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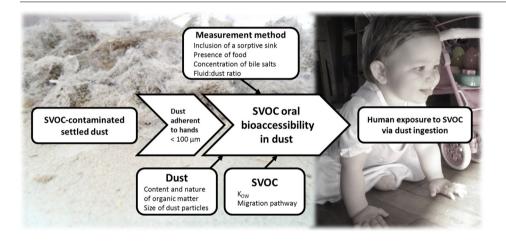
Oral bioaccessibility of semi-volatile organic compounds (SVOCs) in settled dust: A review of measurement methods, data and influencing factors



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GRAPHICAL ABSTRACT



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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.

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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-tomouth 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

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

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 $< 100 \,\mu m$ 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 & 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 (Fig. 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 multichamber 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.

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