influence of bile concentration varies according to the polarity of the substance: the less polar substances will rapidly be mobilized in the form of micelles while the more polar will remain solubilized in the water and can be readsorbed on the matrix, hence a greater variability of their bioaccessibility [84]. In dust samples, increasing the quantity of bile salts in the in vitro model caused an increase of the bioaccessibility of OPFRs and phthalates [42], PCBs [75], and PBDEs [47]. The concentration of bile added to the in vitro system should therefore be physiologically relevant and not exceed 5g/L in the presence of food in the model.

Fluid to dust ratio. The massic ratio between synthetic fluid and dust is a parameter to consider because larger volumes of fluid will lead to a better migration of SVOCs towards digestive fluids. Conversely, in Yu et al. study, an increase of the solid phase, or a decrease of the liquid phase caused the partition equilibrium of PBDEs to shift towards the solid phase, thus leading to the decrease of their bioaccessibility [47]. The mean gastric and intestinal volumes reported by Mudie et al. were < 30 mL and from 81 to 165 mL, respectively, for the fasted state and from 250 to 664 mL and from 47 to 590 mL, respectively, for the fed state [49]. Even if the upper percentile for daily dust intake of 100 mg recommended by the US EPA [85] was ingested in one single intake, ratios would go from 300:1 (for gastric volume in fasted state) to 6640:1 (for max

gastric volume in fed state). In the methods used for the measurements of dust bioaccessibility, the fluid:dust ratio ranged from 20 to 133 for gastric fluids and from 67 to 300 for intestinal fluids. Yu et al. studied this ratio and concluded that it should be between 150 and 200 [47]. Collins et al. recommend a minimum ratio of 100:1, even though they appreciate that a higher ratio may be more realistic, but would lead to detection problems [24]. Besides, in their review of bioaccessibility in soil, Rostami and Juhasz reported that little difference was observed in metal bioaccessibility in soil when fluid:soil ratios varied from 100:1 to 5000:1 [23]. The fluid:dust ratio should therefore not fall below 100:1, as a compromise between physiological relevance and analytical feasibility.

Calculation of bioaccessibility. There are two different approaches for the calculation of bioaccessibility. The first one, more widely used [42,44–46,51,52,74–77], is based on the ratio between bioaccessible SVOCs and total SVOC concentration, originally present in dust:

$$bioaccessibility\ (\%) = \frac{[bioaccessible\ SVOCs]}{[total\ SVOCs]} x100$$

The second approach considers the ratio between bioaccessible SVOCs and the sum of bioaccessible SVOCs and non-bioaccessible SVOCs, measured in the residual dust pellet left after the in vitro test [47,48,50,73]:

$$bioaccessibility\ (\%) = \frac{[bioaccessible\ SVOCs]}{[bioaccessible\ SVOCs] + [non - bioaccessible\ SVOCs]} x100$$

The two approaches would give the same results if [total SVOCs] = [bioaccessible SVOCs] + [non bioaccessible SVOCs], but this might not be true, depending on the efficiency of the extraction protocols. Moreover, the first equation assumes that the dust is homogeneous, and that the test samples used for the determination of [total SVOCs] and [bioaccessible SVOCs] are

identical, which might not be true, particularly if the sieving fraction is high (>250 µm). The second equation should therefore be favored when possible in the study design.

Collins et al. suggested an harmonized protocol where most of the above parameters, i.e., colon simulation, dietary components and an sorptive sink, are considered [24]. This harmonization protocol should be applied in further bioaccessibility studies, and an effort should be made toward the simplification of the method. Even though bioaccessibility studies will always be simpler to implement than bioavailability assessment studies, they remain long and tedious and have not yet been applied on many samples in large-scale studies. A simpler method, based on Collins et al. recommendations, physiologically relevant in terms of body temperature and pH should be developed. Efforts should be concentrated on the main influencing factors, ie inclusion of a sorption sink, concentration of bile salts, and fluid:dust ratio. The method should be validated versus in vivo studies, as it was done with the UBM for metals, and eventually included in an ISO standard.

3.3.2. Influence of dust as a matrix.

The second category of factors influencing the bioaccessibility of SVOC in dust are those related to dust as a matrix. In 2003, Morawska and Salthammer described dust as "an undefined matrix, the composition of which is essentially dependent on the type of indoor fittings, the general behavior and standard hygiene of the room occupants, and the possibility of introducing dirt, soil and sand from the surroundings of the indoor environment" [86]. Dust is made of human fragments, mainly skin flakes containing squalene and cholesterol, cellulose and petrochemical fibers, microplastics, particles originating from the abrasion of fabrics, furniture and surfaces,

pollen, living organisms (bacteria, fungi), fuel soot as well as inorganic particle made of quartz, albite, calcite, dolomite, etc.) [54,87–92]. Moreover, dust particles were reported as having different morphologies (micro-aggregates, spherical, angular, etc.) [91]. Dust is therefore a complex matrix that can bind with SVOCs and retain them in its pores, thus influencing their bioaccessibility in a varying extent depending on dust chemical and physical characteristics.

Carbon or organic matter content. The amount of organic matter (OM) contained in dust may vary from 5 to 95% percent [92], although a narrower range (8% - 61%) was described in the literature [50–52,72]. The effect of an increase of carbon or organic matter was investigated: while no effect could be observed for flame retardants [45], PBDEs [93], and the less hydrophobic OPFRs and phthalates [42], a decrease of the average bioaccessibility of PBDEs [72], tri- to hepta- BDEs [50], BDE-209 [52], the more hydrophobic OPFRs and phtalates [42], and fipronil [40] was observed. Similar effects were also observed in soils, for example for phenanthrene [64] and PCBs [67,94]. Delannoy et al. also compared different types of organic matter in soil and found that the reducing effect of OM on PCBs' bioaccessibility increased as following: fulvic acid > sphagnum peat ≥ sphagnum peat and activated carbon ≥ humic acid >> activated carbon. Yu et al. tried to better characterize OM in dust by assessing its aromaticity (using the H/C ratio: the lower the ratio, the higher the aromaticity) and its polarity (using the N/C ratio: the higher the ratio, the higher the polarity), and their impact on the bioaccessibility of tri- to hepta-BDE. Their bioaccessibility increased with decreasing OM aromaticity, while increased with increasing OM polarity [50]. The effect of OM on bioaccessibility is therefore not only due to the OM content but also to the complexity of its nature.

Dust particle size and pore volumes. An increase of SVOC bioaccessibility associated to the decrease of dust particles was observed for PAHs [95], PBDEs [50], OCPs [44], and phthalates [76]. These observations are expected because smaller dust particles have larger specific surface area per mass unit, allowing better contact and dissolution in digestive fluids. Therefore, the right particle size to be analyzed has to be chosen for relevant human exposure assessment: not only will this have an impact on total concentration of SVOCs in dust, but also on their bioaccessibility. Similarly to smaller particle size, larger pore volumes were associated with higher bioaccessibility because they also offer a larger specific area more easily accessible to digestive fluids [50].

Sample aging. In soils, the bioaccessibility of persistent organic pollutants (POPs) decreases when their residence time increases, through the aging process which allows POPs to be absorbed in organic matter and diffuse into the matrix nanopores [23]. Fang and Stapleton compared the bioaccessibility of OPFRs and BDEs in two series of samples, sampled in 2006 and 2010, respectively [45]. Except for BDE-209, the 2006 bioaccessibility serie was significantly lower than the 2010's, thus confirming the observations made on soils. BDE-209 might be present in the dust, not only via sorption on dust surface, but also within the fibers, via materials abrasion, and would therefore be less concerned by the aging process (see also "Influence of the SVOC migration pathway**"** below).

The bioaccessibility of SVOC could be predicted based on a knowledge of the matrix and the total SVOC content, which are easier to measure than the bioaccessibility itself. To this end, the matrix influence parameters need to be ranked depending on their respective impact on bioaccessibility. Yu et al. compared the different parameters, i.e., OM content, polarity and

aromaticity of OM, particle size, surface area, and pore volume of dust, using multiple linear regression [50]. Only OM content and pore volume remained in the statistical model. The bioaccessibility of tri- to hepta-BDEs could thus be calculated according to the equation: bioaccessibility (%) = 45.05 - 0.49 x OM% + 1.79 x pore volume [50]. For the same reasons as stated above, BDE-209 measurements did not fit this equation. Further studies should be undertaken to integrate the aging process and the way the SVOC integrated dust in the model and a more comprehensive equation proposed.

3.3.3. Influence of the SVOC's chemical properties

The third category of factors that influence the bioaccessibility are those related to the SVOC chemical properties, such as the octanol/water partition coefficient (K_{OW}) that could be used to predict the propensity of SVOCs to migrate from dust to digestive fluids.

Kow. SVOCs with higher K_{OW} are more hydrophobic and less likely to solubilize in aqueous digestive fluids. A decreasing trend in bioaccessibility was thereby observed with increasing log K_{ow} for OPFRs [41,45], BFRs [45,46,48], PCBs [74,75], phthalates [43], and PAHs [77], although this trend could not be confirmed in two others studies related to PBDEs [46,51,72], showing that other parameters are also to consider.

SVOC migration pathway. The presence of SVOC in indoor dust can arise through three mechanisms: (i) via volatilization and re-condensation of the SVOC on dust particles (air mediated transfer), (ii) via direct transfer from horizontal surfaces to dust, and (iii) via weathering or abrasion of polymers [96–98]. In the first two cases, the SVOC is sorbed onto the surfaces of dust particles, whereas in the third case, the SVOC is a constituent of dust particles

[73,96]. These migration pathways could lead to different bioaccessibilities, and sorbed SVOCs could be more bioaccessible than constitutive SVOCs. Yu et al. hypothesized that these different migration pathways could explain the lower PBDEs bioaccessibility in indoor dust than in outdoor dust since indoor dust is more likely to contain fragments of materials than outdoor dust [72]. In their next study, they compared the bioaccessibility of PBDE-spiked dust versus unspiked dust and observed no change in the bioaccessibility of tri- to hepta- BDEs whereas BDE-209 bioaccessibility was higher in the spiked dust, thus confirming a different behavior of BDE-209, that could originate from material abrasion [50]. Indeed, Webster et al. observed that the repartition of bromine of highly BDE-209 contaminated dust was heterogeneous in house dust and concentrated in scattered highly contaminated particles, suggesting an abrasion origin of BDE-209 in dust [96], although Abdallah et al. did not observe this heterogeneous repartition when trying to explain the lower bioaccessibility of BDE-209 in their dust samples [46]. However, in a more recent study, an experimental chamber was used to compare the bioaccessibility of HBCDs in a pre-characterized dust that had been enriched by HBCDs originating from treated textile via the two migration pathway: HBCDs bioaccessibility in dust contaminated via volatilization (35%) was greater than in dust contaminated by abrasion (15%) [73]. This study confirms the general tendency of sorbed compounds being more bioaccessible than constitutive ones, although more studies need to be performed with other SVOCs sources.

Level of SVOC concentration. A variation of the amount of SVOC present in dust before it is submitted to bioaccessibility test showed no impact of the SVOC concentration [47,72].

Enantiomeric form of the SVOC. No difference was observed in the bioaccessibility of the 3 main HBCDs diastereoisomers (α, β, and γ), but this does not preclude the existence of an effect on their bioavailability [46].

A summary of the influencing factors related to the measurement method, the matrix and the SVOC is shown in Table 7.

4. Conclusion

SVOC bioaccessibilities show large variations, from 1 to 100 %. It is therefore important to take bioaccessibility into account for a better assessment of human exposure. It is particularly relevant for PAHs, which is the chemical family displaying the lowest bioaccessibilities and would therefore be more prone to exposure assessment errors. It is also important for phthalates, because the high concentrations measured in indoor dust could be put into perspective knowing their bioaccessibility. Bioaccessibility studies are easier to implement than bioavailability studies. However existing methods need to be (i) simplified, based on their most influencing parameters: inclusion of a sorptive sink and/or food, bile concentration and fluid:dust ratio, (ii) harmonized via interlaboratory calibrations, and (iii) validated versus in-vivo studies, preferably using swine. Predictions of the bioaccessible fraction could be made for compounds mainly concerned by the adsorption migration pathways, based on a knowledge of the SVOC content of the dust, its organic matter content and its pore sizes. Within a chemical family, further equations could be established based on their K_{ow}. However, more bioaccessibility data need to be acquired, on many different dust samples, for building and validating such models. Moreover, the bioaccessibility of SVOCs in dust has been assessed for

different chemical families, including OPFRs, BFRs, phthalates, OCP pesticides, and PAHs, but more studies are needed to address the lack of knowledge on other compounds and chemical families found in settled dust, such as bisphenols, triclosan, perfluorinated compounds, pyrethroids, etc.

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Figures:

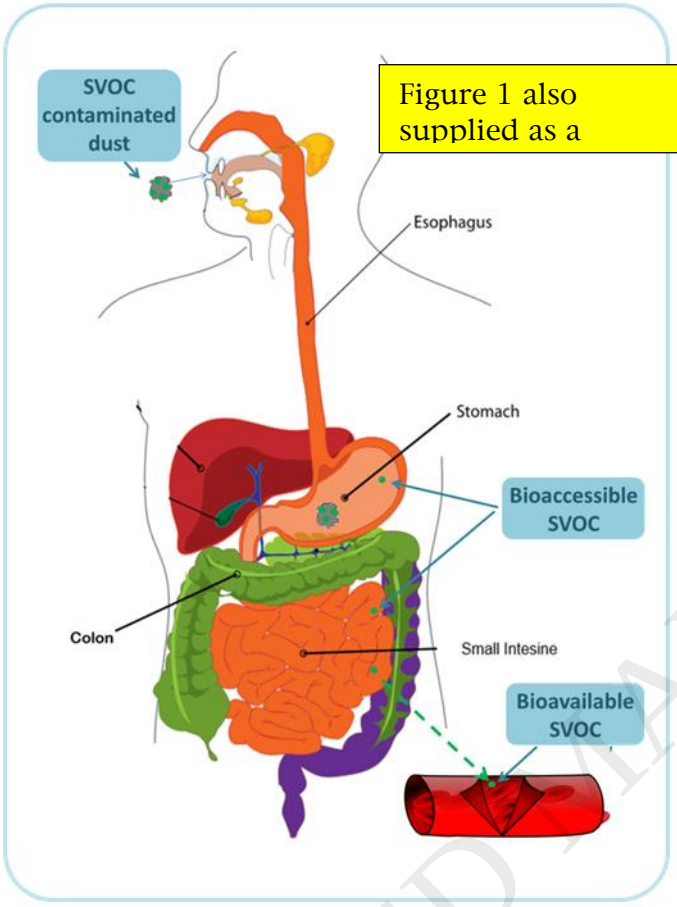

Figure 1: Human digestive system showing SVOC oral bioaccessibility and bioavailability

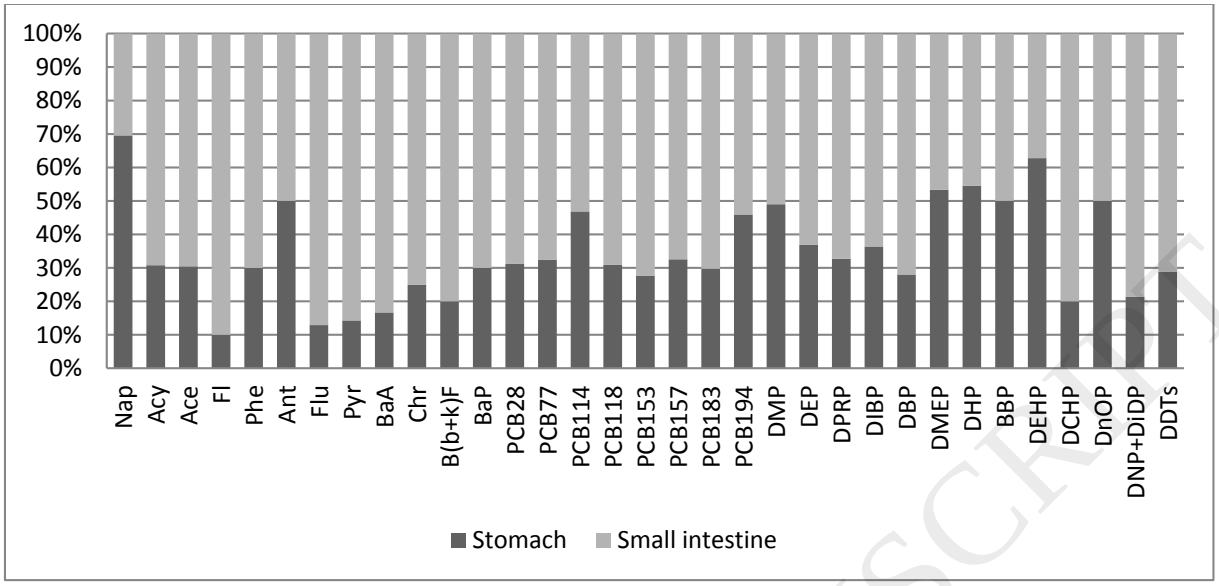

Figure 2: Partition of in vitro evaluation of SVOC absorption between stomach and small intestine.
PAH, phthalate, and DDT data are from the work of Wang et al. [44,76,95]. PCB data are from the work of Kang et al. [75].
Nap: naphthalene, Acy: acenaphthylene, Ace acenaphthene, Fl: fluorene, Phe phenanthrenes, Ant: anthracene, Flu: fluoranthene, Pyr: pyrene, BaA: benzo(a) anthracene, Chr: chrysene, B(b + k)F: benzo(b + k)fluoranthene, BaP: Benzo(a)Pyrene, DMP: dimethyl phthalate, DEP: diethyl phthalate, DPRP: di-n-propyl phthalate, DiBP: diisobutyl phthalate, DBP: di-n- butyl phthalate, DMEP: bis (2-methoxyethyl) phthalate, DHP: di-n-hexyl phthalate, BBP: butyl benzyl phthalate, DEHP: di- 2-ethylhexyl phthalate, DCHP: dicyclohexyl phthalate, DnOP: di-n-octyl phthalate, DNP: dinonyl phthalate, DiDP: di-iso-decyl phthalate, DDT: dichlorodiphenyltrichloroethane.

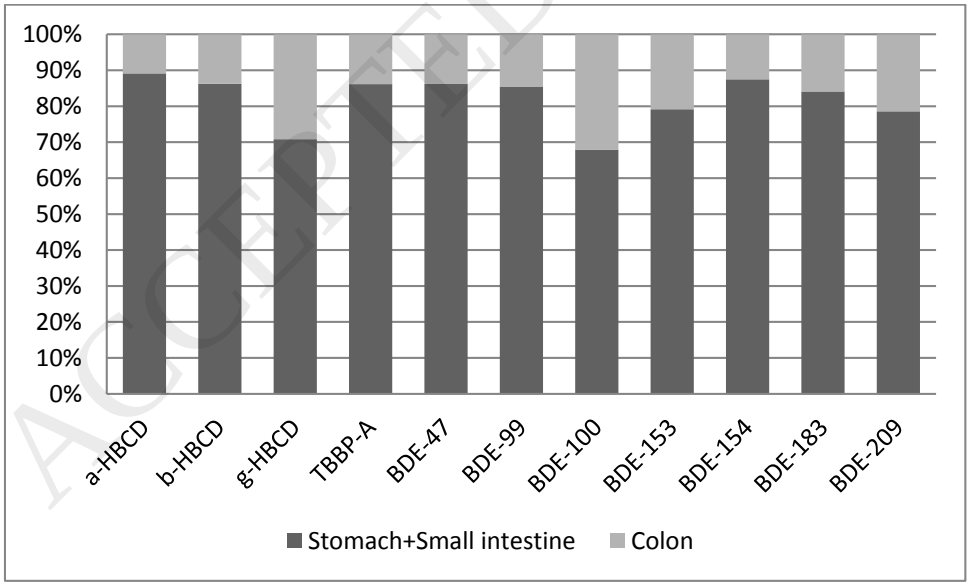

Figure 3: Partition of in vitro evaluation of SVOC absorption between stomach+small intestine and colon. Data are from the work of Abdallah et al. [46].
HBCD: hexabromocyclododecane, TBBP: tetrabromobisphenol, BDE: bromodiphenylether.

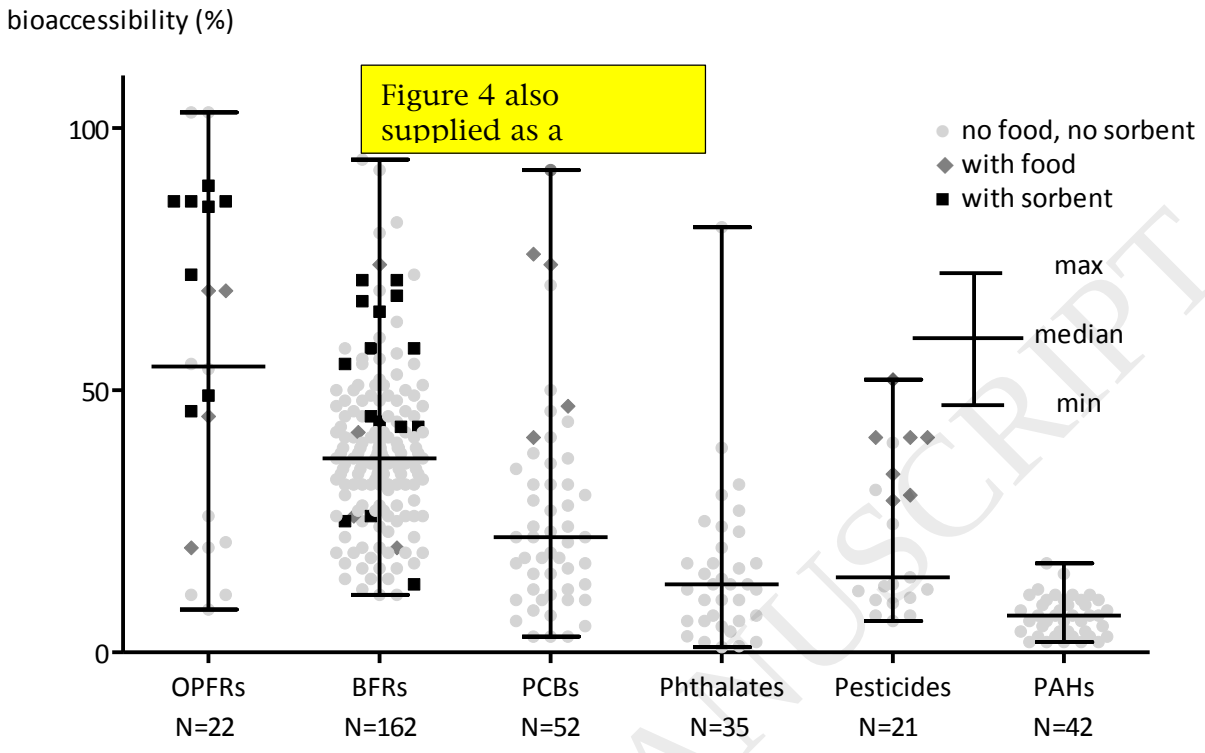

Figure 4: Published (20011-2017) SVOC bioaccessibility data in indoor settled dust according to measurement design. Each dot represents the median value for one compound in one study
OPFRs: organophosphorus flame retardants, BFRs: brominated flame retardants PCBs: polychlorobiphenyls, PAHs: polycyclic aromatic hydrocarbons, respectively

Tables:

Method	CE-PBET	CE-PBET	CE-PBET	PBET	PBET	CE-PBET + Tenax® TA	PBET	PBET	CE-PBET	PBET	PBET	PBET	PBET	PBET	PBET	PBET	PBET
n	1[a]	1[b]	1[c]	6	6	17	2	3	3	44[d]	44[e]	44[f]	44[g]	1[h]home	1[i]	1[j]	1[k]
Sieving	< 250 µm	< 250 µm	< 250 µm	< 100 µm	< 100 µm	< 53 µm	63-125 µm	25-500 µm	25-500 µm	< 250 µm	< 250 µm	< 250 µm	< 250 µm	< 250 µm	< 250 µm	< 250 µm	< 250 µm
EH-TBB						43											
BEH-TEBP						13											
α-HBCD	12	32	16					82	92								
β-HBCD	16	34	14					69	80								
γ-HBCD	19	37	14					51	72								
TBBP-A								51	94								
BDE 17						45				48	56	35	20	60	56	55	49
BDE 28				74						38	35	29	37	36	50	33	40
BDE 28, 33						65	48										
BDE 49						58											
BDE 47				26		71	34	50	58	38	32	26	22	34	43	39	45
BDE 66							36			38	34	28	26	33	57	38	39
BDE 100						68	34	36	53	46	37	26	20	40	42	45	45
BDE 99				20		71	32	35	41	32	24	18	16	27	34	35	47
BDE 85							32			50	39	48	19	42	37	45	40
BDE 85, 155						67											
BDE 154						58	39	28	32	49	36	32	26	36	55	42	47
BDE 153				42		55	39	38	48	41	36	25	26	32	49	33	42
BDE 138						43	27			42	52	25	35	30	41	35	39
BDE 183						44	32	37	44	38	41	27	28	17	39	22	36
BDE 190										51	31	41	35	46	17	51	36
BDE 203, 200						25											
BDE 209					63	26	11	11	14	23	19	19	19				
Reference	[73]			[51]	[52]	[45]	[50]	[46]		[72]				[47]			

Table 1: Bioaccessibility (%)of brominated flame retardants in indoor settled dust

[a]pooled dust samples not enriched, [b]pooled dust samples enriched by volatilization, [c]pooled dust samples enriched by abrasion, [d]Spring, [e]Summer, [f]Autumn, [g]Winter, [h]home, [i]laboratory, [j]office, 1[k]air conditionner

PBET: physiologically-based extraction test, CE: colon-extended, BEH-TEBP: bis(2-ethylhexyl) tetrabromophthalate, HBCD: hexabromocyclododecane, TBBP-A: tetrabromobisphenol A, BDE: bromodiphenyl ether

Method	UBM (without food)		FOREhST (with food)		PBET	PBET + Tenax® TA	CE-PBET + Tenax® TA
n	1 pooled sample of 10 house dust	1 pooled sample from 5 car dust	1 pooled sample of 10 house dust	1 pooled sample from 5 car dust	19	1	17
Sieving	20-60 µm	20-60 µm	20-60 µm	20-60 µm	< 150 µm		< 53 µm
TCEP	103	103	69	69	54	72	86
TCPP	26	11	45	20	55	89	86
TDCPP	21	11			20	49	85
TPP					8.2	46	86
Reference	[41]				[42]		[45]

Table 2: Bioaccessibility (%) of organophosphate flame retardants in indoor settled dust

UBM: Unified BioAccessibility Research Group of Europe (BARGE) Method, FOREhST: Fed ORganic estimation human Simulation Test, PBET: physiologically-based extraction test, TCEP: tris(2-chloroethyl) phosphate, TCPP: tris(2-chloroisopropyl) phosphate, TDCPP: tris(1,3-dichloro-2-propyl) phosphate, TPP: triphenylphosphate.

Method	PBET	PBET	DIN 19738	DIN 19738 + milk powder
n	18	120 outdoor, 40 indoor dust samples	6 to 9	3
Sieving	< 100 µm	<100 µm	< 63 µm	< 63 µm
PCB 18		30		
PCB 28	38	36	70	74
PCB 37		46		
PCB 44		17		
PCB 52		22		
PCB 70		32		
PCB 74		12		
PCB 77	32	6		
PCB 81		28		
PCB 87		37		
PCB 99		10		
PCB 101		3	50	76
PCB 105		3		
PCB 114	27			
PCB 118	23	10		
PCB 119		3		
PCB 123		12		
PCB 126		41		
PCB 128/158		44		
PCB 138		22	19	47
PCB 144		32		
PCB 151		5		
PCB 153	24		16	41
PCB 153/157		35		
PCB 156		10		
PCB 157	18			
PCB 167		18		
PCB 168		18		
PCB 169		29		
PCB 170		21		
PCB 177		11		
PCB 180		7	13	92
PCB 183	15	24		
PCB 187		22		
PCB 189		8		
PCB 194	15	10		
PCB 199		17		
Reference	[75]	[74]	[39]	

Table 3: Bioaccessibility (%) of polychlorobiphenyls (PCBs) in indoor settled dust
PBET: physiologically-based extraction test

Method	PBET	PBET	PBET	PBET
n	19	40	40	14
Sieving	< 150 µm	< 63 µm	63-100 µm	<100 µm
DMP	81	39	27	32
DEP		30	20	25
DPRP		23	24	
DiBP		13	13	17
DBP	3	10	7	15
DMEP		6	1	
DHP		17	12	
BBP	5	14	17	12
DEHP	1	16	6	10
DCHP		7	4	
DnOP		2	2	13
DNP+DiDP		6	10	
Reference	[42]	[76]		[43]

Table 4: Bioaccessibility (%) of phthalates in indoor settled dust

PBET: physiologically-based extraction test, DMP: dimethyl phthalate, DEP: diethyl phthalate, DPRP: di-n-propylphthalate, DiBP: diisobutyl phthalate, DBP: dibutyl phthalate, DMEP: bis (2-methoxyethyl) phthalate, DHP: di-n-hexyl phthalate, BBP: butyl benzyl phthalate, DEHP: di-2-ethylhexyl phthalate, DCHP: dicyclohexyl phthalate, DnOP: di-n-octyl phthalate, DNP: dinonyl phthalate, DiDP: di-isodecyl phthalate (DiDP)

Method	DIN 19738	PBET	DIN 19738	DIN 19738 + milk powder
n	37	120 outdoor, 40 indoor dust samples	6 to 9	3
Sieving	< 150 µm	<100 µm	< 63 µm	< 63 µm
DDTs		24.5	7[a]	30[a]
HCHs		10.4	31[b]	52[b]
CHLs		12.6		
Drins		11.7		
HCB		14.3		
Mirex		9.4		
PCP			12	34
PBO			7	41
Methoxychlor			10	29
Chlorpyrifos			13	41
Permethrine			6	41
Fipronil	40			
Reference	[40]	[44]	[39]	

Table 5: Bioaccessibility (%) of pesticides in indoor settled dust

PBET: physiologically-based extraction test, DDTs: dichlorodiphenyltrichloroethanes ([a]p,p'-DDT), HCHs: hexachlorocyclohexane([b]Lindane), CHLs: Heptachlor, transchlordane, cis-chlordane, trans-nonachlor, and cis-nonachlor, Drins: aldrin, dieldrin and endrin, HCB: hexachlorobenzene, PCP: pentachlorophenol, PBO: piperonyl butoxide

Method	PBET						
n	20[a]	4[b]	5[c]	16[d]	6[e]	4[f]	23[g]
Sieving	< 100 µm						
benzo(a)anthracene	12	11	17	8	11	11	10
chrysene	11	10	15	6	9	7	10
benzo(b+k)fluoranthene	7	10	3	3	3	3	4
benzo(a)pyrene	8	7	5	2	3	4	9
indeno(1, 2, 3-c, d)pyrene	6	4	2	2	2	1	4
dibenz(a,h)anthracene	6	7	5	6	8	7	9
Reference	[77]						

Table 6: Bioaccessibility (%) of PAHs in indoor settled dust and air conditioning filter dust

[a]air conditionning filter dust from commercial offices, [b]air conditionning filter dust from secondary schools, [c]air conditionning filter dust from shopping malls, [d]air conditionning filter dust from hospitals, [e]air conditionning filter dust from electronic factories, [f]air conditionning filter dust from commercial manufacturing plants, [g]house floor settled dust

Influencing factor	**Effect on SVOC bioaccessibility**
Factor related to the measurement method:	
Presence of a sorptive sink	↗ (OPFRs [42,45], PBDEs [45,48])
Presence of food	↗ (pesticides and PCBs [39]) ↘ (OPFRs [41])
Concentration of bile salts ↗	↗ (OPFRs and phthalates [42], PCBs [75], PBDEs [47])
Fluid :dust ratio ↗	↗ (PBDEs [47])
Factor related to the matrix:	
Dust organic matter ↗	↘ (PBDEs [50,52,72], fipronil [40], and the more hydrophobic OPFRs and phthalates [42]) → (FRs [45], PBDEs [93], and the less hydrophobic OPFRs and phthalates [42])
Dust particle ↗	↘ (PAHs [95], PBDEs [50], OCs [44], and phthalates [76])
Factor related to SVOC characteristics:	
K_{OW} ↗	↘ (OPFRs [41,45], BFRs [45,46], PCBs [74,75], phthalates [43], and PAHs[77]) → (PBDEs [46,51,72])
SVOC migration pathway (sorption → abrasion)	↘ (PBDEs [50] and HBCDs [73]) → (PBDEs [46])
Level of SVOC concentration ↗	→ (PBDEs [47,72])

Table 7 : Summary of the main factors influencing SVOC bioaccessibility in dust

OPFRs: organophosphate flame retardants, PBDEs: polybromodiphenylethers, PCBs: polychlorobiphenyls, FRs: flame retardants, PAHs: polycyclic aromatic hydrocarbons, OCs: organochlorine pesticides, and HBCDs: hexabromocyclododecanes