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Exposition humaine aux composés organiques semi-volatils (COSV) en environnement intérieur par ingestion de poussières : évaluation de la bioaccessibilité orale des COSV

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SOMMAIRE

LISTE DES SIGLES & ACRONYMES 9

LISTE DES TABLEAUX 13

LISTE DES FIGURES 15

INTRODUCTION 17

CHAPITRE 1 : CONTEXTE SCIENTIFIQUE 19

1. LES COMPOSES ORGANIQUES SEMI-VOLATILS (COSV) 19

1.1. DEFINITION DES COSV 19

1.1. SOURCES DE COSV EN ENVIRONNEMENT INTERIEUR 19

1.2. REPARTITION DES COSV EN ENVIRONNEMENT INTERIEUR 25

1.3. TOXICITE DES COSV 26

2. CONTAMINATION DE L'AIR ET DES POUSSIERES EN ENVIRONNEMENT INTERIEUR 29

2.1. CONTAMINATION DE L'AIR ET DES POUSSIERES DES LOGEMENTS. 30

2.1. CONTAMINATION DE L'AIR ET DES POUSSIERES DES ECOLES (ARTICLE SCIENTIFIQUE N°1) 31

3. LES VOIES D'EXPOSITION AUX COSV 67

3.1. L'INGESTION 67

3.2. L'INHALATION 68

3.3. LE CONTACT CUTANE 68

3.4. CONTRIBUTION RELATIVE DE CHAQUE VOIE 68

4. NOTIONS DE BIOACCESSIBILITE ET BIODISPONIBILITE 69

4.1. DEFINITION DE LA BIOACCESSIBILITE 70

4.2. DEFINITION DE LA BIODISPONIBILITE 70

5. QUESTIONS DE RECHERCHE 72

6. OBJECTIFS DE LA THESE 72

CHAPITRE 2 : LA BIOACCESSIBILITE DES COSV DANS LES POUSSIERES- REVUE DE LA LITTERATURE (ARTICLE SCIENTIFIQUE N°2) 73

CHAPITRE 3 : PROPOSITION D'UNE METHODE SIMPLIFIEE DE MESURE DES COSV DANS LES POUSSIERES 99

1. DEVELOPPEMENT DE LA METHODE (ARTICLE SCIENTIFIQUE N°3) 100

2. APPLICATION A DES ECHANTILLONS REELS 151

2.1. SELECTION DES ECHANTILLONS 152

2.2. BIOACCESSIBILITE DES COSV DANS 7 ECHANTILLONS DE POUSSIERE DE SALLES DE CLASSE 157

CONCLUSION ET PERSPECTIVES 171

1. ACQUISITION DE DONNEES COMPLEMENTAIRES SUR LA BIOACCESSIBILITE DES COSV 171

2. EVOLUTION DE LA METHODE SIMPLIFIEE 171

3. VALIDATION *IN VIVO* DES DONNEES 172

4. PERSPECTIVES SUR L'INHALATION 173

5. PERSPECTIVES SUR LE CONTACT CUTANE 174

6. EVALUATION GLOBALE DE L'EXPOSITION HUMAINE AUX COSV EN ENVIRONNEMENT INTERIEUR 175

REFERENCES 177

VALORISATION SCIENTIFIQUE 187

LISTE DES SIGLES & ACRONYMES

4,4'-DDE : 2,2-bis(p-chlorophényl)-1,1-dichloroéthylène

4,4'-DDT : 4,4'-dichlorodiphényltrichloroéthane

ADEME : Agence de l'Environnement et de la Maîtrise de l'Energie

AHTN : 7-Acétyl-1,1,3,4,4,6-hexaméthyl-1,2,3,4-tetrahydronaphthalène (tonalide)

ANSES : Agence nationale de sécurité sanitaire en charge de l'alimentation, de l'environnement et du travail

BA : bioacessibilité

BARGE : Bioaccessibility research group of Europe

BBP : butyl benzyl phtalate

BDE : bromodiphényl éther

BPA : Bisphenol A

CG/MS/MS : chromatographie gazeuse couplée à la spectrométrie de masse en tandem

CIRC : Centre International de Recherche sur le Cancer

CLP : *classification, labelling and packaging*

CLS : concentration limite de sélection

COSV: composé organique semi-volatil

COTV : composé organique très volatil

COV : composé organique volatil

CSTB : Centre Scientifique et Technique du Bâtiment

DBP : dibutyl phtalate

DEHP : di-2-ethylhexyl phtalate

DEP : diethyl phtalate

DiBP : diisobutyl phtalate

DiDP : diisodecyl phtalate

DiNP : diisononyl phtalate

DiUP : diisoundecyl phtalate

DL : *dioxin like*

DMEP : di-2-méthoxyéthyl phtalate

DMP : dimethyl phtalate

DNOP : dioctyl phtalate

DPHP : di-2-propylheptyl phtalate

DTDP : diisotridecyl phtalate

ECHA : *European Chemicals agency*

ECOS : Exposition cumulée aux composés organiques semi-volatils

EHESP : Ecole des Hautes Etudes en Santé Publique

HAP : hydrocarbure aromatique polycyclique

HCH : hexachlorocyclohexane

HHCB : 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8,-hexamethyl-cyclopenta[g]benzopyran (galaxolide)

Irset : Institut de recherche en santé, environnement et travail

ISO : *International Organization for Standardization*

K_{OA} : coefficient de partage entre l'octanol et l'air

K_{OW} : coefficient de partage entre l'octanol et l'eau

LD : limite de détection

LERES : Laboratoire d'Etudes et de Recherche en Environnement et Santé

LQ : limite de quantification

NDL : *non dioxin like*

NF : Norme Française

NIST : *National Institute of Standards & Technology*

OQAI : Observatoire de la Qualité de l'Air Intérieur

PBDE : polybromodiphényléther

PBT : persistant, bioaccumulable et toxique

PCB : polychlorobiphényle

PLE : pressurized liquid extraction (extraction liquide à haute pression)

PNSE : Plan National Santé Environnement

POP : polluant organique persistant

PVC : Polychlorure de vinyle

SRM : *Standard Reference Material*

TBP : tributylphosphate

TD : thermodésorption

tPtB : très persistant et très bioaccumulable

US EPA : agence américaine de protection de l'environnement

VTR : valeur toxicologique de référence

LISTE DES TABLEAUX

Tableau 1 : Usages et sources de COSV dans les poussières sédimentées 20

Tableau 2 : HAP présents dans la liste de l'ECHA des substances extrêmement préoccupantes candidates en vue d'une autorisation 28

Tableau 3 : liste des COSV retenus pour les mesures de bioaccessibilité orale 151

Tableau 4: Concentrations limite de sélection (CLS) des phtalates et des PBDE 155

Tableau 5 : Liste des échantillons sélectionnés 156

Tableau 6 : Concentrations des COSV dans les blancs et les contrôles d'extraction fortifiés 159

Tableau 7 : Concentrations des COSV dans le blanc et les contrôles d'incubation fortifiés 160

Tableau 8 : Concentrations des COSV bioaccessibles, non-bioacessibles et totales dans le SRM 2585 162

Tableau 9 : Concentrations en COSV bioaccessibles et non-bioaccessibles dans 7 échantillons de poussières d'école (France, 2013-2017) 164

Tableau 10 : Bioaccessibilité des COSV dans 7 échantillons de poussières d'école (France, 2013-2017) 165

Tableau 11 : Comparaison de la bioacessibilité des HAP avec les données de la litérature 168

Tableau 12 : Comparaison entre bioaccessibilité et biodisponibilité de quatre phtalates 169

LISTE DES FIGURES

Figure 1 : Structure chimique générique des phthalates 21

Figure 2 : Structure chimique de quelques HAP 22

Figure 3 : Structure chimique des PCB 23

Figure 4 : Structure chimique des PBDE 24

Figure 5 : Structure chimique de la pyréthrine et de quelques exemples de pyréthrinoïdes 25

Figure 6 : Equilibre des COSV en environnement intérieur 26

Figure 7 : Effets sur la santé des expositions aux HAP 27

Figure 8 : Les principales étapes du projet ECOS-Habitat 30

Figure 9 : Les voies d'exposition aux COSV en environnement intérieur 67

Figure 10 : Contribution relative de chaque voie d'exposition 69

Figure 11 : Représentation schématique des notions de bioaccessibilité et biodisponibilité orale 71

Figure 12 : Relation entre bioaccessibilité et biodisponibilité 72

Figure 13 : Concentrations en phtalates mesurées dans les échantillons de la campagne nationale « écoles » de l'OQAI (2013-2017) 153

Figure 15 : Concentrations en PBDE mesurées dans les échantillons de la campagne nationale « écoles » de l'OQAI (2013-2017) 153

Figure 16 : Classement des échantillons selon leur masse de poussière disponible (reliquat) ... 154

Figure 17 : concentrations totale et bioaccessible, et bioaccessibilité des COSV dans 7 échantillons de poussières d'école (France 2013-2017) 166

Figure 18 : Relation entre bioaccessibilité et K_{ow} des COSV de 7 échantillons de poussières d'école (France, 2013-2017)..... 167

Figure 19 : Relation entre bioaccessibilité et K_{ow} des PCB de 7 échantillons de poussières d'école (France 2013-2017)..... 168

Figure 20 : Schéma d'une monocouche de Caco-2 cultivée sur un support filtrant perméable .....**Erreur ! Signet non défini.**

Figure 21 : Considérer la bioaccessibilité pour évaluer l'exposition aux COSV en environnement intérieur..... 175

Figure 22 : Support de médiation scientifique..... 188

INTRODUCTION

Poussière : «particules qui se sont déposées sur des objets, des surfaces, des planchers et de la moquette à l'intérieur d'un bâtiment. Ces particules peuvent comprendre des particules de sol qui ont été apportées dans l'environnement intérieur à partir de l'extérieur ainsi que de la matière organique » [1]. Ainsi est définie la poussière par l'agence américaine de protection de l'environnement (US EPA) dans son Manuel sur les facteurs d'exposition (*Exposure Factor Handbooks*). Cette définition est celle retenue dans le cadre de ces travaux de thèse, en lien avec une exposition de la population générale à l'exclusion de toute exposition professionnelle.

La poussière est une matrice hétérogène faite de particules provenant de sources intérieures (érosion des matériaux, desquamation de la peau) et extérieures (particules de sol transférées à l'intérieur par le vent, les animaux de compagnie, les chaussures, etc.). Sa composition dépend essentiellement du type d'aménagement intérieur, du comportement des occupants et des environs du bâtiment. La poussière est ainsi constituée de matières organiques : fragments d'origine humaine (principalement des squames contenant du squalène et du cholestérol), fibres (d'origine naturelle comme le coton ou la cellulose, ou issues de la pétrochimie (polypropylène)), micro-plastiques, particules provenant de l'abrasion des tissus, des meubles et des surfaces, suies, pollen, etc. ; de particules inorganiques : quartz, albite, calcite, dolomie, etc. ; et d'organismes vivants (bactéries, moisissures) [2–11].

La poussière domestique sert donc de réservoir pour divers polluants provenant de l'intérieur et de l'extérieur. Elle peut contenir des métaux toxiques comme l'antimoine, l'arsenic, le cadmium, le chrome, le cuivre, le manganèse, le plomb, le strontium et le vanadium, ainsi que des polluants organiques non volatils ou semi-volatils, comme des composés bromés, fluorés, chlorés, etc. [8,9,12]. Les composés organiques semi-volatils (COSV) sont parfois suspectés d'effets néfastes pour la santé et notamment de perturbation endocrinienne. C'est sur ces derniers que se portent les présents travaux de thèse.

La poussière est un important vecteur d'exposition humaine aux COSV. Les populations y sont en effet exposées par ingestion et en particulier les enfants qui passent du temps au sol, ont de fréquents contacts mains-bouche ou mettent à la bouche des jouets ou de la nourriture tombés au sol. On estime à 40, 30, et 20 mg/jour les quantités de poussières ingérées par les enfants de 1 à 6 ans, de 6 à

12 ans et de plus de 12 ans, respectivement [1]. Les populations sont également exposées à la poussière par contact cutané et par inhalation des particules les plus fines.

Cette problématique est un enjeu de santé publique. L'Observatoire de la Qualité de l'air intérieur, missionné par les pouvoirs publics pour mieux connaître la qualité de l'air intérieur, a inclus la thématique « poussières » dans ses programmes de recherche[1]. Dans la continuité de son prédécesseur, le Plan National Santé Environnement 3 (2015-2019) prévoit d'une part d'« agir pour une meilleure qualité de l'air intérieur », d'autre part de « réduire l'exposition aux perturbateurs endocriniens »[2].

Dans le domaine de l'air, des valeurs limites réglementaires ont déjà été établies pour certains composés organiques volatils (COV) dont le benzène et le formaldéhyde, mais à ce jour, aucune valeur de référence n'a été préconisée pour les COSV dans les poussières. Établir de telles préconisations requiert de bien estimer la dose à laquelle est exposée la population en environnement intérieur.

Dans ce contexte, cette thèse a pour objet de mieux caractériser l'exposition humaine aux COSV en environnement intérieur par ingestion de poussière, et pour ce faire, de considérer la fraction bioaccessible (libérée dans le tractus gastro-intestinal après ingestion).

Ce manuscrit est constitué de trois chapitres :

Le premier chapitre présente les COSV en termes de sources et de toxicité, puis établit leur présence et leurs niveaux de concentration en environnement intérieur, plus particulièrement dans les écoles, en s'appuyant sur un premier article scientifique. Les différentes voies d'exposition sont ensuite décrites avec les notions importantes de bioaccessibilité et biodisponibilité.

Le deuxième chapitre présente la bioaccessibilité orale des COSV en se basant sur un article scientifique de type revue de la littérature.

Le troisième chapitre propose une nouvelle méthode simplifiée pour la mesure de la bioaccessibilité de ces COSV, qui fait l'objet d'un troisième article scientifique.

Enfin la dernière partie inscrit ce projet dans un contexte plus large que l'exposition par ingestion en établissant des perspectives considérant également la bioaccessibilité par inhalation et par contact cutané, afin de caractériser de manière globale l'exposition aux COSV en environnement intérieur.

[1] http://www.oqai.fr

[2] https://solidarites-sante.gouv.fr/sante-et-environnement/les-plans-d-action-nationaux/article/le-plan-national-sante-environnement-pnse3-2015-2019

CHAPITRE 1 : CONTEXTE SCIENTIFIQUE

1. LES COMPOSES ORGANIQUES SEMI-VOLATILS (COSV)

1.1. DEFINITION DES COSV

Selon la norme NF ISO 16000-6 [13], les COSV sont définis par leur point d'ébullition, situé entre (240°C à 260°C) et (380°C à 400°C). Ils se distinguent ainsi des composés organiques volatils (COV) dont le point d'ébullition se situe entre (50°C à 100°C) et (240°C à 260°C) et des composés organiques très volatils (COTV) dont le point d'ébullition se situe entre <0°C et (50°C à 100°C). La norme précise toutefois que le point d'ébullition peut être difficile à déterminer pour certains composés qui se décomposent avant l'ébullition à pression atmosphérique. Les COSV peuvent alors être définis selon leur tension de vapeur, et c'est ainsi que Weschler et Nazaroff, dans leur article de référence de 2008 sur les COSV dans les environnements intérieurs [14], définissent les COSV comme des composés organiques avec une tension de vapeur comprise entre 10^{-14} et 10^{-4} atm (10^{-9} à 10 Pa).

Une approche originale pour définir les COSV a également été proposée par Võ et Morris [15]. Ces auteurs se basent sur le ratio d'évaporation d'un composé dans des conditions ambiantes d'évaporation : un composé volatil est défini comme un composé qui s'évapore de plus de 95 % de sa masse en 6 mois , un composé non volatil comme un composé qui s'évapore de moins de 5 % de sa masse en 6 mois, et un composé semi-volatil est un composé qui s'évapore entre 5 et 95 % de sa masse en 6 mois.

1.1. SOURCES DE COSV EN ENVIRONNEMENT INTERIEUR

De nombreuses études bibliographiques internationales ont investigué la présence de COSV en environnement intérieur [14,16–18]. Pas moins de 25 familles chimiques de COSV ont été répertoriées, parmi lesquelles alcaloïdes, alkylphénols, dioxines et furanes, muscs, esters organophosphatés, organo-étains, parabènes et triclosan, composés perfluorés, phénols, phtalates, polybromodiphényléthers (PBDE), polychlorobiphényles (PCB), polychlorobenzènes, hydrocarbures aromatiques polycycliques (HAP), etc.

Le Tableau 1, issu des travaux de Mercier et al. [12], présente les différents usages et sources de COSV en environnement intérieur. Ces sources sont liées aux activités des occupants (tabagisme, sous-produits de combustion, utilisation de cosmétiques, produits de soins, produits d'entretien et détergents, biocides), à l'équipement et à l'ameublement (télévisions, ordinateurs, textiles, mousses de polyuréthane, moquettes), aux matériaux de construction (sols synthétiques, peintures, joints) ainsi qu'à la contamination apportée par l'air extérieur (fumées industrielles, trafic routier, applications de pesticides, sous-produits de combustion).

TABLEAU 1 : USAGES ET SOURCES DE COSV DANS LES POUSSIERES SEDIMENTEES

Familles chimiques	Usages	Sources
Alkylphénols	Surfactants, conservateurs	Détergents et produits d'entretien, lessives, cosmétiques
Bisphénol A (BPA)	Composant de polymère, révélateur chimique	Plastiques de type polycarbonate et résines époxydes, papiers thermiques
Hydrocarbures aromatiques polycycliques (HAP)	Non intentionnels (présents dans les produits pétroliers ; résidus de combustion)	Tabagisme, cuisson, combustion d'encens, chauffage domestique (charbon, bois) Air extérieur (trafic, émissions industrielles, feux de forêt, etc.)
Muscs de synthèse	Parfums	Produits de soin, cosmétiques, produits d'entretien
Pesticides organochlorés et organophosphorés, pyréthrinoïdes	Pesticides, biocides	Produits insecticides, antiparasitaires humain et animal, de traitement des plantes Air extérieur (traitement des cultures)
Phtalates	Plastifiants	Matières plastiques souples (revêtements de sol ou muraux, câbles électriques, rideaux de douche, matériel médical, etc.), lubrifiants, parfums
Polybromodiphényléthers (PBDE)	Retardateurs de flamme	Textiles, mobiliers rembourrés, plastiques durs (ordinateurs, téléviseurs, etc.)
Polychlorobiphényles (PCB)	Stabilisateurs, retardateurs de flamme	Vieux joints d'étanchéité (ouvrants, revêtements de sol)
Tributylphosphate (TBP)	Solvant, plastifiant, retardateur de flamme	Revêtements, peintures
Triclosan	Désinfectant, biocide	Produits d'hygiène corporelle, produits de consommation courante

Tableau adapté de la publication de Mercier et al. (2011), Environ. Sci. Technol [12]

Parmi les familles les plus fréquemment retrouvées en environnement intérieur, les phtalates, les HAP, les PCB, les PBDE et les pyréthrinoïdes sont présentés plus en détails ci-après.

LES PHTALATES

Les phtalates, ou esters de l'acide phtalique, peuvent se classer en trois groupes [19]:

- Les phtalates de poids moléculaire élevé, qui comptent de 7 à 13 atomes de carbones le long de leur radical carboné R (Figure 1), comprennent le diisodecyl phtalate (DiDP), le diisononyl phtalate (DiNP), le di-2-propylheptyl phtalate (DPHP), le diisoundecyl phtalate (DiUP) et le diisotridecyl phtalate (DTDP). Ces phtalates sont utilisés comme plastifiants pour assouplir les polymères comme le PVC. Ils ne sont pas liés chimiquement aux polymères et sont donc à même de migrer dans l'environnement.
- Les phtalates de faible poids moléculaire, comprenant notamment le dibutyl phtalate (DBP), le diisobutyl phtalate (DiBP), le butyl benzyl phtalate (BBP) et le di-2-ethylhexyl phtalate (DEHP), sont utilisés comme plastifiants non seulement pour le PVC, mais également pour les dispositifs médicaux, les adhésifs, les peintures et les encres. De même que les phtalates à longues chaines, ils ne sont pas non plus liés chimiquement aux polymères et peuvent donc migrer facilement dans l'environnement.
- Le dimethyl phtalate (DMP) et le diethyl phtalate (DEP), comptant respectivement un et deux atomes de carbone sur leurs radicaux, sont utilisés dans les cosmétiques, produits de soin et produits d'entretien.

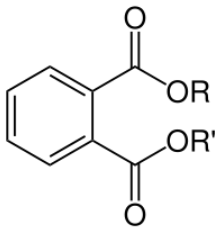


FIGURE 1 : STRUCTURE CHIMIQUE GENERIQUE DES PHTHALATES

Des limitations d'usage de certains phtalates ont été mises en places au niveau réglementaire : la directive européenne 2005/84/CE limite à 0,1 % la concentration du DiNP, du DIDP et du DNOP dans les jouets pouvant être mis à la bouche des enfants de moins de 3 ans, et du DEHP, du DBP et du BBP dans tous les jouets et articles de puériculture. La directive 2004/93/CE interdit l'utilisation du DEHP, du DBP et du DMEP dans les produits cosmétiques. La directive 2007/19/CE interdit l'utilisation du DEHP et du DBP dans les plastiques en contact avec des aliments gras. En France, l'arrêté du 30 avril 2009 relatif aux conditions de mise sur le marché des produits de construction et de décoration contenant des substances cancérigènes, mutagènes ou repro-

toxiques de catégorie 1 ou 2, limite à 1 µg/m³ les émissions en DEHP et de DBP des produits de construction et de décoration.

LES HAP

Les hydrocarbures aromatiques polycycliques (HAP) forment un grand groupe de composés organiques composés d'au moins deux noyaux benzéniques fusionnés et disposés selon diverses configurations (Figure 2).

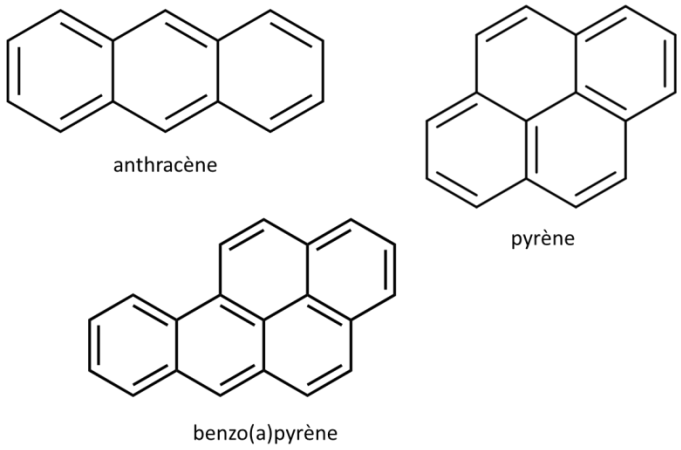


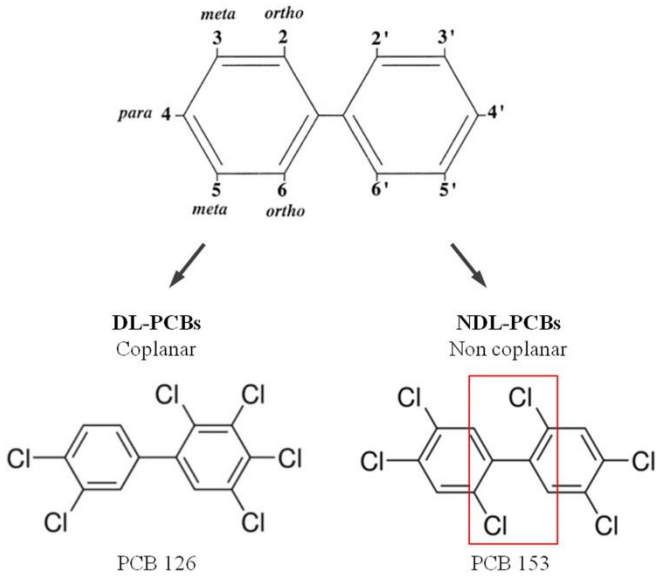
FIGURE 2 : STRUCTURE CHIMIQUE DE QUELQUES HAP

Bien qu'il existe des sources naturelles de HAP, comme les feux de forêt ou les éruptions volcaniques, les sources anthropogéniques prédominent. A l'intérieur des bâtiments, les HAP proviennent de la consommation de tabac, de la cuisson d'aliments, des cheminées ou poêles à foyer ouverts ou de la combustion de bougies et d'encens. A l'extérieur, la combustion incomplète des carburants pour le trafic automobile ou le chauffage des bâtiments, l'incinération des déchets et d'autres procédés industriels et chimiques à haute température, émettent également des HAP qui peuvent migrer à l'intérieur des bâtiments. Les concentrations de HAP varient d'une saison à l'autre, et sont plus fortes pendant les périodes hivernales durant lesquelles le chauffage central est en activité.[20–22]

LES PCB

Les polychlorobiphényles (PCB) sont composés de deux noyaux benzéniques dont les atomes d'hydrogène sont plus ou moins substitués par des atomes de chlore. Il existe ainsi 209 PCB différents, dont les coefficients octanol-eau (K_{OW}), indicateurs de leur lipophilie et donc de leur propension à la bioaccumulation, varient d'un facteur 10000 entre le chlorobiphényl (mono-

substitué) et le décachlorobiphényl (entièrement substitué).[23] Les PCB se distinguent en deux catégories, selon le rapprochement de leur structure et de leur toxicité avec les dioxines (Figure 3) [24]. Les NDL (*non dioxin like*) –PCB sont moins toxiques que les DL(*dioxin like*)-PCB, mais ils sont retrouvés plus abondamment dans l'environnement [25].



Repris de la publication de Abella et al. (2016), life sciences.[26]

FIGURE 3 : STRUCTURE CHIMIQUE DES PCB

Les PCB ont été produits à l'échelle industrielle pendant plus de cinquante ans, en raison de leurs remarquables propriétés physico-chimiques (stabilité chimique et thermique, faible volatilité, propriétés diélectriques, ininflammabilité, point d'ébullition élevé, miscibilité aux solvants organiques, etc.). Ils ont ainsi été utilisés comme fluides caloporteurs, lubrifiants hydrauliques, fluides diélectriques pour transformateurs et condensateurs, etc. A l'intérieur des bâtiments, ils étaient utilisés pour l'isolation des fils en PVC, comme retardateurs de flamme, comme additifs (dans les produits d'étanchéité, les adhésifs, les peintures), etc. La production de PCB a été interdite en 1987 par le congrès américain et par la convention de Stockholm sur les polluants organiques persistants (POPs) en 2001 [23]. Cependant, les PCB, du fait même de cette persistance, sont toujours présents aujourd'hui en environnement intérieur [27].

LES PBDE

Les polybromodiphényléthers (PBDE) sont constitués de deux noyaux benzéniques aux atomes d'hydrogène substitués par des atomes de brome dans diverses proportions (Figure 4). De même que les PCB, les PBDE comptent 209 congénères, qui sont regroupés en fonction du nombre

d'atomes de brome qu'ils comptent, en mono-, di-, tri-, tétra-, penta-, hexa-, hepta-, octa-, nona- et déca-BDE. Les principaux mélanges commerciaux sont constitués majoritairement de penta-BDE, octa-BDE et déca-BDE (BDE 209).

Les PBDE ont été utilisés comme retardateurs de flamme dans les mousses de polyuréthane pour l'ameublement, l'isolation des fils électriques, ainsi que dans le matériel électronique et informatique [28]. En 2003, la directive européenne 2003/11/CE a limité la mise sur le marché et l'emploi des penta- et octa- BDE en Europe. Le règlement (UE) 2017/227 de la Commission du 9 février 2017 restreint quant à lui l'usage du déca-BDE. Cependant, les PBDE sont persistants en environnement intérieur en raison de leur stabilité chimique, bien que la débromation des congénères les plus bromés sous l'effet de la lumière du soleil puisse mener à un enrichissement en congénères plus faiblement bromés [29].

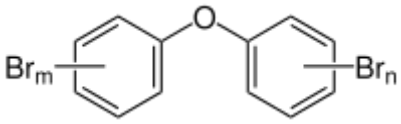


FIGURE 4 : STRUCTURE CHIMIQUE DES PBDE

LES PYRETHRINOÏDES

Les pyréthrinoïdes sont des substances synthétiques dont la formule est inspirée des pyréthrines naturelles présentes dans les fleurs de chrysanthème. Les pyréthrinoïdes se divisent en deux groupes (Figure 5) :

- les pyréthrinoïdes de type I, ne contenant pas de groupe α-cyano, qui comprennent notamment l'alléthrine, la bifenthrine, la d-phénothrine, la perméthrine, la resméthrine et la tétraméthrine [30,31] ;
- les pyréthroïdes de type II, contenant un groupe α-cyano, qui comprennent des composés tels que la cyperméthrine, la deltaméthrine, la cyhalothrine, la cyfluthrine, et le fenvalerate [30,31].

Les pyréthrinoïdes sont de plus en plus utilisés pour remplacer les substances pesticides restreintes ou interdites comme les pesticides organochlorés et organophosphorés [32]. Ils sont utilisés à l'extérieur comme pesticides pour les cultures, la forêt, l'horticulture et les jardins. En environnement intérieur, la perméthrine est utilisée comme biocide pour lutter contre les poux et les puces et comme répulsif pour les arthropodes dans les vêtements et les tapis [32]. Dans les

régions tropicales, la deltaméthrine et la perméthrine sont utilisées pour imprégner les moustiquaires et réduire la transmission de la malaria [33].

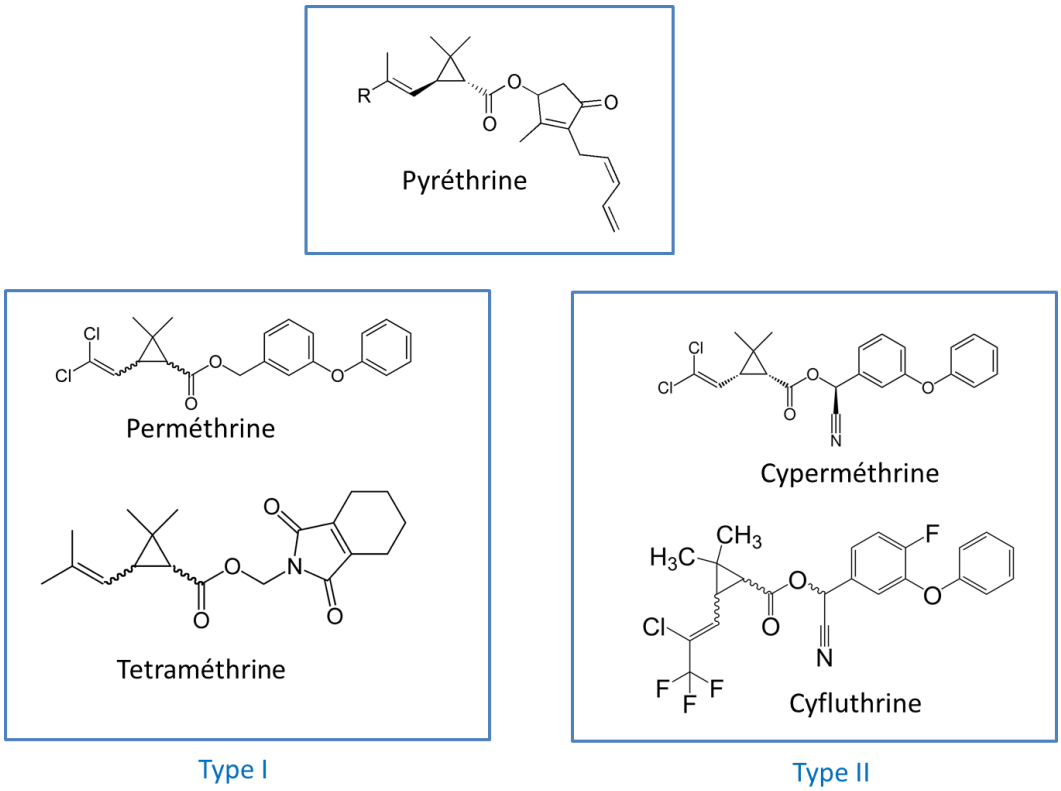


FIGURE 5 : STRUCTURE CHIMIQUE DE LA PYRETHRINE ET DE QUELQUES EXEMPLES DE PYRETHRINOÏDES

1.2. Repartition des COSV en environnement interieur

Une fois émis dans l'environnement intérieur par volatilisation ou abrasion de leur matériau d'origine, par intervention humaine (application de biocide ou combustion), ou venus de l'extérieur, les COSV, en raison de leurs propriétés semi-volatiles, s'équilibrent entre la phase gazeuse de l'air, les particules en suspension, la poussière sédimentée et les surfaces disponibles (murs, plafonds, sols), y compris humaines [14,34,35]. Ces équilibres, illustrés dans la Figure 6, varient en fonction de la température intérieure, de l'humidité, de la ventilation, de la concentration des particules en suspension dans l'air, de la concentration de la source, de la réactivité des COSV, ainsi que des activités des occupants [36].

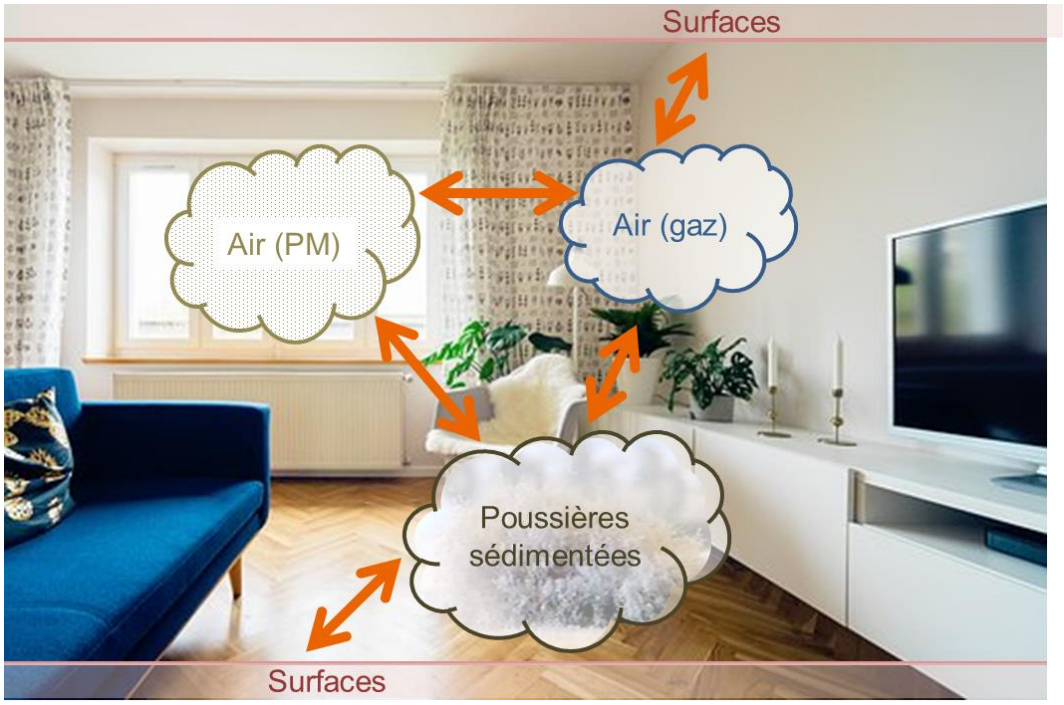


FIGURE 6 : EQUILIBRE DES COSV EN ENVIRONNEMENT INTERIEUR

1.3. TOXICITE DES COSV

La présence de COSV dans les environnements intérieurs questionne les autorités de santé en raison de leur toxicité. Les COSV sont en effet pour la plupart suspectés de perturbation endocrinienne avec des effets reprotoxiques, neurotoxiques et cancérogènes.

TOXICITE DES PHTALATES

Chez les humains, il existe de plus en plus de preuves d'une association entre l'exposition aux phtalates et les troubles congénitaux de la reproduction chez les hommes, incluant notamment une inhibition de la production de testostérone, une détérioration de la qualité du sperme, des distances anogénitales plus courtes et des hypospadias [19,37–40].

Des associations avec des niveaux anormaux d'hormones thyroïdiennes [41,42], le diabète, la résistance à l'insuline et l'obésité sont également suspectés [37] ainsi que des liens avec l'asthme et l'allergie. [43–45]

Le DEHP, le DBP, le BBP et le DiBP sont inscrits à l'annexe VI du règlement CLP (*Classification, Labelling and Packaging*) comme substances présumées toxiques pour la reproduction humaine (Repr. 1B). Ils ont également été ajoutés en juin 2017 à la liste de l'ECHA (*European Chemicals*

Agency) des substances extrêmement préoccupantes candidates en vue d'une autorisation, en raison de leurs propriétés perturbatrices du système endocrinien.

Par ailleurs, le DEHP a été classé en 2013 comme agent peut-être cancérogène par le Centre International de Recherche sur le Cancer (CIRC).

TOXICITE DES HAP

Certains HAP, dont le benzo[a]anthracène, le benzo[a]pyrène et le dibenz[ah]anthracène, représentent une menace sérieuse pour la santé et le bien-être des humains du fait de leurs effets cancérigènes, mutagènes et tératogènes [22]. Bien que les HAP plus légers soient considérés comme moins toxiques, ils peuvent réagir avec d'autres polluants (comme l'ozone, les oxydes d'azote et le dioxyde de soufre) pour former d'autres molécules plus toxiques. Les effets à court-terme et à long terme sur la santé des HAP ont fait l'objet d'une revue bibliographique [22] et sont résumés dans le schéma ci-dessous.

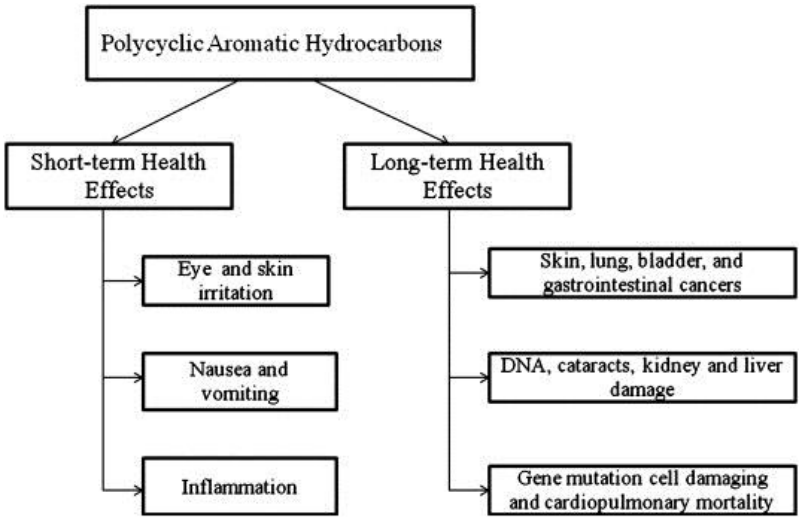


Diagramme repris de la publication de Ki-Hyun Kim (2013), Environment International [22]

FIGURE 7 : EFFETS SUR LA SANTE DES EXPOSITIONS AUX HAP

Parmi les 16 substances jugées prioritaires par l'agence américaine de protection de l'environnement (US EPA), le CIRC a classé le benzo(a)pyrène comme cancérogène pour l'Homme (groupe 1), le dibenzo(a,h)anthracène comme probablement cancérogène (groupe 2A) et le naphtalène, le benzo(a)anthracène, le chrysène, le benzo(b)fluoranthène, le benzo(k)fluoranthène et l'indeno(1,2,3-cd)pyrène comme peut-être cancérogène (groupe 2B). En Europe, 5 substances ont été ajoutées à la liste de l'ECHA des substances extrêmement préoccupantes candidates en vue d'une autorisation (Tableau 2).

TABLEAU 2 : HAP PRESENTS DANS LA LISTE DE L'ECHA DES SUBSTANCES EXTREMEMENT PREOCCUPANTES CANDIDATES EN VUE D'UNE AUTORISATION[3]

Nom de la substance	numéro CAS	Date d'inclusion	Raison de l'inclusion
Benzo[ghi]perylène	191-24-2	27/06/2018	PBT tPtB
Benz[a]anthracène	56-55-3 1718-53-2	15/01/2018	Cancérigène PBT tPtB
Chrysène	218-01-9 1719-03-5	15/01/2018	Cancérigène PBT tPtB
Benzo[a]pyrène	50-32-8	20/06/2016	Cancérigène Mutagène Reprotoxique PBT tPtB
Anthracène	120-12-7	28/10/2008	PBT

PBT : Persistant, Bioaccumulable et Toxique, tPtB : très Persistant et très Bioaccumulable.

TOXICITE DES PCB

Les PCBs sont impliqués de manière causale dans l'apparition de troubles neurodéveloppementaux [46]. L'exposition humaine aux PCB est également liée à des dysfonctionnements du comportement reproductif [24] et à la survenue de cancers, dont le lymphome non-hodgkinien [23]. En 2016, le CIRC a reclassé les PCB dans le groupe 1 "Cancérogène pour l'Homme" au lieu du groupe 2A "Probablement cancérogène pour l'Homme".

TOXICITE DES PBDE

La présence des PBDE en environnement intérieur est préoccupante, et une exposition humaine précoce a été associée à des signes d'altération de la santé neurodéveloppementale [47–49]. L'exposition aux PBDE provenant de la poussière domestique pourrait également interférer avec la fonction thyroïdienne [50,51], la survenue précoce de la puberté [52], et être liée à une altération de la qualité du sperme [53]. Les penta-, octa-, et déca-BDE sont listés dans l'annexe A (Elimination) de la convention de Stockholm.

[3] https://echa.europa.eu/fr/candidate-list-table

TOXICITE DES PYRETHRINOÏDES

Les pyréthrinoïdes sont considérés comme moins toxiques pour les humains que les pesticides organochlorés et organophosphorés, même si le groupement α-cyano confère une plus forte toxicité aux pyréthrinoïdes de type II [31]. Bien que leur toxicité soit en théorie spécifique aux insectes, les pyréthrinoïdes synthétiques sont également très toxiques pour les organismes aquatiques [54]. Chez les humains, une exposition environnementale et professionnelle aux pyréthrinoïdes pourrait être liée à l'altération de la qualité du sperme et à des modifications des taux d'hormones thyroïdiennes et reproductrices [32]. L'exposition pendant la grossesse pourrait affecter la taille à la naissance, le système immunitaire, le développement neurologique et l'équilibre hormonal chez les enfants [32,55,56]. L'évaluation par le CIRC de la deltaméthrine, de l'ensfenvalerate et de la perméthrine, réalisée en 1991, n'a pas permis de statuer quant au caractère cancérogène de ces substances (groupe 3).

2. CONTAMINATION DE L'AIR ET DES POUSSIERES EN ENVIRONNEMENT INTERIEUR

La toxicité suspectée ou avérée des COSV pour la santé humaine, associée à la multiplicité des sources de COSV à l'intérieur des bâtiments, a rendu nécessaire la mesure de leurs concentrations dans les différents milieux de l'environnement intérieur. Ces mesures sont en effet nécessaires pour évaluer l'exposition humaine à ces composés et les risques pour la santé associés à leur présence.

Missionné par les Pouvoirs Publics, l'Observatoire de la qualité de l'air intérieur (OQAI) a été créé en 2001 pour « mieux connaître la pollution intérieure, ses origines et ses dangers, notamment grâce à des campagnes de mesures »[4]. Sous tutelle des ministères en charge du Logement, de l'Ecologie et de la Santé, de l'Agence de l'environnement et de la maîtrise de l'énergie (ADEME) et de l'Agence nationale de sécurité sanitaire en charge de l'alimentation, de l'environnement et du travail (ANSES), l'OQAI est opéré par le Centre Scientifique et Technique du bâtiment. Les travaux réalisés dans le cadre de l'OQAI ont permis de documenter les concentrations intérieures en COSV dans les bâtiments en France.

[4] http://www.oqai.fr

2.1. CONTAMINATION DE L'AIR ET DES POUSSIERES DES LOGEMENTS.

En partenariat avec l'EHESP, l'OQAI a tout d'abord dressé une image représentative de la contamination des logements français dans le cadre du projet ECOS-Habitat (Exposition cumulée aux composés organiques semi-volatils dans l'habitat) [57]. Décliné en 8 étapes (Figure 8) allant de la sélection des substances d'intérêt jusqu'à l'évaluation des risques liés à la présence cumulée de multiples COSV dans les logements, le projet s'est construit sur deux campagnes nationales de collecte d'échantillons organisées entre 2003 et 2009 : la campagne « Logements » conduite en 2003-2005, qui a permis la collecte de filtres de prélèvements de particules en suspension dans l'air intérieur [58], et le projet Plomb-Habitat, en 2008-2009, durant lequel ont été collectées des poussières sédimentées [59].

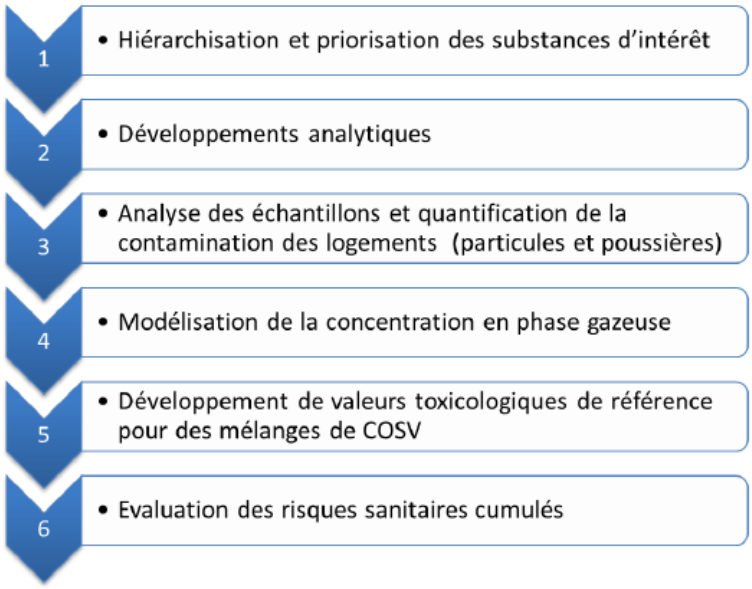


Figure reprise de Pelletier (2017), mémoire de thèse [60]

FIGURE 8 : LES PRINCIPALES ETAPES DU PROJET ECOS-HABITAT

Dans les poussières sédimentées, la fréquence de détection des phtalates, de trois HAP (anthracène, benzo(a)pyrène et phénanthrène), des muscs (galaxolide et tonalide), du BDE 209, de la perméthrine, du bisphénol-A et du tributylphosphate était supérieure à 98 %, tandis que la plupart des BDE (congénères 28, 85, 100, 119, 153 et 154) et 4 PCB sur 10 (congénères 28, 31, 77 et 126) étaient détectés dans moins de la moitié des logements. En termes de concentrations, les plus élevées ont été mesurées pour les phtalates, le bisphénol-A, la perméthrine et la galaxolide, allant de plusieurs µg/g à des valeurs maximales supérieures à 1 mg/g pour le DEHP, le DiBP, le DiNP, le BBP et la perméthrine. Des concentrations médianes de plusieurs centaines de ng/g

étaient ensuite observées pour le BDE 209, la tonalide, le phénanthrène et le tributylphosphate.[61]

Dans les particules en suspension dans l'air, les HAP, le DEHP, le DiNP et le triclosan ont été détectés dans plus de 98 % des logements et 27 autres COSV ont été quantifiés dans plus de la moitié des logements. En termes de concentration, les médianes les plus élevées ont été mesurées pour les phtalates avec des valeurs allant de 1 ng/m^3 jusqu'à 46 ng/m^3 pour le DEHP. Des valeurs médianes de plusieurs centaines de pg/m^3 ont ensuite été mesurées pour certains HAP, suivis par le triclosan, la perméthrine et les autres HAP avec des concentrations jusqu'à 100 pg/m^3.[62]

Cette étude d'envergure nationale a permis de rendre compte des niveaux de concentrations et de la multiplicité du nombre de substances auxquelles est exposée la population.

2.1. CONTAMINATION DE L'AIR ET DES POUSSIERES DES ECOLES (ARTICLE SCIENTIFIQUE N°1)

L'OQAI s'intéresse également et prioritairement à la qualité de l'air des lieux de vie fréquentés par des populations plus vulnérables comme les enfants. Lors de la phase pilote de la campagne nationale « écoles », l'OQAI a travaillé avec l'EHESP pour définir les techniques de prélèvement à mettre en place pour la campagne nationale. Testé dans 90 salles de classe de 30 écoles bretiliennes, le protocole de mesure a permis une première description des concentrations en COSV dans les écoles. Ce projet pilote a donné lieu à une publication, qui constitue le premier article scientifique sur lequel repose ce travail de thèse. Cet article comporte deux volets principaux : la description des niveaux de contamination, ainsi que la comparaison de deux méthodes de prélèvements des poussières sédimentées, à l'aide d'une lingette ou avec un aspirateur. Concernant les données de contamination des poussières, la comparaison des résultats entre logements et écoles montre des niveaux de contamination similaires pour la plupart des COSV, à l'exception de certains phtalates : le DiBP et le DBP sont ainsi environ trois fois, le DEHP cinq fois, le DiNP huit fois, et le BBP douze fois plus concentrés dans les poussières des écoles que dans les poussières des logements. De telles observations ont également été faites en 2010 au Danemark [63] et en 2018 en Espagne [64]. L'exposition plus élevée des enfants aux DiBP, DBP, BBP, DEHP et DiNP à l'école qu'à la maison doit donc être prise en compte dans les évaluations des risques et les études épidémiologiques, car elle est non négligeable.

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Semi-volatile organic compounds in the air and dust of 30 French schools: a pilot study

Abstract The contamination of indoor environments with chemical compounds released by materials and furniture, such as semi-volatile organic compounds (SVOCs), is less documented in schools than in dwellings—yet children spend 16% of their time in schools, where they can also be exposed. This study is one of the first to describe the contamination of the air and dust of 90 classrooms from 30 nursery and primary schools by 55 SVOCs, including pesticides, phosphoric esters, musks, polycyclic aromatic hydrocarbons (PAHs), polychlorobiphenyls (PCBs), phthalates, and polybromodiphenylethers (PBDEs). Air samples were collected using an active sampling method, and dust samples were collected via two sampling methods (wiping and vacuum cleaning). In air, the highest concentrations (median >100 ng/m^3) were measured for diisobutyl phthalate (DiBP), dibutyl phthalate (DBP), diethyl phthalate (DEP), bis(2-ethylhexyl) phthalate (DEHP), and galaxolide. In dust, the highest concentrations (median >30 μg/g) were found for DEHP, diisononyl phthalate (DiNP), DiBP, and DBP. An attempt to compare two floor dust sampling methods using a single unit (ng/m²) was carried out. SVOC concentrations were higher in wiped dust, but frequencies of quantification were greater in vacuumed dust.

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Key words: SVOCs; Children's exposure; Indoor air; Dust; School; Sampling.

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Practical Implications
This pilot study shows that phthalate concentrations in schools are not negligible and should be considered in risk assessment via air inhalation or dust ingestion.

Introduction

People spend more than 80% of their time indoors (Hussein et al., 2012; Klepeis et al., 2001), where they are exposed to a wide range of chemical compounds such as semi-volatile organic compounds (SVOCs), emitted by building materials and consumer products. SVOCs include a group of chemical compounds defined by their volatility and vapor pressure: Their boiling point is between 240°C and 400°C, and their vapor pressure ranges from $1/10^{14}$ to $1/10^4$ atm (Weschler and Nazaroff, 2008; WHO, 1989).

Some SVOCs have been present in indoor environments since the 1950s (Weschler, 2009). Polybromodiphenylethers (PBDEs), for example, have been used as flame retardants in products such as foam cushioning, mattresses, and electronic devices; polychlorobiphenyls (PCBs) originated from heat transfer fluids or joint sealants (Kohler et al., 2005), and although no longer manufactured, are still present in indoor environments; phthalates are used as plasticizers, especially for flexible polyvinyl chloride (PVC) (Weschler, 2009); polycyclic aromatic hydrocarbons (PAHs) develop during incomplete combustion processes such as heating with fossil fuels, cooking, or outdoor motorized traffic (Fromme et al., 2004). Pesticides may be added to carpets, paints, or furnishings, or they can be brought into the home after being

used outdoors (Rudel and Perovich, 2009). Synthetic musks, as a group of fragrance ingredients, have been widely used in a range of personal care products (Roosens et al., 2007).

SVOCs are suspected of having adverse health effects such as reprotoxic and neurotoxic effects (Fournier et al., 2014). Children are more vulnerable to the harmful effects of pollutants because major systems of their organism are still immature. Children's exposure to SVOCs during development (in utero, infants, and children) can result in permanent alterations in tissue structure and function, notably because of endocrine-disrupting mechanisms (Rudel and Perovich, 2009).

The physical and chemical properties of SVOCs lead to their emission into indoor air and then to their partition between air (gas and particulate phases) and surfaces (settled dust) (Weschler and Nazaroff, 2010). People are thus exposed through air inhalation, dust ingestion, and dermal contact. Children are more exposed than adults because they have higher ventilation rates and higher levels of physical activity (Rivas et al., 2014). Their specific behavior (crawling on the floor, hand-to-mouth contact, object-to-mouth contact) may also contribute to a higher ingestion of settled dust (EPA, 2011; Oomen, 2008), even though current estimates of children's exposure to SVOC via dust are subject to a high level of uncertainty.

Numerous studies relating to household contamination by SVOCs (Ali et al., 2012; Blanchard et al., 2014; Kanazawa et al., 2010; Le Cann et al., 2011; Meeker and Stapleton, 2010; Mercier et al., 2011) have been published in recent years. Studies investigating SVOC contamination in air and/or dust at school are less numerous (Cequier et al., 2014; Harrad et al., 2010; Lim et al., 2014; Mizouchi et al., 2015; Sofuoglu et al., 2010; Toms et al., 2015; Wallner et al., 2012; Wu et al., 2010), but they indicate that SVOCs are also present in school environments. It is important to gain better knowledge of SVOC contamination in school buildings. Indeed, although children spend nearly 70% of their time at home, where they are exposed to SVOCs, they also spend 16% of their time at school (Conrad *et al*., 2013; Zmirou et al., 2002), so the exposure to SVOCs within the school environment might also contribute to children's personal exposure. In this context, the French indoor air quality observatory (OQAI), already concerned about schools' indoor pollutants (Canha et al., 2015; Wei et al., 2015), decided to include the SVOC measurements in its nationwide survey involving 600 classrooms between 2013 and 2017. Ahead of this, a pilot study was necessary to develop an appropriate strategy for measuring SVOCs, using the most suitable sampling and analytical tools. During this exploratory phase, and without any prior knowledge of SVOC concentrations in French schools, several issues had to be faced—such as blank pollutions and suitability of the calibration range.

Nevertheless, the prime objective of this study was to report the contamination levels of 55 SVOCs in the air and dust of 90 classrooms. These SVOCs had already been selected for their health interest (Bonvallot et al., 2010). They belong to several chemical families (organochlorines, organophosphates, pyrethroids, phosphoric ester, musks, PAHs, phthalates, PBDEs, and PCBs) and were to be analyzed simultaneously, using a single analytical method. This study also presented an opportunity to compare two settled dust sampling methods—one using wipes, the other a vacuum cleaner. This comparison, carried out using a mass/surface unit for both types of sampling, aimed at selecting the more appropriate sampling method for the national campaign—although it was also of interest because it had not often been reported in the scientific literature.

Materials and methods

School selection

Thirty schools located in Ille-et-Vilaine, Brittany, France, joined the study on a voluntary basis during the 2009–2010 academic year. There were 16 nursery schools (attended by children aged 2–5) and 14 primary schools (children aged 6–11). Further characteristics are described in Supporting Information (SI) (Table S1). Three classrooms were investigated in each school.

SVOC selection

SVOCs were selected using a ranking method based on toxicity and indoor exposure levels (Bonvallot et al., 2010). In short, data on settled dust concentrations in dwellings were collected with a literature review for 156 SVOCs. These concentrations were then compared to toxicity reference doses retrieved from toxicity databases or calculated from no observed effect levels (NOELs) (or lowest observed effect levels (LOELs)) and uncertainty factors. The top-ranked compounds were phthalates, pesticides, short-chain chlorinated paraffins, pentaBDEs (BDE-85, 99, 100 and 119), perfluorinated compounds, organotins, PCBs, and PAHs. Of these chemicals, we studied those which could be simultaneously analyzed using gas chromatography coupled with mass spectrometry (GC/MS). The final list of compounds included 55 SVOCs from 11 chemical classes: 12 organochlorines (α-endosulfan, α-hexachlorocyclohexane (α-HCH), γ-hexachlorocyclohexane (γ-HCH also known as lindane), aldrin, *cis*-chlordane, dichlorodiphenyldichloroethylene (4,4′-DDE), dichlorodiphenyltrichloroethane (4,4′-DDT), dieldrin, endrin, heptachlor, metolachlor, and *trans*-chlordane), three organophosphates (diazinon, dichlorvos, and chlorpyrifos), one triazine (atrazine), one oxadiazolone (oxadiazon), five pyrethroids (cyfluthrin, cypermethrin,

deltamethrin, permethrin, and tetramethrin), one phosphoric ester (tributylphosphate), two polycyclic musks (galaxolide and tonalide), seven PAHs (acenaphthene, anthracene, benzo(a)pyrene, fluoranthene, fluorene, phenanthrene, and pyrene), 11 PCBs (PCB 28, 31, 52, 77, 101, 105, 118, 126, 138, 153, and 180), eight phthalates (bis(2-ethylhexyl) phthalate (DEHP), butyl benzyl phthalate (BBP), di(methoxyethyl) phthalate (DMEP), dibutyl phthalate (DBP), diethyl phthalate (DEP), diisobutyl phthalate (DiBP), diisononyl phthalate (DiNP), and dimethyl phthalate (DMP), and 4 PBDEs (BDE 85, 99, 100, and 119).

Air sampling

Air samples were collected on a 76-mm polyurethane foam (PUF) (SKC, Eighty Four, PA, USA) that had previously been cleaned with dichloromethane (DCM) using pressurized liquid extraction (PLE) and inserted in a 22 × 100 mm glass tube (SKC, Eighty Four, PA, USA). Particulate matter was collected on a 25-mm quartz fiber filter (QFF) (Whatman, Maidstone, Kent) fitted in front of the PUF. The air was pumped through the device using a GilAir-5 pump (Sensidyne, St. Petersburg, FL, USA). The sampling device was installed in a position representative of the whole classroom, and if possible, in the middle of the room, away from emitting materials and drafts, and at the children's airway height (1.30 m). To avoid introducing potentially emitting materials to the classroom, silicone was chosen (for its inertness) for the tubing between the glass tube and the pump, while metallic laboratory clamps and holders were used to secure the sampling device in place. The pump was stored in a noise-insulated wooden box to avoid disturbing the occupants of the classroom. The air sampling method was inspired by Bouvier et al. (2006). Air was sampled continuously for 4.5 days during a normal school week (from Monday morning to Friday afternoon) at 2 l/min, thus allowing about 12.6 m^3 of air to be collected. The flow rate was checked before and after sampling with a Gilibrator-2 flowrate meter (Sensidyne, St. Petersburg, FL, USA). At the end of the sampling period, the sampling device was transported back to the laboratory in an icebox. The PUF and filters were then wrapped together in foil paper previously cleaned with DCM and stored at −18°C in an amber glass vial for up to a month (Blanchard, 2001) prior to analysis. A field blank sample was taken for each investigated school (i.e., one field blank for three classrooms).

Dust sampling

To avoid any disturbance of air sampling, dust was sampled either during the week preceding air sampling or just after the end of air sampling**.** Two different methods were used for sampling settled dust. The first method consisted of vacuuming dust settled on the floor in a cellulose thimble using a modified vacuum cleaner. A 10–12 m² area in which children spend most time was measured and vacuumed slowly (about 0.5 m²/min). This dust sampling method is fully described elsewhere (Blanchard et al., 2014) and in SI page 2. The second method consisted of collecting settled dust using a damp wipe on a 0.1 m² floor surface. The floor area to be sampled was a smooth surface such as stone, wooden, or plastic floor, chosen in an area where the children spend most time. Three wipes per classroom were collected, and a sampling blank was made for each school investigated (i.e., one field blank for every 3 classrooms). This dust sampling method was adapted from elsewhere (Le Bot et al., 2010) and is also fully described in SI page 2.

Vacuumed dust preparation

After collection, the content of each cellulose cartridge was passed through a pre-cleaned (DCM) 100-μm sieve using a vibrating stainless steel sieve apparatus to remove coarse material (cotton and debris) and thus obtain a more homogeneous sample. The sieved dust was then weighed and stored at −18°C in an amber glass flask hermetically sealed until chemical analysis (Blanchard et al., 2013).

Sample extraction and analysis

Full details on the reagents and chemicals used for analyses are provided in SI page 2. A detailed description of the extraction method for vacuumed dust and air samples, using pressurized liquid extraction, is already available elsewhere (Blanchard et al., 2014; Mercier et al., 2014) and is also provided in SI page 3. For wiped dust, extraction was performed on 200 mg of sieved dust. Wiped dust samples were defrosted (1 hour at room temperature in amber vials) and then transferred into glass centrifuge tubes. After adding 8 ml of DCM and 100 ng of each surrogate standard (fenpropathrin and methoprotryne), the tubes were centrifuged at 630 ***g*** for 2 min, then sonicated for 20 min at a temperature below 30°C and centrifuged again at 1400 ***g*** for 5 min. After freezing the sample to separate the water released by the wipe from the solvent, 5 ml of the DCM extract was collected and mixed with the other two wipe extracts from the same classroom. The combined extract was then concentrated to 1 ml, cleaned up on Chromabond® NH_2 glass columns (Macherey-Nagel, Düren, Germany) prewashed with 6 ml of DCM and eluted with 5 ml of DCM. After concentrating to 0.5 ml and adding 1 μg of 2,3,4-trichloronitrobenzene (TCNB) as internal standard (ISTD), the final extract was stored at −18°C prior to analysis. All extracts were then analyzed using gas chromatography coupled to tandem mass

spectrometry. A detailed description of the analytical method is already available elsewhere (Mercier et al., 2014) and is also fully described in SI page 3.

Analysis of highly concentrated compounds

As little data about concentrations found in schools was available prior to this study, concentrations of several compounds appeared to exceed the top of the calibration range, and analyses of less concentrated extracts were needed. However, analyzing each sample twice or more would have exceeded the initial budget. Therefore, in an attempt to evaluate the SVOC concentrations above the upper limit (UL) of the calibration range, seven extracts for air samples and 32 extracts for dust samples were diluted by a factor of 20 for air samples, up to 200 for vacuumed dust samples and up to 1000 for wiped dust samples. These extracts were chosen from those that needed dilution and are therefore not representative. The calculated concentrations, presented in Tables S10–S12, were only used for dust sampling method comparison and as information for the upcoming nationwide survey. However, as the concentrations of BBP, DEHP, and DiNP in vacuumed dust and BBP and DEHP in wiped dust were greater than UL in all the samples, results from the diluted extracts could be considered characteristic of the schools studied and were used in this work.

Comparison between floor dust sampling methods

To compare the concentrations found in vacuumed dust and in wiped dust, the classrooms where vacuumed dust had been collected on a soft surface (such as carpets or rugs) were removed from the database because wiped dust was never sampled on such surfaces. Only those samples collected on hard surfaces were therefore considered for comparison. Regarding vacuumed dust, the total mass of sampled dust was weighed and the sampled surface was measured. Concentration in vacuumed dust in ng/m² could thus be calculated to compare concentrations using the same unit: *concentration per surface (ng/m²) = concentration per mass (ng/g) × total mass (g)/sampled surface (m²)*. The comparison was performed for the 14 compounds quantified at least 10 times in matching vacuumed and wiped dust samples (i.e., paired data from the same classroom). Greater than UL concentrations were not included in this comparison unless they belonged to the 32 extracts that were diluted.

Quality assurance and quality control

Limits of quantification (LOQs) were defined as the lowest concentration of a substance for which the relative standard deviation (RSD) of replicate analyses was lower than 20% (González et al., 2014). Quadratic calibration curves were established for each compound by analyzing at least five calibration solutions ranging from LOQs to ULs. The values for LOQs and ULs for each matrix are displayed in Table S2. Compounds were quantified with TCNB as ISTD. Laboratory blank and quality control (QC) samples were extracted and analyzed to control contamination from all consumables and check for method accuracy. A detailed description of their preparation is provided in SI page 4. Field blank samples were extracted and analyzed like other samples. When either a field blank sample or a laboratory blank sample showed a concentration greater than 30% of the concentration found in the associated samples, the results in these samples were not validated and were removed from the data. Where the contamination was less than 30% of the concentration found in associated samples, the concentrations for these samples were reported without blank correction. Other conditions regarding data validation are detailed in SI page 4.

Air sampling conditions were tested with an evaluation of PUF retention capacity according to the French norm XP X 43-058 (AFNOR, 2007). A mix of 44 SVOCs was spiked onto the QFFs fitted in front of three clean PUFs, at a concentration greater than the maximum observed in samples. A second PUF was installed in series after one of the PUFs. Air was then sampled through the devices at 2 l/min for 4.5 days. Air was also sampled in parallel through three clean, non-spiked, witness PUFs, with a second PUF in series for one of these. The recovery of each SVOC in the spiked devices was then assessed after correction by the concentration measured in the witness PUFs. According to the norm, the method is valid for a substance if it has a recovery between 60 and 120%. PUFs in series were analyzed for substances not fitting these requirements.

Statistical analysis

Descriptive statistics of the data were produced using Excel (Microsoft® Office, Redmond, WA, USA). To be able to rank the values for the calculation of percentiles, concentrations below the LOQ were assigned a value of LOQ/2 and concentrations above the UL of the calibration range were assigned a value equal to UL. This practice has an impact on percentiles: for example, if more than 5% of values are >UL then the 95th percentile and any above will be >UL. Percentiles were therefore described as '> UL' where relevant in Table 1 and in Tables S6–S9. Spearman rank correlation was used to test the association between SVOC levels in each type of dust (error rate of 5%) (XL STAT® software, Microsoft® Office). Boxplots were represented graphically by GraphPad Prism version 5.01 for Windows, GraphPad Software, San Diego, California, USA, http://www.graphpad.com.

Results

Field blank samples for air & wiped dust

In air samples, five phthalates (BBP, DEHP, DMP, DiNP, and DEP) were present in field blank samples at various concentrations. DiNP was most frequently detected, resulting in the cancellation of 32 results. For the other phthalates, five to seven results could not be validated. Insufficient cleaning of the polyurethane foam was suspected to be the source of DiNP contamination, and this was addressed in subsequent works (Blanchard et al., 2014). Field blank wipe samples were also affected by phthalate contamination: BBP, DBP, DEHP, DiNP, DEP, DiBP, and DMP were found in 2–10 samples (depending on the molecule), and this caused the cancellation of 36 results, for which an obvious source has yet to be clearly identified.

Evaluation of the air sampling method

As shown in Table S3, recoveries were within 60% and 120% for 38 of 44 compounds. Of these 38 compounds, the lowest recovery was observed for diazinon (66%), whereas all other recoveries were between 80 and 110%. For these compounds and for a 4.5-day sampling at 2 l/min, PUF retention capacities were ≥200 ng for PCBs and certain pesticides, ≥500 ng for pyrethroids, PAHs, PBDEs and other pesticides, ≥2.5 μg for tributylphosphate, ≥10 μg for musks, and ≥100 μg for phthalates. However, null or poor recoveries were observed for aldrin (0%), dichlorvos (13%), tetramethrin (0%), acenaphthene (8%), anthracene (37%), and benzo(a)pyrene (1%). The conditions of this test were those of a worst case scenario, as the whole substance was present at the beginning of the sampling period and would therefore have 4.5 days to reach its breakthrough volume or suffer from degradation—whereas in real conditions, substances would be caught on the PUF throughout the sampling period and might not reach their breakthrough volume or have time to be degraded. Nevertheless, concentrations reported in this work for these six compounds could not be validated and were removed from the reported results (Table 1 and Tables S6 and S7).

SVOC concentrations in air QC samples and SRM 2585

Concentrations and associated RSD and recovery data were satisfactory as presented in SI pages 4 & 5 and summarized in Tables S4 and S5.

SVOC concentrations in air

Of the 90 classrooms investigated, 84 air samples were kept for analysis. The remaining six were not analyzed because the sampled air volume was less than 90% of the expected volume of 12.6 m^3. For the first 22 extracts analyzed, the concentration of several compounds—particularly musks and several phthalates—could not be evaluated because they were very often above the UL of the calibration range, and so were not reported in the final results. An upper concentration level was added to the calibration range for the remaining 62 samples. For these 62 samples, the results of the most frequently quantified substances are displayed in Table 1 while results for all substances can be seen in Tables S6 and S7. Of the 55 compounds analyzed, 33 were quantified at least once while 22 were never quantified (*cis*-chlordane, *trans*-chlordane, 4,4′-DDE, heptachlor, PCB 77, 105, 118, 126, 138, 153, and 180, 4,4′-DDT, endrin, metolachlor, atrazine, oxadiazon, cyfluthrin, deltamethrin, tetramethrin, benzo(a)pyrene, and BDE 85 and 119). The concentration of most of the compounds was in the calibration range with the exception of eight (galaxolide, tonalide, phenanthrene, DMP, DiBP, DBP, BBP, and DEHP). The highest concentrations (median >50 ng/m^3) were measured for four phthalates (DiBP, DBP, DEP, and DEHP) and one musk (galaxolide). Intermediate concentrations (median from 1 to 40 ng/m^3) were measured for DiNP, tonalide, BBP, DMP, phenanthrene, fluorene, tributylphosphate, γ-HCH, and acenaphthene, in decreasing order of concentration. Seven compounds were only found in 10% to 30% of the samples (fluoranthene, α-HCH, PCB28, pyrene, PCB 52, PCB31, and BDE 99).

SVOC concentrations in vacuumed settled dust

Of the 55 compounds analyzed, 42 were quantified at least once and 13 were never quantified (cis-chlordane, aldrin, heptachlor, metolachlor, dichlorvos, cyfluthrin, deltamethrin, tetramethrin, atrazine, PCB 126, acenaphthene, and BDE 85 and 119). Results of the most frequently quantified substances are displayed in Table 1, and all results can be seen in Tables S6 and S8. Greater than 30 μg/g median concentrations were reached for DEHP, DiNP and DiBP (>50 μg/g), and DBP (36 μg/g). The median concentrations measured for 10 compounds (BBP, DEP, galaxolide, phenanthrene, tonalide, pyrene, permethrin, DMP, fluoranthene, and tributylphosphate) ranged from 0.1 to more than 3 μg/g. Eight compounds were only quantified in 10–40% of the samples (fluorene, anthracene, benzo(a) pyrene, γ-HCH, 4,4′-DDT, PCB 101, BDE99, and PCB 138).

SVOC concentrations in wiped settled dust

Of the 55 compounds analyzed, 34 were quantified at least once while 21 were never quantified (*cis*-chlordane, *trans*-chlordane, 4,4′-DDE, aldrin, endrin, heptachlor, metolachlor, dichlorvos, diazinon, cyfluthrin,

Table 1 SVOC concentrations in French classrooms (Brittany, France, 2010)

	Air (ng/m^3)							Vacuumed dust (<100 μm fraction) (ng/g)							Wiped dust (ng/m^2)						
Substance	LOQ	UL	*N*	5th%	50th%	95th%	*F*	LOQ	UL	*N*	5th%	50th%	95th%	*F*	LOQ	UL	*N*	5th%	50th%	95th%	*F*
Organochlorinated pesticides																					
α-HCH	0.4	20	59	<0.4	<0.4	3.4	24%	26	1 320	89	<26.3	<26.3	<26.3	2%	20	830	81	<20	<20	<20	1%
γ-HCH	1.0	50	62	<1.0	2.0	7.2	79%	66	3 290	89	<65.8	<65.8	247	18%	40	2 080	81	<40	<40	<40	4%
4,4′-DDT	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	177	15%	40	2 080	81	<40	<40	<40	2%
Pyrethroids																					
Permethrin	1.0	50	62	<1.0	<1.0	<1.0	2%	66	3 290	89	<65.8	279	1 961	61%	40	2 080	81	<40	<40	578	27%
Phosphoric ester																					
Tributylphosphate	1.0	50	62	2.0	4.7	12.4	100%	66	3 290	89	<65.8	103	401	74%	40	2 080	79	<40	<40	190	20%
Musks																					
Galaxolide	1.0	50	62	46	>50	>50	100%	66	3 290	89	304	965	2 191	98%	40	2 080	65	148	335	1 213	97%
Tonalide	1.0	50	62	10	20	>50	100%	66	3 290	89	<65.8	337	915	88%	40	2 080	81	<40	170	642	63%
PAHs																					
Acenaphthene	1.0	50	62	*	*	*	53%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Fluorene	1.0	50	62	2.5	5.5	13	100%	66	3 290	89	<65.8	<65.8	268	40%	40	2 080	81	<40	<40	175	9%
Phenanthrene	1.0	50	62	4.8	8.7	18	100%	66	3 290	89	<65.8	363	907	92%	40	2 080	75	<40	<40	539	45%
Anthracene	1.0	50	62	*	*	*	2%	66	3 290	89	<65.8	<65.8	127	40%	40	2 080	81	<40	<40	<40	1%
Fluoranthene	1.0	50	62	<1.0	<1.0	1.6	29%	66	3 290	89	<65.8	184	751	85%	40	2 080	81	<40	<40	441	32%
Pyrene	1.0	50	62	<1.0	<1.0	1.2	18%	66	3 290	89	<65.8	285	760	90%	40	2 080	80	<40	<40	525	40%
Benzo(a)pyrene	1.0	50	62	*	*	*	0%	66	3 290	89	<65.8	<65.8	172	27%	40	2 080	81	<40	<40	125	6%
PCBs																					
PCB 31	0.4	20	62	<0.4	<0.4	0.6	15%	26	1 320	89	<26.3	<26.3	<26.3	2%	20	830	81	<20	<20	<20	0%
PCB 28	0.4	20	62	<0.4	<0.4	0.9	19%	26	1 320	89	<26.3	<26.3	<26.3	6%	20	830	81	<20	<20	<20	0%
PCB 52	0.4	20	62	<0.4	<0.4	0.5	16%	26	1 320	89	<26.3	<26.3	48	7%	20	830	81	<20	<20	<20	2%
PCB 101	0.4	20	62	<0.4	<0.4	<0.4	2%	26	1 320	89	<26.3	<26.3	107	13%	20	830	81	<20	<20	<20	1%
PCB 138	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	79	10%	20	830	81	<20	<20	<20	1%
Phthalates																					
DMP	1.0	50	53	6.7	13	>50	100%	66	3 290	54	<65.8	252	1 680	87%	40	2 080	79	<40	<40	555	39%
DEP	8.0	800	53	85	221	515	100%	526	52 600	76	739	2 890	6 560	93%	333	33 300	65	<333	1 310	5 200	66%
DiBP	8.0	800	62	352	>800	>800	100%	526	52 600	89	41 000	> 52 600	> 52 600	100%	333	33 300	71	11 000	>33 300	>33 300	100%
DBP	8.0	800	62	66	228	744	100%	526	52 600	89	11 000	38 200	> 52 600	100%	333	33 300	64	4 220	15 200	>33 300	100%
BBP[a,b]	1.0	50	56	3.7	19	>50	100%	66	3 290	22	11 400	105 000	468 000	100%	40	2 080	22	6 750	73 600	1 940 000	100%
DEHP[a,b]	8.0	800	58	49	108	417	100%	526	52 600	28	275 000	1 430 000	5 830 000	100%	333	33 300	28	86 900	1 210 000	4 520 000	100%
DiNP[a]	8.0	800	30	8.2	35	214	93%	526	52 600	32	258 000	1 030 000	4 100 000	100%	333	33 300	77	33 000	>33 300	>33 300	100%
PBDEs																					
BDE 99	1.0	50	62	<1.0	<1.0	4.9	13%	66	3 290	89	<65.8	<65.8	340	12%	40	2 080	81	<40	<40	<40	2%

LOQ, limit of quantitation; UL, upper limit of the calibration range; *N*, number of classrooms, *F*, frequency of classrooms with concentrations >LOQ; α-HCH, α-hexachlorocyclohexane; γ-HCH, γ -hexachlorocyclohexane (Lindane); 4,4′-DDT, dichlorodiphenyltrichloroethane; PAH, polycyclic aromatic hydrocarbon; PCB, polychlorobiphenyl; DMP, dimethyl phthalate; DEP, diethyl phthalate; DiBP, diisobutyl phthalate; DBP, dibutyl phthalate; BBP, butyl benzyl phthalate; DEHP, bis(2-ethylhexyl) phthalate; DiNP, diisononyl phthalate; PBDE, polybromodiphenylether.

[a]Concentrations from less concentrated extracts for vacuumed dust.

[b]Concentrations from less concentrated extracts for wiped dust.

*Unvalidated air sampling method, substance subject to degradation.

deltamethrin, tetramethrin, atrazine, acenaphthene, PCB 28, 31, 77, 126 and 180, and BDE 85 and 119). Results of the most frequently quantified substances are displayed in Table 1, and all results can be seen in Tables S6 and S9. Greater than 2 $\mu g/m^2$ median concentrations were reached for DEHP, BBP, DiNP and DiBP (>33 $\mu g/m^2$), and DBP (15 $\mu g/m^2$). The median concentrations measured for musks and DEP ranged from 0.2 to 1.5 $\mu g/m^2$. Six compounds (phenanthrene, pyrene, DMP, fluoranthene, permethrin, and tributylphosphate) were only found in 10–45% of the samples.

SVOC concentrations in vacuumed dust vs. wiped dust

Frequencies of quantification for the 14 compounds quantified more than 10 times in paired dust samples are shown in Table 2. These were higher in vacuumed dust than in wiped dust, except in the case of five phthalates (DiBP, DBP, BBP, DEHP, and DiNP) found in 100% of the samples with both methods. Figure 1 shows the distribution of SVOC concentrations in vacuumed dust and wiped dust for these 14 compounds: concentrations measured in wiped dust were always larger than in vacuumed dust by a factor of 9–26 (ratio of the medians shown in Table 2).

Concentrations measured in the same room with both sampling methods were compared for each individual substance using Spearman correlation coefficients. These coefficients are summarized in Table 2. Significant correlations were observed for galaxolide, tonalide, fluoranthene, pyrene, DBP, DEHP, DiBP, and DiNP ($P < 0.05$). No significant correlations were observed for permethrin, tributylphosphate, phenanthrene, BBP, DEP, and DMP.

Discussion

SVOC selection

The ranking method used for the selection of SVOCs was preliminary based on dust contamination in dwellings, so SVOCs present in products having specific uses in schools may have been missed. However, the selection of SVOCs was initially based on a bibliographic search, then extended using expert judgment, so that the number of compounds potentially not included would be limited—as proven by the large number of SVOCs ultimately included in the ranking ($n = 156$). Nevertheless, the differences in the contamination levels between schools and dwellings may have constituted a limit to this exercise because SVOCs may have ended up being differently ranked, had contamination in schools been considered. This limit was reduced by the choice of the analytical method allowing measurement of 55 compounds,

Table 2 Paired data comparison of wiped dust vs. vacuumed dust

	Frequencies of quantification		Median concentration (5th–95th%) (ng/m^2)				Spearman's correlation coefficient	
	Vacuumed dust (<100 μm fraction) (%)	Wiped dust (%)	*N*	Vacuumed dust (<100 μm fraction)	Wiped dust	Ratio Wd/Vd[a]	*r*	*P* value
Pyrethroids								
Permethrin	56	25	10	13 (9–74)	310 (267–855)	23	0.59	0.077
Phosphoric ester								
Tributylphosphate	66	19	11	17 (3–43)	158 (142–190)	9	0.05	0.892
Musks								
Galaxolide	97	96	48	22 (10–51)	433 (273–719)	20	**0.36**	**0.011**
Tonalide	83	61	34	18 (7–47)	215 (177–362)	12	**0.55**	**0.001**
PAHs								
Fluoranthene	78	30	16	9 (4–70)	211 (161–404)	23	**0.70**	**0.003**
Phenanthrene	89	46	23	12 (7–82)	234 (170-355)	11	0.25	0.252
Pyrene	86	40	21	11 (6–44)	221 (154–492)	20	**0.73**	**0.000**
Phthalates								
BBP	100	100	13	5500 (1590–23 300)	73 600 (18 900–305 000)	13	0.38	0.199
DBP	100	100	36	600 (278–2600)	10 900 (6490–17 000)	18	**0.41**	**0.013**
DEHP	100	100	14	88 700 (9600–189 000)	1 390 000 (146 000–2 440 000)	16	**0.72**	**0.005**
DEP	92	64	24	84 (51–229)	1930 (1330–2740)	23	0.24	0.262
DiBP	100	100	27	3140 (881–20 100)	41 300 (22 300–197 000)	13	**0.51**	**0.007**
DiNP	100	100	17	60 700 (18 400–121 000)	661 000 (326 000–1 200 000)	11	**0.66**	**0.005**
DMP	83	39	15	7 (5–29)	183 (141–319)	26	0.36	0.189

In bold: significant correlation (*P* value <0.05).

PAH, polycyclic aromatic hydrocarbon; BBP, butyl benzyl phthalate; DBP, dibutyl phthalate; DEHP, bis(2-ethylhexyl) phthalate; DEP, diethyl phthalate; DiBP, diisobutyl phthalate; DiNP, diisononyl phthalate; DMP, dimethyl phthalate.

[a]Ratio of median in wiped dust vs median in vacuumed dust.

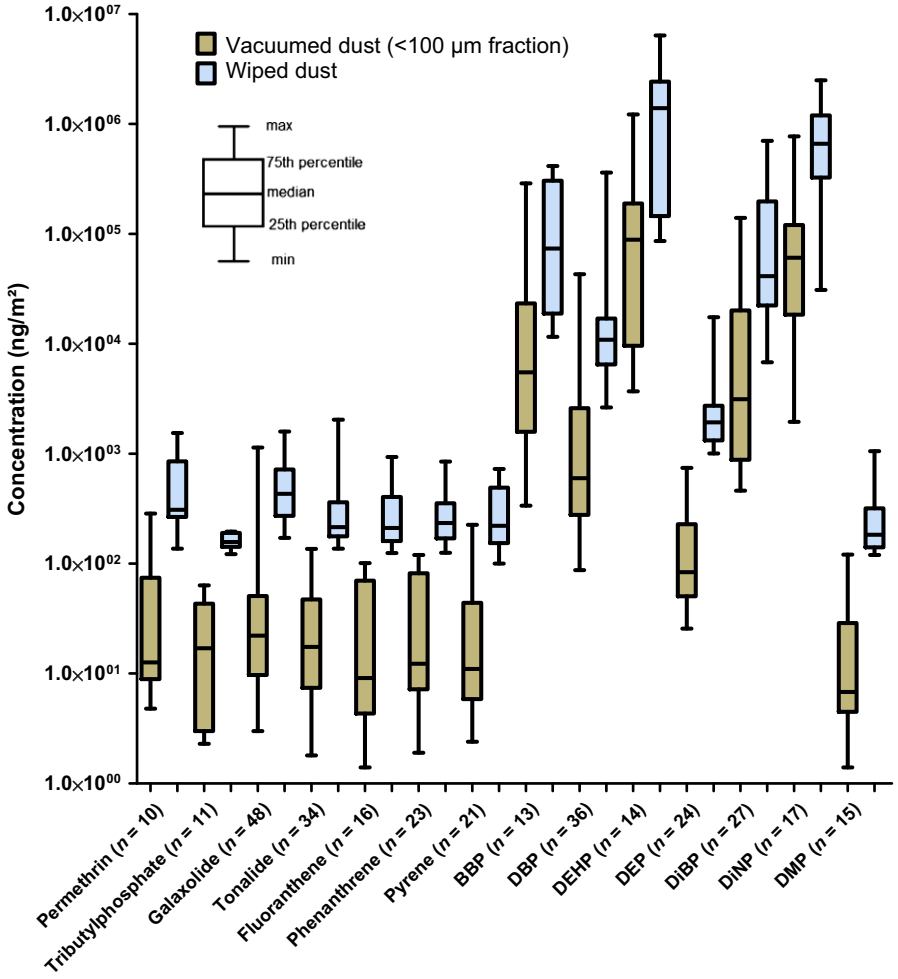

Fig. 1 SVOC concentrations in vacuumed and wiped dust for substances quantified in matched samples

rather than just those SVOCs that were initially sorted. Moreover, it was useful to measure the same compounds in schools and dwellings as this helped compare the profiles of SVOC contamination in different indoor environments.

Analytical method

The analysis of 55 target compounds from different chemical classes does present an analytical challenge. Most methods previously published were dedicated to the analysis of a specific family of compounds, whereas multiresidue analytical methods were rarely reported (Mercier et al., 2014). However, the ultimate goal of the method development was to be able to analyze hundreds of samples within a nationwide survey. This is why the multiresidue approach was adopted, entailing compromises between analytical performance and the constraints that are inherent to large-scale studies, such as environmental sampling issues (e.g., limited availability of daily dust samples) and economic viability. As described by Mercier et al. (2014), these compromises were achieved by (i) the choice to use only PUF for air sampling without any resin adsorbents, which are more expensive and require more complex extraction procedures, (ii) automation of the extraction procedure, (iii) simplification of the clean-up procedure, (iv) the use of native rather than labeled surrogate standards, and (v) the use of tandem mass spectrometry for its selectivity and sensitivity. The laboratory obtained Cofrac (French Committee for Accreditation) accreditation in accordance with the ISO/CEI 17025 standard for this method.

Our LOQs, however, were relatively high for 4 chemical families (organochlorines, organophosphates, PCBs, and PBDEs). In air (Table S13), Wilson et al. (2003), Lim et al. (2014), and Bradman et al. (2014) reported concentrations below our LOQ for PBDEs. In dust (Table S14), concentrations lower than our LOQ were also reported by Wilson et al. (2003), Dalvie et al. (2014), and Harrad et al. (2010). LOQs are often based on the signal-to-noise (S/N) ratio approach. This approach was impractical with our system, because smoothing was applied to the signal, making S/N ratios meaningless. The standard

deviation approach, described by González et al. (2014), was used instead, making comparison with other studies more difficult. However, these higher LOQs might also be a consequence of our multiresidue approach and would probably have been lower using dedicated methods. Nevertheless, the multiresidue method allowed for the simultaneous analysis of multiple compounds in an economically sound way while still providing valuable information about the relative presence of SVOCs in classrooms.

Evaluation of air sampling method

Tested concentrations were greater than the highest concentrations reported in samples and showed that the air sampling method was fit for purpose, except for the six compounds for which null or poor recoveries were observed. The hypothesis of a low breakthrough volume was verified on acenaphthene for which 4% of the spiked amount was measured in the second, in series, PUF (Table S3). However, for aldrin, dichlorvos, tetramethrin, anthracene, and benzo(a)pyrene, the amount left in the second PUF was null, which means that these molecules are probably also subject to degradation. During the 4.5-day sampling period, PUFs were only kept in their glass cartridge and were therefore exposed to sunlight and variations of room temperature. Photolysis has indeed been reported, for example, for aldrin (Burrows et al., 2002), tetramethrin (EPA 2010), and benzo(a)pyrene (Zhang et al., 2006).

Contamination levels of SVOCs in schools

The data presented in this study were compared to other studies reported in scientific literature from 2003 to 2015, including studies in primary or elementary schools and in nursery schools and day care centers where the children's age matched those attending French nursery schools (2–5 years old). Summaries of these comparisons are available in Supporting Information (Tables S13 and S14). These summaries mention the sampling techniques used, as SVOC concentrations can only be compared if sampled in a similar manner. Sampling for the present study was conducted from November 2009 to June 2010, covering three seasons (autumn, winter, and spring). Ambient and indoor meteorological conditions were not monitored in this study, although these would affect SVOC emissions (Clausen et al., 2012; Wu et al., 2016). Likewise, seasonal effects on SVOC emissions were reported (Cao et al., 2014). Moreover, the choice of dust fraction to be analyzed is also important, as SVOC concentrations vary significantly with particle size: in general, concentration of toxic chemicals in dust increases as particle size decreases (Cao et al., 2012; Mercier et al., 2011). Cao et al. also emphasize that dust with particle size less than 100 μm, which we chose, should be paid more attention because it is more relevant to human exposure. Sieved fractions between 63 μm to 500 μm were reported in the literature relating to SVOCs in schools (Bradman et al., 2014; Clausen et al., 2003; Gaspar et al., 2014; Harrad et al., 2010; Mizouchi et al., 2015; Wallner et al., 2012; Wilson et al., 2003). Sometimes larger particles and sand deposits were removed, but the dust was not sieved (Fromme et al., 2013, 2014). Nevertheless, the number of studies in schools was limited so different sampling conditions and dust particle size fractions were considered even though this constitutes a limitation of the comparison of our results with the literature.

In air (Table S13), in comparison with other studies, concentrations measured in these 30 French schools were always similar or slightly lower than what had been observed elsewhere, except DiBP which was more concentrated in our study (>800 ng/g) than in that of Fromme et al. (2013) (468 ng/g) or Gaspar et al. (2014) (100 ng/g). Such a discrepancy was also observed in French dwellings (Blanchard et al., 2014) and could be explained by the gradual substitution of DBP by DiBP.

In dust, Morgan et al. (2007) used wipes to sample dust settled on the floor in Ohio day care centers. They reported 140 ng/m² of (*cis* + *trans*) permethrin which is more than reported in the present study (<40 ng/m²). This higher level was confirmed in vacuumed dust (1554 ng/g vs. 279 ng/g). Regarding other compounds in vacuumed dust (Table S14), PAH concentrations were of the same order as in North Carolina, USA: phenanthrene, fluoranthene, and pyrene concentrations were 338, 437, and 354 ng/g, respectively (Wilson et al., 2003), vs. 363, 184, and 285 ng/g, respectively, in this study. A slightly lower concentration of 98 ng/g was measured for pyrene in Denmark (Langer et al., 2010). In all studies, phthalates, and particularly DEHP and DiNP, are found in higher concentrations than other substances. Medians found for DEP, DBP, DEHP, and DiNP in our study are within the range of other studies: DEP, measured at 2.89 μg/g in this study, is at most twice as concentrated as in Denmark (2.20 μg/g), Germany or California, USA (1.40 μg/g for both); the range of concentrations for DBP, measured at 38.2 μg/g in this study, go from 1.87 μg/g (North Carolina, USA) to 52.0 μg/g (South Korea); likewise, DEHP and DiNP, respectively, quantified at 1430 μg/g and 1030 μg/g in this study are within the range of other studies (from 172 μg/g in California, USA, to 3350 μg/g in Austria for DEHP and from 302 μg/g in Germany to 946 μg/g in South Korea for DiNP). However, DiBP and BBP were at least twice as concentrated in French schools: the median concentration for DiBP, greater than 52 μg/g, is higher than in Denmark (23 μg/g), Germany (20 μ/g) or California, USA (9.3 μg/g); the French concentration for BBP

(105 μg/g) was also higher than in other studies, ranging from 3.72 (North Carolina, USA) to 46.8 μ/g (California, USA) (Clausen et al., 2003; Fromme et al., 2013; Gaspar et al., 2014; Hutter et al., 2013; Kim et al., 2013; Langer et al., 2010; Wallner et al., 2012; Wilson et al., 2003). The frequent presence of PVC flooring (in 70% of classrooms) could explain the higher concentration of BBP in school dust, as more than 70% of BBP produced is used as a plasticizer in polymer products, mainly PVC for flooring (ECHA, 2009). The presence of DiBP might be related to its use in such children's products as crayons, erasers, and school bags (ECHA, 2010).

Our results were compared to two others French surveys that investigated a similar list of compounds: Blanchard et al. (2014) investigated air and dust in 30 dwellings in Brittany, using similar sampling techniques and the same analytical method and Mandin et al. (Mandin et al., 2013) measured SVOCs in 145 dust samples from household vacuum cleaners using the same (albeit more sensitive) analytical method. In air, compared to the 30 dwellings, concentrations found in schools are up to twice as high for tributylphosphate, musks, PAHs and phthalates except BBP which is about eight times more concentrated in schools than in dwellings. Concentrations found in dust are similar for tributylphosphate, musks, PAHs, and the three less concentrated phthalates (DMP, DEP, and DMEP). However, the other phthalates are more concentrated in schools by factors of around three (DiBP, DBP), five (DEHP), eight (DiNP), and twelve (BBP). Langer et al. (2010) compared phthalate and PAH contamination in homes and day care centers. They found that with the exception of DEP, concentrations of phthalates in dust were higher in day care centers than in homes, whereas PAH concentrations were similar, confirming our observations in schools and pre-schools.

Sources of phthalates include personal care products and cosmetics, PVC flexible pipe, PVC flooring, and wall covering (Mercier et al., 2011). In nursery schools, Kim et al. (2013) found that DEHP concentrations correlated significantly with the area of PVC flooring. DiNP probably follows the same trend, as it started replacing DEHP, as well as DBP and BBP, in response to the restriction of their use in Europe (Blanchard et al., 2014). Descriptions of French dwellings available on the OQAI website (www.oqai.fr) show the presence of PVC or linoleum flooring in 18–26% of rooms, vs 60% of classrooms at a national level (70% in this study) for PVC flooring only. This supports the hypothesis that higher phthalate concentrations in schools might be associated with the presence of PVC flooring, either because of the material itself or because of the application of floor care chemical products (Bi et al., 2015). Children's higher exposure to DiBP, DBP, BBP, DEHP, and DiNP at school compared to at home should thus be considered in both risk assessments and epidemiological studies, as it may contribute substantially to exposure.

Comparison of vacuum and wipe sampling methods and results

The wipe sampling method is easy to implement, silent, and fast (less than 10 min per classroom) whereas the vacuum cleaner sampling method that requires more preparation is slower (about 20 minutes per classroom) and noisy. In addition, a recurrent issue that occurred in this study and was also observed by Kim et al. (2013) and Harrad et al. (2010), was the lack of dust for vacuuming. In general, classrooms are cleaned on a daily basis, so reaching the mass of dust necessary for analysis meant sampling large areas and organizing the sampling according to the school cleaning schedule, which sometimes could not be achieved.

More compounds can be quantified using the vacuum cleaner, which is inherent to the sampling method: LOQs were based on analysis of 200 mg of dust when available, or three wipes. The median quantity of dust sampled with a wipe is 30 mg (Le Bot et al., 2010) (i.e., 90 mg for three wipes), so the LOQs in wipes were often more than double those in vacuumed dust. However, concentrations measured in wiped dust were higher than in vacuumed dust. Several hypotheses may explain this difference. First, as shown by Cettier et al. (2015) for the collection of PCBs and pesticides, wipe sampling is efficient, particularly in the presence of dust. Indeed, wipe sampling allows the thorough collection of all dust present on the floor, including fine and large particles, as the wipe's moisture can help unstick stuck dust or collect SVOCs released by the surface of the floor material. Second, the fraction collected with the vacuum cleaner misses those fine and large particles, as the finest pass through the cellulose thimble or are stuck in it and the largest (fraction greater than 100 μm) are eliminated through the sieving process. Third, the depression created by the vacuum cleaner may disturb the partitioning of the molecules between gas-phase and dust, possibly according to their volatility. These hypotheses may explain the absence of significant correlation between the two sampling methods for permethrin, tributylphosphate, phenanthrene, BBP, DEP, and DMP as the dust composition may have differed between classrooms.

In the past 10 years, sampling involving both vacuuming and wiping methods has been described in scientific literature: Watkins et al. (2013) measured PBDEs in office air, vacuumed dust, and surface wipes and observed a significant correlation between BDE 209 in dust and in surface wipes ($r = 0.69$, $P = 0.007$), although their methodology was different to ours; the surface wipes were sampled on undisturbed 'dusty' surfaces such as bookshelves or

filing cabinets. In addition, they compared concentrations in mass per mass for dust versus mass per surface for wipes. Wu et al. (2010) found significant correlations between floor dust (in ng/g) and surface dust (in pg/cm²) for BDE 183, 100, and 99, but not for the other PBDEs. Morgan et al. (2007) measured pyrethroid concentrations in dust and hard floor surface wipes, but again these concentrations cannot be compared due to different concentration units (ng/g vs. ng/cm²). Wason et al. (2013) studied correlations of organophosphate and pyrethroid concentrations between dust and kitchen or living room floor wipes, still in inhomogeneous units, in which diazinon, chlorpyrifos, permethrin, and cyfluthrin showed significant correlations, at least for kitchen wipes, whereas no significant correlation was established for cypermethrin. Comparisons between vacuumed and wiped dust using a homogeneous unit (mass/surface) are rarely performed despite the usefulness of considering dust contamination, not only in ng/g of a specific sieved fraction, but also in ng/m². Both types of dust sampling have been shown to be useful to characterize human exposure to dust. The wipe method represents surface loading, and as Lioy et al. (2002) explained, it can be used to estimate the amount of material available on a surface and the amount available for contact by a person. It was designed and used to imitate the hand's ability to pick up and retain particles (Le Bot et al., 2010), so wiped dust seems suitable for the evaluation of children's exposure. Vacuumed dust provides more knowledge in terms of dust contamination and is useful to characterize potential sources inside or outside a home (Lioy et al., 2002), yet can also be used as a proxy of dust exposure: Meeker et al. (2013) showed that some organophosphate flame retardants in vacuumed house dust were related to human urinary metabolites; Bennett et al. (2014) showed that PBDEs, not only in floor wipes but also in vacuumed dust, were correlated with serum levels.

Conclusion

This study which presents the contamination levels of SVOCs in schools for the first time in France has certain limitations relating to relatively high LOQs for some substances, the lack of data above the upper limit of the calibration range, the as yet unresolved issue of contaminated wipe blanks and the occasional difficulty vacuuming enough dust. Furthermore, the glass cartridges used for air sampling might not be suitable for the analysis of photosensitive compounds. Some of these limitations could be overcome: for example, the mass of vacuumed dust could be maximized with well-timed dust sampling performed before any scheduled housekeeping and allowing enough time to sample a large floor surface; alternatively, an extraction technique such as thermal desorption, requiring less dust, could be developed; air could be sampled using a light-proof device; LOQs could be lowered using a last generation, more sensitive, detector or with an increase of the injection volume. Nevertheless, the multiresidue method allows simultaneous analysis of multiple compounds in an economically sound way while still providing valuable information about the relative presence of SVOCs in classrooms. This shows in particular that DiBP, DBP, BBP, DEHP, and DiNP in dust are found more frequently in schools than in homes. These findings suggest that school exposure is not negligible for phthalates, demanding further investigation as the exposure would be underestimated in this work as a result of the lack of data above ULs. The comparison carried out between dust sampling with wipes, or with a vacuum cleaner, was for the first time reported using the same unit (ng/m²) and shows that sampling technique has an impact on SVOC measurement in dust: Dust sampling allows more compounds to be measured whereas wipe sampling leads to greater concentrations. The choice of the sampling method should of course be objective driven and consider the practical implementation and contamination levels. The use of vacuumed dust could be favored when the concentrations are too low to be quantified with the wipe method.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Table S1. Characteristics of schools and classrooms.
Table S2. SVOCs of interest for the study.
Table S3. Air sampling method evaluation.
Table S4. SVOC concentrations in air QC samples (ng/m^3).

Table S5. SVOC concentrations in SRM 2585 (ng/g).
Table S6. SVOC concentrations in French classrooms (Brittany, France, 2010).
Table S7. SVOC concentrations in air (ng/m^3) in classrooms (Brittany, France, 2010).
Table S8. SVOC concentrations in vacuumed dust (< 100 μm fraction) (ng/g) in classrooms (Brittany, France, 2010).
Table S9. SVOC concentrations in wiped dust (ng/m²) in classrooms (Brittany, France, 2010).
Table S10. SVOC concentrations from less concentrated extracts in air (ng/m^3) in classrooms (Brittany, France).
Table S11. SVOC concentrations from less concentrated extracts in vacuumed dust (< 100 μm fraction) (ng/g) in classrooms (Brittany, France).
Table S12. SVOC concentrations from less concentrated extracts in wiped dust (ng/m²) in classrooms (Brittany, France).
Table S13. SVOCs in air of nursery and primary schools in ng/m^3.
Table S14. SVOCs in dust of nursery and primary schools in ng/g.

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Semi-volatile organic compounds in the air and dust of 30 French schools: a pilot study

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Supporting information

Dust sampling. 2
Reagents and chemicals 2
Sample extraction 3
Sample analysis 3
Preparation of laboratory blank and quality control (QC) samples 4
Data validation process 4
SVOC concentrations in air QC samples 4
SVOC concentrations in SRM 2585 5
References 20

Table S1. Characteristics of schools and classrooms 5
Table S2. SVOCs of interest for the study 6
Table S3. Air sampling method evaluation 7
Table S4. SVOC concentrations in air QC samples (ng/m^3) 8
Table S5. SVOC concentrations in SRM 2585 (ng/g) 9
Table S6. SVOC concentrations in French classrooms (Brittany, France, 2010) 10
Table S7. SVOC concentrations in air (ng/m^3) in classrooms (Brittany, France, 2010) 12
Table S8. SVOC concentrations in vacuumed dust (< 100 µm fraction) (ng/g) in classrooms (Brittany, France, 2010) 13
Table S9. SVOC concentrations in wiped dust (ng/m²) in classrooms (Brittany, France, 2010) 14
Table S10. SVOC concentrations from less concentrated extracts in air (ng/m^3) in classrooms (Brittany, France) 15
Table S11. SVOC concentrations from less concentrated extracts in vacuumed dust (< 100 µm fraction) (ng/g) in classrooms (Brittany, France) 15
Table S12. SVOC concentrations from less concentrated extracts in wiped dust (ng/m²) in classrooms (Brittany, France) 15
Table S13. SVOCs in air of nursery and primary schools in ng/m^3 16
Table S14. SVOCs in dust of nursery and primary schools in ng/g 18

Dust sampling.

To avoid any disturbance of air sampling, dust was sampled either during the week preceding air sampling or just after the end of air sampling. Two different methods were used for sampling settled dust. The first method consisted of vacuuming dust settled on the floor using a modified vacuum cleaner (LG Electronics, Seoul, South Korea): the nozzle was covered with aluminum foil and dust was collected in a cellulose thimble (Whatman, Maidstone, Kent) placed at the entrance of the tube in order to avoid any contact with the internal parts of the vacuum cleaner, thus limiting foreign contamination of the sample. A 10 to 12 m² area in which children spend most time was measured and vacuumed slowly (about 0.5 m² per minute). The amount of dust present in the cellulose cartridge was then visually checked: if it was insufficient, another area was selected, measured and vacuumed. This procedure was repeated until the cellulose cartridge was at least half full. The cartridge was then wrapped in aluminum foil previously cleaned with DCM, transported back to the laboratory in an ice-box and kept in a freezer prior to extraction. The second method consisted of collecting settled dust using a damp wipe (Aramsco, Paulsboro, USA) on a 0.1 m² square floor surface delimited by a cardboard template (atelier du cadre, Carentoir, France). The cardboard template was cleaned using a wipe and phthalate free gloves were worn in order to avoid external contamination of the sample. The floor surface area to be sampled was a smooth surface such as stone, wooden or plastic floor, chosen in an area where the children spend most time, and where possible, was a smooth surface such as a stone, wooden or plastic floor. A wipe was removed from its package and laid flat in a corner of the template. It was then slowly moved from side to side and from top to bottom, as if drawing an “S” shape. The wipe was then folded in two, keeping the collected dust inside the fold and applied with the same slow motion, perpendicular to the previous passage. The wipe was folded once more, keeping the dust inside, and applied over the edges and corners of the template (NF X 46-032, 2008). The wipe was then rolled and inserted into a glass amber vial, previously cleaned with DCM. The same procedure was performed twice more, to collect three wipes per classroom. A sampling blank was made for each school investigated (i.e. one field blank for every 3 classrooms) using another wipe that was taken out of its package, folded, rolled and inserted into a glass amber vial in the same way as for the samples. Wipes were transported back to the laboratory in an ice-box and kept in a freezer prior to analysis.

Reagents and chemicals

Certified standards of aldrin, cis- and trans-chlordane, 4,4’-DDE, 4,4’-DDT, dieldrin, alpha-endosulfan, endrin, heptachlor, metolachlor, alpha-HCH, gamma-HCH (lindane), chlorpyrifos, diazinon, dichlorvos, atrazine, oxadiazon, cyfluthrin, cypermethrin, deltamethrin, permethrin, tetramethrin, tributylphosphate, acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, phenanthrene, pyrene, PCB 77, 105, 126, butylbenzylphthalate (BBP), di-n-butylphthalate (DBP), di(2-ethylhexyl)phthalate (DEHP), diethylphthalate (DEP), diisobutylphthalate (DiBP), diisononylphthalate (DiNP), dimethoxyethylphthalate (DMEP), dimethylphthalate (DMP), fenpropathrin (surrogate standard), methoprotryne (surrogate standard) and the internal standard (ISTD) 2,3,4-trichloronitrobenzene (TCNB) were purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany). Purity of certified standards was above 97 %, except for permethrin (94 %). Acetone and dichloromethane (DCM) (PLUS-for residual pesticide analysis) were purchased from Carlo Erba Reagents (Val

de Reuil, France). Individual standard stock solutions (1 g/L) were prepared in acetone by accurately weighing 25 mg (± 0.1 mg) of certified standards into 25 mL volumetric flasks and stored at -18°C. Nonane solutions (50 mg/L) of BDE 85, 99, 100 and 119 were purchased from Wellington Laboratories (Guelph, ON, Canada). Cyclohexane solutions (10 mg/L) of galaxolide (HHCB) and tonalide (AHTN) were obtained from Dr. Ehrenstorfer GmbH (Augsburg, Germany). A mixture (PCB Mix 21) containing 10 mg/L of 8 PCBs (PCB 28, 31, 52, 101, 118, 138, 153 and 180) in cyclohexane was supplied by Dr. Ehrenstorfer GmbH (Augsburg, Germany). Calibration solutions were prepared by appropriate dilution of individual standard stock solutions and commercial solutions in DCM.

The Standard Reference Material SRM 2585 (Organic Contaminants in House Dust) was purchased from the National Institute of Standards and Technology (NIST, Gaithersburg, MD, USA). Celite® 545 was purchased from Merck KGaA (Darmstadt, Germany). Chromabond® NH_2 (aminopropyl modified silica) glass columns (3 mL / 500 mg) were purchased from Macherey-Nagel GmbH & Co. KG (Düren, Germany).

Sample extraction

For air samples (gas and particulate phases), semivolatile organic compounds (SVOCs) were extracted from polyurethane foam (PUF) and quartz fiber filter (QFF) together using a pressurized liquid extractor (PLE) ASE (Accelerated Solvent Extractor) 350 (Dionex Corporation, Sunnyvale, USA). The QFF was placed on top of a cellulose filter at the bottom of each stainless steel cell. The PUF was then inserted into the cell and another cellulose filter was placed on top after adding 100 ng of each surrogate standard (fenpropathrin and methoprotryne). Extractions were performed once with DCM. Organic extracts were concentrated to 0.5 mL at 30°C under a nitrogen stream, spiked with 1 µg of ISTD and stored at -18°C prior to analysis.

SVOC extractions from vacuumed dust were performed on 200 mg of sieved dust. After adding 100 ng of each surrogate standard, extractions were performed using PLE. Organic extracts were concentrated to 10 mL at 30°C under a nitrogen stream. A volume of 500 µL was transferred into a 1.5 mL amber glass vial and spiked with 1 µg of ISTD. This aliquot was dedicated to quantification of the most concentrated compounds, such as phthalates. The remaining 9.5 mL were concentrated to 1 mL and transferred onto Chromabond® NH_2 glass columns prewashed with 6 mL of DCM. Elution was performed with 5 mL of DCM. The extracts were then concentrated to 0.5 mL and spiked with 1 µg of ISTD. All extracts were stored at -18°C prior to analysis.

Sample analysis

All extracts were analyzed using a gas chromatograph (GC) (Trace GC Ultra) coupled to a mass spectrometer (MS) (TSQ Quantum GC) operated in electron impact ionization (EI) mode (70 eV) (Thermo Scientific). The GC system was equipped with a TriPlus Autosampler and a Programmable Temperature Vaporizing (PTV) injector fitted with an empty baffled glass liner. Calibration solutions and sample extracts were injected (1 µL) in splitless mode. Helium was used as column carrier gas at a constant flow rate of 2 mL/min. Chromatographic separation was performed on a Rtx-PCB capillary column (60 m length x 0.25 mm I.D., 0.25 µm film thickness)

supplied by Restek (Lisses, France). The triple quadrupole MS was operated in multiple reaction monitoring (MRM) mode and the two most sensitive and specific transitions were monitored for each compound.

Preparation of laboratory blank and quality control (QC) samples

For air samples, cleaned PUFs were used as laboratory blank samples and QC samples consisted of cleaned PUFs spiked with the calibration solution at a concentration of twice or eight times the LOQ. These were prepared with each batch of nine samples. For vacuumed dust samples, laboratory blank samples consisted of Celite (2800 mg) and QC samples were made of 200 mg of the NIST (National Institute of Standards and Technology) SRM 2585 which contains indicative, reference or certified concentrations of several target compounds (Mercier et al., 2014). Both were prepared with each batch of nine samples. For wiped dust samples, wipes freshly removed from their packaging were used as laboratory blank samples and QC samples were performed by spreading 200 mg of SRM 2585 onto wipes also freshly removed from their packaging. These were prepared with the samples of each six classrooms.

Data validation process

The data validation protocol of the method contained several conditions including (i) the area of the ISTD in samples had to be within ± 25% of its area in calibration solutions, (ii) the determination coefficient of the calibration curve had to be greater than 0.995, (iii) the concentration of a substance in the laboratory blank sample had to be lower than 30% of the concentration measured in the associated samples, (iv) the measured concentration in calibration check solutions, injected every 10 samples, had to be within ±25% of its nominal concentration value, (v) the measured concentration of the calibration solution at the LOQ level had to be within ±50% of its nominal concentration value, and (vi) the concentration measured in the Standard Reference Material 2585 had to be within the limits set for the current year. If those conditions were not met, samples would either be re-analyzed or re-extracted if possible. For laboratory blanks, the validation conditions were as described in the main document ("When either a field blank sample or a laboratory blank sample showed a concentration greater than 30 % of the concentration found in the associated samples, the results in these samples were not validated and were removed from the data. If the contamination was less than 30% of the concentration found in associated samples, the concentrations for these samples were reported without blank correction").

SVOC concentrations in air QC samples

Concentrations measured in air QC samples and associated RSD and recovery data are summarized in SI Table 4. For low level (LOQ x 2) and high level (LOQ x 8) QCs, measured concentrations ranged from 77 to 124% and 79 to 119% respectively of the spiked concentrations, indicating good accuracy of results. For the low level QCs, RSD ranged from 11% to 34% for all compounds except phthalates, for which RSD ranged from 13% to 48%, because of occasional background contamination. For the high level QCs, RSD ranged from 8% to 33%. Overall, precision of the results was satisfactory: of the 55 compounds analyzed, RSD were below 25% for 47 compounds in low level QCs, and for 50 compounds in high level QCs.

SVOC concentrations in SRM 2585

Concentrations measured in SRM 2585 are summarized in SI Table 5. Overall they were in a good agreement with the indicative, reference or certified concentrations for the SRM 2585 extracted as vacuumed dust where they ranged from 75% to 125% of the indicative, reference or certified concentrations with the exception of heptachlor (60%), 4,4'-DDE (68%) and PCB 153 (73%). Measured concentrations were less accurate in SRM2585 extracted as wiped dust, where they ranged from 50% to 140% - although they fell between 75% and 125% for 25 of the 31 quantified compounds. The measured concentration of anthracene was about twice the certified value in SRM 2585 extracted as vacuumed dust (217%) or wiped dust (194%), confirming the findings of Mercier et al (2012, 2014). Method precision was satisfactory: RSDs for SRM 2585 extracted as vacuumed dust ranged from 10% to 24% and from 14% to 30% for SRM 2585 extracted as wiped dust.

Table S1. Characteristics of schools and classrooms

	This study (2009-2010)	**French Survey** (Guillam et al., 2011) (2010)
Schools characteristics	n=30	n=466
Building's year of construction		
Before 1946	22%	27%
Between 1946 and 2000	64%	56%
After 2000	13%	8%
Heating energy		
gas	63%	43%
oil	13%	30%
electricity	10%	20%
Ventilation		
Natural	70%	85%
Mechanical	30%	15%
Outdoor environment		
Urban	47%	44%
Rural	53%	35%
Residential		18%
Classrooms characteristics		
Age of children	n=90	n=985
2 to 5 years old	49%	49%
6 to 11 years old	51%	51%
Number of Children	n=90	n=936
Average	24.4	23.7
Story	n=90	n=924
Ground floor	80%	76%
2nd floor	16%	21%
3rd floor	4%	3%
Floor covering	n=90	n=960
PVC	70%	60%
Stone	34%	32%
Wood	10%	9%
Wall covering	n=90	n=949
Paint	78%	90%
Wall paper	29%	12%

Table S2. SVOCs of interest for the study

	Air (ng/m^3)		Vacuumed dust (< 100 µm fraction) (ng/g)		Wiped dust (ng/m^2)	
Substance	**LOQ**	**UL**	**LOQ**	**UL**	**LOQ**	**UL**
Organochlorinated pesticides:						
α-HCH	0.4	20	26	1 320	20	830
γ-HCH	1.0	50	66	3 290	40	2 080
Heptachlor	0.4	20	26	1 320	20	830
Metolachlor	1.0	50	66	3 290	40	2 080
Aldrin	1.0	50	66	3 290	40	2 080
Trans-chlordane	0.4	20	26	1 320	20	830
Cis-chlordane	0.4	20	26	1 320	20	830
Alpha-endosulfan	1.0	50	66	3 290	40	2 080
4,4'-DDE	0.4	20	26	1 320	20	830
Dieldrin	1.0	50	66	3 290	40	2 080
Endrin	1.0	50	66	3 290	40	2 080
4,4'-DDT	1.0	50	66	3 290	40	2 080
Organophosphorus pesticides:						
Dichlorvos	1.0	50	66	3 290	40	2 080
Diazinon	1.0	50	66	3 290	40	2 080
Chlorpyrifos	1.0	50	66	3 290	40	2 080
Other pesticides:						
Atrazine	1.0	50	66	3 290	40	2 080
Oxadiazon	1.0	50	66	3 290	40	2 080
Pyrethroids:						
Tetramethrin	1.0	50	66	3 290	40	2 080
Permethrin	1.0	50	66	3 290	40	2 080
Cyfluthrin	1.0	50	66	3 290	40	2 080
Cypermethrin	1.0	50	66	3 290	40	2 080
Deltamethrin	1.0	50	66	3 290	40	2 080
Phosphoric ester :						
Tributylphosphate	1.0	50	66	3 290	40	2 080
Musks:						
Galaxolide	1.0	50	66	3 290	40	2 080
Tonalide	1.0	50	66	3 290	40	2 080

	Air (ng/m^3)		Vacuumed dust (< 100 µm fraction) (ng/g)		Wiped dust (ng/m^2)	
	LOQ	**UL**	**LOQ**	**UL**	**LOQ**	**UL**
PAHs:						
Acenaphtene	1.0	50	66	3 290	40	2 080
Fluorene	1.0	50	66	3 290	40	2 080
Phenanthrene	1.0	50	66	3 290	40	2 080
Anthracene	1.0	50	66	3 290	40	2 080
Fluoranthene	1.0	50	66	3 290	40	2 080
Pyrene	1.0	50	66	3 290	40	2 080
Benzo(a)pyrene	1.0	50	66	3 290	40	2 080
PCBs:						
PCB 31	0.4	20	26	1 320	20	830
PCB 28	0.4	20	26	1 320	20	830
PCB 52	0.4	20	26	1 320	20	830
PCB 101	0.4	20	26	1 320	20	830
PCB 77	0.4	20	26	1 320	20	830
PCB 118	0.4	20	26	1 320	20	830
PCB 153	0.4	20	26	1 320	20	830
PCB 105	0.4	20	26	1 320	20	830
PCB 138	0.4	20	26	1 320	20	830
PCB 126	0.4	20	26	1 320	20	830
PCB 180	0.4	20	26	1 320	20	830
Phthalates:						
DMP	1.0	50	66	3 290	40	2 080
DEP	8.0	800	526	52 600	333	33 300
DiBP	8.0	800	526	52 600	333	33 300
DBP	8.0	800	526	52 600	333	33 300
DMEP	1.0	50	66	3 290	40	2 080
BBP	1.0	50	66	3 290	40	2 080
DEHP	8.0	800	526	52 600	333	33 300
DiNP	8.0	800	526	52 600	333	33 300
PBDEs:						
BDE 100	1.0	50	66	3 290	40	2 080
BDE 119	1.0	50	66	3 290	40	2 080
BDE 99	1.0	50	66	3 290	40	2 080
BDE 85	1.0	50	66	3 290	40	2 080

LOQ: limit of quantitation. UL: upper limit of the calibration range.

α-HCH: α-hexachlorocyclohexane, γ-HCH: γ-hexachlorocyclohexane (Lindane), 4,4'-DDE: dichlorodiphenyldichloroethylene, 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, DMEP: di(methoxyethyl)-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

Table S3. Air sampling method evaluation

	Spiked mass (ng)	Spiked concentration (ng/m^3)[a]	Measured / spiked concentration (%) for glass cartridges (n=3)	Measured / spiked concentration (%) in second PUF in series (n=1)[b]
Organochlorinated pesticides:				
α -HCH	200	16	102 ± 6	
γ -HCH	500	40	98 ± 5	
Aldrin	500	40	0 ± 0	0
Alpha-endosulfan	500	40	86 ± 3	
4,4'-DDE	200	16	96 ± 2	
Dieldrin	500	40	97 ± 5	
4,4'-DDT	500	40	110 ± 6	
Organophosphated pesticides:				
Dichlorvos	500	40	13 ± 1	0
Diazinon	500	40	66 ± 2	
Chlorpyrifos	500	40	91 ± 5	
Other pesticides:				
Oxadiazon	500	40	102 ± 5	
Pyrethroids:				
Tetramethrin	500	40	0 ± 0	0
Permethrin	2500	200	95 ± 3	
Cyfluthrin	500	40	89 ± 3	
Cypermethrin	500	40	87 ± 6	
Deltamethrin	500	40	81 ± 17	
Phosphoric ester :				
Tributylphosphate	2500	200	99 ± 4	
Musks:				
Galaxolide	10000	800	91 ± 4	
Tonalide	10000	800	93 ± 2	
PAHs:				
Acenaphtene	500	40	8 ± 0	4
Fluorene	500	40	81 ± 8	
PAHs (continued):				
Phenanthrene	500	40	100 ± 4	
Anthracene	500	40	31 ± 6	0
Fluoranthene	500	40	106 ± 4	
Pyrene	500	40	85 ± 4	
Benzo(a)pyrene	500	40	1 ± 1	0
PCBs:				
PCB 31	200	16	97 ± 8	
PCB 28	200	16	99 ± 1	
PCB 52	200	16	99 ± 2	
PCB 101	200	16	96 ± 7	
PCB 118	200	16	98 ± 3	
PCB 153	200	16	97 ± 3	
PCB 105	200	16	99 ± 5	
PCB 138	200	16	99 ± 2	
PCB 180	200	16	99 ± 6	
Phthalates:				
DEP	1E+05	8000	97 ± 2	
DiBP	1E+05	8000	96 ± 1	
DBP	1E+05	8000	93 ± 2	
BBP	1E+05	8000	100 ± 4	
DEHP	1E+05	8000	95 ± 1	
DiNP	1E+05	8000	85 ± 4	
PBDEs:				
BDE 100	500	40	85 ± 5	
BDE 99	500	40	95 ± 7	
BDE 85	500	40	86 ± 8	

[a]based on 12,5m^3 sampled at 2 L/min from Monday 8:30 to Friday 16:30 ; [b]Measured / spiked concentration (%) in PUF in series = (concentration in PUF in series after spiked PUF - concentration in PUF in series after witness PUF)/spiked concentration .

α-HCH: α-hexachlorocyclohexane, γ-HCH: γ-hexachlorocyclohexane (Lindane), 4,4'-DDE: dichlorodiphenyldichloroethylene, 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

This evaluation was carried out for the 44 compounds that were more often quantified and later selected for the national campaign.

Table S4. SVOC concentrations in air QC samples (ng/m^3)

Substance	SVOC concentrations (ng/m^3) in air QC sample Level 1 (LOQx2) (n=14)			SVOC concentrations (ng/m^3) in air QC sample Level 2 (LOQx8) (n=12)		
	Measured concentration (RSD (%))	Spiked concentration	Measured / spiked concentration (%)	Measured concentration (RSD (%))	Spiked concentration	Measured / spiked concentration (%)
Organochlorinated pesticides:						
α-HCH	0.740 (31)	0.800	92	3.02 (23)	3.20	94
γ-HCH	1.84 (19)	2.00	92	7.59 (21)	8.00	95
Heptachlor	0.745 (20)	0.800	93	3.07 (17)	3.20	96
Metolachlor	2.12 (17)	2.00	106	8.24 (12)	8.00	103
Aldrin	1.67 (20)	2.00	83	6.93 (15)	8.00	87
Trans-chlordane	0.706 (17)	0.800	88	3.16 (16)	3.20	99
Cis-chlordane	0.686 (16)	0.800	86	3.00 (13)	3.20	94
Alpha-endosulfan	1.88 (17)	2.00	94	7.63 (14)	8.00	95
4,4'-DDE	0.697 (18)	0.800	87	2.90 (11)	3.20	91
Dieldrin	1.89 (14)	2.00	95	7.60 (10)	8.00	95
Endrin	2.10 (11)	2.00	105	8.33 (13)	8.00	104
4,4'-DDT	2.48 (25)	2.00	124	8.37 (27)	8.00	105
Organophosphated pesticides:						
Dichlorvos	1.66 (34)	2.00	83	6.38 (33)	8.00	80
Diazinon	1.89 (18)	2.00	95	8.03 (17)	8.00	100
Chlorpyrifos	2.18 (21)	2.00	109	9.18 (24)	8.00	115
Other pesticides:						
Atrazine	1.88 (19)	2.00	94	7.30 (15)	8.00	91
Oxadiazon	1.88 (15)	2.00	94	7.94 (15)	8.00	99
Pyrethroids:						
Tetramethrin	2.10 (14)	2.00	105	8.65 (13)	8.00	108
Permethrin	1.96 (10)	2.00	98	8.31 (10)	8.00	104
Cyfluthrin	2.10 (17)	2.00	105	8.74 (14)	8.00	109
Cypermethrin	2.09 (13)	2.00	105	8.37 (13)	8.00	105
Deltamethrin	2.29 (18)	2.00	114	8.94 (17)	8.00	112
Phosphoric ester :						
Tributylphosphate	1.97 (19)	2.00	99	7.82 (15)	8.00	98
Musks:						
Galaxolide	2.27 (31)	2.00	113	7.70 (20)	8.00	96
Tonalide	1.86 (22)	2.00	93	7.04 (18)	8.00	88
PAHs:						
Acenaphtene	1.54 (30)	2.00	77	6.30 (34)	8.00	79
Fluorene	1.64 (25)	2.00	82	6.42 (19)	8.00	80
Phenanthrene	1.91 (15)	2.00	96	7.87 (17)	8.00	98
Anthracene	1.97 (11)	2.00	99	7.92 (13)	8.00	99
Fluoranthene	1.93 (14)	2.00	96	7.95 (10)	8.00	99
Pyrene	2.00 (12)	2.00	100	7.77 (8)	8.00	97
Benzo(a)pyrene	1.99 (24)	2.00	100	7.94 (14)	8.00	99
PCBs:						
PCB 31	0.730 (16)	0.800	91	3.11 (15)	3.20	97
PCB 28	0.683 (19)	0.800	85	2.83 (15)	3.20	88
PCB 52	0.703 (18)	0.800	88	3.01 (16)	3.20	94
PCB 101	0.736 (17)	0.800	92	3.07 (15)	3.20	96
PCB 77	0.786 (14)	0.800	98	3.25 (11)	3.20	101
PCB 118	0.768 (16)	0.800	96	3.09 (13)	3.20	96
PCB 153	0.743 (18)	0.800	93	3.13 (15)	3.20	98
PCB 105	0.751 (16)	0.800	94	3.19 (13)	3.20	100
PCB 138	0.747 (16)	0.800	93	3.11 (12)	3.20	97
PCB 126	0.789 (13)	0.800	99	3.27 (12)	3.20	102
PCB 180	0.723 (18)	0.800	90	3.14 (13)	3.20	98
Phthalates:						
DMP	2.20 (48)	2.00	110	7.55 (30)	8.00	94
DEP	16.7 (35)	16.0	104	76.4 (31)	64.0	119
DiBP	20.4 (26)	16.0	127	68.6 (16)	64.0	107
DBP	17.8 (18)	16.0	111	65.0 (14)	64.0	102
DMEP	2.02 (13)	2.00	101	7.90 (13)	8.00	99
BBP	2.24 (31)	2.00	112	8.72 (12)	8.00	109
DEHP	19.9 (22)	16.0	125	74.2 (11)	64.0	116
DiNP	18.6 (21)	16.0	116	79.7 (30)	64.0	125
PBDEs:						
BDE 100	1.96 (14)	2.00	98	7.86 (18)	8.00	98
BDE 119	1.95 (19)	2.00	98	7.95 (17)	8.00	99
BDE 99	1.94 (18)	2.00	97	8.01 (20)	8.00	100
BDE 85	2.04 (22)	2.00	102	8.26 (17)	8.00	103

LOQ: limit of quantitation. RSD: Relative Standard Deviation

α-HCH: α-hexachlorocyclohexane, γ-HCH: γ-hexachlorocyclohexane (Lindane), 4,4'-DDE: dichlorodiphenyldichloroethylene, 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, DMEP: di(methoxyethyl)-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

Table S5. SVOC concentrations in SRM 2585 (ng/g)

		SVOC concentrations (ng/g) in SRM 2585 extracted as vacuumed dust QC control (n=12)[d]		SVOC concentrations (ng/g) in SRM 2585 extracted as wiped dust QC control (n=10)	
Substance	**Indicative, reference or certified concentration**	**Measured concentration (RSD (%))**	**Measured / Indicative, reference or certified concentration (%)**	**Measured concentration (RSD (%))**	**Measured / Indicative, reference or certified concentration (%)**
Organochlorinated pesticides:					
γ-HCH	4.1[b]	< 65.8	-	< 62.5	-
Heptachlor	166[b]	99.9 (12)	60	83.0 (18)	50
Trans-chlordane	277[b]	341 (17)	123	294 (18)	106
Cis-chlordane	174[b]	166 (15)	95	150 (22)	86
4,4'-DDE	261[a]	177 (14)	68	165 (21)	63
Dieldrin	88.0[b]	89.5 (21)	102	109 (23)	124
4,4'-DDT	111[a]	125 (18)	113	131 (29)	118
Organophosphated pesticides:					
Diazinon	396[c]	380 (14)	96	343 (17)	87
Chlorpyrifos	279[c]	244 (21)	87	282 (19)	101
Pyrethroids:					
Tetramethrin	356[c]	350 (22)	98	361 (24)	101
Permethrin	4970[c]	4322 (22)	87	3910 (17)	79
Cyfluthrin	3730[c]	3024 (24)	81	3280 (16)	88
Cypermethrin	4050[c]	3439 (19)	85	3680 (19)	91
Phosphoric ester :					
Tributylphosphate	306[c]	255 (20)	83	247 (16)	81
Musks:					
Galaxolide	1540[c]	1460 (14)	95	1350 (15)	88
Tonalide	1840[c]	1730 (14)	94	1680 (17)	91
PAHs:					
Phenanthrene	1920[a]	1710 (12)	89	1480 (18)	77
Anthracene	96.0[a]	208 (21)	217	186 (26)	194
Fluoranthene	4380[a]	2630 (16)	83	3370 (19)	77
Pyrene	3290[a]	2740 (17)	83	2620 (20)	80
Benzo(a)pyrene	1140[a]	897 (23)	79	1230 (30)	108
PCBs:					
PCB 31	14.0[a]	<26.3	-	< 25	-
PCB 28	13.4[a]	<26.3	-	< 25	-
PCB 52	21.8[a]	20.4 (18)	94	20.6 (15)	94
PCB 101	29.8[a]	34.5 (15)	116	31.9 (17)	107
PCB 118	26.3[a]	29.6 (12)	112	< 25	-
PCB 153	40.2[a]	29.3 (15)	73	< 25	-
PCB 105	13.2[a]	<26.3	-	< 25	-
PCB 138	27.6[a]	33.1 (14)	120	30.7 (14)	111
PCB 180	18.4[a]	20.3 (21)	110	19.8 (18)	108
Phthalates:					
DMP	2550[c]	2104 (10)	83	2350 (20)	92
DEP	8240[c]	7700 (11)	93	7650 (20)	93
DiBP	6670[c]	6370 (18)	96	5230 (21)	78
DBP	33300[c]	28900 (16)	87	23900 (19)	72
BBP[d]	98700[c]	82700 (22)	84	> 3130	-
DEHP[d]	552000[c]	436000 (16)	79	> 50000	-
DiNP[d]	182000[c]	157000 (13)	86	> 50000	-
PBDEs:					
BDE 100	145[a]	134 (20)	92	118 (22)	81
BDE 99	892[a]	753 (14)	84	647 (21)	73
BDE 85	43.8[a]	47.4 (20)	108	61.1 (18)	140

LOQ: limit of quantitation. RSD: Relative Standard Deviation

γ-HCH: gamma-hexachlorocyclohexane (Lindane), 4,4'-DDE: dichlorodiphenyldichloroethylene, 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

[a] Certified concentration.

[b] Reference concentration.

[c] Indicative concentration taken from Mercier et al. (J. Chromatogr. A 1336 (2014) 101-111)

[a] Concentrations from less concentrated extracts used for SRM2585 extracts extracted as vacuumed dust QC sample (n=3)

Table S6. SVOC concentrations in French classrooms (Brittany, France, 2010)

	Air (ng/m³)							Vacuumed dust (< 100 µm fraction) (ng/g)							Wiped dust (ng/m²)						
Substance	**LOQ**	**UL**	**N**	**5th%**	**50th%**	**95th%**	**F**	**LOQ**	**UL**	**N**	**5th%**	**50th%**	**95th%**	**F**	**LOQ**	**UL**	**N**	**5th%**	**50th%**	**95th%**	**F**
Organochlorinated pesticides:																					
α-HCH	0.4	20	59	<0.4	<0.4	3.4	24%	26	1 320	89	<26.3	<26.3	<26.3	2%	20	830	81	<20	<20	<20	1%
γ-HCH	1.0	50	62	<1.0	2.0	7.2	79%	66	3 290	89	<65.8	<65.8	247	18%	40	2 080	81	<40	<40	<40	4%
Heptachlor	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	0%	20	830	81	<20	<20	<20	0%
Metolachlor	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Aldrin	1.0	50	62	*	*	*	2%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Trans-chlordane	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	1%	20	830	81	<20	<20	<20	0%
Cis-chlordane	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	0%	20	830	81	<20	<20	<20	0%
Alpha-endosulfan	1.0	50	62	<1.0	<1.0	<1.0	5%	66	3 290	89	<65.8	<65.8	<65.8	1%	40	2 080	81	<40	<40	<40	1%
4,4'-DDE	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	2%	20	830	81	<20	<20	<20	0%
Dieldrin	1.0	50	62	<1.0	<1.0	1.0	6%	66	3 290	89	<65.8	<65.8	<65.8	2%	40	2 080	81	<40	<40	<40	1%
Endrin	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	<65.8	4%	40	2 080	81	<40	<40	<40	0%
4,4'-DDT	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	177	15%	40	2 080	81	<40	<40	<40	2%
Organophosphated pesticides:																					
Dichlorvos	1.0	50	62	*	*	*	2%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Diazinon	1.0	50	62	<1.0	<1.0	1.2	6%	66	3 290	89	<65.8	<65.8	<65.8	2%	40	2 080	81	<40	<40	<40	0%
Chlorpyrifos	1.0	50	62	<1.0	<1.0	<1.0	2%	66	3 290	89	<65.8	<65.8	<65.8	3%	40	2 080	81	<40	<40	<40	2%
Other pesticides:																					
Atrazine	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Oxadiazon	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	110	9%	40	2 080	81	<40	<40	<40	1%
Pyrethroids:																					
Tetramethrin	1.0	50	62	*	*	*	0%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Permethrin	1.0	50	62	<1.0	<1.0	<1.0	2%	66	3 290	89	<65.8	279	1 961	61%	40	2 080	81	<40	<40	578	27%
Cyfluthrin	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Cypermethrin	1.0	50	62	<1.0	<1.0	<1.0	2%	66	3 290	89	<65.8	<65.8	<65.8	4%	40	2 080	81	<40	<40	<40	1%
Deltamethrin	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Phosphoric ester :																					
Tributylphosphate	1.0	50	62	2.0	4.7	12.4	100%	66	3 290	89	<65.8	103	401	74%	40	2 080	79	<40	<40	190	20%
Musks:																					
Galaxolide	1.0	50	62	46	>50	>50	100%	66	3 290	89	304	965	2 191	98%	40	2 080	65	148	335	1 213	97%
Tonalide	1.0	50	62	10	20	>50	100%	66	3 290	89	<65.8	337	915	88%	40	2 080	81	<40	170	642	63%
PAHs:																					
Acenaphtene	1.0	50	62	*	*	*	53%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
Fluorene	1.0	50	62	2.5	5.5	13	100%	66	3 290	89	<65.8	<65.8	268	40%	40	2 080	81	<40	<40	175	9%
Phenanthrene	1.0	50	62	4.8	8.7	18	100%	66	3 290	89	<65.8	363	907	92%	40	2 080	75	<40	<40	539	45%
Anthracene	1.0	50	62	*	*	*	2%	66	3 290	89	<65.8	<65.8	127	40%	40	2 080	81	<40	<40	<40	1%
Fluoranthene	1.0	50	62	<1.0	<1.0	1.6	29%	66	3 290	89	<65.8	184	751	85%	40	2 080	81	<40	<40	441	32%
Pyrene	1.0	50	62	<1.0	<1.0	1.2	18%	66	3 290	89	<65.8	285	760	90%	40	2 080	80	<40	<40	525	40%
Benzo(a)pyrene	1.0	50	62	*	*	*	0%	66	3 290	89	<65.8	<65.8	172	27%	40	2 080	81	<40	<40	125	6%

Substance	Air (ng/m³) LOQ	UL	N	5th%	50th%	95th%	F	Vacuumed dust (< 100 µm fraction) (ng/g) LOQ	UL	N	5th%	50th%	95th%	F	Wiped dust (ng/m²) LOQ	UL	N	5th%	50th%	95th%	F
PCBs:																					
PCB 31	0.4	20	62	<0.4	<0.4	0.6	15%	26	1 320	89	<26.3	<26.3	<26.3	2%	20	830	81	<20	<20	<20	0%
PCB 28	0.4	20	62	<0.4	<0.4	0.9	19%	26	1 320	89	<26.3	<26.3	<26.3	6%	20	830	81	<20	<20	<20	0%
PCB 52	0.4	20	62	<0.4	<0.4	0.5	16%	26	1 320	89	<26.3	<26.3	48	7%	20	830	81	<20	<20	<20	2%
PCB 101	0.4	20	62	<0.4	<0.4	<0.4	2%	26	1 320	89	<26.3	<26.3	107	13%	20	830	81	<20	<20	<20	1%
PCB 77	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	2%	20	830	81	<20	<20	<20	0%
PCB 118	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	42	8%	20	830	81	<20	<20	<20	1%
PCB 153	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	73	9%	20	830	81	<20	<20	<20	1%
PCB 105	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	3%	20	830	81	<20	<20	<20	1%
PCB 138	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	79	10%	20	830	81	<20	<20	<20	1%
PCB 126	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	0%	20	830	81	<20	<20	<20	0%
PCB 180	0.4	20	62	<0.4	<0.4	<0.4	0%	26	1 320	89	<26.3	<26.3	<26.3	4%	20	830	81	<20	<20	<20	0%
Phthalates:																					
DMP	1.0	50	53	6.7	13	>50	100%	66	3 290	54	<65.8	252	1 680	87%	40	2 080	79	<40	<40	555	39%
DEP	8.0	800	53	85	221	515	100%	526	52 600	76	739	2 890	6 560	93%	333	33 300	65	<333	1 310	5 200	66%
DiBP	8.0	800	62	352	>800	>800	100%	526	52 600	89	41 000	> 52 600	> 52 600	100%	333	33 300	71	11 000	>33 300	>33 300	100%
DBP	8.0	800	62	66	228	744	100%	526	52 600	89	11 000	38 200	> 52 600	100%	333	33 300	64	4 220	15 200	>33 300	100%
DMEP	1.0	50	62	<1.0	<1.0	<1.0	2%	66	3 290	89	<65.8	<65.8	<65.8	4%	40	2 080	81	<40	<40	142	9%
BBP[ab]	1.0	50	56	3.7	19	>50	100%	66	3 290	22	11 400	105 000	468 000	100%	40	2 080	22	6 750	73 600	1 940 000	100%
DEHP[ab]	8.0	800	58	49	108	417	100%	526	52 600	28	275 000	1 430 000	5 830 000	100%	333	33 300	28	86 900	1 210 000	4 520 000	100%
DiNP[a]	8.0	800	30	8.2	35	214	93%	526	52 600	32	258 000	1 030 000	4 100 000	100%	333	33 300	77	33 000	>33 300	>33 300	100%
PBDEs:																					
BDE 100	1.0	50	62	<1.0	<1.0	1.9	8%	66	3 290	89	<65.8	<65.8	140	8%	40	2 080	81	<40	<40	<40	1%
BDE 119	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%
BDE 99	1.0	50	62	<1.0	<1.0	4.9	13%	66	3 290	89	<65.8	<65.8	340	12%	40	2 080	81	<40	<40	<40	2%
BDE 85	1.0	50	62	<1.0	<1.0	<1.0	0%	66	3 290	89	<65.8	<65.8	<65.8	0%	40	2 080	81	<40	<40	<40	0%

LOQ: limit of quantitation. UL: upper limit of the calibration range. N: number of classrooms. F: frequency of classrooms with concentrations > LOQ.
α-HCH: α-hexachlorocyclohexane, γ-HCH: γ -hexachlorocyclohexane (Lindane), 4,4'-DDE: dichlorodiphenyldichloroethylene, 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, DMEP: di(methoxyethyl)-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.
[a]Concentrations from less concentrated extracts for vacuumed dust
[b]Concentrations from less concentrated extracts for wiped dust
*Unvalidated air sampling method, substance subject to degradation or low breakthrough volume.
In grey : substance never quantified

Table S7. SVOC concentrations in air (ng/m^3) in classrooms (Brittany, France, 2010)

Substance[a]	LOQ	UL	N	$N_{c<LOQ}$	$N_{LOQ<c<UL}$	$N_{c>UL}$	min	5th%	25th%	50th%	75th%	95th%	max	F
Organochlorinated pesticides:														
a-HCH	0.4	20	59	45	14	0	<0.4	<0.4	<0.4	<0.4	<0.4	3.4	12	24%
g-HCH	1.0	50	62	13	49	0	<1	<1	1.1	2.0	2.6	7.2	12	79%
Chlorpyrifos-ethyl	1.0	50	62	61	1	0	<1	<1	<1	<1	<1	<1	4.1	2%
Aldrin[b]	1.0	50	62	61	1	0	*	*	*	*	*	*	*	2%
Alpha-endosulfan	1.0	50	62	59	3	0	<1	<1	<1	<1	<1	<1	2.0	5%
Dieldrin	1.0	50	62	58	4	0	<1	<1	<1	<1	<1	1.0	2.4	6%
Organophosphated pesticides:														
Dichlorvos[b]	1.0	50	62	61	1	0	*	*	*	*	*	*	*	2%
Diazinon	1.0	50	62	58	4	0	<1	<1	<1	<1	<1	1.2	3.1	6%
Pyrethroids:														
Permethrin	1.0	50	62	61	1	0	<1	<1	<1	<1	<1	<1	2.1	2%
Cypermethrin	1.0	50	62	61	1	0	<1	<1	<1	<1	<1	<1	2.9	2%
Phosphoric ester :														
Tributylphosphate	1.0	50	62	0	62	0	1.3	2.0	3.5	4.7	6.7	12	28	100%
Musks:														
Galaxolide	1.0	50	62	0	5	57	14	46.2	>50	>50	>50	>50	>50	100%
Tonalide	1.0	50	62	0	51	11	3.5	10	16	20	36	>50	>50	100%
PAHs:														
Acenaphtene[b]	1.0	50	62	29	33	0	*	*	*	*	*	*	*	53%
Fluorene	1.0	50	62	0	62	0	1.1	2.5	4.1	5.5	7.3	13	18	100%
Phenanthrene	1.0	50	62	0	61	1	1.6	4.8	6.4	8.7	12	18	>50	100%
Anthracene[b]	1.0	50	62	61	1	0	*	*	*	*	*	*	*	2%
Fluoranthene	1.0	50	62	44	18	0	<1	<1	<1	<1	1.1	1.6	8.3	29%
Pyrene	1.0	50	62	51	11	0	<1	<1	<1	<1	<1	1.2	3.6	18%
PCBs:														
PCB31	0.4	20	62	53	9	0	<0.4	<0.4	<0.4	<0.4	<0.4	0.6	2.6	15%
PCB28	0.4	20	62	50	12	0	<0.4	<0.4	<0.4	<0.4	<0.4	0.9	4.2	19%
PCB52	0.4	20	62	52	10	0	<0.4	<0.4	<0.4	<0.4	<0.4	0.5	0.5	16%
PCB101	0.4	20	62	61	1	0	<0.4	<0.4	<0.4	<0.4	<0.4	<0.4	0.6	2%
Phthalates:														
DMP	1.0	50	53	0	49	4	4.1	6.7	10.0	12.6	27.9	>50	>50	100%
DEP	8.0	800	53	0	53	0	40	85	158	221	282	515	684	100%
DiBP	8.0	800	62	0	22	40	207	352	652	>800	>800	>800	>800	100%
DBP	8.0	800	62	0	59	3	37	66	146	228	352	744	>800	100%
DMEP	1.0	50	62	61	1	0	<1	<1	<1	<1	<1	<1	1.1	2%
BBP	1.0	50	56	0	37	19	1.5	3.7	8.0	19	>50	>50	>50	100%
DEHP	8.0	800	58	0	57	1	27	49	72	108	165	417	>800	100%
DiNP	8.0	800	30	2	28	0	<8	8.2	25	35	62	214	416	93%
PBDEs:														
BDE 100	1.0	50	62	57	5	0	<1	<1	<1	<1	<1	1.9	3.1	8%
BDE 99	1.0	50	62	54	8	0	<1	<1	<1	<1	<1	4.9	8.5	13%

LOQ: limit of quantitation. UL: upper limit of the calibration range. N: number of classrooms. $N_{c<LOQ}$: number of samples whose concentration is less than LOQ. $N_{LOQ<c<UL}$: number of samples whose concentration is between LOQ and UL. $N_{c>UL}$: number of samples whose concentration is above UL. F: frequency of classrooms with concentrations > LOQ.

α-HCH: α-hexachlorocyclohexane, γ-HCH: γ-hexachlorocyclohexane (Lindane), PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, DMEP: di(methoxyethyl)-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

[a]Only substances quantified at least once reported.
*Unvalidated sampling method, substance subject to degradation or low breakthrough volume

Table S8. SVOC concentrations in vacuumed dust (< 100 µm fraction) (ng/g) in classrooms (Brittany, France, 2010)

Substance[a]	LOQ	UL	N	$N_{c<LO}$	$N_{LOQ<c<}$	$N_{c>U}$	min	5th%	25th%	50th%	75th%	95th%	max	F
Organochlorinated pesticides:														
α-HCH	26.3	1 320	89	87	2	0	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	33.8	2%
γ-HCH	65.8	3 290	89	73	16	0	<65.8	<65.8	<65.8	<65.8	<65.8	247	482	18%
Trans-chlordane	26.3	1 320	89	88	1	0	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	84.3	1%
Alpha-endosulfan	65.8	3 290	89	88	1	0	<65.8	<65.8	<65.8	<65.8	<65.8	<65.8	144	1%
4,4'-DDE	26.3	1 320	89	87	2	0	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	116	2%
Dieldrin	65.8	3 290	89	87	2	0	<65.8	<65.8	<65.8	<65.8	<65.8	<65.8	331	2%
Endrin	65.8	3 290	89	85	4	0	<65.8	<65.8	<65.8	<65.8	<65.8	<65.8	606	4%
4,4'-DDT	65.8	3 290	89	76	13	0	<65.8	<65.8	<65.8	<65.8	<65.8	177	583	15%
Organophosphated pesticides:														
Diazinon	65.8	3 290	89	87	2	0	<65.8	<65.8	<65.8	<65.8	<65.8	<65.8	160	2%
Chlorpyrifos	65.8	3 290	89	86	3	0	<65.8	<65.8	<65.8	<65.8	<65.8	<65.8	1 250	3%
Other pesticides:														
Oxadiazon	65.8	3 290	89	81	8	0	<65.8	<65.8	<65.8	<65.8	<65.8	110	373	9%
Pyrethroids:														
Permethrin	65.8	3 290	89	35	52	2	<65.8	<65.8	<65.8	279	730	1 960	4 500	61%
Cypermethrin	65.8	3 290	89	85	4	0	<65.8	<65.8	<65.8	<65.8	<65.8	<65.8	2 470	4%
Phosphoric ester :														
Tributylphosphate	65.8	3 290	89	23	64	2	<65.8	<65.8	<65.8	103	166	401	> 3290	74%
Musks:														
Galaxolide	65.8	3 290	89	2	87	0	<65.8	304	564	965	1 358	2 190	3 480	98%
Tonalide	65.8	3 290	89	11	78	0	<65.8	<65.8	187	337	506	915	12 700	88%
PAHs:														
Fluorene	65.8	3 290	89	53	36	0	<65.8	<65.8	<65.8	<65.8	111	268	465	40%
Phenanthrene	65.8	3 290	89	7	81	1	<65.8	<65.8	240	363	521	907	> 3290	92%
Anthracene	65.8	3 290	89	53	36	0	<65.8	<65.8	<65.8	<65.8	86	127	702	40%
Fluoranthene	65.8	3 290	89	13	75	1	<65.8	<65.8	122	184	323	751	> 3290	85%
Pyrene	65.8	3 290	89	9	79	1	<65.8	<65.8	194	285	449	760	> 3290	90%
Benzo(a)pyrene	65.8	3 290	89	65	24	0	<65.8	<65.8	<65.8	<65.8	70	172	860	27%
PCBs:														
PCB31	26.3	1 320	89	87	1	1	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	> 1320	2%
PCB28	26.3	1 320	89	84	4	1	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	> 1320	6%
PCB52	26.3	1 320	89	83	5	1	<26.3	<26.3	<26.3	<26.3	<26.3	48.1	> 1320	7%
PCB101	26.3	1 320	89	77	12	0	<26.3	<26.3	<26.3	<26.3	<26.3	107	608	13%
PCB77	26.3	1 320	89	87	2	0	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	209	2%
PCB118	26.3	1 320	89	82	7	0	<26.3	<26.3	<26.3	<26.3	<26.3	42.2	391	8%
PCB153	26.3	1 320	89	81	8	0	<26.3	<26.3	<26.3	<26.3	<26.3	73.3	541	9%
PCB105	26.3	1 320	89	86	3	0	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	292	3%
PCB138	26.3	1 320	89	80	9	0	<26.3	<26.3	<26.3	<26.3	<26.3	78.5	556	10%
PCB180	26.3	1 320	89	85	4	0	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	261	4%
Phthalates:														
DMP	65.8	3 290	54	7	47	0	<65.8	<65.8	122	252	531	1 680	2 780	87%
DEP	526	52 600	76	5	71	0	263	739	2 330	2 890	3 840	6 560	10 400	93%
DiBP	526	52 600	89	0	26	63	23 050	41 020	> 52600	> 52600	> 52600	> 52600	> 52600	100%
DBP	526	52 600	89	0	64	25	8 010	11 000	23 200	38 200	> 52600	> 52600	> 52600	100%
DMEP	65.8	3 290	89	85	4	0	<65.8	<65.8	<65.8	<65.8	<65.8	<65.8	5 890	4%
BBP[b]	65.8	3 290	22				8 520	11 400	53 000	105 000	216 000	468 000	1 930 000	100%
DEHP[b]	526	52 600	28				226 000	275 000	709 000	1 430 000	2 240 000	5 830 000	9 280 000	100%
DiNP[b]	526	52 600	32				166 000	258 000	617 000	1 030 000	2 150 000	4 100 000	9 570 000	100%
PBDEs:														
BDE100	65.8	3 290	89	82	7	0	<65.8	<65.8	<65.8	<65.8	<65.8	140	241	8%
BDE99	65.8	3 290	89	78	11	0	<65.8	<65.8	<65.8	<65.8	<65.8	340	575	12%

LOQ: limit of quantitation. UL: upper limit of the calibration range. N: number of classrooms. $N_{c<LOQ}$: number of samples whose concentration is less than LOQ. $N_{LOQ<c<UL}$: number of samples whose concentration is between LOQ and UL. $N_{c>UL}$: number of samples whose concentration is above UL. F: frequency of classrooms with concentrations > LOQ.
α-HCH: α-hexachlorocyclohexane, γ-HCH: γ-hexachlorocyclohexane (Lindane), 4,4'-DDE: dichlorodiphenyldichloroethylene, 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl-phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, DMEP: di(methoxyethyl)-phthalate, BBP: butyl-benzyl-phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

[a]Only substances quantified at least once reported.

[b]Concentrations from less concentrated extracts

Table S9. SVOC concentrations in wiped dust (ng/m²) in classrooms (Brittany, France, 2010)

Substance[a]	LOQ	UL	N	$N_{c<LOQ}$	$N_{LOQ<c<UL}$	$N_{c>UL}$	min	5th%	25th%	50th%	75th%	95th%	max	F
Organochlorinated pesticides:														
α-HCH	20	830	81	80	1	0	<20	<20	<20	<20	<20	<20	78	1%
γ-HCH	40	2 080	81	78	3	0	<40	<40	<40	<40	<40	<40	329	4%
Alpha-endosulfan	40	2 080	81	80	1	0	<40	<40	<40	<40	<40	<40	337	1%
Dieldrin	40	2 080	81	80	1	0	<40	<40	<40	<40	<40	<40	146	1%
4,4'-DDT	40	2 080	81	79	2	0	<40	<40	<40	<40	<40	<40	229	2%
Organophosphated pesticides:														
Chlorpyrifos	40	2 080	81	79	2	0	<40	<40	<40	<40	<40	<40	328	2%
Other pesticides:														
Oxadiazon	40	2 080	81	80	1	0	<40	<40	<40	<40	<40	<40	600	1%
Pyrethroids:														
Permethrin	40	2 080	81	59	21	1	<40	<40	<40	<40	146	578	>2080	27%
Cypermethrin	40	2 080	81	80	1	0	<40	<40	<40	<40	<40	<40	1 442	1%
Phosphoric ester :														
Tributylphosphate	40	2 080	79	63	14	2	<40	<40	<40	<40	<40	190	>2080	20%
Musks:														
Galaxolide	40	2 080	65	2	63	0	<40	148	258	335	703	1 213	1 624	97%
Tonalide	40	2 080	81	30	51	0	<40	<40	<40	170	232	642	2 044	63%
PAHs:														
Fluorene	40	2 080	81	74	7	0	<40	<40	<40	<40	<40	175	376	9%
Phenanthrene	40	2 080	75	41	33	1	<40	<40	<40	<40	225	539	>2080	45%
Anthracene	40	2 080	81	80	1	0	<40	<40	<40	<40	<40	<40	296	1%
Fluoranthene	40	2 080	81	55	25	1	<40	<40	<40	<40	161	441	>2080	32%
Pyrene	40	2 080	80	48	32	0	<40	<40	<40	<40	182	525	1 924	40%
Benzo(a)pyrene	40	2 080	81	76	5	0	<40	<40	<40	<40	<40	125	308	6%
PCBs:														
PCB52	20	830	81	79	2	0	<20	<20	<20	<20	<20	<20	200	2%
PCB101	20	830	81	80	1	0	<20	<20	<20	<20	<20	<20	366	1%
PCB118	20	830	81	80	1	0	<20	<20	<20	<20	<20	<20	290	1%
PCB153	20	830	81	80	1	0	<20	<20	<20	<20	<20	<20	128	1%
PCB105	20	830	81	80	1	0	<20	<20	<20	<20	<20	<20	96	1%
PCB138	20	830	81	80	1	0	<20	<20	<20	<20	<20	<20	150	1%
Phthalates:														
DMP	40	2 080	79	48	31	0	<40	<40	<40	<40	161	555	1 058	39%
DEP	333	33 330	65	22	43	0	<333	<333	<333	1 314	1 951	5 201	17 520	66%
DiBP	333	33 333	71	0	32	39	6 785	10 954	22 405	>33330	>33330	>33330	>33330	100%
DBP	333	33 330	64	0	46	18	2 636	4 219	8 380	15 200	>33 330	>33 330	>33 330	100%
DMEP	40	2 080	81	74	7	0	<40	<40	<40	<40	<40	142	310	9%
BBP[b]	40	2 080	22				5 238	6 752	13 760	73 630	404 300	1 937 000	4 378 000	100%
DEHP[b]	333	33 333	28				48 180	86 870	380 700	1 212 000	2 345 000	4 522 000	6 395 000	100%
DiNP	333	33 333	77	0	4	73	17 056	32 959	>33330	>33330	>33330	>33330	>50000	100%
PBDEs:														
BDE100	40	2 080	81	80	1	0	<40	<40	<40	<40	<40	<40	193	1%
BDE99	40	2 080	81	79	2	0	<40	<40	<40	<40	<40	<40	406	2%

LOQ: limit of quantitation. UL: upper limit of the calibration range. N: number of classrooms. $N_{c<LOQ}$: number of samples whose concentration is less than LOQ. $N_{LOQ<c<UL}$: number of samples whose concentration is between LOQ and UL. $N_{c>UL}$: number of samples whose concentration is above UL. F: frequency of classrooms with concentrations > LOQ.
α-HCH: α-hexachlorocyclohexane, γ-HCH: γ-hexachlorocyclohexane (Lindane), 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, DMEP: di(methoxyethyl)-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

[a]Only substances quantified at least once reported.

[b]Concentrations from less concentrated extracts

Table S10. SVOC concentrations from less concentrated extracts in air (ng/m^3) in classrooms (Brittany, France)

Substance	N	min	5th%	25th%	50th%	75th%	95th%	max
Musks:								
Galaxolide	7	54	59	75	108	124	145	150
Phthalates:								
DiBP	5	593	605	653	730	2030	2220	2260

N: number of classrooms.

DiBP: diisobutyl-phthalate

Table S11. SVOC concentrations from less concentrated extracts in vacuumed dust (< 100 µm fraction) (ng/g) in classrooms (Brittany, France)

Substance	N	min	5th%	25th%	50th%	75th%	95th%	max
Phthalates:								
DiBP	30	58 600	88 800	132 000	273 000	890 000	1 880 000	2 300 000
BBP	22	8 520	11 400	53 000	105 000	216 000	468 000	1 930 000
DEHP	28	226 000	275 000	709 000	1 430 000	2 240 000	5 830 000	9 280 000
DiNP	32	166 000	258 000	616 000	1 030 000	2 150 000	4 100 000	9 570 000

N: number of classrooms.

DiBP: diisobutyl-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate.

Table S12. SVOC concentrations from less concentrated extracts in wiped dust (ng/m²) in classrooms (Brittany, France)

Substance	N	min.	perc. 5	perc. 25	median	perc. 75	perc. 95	max.
Phthalates:								
DiBP	16	41310	49060	87830	173900	339900	977600	1797000
BBP	27	5238	6752	13760	73630	404300	1937000	4378000
DEHP	24	48180	86870	380700	1212000	2345000	4522000	6395000
DiNP	21	112700	241900	614900	894200	1479000	2499000	6550000

N: number of classrooms.
DiBP: diisobutyl-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate

Table S13. SVOCs in air of nursery and primary schools in ng/m^3

Organochlorinated pesticides

Reference	Country, year	Type of school	Sampling method	mean / median	n	γ-HCH	Chlorpyrifos	Aldrin
Wilson 2003	USA (North Carolina), 1997	Daycare center	XAD-2/QFF	mean	4	5.74	13.7	2.08
Kawahara, 2005	Japan, 2003	3 Nursery school / 1 kindergaten	Chromosorb 102 / QFF	median	2		0	
Morgan 2014	USA (North Carolina), 2002	Daycare center	XAD-2/QFF	median	13	< 0.09		0.82
Cequier 2014	Norway, 2012	Primary school	PUF/QFF	median	6			
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	2.0	<1	<1

Organophosphated pesticides

Reference	Country, year	Type of school	Sampling method	mean / median	n	Dichlorvos	Diazinon
Wilson 2003	USA (North Carolina), 1997	Daycare center	XAD-2/QFF	mean	4		4.3
Kawahara, 2005	Japan, 2003	3 Nursery school / 1 kindergaten	Chromosorb 102 / QFF	median	2	13	0
Morgan 2014	USA (North Carolina), 2002	Daycare center	XAD-2/QFF	median	13		2.27
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	<1	<1

Phosphoric ester

Reference	Country, year	Type of school	Sampling method	mean / median	n	Tributylphosphate
Marklund 2005	Sweden, 2005	Daycare center	Isolute NH2 SPE columns	mean	-	3.7
Fromme 2014	Germany, 2012	Daycare center	PUF	median		2.2
Cequier 2014	Norway, 2012	Primary school	PUF/QFF	median	6	3
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	4.7

Musks

Reference	Country, year	Type of school	Sampling method	mean / median	n	Galaxolide	Tonalide
Sofuoglu 2010	Turkey, 2009	Primary school	PUF / GFF	mean	10[a]	269.8	13.8
Fromme 2004	Germany, 2000/2001	Kindergartens	PUF	median	74	101	44
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	>50	20.5

PAHs

Reference	Country, year	Type of school	Sampling method	mean / median	n	Acenaphtene	Fluorene	Phenanthrene	Anthracene	Fluoranthene	Pyrene
Wilson 2003	USA (North Carolina), 1997	Daycare center	XAD-2/QFF	mean	4	26	6.09	17.4	0.68	0.71	0.364
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	1.1	5.5	8.7	<1	<1	<1

PCBs ***PBDEs***

Reference	Country, year	Type of school	Sampling method	mean / median	n	PCB28	PCB52	PCB101	BDE100	BDE99
Wilson 2003	USA (North Carolina), 1997	Daycare center	XAD-2/QFF	mean	4	12.9	5.29	0.647	0.135	0.279
Lim 2014	Korea 2010/2011	Elementary school	PUF/GFF	mean	54				0.135	0.279
Bradman 2014	USA (California), 2010/2011	Child care or preschool	PUF	median	40				0.12	
Cequier 2014	Norway, 2012	Primary school	PUF/QFF	median	6				0.008	0.023
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	<0,4	<0,4	<0,4	<1	<1

Phthalates

Reference	Country, year	Type of school	Sampling method	mean / median	n	DMP	DEP	DiBP	DBP	BBP	DEHP	DiNP
Wilson 2003	USA (North Carolina), 1997	Daycare center	XAD-2/QFF	mean	4				488	144		
Fromme 2004	Germany, 2000/2001	Kindergartens	PUF	median	74	331	353		1188		458	
Fromme 2013	Germany 2011/2012	Daycare center	PUF/GFF	median	60	76	183	468	227		194	102
Gaspar 2014	USA (California), 2014	Child care or preschool	PUF	median	40		210	100	520	10	10	
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	12.6	221	> 800	228	19.1	108	35.2

PBDEs

Reference	Country, year	Type of school	Sampling method	mean / median	n	BDE100	BDE99
Wilson 2003	USA (North Carolina), 1997	Daycare center	XAD-2/QFF	mean	4	0.135	0.279
Lim 2014	Korea 2010/2011	Elementary school	PUF/GFF	mean	54	0.135	0.279
Bradman 2014	USA (California), 2010/2011	Child care or preschool	PUF	median	40	0.12	
Cequier 2014	Norway, 2012	Primary school	PUF/QFF	median	6	0.008	0.023
This study	France, 2009/2010	Primary school	PUF/QFF	median	62	<1	<1

[a] 10 replicates in 1 school

GFF: Glass Fiber Filter, QFF: quartz fiber filter, SPE: solid phase extraction.

γ-HCH: gamme-hexachlorocyclohexane (Lindane), PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

Table S14. SVOCs in dust of nursery and primary schools in ng/g

Organochlorinated pesticides

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	γ-HCH	Alpha-endosulfan	Dieldrin	Endrin	4,4'-DDT
Wilson 2003	USA (North Carolina), 1997	Daycare	HVS3; 150µm	mean	4	19		9	70	11
Dalvie 2014	South Africa, 2010	1 Primary / 1 preschool	vacuuming in bag by technician; NA	single value	1/1		20/20			
Morgan 2014	USA (North Carolina), 2000/2001	Daycare	HVS3; 150µm	median	13	< 2				< 2
This study	France, 2009/2010	Primary school	vacuuming in cellulose thimble; 100µm	median	89	<65.8	<65.8	<65.8	<65.8	<65.8

Organophosphated pesticides

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	Diazinon	Chlorpyrifos
Wilson 2003	USA (North Carolina), 1997	Daycare	HVS3; 150µm	mean	4	34	107
Dalvie 2014	South Africa, 2010	1 Primary / 1 preschool	vacuuming in bag by technician; NA	single value	1/1		60/30
Morgan 2014	USA (North Carolina), 2000/2001	Daycare	HVS3; 150µm	median	13	65.2	142
This study	France, 2009/2010	Primary school	vacuuming in cellulose thimble; 100µm	median	89	<65.8	<65.8

Pyrethroids

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	Permethrin	Cypermethrin
Dalvie 2014	South Africa, 2010	1 Primary / 1 preschool	vacuuming in bag by technician; NA	single value	1/1		170/170
Morgan 2007	USA (Ohio), 2001	Daycare center	HVS3	median	23	1554 (cis+trans)	
Morgan 2014	USA (North Carolina), 2000/2001	Daycare	HVS3; 150µm	median	13	1662 (cis+trans)	
This study	France, 2009/2010	Primary school	vacuuming in cellulose thimble; 100µm	median	89	279	<65.8

Phosphoric ester

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	Tributylphosphate
Fromme 2014	Germany, 2012	Daycare center	vacuuming with a dust filder holder	median	10	< 300
Mizouchi 2015	Japan, 2009/2010	Elementary schools	vacuuming with paper bag ; 250 µm	median	12	<10
Cequier 2014	Norway 2014	Primary school	vacuuming using forensic filter ; large particles and hair removed	median	6	43.5
Brommer 2015	UK, 2011/2012	Primary schools / daycare centers	vacuuming in a 25 µm nylon sock	median	28	120
This study	France, 2009/2010	Primary school	vacuuming in cellulose thimble; 100µm	median	89	103

PAHs

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	Fluorene	Phenanthrene	Anthracene	Fluoranthene	Pyrene	Benzo(a)pyrene
Wilson 2003	USA (North Carolina), 1997	Daycare	HVS3 vacuuming; 150µm	mean	4	25	338	45	437	354	191
Langer 2010	Denmark, 2009	Daycare center	Vacuuming on a glass fiber filter; -	median	151					98	11
This study	France, 2009/2010	Primary school	vacuuming in cellulose thimble; 100µm	median	89	<65.8	363	<65.8	184	285	<65.8

PCBs

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	PCB31	PCB28	PCB52	PCB101	PCB77	PCB118	PCB153	PCB105	PCB138	PCB180
Wilson 2003	USA (North Carolina), 1997	daycare	HVS3 vacuuming; 150µm	mean	4		37	32	19	4	20	17	11	19	11
Harrad 2010	UK, 2007/2008	primary school	vacuuming in a 25µm mesh size sock; -	median	36	3.6	3.6	2.8	1.6		1.1	1.7		1.6	0.7
This study	France, 2009/2010	primary school	vacuuming in cellulose thimble; 100µm	median	89	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3	<26.3

Phthalates

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	DMP	DEP	DiBP	DBP	BBP	DEHP	DiNP
Wilson 2003	USA (North Carolina), 1997	Daycare	HVS3 vacuuming; 150µm	mean	4				1 870	3 720		
Langer 2010	Denmark, 2009	Daycare center	Vacuuming on a glass fiber filter; -	median	151		2 200	23 000	38 000	17 000	500 000	
Kim 2013	Seoul, 2012	Nursery school	vacuuming of surface dust in thimble; 100µm	median	50	2 100			52 000	50 400	3 030 000	946 000
Fromme 2013	Germany 2011/2012	Daycare center	Vacuuming on a glass fiber filter; -	median	60-63	300	1 400	20 000	21 000	6 000		302 000
Wallner 2012	Austria, 2012	Primary school	vacuuming by school personnel; 63µm	median	36					34 000		
Clausen 2003	Denmark, 2003	School	HVS3 vacuuming; 500µm	mean	15						3 214 000	
Gaspar 2014	USA (California), 2010/2011	Child care or preschool	HVS3 vacuuming on carpet; 150µm	median	39		1 400	9 300	13 700	46 800	172 200	
Hutter 2013	Austria, 2012	Elementary schools	vacuuming by school personnel; 63µm	median	9						3 350 000	
This study	France, 2009/2010	Primary school	vacuuming in cellulose thimble; 100µm	median	89	252	2 890	> 52 600	38 200	105 000	1 430 000	1 030 000

PBDEs

Reference	Country, year	Type of school	Sampling method; sieving fraction	mean / median	n	BDE100	BDE99
Wilson 2003	USA (North Carolina), 1997	daycare	HVS3 vacuuming; 150µm	mean	4		
Harrad 2010	UK, 2007/2008	primary school	vacuuming in a 25µm mesh size sock; -	median	36	6.6	36
Wu 2010	South Korea, 2010	Elementary school	vaccuming in washable dust collector; 212µm	medians	13/6	1,16/3,54	6,44/50,9
Lim 2014	Korea 2010/2011	Elementary school	vacuuming in bag by technician; 500µm	mean	54	67.7	215.8
Bradman 2014	USA (California), 2010/2011	Child care or preschool	HVS3 vacuuming on carpet; 150µm	median	39	211.5	1031.1
Toms 2015	Australia, 2011/2012	primary school	vacuuming in a 25µm mesh size sock; 500 µm	mean	28	10.0	101.7
Cequier 2014	Norway 2014	Primary school	vacuuming using forensic filter ; large particles and hair removed	median	6	7.95	42.4
This study	France, 2009/2010	primary school	vacuuming in cellulose thimble; 100µm	median	89	<65.8	<65.8

HVS3: High Volume Small Surface Sampler
γ-HCH: gamme-hexachlorocyclohexane (Lindane), 4,4'-DDT: dichlorodiphenyltrichloroethane, PAHs: polycyclic aromatic hydrocarbons, PCBs: polychlorobiphenyls, DMP: dimethyl-phthalate, DEP: diethyl phthalate, DiBP: diisobutyl-phthalate, DBP: dibutyl-phthalate, BBP: butyl benzyl phthalate, DEHP: bis(2-ethylhexyl)-phthalate, DiNP: diisononyl-phthalate, PBDEs: polybromodiphenylethers.

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3. LES VOIES D'EXPOSITION AUX COSV

Comme mentionné dans le paragraphe 1.2, les COSV sont présents en environnement intérieur en équilibre entre l'air, les particules en suspension, les poussières sédimentées et les surfaces, avec des ratios dépendant des conditions ambiantes et de la nature des COSV. Les trois voies d'exposition humaine sont l'inhalation, l'ingestion et le contact cutané. En environnement intérieur, les populations sont donc exposées aux COSV par inhalation des phases gazeuse et particulaire de l'air, par ingestion des COSV adsorbés sur les particules sédimentées ou en suspension dans l'air, et par contact cutané avec l'air (gaz et particules), les poussières sédimentées et les surfaces (Figure 9).

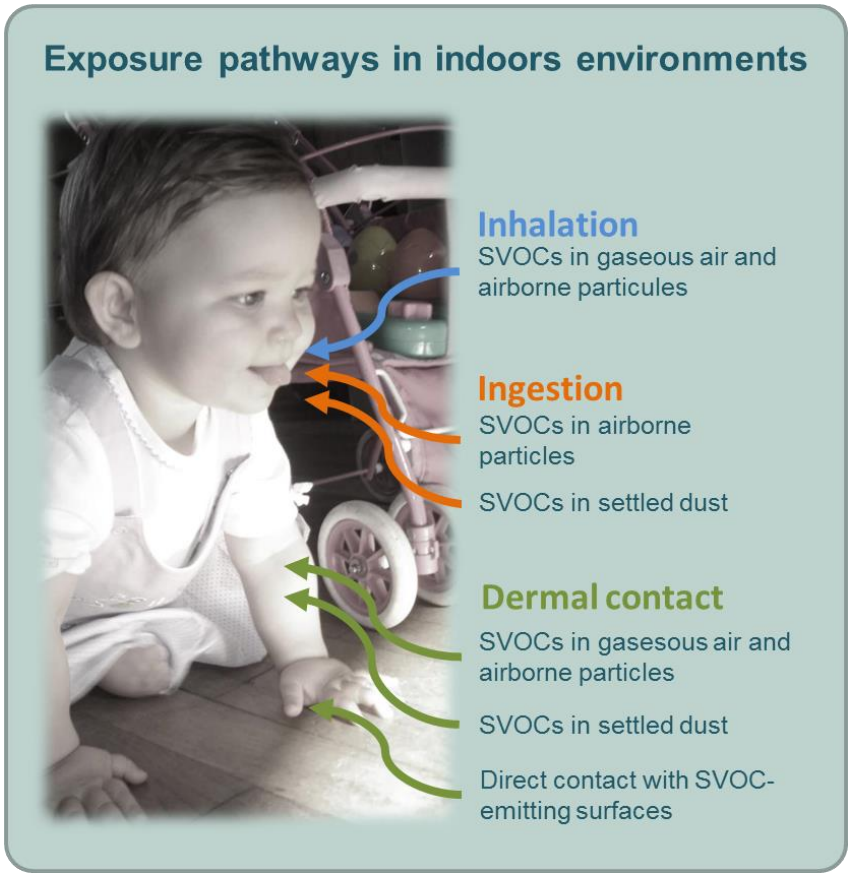

FIGURE 9 : LES VOIES D'EXPOSITION AUX COSV EN ENVIRONNEMENT INTERIEUR

3.1. L'INGESTION

Les enfants absorbent chaque jour de manière involontaire jusqu'à 100 mg de poussières et les adultes 30 mg [65]. L'ingestion de poussière est probablement la voie d'exposition aux COSV la plus étudiée dans la littérature ; elle représente la voie majoritaire d'exposition pour plusieurs

phtalates [66], notamment le DEHP [67,68] et certains retardateurs de flamme halogénés [69,70] dont les PBDE [71–73].

3.2. L'INHALATION

L'homme respire jusqu'à 16 m^3 d'air par jour [74] et se retrouve ainsi exposé aux COSV présents dans l'air. L'inhalation comme voie d'exposition aux COSV a été étudiée dans la littérature [75,76]. Elle est considérée comme voie d'exposition majoritaire pour les COSV les plus volatils, en particulier en l'absence d'évaluation de l'exposition par contact cutané. [77,78]

3.3. LE CONTACT CUTANE

L'exposition aux COSV par contact cutané a longtemps été ignorée ou considérée négligeable. En 2012, Weschler et Nazaroff ont commencé à s'y intéresser et se sont rendu compte que cette voie pourrait être responsable d'une exposition égale ou supérieure à l'inhalation pour certains COSV [79]. Elle est désormais de plus en plus étudiée et parfois considérée comme voie majoritaire, notamment pour les phtalates les plus légers [67,68,80–82] et les HAP [81]. De plus le port de vêtements pourrait accélérer ou retarder l'exposition cutanée selon le nombre de jours écoulés depuis le dernier lavage [83,84]. Pour les retardateurs de flamme bromés, Abdallah et Harrad ont montré que l'exposition due au contact direct avec du tissu d'ameublement traité est supérieure au contact direct avec de la poussière contaminée [85].

3.4. CONTRIBUTION RELATIVE DE CHAQUE VOIE

La contribution de chaque voie d'exposition a été calculée pour le projet ECOS-Habitat durant les travaux de thèse de Maud Pelletier. La Figure 10 montre les résultats médians pour les enfants âgés de 2 à 3 ans. La contribution relative de chaque voie diffère selon le composé en fonction de leur volatilité. Pour les COVS les plus volatils[5] (fluorène, anthracène, aldrine, dieldrine, tonalide, galaxolide, tributylphosphate, DEP, DBP, DiBP, PCB 28, PCB 31 et PCB 52), l'inhalation et le contact cutané avec la phase gazeuse sont les principales voies d'exposition, tandis que pour les

[5] Log Koa (coefficient de partage octanol air) < 9[34]

COVS moins volatils[6] (DEHP, DiNP et BDE 154), l'ingestion de poussière est la principale voie d'exposition.

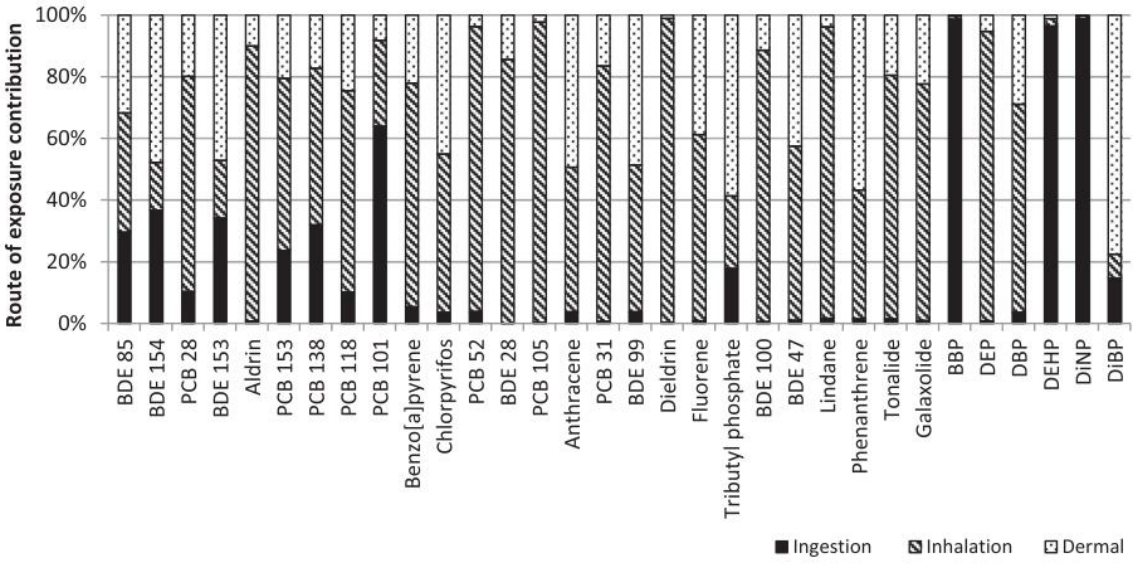

Figure reprise de la publication de Pelletier et al. (2017), Environ. Int. [35]

FIGURE 10 : CONTRIBUTION RELATIVE DE CHAQUE VOIE D'EXPOSITION

4. NOTIONS DE BIOACCESSIBILITE ET BIODISPONIBILITE

Afin d'évaluer les risques associés à la présence de COSV dans les environnements intérieurs ou d'établir un lien entre COSV et problématique de santé dans les études épidémiologiques, l'exposition humaine aux COSV dans les environnements intérieurs doit être évaluée précisément. À cette fin, les trois voies d'exposition : (1) exposition par ingestion de poussière ou de particules, (2) exposition par inhalation d'air et (3) exposition par contact cutané doivent être agrégées.[35,77]

Les concentrations utilisées pour ce faire sont en général les concentrations totales présentes dans les milieux. Or, la totalité de la concentration n'est pas absorbée par l'organisme et il convient ici d'introduire les notions de biodisponibilité et de bioaccessibilité.

[6] Log Koa (coefficient de partage octanol air) > 9[34]

4.1. DEFINITION DE LA BIOACCESSIBILITE

La fraction bioaccessible d'un composé est la quantité qui est libérée dans un fluide biologique et devient disponible pour l'absorption.[86] On parle de bioaccessibilité orale pour définir la quantité libérée par la salive et les fluides gastro-intestinaux après ingestion de poussières ou de particules [87–89]. On parle de bioaccessibilité par inhalation concernant la fraction libérée par les fluides pulmonaires après inhalation de particules [90]. Enfin, on parle de bioaccessibilité cutanée concernant la fraction libérée par la sueur et le sébum après un contact cutané avec des poussières ou des particules [91]. Ainsi, la bioaccessibilité est toujours relative à une matrice (poussières, particules, sols, aliments, médicaments, etc.).

La bioaccessibilité absolue est le ratio entre la quantité libérée dans le fluide et la quantité totale initialement présente dans la matrice.

$$bioaccessibilité\ absolue\ (\%) = \frac{teneur\ en\ COSV\ bioaccessible}{teneur\ totale\ en\ COSV}\ x100$$

Pour les substances dont on connait la valeur toxicologique de référence (VTR), la bioaccessibilité peut également être exprimée par rapport à la bioaccessibilité dans la matrice avec laquelle la VTR a été calculée (par exemple dans l'huile). On parle alors de bioaccessibilité relative.

4.2. DEFINITION DE LA BIODISPONIBILITE

La fraction biodisponible est définie comme la quantité qui a traversé une membrane biologique et atteint la circulation systémique [86,89]. Cette membrane est la paroi intestinale pour la biodisponibilité orale [87–89], la barrière pulmonaire pour la biodisponibilité pulmonaire [90,92] et la peau pour la biodisponibilité cutanée [93].

La biodisponibilité absolue est le ratio entre la quantité absorbée dans la circulation systémique et la quantité initialement présente dans la matrice.

$$biodisponibilité\ absolue\ (\%) = \frac{teneur\ en\ COSV\ biodisponible}{teneur\ totale\ en\ COSV}\ x100$$

De même que pour la bioaccessibilité, on peut exprimer la biodisponibilité de manière relative par rapport à la matrice à partir de laquelle on a calculé la VTR d'une substance donnée.

Les notions de bioaccessibilité et biodisponibilité pour la voie orale sont illustrées sur la Figure 11.

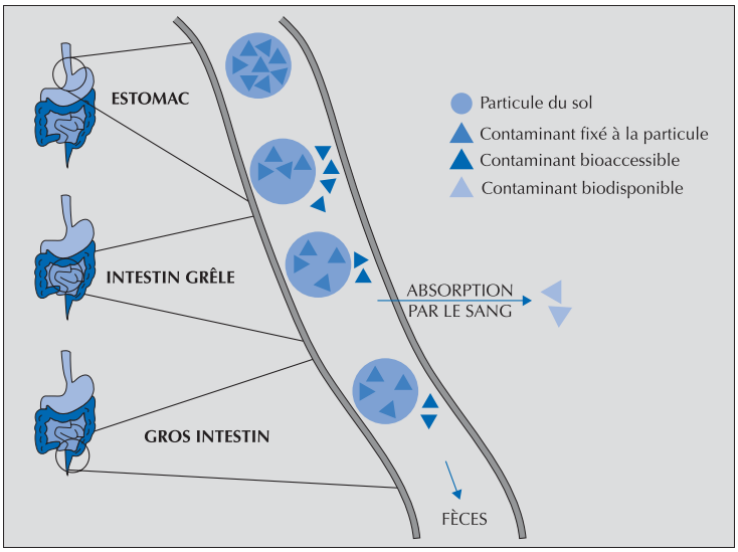

Figure reprise de la publication de Denys et al. (2009), Environnement, Risques & Santé [88]

FIGURE 11 : REPRESENTATION SCHEMATIQUE DES NOTIONS DE BIOACCESSIBILITE ET BIODISPONIBILITE ORALE

La biodisponibilité est la notion la plus pertinente à connaître pour affiner la dose d'exposition et établir le lien entre contamination environnementale et exposition humaine. Cependant, la biodisponibilité est difficile à évaluer, principalement pour des raisons éthiques, puisqu'elle suppose une ingestion de poussière contaminée, et des mesures dans des matrices biologiques qui peuvent être invasives.

La bioaccessibilité, qui peut se mesurer en laboratoire par des tests *in vitro*, offre donc une alternative intéressante à la biodisponibilité. La bioaccessibilité n'intègre pas les pertes dues au passage à travers les parois et à des réactions métaboliques. Elle sera donc toujours égale ou supérieure à la biodisponibilité (Figure 12), ce qui peut être un atout du fait de son caractère conservatoire [87], dans d'autres domaines que celui de cette thèse, comme par exemple dans la gestion des sols pollués.

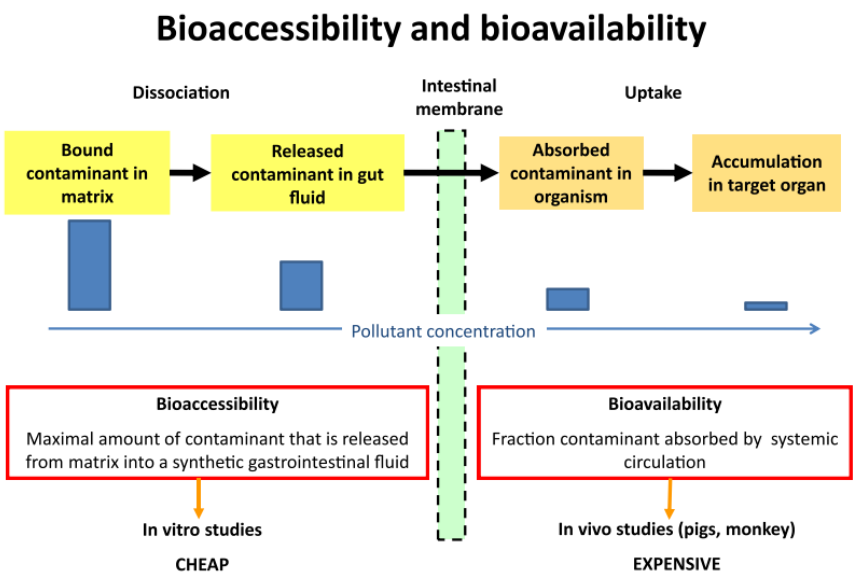

Figure reprise de la publication de Collins et al. (2015), Environ. Int. [87]

FIGURE 12 : RELATION ENTRE BIOACCESSIBILITE ET BIODISPONIBILITE

5. QUESTIONS DE RECHERCHE

Dans ce contexte et dans la perspective d'une meilleure connaissance de la contribution environnementale dans l'exposition humaine aux COSV, les questions posées à la recherche sont :

- Comment mesurer les concentrations environnementales en COSV pour mieux évaluer l'exposition humaine à ces substances ?
- Quelle est la bioaccessibilité des COSV présents dans les particules et les poussières ?

6. OBJECTIFS DE LA THESE

L'objectif de cette thèse est de répondre au volet « ingestion » de la question de recherche. Ces travaux de thèse se sont donc concentrés sur l'exposition par ingestion de poussière et sur la bioaccessibilité orale des COSV. Ils se sont organisés en trois points :

- Revue de la littérature scientifique du domaine
- Développement et validation d'une méthode simple de mesure de la bioaccessibilité des COSV dans les poussières
- Production de données de bioaccessibilité pour plusieurs familles de COSV

CHAPITRE 2 : LA BIOACCESSIBILITE DES COSV DANS LES POUSSIERES- REVUE DE LA LITTERATURE (ARTICLE SCIENTIFIQUE N°2)

La première partie de ce travail de thèse a consisté en une revue bibliographique axée sur la bioaccessibilité orale des COSV dans les poussières. Nombreuses quand la matrice considérée est le sol, ou quand les substances d'intérêt sont les métaux, les recherches sont plus rares et encore jeunes en ce qui concerne les polluants organiques dans les poussières. Toutefois une vingtaine d'articles ont été réunis, qui montrent une forte disparité des bioaccessibilités mesurées. Dues à la nature des COSV ou des poussières étudiées, ces disparités peuvent également avoir pour origine des méthodes de mesures très différentes. Cette revue bibliographique souligne ainsi la nécessité d'une méthode harmonisée, en écho aux propositions de Collins et son équipe [87], mais également d'une méthode de mesure simplifiée.

Les résultats de cette revue de la littérature ont fait l'objet d'un article publié en mars 2018 dans *Journal of Hazardous Materials*, qui est présenté dans la suite du chapitre.

Un tableau récapitulatif des réactifs et conditions opératoires des méthodes reportées dans la littérature pour la mesure de la bioaccessibilité des COSV est également disponible en fin de chapitre (page 87).

Par ailleurs, les valeurs de bioaccessibilité documentées dans cette revue ont été utilisées dans le cadre de la thèse de Maud Pelletier pour estimer l'exposition de la population aux COSV dans les logements français [35] (article disponible dans la partie « Valorisation scientifique de ce manuscrit »).

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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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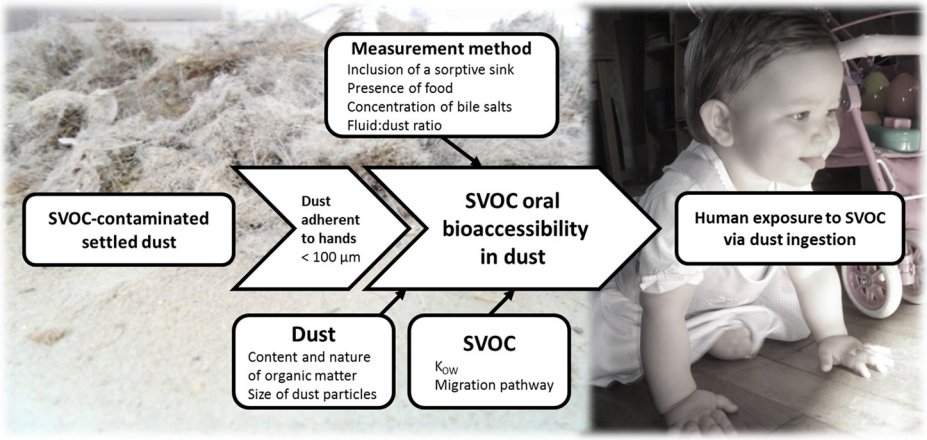
GRAPHICAL ABSTRACT



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Pollutant

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-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 & 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.

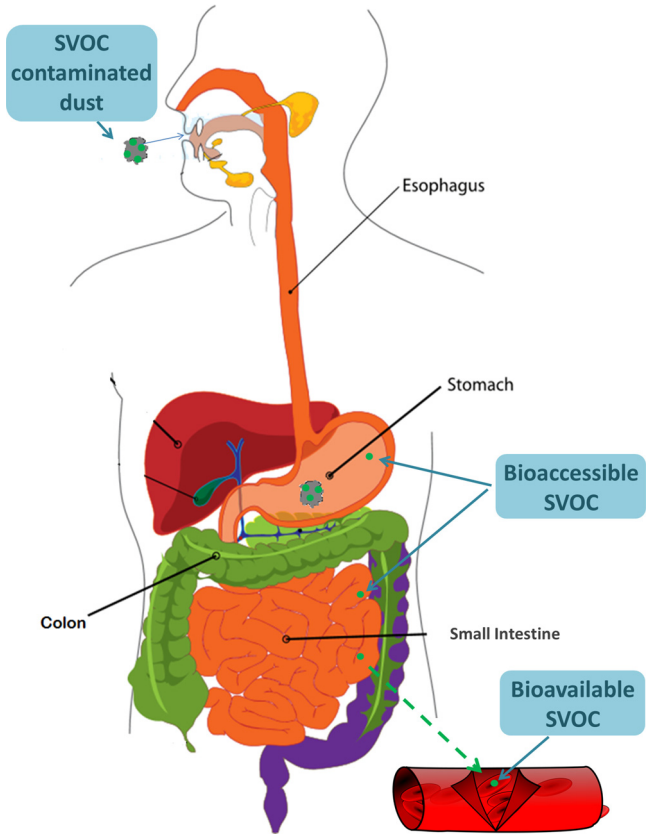

Fig. 1. Human digestive system showing SVOC oral bioaccessibility and bioavailability.

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.

3.1.1. 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 min at 37 °C. This first process is sometimes considered of limited interest because the extraction time, which should not exceed 2 min 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].

3.1.2. 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 19738 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 h at 37 °C.

3.1.3. Small intestine in vitro process

The 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 h 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 Fig. 2, where the distribution of bioaccessible SVOC is on average 35% in the gastric fluid and 65% in the small intestine fluid.

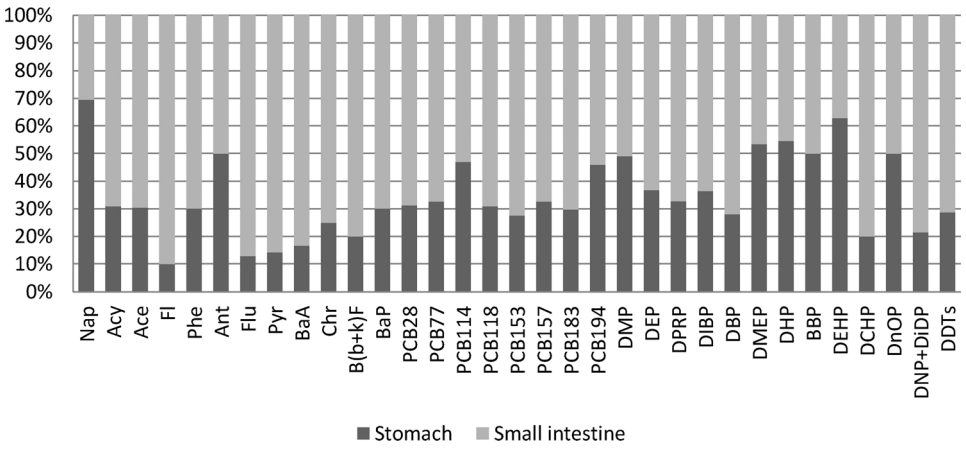

Fig. 2. Partition of in vitro evaluation of SVOC absorption between stomach and small intestine.
PAH, phthalate, and DDT data are from the work of Wang et al. [44,76,95]. PCB data are from the work of Kang et al. [75].
Nap: naphthalene, Acy: acenaphthylene, Ace acenaphthene, Fl: fluorene, Phe phenanthrenes, 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.

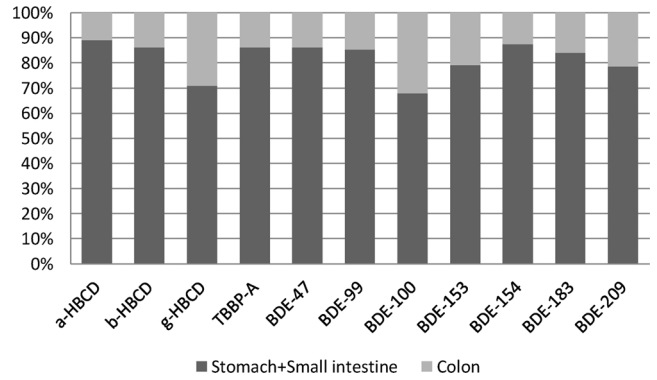

Fig. 3. Partition of in vitro evaluation of SVOC absorption between stomach + small intestine and colon. Data are from the work of Abdallah et al. [46].
HBCD: hexabromocyclododecane, TBBP: tetrabromobisphenol, BDE: bromodiphenylether.

3.1.4. 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 h. For flame retardants, the additional bioaccessibility provided by the colon incubation ranged from 11 to 32% of the total bioaccessibility [46], as shown in Fig. 3.

3.1.5. 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.

3.1.6. 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 min [39,40]. All authors also apply shaking to their system to simulate the peristaltic movements of human digestion.

3.1.7. 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.

3.1.8. 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 (Fig. 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.

3.1.9. 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%–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 Fig. 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 Fig. 4.

3.2.1. 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 Fig. 4.

3.2.2. 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 Fig. 4, ranged from 8% to 103%, depending on the compound and the measurement method.

3.2.3. 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 Fig. 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.

3.2.4. 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 Fig. 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.

3.2.5. 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 Fig. 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.

3.2.6. 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 (Table 6). 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 to 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

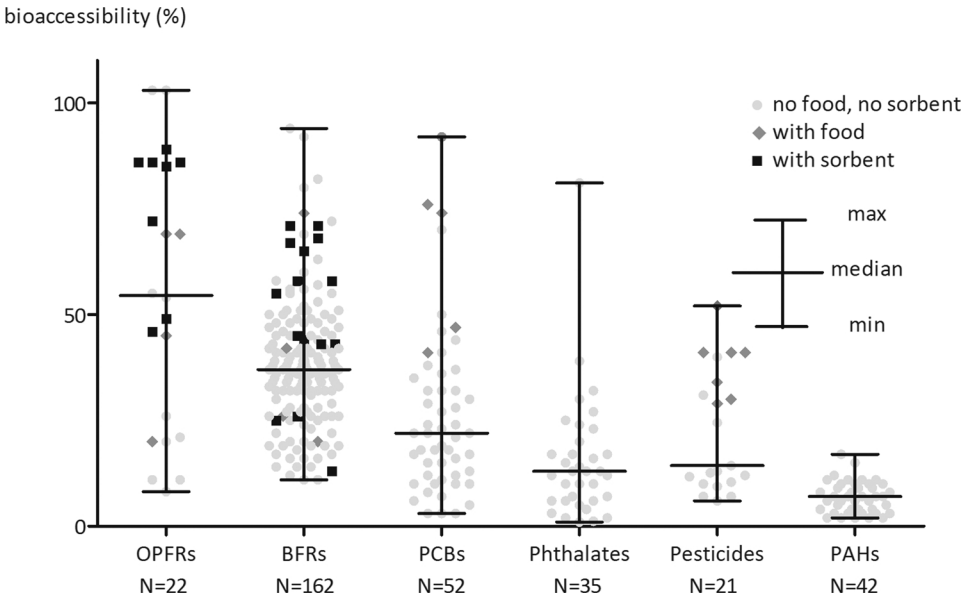

Fig. 4. Published (20011-2017) SVOC bioaccessibility data in indoor settled dust according to measurement design. Each dot represents the median value for one compound in one study. OPFRs: organophosphorus flame retardants, BFRs: brominated flame retardants PCBs: polychlorobiphenyls, PAHs: polycyclic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

(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 5 g/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

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

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	1	1	6	6	17	2	3	3	44	44	44	44	1	1	1	1
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]	[73]	[73]	[51]	[52]	[45]	[50]	[46]	[46]	[72]	[72]	[72]	[72]	[47]	[47]	[47]	[47]

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

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

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]	[41]	[41]	[41]	[42]	[42]	[45]

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.

Table 3
Bioaccessibility (%) of polychlorobiphenyls (PCBs) in indoor settled dust.

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]	[39]

PBET: physiologically-based extraction test.

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

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

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]	[76]	[43]

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).

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

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]	[39]

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.

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

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]	[77]	[77]	[77]	[77]	[77]	[77]

[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.

Table 7
Summary of the main factors influencing SVOC bioaccessibility in 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])
Increase of bile concentration	↗ (OPFRs and phthalates [42], PCBs [75], PBDEs [47])
Increase of fluid :dust ratio	↗ (PBDEs [47])
Factor related to the matrix:	
Increase of 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])
Increase of dust particle size	↘ (PAHs [95], PBDEs [50], OCs [44], and phthalates [76])
Factor related to SVOC characteristics:	
Increase of 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])
Increase of SVOC concentration	→ (PBDEs [47,72])

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

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 towards 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 × OM% + 1.79 × 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.

5. Declaration of interest

None.

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		1	2	3
		BARGE	DIN 19738 (Saliva + PBET)	DIN 19738 (Saliva + PBET + milk powder)
	Réactifs pour 1L		**mg**	
	NaCl	298 mg	1670	x
	NaSCN ou KSCN	200 mg (K)	500 (Na)	x (Na)
	Na_2SO_4	570 mg	1830	x
	$NaHCO_3$		500	x
	NaOH	1.80 ml of 1.0 M		
	KCl	896 mg	1500	x
	KH_2PO_4 ou NaH_2PO_4	888 mg (Na)	2000 (K)	x (K)
	$CaCl_2 \cdot 2\ H_2O$		500	x
Bouche	Mucin	50 mg	62.5	x
	α-amylase	145 mg	20.8	x
	Urea	200 mg (K)	8.33	x
	Uric acid	15 mg	0.83	x
	Conditions opératoires			
	Ratio Volume de solution / Masse de poussière (mL/g)	15	15	15
	pH	6.5 ± 0.5		6.4
	température	37°C	37°C	37°C
	agitation	shake	200 rpm	
	durée	5 - 15 min	30 min	30 min
	Réactifs pour 1L		**mg**	
	NaCl	2752 mg	2900	x
	KCl	824 mg	700	x
	KH_2PO_4ou NaH_2PO_4	266 mg (Na)	270 (K)	x (K)
	HCl (for adjusting pH)	8.3 ml of 37% HCl		x
	CaCl2	400 mg		
	NH_4Cl	306 mg		
	$KHCO_3$			
	Pepsin	**1000 mg**	**17.5**	**x**
	Mucin	1000 mg	52.5	x
	Whole milk powder			x
	Sodium malate			
	Tri-sodium citrate			
	Lactic acid			
	Glacial acetic acid			
	Glucose	650 mg		
	Glucuronic acid	20.0 mg		
	Urea	85.0 mg		
	Glucosaminehydrochloride	330 mg		
	Bovine Serum Albumine	1000 mg		
	Cystein			
Estomac	Glycine			
	Dietary components :			
	Nutrilon (56% lactose, 12% fat, 10% casein)			
	Starch (potato)			
	Peptone water			
	Tryptone (vegetable)			
	Yeast extract			
	Casein			
	Pectin (citrus)			
	Xylan (oat)			
	Arabinogalactan (larch)			
	Guar gum			
	Inulin (chicory)			
	Conditions opératoires			
	Ratio Volume de solution / Masse de poussière (mL/g)	32.5	50	50
	pH	0.9 - 1.0	2	2
	durée	1 hr	2hrs	2hrs
	température	37°C	37°C	37°C
	agitation	end-over-end rotation	200 rpm	

Adsorbent		1 BARGE	2 DIN 19738 (Saliva + PBET)	3 DIN 19738 (Saliva + PBET + milk powder)
Intestin	**Réactifs pour 1L**			
	KCl	564 mg (duodenal) / 376 mg (bile)	300	x
	NaCl	7012 mg (duodenal) / 5259 mg (bile)		
	$CaCl_2 \cdot 2\ H_2O$	200 mg (duodenal) / 222 mg (bile)	500	x
	$MgCl_2 \cdot 6\ H_2O$	50.0 mg (duodenal)	200	x
	$NaHCO_3$	5607 mg (duodenal) / 5785 mg (bile)	1000	x
	$Na_2HPO_4 \cdot 12H_2O$			
	$NaH_2PO_4 \cdot 2H_2O$			
	KH_2PO_4	80 mg (duodenal)		
	HCl (for adjusting pH)	180 µL of 37% HCl x2 (duodenal + bile)		
	Trypsin		7.5	x
	Pancreatin	**3000 mg (duodenal)**	**225**	**x**
	Bile	**6000 mg**	**225**	**x**
	Urea	100 mg (duodenal) / 250 mg (bile)	7.5	x
	Lipase	**500 mg (duodenal)**		
	Bovine Serum Albumine	1000 mg (duodenal) / 1800 mg (bile)		
	Dietary components :			
	Nutrilon (56% lactose, 12% fat, 10% casein)			
	Starch (potato)			
	Peptone water			
	Tryptone (vegetable)			
	Yeast extract			
	Casein			
	Pectin (citrus)			
	Xylan (oat)			
	Arabinogalactan (larch)			
	Guar gum			
	Inulin (chicory)			
	Conditions opératoires			
	Ratio Volume de solution / Masse de poussière (mL/g)	92.5	100	100
	pH	7.4 ± 0.2 (duodenal) / 8.0 ± 0.2 (bile)	7.5	7.5
	durée	4 hrs	6 hrs	7 hrs
	température	37°C	37°C	37°C
	agitation	end-over-end rotation	200 rpm	
	% Bioaccessibility			
	Réactifs pour 1L			
	Type II mucin			
	NaCl			
	KCl			
	$NaHCO_3$ (sodium bicarbonate)			
	$MgSO_4.7H_2O$ (magnesium Sulfate)			
	Cysteine hydrochloride			
	KH_2PO_4 (potassium phosphate)			
	K_2HPO_4 (dipotassium phosphate)			
	Bile			
	$CaCl_2 \cdot 2\ H_2O$			
	Haemin			
	$FeSO_4.7H_2O$			
	Dietary components :			
	Starch (potato)			
	Peptone water			
	Tryptone (vegetable)			
	Yeast extract			

		1	2	3
		BARGE	DIN 19738 (Saliva + PBET)	DIN 19738 (Saliva + PBET + milk powder)
Colon	Casein Pectin (citrus) Xylan (oat) Arabinogalactan (larch) Guar gum Inulin (chicory) ***Microbiota (fecal material from a healthy human adult that included Fecal Coliforms, Bifidobacteria, Enterococci, Staphylococci and Clostridia)*** **Anaerobe** **Aerobe**			
	Conditions opératoires Ratio Volume de solution / Masse de poussière (mL/g) pH durée température agitation % Bioaccessibility			
Comparaison avec in-vivo				method validated in-vivo for organic and inorganic contaminants
Référence / Journal / Pays			Starr 2016 / Journal of Hazardous Materials / USA	Ertl 2012 / Journal of Exposure Science and Environmental Epidemiology / Germany

		4	5	6	7
		PBET	PBET	PBET	PBET
	Réactifs pour 1L				
	NaCl				
	NaSCN ou KSCN				
	Na_2SO_4				
	$NaHCO_3$				
	NaOH				
	KCl				
	KH_2PO_4 ou NaH_2PO_4				
	$CaCl_2 \cdot 2\ H_2O$				
Bouche	Mucin				
	α-amylase				
	Urea				
	Uric acid				
	Conditions opératoires				
	Ratio Volume de solution / Masse de poussière (mL/g)				
	pH				
	température				
	agitation				
	durée				
	Réactifs pour 1L				
	NaCl		8.75 g		
	KCl				
	KH_2PO_4ou NaH_2PO_4				
	HCl (for adjusting pH)			x	x
	CaCl2				
	NH_4Cl				
	$KHCO_3$				
	Pepsin	**1.25 g**	**125 mg**	**10 mg**	**10 mg**
	Mucin			3.56 g	3.56 g
	Whole milk powder				
	Sodium malate	500 mg	500 mg		
	Tri-sodium citrate	500 mg	500 mg		
	Lactic acid	420 µL	425 µL		
	Glacial acetic acid	500 µL	500 µL		
	Glucose				
	Glucuronic acid				
	Urea				
	Glucosaminehydrochloride				
	Bovine Serum Albumine				
	Cystein				
Estomac	Glycine				
	Dietary components :				
	Nutrilon (56% lactose, 12% fat, 10% cas				
	Starch (potato)				
	Peptone water				
	Tryptone (vegetable)				
	Yeast extract				
	Casein				
	Pectin (citrus)				
	Xylan (oat)				
	Arabinogalactan (larch)				
	Guar gum				
	Inulin (chicory)				
	Conditions opératoires				
	Ratio Volume de solution / Masse de poussière (mL/g)	100	20	133	40
	pH	2.5	1.5	1.6-1.9	1.6-1.9
	durée	1 hr	1 hr	2 hrs	2 hrs
	température	37°C	37°C	37°C	37°C
	agitation	150 rpm	shaken	shaken	shaken

		4	5	6	7
Adsorbent		PBET	PBET	PBET	PBET
Intestin	**Réactifs pour 1L**				
	KCl				
	NaCl				
	$CaCl_2 \cdot 2\,H_2O$				
	$MgCl_2 \cdot 6\,H_2O$				
	$NaHCO_3$			12.5 g	12.5 g
	$Na_2HPO_4{\cdot}12H_2O$			42.4 g	42.4 g
	$NaH_2PO_4{\cdot}2H_2O$			7.4 g	7.4 g
	KH_2PO_4				
	HCl (for adjusting pH)				
	Trypsin				
	Pancreatin	**0.5 g**	**1.33 g**	**0.9 g**	**0.9 g**
	Bile	**1.78 g**	**6.67 g**	**5.5 g**	**5.5 g**
	Urea				
	Lipase				
	Bovine Serum Albumine				
	Dietary components :				
	Nutrilon (56% lactose, 12% fat, 10% cas				
	Starch (potato)				
	Peptone water				
	Tryptone (vegetable)				
	Yeast extract				
	Casein				
	Pectin (citrus)				
	Xylan (oat)				
	Arabinogalactan (larch)				
	Guar gum				
	Inulin (chicory)				
	Conditions opératoires				
	Ratio Volume de solution / Masse de poussière (mL/g)	100	143	67	60
	pH	7	7	7	7
	durée	4 hrs	4 hrs	6 hrs	6 hrs
	température	37°C	37°C		
	agitation		shaken		
	% Bioaccessibility				
	Réactifs pour 1L				
	Type II mucin				
	NaCl				
	KCl				
	$NaHCO_3$ (sodium bicarbonate)				
	$MgSO_4.7H_2O$ (magnesium Sulfate)				
	Cysteine hydrochloride				
	KH_2PO_4 (potassium phosphate)				
	K_2HPO_4 (dipotassium phosphate)				
	Bile				
	$CaCl_2 \cdot 2\,H_2O$				
	Haemin				
	$FeSO_4.7H_2O$				
	Dietary components :				
	Starch (potato)				
	Peptone water				
	Tryptone (vegetable)				
	Yeast extract				

		4	5	6	7
		PBET	PBET	PBET	PBET
Colon	Casein Pectin (citrus) Xylan (oat) Arabinogalactan (larch) Guar gum Inulin (chicory) ***Microbiota (fecal material from a healthy human adult that included Fecal Coliforms, Bifidobacteria, Enterococci, Staphylococci and Clostridia)*** **Anaerobe** **Aerobe**				
	Conditions opératoires Ratio Volume de solution / Masse de poussière (mL/g) pH durée température agitation % Bioaccessibility				
Comparaison avec in-vivo					
Référence / Journal / Pays		He 2015 / Chemosphère / China	Wang 2013 (PAH) / Journal of Hazardous Materials / China ; Wang 2013 (Phthalates) / Journal of Hazardous Materials / China ; Wang 2013 (PCBs) / Science of the Total Environment / China ; Wang 2013 (Ocs) / Atmospheric Environment / China ; Kang 2012 /Environmental Science & Technology / China ; Kang 2011 / Environmental International / China ; Kang 2013 / Chemosphère / China.	Yu 2012 / Environment International / China	Yu 2011 / Journal of Environmental Sciences / China

		8	9	10	11
		PBET + Tenax	CE-PBET	CE-PBET	CE-PBET
	Réactifs pour 1L				
	NaCl				
	NaSCN ou KSCN				
	Na_2SO_4				
	$NaHCO_3$				
	NaOH				
	KCl				
	KH_2PO_4 ou NaH_2PO_4				
	$CaCl_2 \cdot 2\ H_2O$				
Bouche	Mucin				
	α-amylase				
	Urea				
	Uric acid				
	Conditions opératoires				
	Ratio Volume de solution / Masse de poussière (mL/g)				
	pH				
	température				
	agitation				
	durée				
	Réactifs pour 1L				
	NaCl				
	KCl				
	KH_2PO_4ou NaH_2PO_4				
	HCl (for adjusting pH)		?	x	x
	CaCl2				
	NH_4Cl				
	$KHCO_3$				
	Pepsin	**10 mg**	**1.25 g**	**1.25 g**	**1.25 g**
	Mucin	3.56 g	4 g ?	4g ?	
	Whole milk powder				
	Sodium malate		500 mg	500 mg	500 mg
	Tri-sodium citrate		500 mg	500 mg	500 mg
	Lactic acid		420 µL	420 µL	420 µL
	Glacial acetic acid		500 µL	500 µL	500 µL
	Glucose				
	Glucuronic acid				
	Urea				
	Glucosaminehydrochloride				
	Bovine Serum Albumine				
	Cystein		800 mg ?	800 mg ?	800 mg ?
Estomac	Glycine				
	Dietary components :				
	Nutrilon (56% lactose, 12% fat, 10% cas				
	Starch (potato)		5.0 g	5.0 g	
	Peptone water		3.4 g	3.4 g	
	Tryptone (vegetable)		6.1 g	6.1 g	
	Yeast extract		4.5 g	4.5 g	
	Casein		3.0 g	3.0 g	
	Pectin (citrus)		2.0 g	2.0 g	
	Xylan (oat)		2.0 g	2.0 g	
	Arabinogalactan (larch)		2.0 g	2.0 g	
	Guar gum		1.0 g	1.0 g	
	Inulin (chicory)		1.0 g	1.0 g	
	Conditions opératoires				
	Ratio Volume de solution / Masse de poussière (mL/g)	200	112.5	160	100
	pH	2	2.5	2.5	2.5
	durée	2 hrs	1.5 hrs	1 hr	1 hr
	température	37°C	37°C	37°C	37°C
	agitation		shaken	shaken	gently mixed

		8	9	10	11
		PBET + Tenax	CE-PBET	CE-PBET	CE-PBET
Adsorbent		**200 mg Tenax added just after the addition of intestinal solution**	**500 mg, stored in trap made of 100µm stainless stell mesh, inserted in gastric solution then kept in small intestine solution**	**500 mg, stored in cellulose membrane, inserted in gastric solution then kept in small intestine solution**	
Intestin	**Réactifs pour 1L**				
	KCl				
	NaCl				
	$CaCl_2 \cdot 2\,H_2O$				
	$MgCl_2 \cdot 6\,H_2O$				
	$NaHCO_3$	12.5 g			
	$Na_2HPO_4 \cdot 12H_2O$	42.4 g			
	$NaH_2PO_4 \cdot 2H_2O$	7.4 g			
	KH_2PO_4				
	HCl (for adjusting pH)				
	Trypsin				
	Pancreatin	**0.9 g**	**0.5 g**	**0.5 g**	**0.5 g**
	Bile	**5.5 g**	**1.78 g**	**1.78 g**	**1.78 g**
	Urea				
	Lipase		**1.6 g**		
	Bovine Serum Albumine				
	Dietary components :				
	Nutrilon (56% lactose, 12% fat, 10% cas				
	Starch (potato)		5.0 g	5.0 g	
	Peptone water		3.4 g	3.4 g	
	Tryptone (vegetable)		6.1 g	6.1 g	
	Yeast extract		4.5 g	4.5 g	
	Casein		3.0 g	3.0 g	
	Pectin (citrus)		2.0 g	2.0 g	
	Xylan (oat)		2.0 g	2.0 g	
	Arabinogalactan (larch)		2.0 g	2.0 g	
	Guar gum		1.0 g	1.0 g	
	Inulin (chicory)		1.0 g	1.0 g	
	Conditions opératoires				
	Ratio Volume de solution / Masse de poussière (mL/g)	300	112.5	160	100
	pH	7	6.5	7	7
	durée	6 hrs	4hrs	4hrs	4 hrs
	température				37°C
	agitation				gently mixed
	% Bioaccessibility				
	Réactifs pour 1L				
	Type II mucin		4 g	4 g	4 g
	NaCl		4.5 g	4.5 g	4.5 g
	KCl		4.5 g	4.5 g	4.5 g
	$NaHCO_3$ (sodium bicarbonate)		1.5 g	1.5 g	1.5 g
	$MgSO_4.7H_2O$ (magnesium Sulfate)		1.25 g	1.25 g	1.25 g
	Cysteine hydrochloride		800 mg	800 mg	800 mg
	KH_2PO_4 (potassium phosphate)		500 mg	500 mg	500 mg
	K_2HPO_4 (dipotassium phosphate)		500 mg	500 mg	
	Bile		400 mg	400 mg	400 mg
	$CaCl_2 \cdot 2\,H_2O$		189 mg	189 mg	0.15 g
	Haemin		50 mg	50 mg	50 mg
	$FeSO_4.7H_2O$		5 mg	5 mg	5 mg
	Dietary components :				
	Starch (potato)		5.0 g	5.0 g	5.0 g
	Peptone water		3.4 g	3.4 g	5.0 g
	Tryptone (vegetable)		6.1 g	6.1 g	5.0 g
	Yeast extract		4.5 g	4.5 g	4.5 g

		8	9	10	11
		PBET + Tenax	CE-PBET	CE-PBET	CE-PBET
Colon	Casein		3.0 g	3.0 g	3.0 g
	Pectin (citrus)		2.0 g	2.0 g	2.0 g
	Xylan (oat)		2.0 g	2.0 g	2.0 g
	Arabinogalactan (larch)		2.0 g	2.0 g	2.0 g
	Guar gum		1.0 g	1.0 g	1.0 g
	Inulin (chicory)		1.0 g	1.0 g	1.0 g
	Microbiota (fecal material from a healthy human adult that included Fecal Coliforms, Bifidobacteria, Enterococci, Staphylococci and Clostridia)				
	Anaerobe				
	Aerobe				
	Conditions opératoires				
	Ratio Volume de solution / Masse de poussière (mL/g)		100	100	100 à 120
	pH		6.5	6.5	
	durée		16 hrs	16 hrs	8 hrs
	température				
	agitation				
	% Bioaccessibility				
Comparaison avec in-vivo			measurements in very close agreement with reported PBDE bioavailability measures from an in vivo rat exposure study using indoor dust. (comparaison avec Huwe 2008)		
Référence / Journal / Pays		Yu 2013 / Chemosphere / China	Fang 2014 / Environmental Science & Technology / USA (North Carolina)	Kademoglou 2018 / STOTEN / UK	Abdallah 2012 / Journal of Environmental Monitoring / UK

		12	13	14	15	16
		SHIME Simuator of the human intestinal microbial ecosystem	FOREhST Fed Organic Estimation human Simultation Test	FOREhST Fed Organic Estimation human Simultation Test	IVG (in vitro gastrointestinal method)	RBALP (relative bioaccessibility leaching procedure)
	Réactifs pour 1L					
	NaCl					
	NaSCN ou KSCN		=			
	Na_2SO_4		Barge			
	$NaHCO_3$		+			
	NaOH		Food			
	KCl		Components			
	KH_2PO_4 ou NaH_2PO_4					
	$CaCl_2 \cdot 2\ H_2O$					
Bouche	Mucin					
	α-amylase					
	Urea					
	Uric acid					
	Conditions opératoires					
	Ratio Volume de solution / Masse de poussière (mL/g)			16.6666667		
	pH					
	température			37°C		
	agitation			130 rpm		
	durée			5		
	Réactifs pour 1L					
	NaCl	0.1 M				
	KCl					
	KH_2PO_4ou NaH_2PO_4					
	HCl (for adjusting pH)	1.3 mL of 5 M			x	
	CaCl2					
	NH_4Cl					
	$KHCO_3$	0.1 M				
	Pepsin	**10 mg**				
	Mucin	4 g				
	Whole milk powder					
	Sodium malate					
	Tri-sodium citrate					
	Lactic acid					
	Glacial acetic acid					
	Glucose	0.4 g				
	Glucuronic acid					
	Urea					
	Glucosaminehydrochloride					
	Bovine Serum Albumine					
	Cystein	0.5 g				
Estomac	Glycine					0.4 M
	Dietary components :					
	Nutrilon (56% lactose, 12% fat, 10% cas	5 g				
	Starch (potato)	3 g				
	Peptone water	3 g				
	Tryptone (vegetable)					
	Yeast extract	3 g				
	Casein					
	Pectin (citrus)	2 g				
	Xylan (oat)	1 g				
	Arabinogalactan (larch)	1 g				
	Guar gum					
	Inulin (chicory)					
	Conditions opératoires					
	Ratio Volume de solution / Masse de poussière (mL/g)	10		53.1666667	100	100
	pH	1.5		1.6	1.5	1.5
	durée	2 hrs		2 hrs	2hrs	1 hr
	température	37°C		37°C	37°C	37°C
	agitation	150 rpm			70 rpm	end over end rotation 30 rpm

		12	13	14	15	16
		SHIME Simuator of the human intestinal microbial ecosystem	FOREhST Fed Organic Estimation human Simultation Test	FOREhST Fed Organic Estimation human Simultation Test	IVG (in vitro gastrointestinal method)	RBALP (relative bioaccessibility leaching procedure)
Adsorbent					**addition of a C18 membrane**	
Intestin	**Réactifs pour 1L**					
	KCl					
	NaCl					
	$CaCl_2 \cdot 2\,H_2O$					
	$MgCl_2 \cdot 6\,H_2O$					
	$NaHCO_3$	12.5 g			12.5 g	
	$Na_2HPO_4 \cdot 12H_2O$					
	$NaH_2PO_4 \cdot 2H_2O$					
	KH_2PO_4					
	HCl (for adjusting pH)					
	Trypsin					
	Pancreatin	**0.9 g**			**0.9 g**	**0.5 g**
	Bile	**6 g**			**6 g**	**1.75 g**
	Urea					
	Lipase					
	Bovine Serum Albumine					
	Dietary components :					
	Nutrilon (56% lactose, 12% fat, 10% cas					
	Starch (potato)					
	Peptone water					
	Tryptone (vegetable)					
	Yeast extract					
	Casein					
	Pectin (citrus)					
	Xylan (oat)					
	Arabinogalactan (larch)					
	Guar gum					
	Inulin (chicory)					
	Conditions opératoires					
	Ratio Volume de solution / Masse de poussière (mL/g)	15			150	100
	pH	6.5			6.5	7
	durée	5 hrs			2 hrs	4 hrs
	température	37°C			37°C	
	agitation	150 rpm			70 rpm	30 rpm end over end rotation
	% Bioaccessibility	8.00%				
	Réactifs pour 1L					
	Type II mucin					
	NaCl					
	KCl					
	$NaHCO_3$ (sodium bicarbonate)					
	$MgSO_4.7H_2O$ (magnesium Sulfate)					
	Cysteine hydrochloride					
	KH_2PO_4 (potassium phosphate)					
	K_2HPO_4 (dipotassium phosphate)					
	Bile					
	$CaCl_2 \cdot 2\,H_2O$					
	Haemin					
	$FeSO_4.7H_2O$					
	Dietary components :					
	Starch (potato)					
	Peptone water					
	Tryptone (vegetable)					
	Yeast extract					

		12	13	14	15	16
		SHIME Simuator of the human intestinal microbial ecosystem	FOREhST Fed Organic Estimation human Simultation Test	FOREhST Fed Organic Estimation human Simultation Test	IVG (in vitro gastrointestinal method)	RBALP (relative bioaccessibility leaching procedure)
Colon	Casein Pectin (citrus) Xylan (oat) Arabinogalactan (larch) Guar gum Inulin (chicory) ***Microbiota (fecal material from a healthy human adult that included Fecal Coliforms, Bifidobacteria, Enterococci, Staphylococci and Clostridia)***					
	Anaerobe	**1.1 x 10^8 CFU mL^{-1}**				
	Aerobe	**2.25 x 10^7 CFU mL^{-1}**				
	Conditions opératoires					
	Ratio Volume de solution / Masse de poussière (mL/g)	20		98.1666667		
	pH			6		
	durée	18 hrs		2 hrs		
	température	37°C		37°C		
	agitation	150 rpm		130 rpm		
	% Bioaccessibility	1.2 - 21 %				
Comparaison avec in-vivo					corrélation avec in vivo pour les HAP : slope 0.85, r^2 = 0.45, p< 0.07	Mauvaise corrélation avec in vivo study
Référence / Journal / Pays		Siciliano Chemosphere 2010 / Canada (PAHs Soils)		Quintana, 2016, Stoten	James 2010 / EST / canada	

CHAPITRE 3 : PROPOSITION D'UNE METHODE SIMPLIFIEE DE MESURE DES COSV DANS LES POUSSIERES

La revue bibliographique développée au chapitre précédent a montré l'existence de plusieurs méthodes de mesure de la bioaccessibilité orale des COSV dans les poussières. Elle a également mis en évidence le manque d'harmonisation entre ces méthodes. On peut ici faire un parallèle avec les nombreux travaux menés sur la bioaccessibilité des métaux dans les sols, qui a conduit dans un premier temps à une harmonisation sous la forme de la méthode BARGE (*Bioaccessibility research group of Europe*) [94–96]. Bien que complète et harmonisée, cette méthode présentait une complexité de mise en œuvre qui a pu freiner de nombreux utilisateurs. Une méthode plus simple a alors été proposée, centrée sur la digestion acide en phase gastrique, dont les performances sont équivalentes à la méthode de référence [97].

En ce qui concerne les COSV, les méthodes les plus performantes, comme celle de Fang et Stapleton qui a montré une corrélation entre bioaccessibilité et biodisponibilité des PBDE dans la poussière de référence SRM 2585 [98], n'ont pas été mises en œuvre dans le cadre de grandes campagnes d'analyse. Ce peut être par manque de moyen ou d'intérêt scientifique, mais il est plus probable que ce manque de déploiement à grande échelle soit dû à la complexité de la mise en œuvre, ces méthodes requérant une longue phase de préparation, de nombreux réactifs, de multiples extractions, et plusieurs jours voire semaines entre la préparation des fluides digestifs et l'injection des extraits finaux.

La connaissance de la bioaccessibilité doit pourtant se déployer sur un grand nombre d'échantillons de diverses origines afin de pouvoir cerner et *in fine* modéliser les facteurs d'influence décrits dans le chapitre précédent. L'objet de ce chapitre est donc de proposer une méthode simple et robuste qui permette de mesurer la bioaccessibilité des COSV dans les poussières de nombreux échantillons.

1. DEVELOPPEMENT DE LA METHODE (ARTICLE SCIENTIFIQUE N°3)

Les méthodes existantes les plus complètes mises en exergues lors de la revue bibliographique ont servi de référence pour le développement de la méthode simplifiée. Il s'agit des méthodes proposée par Fang et Stapleton [98] et Kademoglou et al. [99], qui comportent un adsorbant permettant de capter les COSV au fur et à mesure de leur libération dans les fluides digestifs, et ainsi imiter la dynamique du passage des COSV à travers la paroi intestinale. Ces méthodes poursuivent également l'incubation intestinale jusqu'au colon et tiennent compte de l'influence de la présence d'aliments sur la bioaccessibilité.

Quatre étapes de simplification de ces méthodes de référence ont été nécessaires pour aboutir à la méthode simplifiée :

- - changement de type d'adsorbant
  - élimination de la digestion gastrique
  - élimination de l'analyse des fluides digestifs
  - optimisation de l'incubation intestinale

Les deux méthodes de références ont été utilisées pour mesurer la bioaccessibilité de plusieurs PBDE dans la poussière de référence SRM 2585 du NIST (*National Institute of Standards & Technology*). Des données relatives à la biodisponibilité de certains PBDE dans le SRM 2585 existent également [100]. La poussière SRM 2585 a été testée avec la méthode simplifiée, et les données produites ont permis sa validation par comparaison aux données existantes.

Les travaux de développement de cette nouvelle méthode d'analyse ont fait l'objet du troisième article de ce projet de thèse, qui a été préparé en vue d'une soumission à *Environmental Science and Technology*. Les co-auteurs incluent Katerina Kademoglou et Christopher Collins, qui ont partagé leur protocole sur la méthode de référence en me formant à sa mise en œuvre dans leur laboratoire de l'université de Reading (juillet 2016).

Oral bioaccessibility of SVOCs in indoor settled dust: a simplified *in vitro* method applied to polybrominated diphenyl ethers (PBDEs), and pyrethroids.

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KEYWORDS

ABSTRACT

Dust ingestion is a non-negligible pathway of human exposure to indoor chemical pollutants including several semi-volatile organic compounds (SVOCs). To better assess this human exposure, it is necessary to consider the oral bioaccessibility of SVOCs, i.e. the fraction of pollutants released from the dust matrix in the digestive tract following dust ingestion. A few methods have been described in the literature for this purpose, but they were never applied on a large number of samples because of their complexity. In this context, a simple method for the extraction of the bioaccessible fraction of SVOCs was proposed. This novel method consists of incubating 200 mg of dust for 20 hours at 37 °C in 40 mL of neutral pH water containing bile and pancreatin. An insert made of 500 mg of sorptive material (XAD®-2) is added to act as a sink for the SVOCs released in solution. This method produced comparable results to those obtained with non-simplified methods for the bioaccessibility of PBDEs in SRM 2585. It was then used to measure the bioaccessibility of pyrethroids and PBDEs in 30 settled dust samples. For the three compounds that were more frequently detected, i.e. permethrin, BDE 47 and BDE 99, median bioaccessibilities ranged from 37 to 48%. Doses considered for human exposure could therefore be lowered by a minimum of 50 %, thus emphasizing the importance of considering oral bioaccessibility when assessing human exposure to indoor pollutants via dust ingestion.

INTRODUCTION

Since the 1950s, the presence of semivolatile organic compounds (SVOCs) indoors[1] has been reported worldwide in dwellings,[2–8] schools,[9–13] and other indoor environments (cars, offices, hospitals, mosques, etc.).[14–18] This presence is subject of concern for human health since most of the SVOCs are endocrine disruptors with effects on the reproductive tract development, the thyroid function, the nervous system and the development of metabolic diseases.[19–21] SVOCs are characterized by their vapor pressure (from10^{-14} to 10^{-4} atm) and their boiling point (between 240 °C and 400 °C).[22,23] Due to these properties, SVOCs equilibrate between the gaseous and particulate phases of air, surfaces, and settled dust. Human are thus exposed to SVOCs via inhalation of air, dermal contact with air, dust and surfaces, and also by ingestion of dust. Human exposure is most often quantified based on the environmental concentration.[24] However, only a fraction of this concentration penetrates the body. For dust ingestion, the bioaccessible concentration is defined as the concentration that is released in the gastro-intestinal tract, from the dust into the gastric and intestinal fluids, and is susceptible to become bioavailable.[25] The bioavailable concentration is the fraction reaching the digestive system and absorbed into the systemic circulation; it is consequently the concentration of interest to accurately assess human exposure. However, assessing the bioavailability of SVOCs necessitates performing *in vivo* studies that are costly and ethically challenging. On the other hand, bioaccessibility can be assessed with *in vitro* studies, and provides an interesting proxy to bioavailability.

Studies investigating the bioaccessibility of SVOCs in indoor dust are still scarce and new. Nonetheless, about twenty studies have been reported since 2011.[26] So far these studies have only been used to document data on a limited number of samples due to the complexity and cost of the measurement methods, even though they are easier to implement than *in vivo* methods. Some of these studies were of particular interest because the measurement methods used were

the most advanced and conservative, as they included a sorbent to simulate the dynamic of the digestion, and pursued the *in vitro* digestion process to the colon stage. These methods were used to produce bioaccessibility data for polybrominated diphenyl ethers (PBDEs)[27,28] and pyrethroids[29], which are two chemical families belonging to SVOCs.

PBDEs were used as flame retardants in furniture polyurethane foam, wire and cable insulation, electronics, and computers.[30] Their use has been limited in Europe and the United States,[31,32] but they are persistent in indoor dust because of their chemical stability, although debromination of higher brominated congeners via the effect of natural sunlight might lead to an enrichment of the lower brominated congeners' content.[33] Their presence indoors is subject to concern: suggestion for impaired neurodevelopmental health [34–36] associated with early life exposure to PBDEs was reported. Exposure to PBDEs from house dust could also interfere with the thyroid function, [37,38] the timing of puberty, [39] and be linked to altered semen quality.[40]

Pyrethroids are synthetic substances that have been formulated based on the naturally occurring pyrethrins. They are used outdoors as pesticides for crops, forestry, horticulture and gardens, and indoors to control lice and fleas. They are also used as arthropod repellants in clothing and carpet.[41] Concerns are raised about environmental and occupational exposure to pyrethroids and altered semen quality, changes in serum thyroid and male reproductive hormones. [41] Exposure during pregnancy could affect birth size, immune system, neurodevelopment and hormonal balance in children.[41–43] Indoor settled dust plays a role in human exposure to pyrethroids, as the pyrethroid dust content in French dwellings was associated with the household insecticide use,[44] and dust ingestion accounted for 11% of permethrin exposure via ingestion.[45]

A better knowledge of the bioaccessibility of these compounds is necessary to better assess to what extent humans are exposed to them indoors via dust ingestion. So far, existing measurement methods have never been deployed on a large number of samples because of their cost and complexity, thus emphasizing the need of a simple and robust bioaccessibility measurement method.

Within this context and in order to provide a tool for a finer assessment of human exposure to these compounds, the present work has three objectives: (i) to develop a simplified method for the evaluation of the oral bioaccessibility of SVOCs in indoor dust, (ii) to validate this simplified method by comparing its results with data from the literature, and (iii) to document the oral bioaccessibility of five PBDEs (BDE 47, 85, 99, 100, and 153) and four pyrethroids (tetramethrin, permethrin, cyfluthrin, and cypermethrin) in 30 settled dust samples collected in French classrooms.

MATERIALS AND METHODS

Selection of PBDEs and pyrethroids. The list of compounds of interest selected for this project was based on a hierarchization work that considered SVOC toxicity and indoor concentrations reported in the literature.[19] Briefly, data on the SVOC concentrations found in residential indoor settled dust were collected from the scientific literature and compared with toxicity reference doses. Among the top-ranked compounds that included phthalates, short-chain chlorinated paraffins, organophosphorus compounds, polychlorinated biphenyls, organochlorines, perfluorinated compounds, polycyclic aromatic hydrocarbons, etc., we chose the two families of compounds for which bioaccessibility data had already been reported in the literature using advanced method as mentioned in the introduction. More specifically, we chose one tetra-BDE

(BDE 47), 3 penta-BDEs (BDE 85, 99, and 100) and one hexa-BDE (BDE 153). For pyrethroids, in addition to permethrin and cyfluthrin that were ranked in the hierarchization, we also added tetramethrin and cypermethrin, since they were present in the standard reference material (SRM 2585) used to control analyses.

Reagents and chemicals. Certified standards of tetramethrin, permethrin, cyfluthrin, cypermethrin, fenpropathrin, and 2,3,4-trichloronitrobenzene (TCNB) were purchased from LGC Labor GmbH (Augsburg, Germany). Nonane/toluene (10%) solutions (50 mg/L) of BDE 47, 85, 99, 100 and 153, and nonane/toluene (3%) mixture (5 mg/L) of $^{13}C_{12}$-BDE 47, 99 and 153 were purchased from Wellington Laboratories Inc. (Guelph, ON, Canada). The Standard Reference Material SRM 2585 (Organic Contaminants in House Dust) [46] was purchased from the National Institute of Standards and Technology (NIST, Gaithersburg, MD, USA). Bile salts, pepsin from porcine gastric mucosa, pancreatin from porcine stomach, and Celite® 545 were purchased from Merck KGaA (Darmstadt, Germany). Chromabond® NH_2 (aminopropyl modified silica) glass columns (3 mL / 500 mg) were purchased from Macherey-Nagel GmbH & Co. KG (Düren, Germany). Evian mineral water in glass bottles (Cachat source, SAEME, France) was purchased from France Boisson (Rueil-Malmaison; France).

Selection of dust samples. A national campaign was organized in France by the Indoor Air Quality Observatory (OQAI), between 2013 and 2017, to assess indoor air quality in French schools. Air and dust samples were collected in 600 classrooms and analyzed for several parameters (airborne particles, volatile and semi-volatile organic compounds, nitrogen dioxide, metals, etc.). For this study, we selected 30 samples from the national campaign based on two criteria: (i) the amount of dust remaining after analysis had to be sufficient (> 220 mg) and (ii) the PBDE content, assessed as part of the national campaign, had to represent as many

126 concomitant congeners as possible, in relatively high concentration, in order to be able to
127 measure their bioaccessibility. The pyrethroids content could not be used as a criterion at this
128 stage, because they were not included in the national campaign analysis, except permethrin,
129 which was quantified in all samples. The 30 samples correspond to 13 preschools and 17
130 elementary schools, located in all of the French regions.

131 **Dust sample collection and preparation.** Dust collection was performed by trained technical
132 operators. Dust samples were collected on classrooms' floor using a vacuum cleaner specifically
133 designed to avoid any contamination resulting from the contact between the sample and the
134 vacuum cleaner's parts: dust was collected in a cellulose thimble fitted at the entrance of the
135 tube, where a custom-made Teflon nozzle was fitted. Teflon was chosen as an inert material
136 towards the organic pollutants of this study. Upon reception in the laboratory, samples were
137 stored in the freezer at -20 °C before being sieved through a 100 µm sieve. The <100 µm fraction
138 was stored in the freezer at -20 °C in clean amber glass vials until analysis.

139 ***In vitro*** **release of bioaccessible SVOCs.** The simplified method for extracting the
140 bioaccessible SVOC content in dust consists of an *in vitro* simulation of the intestinal digestion,
141 including only the small intestine (4 hours) and colon (16 hours) incubations, in the presence of
142 an adsorbent, which serves as a sink for SVOCs, thus mimicking the transfer of SVOCs through
143 the intestinal wall and promoting the liberation of SVOCs from the dust matrix[47]. The adsorbent
144 used in this work is Amberlite® XAD®-2, a polymeric adsorbent widely used to adsorb organic
145 compounds from air[48] and water[49]. An XAD®-2 insert was designed to allow the intestinal
146 solution to flow freely around the XAD®-2 beads, while retaining the beads apart from the dust
147 particles. This insert consists of 500 mg of XAD®-2 trapped in a 70 x 58 mm, 110 mesh, nylon
148 gauze pocket (Hebei Reking Wire Mesh CO., Ltd, Hebei, China). In order to maintain the

149 XAD®-2 insert submerged, a 9 mm diameter glass marble was added in the pocket before closing
150 it using 25 mm paper clips (Lyreco, Marly, France) A picture of the insert in available in
151 Supplement Information (SI) (SI Figure 1). XAD®-2 inserts were cleaned prior to use with
152 dichloromethane using an Accelerated Solvent Extractor ASE 350 (Dionex Corporation,
153 Sunnyvale, California, United States). Intestinal solution was prepared by adding 1.78 g of bile
154 salts and 0.5 g of pancreatin to 1 L of water, in accordance with previous work[28]. Evian water, a
155 natural mineral groundwater known for its very stable mineral content and conductivity (509
156 µS/cm), was used for this purpose.[50] A fluid:dust ratio of 200:1 was respected as a safe
157 compromise between physiological relevance and analytical feasibility[26]: 200 mg of dust were
158 added to 40 mL of intestinal solution in a Duran® 100 mL amber glass bottle (DWK Life
159 Sciences GmbH, Wertheim, Germany). The solution was left to incubate at 37 °C in a TH 15
160 incubator hood (Edmund Bühler GmbH, Bodelshausen, Germany) for 20 hours with a 125 rpm
161 agitation to mimic the gastro-intestinal tract peristaltic movement. At the end of the incubation,
162 the XAD®-2 inserts were removed from the solution, rinsed with the intestinal solution to
163 remove any dust left on surface, and hang out on a metallic wire under the hood until dry.
164 Meanwhile the intestinal solution and its dust content were transferred to 50 mL Kimax
165 centrifuged tubes (Gerresheimer, Düsseldorf, Germany) and centrifuged at 2500 g for 20 min.
166 After separation, the intestinal solution was discarded and the residual dust was lyophilized in an
167 Alpha 1-2 freeze drier (Christ, Osterode am Harz, Germany) until dry. The XAD®-2 insert,
168 containing the bioaccessible SVOC content, and the residual dust, containing the non-
169 bioaccessible SVOC content, were then treated separately, albeit using the same extraction and
170 analytical methods (Figure 2).

171 **Extraction of PBDEs and pyrethroids in XAD®-2 and residual dust.** The extraction
172 procedure has already been described in previous works[51]. Briefly, surrogate standards
173 (fenpropathrin, and $^{13}C_{12}$-BDE 47, 99, and 153) were added to each sample then extractions were
174 performed with dichloromethane by pressurized liquid extraction (PLE) using the Accelerated
175 Solvent Extractor ASE 350 (Dionex Corporation, Sunnyvale, California, United States). Organic
176 extracts were concentrated to 1 mL and quantitatively transferred onto Chromabond® NH_2 glass
177 columns prewashed with 6 mL of dichloromethane. Elution was performed with 5 mL of
178 dichloromethane. Organic extracts were then concentrated to 0.5 mL, spiked with an internal
179 standard (2,3,4-TCNB), transferred into a 1.5 mL amber glass vial and stored at -18 °C prior to
180 analysis.

181 **Analysis of PBDEs and pyrethroids in XAD®-2 and residual dust.** The analytical method
182 was also described previously[51]. Briefly, analyses of organic extracts were performed using a gas
183 chromatograph (GC) Trace GC Ultra coupled to a mass spectrometer (MS/MS) TSQ Quantum
184 GC operated in electron impact ionization (EI) mode (70 eV) (Thermo Scientific, Waltham,
185 Massachusetts, United States). The GC system was equipped with a TriPlus Autosampler and a
186 PTV (Programmable Temperature Vaporizing) injector. Calibration solutions and organic
187 extracts were injected (1 µL) in splitless mode. Helium was used as column carrier gas at a
188 constant flow rate of 2 mL/min. Chromatographic separation was performed on a Rtx-PCB
189 capillary column (60 m length x 0.25 mm I.D., 0.25 µm film thickness) supplied by Restek
190 (Lisses, France). The mass spectrometer (triple quadrupole) was operated in the Multiple
191 Reaction Monitoring (MRM) mode and the two most sensitive and specific transitions were
192 monitored for each compound. The concentration in each sample was calculated by internal
193 calibration, using at least 5 of the 8 points calibration curves.

194 **Calculation of bioaccessibility.** The percentage of bioaccessibility was calculated according
195 to the following formulae:

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

196 **QA/QC.** The limits of detection (LODs) and limits of quantification (LOQs) are reported in
197 Table 4. Incubation blank and quality control (QC) samples were incubated, extracted and
198 analyzed to control contamination from all consumables and to check for method accuracy.
199 Incubation blanks consisted of an XAD®-2 insert immerged in 40 mL of the intestinal solution.
200 Incubation QC samples consisted of XAD®-2 inserts immerged in 40 mL of the intestinal
201 solution previously spiked with the target compounds at a concentration of once (Level 1) or
202 eight times (Level 2) the analytical LOQ. The NIST standard reference material SRM 2585 was
203 also tested: an XAD®-2 insert was immerged in 40 mL of intestinal solution containing 200 mg
204 of SRM 2585. One incubation blank, and two each of Level 1, Level 2 and SRM 2585 incubation
205 QC samples were prepared for every batch of 7 or 8 samples. Extraction blanks and QC samples
206 were also analyzed with each XAD®-2 or dust extraction batch to monitor the pollution and the
207 accuracy of the ASE extraction method. Extraction blanks samples consisted of a cleaned
208 XAD®-2 insert for XAD®-2 extractions, and of diatomaceous earth (Celite® 545) for dust
209 extractions. Extraction QC samples consisted of a cleaned XAD®-2 insert or Celite® 545, spiked
210 at Level 2. In addition, for dust extractions, 200 mg of SRM 2585 were extracted to assess the
211 concentration of the reference material, as certified or indicative values are known for several
212 compounds. These QC procedures comply with the principles described by Rodríguez-Navas,
213 Rosende and Mir to ensure a proper validation of analytical results.[52]

214 **Statistical analysis.** GraphPad Prism® version 5.01 for Windows (GraphPad Software, LaJolla
215 CA, USA) was used for graphical data display and statistical analysis. Prior to statistical

analysis, all bioaccessibility percentages were converted into fractions and arc-sine transformed[28]. Multiple t-tests (unpaired; $p < 0.05$) were performed to assess statistically significant differences between bioaccessibility and bioavailability.

RESULTS AND DISCUSSION

Four steps towards simplifying the *in vitro* method

As mentioned in the introduction, the methods developed and / or used previously by the authors,[28] Fang and Stapleton[27] and Wang et al.,[29] are the most inclusive. In addition to the gastric and small intestine process that are present in all *in vitro* methods[26], they also consider the colon stage in the incubation process and they mimic the dynamic of the digestion using Tenax® TA as a sorptive sink. These common characteristics along with the whole *in vitro* process are represented in Figure 1, and these inclusive methods have been used as a reference based on which we started a four-step simplification process.

First step – Use of an XAD®-2 insert. Prior to Kang et al. investigating different sorptive sink solutions (silica, poly(ethylene-co-vinyl acetate) (polyE), Tenax® TA, and C18) and recommending silica polyE to predict PAHs bioavailability of indoor dust[53], Tenax® TA used to be the favored option and has been used by Fang and Stapleton to measure the bioaccessibility of PBDEs in the reference material SRM 2585[27], with a very good correlation to their bioavailability measured *in vivo* on rats that had ingested the same material[54]. However Tenax® TA is rather expensive, and would not be appropriate in the prospect of documenting the bioaccessibility of a large number of dust samples, since the cost, either for using new material for each sample, or for the operator time required to recycle the materiel for several successive uses, would be prohibitive and contrary to the aim of simplifying the method. In this project, XAD®-2 was tested as an alternative to Tenax® TA. XAD®-2 presents several advantages: (i) it

is quite inexpensive so it can be disposed of after use, without the need of being recycled, (ii) its mesh size (20-60) is appropriate for the mesh size of the nylon mesh (110) that is used for the insert in the present study, and (iii) it is suitable for extraction with dichloromethane, which has been the solvent of choice for the extraction of SVOCs in dust in our previous works[7,13,51]. The suitability of XAD®-2 for measuring the bioaccessibility of SVOCs in dust was assessed by comparison to Tenax® TA using the SRM 2585 reference material, which was submitted to one hour of gastric incubation followed by four hours of intestinal incubation in the presence of 500 mg of sorbent. Since no bioaccessible BDE 153 was detected in the presence of Tenax® TA, which could be due to an insufficient incubation time for this compound, the comparison was only carried out for the pyrethroids and the remaining PBDEs. As shown in SI Chart1, a good correlation (slope = 0.945, $r^2 = 0.978$) was established between the bioaccessibility results obtained with Tenax® TA and XAD®-2. Therefore, the insert made of 500 mg of XAD®-2 was deemed suitable for the measurement of the bioaccessibility of SVOCs in indoor settled dust.

Second step – removal of the analysis of the digestive fluid. After leaving the dust matrix, SVOCs are released into the synthetic digestive fluid, from where they are adsorbed onto XAD®-2. XAD®-2 is an infinite sink from which SVOCs will not desorb in the conditions of the incubation. The pyrethroids and PBDEs, with Log K_{OW} (octanol/water partition coefficient) greater than 4.73, are hydrophobic compounds. Once released in the fluid, they would either be adsorbed on XAD® -2 or back trapped in dust, but they should not remain in the fluid. To check this hypothesis, SVOC concentrations in the digestive fluid were monitored at two different stages of the incubation (after intestinal incubation (4 hours) and after colon incubation (20 hours) for triplicates of SRM 2585. The percentage of bioaccessible SVOC in the digestive fluid was calculated:

$$bioaccessible\ SVOC\ in\ the\ digestive\ fluid\ (\%) = \frac{mass\ of\ SVOC\ in\ the\ digestive\ fluid\ (ng)}{masse\ of\ SVOC\ in\ the\ digestive\ fluid\ (ng) + masse\ of\ SVOC\ on\ \text{XAD®} - 2\ (ng)}$$

The results in the fluid, presented in SI Table 1, are below the LOD for all PBDEs and reach a maximum of 3% of the total bioaccessible content after 4 hours and 1% after 20 hours for pyrethroids. The contribution of SVOC concentration in digestive fluid in the assessment of bioaccessible SVOC can therefore be considered negligible and the analysis of digestive fluid removed from the protocol as a way towards simplification and saving of operator's time.

Third step – optimization of the intestinal incubation

The intestinal phase is one of the main steps of human digestion because it is there that the absorption of nutriments through the intestinal wall takes place. It is a crucial step in *in vitro* digestive systems because of the duration of incubation that allows more time for the dynamic of the release of SVOCs from the dust matrix.[26] While intestinal incubation, representing digestion in the small intestine, ends after about 4 hours, it can be pursued further to also consider the large intestine or colon, which has been shown to considerably increase the resulting bioaccessibility. Synthetic digestive fluid simulating colon fluid is different from small intestine fluid, as it contains mucin, L-cystein, haemin, iron and different salts, but no pancreatin.[28]. In addition, durations of incubation differ with 4 hours in small intestine and 16 hours in colon, within the range of physiologically relevant values.[55] In the present effort of simplification, the hypothesis was made that the duration of incubation was the crucial step in the additional bioaccessibility brought by colon incubation, as it would give more time to SVOCs with slower kinetics to be released from the dust and adsorbed onto XAD®-2. To test this hypothesis, triplicates of SRM 2585 where submitted to one hour of gastric incubation in Evian water at pH 2.5, followed,

after pH neutralization to 7 using saturated sodium bicarbonate, by either 4 or (4 + 16 =) 20 hours of incubation in the presence of bile salts. Results are shown in Chart 1. The additional incubation time increased the bioaccessibility by a factor of 1.2 for tetramethrin, about 3 for the other pyrethroids, and about 2.5 for PBDEs. Tetramethrin, being the less hydrophobic compound (log K_{OW} = 4.73), is already more bioaccessible after 4 hours than the other compounds (54% vs. max 21%) and would be less impacted by the additional incubation. Bioaccessibility results obtained after the 20 hours-incubation are in agreement with the authors' previous results, obtained with the non-simplified method, for BDE 47 (54% in the current study, 51% in the previous study), BDE 100 (39% current, 40% previous), and BDE 153 (26% current, 32% previous)[28]. These results confirmed the hypothesis that the most important factor for assessing SVOC bioaccessibility is the duration of incubation. Moreover, the change of synthetic fluid between intestinal and colon incubation is not necessary and a simplified media made of bile salts is sufficient to reproduce results obtained for intestinal and colon digestion with more complex media.

Fourth step – removal of the gastric incubation

Incubation in gastric conditions is an important step for the *in vitro* assessment of bioaccessibility of metals and is in fact the only relevant compartment as metals are liberated in the stomach via the action of acidity.[56] However, for organic compounds, liberation in gastric conditions have been shown inferior to intestinal conditions for polycyclic aromatic hydrocarbons (PAHs),[57] phthalates,[58] and polychlorinated biphenyls (PCBs).[59]

When dust is submitted to immersion, part of it dissolves in the digestive fluid, thus favoring the release of the SVOCs that it contained. We made the hypotheses that (i) dust dissolution in digestive fluids may be impacted by the gastric and intestinal conditions of the experiment, and

(ii) a greater amount of dissolved dust could be linked to a greater SVOC bioaccessibility. To test these hypotheses, the amount of dissolved dust and the associated SVOC bioaccessibilities in SRM 2585 triplicates were tested for sixteen different gastric and intestinal conditions, described in SI Table 2. Results are shown in SI Chart 2. An increase of the percentage of dissolved dust was always associated with an increase of bioaccessibility, although the strength of the correlation varied depending on the compound, with r^2 ranging from 0.17 for BDE 99, to 0.54 for tetramethrin. A non-parametric correlation test was also performed, which showed that the correlation was significant for all the compounds but BDE 99 and BDE 153 (SI Table 3).

Moreover, the highest percentages of dust dissolution (> 58%) were obtained in the presence of pancreatin (tests 13, 15 and 16 in SI Table 2) even if dust was not submitted to gastric incubation. Pancreatin is a mixture of digestive enzymes (amylase, lipase, trypsin, and protease) produced by the pancreas to break down proteins, fats and carbohydrates in the small intestine.[25,61,62] The role of pancreatin in bioaccessibility tests has already been documented in the literature: it was involved in the dehalogenation process of halonitromethanes[63] and on the degradation of pyrethroids in the digestive fluid prior to absorption.[29] It was also reported as a surfactant that, along with bile salts, enhances the bioaccessibility of p,p′-DDT in contaminated soils,[64] although this effect was weak on PAHs.[65] A comparison between bioaccessibility results obtained in the presence of pancreatin with or without gastric incubation was carried out for SRM 2585. Results are shown in Chart 2. The intestinal-only process, including bile salts and pancreatin, produced greater results than those obtained with the gastro-intestinal process including bile salts for most compounds, and comparable results to those obtained with the gastro-intestinal process based on a buffer solution.

Therefore the gastric incubation was not considered necessary for measuring SVOC bioaccessibility in dust and the step was removed from the process. This is a major event for the simplification of the method, because it eliminates the need for pH adjustment to 2.5, the necessity to handle the XAD®-2 inserts between the gastric and intestinal phases, and last the need for pH readjustment to 7.0, such saving operator labor time.

Evaluation of time and money saving. An attempt to compare the time necessary to perform each step of the reference and simplified methods has been made and is summarized in Table 1. The time spent for one sample with the simplified method (2 hours and 20 minutes) has been evaluated to less than half the time spent on the reference method (nearly 5 hours), which can be translated in money saving as operator's time often contributes to more than half to the cost of an analysis. Further substantial savings could be obtained with the change of sorbent, with an estimated 1 to 12 ratio between the cost of 500 mg of XAD®-2 and the cost of 500 mg of Tenax® TA. These savings would be very valuable when assessing the SVOC bioaccessible content of many samples in larger studies.

Method validation.

A comparison was first carried out between bioaccessibilities measured for PBDEs in SRM 2585 with this method and the two non-simplified methods for which data for PBDEs were also available. The first non-simplified method (method A) is the authors' previous work, based on Tilston et al.'s method,[66] including Tenax® TA, retained in a dialysis membrane, as an adsorbent.[28] The other method (method B) is the one developed by Fang and Stapleton, also based on Tilston et al.'s work,[66] with Tenax® TA retained in a stainless steel gaze and with the addition of lipase among the intestinal components.[27] As shown in Chart 3, bioaccessibility data

produced by the simplified method were greater than those obtained with the non-simplified method A, but lower than those obtained with the non-simplified method B. The fact that method B produces greater results could be linked to the presence of lipase, which may act as an additional component favoring the release of hydrophobic compounds from dust. On the contrary, the lower results obtained with method A could be due to the membrane which can slow down the kinetics of the adsorption on Tenax® TA with the increase of molecular weight.[67] It is satisfactory that the simplified method should produce intermediate results compared to non-simplified methods as this comforts its reliability.

We also compared the results obtained through the simplified method with *in vivo* bioavailability data, bearing in mind that bioaccessibility data should be greater than bioavailability as they do not include any metabolism past the intestinal barrier.[68] In 2008, Huwe et al. administered SRM 2585 to rats and measured the concentrations of 15 PBDEs, including those of interest in the present study, in liver and adipose tissues, as well as in feces[54]. To calculate the resulting bioavailability, shown in Chart 3, the following equation was applied:

$$bioavailability\ (\%) = \frac{\%PBDE\ retained}{sum(\%\ PBDE\ retained + \%\ PBDE\ excreted\ in\ feces)}\ x100.$$

Non-significant differences were observed between bioavailability and bioaccessibilities measured with the simplified method for BDE 47 and BDE 85 ($p>0.05$). A lower recovery of BDE 99 (65%) was observed by Huwe et al., which caused the calculated bioavailability to rise (from 43.7% to 67.1%). While we are not able to assess the origin of this lower recovery, it is worth noting that the non-corrected percentage retained of 43.7 ±5.2% is not significantly different from our simplified bioaccessibility of 48.2 ±7.7% ($p>0.05$). Nonetheless, bioavailability was significantly higher than simplified bioaccessibility for BDE 100 ($p=0.0002$) and BDE 153 ($p<0.001$). Two phenomena, hypothesized by Abdallah and Stuart in their work on

373 human milk, [69] could explain these higher values: the first one is the debromination of more
374 highly brominated BDE compound such as BDE 209, although this is unlikely to be the main
375 mechanism in rats, contrary to fish species.[54] Debromination was also reported in indoor
376 environments by the action of sunlight or bacteria degradation, but SRM 2585 is unlikely to be
377 subject to debromination as the dust was sterilized[46] and stored in darkness. The second
378 phenomena hypothesized by Abdallah and Stuart was the bioaccumulation of BDE 153 over time
379 in fatty tissues, explained by the longer BDE 153 half-life (6.5 years), although this is not
380 relevant to the length of rat studies (<14 weeks). Huwe at al. observed that BDE 153 has a higher
381 bioconcentrating potential than BDE 154, another hexa-brominated congener, which could be
382 explained by the low metabolism of BDE 153 compared to BDE 154.[54] The case of BDE 153
383 seems peculiar and more studies, on different types of dust, would be necessary to assess
384 whether the bioaccessibility measurement method needs to be optimized for this compound or if
385 a correction factor should be applied based on *in vivo* phenomena explaining the difference
386 between this BDE and the other congeners. Regarding pyrethroids, there is neither
387 bioaccessibility data nor bioavailability data available to date for SRM 2585. Such data would be
388 necessary to validate the results from the present work.

389 **QA/QC results.**

390 All extraction blank and QC samples in this study were compliant to our protocols. SVOC
391 measurements were < limit of detection (LOD) in all extraction blanks. For XAD-2 extraction
392 QCs, measured concentrations were within 89 and 106% of the spiked value, with a relative
393 standard deviation (RSD) ranging from 5 to 17% (SI Table 4-A). For dust extraction QCs spiked
394 in Celite® 545, performances were also satisfactory, with measured concentrations between 93
395 and 104% of the spiked value, and RSDs ranging from 3 to 16% (SI Table 4-B). Regarding the

396 extractions of SRM 2585, measured concentrations were between 82 and 115% of the certified
397 or reference value, and RSDs ranged between 3 and 18% (Table 2).

398 Incubation blank and QC samples were also assessed: concentrations in incubation blanks were
399 all below the LOD and confirm the absence of any source of contamination from the XAD-2
400 insert, intestinal fluid, and glassware. Incubation QCs confirm the capacity of XAD®-2 to adsorb
401 the SVOCs released in the intestinal fluid. For the lower spiking level, the concentrations
402 measured were between 62 and 100% of the spiked concentrations, with RSD ranging from 14 to
403 38% (SI Table 5-A). These greater RSD percentages are not surprising because SVOCs were
404 spiked at the LOQ level. For the higher spiking level, measured concentrations were within 67
405 and 94% of the spiked concentrations with RSDs ranging from 12 to 23%, except for BDE 153
406 that showed a 49% RSD, which could be due to an occasional lack of instrumental sensibility (SI
407 Table 5-B). For both spiking levels, the lowest recoveries concerned tetramethrin. This is also
408 true for SRM 2585, when comparing the sum of the bioaccessible and non-bioaccessible
409 concentrations to the total measured concentration (Table 3). While recoveries were all
410 satisfactory, ranging from 77% to 110%, the lowest value concerns tetramethrin and the
411 possibility of a minor loss caused by degradation during the incubation process cannot be
412 excluded.

413 **Bioaccessibility of pyrethroids and PBDEs in 30 school dust samples.**

414 The distribution of bioaccessible and total (bioaccessible + non-bioaccessible) pyrethroid and
415 PBDE concentrations found in classrooms are shown in Table 4 and graphically represented in
416 Chart4. To allow for a meaningful calculation of bioaccessibility for each sample, after removal
417 of all concentrations < LOD/2 in XAD®-2 or dust, results between LOD/2 and LOQ for XAD®-2
418 were kept, provided that the concentration in the corresponding residual dust was > LOQ, in

order to avoid a meaningless null bioaccessibility. If the concentration in the corresponding dust was < LOQ then the results in XAD®-2 and residual dust were both removed. Likewise, results between LOD/2 and LOQ for dust were kept if the corresponding XAD®-2 concentration was >LOQ, to avoid a meaningless 100% bioaccessibility. If the concentration in the corresponding XAD®-2 was < LOQ then the results in residual dust and XAD®-2 were both removed. Bioaccessibility data are shown in Chart4. Median bioaccessibilities ranged from 0% (for BDE 153) to 100 % (for tetramethrin), even though these two compounds might not be the most representative of the study as they were only quantified 5 times and once, respectively. For the three compounds that were more frequently detected, i.e. permethrin (n=28), BDE 47 (n=26) and BDE 99 (n=24), median bioaccessibilities ranged from 37 to 48%. The variability between samples was moderate, with a difference between the 75th and 25th percentiles of 25, 22, and 28% for permethrin, BDE 47, and BDE 99, respectively, although values as low as 10% (for BDE 99) or as high as 92 % (also for BDE 99) could also be observed. Chart4 also shows that measured bioaccessibilities were not dependent on the initial SVOC content present in the dust. A comparison with results from the literature was undertaken. As explained in our previously published literature review, SVOC bioaccessibilities can vary according to the measurement method that is being used, one of the main influencing factors being the presence of an adsorbent acting as a "sink" for SVOCs released from the dust into the digestive solution[26,68]. The scientific literature on the subject is still scarce, and to the best of our knowledge, only four articles documenting the bioaccessibility of SVOCs in dust, measured in the presence of an adsorbent, have been published so far, on organophosphate flame retardants (OPFRs)[27], PBDEs[27,28], and more recently on pyrethroids[29] and polycyclic aromatic hydrocarbons (PAHs)[53]. For pyrethroids and PBDEs, our results are in accordance with those published previously (Table 5). While more

data are needed for the compounds not frequently detected in our studies, it is worth considering the bioaccessibility of PBDEs and the less volatile pyrethroids permethrin and cypermethrin, as the resulting impact on human exposure could be lowered by a minimum of 50 %. Moreover, for an accurate assessment of the effect of environmental exposure on human health, the bioaccessibility of SVOCs should be considered individually for each sample, because of the wide range between minima and maxima.

Proposal of a simplified method. In this project, a new simplified method is proposed for the evaluation of the bioaccessibility of SVOCs in indoor settled dust. This simplified method, which no longer includes a gastric compartment, consists of 20 hours of incubation at a neutral pH in the presence of bile, pancreatin, and XAD-2 as sorbent sink. The analysis of indoor environmental samples showed some limitations to the use of the XAD®-2 insert as dust fibers tend to be caught in the insert's creases, which necessitate some tedious manual removal. One way around this problem could be to heat seal the insert and give it a flat square shape that would eliminate the presence of creases. Another way around this problem would be to pursue the use of a cellulose membrane, as in the authors' previous work,[28] only by selecting a membrane with bigger pore size, to favor the adsorption of SVOC with slower kinetics of release and adsorption. Another limit to this method is the lack of inter-laboratory studies carried on the same environmental samples. However, the validation data are satisfactory and the first results are promising as they are consistent with previous studies. The bioaccessible SVOC fraction is the concentration of choice for human exposure assessment studies and for more precise associations between indoor environmental exposure to dust and health outcome in epidemiological studies. Using the present method, the knowledge of this bioaccessible fraction is made easy and cost

efficient as it only necessitates the analysis of the XAD®-2 inserts, emphasizing the simplicity of the method as a strength for the analysis of numerous samples in the future.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

SI Figure 1: Design of the XAD®-2 insert

SI Table 1: Percentage of bioaccessible SVOC in the digestive fluid after 4 or 20 hours of intestinal incubation for SRM 2585 triplicates.

SI Table 2: Impact of sixteen different gastric and intestinal conditions on SRM 2585 dissolution

SI Table 3: Spearman test of the correlation between bioaccessibility and dust dissolution

SI Table 4: SVOC concentrations in extraction QC samples

SI Table 5: SVOC concentrations in incubation QC samples

SI Chart 1: Comparison between SVOC bioaccessibilities measured with Tenax® TA and XAD®-2 in 3 replicates of SRM 2585.

SI Chart 2: Effect of dust dissolution on SVOC bioaccessibility

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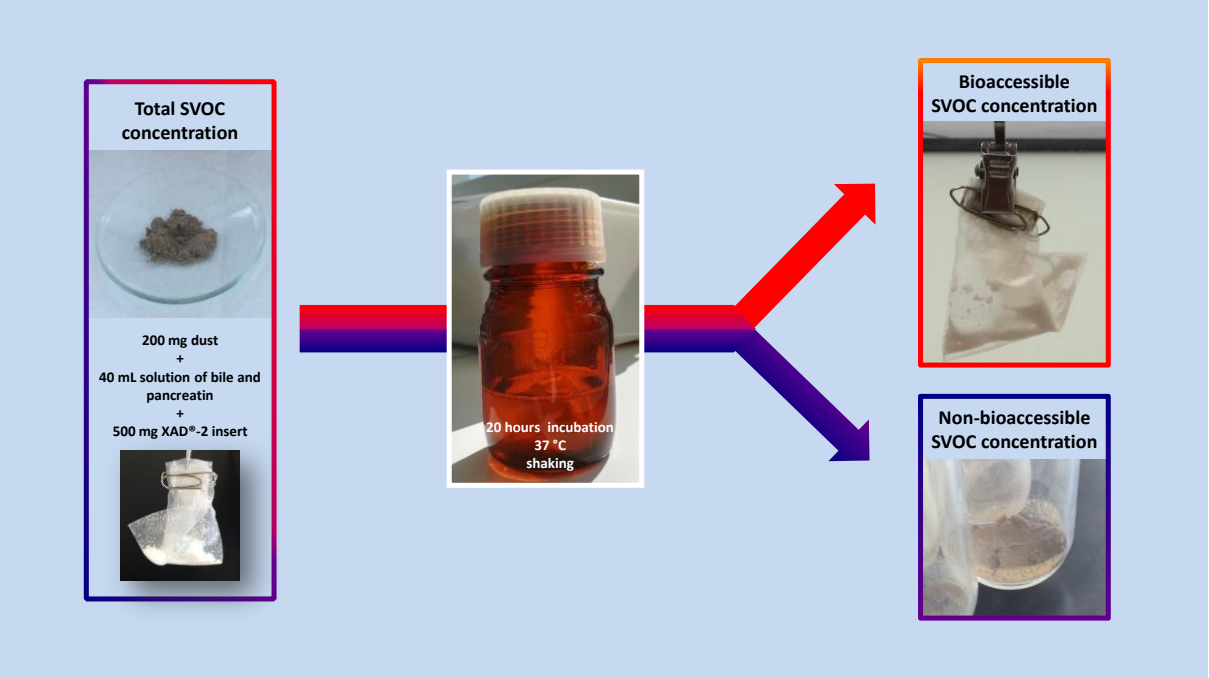
696 TOC Art



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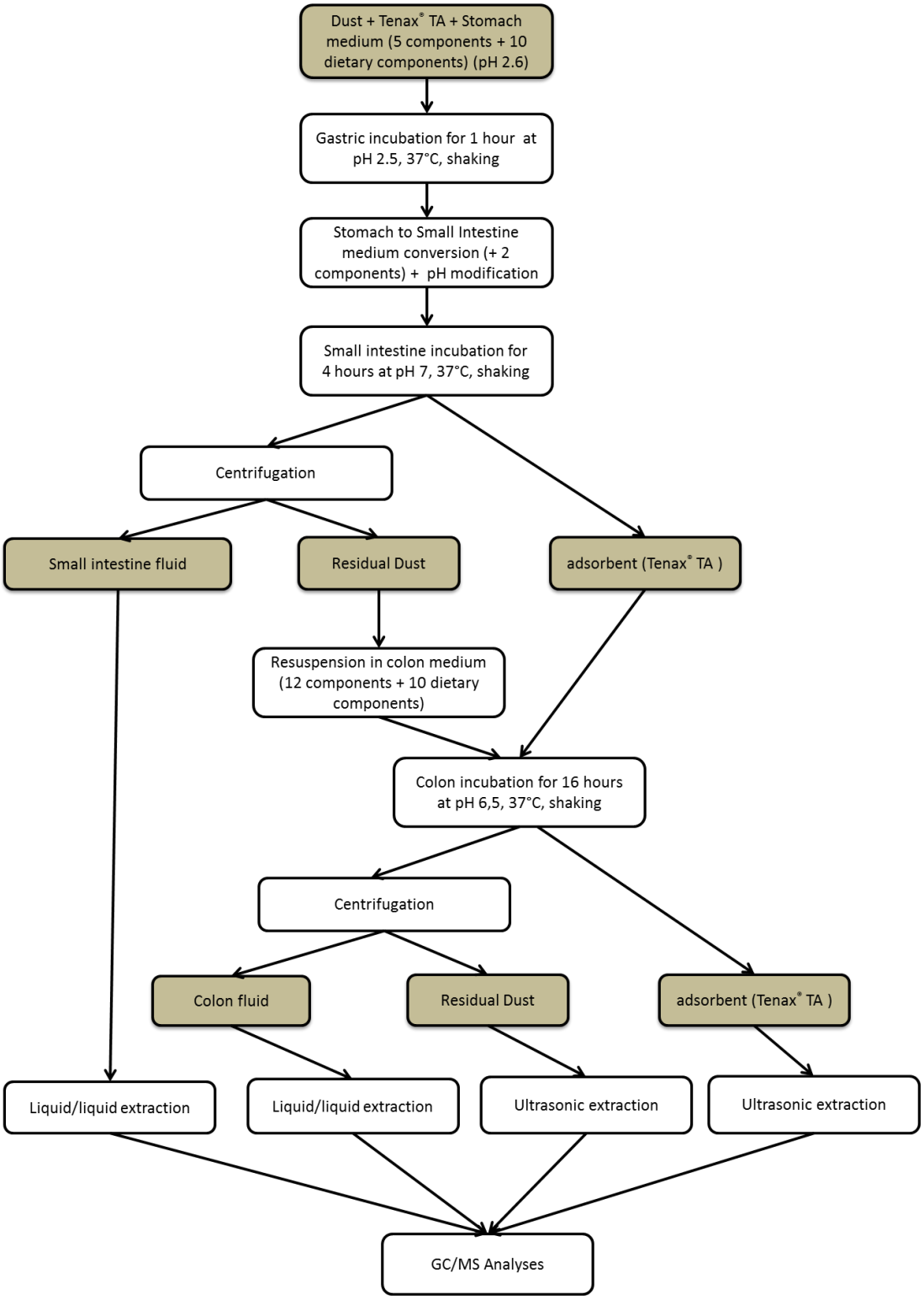
698 FIGURES



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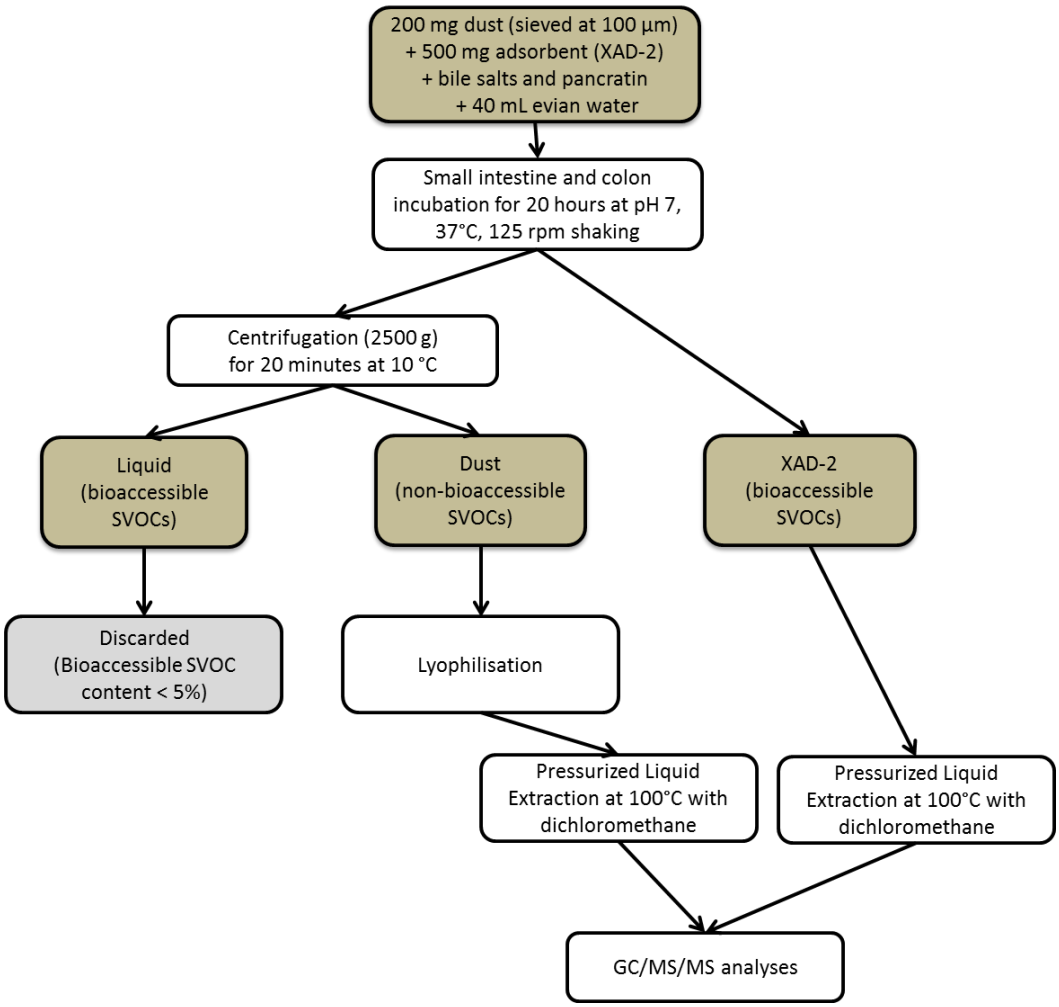
700 Figure 1: Reference *in vitro* method for measuring SVOC bioaccessibility



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702 Figure 2: Simplified *in vitro* method for measuring SVOC bioaccessibility

703

704 TABLES

705 Table 1: Evaluation of operator's time in hours, for a batch of 8 samples

	Reference method	Simplified method
Media preparation	2:00	0:30
Inserts preparation	1:00	1:00
Sample preparation	0:30	0:30
Gastric incubation	0:15	
Conversion to intestinal conditions	2:00	
Intestinal incubation		0:15
Small intestine incubation	0:15	
Centrifugation	0:30	0:30
Resuspension of residual dust in colon fluid	0:30	
Colon incubation	0:15	
Centrifugation	0:30	
Small intestinal fluid LL extraction + concentration + purification	8:00	
Colon fluid extraction + concentration + purification	8:00	
Dust extraction + concentration + purification	8:00	8:00
Sorbent extraction + concentration + purification	8:00	8:00
Total time	39:45	18:45
Time per sample	4:58	2:20

706

707 Table 2: Total SVOC concentrations in SRM 2585

	n	Total concentration (ng/g)	RSD (%)	Certified or reference concentration in SRM 2585 (ng/g)	Total / Certified or reference concentration (%)
Pyrethroids					
Cyfluthrin	4	3063	15%	3730	82%
Cypermethrin	4	3192	18%	4050	79%
Permethrin	4	5710	3%	4970	115%
Tetramethrin	4	330	18%	356	93%
PBDEs					
BDE 47	4	531	6%	497	107%
BDE 85	4	42.7	10%	43.8	97%
BDE 99	4	823	5%	892	92%
BDE 100	4	130	8%	145	90%
BDE 153	3	137	10%	119	115%

708

709

710 Table 3: bioaccessible and non-bioaccessible SVOC concentrations in SRM 2585.

	n	Bioaccessible concentration (ng/g)	RSD (%)	Non-bioaccessible concentration (ng/g)	RSD (%)	Bioaccessible + non-bioaccessible concentrations (ng/g)	Bioaccessible + non-bioaccessible / total concentration in Table 2 (%)	Bioaccessibility (%)	RSD (%)
Pyrethroids									
Cyfluthrin	8	1530	14%	1480	45%	3008	98%	53%	16%
Cypermethrin	8	1680	16%	1530	19%	3213	101%	52%	13%
Permethrin	8	3310	12%	2510	15%	5813	102%	57%	7%
Tetramethrin	8	211	22%	44.0	69%	255	77%	83%	13%
PBDEs									
BDE 47	8	396	13%	188	23%	583	110%	68%	9%
BDE 85	8	18.9	25%	23.3	22%	42.2	99%	45%	14%
BDE 99	8	373	12%	389	10%	762	93%	49%	8%
BDE 100	8	68.6	4%	67.9	13%	136	105%	50%	7%
BDE 153	6	45.2	44%	77.6	60%	123	89%	40%	41%

711

712

713 Table 4: Distribution of the bioaccessible, non-bioaccessible, and total concentrations of
714 pyrethroids and PBDEs in the indoor settled dust of 30 French classrooms (ng/g)

				Bioaccessible concentrations			Non-bioaccessible concentrations			Total concentrations		
	LOD	LOQ	n	min	median	max	min	median	max	min	median	max
Cyfluthrin	12.5	25	0	-	-	-	-	-	-	-	-	-
Cypermethrin	25	37.5	10	40	93	320	110	190	430	53	190	590
Tetramethrin	12.5	25	5	69	260	490	390	390	390	69	270	650
Permethrin	25	62.5	28	79	420	2100	190	780	3800	440	1300	5900
BDE 47	5.0	12.5	26	8.7	25	910	7.0	28	2400	21	57	3300
BDE 85	5.0	12.5	4	5.9	10	15	9.8	12	23	21	24	29
BDE 99	5.0	12.5	24	3.3	34	510	3.4	45	800	16	87	990
BDE 100	5.0	12.5	11	4.6	20	87	7.9	30	250	18	51	320
BDE 153	25	50	1	-	-	-	62	62	62	62	62	62

715

716 Table 5: Comparison of SVOC bioaccessibilities with the literature data

	This study				Fang and Stapleton[27]				Kademoglou et al.[28]		Wang et al.[29]	
Substance	n	min	median	max	n	min	median	max	n	median	n	median
Cyfluthrin	0	-	-	-							1	53%
Cypermethrin	10	23%	43%	100%							1	33%
Permethrin	28	12%	38%	83%							1	48%
Tetramethrin	5	40%	100%	100%							-	-
BDE 47	26	20%	48%	84%	17	53%	71%	89%	1	59%		
BDE 85	4	20%	47%	60%					-	-		
BDE 99	24	10%	37%	92%	17	43%	71%	85%	-	-		
BDE 100	11	13%	36%	72%	17	41%	68%	84%	1	46%		
BDE 153	1	0%	0%	0%	17	38%	55%	79%	1	45%		

717

718 CHARTS

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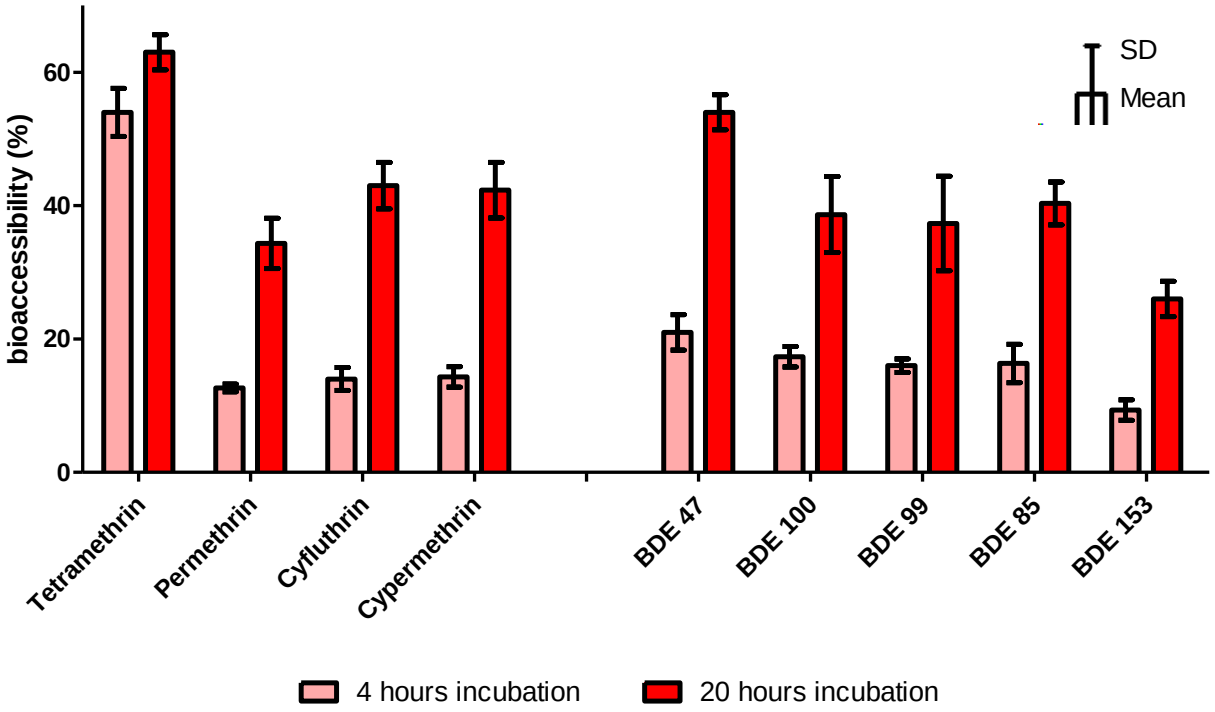
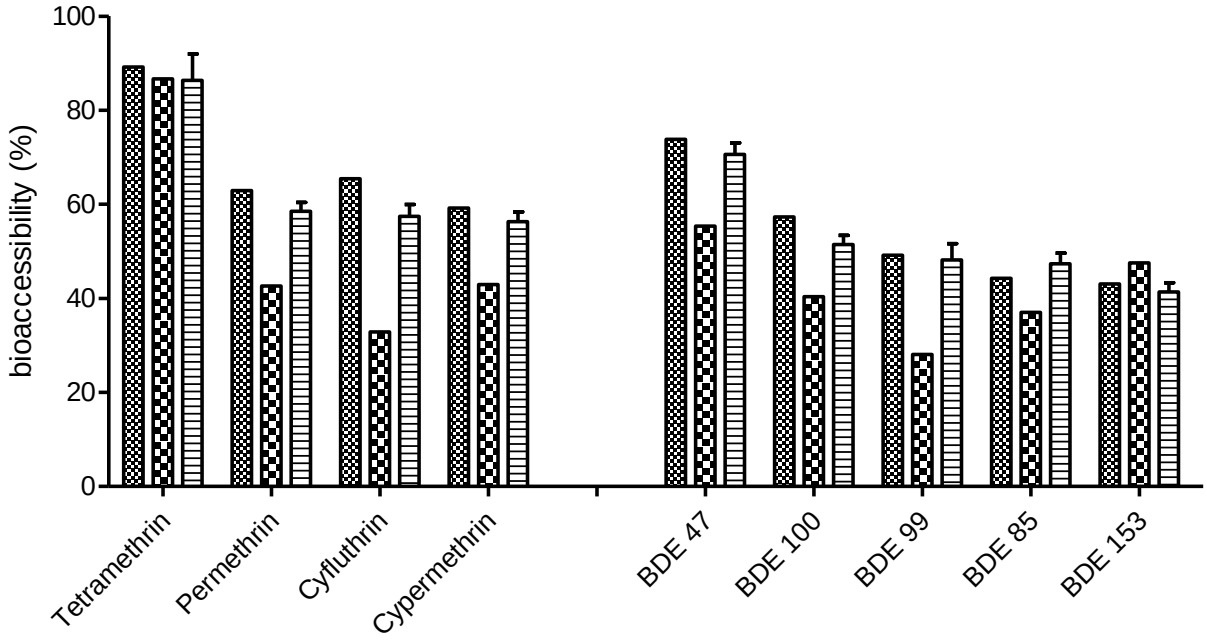


720

721 Chart 1: Effect of the duration of intestinal incubation on the bioaccessibility of pyrethroids and

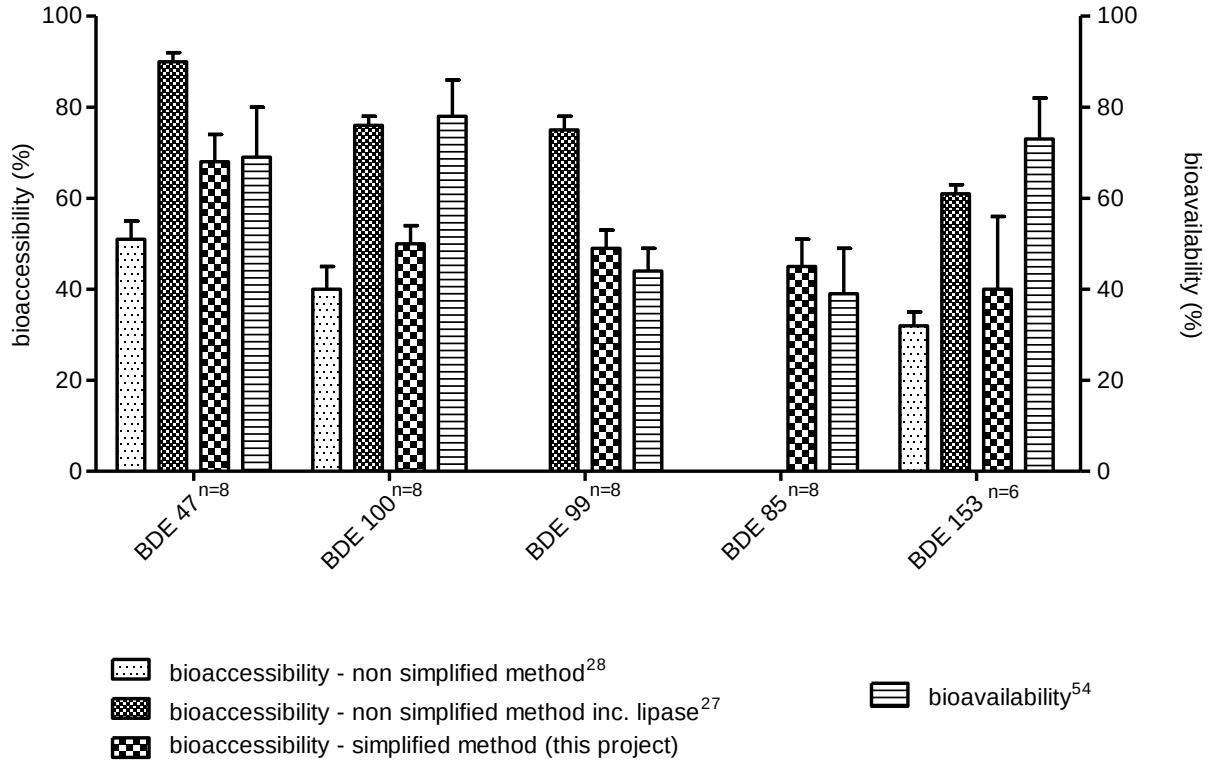
722 PBDEs in triplicates of SRM 2585.



	Test	n	Gastric conditions (37°C, 1 hour)	Intestinal condition (37°C)
	test 13	1	Buffer, pH 2.6[c], pepsin[d]	20 hours, pancreatin[g]
	test 15	1	Evian water, pH 2.5 after[b], pepsin[d]	20 hours, bile salts[e],pancreatin[g]
	test 16	5	/	20 hours, bile salts[e],pancreatin[g]

Chart 2: Effect of *in vitro* gastro-intestinal conditions on SVOC bioaccessibilities in SRM 2585.

[b]immersion of 200 mg of dust in 40 mL of Evian water followed by acidification at pH 2.5 with 35% HCl, [c]immersion of 200 mg of dust in 40 mL of pH 2.6 Citrate-Phosphate Buffer, [d]pepsin concentration: 1.25g/L, [e]bile salts concentration: 1.78g/L, [g]pancreatin concentration: 0.5 g/L.



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730 Chart 3: Bioaccessibility and bioavailability of PBDEs in SRM 2585. Error bars represent one

731 SD of triplicate measurements except indicated otherwise on the chart.

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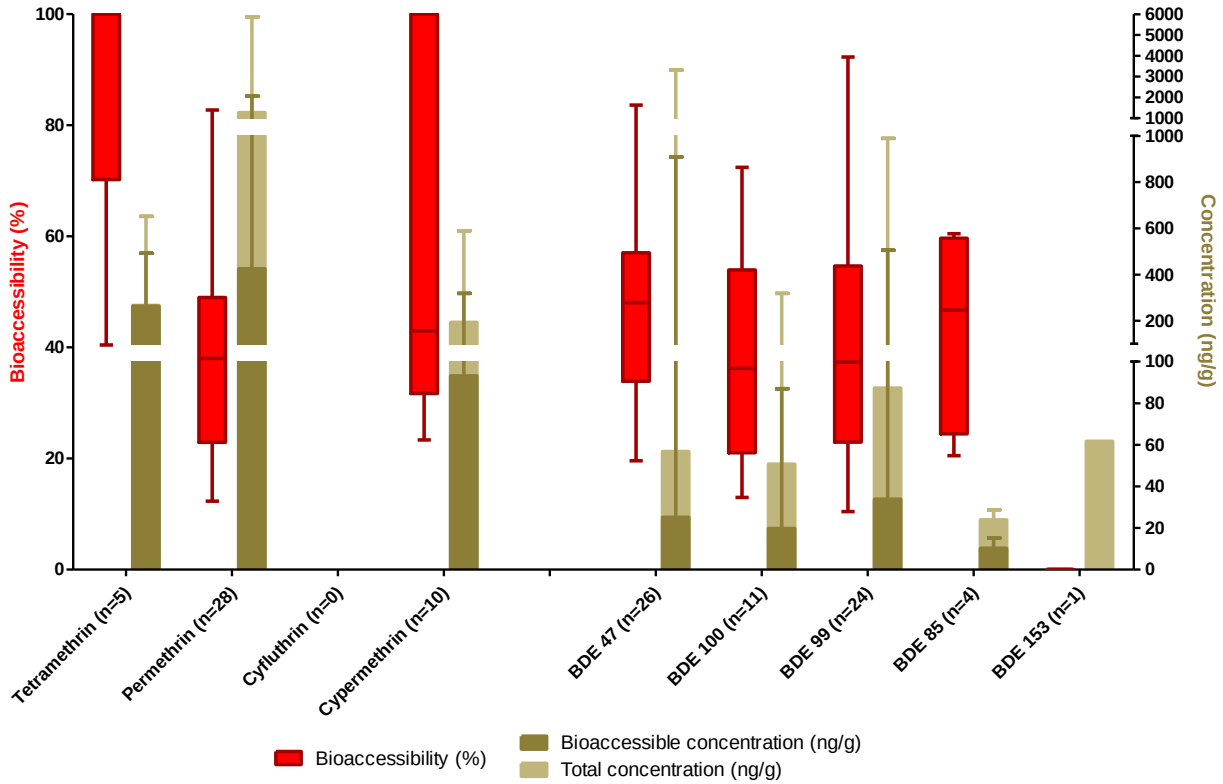

733
734 Chart 4: Bioaccessibility and bioaccessible and total concentrations of pyrethroids and PBDEs in
735 the indoor settled dust of 30 French classrooms

736

SUPPORTING INFORMATION

Oral bioaccessibility of SVOCs in indoor settled dust: a simplified *in vitro* method applied to polybrominated diphenyl ethers (PBDEs), and pyrethroids.

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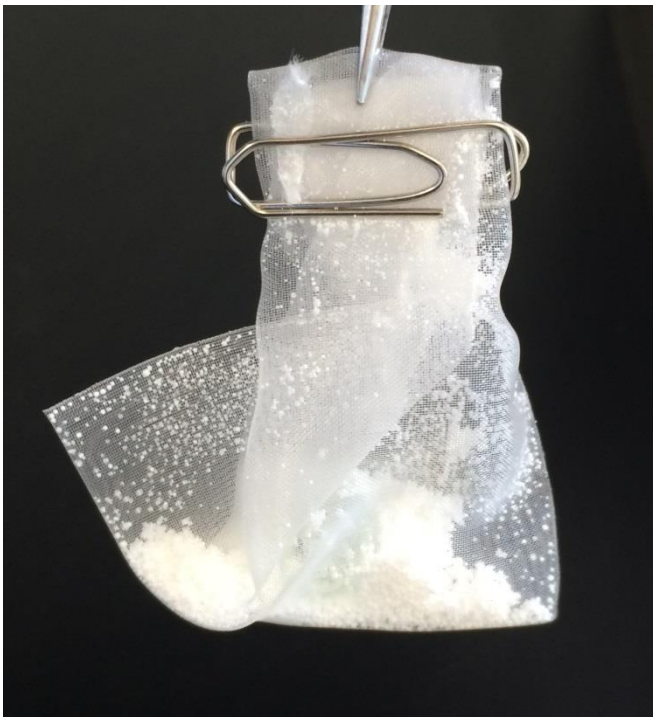
FIGURES



SI Figure 1: Design of the XAD®-2 insert

TABLES

SI Table 1: Percentage of bioaccessible SVOC in the digestive fluid after 4 or 20 hours of intestinal incubation for SRM 2585 triplicates.

% COSV in fluid	4 hours -1	4 hours -2	4 hours -3	20 hours -1	20 hours -2	20 hours -3
Cyfluthrin	0%	0%	3%	1%	1%	1%
Cypermethrin	0%	0%	0%	0%	1%	0%
Permethrin	3%	0%	0%	1%	1%	1%
Tetramethrin	0%	0%	0%	0%	0%	0%
BDE 47	0%	0%	0%	0%	0%	0%
BDE 85	0%	0%	0%	0%	0%	0%
BDE 99	0%	0%	0%	0%	0%	0%
BDE 100	0%	0%	0%	0%	0%	0%
BDE 153	-	-	-	0%	0%	0%

SI Table 2: Impact of sixteen different gastric and intestinal conditions on SRM 2585 dissolution

Test	n	Gastric conditions (37°C, 1 hour)	pH Neutralization	Intestinal conditions (37°C)	% Dust dissolution
1	3	Evian water, pH 2.5 before[a]		4 hours	44.0% ± 2.0%
2	3	Buffer, pH 2.6[c]		/	30.7% ± 6.7%
3	3	Buffer, pH 2.6[c]		4 hours	23.4% ± 9.3%
4	3	Buffer, pH 2.6[c]		24 hours	30.3% ± 1.5%
5	3	Evian water, pH 2.5 after[b]		4 hours	47.5% ± 5.2%
6	3	Evian water, pH 2.5 after[b]		4 hours, bile salts[e]	43.4% ± 2.1%
7	3	Evian water, pH 2.5 after[b]	addition of saturated $NaHCO_3$	20 hours, bile salts[e]	48.2% ± 3.4%
8	3	Evian water, pH 2.5 after[b]		20 hours	43.6% ± 2.7%
9	1	Evian water, pH 2.5 after[b]		24 hours	43.8%
10	1	Evian water, pH 2.5 before[a]		20 hours	53.8%
11	3	Evian water, pH 2.5 after[b]		20 hours, lipase[f]	55.5% ± 2.3%
12	3	Buffer, pH 2.6[c], pepsine[d]		20 hours	48.6% ± 3.2%
13	1	Buffer, pH 2.6[c], pepsine[d]		20 hours, pancreatin[g]	58.3%
14	3	Evian water, pH 2.5 after[b], pepsine[d]		20 hours, bile salts[e]	41.7% ± 3.5%
15	1	Evian water, pH 2.5 after[b], pepsine[d]		20 hours, bile salts[e],pancreatin[g]	58.9%
16	5	/	/	20 hours, bile salts[e],pancreatin[g]	58.6% ± 3.0%

[a]immersion of 200 mg of dust in 40 mL of Evian water previously acidified at pH 2.5 with 35% HCl
[b]immersion of 200 mg of dust in 40 mL of Evian water followed by acidification at pH 2.5 with 35% HCl
[c]immersion of 200 mg of dust in 40 mL of pH 2.6 Citrate-Phosphate Buffer
[d]pespine concentration: 1.25g/L
[e]bile salts concentration: 1.78g/L
[f]lipase concentration: 1.6 g/L
[g]pancreatin concentration: 0.5 g/L

SI Table 3: Spearman test of the correlation between bioaccessibility and dust dissolution

Parameter	Cyfluthrin	Cypermethrin	Permethrin	Tetramethrin	BDE 47	BDE 85	BDE 99	BDE 100	BDE 153
Number of XY Pairs	16	16	16	16	16	16	16	16	16
Spearman r	0.5845	0.5801	0.5816	0.7926	0.5993	0.6849	0.4945	0.5889	0.4694
95% confidence interval	0.1090 to 0.8423	0.1024 to 0.8404	0.1046 to 0.8410	0.4767 to 0.9272	0.1314 to 0.8488	0.2715 to 0.8849	-0.01785 to 0.8011	0.1157 to 0.8443	-0.05049 to 0.7891
P value (two-tailed)	0.0174	0.0185	0.0181	0.0003	0.0142	0.0034	0.0515	0.0164	0.0666
P value summary	*	*	*	***	*	**	ns	*	ns
Exact or approximate P value?	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation
Is the correlation significant? (alpha=0.05)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No

SI Table 4: SVOC concentrations in extraction QC samples

(A) SVOC concentrations in XAD-2 extraction QC samples spiked at Level 2 (8 x LOQ) in XAD-2 insert

	LOQx8 (ng/g)	n	Measured concentration (ng/g)	RSD (%)	Measured / spiked concentration (%)
Pyrethroids					
Cyfluthrin	100	3	92	15%	92%
Cypermethrin	100	3	96	17%	96%
Permethrin	500	3	520	17%	103%
Tetramethrin	100	3	89	11%	89%
PBDEs					
BDE 47	100	3	94	7%	94%
BDE 85	100	3	96	5%	96%
BDE 99	100	3	96	11%	96%
BDE 100	100	3	93	8%	93%
BDE 153	200	3	210	13%	106%

(B) SVOC concentrations in dust extraction QC samples spiked at Level 2 (8 x LOQ) in Celite® 545

	LOQx8 (ng/g)	n	Measured concentration (ng/g)	RSD (%)	Measured / spiked concentration (%)
Pyrethroids					
Cyfluthrin	100	3	93	15%	93%
Cypermethrin	100	3	95	16%	95%
Permethrin	500	3	480	3%	97%
Tetramethrin	100	3	95	15%	95%
PBDEs					
BDE 47	100	3	100	6%	101%
BDE 85	100	3	90	8%	90%
BDE 99	100	3	100	11%	104%
BDE 100	100	3	94	14%	94%
BDE 153	200	2	190	10%	93%

SI Table 5: SVOC concentrations in incubation QC samples

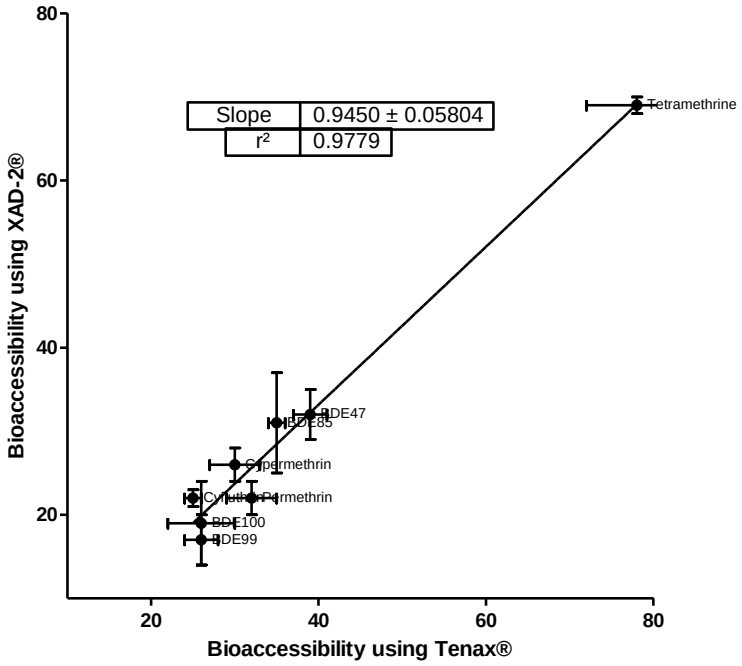
(A) SVOC concentrations in incubation QC samples spiked at Level 1 (LOQ)

	LOQ (ng/g)	n	Measured concentration (ng/g)	RSD (%)	Measured / spiked concentration (%)
Pyrethroids					
Cyfluthrin	25	8	20	38%	78%
Cypermethrin	37.5	8	37	29%	99%
Permethrin	62.5	8	63	14%	100%
Tetramethrin	25	8	15	28%	62%
PBDEs					
BDE 47	12.5	8	11	15%	90%
BDE 85	12.5	8	12	17%	93%
BDE 99	12.5	8	11	29%	85%
BDE 100	12.5	8	9.9	33%	79%
BDE 153	50	5	36	31%	72%

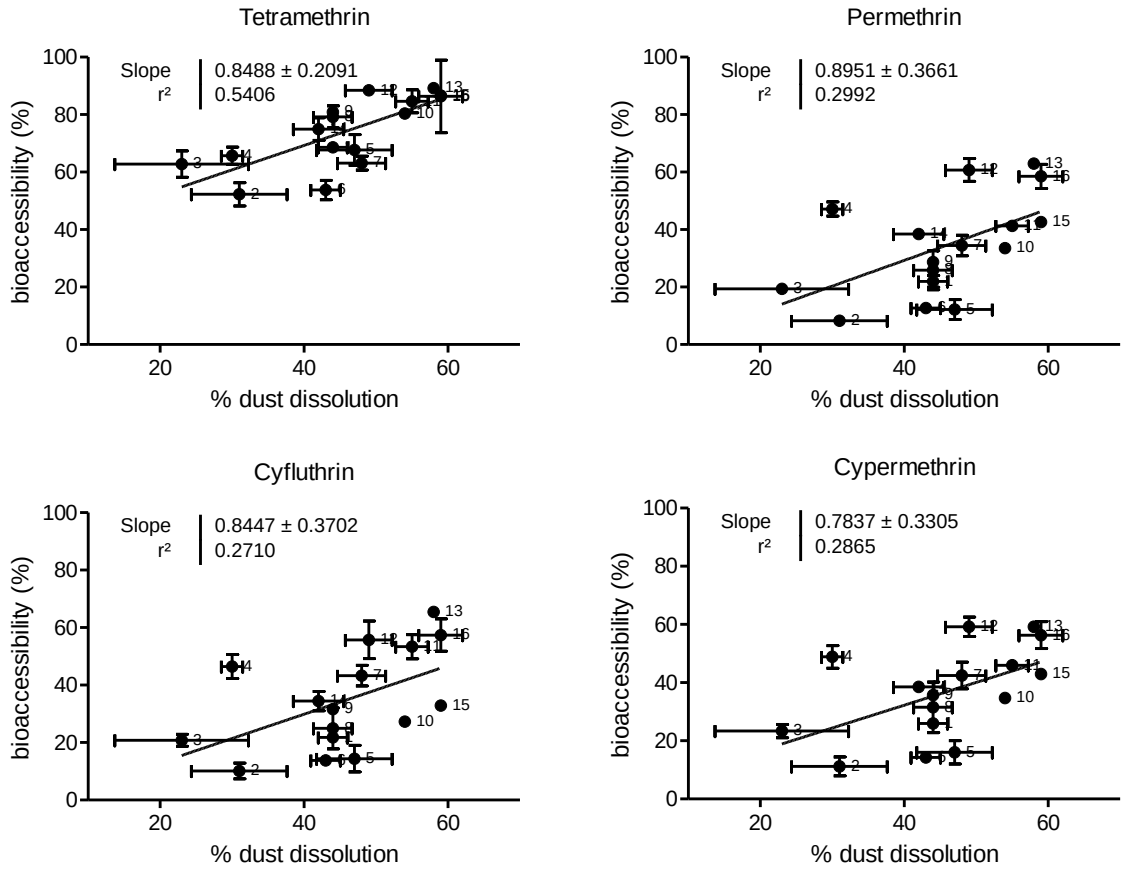
(B) SVOC concentrations in incubation QC samples spiked at Level 2 (8 x LOQ)

	LOQx8 (ng/g)	n	Measured concentration (ng/g)	RSD (%)	Measured / spiked concentration (%)
Pyrethroids					
Cyfluthrin	100	8	76	20%	76%
Cypermethrin	100	8	77	27%	77%
Permethrin	500	8	460	16%	93%
Tetramethrin	100	8	67	23%	67%
PBDEs					
BDE 47	100	8	94	15%	94%
BDE 85	100	8	85	12%	85%
BDE 99	100	8	84	13%	84%
BDE 100	100	8	85	13%	85%
BDE 153	200	6	170	49%	84%

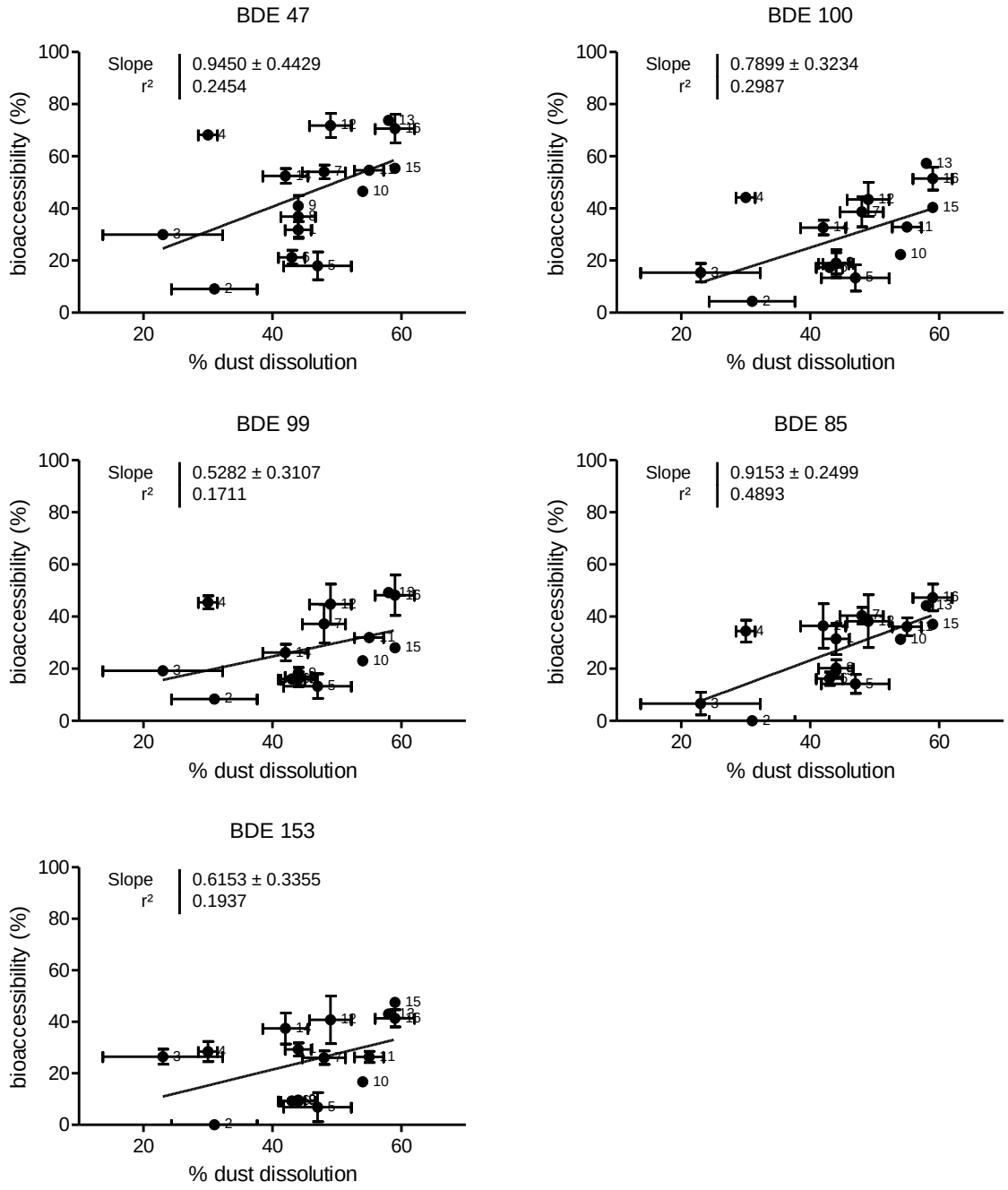
CHARTS



SI Chart 1: Comparison between SVOC bioaccessibilities measured with Tenax® TA and XAD®-2 in 3 replicates of SRM 2585. Error bars represent one SD.



SI Chart 2: Effect of dust dissolution on pyrethroids' bioaccessibility



SI Chart 2: Effect of dust dissolution on PBDEs' bioaccessibility

2. APPLICATION A DES ECHANTILLONS REELS

La méthode simplifiée d'analyse de la bioaccessibilité des COSV dans les poussières a été mise en œuvre sur 30 échantillons, comme indiqué dans l'article précédent, pour les PBDE et les pyréthrinoïdes. Pour 7 de ces échantillons (correspondant à une série d'analyse), une mesure de la bioaccessibilité d'une liste beaucoup plus complète de COSV a également été réalisée. Cette liste est adaptée de la liste des composés d'intérêt présentés dans le premier article de ce mémoire et est détaillée dans le Tableau 3. Elle exclut les composés pour lesquels aucune concentration supérieure à la LQ n'a été mesurée dans aucun des extraits bioaccessibles ou non-bioaccessible des échantillons ni du SRM 2585.

TABLEAU 3 : LISTE DES COSV RETENUS POUR LES MESURES DE BIOACCESSIBILITE ORALE

Famille	Substance
Pesticides organophosphorés	Chlorpyriphos-éthyl et diazinon
Pesticides organochlorés	4,4'-DDE, 4,4'-DDT, aldrine, α-endosulfan, α-HCH, dieldrine et γ-HCH
Oxadiazolones	Oxadiazon
Pyréthrinoïdes	Cyfluthrine, cyperméthrine, perméthrine et tétraméthrine
Esters phosphoriques	Tributylphosphate
Muscs polycycliques	Galaxolide (HHCB) et tonalide (AHTN)
Hydrocarbures aromatiques polycycliques (HAP)	Acénaphtène, anthracène, benzo[a]pyrène, fluoranthène, fluorène, phénanthrène et pyrène
Polychlorobiphényles (PCB)	PCB 28, 31, 52, 101, 105, 118, 138, 153 et 180
Phtalates	BBP, DBP, DEHP, DEP, DiBP et DiNP
Polybromodiphényléthers (PBDE)	BDE 47, 85, 99, 100 et 153

La suite de ce chapitre explique plus précisément le choix de sélectionner des poussières collectées dans des établissements scolaires et la méthode de sélection des 30 échantillons. En deuxième partie sont présentés les résultats de mesure de la bioaccessibilité de la liste complète des COSV pour les 7 échantillons.

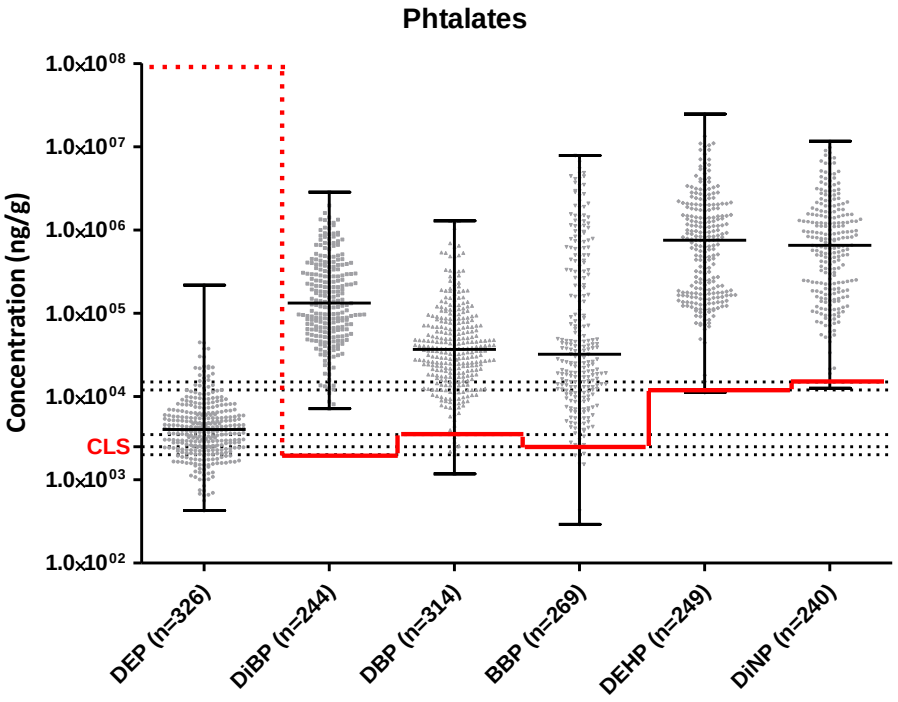
2.1. SELECTION DES ECHANTILLONS

La méthode simplifiée a été appliquée à 30 échantillons de poussière déposée au sol de la campagne nationale « écoles » menée en France par l'Observatoire de la Qualité de l'air intérieur de 2013 à 2017. Le choix de poussières issues de salles de classe est justifié d'une part par les fortes concentrations en certains COSV (notamment les phtalates) qui les caractérisent, d'autre part du fait de l'exposition spécifique des enfants de 3 à 11 ans qui fréquentent l'école 16 % de leur temps. Dans le cadre de la campagne nationale « écoles », des échantillons de poussière sédimentées de 600 salles de classe ont été prélevées entre 2013 et 2017. Pour la détermination de COSV et des métaux, ils ont été tamisés à 100µm, puis stockés au congélateur dans des conditions permettant la conservation des COSV. Trente échantillons de cette collection ont été utilisés pour le présent projet.

La solution du tirage au sort pour la sélection des 30 échantillons n'a pas été retenue, d'une part car pour de nombreux échantillons, le reliquat de poussière disponible était inférieur à la prise d'essai de 200 mg définie dans le cadre du développement de la méthode de mesure de bioaccessibilité. D'autre part, il était pertinent de s'intéresser principalement aux PBDE pour lesquels la validation par des données de biodisponibilité avait été possible pour le SRM 2585. Certaines données *in vivo* sont également disponibles permettant la validation de la bioaccessibilité des phtalates, mais la présence des phtalates dans les échantillons n'a pas été retenue comme critère de sélection, du fait de leur caractère ubiquitaire dans les échantillons de la campagne nationale « écoles » (Figure 13). En revanche les échantillons contenant des PBDE sont plus rares (Figure 14) et ont été sélectionnés de manière privilégiée.

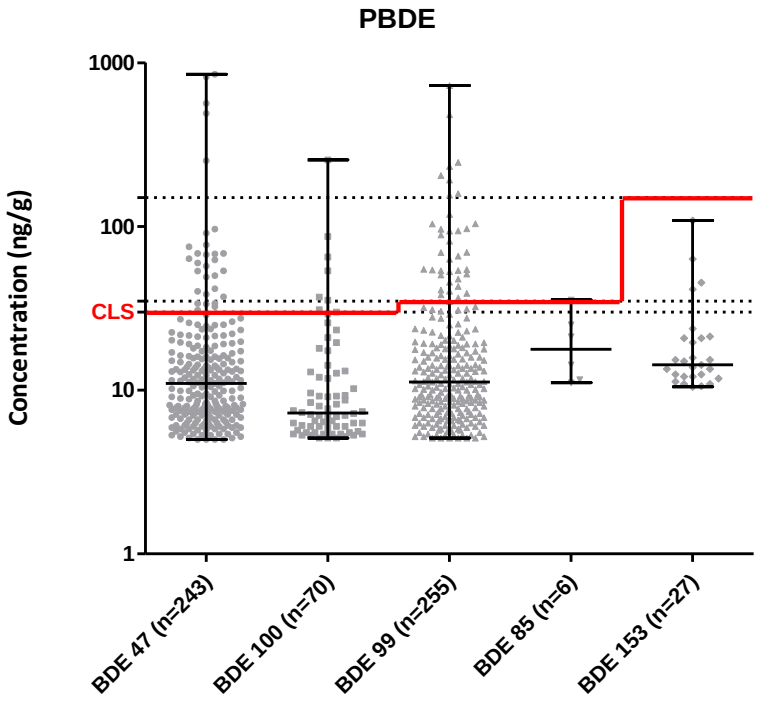
La sélection de 30 échantillons s'est donc opérée selon trois critères :

- Masse de poussière disponible
- Présence de PBDE dans l'échantillon
- Concomitance de plusieurs PBDE différents



CLS: concentration limite de sélection

FIGURE 13 : CONCENTRATIONS EN PHTALATES MESUREES DANS LES ECHANTILLONS DE LA CAMPAGNE NATIONALE « ECOLES » DE L'OQAI (2013-2017)



CLS : concentration limite de sélection

FIGURE 14 : CONCENTRATIONS EN PBDE MESUREES DANS LES ECHANTILLONS DE LA CAMPAGNE NATIONALE « ECOLES » DE L'OQAI (2013-2017)

DISPONIBILITE DE POUSSIERE RESTANTE APRES LES ANALYSES DE COSV ET DE METAUX

La prise d'essai nécessaire pour la détermination de la bioaccessibilité étant de 200 mg, tous les échantillons contenant moins de 220 mg de poussière ont été écartés, les 20 mg d'écart correspondant à une marge de sécurité pour permettre le prélèvement de la prise d'essai de 200 mg et pallier à d'éventuelles incertitudes de pesée ainsi qu'à la possibilité de prises d'essai multiples pour l'analyse des COSV par thermo désorption GC/MS/MS (prise d'essai de 2 mg). Sur les 582 échantillons disponibles au laboratoire, 253 présentaient un reliquat de moins de 220 mg et ont été écartés tandis que les 329 échantillons présentant un reliquat de poussière supérieur à 220 mg ont été conservés pour la suite de la sélection.

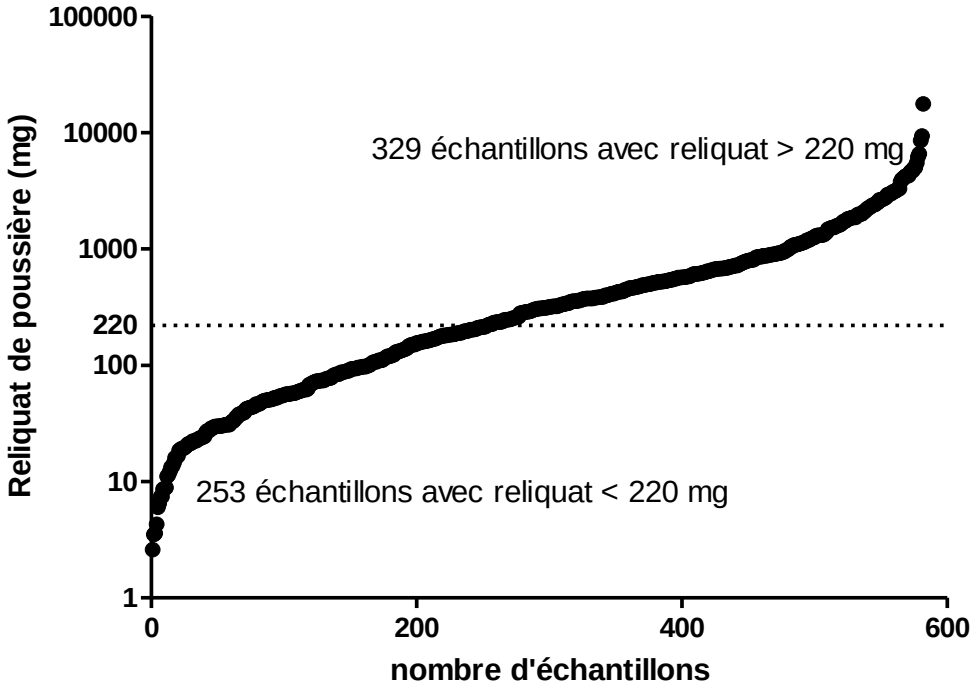


FIGURE 15 : CLASSEMENT DES ECHANTILLONS SELON LEUR MASSE DE POUSSIERE DISPONIBLE (RELIQUAT)

PRESENCE DE PBDE DANS LES ECHANTILLONS

La deuxième étape de la sélection a consisté à se concentrer sur les échantillons contenant un ou plusieurs PBDE avec des concentrations suffisamment élevées pour pouvoir être quantifiés analytiquement en tenant compte de leur bioaccessibilité. Les concentrations mesurées par TD-GC/MS/MS pendant la campagne nationale « écoles » ont été utilisées pour cette étape.

Afin de tenir compte de la répartition des COSV entre le XAD®-2 et la poussière résiduelle et sachant que dans chaque compartiment la concentration mesurée devait être supérieure à la LQ

analytique afin que l'équation « *bioaccessibilité = concentration bioaccessible / (concentration bioaccessible + concentration non-bioaccessible)* » ne soit pas entachée d'une trop forte incertitude, la procédure suivante a été adoptée, basée sur le ratio de bioaccessibilité mesurée lors du développement sur la poussière de référence SRM 2585 :

- Pour les substances dont la bioaccessibilité (« BA ») mesurée dans le SRM 2585 est supérieure à 50 %, la concentration limite de sélection ($CLS_{bioacc>50}$) a été calculée ainsi : $CLS_{bioacc>50}=LQ_{analytique}/(100-BA)$. Par exemple, pour une substance bioaccessible à 70 %, la concentration non-bioaccessible est de 30 %. Si sa LQ analytique est de 12,5 ng/g alors ne seront sélectionnés que les échantillons dont la concentration est supérieure à 42 ng/g.
- Pour les substances dont la bioaccessibilité est inférieure à 50 % dans le SRM 2585, la concentration limite de sélection ($CLS_{bioacc<50}$) a été calculée ainsi : $CLS_{bioacc<50}=LQ_{analytique}/BA$. Par exemple, pour une substance bioaccessible à 30 %, la concentration non-bioaccessible est de 70 %. Si sa LQ analytique est de 12,5 ng/g alors ne seront sélectionnées que les échantillons dont la concentration est supérieure à 18 ng/g.

Les concentrations limite de sélection (CLS) sont détaillées dans le Tableau 4 pour les PBDE ainsi que pour les phtalates et visibles sur les Figure 13s et Figure 14.

TABLEAU 4: CONCENTRATIONS LIMITE DE SELECTION (CLS) DES PHTALATES ET DES PBDE

Substance	Bioaccessibilité dans SRM2585	LQ analytique (ng/g)	CLS (ng/g)	CLS arrondie (ng/g)
DEP	100%	2500	∞	∞
DiBP	50%	1000	2000	2000
DBP	31%	1000	3230	3500
BBP	45%	1000	2220	2500
DEHP	9%	1000	11100	12000
DiNP	7%	1000	14300	15000
BDE47	57%	12.5	29	30
BDE100	49%	12.5	26	30
BDE99	39%	12.5	32	35
BDE85	36%	12.5	35	35
BDE153	68%	50	156	150

Pour la suite de la sélection, les échantillons avec des concentrations mesurées pendant la campagne nationale « écoles » inférieures à la CLS ont été exclus.

Au terme de cette deuxième étape, tous les échantillons contenant au moins un PBDE ont été conservés, soit 49 échantillons sur les 329 issus de l'étape précédente.

CONCOMITANCE DE PLUSIEURS PBDE DIFFERENTS

La troisième étape de la sélection a consisté à classer les 49 échantillons selon le nombre de PBDE différents qu'ils contenaient :

- 7 échantillons contenaient 3 PBDE différents ;
- 13 échantillons contenaient 2 PBDE différents ;
- 29 échantillons ne contenaient qu'un PBDE.

Les 20 échantillons contenant au moins deux PBDE différents ont été sélectionnés. Afin d'arriver à un total de 30, 10 échantillons supplémentaires ont été sélectionnés par tirage sort parmi les 29 ne contenant qu'un PBDE. La sélection finale des 30 échantillons de l'étude est présentée dans le Tableau 5.

TABLEAU 5 : LISTE DES ECHANTILLONS SELECTIONNES

Echantillons sélectionnés	Année de prélèvement	Masse poussière restante	Concentrations mesurées par TD-GC/MS/MS (ng/g)					nombre de PBDE différents
			BDE 47	BDE 85	BDE 99	BDE 100	BDE 153	
Ech. 01	2015	1148.6	489.9		481.9	53.6		3
Ech. 02	2017	1872.0	91.1		158.9	35.4		3
Ech. 03	2015	1980.3	819.3		96.3	37.0		3
Ech. 04	2016	2663.2	252.1		246.3	65.0		3
Ech. 05	2014	568.4	53.5		205.0	30.0		3
Ech. 06	2014	680.8	41.6		69.6			2
Ech. 07	2015	995.1			94.1			1
Ech. 08	2016	1312.5	33.6		65.9			2
Ech. 09	2016	1527.9	38.5		192.3	31.0		3
Ech. 10	2013	402.6	30.8		47.8			2
Ech. 11	2017	2291.8	67.9		155.6	29.2		3
Ech. 12	2013	3307.2	40.1		103.6			2
Ech. 13	2015	704.2			54.9			1
Ech. 14	2015	676.1			103.9			1
Ech. 15	2013	1084.3	59.8					1
Ech. 16	2014	914.2		35.6				1
Ech. 17	2015	308.7	564.8		50.5			2
Ech. 18	2014	223.1	33.8		54.7			2
Ech. 19	2017	374.5	32.4		51.3			2
Ech. 20	2016	376.2	37.1		54.2			2
Ech. 21	2016	378.7			88.9			1
Ech. 22	2014	374.8	26.2		40.9			2
Ech. 23	2013	292.1	49.1					1
Ech. 24	2017	942.2	850.8		233.1	86.8		3
Ech. 25	2017	513.1	63.6		69.3			2
Ech. 26	2017	641.5	75.2		97.0			2
Ech. 27	2017	645.1	96.4		118.5			2
Ech. 28	2016	756.8			725.5	255.2		2
Ech. 29	2017	288.3			43.0			1
Ech. 30	2015	304.4	53.4					1

2.2. BIOACCESSIBILITE DES COSV DANS 7 ECHANTILLONS DE POUSSIERE DE SALLES DE CLASSE

BLANCS ET CONTROLES QUALITE

De même que pour l'analyse des PBDE et des pyréthrinoïdes, l'analyse de la liste complète de COSV s'est accompagnée de blancs et de contrôle qualité relatifs aux méthodes d'extraction et à l'incubation intestinale.

Les blancs et les contrôles de l'étape d'extraction à haute température et à haute pression (PLE – *pressurized liquid extraction*) des COSV sont présentés dans le Tableau 6 dans lequel les colonnes « insert XAD®-2 » correspondent aux conditions d'extraction de la phase bioaccessible, tandis que les colonnes « Celite® » correspondent aux conditions d'extraction de la fraction non-bioaccessible. Les blancs, dont la concentration est inférieure à la LQ pour toutes les substances, témoignent de l'absence de pollution extérieure pendant l'extraction. Les concentrations fortifiées dans les contrôles sont correctement re-quantifiées, avec des concentrations mesurées comprises entre 70 et 130 % de la valeur fortifiée pour toutes les substances, à l'exception de l'acénaphtène, légèrement sous-quantifié pour la fraction non-bioaccessible (66%).

Comme expliqué dans l'article précédent, le blanc et les contrôles d'incubation permettent de s'assurer de l'absence de contamination provenant des réactifs et de la verrerie utilisés pour l'incubation, de vérifier la capacité du XAD-2 à adsorber tous les COSV présents en solution dans le liquide intestinal synthétique, ou de contrôler d'éventuelles dégradations dues à la présence d'enzymes et à des conditions de température relativement élevées (37 ± 1°C) ± pendant un temps relativement long (20 heures). Les concentrations mesurées dans le blanc d'incubation (Tableau 7) sont toutes inférieures à la LQ, à l'exception du DiNP dont la concentration (1600 ng/g) est toutefois négligeable au regard des concentrations bioaccessibles mesurées dans les échantillons de poussières associés (entre 24 900 et 449 000 ng/g). Pour toutes les familles chimiques à l'exception des phtalates et de l'aldrine, les concentrations mesurées dans le contrôle d'incubation fortifiées au Niveau 2, correspondant au milieu de la gamme de calibration (5 x LQ), sont comprises entre 76 et 120 %, de la concentration fortifiée. Pour ces mêmes substances, les concentrations mesurées pour le Niveau 1, correspondant à la LQ, sont comprises entre 71 et 140 % de la concentration fortifiée, à l'exception du tributylphosphate (170 %), du fluorène (200 %), et du phénanthrène (190 %). Les concentrations bioaccessibles proches de la LQ dans les échantillons pourraient donc être également surévaluées. Cependant, le tributylphosphate ne semble pas concerné puisque la plus faible concentration bioaccessible (201 ng/g) est asso-

ciée à la plus faible bioaccessibilité (57 %). Le phénanthrène n'est pas impacté non plus puisque la plus faible concentration bioaccessible retrouvée correspond au Niveau 2 de fortification (94 ng/g). Pour le fluorène, la concentration bioaccessible retrouvée dans l'échantillon numéro 24 (Tableau 9), associée à une bioaccessibilité de 44 % (Tableau 10) pourrait être impactée, bien qu'une bioaccessibilité plus forte (48 %) ait été mesurée dans un autre échantillon. En ce qui concerne l'aldrine, non retrouvée dans le contrôle de Niveau 1 et légèrement sous-quantifiée dans le contrôle de Niveau 2 (64 %), les valeurs non détectées pourraient être des faux-négatifs. L'unique valeur reportée, 34 ng/g pour l'échantillon numéro 29 (Tableau 9), pourrait être sous-évaluée. En ce qui concerne les phtalates, deux cas se distinguent, avec d'un côté le DEP, bien re-quantifié pour les deux niveaux de fortification, et les autres phtalates, re-quantifiés entre 4 % et 26 % seulement de leur concentration de fortification. L'ajout de pancréatine dans le milieu intestinal synthétique semble responsable de cette perte de phtalates. En effet, la pancréatine est un mélange d'enzymes digestives (amylase, lipase, trypsine et protéase) qui hydrolysent les protéines en oligopeptides (trypsine), l'amidon en oligosaccharides (amylase) et les triglycérides en acides gras et glycérol (lipase) [89]. Parmi ces enzymes, la lipase, testée individuellement, n'a pas eu d'impact sur les phtalates, malgré sa capacité à hydrolyser les fonctions esters. En revanche, la trypsine a été reportée dans la littérature pour sa capacité à former des complexes avec les phtalates [101,102] et est donc très probablement responsable de leur faible taux de recouvrement. Ce phénomène est également susceptible de se produire *in vivo* et doit donc être pris en compte.

TABLEAU 6 : CONCENTRATIONS DES COSV DANS LES BLANCS ET LES CONTROLES D'EXTRACTION FORTIFIES

			Extraction inserts XAD-2			Extraction Célite		
			Blanc	Contrôle		Blanc	Contrôle	
	LQ (ng/g)	Concentration fortifiée (ng/g)	Concentration mesurée (ng/g)	Concentration mesurée (ng/g)	Concentration mesurée / concentration fortifiée (%)	Concentration mesurée (ng/g)	Concentration mesurée (ng/g)	Concentration mesurée / concentration fortifiée (%)
Pesticide organophosphoré								
Diazinon	12.5	100	< LQ	81	81%	< LQ	84	84%
Chlorpyrifos-ethyl	12.5	100	< LQ	120	123%	< LQ	100	101%
Pesticide organochloré								
a-HCH	5	40	< LQ	46	115%	< LQ	49	123%
g-HCH	12.5	100	< LQ	89	89%	< LQ	88	88%
Aldrin	12.5	100	< LQ	76	76%	< LQ	92	92%
Alpha-endosulfan	12.5	100	< LQ	78	78%	< LQ	71	71%
4,4'-DDE	5	40	< LQ	39	99%	< LQ	39	97%
Dieldrin	12.5	100	< LQ	81	81%	< LQ	130	130%
4,4'-DDT	12.5	100	< LQ	110	113%	< LQ	100	104%
Oxadiazolone								
Oxadiazon	12.5	100	< LQ	92	92%	< LQ	88	88%
Retardateur de flamme organophosphoré								
Tributylphosphate	187.5	500	< LQ	470	93%	< LQ	500	100%
Musc								
Galaxolide	62.5	500	< LQ	470	94%	< LQ	470	94%
Tonalide	62.5	500	< LQ	460	92%	< LQ	490	98%
HAP								
Acenaphtene	12.5	100	< LQ	70	70%	< LQ	66	66%
Fluorene	12.5	100	< LQ	84	84%	< LQ	87	87%
Phenanthrene	25	100	< LQ	81	81%	< LQ	79	79%
Anthracene	25	100	< LQ	76	76%	< LQ	77	77%
Fluoranthene	12.5	100	< LQ	91	91%	< LQ	93	93%
Pyrene	12.5	100	< LQ	97	97%	< LQ	94	94%
Benzo(a)pyrene	12.5	100	< LQ	98	98%	< LQ	100	100%
PCB								
PCB31	5	40	< LQ	35	87%	< LQ	37	92%
PCB28	5	40	< LQ	35	87%	< LQ	38	94%
PCB52	5	40	< LQ	37	92%	< LQ	40	100%
PCB101	5	40	< LQ	33	83%	< LQ	36	91%
PCB118	5	40	< LQ	42	106%	< LQ	38	96%
PCB153	5	40	< LQ	44	111%	< LQ	39	98%
PCB105	5	40	< LQ	40	99%	< LQ	40	101%
PCB138	5	40	< LQ	45	112%	< LQ	48	121%
PCB180	5	40	< LQ	50	125%	< LQ	49	123%
Phtalate								
DEP	2500	4000	< LQ	3300	81%	< LQ	3600	89%
DiBP	1000	4000	< LQ	3300	84%	< LQ	3500	88%
DBP	1000	4000	< LQ	3400	85%	< LQ	3500	88%
BBP	1000	4000	< LQ	3600	90%	< LQ	4100	102%
DEHP	1000	4000	< LQ	3200	79%	< LQ	3800	95%
DiNP	1000	4000	< LQ	3600	89%	< LQ	3900	97%

TABLEAU 7 : CONCENTRATIONS DES COSV DANS LE BLANC ET LES CONTROLES D'INCUBATION FORTIFIES

	Concentration fortifiée		Blanc	Niveau 1 (n=2)		Niveau 2 (n=2)	
	Niveau 1 (LQ) (ng/g)	Niveau 2 (5 x LQ) (ng/g)	Concentration mesurée (ng/g)	Concentration mesurée (ng/g)	Concentration mesurée / concentration fortifiée (%)	Concentration mesurée (ng/g)	Concentration mesurée / concentration fortifiée (%)
Pesticide organophosphoré							
Diazinon	12.5	100	< LQ	14 ± 1	110%	76 ± 1	76%
Chlorpyrifos-ethyl	12.5	100	< LQ	14 ± 0	110%	100 ± 15	100%
Pesticide organochloré							
a-HCH	5	40	< LQ	6.1 ± 1.1	120%	47 ± 3	120%
g-HCH	12.5	100	< LQ	13 ± 1	100%	99 ± 5	99%
Aldrin	12.5	100	< LQ	0	-	64 ± 9	64%
Alpha-endosulfan	12.5	100	< LQ	8.8 ± 0.7	71%	89 ± 11	89%
4,4'-DDE	5	40	< LQ	5.9 ± 1.0	120%	34 ± 2	85%
Dieldrin	12.5	100	< LQ	15 ± 2	120%	94 ± 4	94%
4,4'-DDT	12.5	100	< LQ	13 ± 1	100%	91 ± 23	91%
Oxadiazolone							
Oxadiazon	12.5	100	< LQ	15 ± 1	120%	79 ± 7	79%
Retardateur de flamme organophosphoré							
Tributylphosphate	187.5	500	< LQ	315 ± 11	170%	520 ± 32	100%
Musc							
Galaxolide	62.5	500	< LQ	87 ± 5	140%	490 ± 4	98%
Tonalide	62.5	500	< LQ	77 ± 0	120%	490 ± 40	98%
HAP							
Acenaphtene	12.5	100	< LQ	16 ± 0	130%	79 ± 1	79%
Fluorene	12.5	100	< LQ	25 ± 1	200%	110 ± 6	110%
Phenanthrene	25	100	< LQ	47 ± 1	190%	120 ± 9	120%
Anthracene	25	100	< LQ	23 ± 0	91%	77 ± 8	77%
Fluoranthene	12.5	100	< LQ	15 ± 3	120%	82 ± 2	82%
Pyrene	12.5	100	< LQ	16 ± 2	130%	89 ± 4	89%
Benzo(a)pyrene	12.5	100	< LQ	14 ± 0	120%	87 ± 1	87%
PCB							
PCB31	5	40	< LQ	5.8 ± 0.4	120%	39 ± 4	97%
PCB28	5	40	< LQ	4.5 ± 0.8	90%	39 ± 6	98%
PCB52	5	40	< LQ	6.0 ± 1.7	120%	42 ± 5	110%
PCB101	5	40	< LQ	5.3 ± 0.9	110%	34 ± 1	86%
PCB118	5	40	< LQ	5.8 ± 0.2	120%	39 ± 1	96%
PCB153	5	40	< LQ	6.9 ± 0.3	140%	41 ± 2	100%
PCB105	5	40	< LQ	5.7 ± 0.3	110%	39 ± 3	98%
PCB138	5	40	< LQ	7.0 ± 1.4	140%	41 ± 1	100%
PCB180	5	40	< LQ	5.5 ± 0.3	110%	42 ± 0	100%
Phtalate							
DEP	2500	4000	< LQ	2500 ± 96	99%	3300 ± 110	82%
DiBP	1000	4000	< LQ	150 ± 9	15%	160 ± 7	4%
DBP	1000	4000	< LQ	160 ± 8	16%	170 ± 6	4%
BBP	1000	4000	< LQ	230	23%	120 ± 25	3%
DEHP	1000	4000	< LQ	260 ± 4	26%	720 ± 520	18%
DiNP	1000	4000	1600	220 ± 9	22%	470 ± 300	12%

SRM 2585

Le Tableau 8 montre les concentrations de COSV bioaccessibles, non-bioaccessibles et totales, ainsi que la bioaccessibilité des COSV dans le matériau de référence SRM 2585. Les bioaccessibilités sont très différentes selon le type de COSV et varient de 14 % pour le DiNP à 100 % pour le tributylphosphate et le lindane (γ-HCH). Outres les données existantes pour les PBDE présentées dans l'article précédent, la bioaccessibilité des retardateurs de flamme organosphosphorés (OPEs) [103,104] et des hexabromocyclododecanes[105] dans le SRM 2585 a déjà été documentée dans la littérature. Cependant, pour la liste des COSV du présent projet, il s'agit de la première mesure de bioaccessibilité dans le SRM 2585. Ces données devront être complétées sur de plus nombreux réplicats, et pourront ainsi servir dans le futur d'éléments de comparaison pour la communauté scientifique.

TABLEAU 8 : CONCENTRATIONS DES COSV BIOACCESSIBLES, NON-BIOACESSIBLES ET TOTALES DANS LE SRM 2585

	Concentration bioaccessible (ng/g, n=2)	Non-bioaccessible concentration (ng/g, n=2)	Concentrations bioaccessible + non-bioaccessible (ng/g, n=2)	Concentration totale (ng/g, n=1)	Cocnentrations bioaccessible + non-bioaccessible / concentration totale (%)	Bioaccessibilité (%, n=2)
Pesticide organophosphoré						
Diazinon	197 ± 22	25 ± 2.8	222 ± 20	219	101 ± 8.9%	89 ± 2.3%
Chlorpyrifos-ethyl	104 ± 8.3	114 ± 40	218 ± 49	287	76 ± 17%	49 ± 7%
Pesticide organochloré						
a-HCH	-	-	-	-	-	-
g-HCH	6.9 ± 0.12	-	6.9 ± 0.12	4.78	144 ± 2.6%	100%
Aldrin	-	-	-	-	-	-
Alpha-endosulfan	-	-	-	-	-	-
4,4'-DDE	134 ± 12	68 ± 1.8	202 ± 13	205	99 ± 6.5%	66 ± 1.3%
Dieldrin	78 ± 1.2	21 ± 2.9	99 ± 1.8	73	135 ± 2.5%	79 ± 2.6%
4,4'-DDT	30 ± 0.25	41 ± 3.2	71 ± 3.4	62	115 ± 5.5%	43 ± 1.7%
Oxadiazolone						
Oxadiazon	14 ± 0.83	5.6 ± 0.41	19 ± 1.2	16	118 ± 7.7%	71 ± 0.25%
Retardateur de flamme organophosphoré						
Tributylphosphate	284 ± 1.7	-	284 ± 1.7	256	111 ± 0.66%	100%
Musc						
Galaxolide	1640 ± 15	202 ± 17	1840 ± 32	1 616	114 ± 2%	89 ± 0.74%
Tonalide	1550 ± 58	200 ± 10	1750 ± 47	1 629	108 ± 2.9%	89 ± 0.90%
HAP						
Acenaphtene	11 ± 0.12	11 ± 0.95	22 ± 0.82	15	152 ± 5.7%	49 ± 2.4%
Fluorene	33 ± 0.27	25 ± 5.7	58 ± 6	43	136 ± 14%	57 ± 5.4%
Phenanthrene	975 ± 20	244 ± 17	1220 ± 3.5	1 218	100 ± 0.29%	80 ± 1.4%
Anthracene	43 ± 0.58	97 ± 1	140 ± 0.44	181	77 ± 0.24%	31 ± 0.51%
Fluoranthene	3180 ± 178	581 ± 68	3760 ± 246	3 977	94 ± 6.2%	85 ± 0.8%
Pyrene	2870 ± 141	517 ± 61	3390 ± 202	3 447	98 ± 5.9%	85 ± 0.89%
Benzo(a)pyrene	355 ± 12	261 ± 2.4	615 ± 9.2	663	93 ± 1.4%	58 ± 1%
PCB						
PCB31	12 ± 0.39	2.7 ± 0.024	15 ± 0.37	14	101 ± 2.5%	82 ± 0.63%
PCB28	8.8 ± 0.81	1.7 ± 0.53	11 ± 1.3	12	88 ± 11%	84 ± 3%
PCB52	17 ± 0.83	5.9 ± 0.18	23 ± 0.65	25	89 ± 2.6%	74 ± 1.5%
PCB101	18 ± 0.027	10 ± 0.24	29 ± 0.27	28	103 ± 0.96%	64 ± 0.51%
PCB118	17 ± 1.3	9.2 ± 0.95	26 ± 2.3	28	93 ± 8.3%	64 ± 0.52%
PCB153	14 ± 0.85	13 ± 2.1	27 ± 3	28	98 ± 11%	52 ± 2.6%
PCB105	6.7 ± 0.49	4 ± 1.4	11 ± 1.9	10	109 ± 20%	63 ± 6.8%
PCB138	16 ± 0.63	11 ± 0.62	27 ± 0.0077	27	102 ± 0.029%	58 ± 2.3%
PCB180	6.5 ± 0.017	12 ± 0.7	19 ± 0.72	21	90 ± 3.4%	34 ± 1.2%
Phtalate						
DEP	7070 ± 45	539 ± 24	7610 ± 21	6 965	109 ± 0.3%	93 ± 0.34%
DiBP	2300 ± 39	418 ± 5.4	2720 ± 34	5 097	53 ± 0.66%	85 ± 0.39%
DBP	8070 ± 230	2030 ± 122	10100 ± 108	27 180	37 ± 0.4%	80 ± 1.4%
BBP	33800 ± 197	6060 ± 97	39800 ± 294	86 400	46 ± 0.34%	85 ± 0.13%
DEHP	31800 ± 1480	154000 ± 14600	186000 ± 16100	509 800	36 ± 3.2%	17 ± 0.69%
DiNP	11700 ± 548	70100 ± 571	81800 ± 23	169 300	48 ± 0.014%	14 ± 0.67%

ECHANTILLONS DE POUSSIERE DE SALLES DE CLASSE

Les concentrations de COSV bioaccessibles et non-bioaccessibles dans 7 échantillons de poussière de salle de classe sont présentées dans le Tableau 9 et les bioaccessibilités des COSV dans ces échantillons dans le Tableau 10. Les distributions des concentrations et de la bioaccessibilité sont représentées graphiquement sur la Figure 16. Des concentrations totales fortes, avec des médianes supérieures à 50 µg/g et des valeurs maximales dépassant le mg/g sont observées pour certains phtalates (DiBP, DBP, BBP, DEHP et DiNP). Ces concentrations, déjà fortes, pourraient être sous-estimées puisqu'elles résultent de l'addition des fractions bioaccessibles et non-bioaccessibles et qu'elles ne tiennent donc pas compte des éventuelles pertes causées par la pancréatine durant la phase d'incubation. Des concentrations intermédiaires, avec des médianes allant de la centaine de ng/g au µg/g sont observées pour cinq pesticides organochlorés (α-HCH, γ-HCH, aldrine, dieldrine, et 4,4'-DDT), le tributylphosphate, les 2 muscs, quatre HAP (fluorène, phenanthrène, fluoranthène et pyrène) et un phtalate (le DEP). Enfin des concentrations plus faibles, avec des médianes allant de l'ordre du ng/g à la dizaine de ng/g, sont observées pour les deux pesticides organophosphorés, deux pesticides organochlorés (α-endosulfan et 4,4'-DDE), l'oxadiazon, trois HAP (acénaphtène, anthracène et benzo(a)pyrène) et tous les PCB.

En termes de bioaccessibilité, les résultats varient de 69 à 80 % pour les pesticides organophosphorés, de 24 à 94 % pour les pesticides organochlorés, de 59 à 67 % pour l'oxadiazon, de 57 à 100 % pour le tributylphosphate, de 59 à 75 % pour les muscs, de 16 à 77 % pour les HAP, de 10 à 58 % pour les PCB et de 7 à 93 % pour les phtalates. Les substances les plus bioaccessibles (bioaccessibilité > 70 %) sont le chlorpyrifos-ethyl, l'α-HCH, le g-HCH, le tributylphosphate, et les phtalates les plus légers (DEP, DiBP, DBP et BBP). Des bioaccessibilités intermédiaires, entre 30 % et 70 %, sont observées pour le diazinon, l'α-endosulfan, le 4,4'-DDE, la dieldrine, le 4,4'-DDT, l'oxadiazon, la galaxolide, la tonalide, la majorité des HAP (acénaphtène, fluorène, phénanthrène, anthracène, fluoranthène et pyrène), et les PCB les plus légers (PCB31, 28, 52 et 101). Enfin les COSV les moins bioaccessibles (bioacessibilité < 30 %) sont l'aldrine, le benzo(a)pyrène, les PCB les plus lourds (PCB 118, 153, 138, 180), le DEHP et le DinP.

TABLEAU 9 : CONCENTRATIONS EN COSV BIOACCESSIBLES ET NON-BIOACCESSIBLES DANS 7 ECHANTILLONS DE POUSSIERES D'ECOLE (FRANCE, 2013-2017)

				Concentrations bioaccessibles							Concentrations non-bioaccessibles						
Substance	LD	LQ	n	Ech-24X 030918	Ech-25X 030918	Ech-26X 030918	Ech-27X 030918	Ech-28X 030918	Ech-29X 030918	Ech-30X 030918	Ech-24D 060918	Ech-25D 060918	Ech-26D 060918	Ech-27D 060918	Ech-28D 060918	Ech-29D 060918	Ech-30D 060918
Diazinon		12.5	1				16							7			
Chlorpyrifos-ethyl	5	12.5	1				17							4			
a-HCH	2	5	1						1 070							111	
g-HCH	5	12.5	6	145	16	75	96	14	947	111	9	4	13	8		92	11
Aldrin	5	12.5	1						34							109	
Alpha-endosulfan	5	12.5	4	66		16	29			52	32		16	20			26
4,4'-DDE	2	5	4			2	2		3	7			5	5		6	15
Dieldrin	5	12.5	3			44	64		183				37	70		172	
4,4'-DDT	5	12.5	1							32							70
Oxadiazon	5	12.5	4	18	16	15	18				9	8	10	13			
Tributylphosphate	62.5	187.5	4			201	301	434		608			151	202			49
Galaxolide	25	62.5	7	1 360	2 360	2 600	2 570	1 090	978	3 000	490	1 020	1 620	1 060	369	508	1 550
Tonalide	25	62.5	7	239	1 140	606	470	197	126	515	105	598	423	212	72	58	255
Acenaphtene	5	12.5	6		17	14	19	19	18	23		58	47	44	19	20	14
Fluorene	5	12.5	7	34	93	80	91	69	64	85	42	443	415	369	148	136	93
Phenanthrene	12.5	25	7	94	190	287	328	212	193	285	28	223	137	146	111	119	102
Anthracene	12.5	25	5		14	16	47	7		26		45	28	32	28		22
Fluoranthene	5	12.5	7	35	106	183	179	81	63	121	19	120	125	104	94	82	70
Pyrene	5	12.5	7	67	145	260	257	101	82	174	36	137	179	134	102	101	107
Benzo(a)pyrene	5	12.5	6		14	11	17	12	6	14		60	36	43	52	28	32
PCB31	2	5	1							8							5
PCB28	2	5	1							6							4
PCB52	2	5	3			6	7			6			9	8			9
PCB101	2	5	5			7	10	3	2	4			19	23	8	5	6
PCB118	2	5	3			5	5	4					13	13	10		
PCB153	2	5	3			7	10	1					36	41	7		
PCB105	2	5	0														
PCB138	2	5	3			8	9	3					30	36	11		
PCB180	2	5	2			2	4						14	30			
DEP	1000	2500	2	1 780	5 940	6 840	4 890	2 850	2 780	5 200		646	518				
DiBP	200	1000	7	111 000	330 000	264 000	109 000	124 000	129 000	64 200	12 900	80 800	98 200	24 400	23 900	47 400	11 000
DBP	200	1000	7	6 600	56 700	447 000	366 000	43 700	51 500	26 700	1 330	17 500	139 000	77 000	8 610	14 600	4 740
BBP	200	1000	7	24 100	99 800	1 100 000	994 000	20 000	103 000	640 000	4 250	37 600	592 000	416 000	4 090	32 000	227 000
DEHP	200	1000	7	385 000	211 000	59 900	55 000	73 800	82 900	36 100	825 000	1 470 000	463 000	426 000	784 000	629 000	239 000
DiNP	200	1000	7	449 000	31 300	38 500	33 700	157 000	145 000	24 900	1 030 000	259 000	294 000	298 000	2 140 000	1 180 000	220 000

TABLEAU 10 : BIOACCESSIBILITE DES COSV DANS 7 ECHANTILLONS DE POUSSIERES D'ECOLE (FRANCE, 2013-2017)

Famille Chimique	Substance	LD	LQ	n	Ech 24	Ech 25	Ech 26	Ech 27	Ech 28	Ech 29	Ech 30
Pesticide organophosphoré	Diazinon		12.5	1				69%			
	Chlorpyrifos-ethyl	5	12.5	1				80%			
Pesticide organochloré	a-HCH	2	5	1						91%	
	g-HCH	5	12.5	6	94%	80%	85%	92%		91%	91%
	Aldrin	5	12.5	1						24%	
	Alpha-endosulfan	5	12.5	4	67%		49%	60%			67%
	4,4'-DDE	2	5	4			24%	28%		31%	31%
	Dieldrin	5	12.5	3			55%	48%		51%	
	4,4'-DDT	5	12.5	1							31%
Oxadiazolone	Oxadiazon	5	12.5	4	66%	67%	60%	59%			
Retardateur de flamme organophosphoré	Tributylphosphate	62.5	187.5	4			57%	60%	100%		93%
Musc	Galaxolide	25	62.5	7	73%	70%	62%	71%	75%	66%	66%
	Tonalide	25	62.5	7	69%	66%	59%	69%	73%	69%	67%
HAP	Acenaphtene	5	12.5	6		22%	22%	30%	49%	47%	61%
	Fluorene	5	12.5	7	44%	17%	16%	20%	32%	32%	48%
	Phenanthrene	12.5	25	7	77%	46%	68%	69%	66%	62%	74%
	Anthracene	12.5	25	5		24%	36%	60%	20%		54%
	Fluoranthene	5	12.5	7	65%	47%	59%	63%	46%	44%	63%
	Pyrene	5	12.5	7	65%	51%	59%	66%	50%	45%	62%
	Benzo(a)pyrene	5	12.5	6		18%	24%	28%	19%	18%	30%
PCB	PCB31	2	5	1							58%
	PCB28	2	5	1							58%
	PCB52	2	5	3			40%	46%			38%
	PCB101	2	5	5			28%	30%	30%	27%	35%
	PCB118	2	5	3			29%	29%	30%		
	PCB153	2	5	3			16%	19%	15%		
	PCB105	2	5	0							
	PCB138	2	5	3			20%	21%	20%		
	PCB180	2	5	2			10%	12%			
Phthalate	DEP	1000	2500	2		90%	93%				
	DiBP	200	1000	7	90%	80%	73%	82%	84%	73%	85%
	DBP	200	1000	7	83%	76%	76%	83%	84%	78%	85%
	BBP	200	1000	7	85%	73%	65%	70%	83%	76%	74%
	DEHP	200	1000	7	32%	13%	11%	11%	9%	12%	13%
	DiNP	200	1000	7	30%	11%	12%	10%	7%	11%	10%

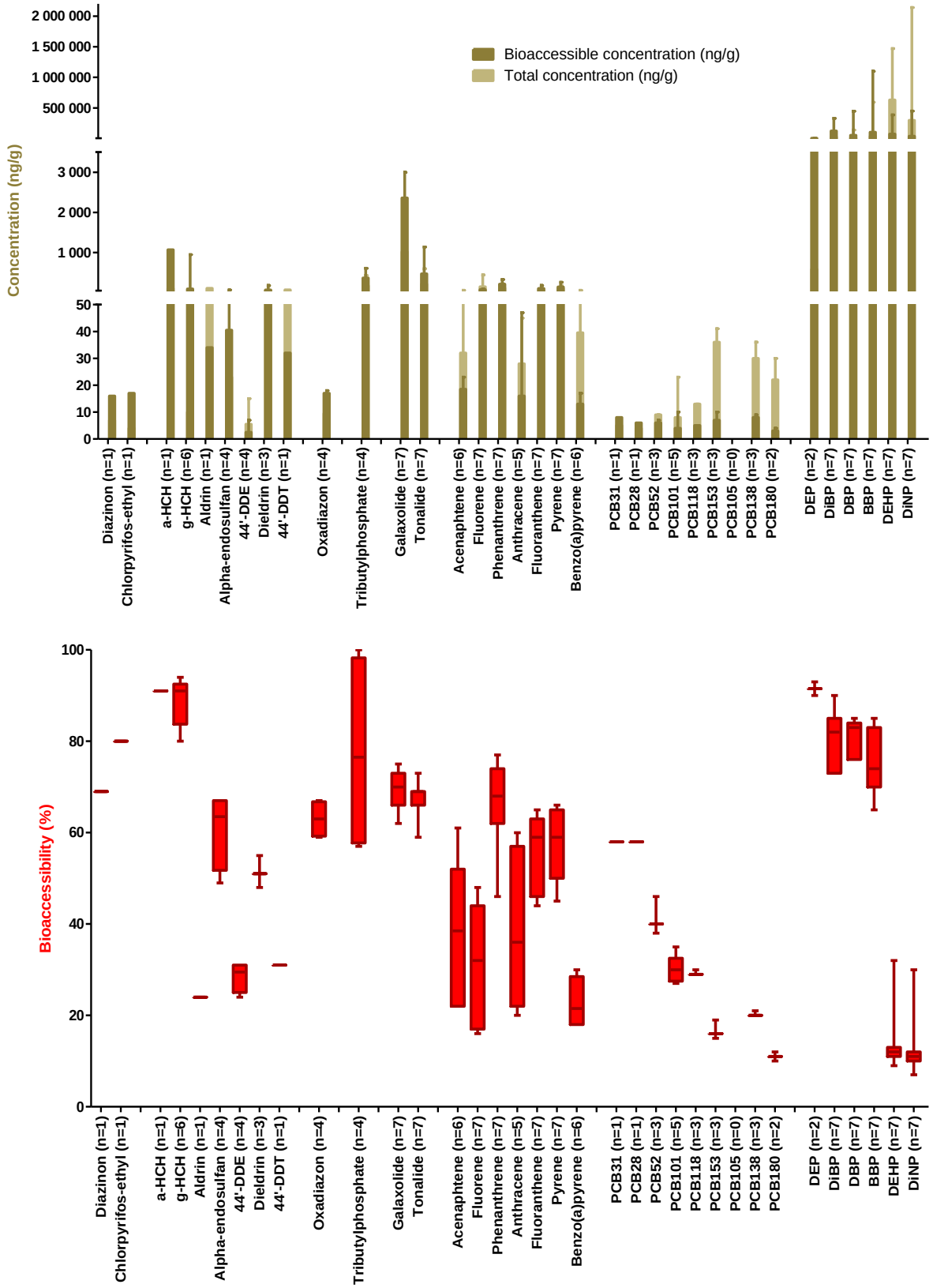


FIGURE 16 : CONCENTRATIONS TOTALE ET BIOACCESSIBLE, ET BIOACCESSIBILITE DES COSV DANS 7 ECHANTILLONS DE POUSSIERES D'ECOLE (FRANCE 2013-2017)

Pour les substances détectées dans plus de trois échantillons différents, les plus faibles variations inter-échantillons (écart-type < 10 %) sont atteintes pour les pesticides organochlorés, l'oxadiazon, les muscs, trois HAP (le fluoranthène, le pyrène et le benzo(a)pyrène) et les phtalates. Des variations inter-échantillons plus importantes (écart-type > 10 %) sont atteintes pour le tributylphosphate et quatre HAP (acénaphtène, fluorène, phénanthrène et anthracène). Si cette tendance se confirmait, les implications seraient importantes, puisqu'au premier groupe pourrait être attribuée une valeur de bioaccessibilité estimée et assortie d'une incertitude connue, tandis que pour le second groupe, la mesure *in vitro* de la bioaccessibilité serait nécessaire.

La Figure 17 montre la relation entre le coefficient octanol-eau (K_{OW}) des COSV et leur bioaccessibilité. Une corrélation est observée entre augmentation du K_{OW} et baisse de la bioaccessibilité (r^2= 0.64). Si l'on ne considère que les PCB (Figure 18), alors cette corrélation est beaucoup plus marquée (r^2 = 0.84). Ainsi pour les PCB, du fait de la faible variabilité inter échantillon et de cette corrélation, un modèle de prédiction de leur bioaccessibilité peut être facilement envisagé.

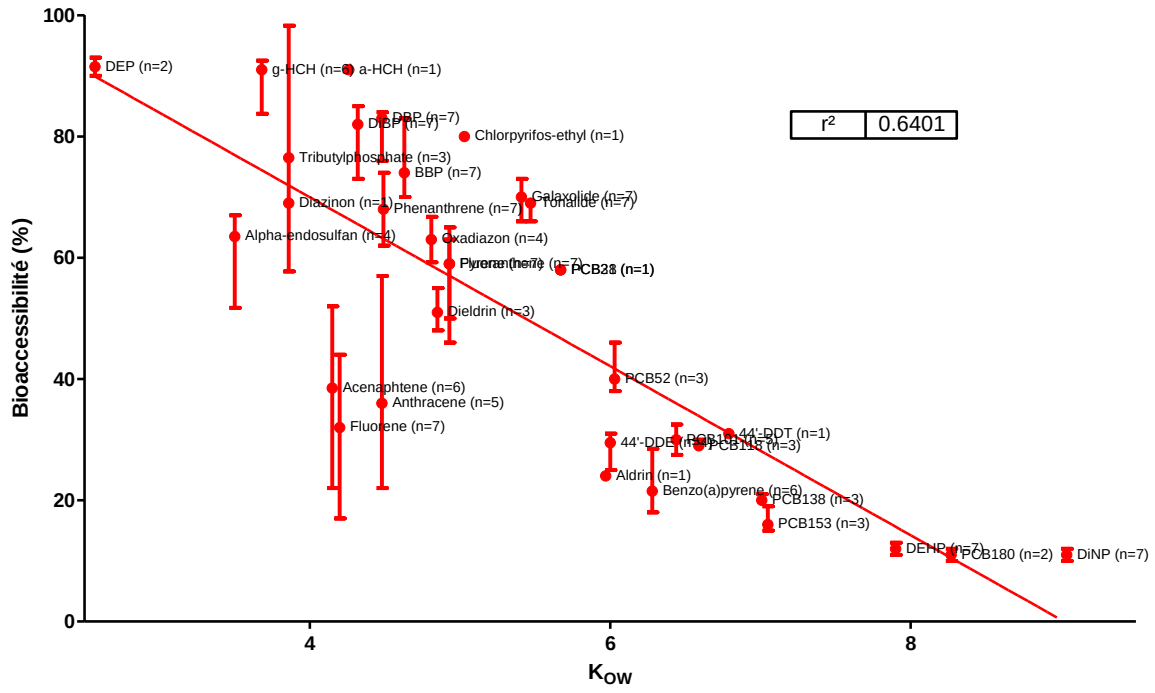


FIGURE 17 : RELATION ENTRE BIOACCESSIBILITE ET K_{OW} DES COSV DE 7 ECHANTILLONS DE POUSSIERES D'ECOLE (FRANCE, 2013-2017)

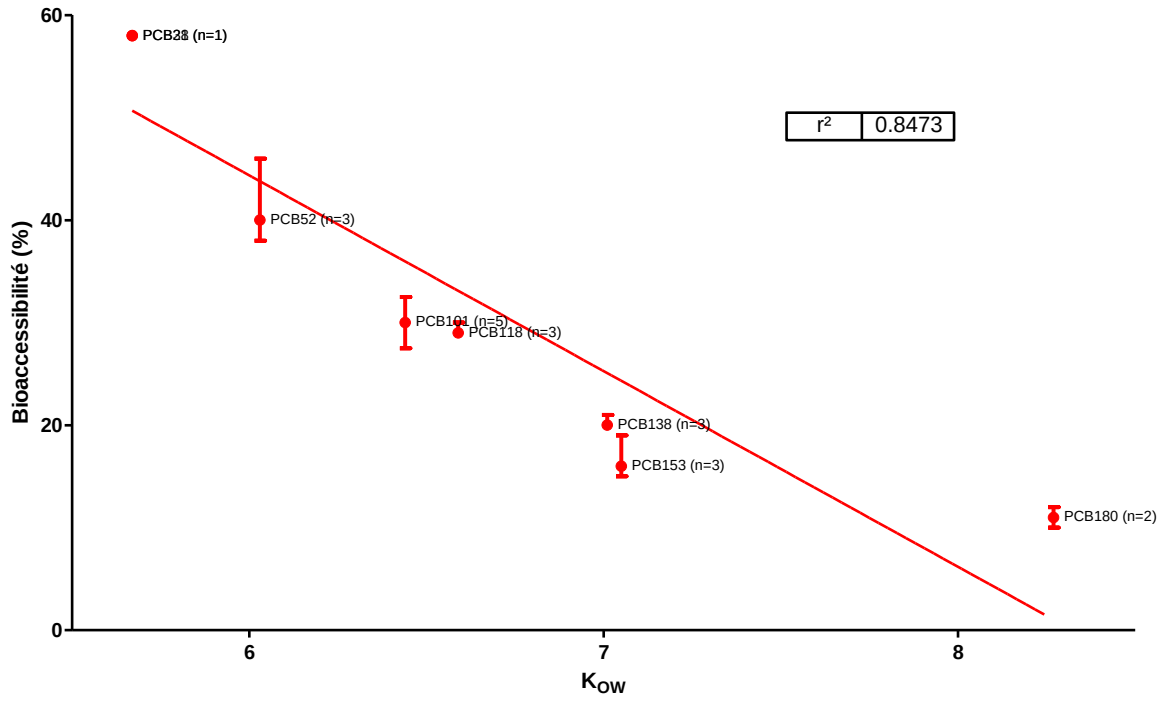


FIGURE 18 : RELATION ENTRE BIOACCESSIBILITE ET K_{OW} DES PCB DE 7 ECHANTILLONS DE POUSSIERES D'ECOLE (FRANCE 2013-2017)

Pour quatre HAP, des données de bioaccessibilité ont été produites très récemment par Kang et al. [106] pour 8 échantillons de poussière en utilisant une méthode de mesure intégrant différents types d'adsorbants, dont le Tenax®-TA. Les auteurs ont également documenté la biodisponibilité des COSV pour ces huit mêmes échantillons, obtenus à partir d'une étude *in vivo* chez la souris. Ces résultats ont été comparés aux résultats obtenus sur les 7 échantillons dans le Tableau 11.

TABLEAU 11 : COMPARAISON DE LA BIOACCESSIBILITE DES HAP AVEC LES DONNEES DE LA LITERATURE

	Cette étude (bioaccessibilité)			Kang et al. [92] (bioaccessibilité (Tenax-Ta))			Kang et al. [92] (biodisponibilité)		
Substance	n	min	max	n	min	max	n	min	max
Phenanthrène	7	46%	77%	8	38%	69%	8	45%	91%
Fluoranthène	7	44%	65%	8	30%	68%	8	19%	72%
Pyrene	7	45%	66%	8	40%	63%	8	15%	56%
Benzo(a)pyrène	6	18%	30%	8	40%	82%	8	32%	75%

Les résultats de bioaccessibilité obtenus sont très comparables avec ceux de cette étude pour le phénanthrène, le fluoranthène et le pyrène, mais ils sont supérieurs pour le benzo(a)pyrène. De même, si l'on s'intéresse aux résultats de biodisponibilité, ils sont comparables bien que légèrement plus dispersés pour les trois premiers HAP, et supérieurs pour le benzo(a)pyrène. La méthode de bioaccessibilité semble donc adaptée pour certains phtalates, mais reste toutefois à valider pour le benzo(a)pyrène, qui est le HAP le plus hydrophobe de la liste investiguée.

En ce qui concerne les phtalates, des travaux ont été menés en Allemagne par Veronika Plichta, dans le cadre de son doctorat encadré par Pr. Hermann Fromme. Ces travaux ont permis de documenter la biodisponibilité de quatre phtalates, à partir d'une étude basée sur l'analyse des taux d'excrétion urinaire de cochons ayant ingéré 5 échantillons de poussières différents [107]. Les résultats sont présentés dans le Tableau 12 et permettent de distinguer deux cas de figure : pour le DBP et le BBP, la bioaccessibilité mesurée à l'aide de la méthode simplifiée produit des résultats supérieurs à la biodisponibilité, tandis que pour le DEHP et le DiNP, la biodisponibilité des phtalates est plus forte que la bioaccessibilité mesurée avec la méthode simplifiée. Ces résultats sont obtenus pour des échantillons de poussières distincts, mais cela ne suffit pas à expliquer une telle disparité, du moins pour le DEHP. En effet, l'une des conclusions des travaux de Veronika Plichta porte sur la faible variabilité inter-échantillons de la biodisponibilité du DEHP. Une valeur supérieure à 40 % est donc attendue pour la bioaccessibilité des phtalates sur les poussières de cette étude.

TABLEAU 12 : COMPARAISON ENTRE BIOACCESSIBILITE ET BIODISPONIBILITE DE QUATRE PHTALATES.

	Cette étude (bioacessibilité)			Plichta [107] (biodisponibilité)		
Substance	n	min	max	n	min	max
DBP	7	76%	85%	5	39%	69%
BBP	7	65%	85%	7	9%	54%
DEHP	7	9%	32%	7	39%	45%
DiNP	7	7%	30%	7	23%	75%

CONCLUSION SUR LA METHODE

Ce chapitre a décrit le développement d'une méthode de mesure simplifiée de la bioaccessibilité des COSV dans les poussières, et a montré l'intérêt d'une telle méthode pour des applications sur de grands nombres d'échantillons. Les résultats obtenus sont cohérents avec des résultats de bioaccessibilité produits par des méthodes de référence pour plusieurs familles de COSV dont les

PBDE, les pyréthrinoïdes et les HAP (à l'exception du benzo(a)pyrène). Par rapport aux données de biodisponibilité existantes, les bioaccessibilités résultantes de la méthode simplifiée sont globalement comparables pour les PBDE et les HAP (toujours à l'exception du benzo(a)pyrène). Elles sont en revanche surestimées pour deux phtalates (le DBP et le BBP) et sous estimées pour les deux phtalates les plus lourds (DEHP et DiNP), ainsi que pour le benzo(a)pyrène. Ces résultats demandent à être confirmés dans un premier temps sur les 23 échantillons non retraités. Cependant, alors qu'il est attendu que la bioaccessibilité soit supérieure à la biodisponibilité, l'inverse est inconcevable et une évolution de la méthode sera certainement nécessaire pour ces substances. La documentation de la bioaccessibilité orale des COSV est également nécessaire pour un plus grand nombre d'échantillons afin de voir si se confirment les tendances observées pour certaines substances comme les PCB, dont les bioaccessibilités, peu variables d'un échantillon à l'autre pourraient être estimées sans besoin de mesure.

CONCLUSION ET PERSPECTIVES

Ces travaux de thèse avaient pour objectif de mettre au point une méthode simplifiée permettant de mesurer la bioaccessibilité des COSV dans les poussières afin d'évaluer plus finement l'exposition humaine aux COSV en environnement intérieur par ingestion de poussière. Une telle méthode a été développée, qui a pu être validée en partie pour certaines familles de COSV et qui demande à être améliorée pour d'autres. Dans tous les cas les éléments permettant la validation de cette méthode sont perfectibles, ce qui ouvre des perspectives pour la suite de ce travail de thèse. De plus, ce projet de thèse s'intéressait au volet « ingestion de poussière » de l'exposition humaine aux COSV, laissant les volets « inhalation » et « contact cutané » à explorer. Ces différentes perspectives sont détaillées dans cette partie finale du manuscrit.

1. ACQUISITION DE DONNEES COMPLEMENTAIRES SUR LA BIOACCESSIBILITE DES COSV

Dans le cadre de ce manuscrit, la bioaccessibilité a été documentée pour 30 échantillons pour les PBDE et les pyréthrinoïdes, mais seulement pour 7 échantillons pour les autres familles de COSV. Pour les 23 échantillons complémentaires, les acquisitions GC/MS/MS ont été réalisées et les données brutes sont disponibles. Leur retraitement permettra de documenter davantage la bioaccessibilité de ces COSV et en particulier leur dispersion selon les échantillons.

2. EVOLUTION DE LA METHODE SIMPLIFIEE

A l'heure actuelle, la méthode simplifiée n'est pas satisfaisante pour documenter la bioaccessibilité des phtalates, en particulier du DiNP et du DEHP. Non seulement ces substances sont retrouvées en environnement intérieur avec les concentrations les plus fortes (jusqu'à 2 mg/g dans ce projet) mais c'est également la voie d'exposition la plus importante [35]. Il est donc crucial d'estimer correctement la bioaccessibilité orale de ces substances. L'évolution de la méthode simplifiée est possible en jouant sur l'ajustement d'un ou plusieurs paramètres, dont la prise d'essai de la poussière, la masse ou la nature de l'adsorbant présent dans l'insert, la durée d'incubation, et les concentrations de bile et de pancréatine dans le milieu intestinal. Sachant que les phtalates sont au minimum 20 fois plus concentrés que la plupart des autres substances,

l'optimisation du premier curseur (taille de la prise d'essai) sera à privilégier dans un premier temps.

3. VALIDATION *IN VIVO* DES DONNEES

Bien que l'avantage des méthodes d'évaluation de bioaccessibilité provienne du fait qu'elles utilisent des outils *in vitro* plutôt qu'*in vivo*, elles ne peuvent s'affranchir d'une étape finale de validation. Des études *in vivo* sont alors nécessaires pour documenter la biodisponibilité des substances d'intérêt, qui sera ensuite utilisée comme valeur de référence pour valider la méthode *in vitro.*

A ce jour, il n'existe que très peu de données documentant la biodisponibilité des COSV dans la poussière. Concernant la liste des COSV d'intérêt pour ce projet, il n'existe à ma connaissance que les 3 études décrites dans le Chapitre 3 de ce mémoire :

- L'étude de Huwe et al. sur la biodisponibilité des PBDE dans le SRM 2585 mesurée chez le rat [100], qui a été utilisée pour le présent projet ainsi qu'il est décrit dans l'Article Scientifique n°3 ;
- L'étude de Veronika Plichta sur la biodisponibilité des phtalates dans 5 poussières différentes mesurée chez le cochon [107]. Ces 5 échantillons de poussières sont disponibles au Léres dans le cadre d'un accord avec Veronika Plichta et Hermann Fromme de l'Autorité bavaroise de la santé et de la sécurité alimentaire (*Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit*) en Allemagne. Ils seront utilisés pour valider la méthode simplifiée sur les phtalates, une fois qu'elle sera opérationnelle après son évolution.
- L'étude de Kang et al. sur la biodisponibilité des HAP dans 8 poussières différentes mesurées chez la souris [106], qui ne sont à l'heure actuelle pas disponibles au Léres.

De nouvelles études sont donc nécessaires pour compléter ces données de validation et couvrir l'ensemble des COSV d'intérêt.

Pour investiguer la biodisponibilité orale d'une substance, plusieurs étapes préalables seront nécessaires :

- Identification des COSV prioritaires, c'est-à-dire ceux pour lesquels l'ingestion est une voie importante d'exposition ;

- Identification de l'espèce animale la plus pertinente : bien que les rats soient plus souvent considérés pour les mesures *in vivo*, les porcs sont recommandés parce que leur système digestif est comparable à celui des humains en termes anatomiques et physiologiques [108]. Cependant les quantités de poussières contaminées nécessaires pour que la concentration des biomarqueurs soit mesurable dans les tissus peut constituer un frein à l'utilisation des porcs ;
- Identifications des biomarqueurs biologiques et de leur localisation chez l'animal (sang, foie, tissus adipeux, etc.), grâce à des recherches bibliographiques sur le métabolisme des substances d'intérêt. L'étude de Mi et al. qui s'intéresse à l'absorption, à la distribution dans les tissus, au métabolisme et à l'élimination du BDE 209 chez les rats [109] est un modèle, mais la métabolomique peut également être mise à contribution, comme le décrivent Gao et al. concernant l'exposition humaine aux HAP [110] ;
- Constitution de stocks de plusieurs échantillons de poussières aux caractéristiques physico-chimiques variées permettant de couvrir la plus grande diversité de types de poussière possible ;
- Définition d'un plan d'expérience respectueux des 3 R (*Replacement, Reduction, Refinement*).

Ces étapes constituent ainsi les composantes d'une des principales perspectives de ce projet de thèse.

4. PERSPECTIVES SUR L'INHALATION

Le paragraphe 3 du 1er Chapitre de ce manuscrit (page 67) présentait les différentes voies d'exposition humaine aux COSV en environnement intérieur. Pour l'inhalation comme pour l'ingestion, les notions de bioaccessibilité et de biodisponibilité sont à considérer. Un travail bibliographique a déjà été réalisé sur ce sujet dans le cadre d'une collaboration entre le CSTB, l'EHESP et l'institut suédois Swetox (*Swedisk Toxicology Research Center*), qui a donné lieu à un article de revue publié dans le journal *Environment International,* dont le titre est *« Bioaccessibility and bioavailability of environmental semi-volatile organic compounds via inhalation: A review of methods and models* ». Cet article est disponible dans la partie « Valorisation Scientifique » de ce manuscrit. Il aborde la bioaccessibilité et la biodisponibilité des COSV sous les angles de l'expérimentation et de la modélisation et met en évidence deux grands défis : le développe-

ment et la validation des méthodes *in vitro* et *in vivo* pour un large éventail de COSV, et des approches de modélisation qui doivent tenir compte de l'ensemble du système respiratoire et de la variabilité biologique humaine [86].

Comme pour la bioaccessibilité orale, la bioaccessibilité pulmonaire s'arrête à la membrane. Cependant, et en parallèle avec l'utilisation des cellules Caco-2 pour l'ingestion, des approches biologiques utilisant des cultures de cellules hAECN (*human Airway Epithelial Cells of Nasal origin*) ont été documentées pour évaluer l'exposition à des polluants gazeux à l'interface air-liquide, qui pourraient faire le lien entre les études *in vitro* et *in vivo* [111]. Ici encore de plus nombreuses études sont toutefois nécessaires pour mieux cerner cette approche.

5. PERSPECTIVES SUR LE CONTACT CUTANE

La troisième voie d'exposition est le contact cutané. L'intérêt pour cette voie n'est que récent, comme expliqué au Chapitre 1 (page 68), mais l'exposition cutanée est moins négligeable qu'on ne le supposait a priori [112]. La bioaccessibilité cutanée des COSV dans les particules adhérant à la peau n'a été que très étudiée. Néanmoins deux revues de la littérature ont été réalisées, l'une par Abdallah et al. sur l'absorption cutanée des retardateurs de flamme [113], l'autre par Beriro et al. sur la biodisponibilité *in vitro* des HAP dans le sol [93]. Les connaissances de la barrière cutanée acquises dans le domaine de la recherche pharmaceutique et cosmétique sont mises à profit, et des modèles équivalents à la peau humaine (HSE, *Human Skin Equivalent model*) sont notamment utilisés pour mesurer la biodisponibilité des substances [113]. Enfin Beriro et al. soulignent la complémentarité des études *in vitro* avec des approches *in vivo* et *in silico* [93].

6. EVALUATION GLOBALE DE L'EXPOSITION HUMAINE AUX COSV EN ENVIRONNEMENT INTERIEUR

L'agrégation de toutes les voies d'exposition permet de caractériser globalement l'exposition humaine aux COSV en environnement intérieur [35]. La prise en compte de la bioaccessibilité dans la caractérisation de chaque voie d'exposition permet d'évaluer plus finement cette exposition, comme l'illustre la Figure 19, qui complète la Figure 9 du Chapitre 1 (page 67).

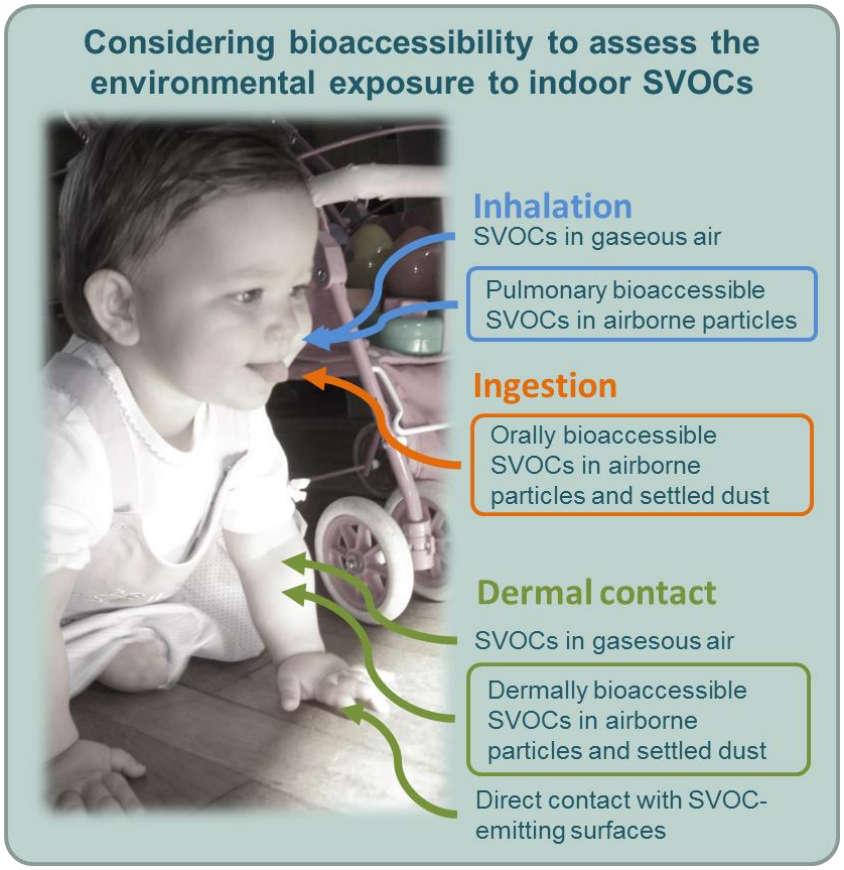


FIGURE 19 : CONSIDERER LA BIOACCESSIBILITE POUR EVALUER L'EXPOSITION AUX COSV EN ENVIRONNEMENT INTERIEUR

En 2005, Christopher Wild a introduit le concept d'exposome, défini comme l'ensemble des expositions à des facteurs environnementaux subis par un organisme humain à partir de sa conception, pour expliquer, en parallèle du génome, les causes d'apparition des maladies [114]. Les approches « top-down » consistent à mesurer dans des matrices biologiques, des biomarqueurs qui sont liés à l'environnement chimique interne de la personne. Ces approches sont complétées par des approches « bottom-up » qui permettent, à partir de mesures environnementales, de déterminer les sources et les méthodes pour les réduire [115]. Comme le soulignent Peters et al. [116] et Cui et Balshaw [117], la caractérisation des expositions externes est nécessaire pour bien comprendre l'exposome et les perspectives du présent projet sont de contribuer à l'acquisition de ces connaissances.

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VALORISATION SCIENTIFIQUE

ARTICLES SCIENTIFIQUES ASSOCIES AU PROJET

M. Pelletier, N. Bonvallot, O. Ramalho, C. Mandin, W. Wei, G. Raffy, F. Mercier, O. Blanchard, B. Le Bot, P. Glorennec, Indoor Residential Exposure to Semivolatile Organic Compounds in France, Environ. Int. 109 (2017) 81–88. doi:https://doi.org/10.1016/j.envint.2017.08.024.

W. Wei, N. Bonvallot, Å. Gustafsson, G. Raffy, P. Glorennec, A. Krais, O. Ramalho, B. Le Bot, C. Mandin, Bioaccessibility and bioavailability of environmental semi-volatile organic compounds via inhalation: A review of methods and models, Environ. Int. 113 (2018) 202–213. doi:10.1016/j.envint.2018.01.024.

COMMUNICATIONS ORALES DANS DES CONGRES SCIENTIFIQUES INTERNATIONAUX

Human exposure to semi-volatile organic compounds (SVOCs) via dust ingestion: a review of influencing factors, Indoor Air 2016 (Gand, Belgique, 3-8/07/2016)

Bioaccessibility of semi-volatile organic compounds (SVOCs) in settled dust, ISES (International Society of Exposure Sciences - Utrecht, Pays-Bas, 9-13/10/2016)

Assessment of the oral bioaccessibility of semi-volatile organic compounds in indoor settled dust using a simplified method, 9th International Workshop on Chemical Bioavailability in the Terrestrial Environment (Varsovie, Pologne, 5-8/11/2017)

COMMUNICATIONS AFFICHEES DANS DES CONGRES NATIONAUX ET INTERNATIONAUX

Characterisation of human exposure to semivolatile organic compounds (SVOCs) through indoor dust ingestion: measurement of SVOC bioaccessibility, 4th Day of the Young Researchers of Irset (Rennes, France, 8/12/2015)

Bioaccessibility of semivolatile organic compounds (SVOCs) in settled dust, EDCEH (European Doctoral College on Environment & Health) (Rennes, France, 6-8/6/2016)

Evaluation de la bioaccessibilité orale des COSV contenus dans les poussières des bâtiments. In: Journée des doctorants du CSTB, Journée des doctorants du CSTB (Paris, France, 4/10/2016)

Assessment of the oral bioaccessibility of semi-volatile organic compounds (SVOCs) in indoor settled dust, Rencontres scientifiques du réseau doctoral en santé publique (Rennes, France, 14/03/2017)

Assessment of the oral bioaccessibility of semi-volatile organic compounds (SVOCs) in indoor settled dust using a simplified method, 6th Day of the Young Researchers of Irset (Rennes, France, 11/1/2018)

Assessment of the oral bioaccessibility of semi-volatile organic compounds (SVOCs) in indoor settled dust using a simplified method, 1st European Exposure Science Strategy Workshop (Dortmund, Germany, 19-20/06/2018)

MEDIATION SCIENTIFIQUE

Participation à la fête de la science : *Pollution domestique : la santé en danger ?* (Rennes, France, 6-8/10/2017)

Intervention dans une école primaire : *Qu'y-a-t-il dans l'air de ma maison ?* (Rennes, France, 5/12/2017)

FIGURE 20 : SUPPORT DE MEDIATION SCIENTIFIQUE

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Indoor residential exposure to semivolatile organic compounds in France

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ABSTRACT

Multiple chemicals are emitted in residential accommodation. Aggregate Daily Doses (ADD) (ng/kg-bw/d) were estimated for 32 semivolatile organic compounds (SVOCs) of different chemical families that are frequently detected in French dwellings in both air and settled dust. Daily doses were determined using steady-state models for the population, categorized into 11 age groups covering birth to age 30. Three routes of exposure were taken into account: dust ingestion, inhalation (gaseous and particulate phases) and dermal contact with the gaseous phase of air. Contamination levels were preferentially retrieved from large, nationwide representative datasets. A two-dimensional probabilistic approach was used to assess parametric uncertainty and identify the most influential factors. For children aged 2 to 3 years, ADD estimates spanned orders of magnitude, with median values ranging from 8.7 pg/kg-bw/d for 2,2′,3,4,4′-pentabromodiphenylether (BDE 85) to 1.3 µg/kg-bw/d for di-isobutyl phthalate (DiBP). Inhalation, ingestion and dermal pathway contributed at varying levels, and depending on compound, air was the dominant medium for 28 of the 32 compounds (either by inhalation or dermal contact). Indoor exposure estimate variance was mainly driven by indoor contamination variability, and secondarily by uncertainty in physical and chemical parameters. These findings lend support to the call for cumulative risk assessment of indoor SVOCs.

1. Introduction

Both consumer product use and the production of chemicals have been rising constantly since the mid-20th century, and many of these chemicals are semivolatile organic compounds (SVOCs). SVOCs include compounds from various chemical families: phthalates, bisphenols, polycyclic aromatic hydrocarbons (PAHs), organophosphorus (OPs), organochlorines (OCs), synthetic musks, polychlorinated biphenyls (PCBs) and polybromodiphenylethers (PBDEs).

The health effects of SVOCs have been assessed by numerous studies on both humans and animals; some are suspected of having reprotoxic (Casas et al., 2013; Rubin, 2011), neurotoxic (Baldi et al., 2001; Blanc-Lapierre et al., 2012; Elbaz et al., 2009; Zaganas et al., 2013) or carcinogenic effects (Armstrong et al., 2004; IARC, 2015a, 2015b).

SVOCs are emitted by volatilization from their source materials and contaminate other compartments; in some cases, they can also migrate directly from source (Sukiene et al., 2017). In the indoor environment, they are found in the gas phase, airborne particles, settled dust (Weschler and Nazaroff, 2008) and on any other available surfaces such as walls, ceiling and flooring – as well as on human skin and clothing. In addition to dietary exposure and dermal contact with consumer products, humans are continuously exposed to these chemicals through various pathways, including inhalation of indoor air (gaseous and particulate phases), ingestion of settled dust and dermal contact with indoor air and settled dust (on floor and other surfaces). Many authors have assessed indoor exposure to certain families of SVOCs (phthalates, PBDEs, etc.), taking into account one or more exposure media via oral, respiratory (and sometimes dermal) pathways (Bekö et al., 2013; Gaspar et al., 2014; Linares et al., 2010; Mitro et al., 2016; Roosens et al., 2010; Trudel et al., 2011; Wilson et al., 2003). Mitro et al. (2016) recently estimated indoor exposures based on US dust surveys and an air contamination model. Here, we seek to use measurement data to assess the exposure of a large population and estimate the associated uncertainty.

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The objective of this study was to estimate the indoor exposure of people of various age groups, to 32 SVOCs from different chemical families frequently detected in French dwellings (Blanchard et al., 2014; Mandin et al., 2014, 2016). Three routes of exposure were taken into account: dust ingestion, inhalation of air (gaseous and particulate phases) and dermal contact with the gaseous phase of air. Contamination levels were preferentially retrieved from large, representative datasets. A two-dimensional probabilistic approach was used to assess the uncertainty associated with the different parameters, and identify the most impacting factors.

2. Methods

2.1. Target population

To address exposure across a broad section of the population, we estimated exposures for 11 age groups from birth to age 30 (as an example of an adult), following the U.S. Environmental Protection Agency (U.S. EPA, 2005) recommendations as to which age groups should be considered within a health risk assessment.

2.2. Compounds selection

32 SVOCs were selected on the basis of their health interest (Bonvallot et al., 2010), and because they were detected in both the air and the settled dust of French dwellings (Blanchard et al., 2014; Mandin et al., 2014, 2016).

2.3. Exposure model

The Aggregate Daily Doses (ADD) (ng/kg-bw/d) were assessed by summing internal (uptake) daily doses from dust ingestion ($DD_{ing\text{-}dust}$), inhalation of air (both gaseous and particulate phases) ($DD_{inh\text{-}air}$) and dermal contact with gas phase ($DD_{derm\text{-}gas}$).

Very few studies included the dermal exposure to dust pathway when assessing aggregate exposures to SVOCs. Trudel et al. (2011) studied dermal exposure to 8 PBDEs in dust. Even though they overestimated this pathway using in vitro experimental data with acetone as carrier vehicle (Roper et al., 2006), they found the contribution of dermal exposure to dust to be consistently < 20%, even for the most contaminated region, and for every age group (below 1 year to 65 years of age). Bekö et al. (2013) estimated indoor exposure to five phthalates and found a very low (< 1%) contribution of dermal exposure to dust, in comparison to other pathways. Since this pathway is typically found to be minor and required uptake parameters are ill-suited to dust exposure even when available, dermal exposure to dust was not addressed in this work.

2.4. Equations for exposure dose estimation

Daily Doses (DD) can be estimated in steady-state conditions using the following equations. These were adapted from relationships developed by Bekö et al. (2013) and Weschler and Nazaroff (2012, 2014).

Ingestion of settled dust:

$$DD_{ing\text{-}dust} = \frac{C_{dust} \times DI \times f_{oral} \times f_{dust} \times t}{BW} \quad (1)$$

where C_{dust} is the SVOC concentration in settled dust (ng/g), DI is the amount of dust ingested by an individual per day (g/d), f_{oral} is the oral bioavailability of the SVOC (−), f_{dust} is the bioaccessibility of the SVOC from the dust (−), t is the fraction of time spent in dwellings (−), BW is the body weight (kg), and $DD_{ing\text{-}dust}$ is expressed in ng/kg-bw/d.

Inhalation of indoor air:

$$DD_{inh\text{-}air} = \frac{(C_{part} + C_{gas}) \times IR \times f_{pulm} \times t}{BW} \quad (2)$$

where C_{part} is the SVOC particulate phase concentration (ng/m^3), C_{gas} is the SVOC gas phase concentration (ng/m^3), IR is the inhalation rate for an individual per day (m^3/d), f_{pulm} is the pulmonary bioavailability of the SVOC (−), t is the fraction of time spent in dwellings (−), BW is the body weight (kg), and $DD_{inh\text{-}air}$ is expressed in ng/kg-bw/d.

Dermal contact with the gas phase:

$$DD_{derm\text{-}gas} = \frac{C_{gas} \times k_{p\text{-}g} \times BSA \times t}{BW} \quad (3)$$

where C_{gas} is the SVOC gas phase concentration (ng/m^3), $k_{p\text{-}g}$ is the SVOC transdermal permeability coefficient (m/h), BSA is the body surface area (m^2), t is the daily duration exposure (h/d), BW is the body weight (kg), and $DD_{derm\text{-}gas}$ is expressed in ng/kg-bw/d. The steady-state model adapted by Weschler and Nazaroff (2012, 2014) used to estimate $k_{p\text{-}g}$ is described in more detail in Supplemental Material (see S1). This requires use of the SVOC octanol/water partition coefficients (log (K_{ow})), Henry's law constants (H) and coefficients describing the external transport of a gaseous SVOC from the bulk indoor air to the boundary layer adjacent to the skin (γ_d).

The ADD for a single SVOC for an individual was then calculated by summing the previous doses according to the following equation, and expressed in ng/kg-bw/d:

$$ADD = DD_{ing\text{-}dust} + DD_{inh\text{-}air} + DD_{derm\text{-}gas} \quad (4)$$

2.5. Parameter estimation for exposure model

Parameter distributions were constructed or retrieved from the literature as detailed below. Some of these parameters will be the same for all SVOCs (γ_d, BW, BSA, IR, DI and t) while others will vary from one compound to another (f_{oral}, f_{dust}, f_{pulm}, log (K_{ow}), H, C_{dust}, C_{part} and C_{gas}).

2.5.1. Physical and chemical parameters

For each SVOC, measured or estimated values of log (K_{ow}) and H at 25 °C were retrieved from: online databases - Hazardous Substances Data Bank (HSBD) and ChemIDplus (http://toxnet.nlm.nih.gov/), Chemspider (http://www.chemspider.com/), and Chemicalize (http://www.chemicalize.org/); toxicological and environmental data sheets from the French National Competence Center for Industrial Safety and Environmental Protection (INERIS) (http://www.ineris.fr/substances/fr/page/21); online calculators - Chemexper (https://www.chemexper.com/) and ACD/Labs (http://www.acdlabs.com/); EPI Suite software (U.S. EPA, 2013, v4.1) and the Handbook of Physical-Chemical Properties and Environment Fate for Organic Chemicals (Mackay et al., 2010a, 2010b, 2010c, 2010d). Particular attention was paid to avoiding duplicates (EPI Suite software, HSBD and ChemIDplus often used the same sources for these parameters). Furthermore, only values at the reference temperature of 25 °C were selected, in order to obtain comparable data between compounds and estimate DD at a constant temperature. At least two values were available for each SVOC. Where at least 15 values for log (K_{ow}) and H were available, distributions were fitted. Otherwise, we used either triangular distributions having at least three values (minimum, average and maximum), or uniform distributions for two retrieved values. See Table S1 for corresponding distributions and input parameters for each SVOC.

2.5.2. Contamination data

Contamination data were provided from measurements taken in recent French housing surveys. Concentration levels in settled dust collected from vacuum cleaner bags were retrieved from a national survey covering the 3.6 million French dwellings that were home to at least one child aged 6 months to 6 years in 2008–2009, using 145 samples (Mandin et al., 2014). Concentration levels in airborne Particulate Matter (PM) of 10 μm in diameter were retrieved from a national survey covering the 24.7 million French main residences, using 285

samples (Mandin et al., 2016). PM samples were collected from each living room over a period of one week, and assumed to be representative of each dwelling as a whole. SVOC gas phase concentrations were not available at national scale; data from 30 French dwellings (Blanchard et al., 2014) were used as a surrogate.

Modeling was established regarding the percentage of samples above the limit of detection (LOD) or the limit of quantification (LOQ) for the retrieved studies. For settled dust and PM measurements, lognormal distributions were fitted using summary statistics when > 75% of data were above LOD (Burmaster and Hull, 1997). This concerns 20 and 14 compounds, for settled dust and PM measurements respectively. Where detection frequency ranged from 20 to 75%, the maximum-likelihood estimation (MLE) was used to estimate lognormal distributions (Helsel, 2011; Helsel and Hirsch, 1992). This statistical method could be used to estimate the undetected data in the studies of Mandin et al. (2014, 2016), because sample sizes were large enough - with 145 and 285 samples for dust and PM respectively. The number of compounds concerned was 7 for settled dust and 11 for PM measurements. Where detection frequency ranged from 1 to 20%, custom distribution was modeled with discrete probability for the quantified values, and continuous uniform probability from 0 to LOD and from LOD to LOQ. The number of compounds concerned was 5 for settled dust and 7 for PM measurements. For the gas phase measurements, the Blanchard et al. (2014) sample size (n = 30) was too small to use MLE. So, where detection frequency ranged from 1 to 99%, custom distribution was modeled using continuous uniform probability from 0 to LOQ and discrete probability for the quantified values. For all three media, a literature survey was conducted to retrieve specific data when detection frequency was < 1%. Publications were selected in the following order of preference: conducted in Europe, post-2000 and providing sample size, measurement method, LOD and/or LOQ values and percentage of samples above the LOD and/or LOQ. Where a lower LOD or LOQ was used, other contamination information was used instead of the initially-selected data (Blanchard et al., 2014; Mandin et al., 2014, 2016). See Table S2 for corresponding distributions and input parameters for each SVOC in each medium.

2.5.3. Exposure media properties

Assessment of $DD_{derm\text{-}gas}$ (Eq. 3) requires use of a transdermal permeability coefficient, $k_{p\text{-}g}$, estimated using the specific physical and chemical parameters of each SVOC, and a non-specific mass transport coefficient, γ_d. This last describes the external transport of an SVOC from the gas phase in the core of a room through the boundary layer adjacent to the skin, see Eq. 1 (Supplemental Material). A triangular distribution was modeled for γ_d, using the minimum and maximum values found in the literature and the generally assumed value of 6 m/h as most likely (Pandrangi and Morrison, 2008; Tamas et al., 2006; Weschler and Nazaroff, 2008). See Table S3 for corresponding distribution and input parameters.

2.5.4. Bioaccessibility and bioavailabilities

Bioaccessibility in dust (f_{dust}) is the fraction of pollutant released from settled dust into the gastrointestinal tract and available for absorption (Rostami and Juhasz, 2011). For each SVOC, f_{dust} was retrieved from the literature survey performed by Raffy et al. (2016). Oral bioavailability (f_{oral}) is the fraction of a contaminant reaching the digestive system and absorbed into systemic circulation (Rostami and Juhasz, 2011). Pulmonary bioavailability (f_{pulm}) is the fraction of a contaminant reaching the alveolar system and absorbed into systemic circulation. For each SVOC, f_{oral} and f_{pulm} were retrieved from the following online databases: the HSBD (https://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB) and the Agency for Toxic Substances and Disease Registry (ATSDR) (https://www.atsdr.cdc.gov/). For each compound displaying at least three available values, triangular distributions were modeled (minimum, average and maximum values). Where only two values were retrieved, uniform distributions were modeled (minimum and maximum). Where only a single value was available, triangular distributions were modeled between this value (as the likeliest), and the minimum and the maximum values retrieved from other compounds belonging to the same chemical family. Finally, if no value was found for an SVOC, a uniform distribution was modeled between the minimum and the maximum values found for the other compounds from the same chemical family - or from the entire studied chemical families taken together if no other compound from the same chemical family was assessed. See Table S4 for corresponding distributions and input parameters for each SVOC.

2.5.5. Human body parameters

The World Health Organization (WHO, 2006) has identified and suggested common critical life stages for use in exposure and risk assessment. Because these were not available for every parameter and age group for populations living in France, we used the U.S. EPA Exposure Factors Handbook (U.S. EPA, 2011). The potential influence of this is covered in the discussion section. We compiled the distribution of human body weight (BW), body surface area (BSA), dust ingestion (DI), inhalation rate (IR) and time spent in dwellings (t). Lognormal distributions were used for BW, BSA and DI. Normal distributions were used for IR and t. See Table S5 for corresponding distributions and input parameters.

2.6. Simulation

DD from all three routes of exposure (Eqs. (1) to (3)) and ADD (Eq. (4)) were estimated using Crystal Ball® software (Oracle©, version 11.1.1.3.00). Latin Hypercube two-dimensional simulations were carried out with 500,000 runs for each SVOC, and each age group. Two-dimensional simulations take into account both the uncertainty (lack of knowledge about a parameter) and the variability (heterogeneity of a parameter in a population) of the input parameters. The following parameters were considered variable (i.e. high variability in relation to uncertainty): C_{dust}, C_{part}, C_{gas}, γ_d, BW, BSA, IR and t, whereas log (K_{ow}), H, f_{oral}, f_{dust} and f_{pulm}, were considered uncertain. DI was considered both uncertain and variable. Sensitivity analysis was performed in a one-dimensional simulation by assessing the contribution of each input parameter to ADD variance (the output), using linear regression.

3. Results

ADD (ng/kg-bw/d) estimates for the 32 SVOCs for children aged 2 to 3 years are shown in Fig. 1. We are presenting results for this specific segment because young children are more vulnerable than the rest of the population in terms of exposure to contaminants (due to more frequent contact with the ground and deposited dust, carrying objects in their mouths, higher inhalation rates, etc.) and more sensitive in terms of effects (due to ongoing development of the main organ systems, which continues after birth). Detailed results for ADD and the three DD from each exposure route for all 11 age groups (birth to age 30) are shown in Tables S8 to S18. ADD estimations spanned orders of magnitude, with median values ranging from 8.7 pg/kg-bw/d for 2,2′,3,4,4′-pentabromodiphenylether (BDE 85) to 1.3 μg/kg-bw/d for diisobutyl phthalate (DiBP) for children aged 2 to 3 years. Variability of ADD (relative interpercentile range, see Table S6) ranged from 1.2 for 2,2′,4,4′,5-pentabromodiphenylether (BDE 99) to 12 for 2,3,3′,4,4′-pentachlorobiphenyl (PCB 105), with a median value of 4. The median uncertainty on the mean was 40%, ranging from 11% for the benzo[*a*]pyrene to 230% for 2,3′,4,4′,5-pentachlorobiphenyl (PCB 118) (see detailed relative errors in Table S13).

The relative contribution of exposure pathways to aggregated median exposure is presented in Fig. 1 (bottom panel) for children aged 2 to 3 years. The relative contributions made by each route of exposure to total indoor estimates differ by compound, and could be related to their degree of volatility. For the most volatile SVOCs - that is those

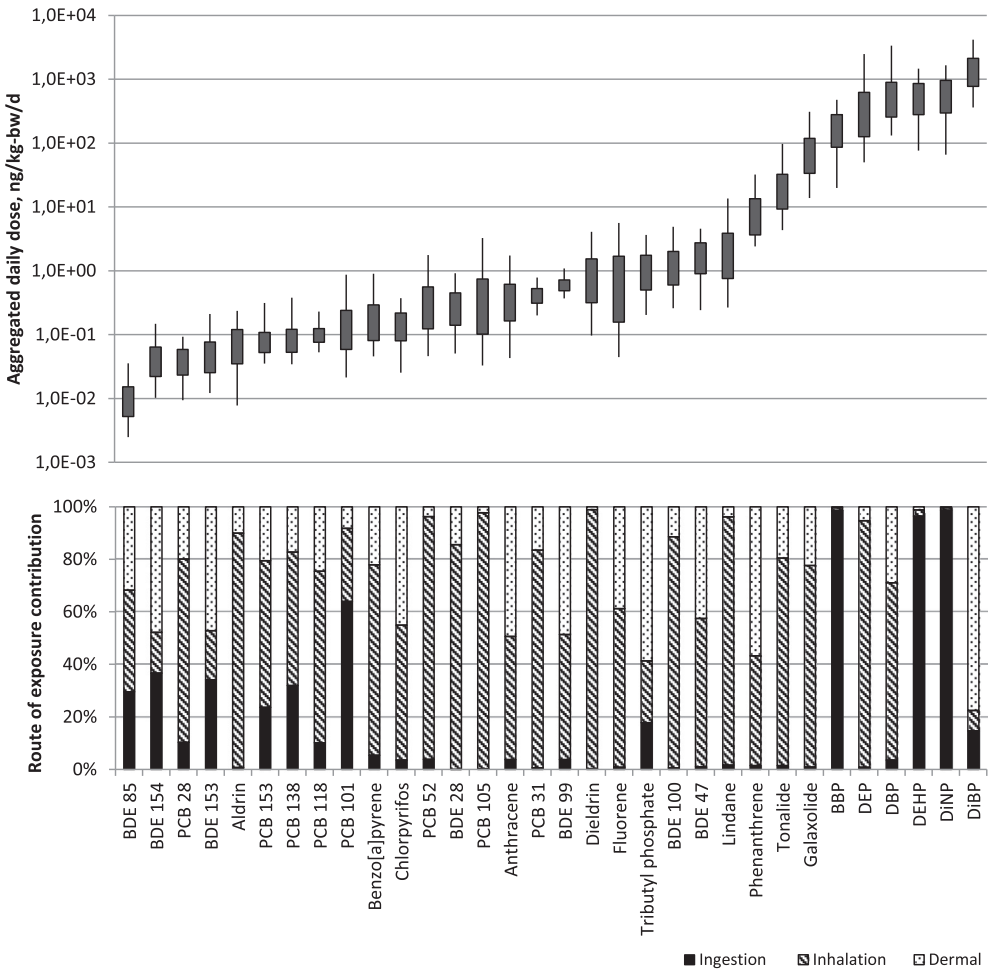

Fig. 1. Top panel of the graph shows Aggregate daily dose of each SVOC for a child aged 2 to 3 years (ng/kg-bw/d), percentiles 5th, 25th, 75th and 95th are presented in box plot format. The bottom panel of the graph shows the contribution made by each route of exposure (ingestion, inhalation and dermal exposure from air) to total indoor exposure, based on the median value estimated for each SVOC for children aged 2 to 3 years (ng/kg-bw/d).

compounds having an octanol-air partition coefficient (log (K_{oa})) value of 9 or less (see Table S1) and expected to be primarily gaseous (Weschler and Nazaroff, 2012), inhalation and dermal contact with the gas phase were the dominant routes of exposure: fluorene, anthracene, aldrin, dieldrin, tonalide, galaxolide, tributylphosphate, diethyl phthalate (DEP), dibutyl phthalate (DBP), DiBP and 2,4,4′-trichlorobiphenyl (PCB 28), 2,4′,5-trichlorobiphenyl (PCB 31) and 2,2′,5,5′-tetrachlorobiphenyl (PCB 52). For less volatile SVOCs - that is those compounds having a log (K_{oa}) value of 13 or greater (see Table S1) and expected to be primarily in the particle phase (Weschler and Nazaroff, 2012), dust ingestion was the dominant route of exposure: diethylhexyl phthalate (DEHP), di-isononyl phthalate (DiNP) and 2,2′,4,4′,5,6′-hexabromodiphenylether (BDE 154). The contribution made by different pathways was more contrasted for SVOCs having a log (K_{oa}) value of between 9 and 13 (see Table S1). On the whole, air was the dominant exposure medium (sum of inhalation and dermal contact > 50% of ADD) for 28 compounds out of 32, while dust was the major contributor for DEHP, DiNP, benzyl butyl phthalate (BBP) and 2,2′,4,5,5′-pentachlorobiphenyl (PCB 101). Overall, dust ingestion is more contributive to exposure for less volatile chemicals, although this is not the case with BBP and PCB 101, both of which are found in relatively high concentrations in dust.

Relative contributions of exposure pathways for P95 values were similar to median values. Notable exceptions were that higher contributions from dust ingestion were found for PCB 118, 2,2′,3,4,4′,5′-hexachlorobiphenyl (PCB 138) and 2,2′,4,4′,5,5′-hexachlorobiphenyl (PCB 153), and higher contributions from inhalation were found for benzo[*a*]pyrene and DBP.

The main sensitivity analysis results are shown in Fig. 2 (see Table S7 for detailed results). These reveal that contamination parameters are most influential: C_{gas}, C_{part} and C_{dust}, the only exception being H for BDE 99. Their relative contributions to ADD variance ranged from 30% for galaxolide (C_{part}) and BDE 99 (H) to 89% for fluorene (C_{gas}). For most compounds, the other influential parameters (having contributions higher than 10%) are the other contamination parameters: C_{gas}, C_{part} and C_{dust}, and also f_{pulm}. For some compounds, other influential parameters are f_{dust} (DEHP and DiNP) alongside physical and chemical parameters: log (K_{ow}) and H (lindane and BDE 99). Furthermore, compounds have been ranked by volatility in Fig. 2 (based on their log (K_{oa}) values), from most volatile (fluorene) to least volatile (DiNP). Among the most volatile SVOCs, C_{gas} tended to be the more influential parameter, while C_{dust} and C_{part} appeared influential for the least volatile. Lastly, we note that within each age group, human parameters were not influential.

ADD (ng/kg-bw/d) estimates for the 32 SVOCs for four age groups are shown in Fig. 3: infants aged 0 to 1 months, infants aged 1 to 3 months, children aged 2 to 3 years and adults aged 21 to 30 years. As expected, ADD decreases with age because of increasing BW - except within the [0–1 month] category where the dust ingestion rate equals 0 mg, and ADD may be lower in comparison with other groups. This is true in particular of compounds making a major contribution to dust ingestion (PCB 101, BBP, DEHP and DiNP). Detailed results for ADD across all 11 age groups (birth to age 30) are shown in Tables S8 to S18.

4. Discussion

Indoor exposure to 32 SVOCs was modeled using contamination measurements from dwellings and human body parameters. ADD

SVOC	Relative contribution (%)							
	[10-20]	[20-30]	[30-40]	[40-50]	[50-60]	[60-70]	[70-80]	[80-90]
Fluorene								**Cgas**
DEP	Cdust	fpulm			**Cgas**			
Anthracene								**Cgas**
Phenanthrene	Cdust						**Cgas**	
PCB 28			fpulm	**Cgas**				
PCB 31		fpulm			**Cgas**			
Tonalide		fpulm		**Cpart**				
Aldrin			fpulm		**Cgas**			
Dieldrin			fpulm		**Cpart**			
Galaxolide		fpulm Cgas	**Cpart**					
Tributylphosphate							**Cgas**	
DiBP		Cdust				**Cgas**		
PCB 52	Cdust	fpulm			**Cpart**			
DBP		fpulm			**Cpart**			
Lindane	fpulm H	Cpart	**Cgas**					
Chlorpyrifos		fpulm			**Cgas**			
BBP	Cpart				**Cdust**			
PCB 101	Cgas					**Cdust**		
BDE 28	fpulm	Cpart		**Cgas**				
PCB 138		Cgas				**Cdust**		
PCB 153			Cgas	**Cdust**				
PCB 118		Cdust			**Cgas**			
PCB 105	fpulm					**Cpart**		
BDE 47								**Cgas**
Benzo[a]pyrene								**Cpart**
BDE 99		Kow	**H**					
BDE 85							**Cgas**	
BDE 100	fpulm					**Cpart**		
BDE 153	Cdust					**Cgas**		
DEHP	fdust					**Cdust**		
BDE 154		Cdust				**Cgas**		
DiNP			fdust	**Cdust**				

Fig. 2. Relative contribution (%) of key parameters (C_{gas}, C_{part}, C_{dust}, f_{pulm}, f_{dust}, log (K_{ow}) and H) to total variation of Aggregate daily doses from exposures to 32 indoor SVOCs (ng/kg-bw/d) for children aged 2 to 3 years. Only relative contributions above 10% are represented. Bold font indicates the more influential parameter for each SVOC. Compounds are ranked according to their volatility (based on their log (K_{oa}) values) from the most volatile (fluorene) to the least volatile (DiNP).

spanned orders of magnitude from 8.7 pg/kg-bw/d to 1.3 μg/kg-bw/d. Inhalation, ingestion and dermal pathway all contributed, though differently across compounds. Indoor exposure estimations were influenced more by variability in indoor concentrations (C_{gas}, C_{part} and C_{dust}) than by uncertainty in physical and chemical parameters.

Study strengths include: 1) estimation of indoor exposure to numerous SVOCs from different chemical families via gas- and particle-phase inhalation, dermal contact with gas phase, and ingestion of settled dust; 2) use of field measurements in dust, particulate and gaseous phases; 3) use, when available, of large and nationwide representative datasets; 4) choice of a two-dimensional probabilistic approach, and 5) consideration of many age groups.

Study limitations include: 1) use of an exposure model that neglects dynamic conditions; 2) use of different data sets for different exposure media, and 3) uncertainty analysis being restricted to parameter uncertainty.

We used steady-state models to estimate indoor exposure to SVOCs. Because indoor air measurements were performed over a period of one week, and settled dust being collected in a vacuum cleaner, we assumed that equilibrium had been reached. Because we frequently move from one environment into another, or between rooms having different concentrations, equilibrium is rarely achieved for the transfer from air to skin. A transient model developed by Gong et al. (2014) considered convective mass transfer resistance in the boundary air layer adjacent

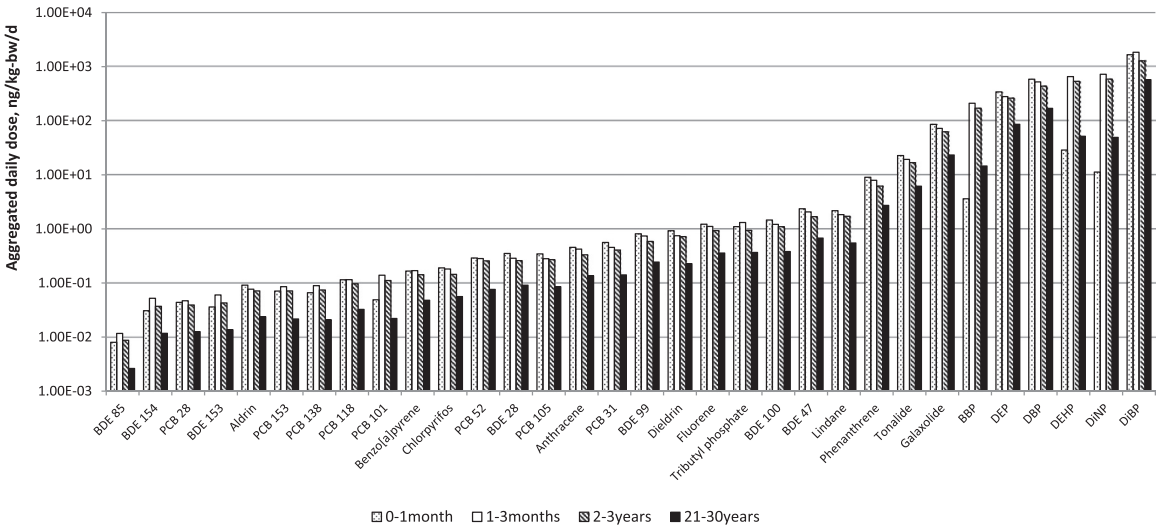

Fig. 3. Aggregate daily dose of each SVOC for four age groups (ng/kg-bw/d).

to the skin. Morrison et al. (2016) have recently improved this model by including skin surface lipids, which increase overall resistance to SVOC uptake from air. However, because these models require parameters that are not available for all compounds, default parameters are employed - rendering a probabilistic assessment difficult.

For contamination data in the three media when the detection frequency was < 1% (Blanchard et al., 2014; Mandin et al., 2014, 2016) a literature survey was conducted to retrieve other contamination information, which was then employed (instead of the initially-targeted data) where a lower LOD or LOQ was used by the authors (see Table S2). This concerned settled dust and gas phase concentrations for the 2,4,4′-tribromodiphenylether (BDE 28), and gas phase concentration alone for 12 other SVOCs: benzo[*a*]pyrene, PCB 31, PCB 105, PCB 118, PCB 138, PCB 153, BDE 47, BDE 85, BDE 99, 2,2′,4,4′,6-pentabromodiphenylether (BDE 100), 2,2′,4,4′,5,5′-hexabromodiphenylether (BDE 153) and BDE 154.

To put our results into perspective, this indoor aggregate multimedia and multipathway exposure assessment was compared to the few other studies investigating the same exposure pathways, namely: Bekö et al. (2013), Gaspar et al. (2014) and Mitro et al. (2016), who investigated phthalates and galaxolide for children aged 3 to 6 years in Denmark, California (US) and 14 states of the US, respectively. Our ADD estimated median values for children aged 3 to 6 years (see Table S14) were compared to: estimated median values for DBP and DEHP (Bekö et al., 2013; Gaspar et al., 2014); estimated median values for DiBP, BBP and DEP (Bekö et al., 2013), and estimated average values for DBP, DEHP, DiBP, BBP, DEP and galaxolide (Mitro et al., 2016). Similar results were found for DBP, DEHP and DEP. For DiBP, we found a median value equal to 1.1 μg/kg-bw/d, consistent with the 1.5 μg/kg-bw/d found by Bekö et al. (2013). Using a dust contamination level for this compound that was seven times lower, Mitro et al. (2016) found a lower exposure level equal to 0.1 μg/kg-bw/d. This difference in concentration data between French and US samples may also reflect a shift in the use of phthalates as a result of changes to the formulation of plasticizers. For BBP, we found a median value equal to 0.1 μg/kg-bw/d, consistent with the 0.2 μg/kg-bw/d of Mitro et al. (2016). Using a dust contamination level for this compound that was four times lower, Bekö et al. (2013) found a lower exposure level equal to 0.01 μg/kg-bw/d. Regarding galaxolide, our exposure level of 0.05 μg/kg-bw/d is consistent with Mitro et al. (2016) who found 0.1 μg/kg-bw/d - in line with dust contamination that was twice as high as ours.

Pathway contributions were found to be similar to Mitro et al. (2016) for DBP, DEP and galaxolide, with inhalation as the main route of exposure (> 50%), followed by dermal absorption from the gas phase and dust ingestion. Pathway contribution estimates from Bekö et al. (2013) for DiBP, BBP and DEHP are also similar to our findings, with total uptake dominated by dermal absorption from the gas phase for DiBP, and dust ingestion for BBP and DEHP. The results of the present study were also comparable to Gaspar et al. (2014), with dust ingestion dominating total uptake of DEHP.

In addition to the indoor exposure in dwellings assessed by this study, other sources of exposure (e.g. diet and personal care products) and other indoor environments (e.g. schools and offices) for many of these compounds contribute to total exposure, as well as direct dermal contact with surfaces. The use of personal care products, directly applied to skin or inhaled from aerosols, could have a non-negligible contribution to total exposure for some compounds, e.g., for certain phthalates (Romero-Franco et al., 2011) and musks (Zhang et al., 2017). Most of the studies addressing SVOC exposure assessment also looked at dietary ingestion (Beamer et al., 2012; Duggan et al., 2003; Lorber, 2007; Roosens et al., 2010; Trudel et al., 2011; Wilson et al., 2003; Wormuth et al., 2006). This could naturally lead to higher ADD estimates and different pathway contributions. Diet has been shown to be an important source of exposure for certain compounds: e.g. some PBDEs (Trudel et al., 2011) and some phthalates (Wilson et al., 2003). However, several authors who have performed exposure assessments on both indoor and diet exposure found that dietary ingestion was not the main route of exposure for chlorpyrifos (Beamer et al., 2012; Duggan et al., 2003), DEP, BBP and DiNP (Wormuth et al., 2006), some PBDEs (Lorber, 2007), some PCBs and some OCs (Wilson et al., 2003). For certain compounds, exposure via dietary ingestion could also equal exposure via non-dietary ingestion: e.g. DEHP (Wormuth et al., 2006), and anthracene, phenanthrene, benzo[*a*]pyrene and fluorene (Wilson et al., 2003). To put our results in perspective, we compared them to those of the French infant total diet study (ANSES, 2016a, 2016b). We compared to lower bound (LB) and upper bound (UB) median estimates for children aged 2 to 3 years. For 6 PCBs (sum of PCB 28, 52, 101, 138, 153 and 2,2′,3,4,4′,5,5′-heptachlorobiphenyl (PCB 180)) our median residential indoor ADDs were about one order of magnitude lower than dietary exposure estimates (LB and UB). For 7 PBDEs (sum of BDE 28, 47, 99, 100, 153, 154 and 2,2′,3,4,4′,5′,6-heptabromodiphenylether (BDE 183)) they were about one order of magnitude higher (LB and UB). For DEHP they were of the same order of magnitude (LB and UB). For DiNP and lindane they were of the same order of magnitude as the LB estimates and about one order of magnitude lower than the UB. For BBP, DEP and DBP they were of the order of magnitude of UB estimates, and one order of magnitude higher than the LB. For DiBP they were about one or two orders of magnitude higher than UB and LB respectively. For chlorpyrifos, dieldrin and aldrin they were of the same order of magnitude, in comparison with the LB estimates, and about two orders of magnitude lower, in comparison with the UB.

Compared to more traditional deterministic approaches, probabilistic methods (e.g. Monte Carlo simulations) have the main advantage of addressing input parameters featuring both uncertainty and variability. ADD estimations were mainly dependent on variability in indoor concentrations (C_{gas}, C_{part} and C_{dust}), and secondarily by uncertainty in f_{pulm} and physical and chemical parameters. Uncertainty of parameters is related to lack of total knowledge, whereas data variability refers to true heterogeneity. An interesting finding is that although input parameter uncertainty has been accused of causing broad uncertainty in exposure estimates (Pelletier et al., 2017; Salthammer and Schripp, 2015), it appeared to contribute less to total variance of ADD than did variability. For every compound but one, variability of a concentration explains at least 40% of ADD variance; in half of all cases, this exceeded 60%. Concentrations of a chemical within dwellings span orders of magnitude, especially as a result of the presence (or absence) of a source in the dwelling. Physical and chemical parameters can either be measured experimentally or calculated using other chemical properties. Depending on which of these methods is used, it follows that values vary by one order of magnitude or more (Finizio et al., 1997) - and these uncertainties are propagated in the calculation of $DD_{derm\text{-}gas}$ and then ADD. Up to 34% of ADD variation for aldrin could be explained by uncertainty in f_{pulm} (see Table S7) because data for most of the SVOCs were unavailable. Indeed, data were available for just two compounds: 2,2′,4,4′-tetrabromodiphenylether (BDE 47) and benzo[*a*]pyrene, leading to modeling of uniform distribution between 0 and 100% for most compounds (see Table S4) and to potential overestimation of inhalation exposure. The same limit was encountered for the other uptake fractions (f_{oral} and f_{dust}), though to a lesser extent. For most SVOCs, in respect of f_{oral}, even where pharmacokinetics studies were available and provided qualitative evidence that the SVOC was absorbed following oral exposure, no quantitative data describing in vivo oral absorption were available in the literature. Moreover, in laboratory animals, absorption of a compound can also depend strongly on experimental parameters, such as the carrier vehicle employed (Huwe et al., 2008). For example, gastrointestinal lindane bioavailability in rats ranged from 6% when the compound was suspended in water to 99% when given in oil. A further aspect is that we used PM_{10} measurements, whereas a smaller sampling fraction would have been more representative of respirable particles - this may result in an overestimation of the inhalation pathway for those SVOCs mainly present in the particulate phase (BDE 47, BDE 99, benzo[*a*]pyrene, PCB 118, PCB 138 and PCB 153). Human

body parameters (BW, BSA, IR, DI and t) are highly variable and, to a lesser extent, uncertain. Özkaynak et al. (2011) found significant uncertainty on DI, and this result led us to consider both uncertainty and variability for this parameter in our study. Nevertheless, we found that human body parameters made a marginal or null contribution (see Table S7) to the variance of ADD for a child aged 2 to 3 years, for each SVOC. It is however important to bear in mind both that we ran the model age-group by age-group, and that these parameters can have a broader impact when applied to a more diverse population.

Recent studies have investigated and modeled the clothing effect. Morrison et al. (2016) have shown that frequency of bathing and changing clothes were influential in terms of dermal uptake. In addition, introduction to the model of a skin surface lipid film, and its interactions with clothing, may affect results. The authors assessed the influence of clothing on the dermal uptake of two phthalates (DEP and DBP). They found that clean clothes were protective against air pollutants, whereas worn clothes, because they had adsorbed air pollutants, increased dermal uptake. Because only clean clothes could be considered protective, we decided to not take into account the role of clothing in this study, making the assumption that the total body surface area was exposed to the gaseous phase.

5. Conclusions

This indoor aggregate multimedia and pathway exposure assessment considered a wide range of pollutants, across a broad population. It reveals that exposure spanned orders of magnitude, from pg/kg-bw/d to μg/kg-bw/d and was mainly dependent on indoor SVOC contaminations. Within the boundaries of the conceptual model we used, exposure variability overwhelmed its uncertainty. Air was the dominant medium for most compounds, either by inhalation or dermal contact. Along with evidence of these compounds causing similar toxic effects (Fournier et al., 2014; Mitro et al., 2016), these findings lend support to the call for cumulative risk assessment of indoor SVOCs.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2017.08.024.

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Review article

Bioaccessibility and bioavailability of environmental semi-volatile organic compounds *via* inhalation: A review of methods and models

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ABSTRACT

Semi-volatile organic compounds (SVOCs) present in indoor environments are known to cause adverse health effects through multiple routes of exposure. To assess the aggregate exposure, the bioaccessibility and bioavailability of SVOCs need to be determined.

In this review, we discussed measurements of the bioaccessibility and bioavailability of SVOCs after inhalation. Published literature related to this issue is available for 2,3,7,8-tetrachlorodibenzo-p-dioxin and a few polycyclic aromatic hydrocarbons, such as benzo[*a*]pyrene and phenanthrene. Then, we reviewed common modeling approaches for the characterization of the gas- and particle-phase partitioning of SVOCs during inhalation. The models are based on mass transfer mechanisms as well as the structure of the respiratory system, using common computational techniques, such as computational fluid dynamics. However, the existing models are restricted to special conditions and cannot predict SVOC bioaccessibility and bioavailability in the whole respiratory system.

The present review notes two main challenges for the estimation of SVOC bioaccessibility and bioavailability *via* inhalation in humans. First, *in vitro* and *in vivo* methods need to be developed and validated for a wide range of SVOCs. The *in vitro* methods should be validated with *in vivo* tests to evaluate human exposures to SVOCs in airborne particles. Second, modeling approaches for SVOCs need to consider the whole respiratory system. Alterations of the respiratory cycle period and human biological variability may be considered in future studies.

1. Introduction

Semi-volatile organic compounds (SVOCs) are defined as molecules with vapor pressures between 10^{-9} and 10 Pa at 25 °C (Weschler and Nazaroff, 2008). SVOCs originate from indoor and outdoor sources and are widely present in people's everyday lives (Blanchard et al., 2014). Common indoor environmental SVOCs include phthalate esters used as plasticizers; polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) used as flame retardants; organochlorine and organophosphorus pesticides; synthetic musks; polycyclic aromatic hydrocarbons (PAHs); and alkylphenols used as additives in detergents, fuels, lubricants, polymers, and other products. These compounds are present in the gas phase and absorbed on airborne particles, settled dust, and indoor surfaces (Bi et al., 2015; Blanchard et al., 2014; Mandin et al., 2016).

Most SVOCs cause adverse health effects, including neurotoxic and reprotoxic effects (Fournier et al., 2014). Chemicals such as organochlorines (*e.g.*, dichlorodiphenyltrichloroethane and PCBs), brominated compounds (*e.g.*, PBDEs), bisphenol A, PAHs, alkylphenols, pesticides, and a variety of phthalate esters have endocrine-disrupting properties (De Coster and Van Larebeke, 2012). In addition, some phthalate esters have been shown to play a role in atopic diseases such as asthma, eczema and rhinitis (Bekö et al., 2015; Bornehag et al., 2004; Hsu et al., 2012; Jaakkola and Knight, 2008; Kolarik et al., 2008). PAHs,

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especially benzo[*a*]pyrene (BaP), and some organochlorine and organophosphate pesticides are also known to be carcinogenic compounds according to the International Agency for Research on Cancer. Inhalation exposure may play an important role in the exposure to SVOC, such as some PAHs and phthalate esters (Jaakkola and Knight, 2008; Kim et al., 2013; Pelletier et al., 2017). If it is less obvious for other SVOCs, the contribution of the inhalation route to indoor SVOC exposure has been estimated as being important for PBDEs, PCBs, pesticides, musks, and phthalate esters with high volatility (Pelletier et al., 2017).

Human exposure to environmental SVOCs can occur *via* the ingestion of settled dust, dermal absorption, and inhalation (Weschler and Nazaroff, 2008), as the compounds partition between different phases in the air, on indoor surfaces, and in settled dust. The SVOC concentrations in the gas phase, particle phase, and settled dust are commonly used for the estimation of human exposure to environmental SVOCs (Pelletier et al., 2017). However, the use of rough concentrations may overestimate the uptake of SVOCs because a fraction of the SVOCs may not be bioaccessible or bioavailable. To improve the health risk assessment associated with the multiple routes of SVOC exposure, the bioaccessible or bioavailable concentrations should be determined (Semple et al., 2004). The definitions of bioaccessibility and bioavailability from the perspectives of toxicologists and environmental scientists are diverse (Reichenberg and Mayer, 2006; Semple et al., 2004). In the present study, the bioaccessible fraction of a compound is defined as the amount that is released into the body fluid and available for absorption (Caboche et al., 2011; Collins et al., 2015; Rostami and Juhasz, 2011), whereas the bioavailable fraction is defined as the amount that can cross a biological membrane and reach systemic circulation (Collins et al., 2015; Rostami and Juhasz, 2011; Yu et al., 2012). Using the bioavailability increases the accuracy of the exposure assessment. Due to difficulties in the measurement of the bioavailability, as it requires measurements in human biological endpoints, SVOC bioaccessible concentrations from environmental media can be used as a substitute. The fraction of a compound released into the fluid of an organism (the bioaccessible fraction) is higher than that subsequently transferred into the bloodstream (the bioavailable fraction) (Kastury et al., 2017).

The bioaccessibility and bioavailability of a number of SVOCs *via* ingestion and dermal contact have been studied through *in vitro* and *in vivo* tests, respectively. In the *in vitro* bioaccessibility studies, the absorption of SVOCs was studied employing real or simulated human gastrointestinal (He et al., 2016; Juhasz et al., 2014; Kang et al., 2012; Wang et al., 2013; Yu et al., 2012) or skin receptor (Beriro et al., 2016) fluids. In the *in vivo* bioavailability studies, human or animal subjects were exposed to SVOCs by ingestion (Wu et al., 2007) or dermal contact (Abdallah et al., 2015; Morrison et al., 2016; Wester et al., 1990), and the SVOC concentration in the blood, urine, or organism was measured (Beriro et al., 2016; Koch et al., 2005).

The bioaccessibility and bioavailability of inhaled metals in ambient particles have been critically reviewed (Boisa et al., 2014; Kastury et al., 2017; Wiseman, 2015). Significant methodological differences were observed among the studies within the compositions of leaching agents used during the extraction and the use of static *versus* dynamic methods. The bioaccessibility and bioavailability of inhaled SVOCs have rarely been studied. Inhaled SVOCs may exist in both the gas and particle phases, which can deposit in respiratory tracts by four mechanisms and become bioaccessible (Fig. 1) (Pankow, 2001): the deposition of gas-phase compounds (GD: gas deposition), deposition of gas-phase compounds evaporated from the inhaled particles (EGD: evaporated gas deposition), deposition of inhaled particles followed by the deposition of the gas-phase compounds evaporated from the deposited particles (PDEGD: particle deposition and evaporated gas deposition), and deposition of inhaled particles followed by the diffusion of compounds from the deposited particles to the fluid of the respiratory tracts (PDD: particle deposition and diffusion). These four general mechanisms can be applied to a number of compounds including SVOCs.

Thus, in this paper we aim to (1) review the existing measurement methods addressing the bioaccessibility and bioavailability of SVOCs *via* inhalation, (2) review the existing mathematical models addressing the bioaccessibility and bioavailability of SVOCs and other chemical compounds relevant for SVOCs *via* inhalation, and (3) discuss the key challenges to determining the SVOC bioaccessibility and bioavailability *via* inhalation.

To carry out the review, peer-reviewed papers were retrieved using "bioaccessibility" OR "bioavailability" AND "inhalation" as key words in the Google Scholar, Science Direct, and PubMed search engines, regardless of the date of publication.

2. Measurements of SVOC bioaccessibility and bioavailability following inhalation

2.1. SVOC bioaccessibility (in vitro tests)

Five articles have been found on the bioaccessible fraction that is soluble in the fluid environment of a target organism that address the desorption of SVOCs due to the PDEGD and PDD mechanisms. Three of them were published after the year 2000. The bioaccessibility of certain particle-phase PAHs was measured *in vitro* using synthetic lung fluids, and the desorbed PAHs were extracted with solvents (Gerde and Scholander, 1989).

The *in vitro* method frequently differs from one study to another. Woodstove particles containing BaP were added into phospholipid vesicles to simulate the transport of particle-phase BaP into biomembranes (Bevan and Yonda, 1985). After 18 h of incubation in phospholipid vesicles at 37 °C, the BaP was extracted with ethyl acetate at 50 °C. Meanwhile, the total extractable amount of BaP in the woodstove particles was assessed by adding 2 g of BaP into 9 ml of toluene and placing the mixture at 70–80 °C for 48–72 h. The results showed that 98–100% of the particle-phase BaP was extractable with toluene, of which 25% entered the phospholipid vesicles. This value has not been compared to data from *in vivo* studies.

Gerde et al. measured the bioaccessibility of 120 μg of inhaled particle-phase BaP by extraction in 17 ml of 1-octanol as a synthetic lung fluid at 37 °C in a cylindrical glass reactor with a two-bladed impeller (Gerde et al., 2001). The inhaled particles were BaP-coated diesel soot containing 14.5 ng BaP per μg soot (25% of a monomolecular layer). The soot-adsorbed BaP decreased from 25% to 16% within 48 h. This value is similar to that of the *in vivo* study obtained 5.6 months after the inhalation exposure of dogs to the same particles. Therefore, the authors concluded that 36% of the total soot-adsorbed BaP, *i.e.*, 9% of the monomolecular layer, was bioaccessible, and that the remaining BaP was retained on the particles in the lung. However, when the carrier particles were composed of silica in powder form with a 3.5 μm diameter and pores of 80 Å in diameter, the bioaccessible fraction of 100 mg of BaP/silica powder extracted with 17 ml of 1-octanol in a stirred reactor under the same temperature was > 85% within 5 min after inhalation (Ewing et al., 2006). This value has not been compared to data from *in vivo* studies.

Borm et al. measured the bioaccessibility of five different inhaled particle-phase PAHs in saline containing dipalmitoylphosphatidylcholine (DPPC) in different concentrations (100–10,000 μg/ml) in the dark in a shaking water bath for 24 h at 37 °C (Borm et al., 2005). The studied particles were reference diesel and four types of carbon black with different properties, *i.e.*, with the surface area ranging from 20 to 300 m^2/g. The carbon black particles contained 0.001–191 ng PAHs per mg particle. The leachable PAHs were extracted for 60 s using tertiary butyl methyl ether. The fraction of PAHs desorbed from the particles into the DPPC solutions was < 1.2% for phenanthrene, < 0.4% for pyrene, < 1.0% for anthracene, < 1.3% for chrysene, and < 1.3% for fluoranthene. These results were compared with the data of the PAH–DNA adducts obtained 13 weeks after the inhalation exposure of rats to the same particles. The results of the *in vivo* study showed that a small fraction of these particle-phase PAHs could become bioavailable

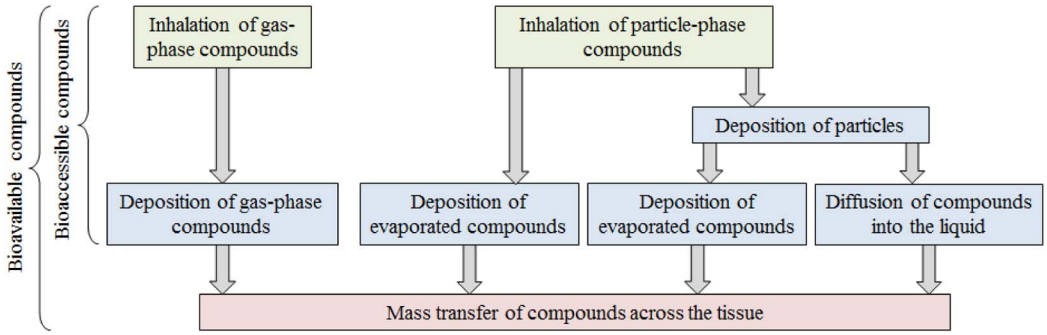

Fig. 1. Model schematics for the evaluation of the bioaccessibility and bioavailability *via* inhalation.

when the particles have a high PAH content.

A summary of the results from these studies on SVOC bioaccessibility is presented in Table 1. Together, the literature describes the bioaccessibility of 7 PAHs (BaP, benzo[*k*]fluoranthene, phenanthrene, pyrene, anthracene, chrysene, and fluoranthene) following an inhalation scenario. The bioaccessibilities of BaP and benzo[*k*]fluoranthene vary between 25% and > 85%, while the bioaccessibilities of the other 5 PAHs are < 1.3%. The methods for measuring the bioaccessibility of SVOCs in lung lining fluids differed between studies. There are many factors that may affect the bioaccessibility, depending on the method. For example, different SVOC-carrier particles were used, including woodstove particles, diesel soot, carbon black, and silica, and their different physical and chemical properties may affect the bioaccessibility of the SVOCs. Additionally, different fluids were used to simulate the lung lining fluid following a scenario of particle deposition within the airways: water, phospholipid vesicles, 1-octanol, and DPPC. The extraction mediums include ethyl acetate, 1-octanol, tertiary butyl methyl ether, and toluene, which also have different properties that may affect the bioaccessibility of the SVOCs. Moreover, the time of incubation and the temperature varied among these studies, and both are factors that can affect the results. More studies are needed to explain the differences across the compounds and studies.

In summary, the determined bioaccessible fraction may depend on many different parameters such as the composition and volume of the simulated lung fluid, the nature of the particles, the extraction time, the temperature, and the agitation. Various methods have been reported, resulting in difficulties in comparing the results among the studies. Therefore, it is important to validate the *in vitro* results using data from *in vivo* studies. Moreover, the proper quality control/quality assurance of the analysis of the extraction fluid is essential for bioaccessibility measurements (Rodríguez-Navas et al., 2017). Guney et al. suggested developing more rigor measurement methods for future studies of inhalation exposure (Guney et al., 2016).

2.2. SVOC bioavailability (in vivo and ex vivo tests)

Ten articles have been found on the bioavailable fraction that reaches the systemic circulation of a subject, and four of them were published after the year 2000. The bioavailability of 2,3,7,8-tetrachlorodibenzo-p-dioxin and some PAHs *via* particle-phase inhalation was measured in human and animal subjects. Measurements of the SVOC bioavailability in humans were performed *in vivo* by Gardiner et al., where the bioavailability of pyrene was analyzed in five non-smokers who worked in plants manufacturing carbon black (Gardiner et al., 1992). In this study, the pyrene in the air of the working environment was assumed to be the only source of exposure, and the concentration of 1-hydroxypyrene was measured in their urine at the end of the working shift as an indicator of the bioavailability of pyrene. The results varied largely from one individual to another. The average concentration of 1-hydroxypyrene was 0.3 μmol 1-hydroxy-pyrene per mol creatinine, while the average pyrene concentration in airborne particles was 8 mg/m^3. Although there were no control groups in the study, the urine values of the workers on the Monday, after a weekend without working in the plant, were lower than the rest of the week's values (p-value = 0.000137). The authors noted that due to the diversity of SVOC sources in everyday human life, this method can be applied to only special cases.

Investigations of bioavailability have more frequently been carried out in animals, *e.g.*, rats and dogs. Gerde et al. measured the *in vivo* bioavailability of inhaled particle-phase BaP in 3 dogs (Gerde et al., 2001). The inhaled particles were BaP-coated diesel soot containing 14.5 ng BaP per μg soot (25% of a monomolecular layer). The particles were pushed once into the dog lungs over a 4–5 s period, and the dogs were apneic for the next 2 min. Blood samples were taken continuously for 1 h directly after the exposure. Eighteen percent of the soot-adsorbed BaP was bioavailable within 4.3 min after inhalation. Other *in vivo* bioavailability tests in animals using similar methods are summarized in Table 2 (Gøtze et al., 1994; Nessel et al., 1992; Ramesh et al., 2002, 2001; Withey et al., 1993, 1992). Samples have been taken of blood, lung tissues, and liver tissues. The bioavailability of particle-phase 2,3,7,8-tetrachlorodibenzo-p-dioxin was found to be 100% (Nessel et al., 1992), while the bioavailability of particle-phase BaP was found to vary between 25% (Ramesh et al., 2002) and 65% (Ramesh et al., 2001). When the concentration of the particle-phase pyrene ranged between 200 and 800 mg/m^3, the pyrene concentration in the blood ranged between 2.5 and 23.4 μg/g (Withey et al., 1992).

Fouchécourt et al. housed 4 rats in cages containing PAH-contaminated soil for 3 days to study the exposure *via* inhalation, ingestion, and dermal absorption (Fouchécourt et al., 1999). The rat lungs were exposed to PAHs directly by the inhalation of contaminated soil and indirectly by blood circulation. However, the contribution of each route was not quantified or distinguished. While the soil contained 13 PAHs, only 3 (BaP, fluoranthene, and pyrene) were detected in the lung after sacrificing the exposed rats. The cytochrome P450-dependent monooxygenase activity, followed by 7-ethoxyresorufin O-deethylase (EROD) activity measurement, a biomarker of chemical exposure (Whyte et al., 2000) in the lungs, showed that the composition of the carrier particles can affect the absorption and bioavailability of the particle-phase SVOCs (Fouchécourt et al., 1999).

The SVOC bioavailability can also be measured *ex vivo* in an isolated and perfused lung (IPL) (Tornquist et al., 1988). Ewing et al. measured the bioavailability of the inhaled particle-phase BaP in 10 rats (Ewing et al., 2006). The inhaled particles were BaP-coated silica in powder form containing 1.3 ng BaP per μg silica powder. The rat lungs were excised and kept ventilated *ex vivo* in an artificial thoracic chamber at 37 °C and perfused with albumin buffer. The particles were pushed into the IPL over a one-minute period while rebreathing was prevented by maintaining a constant downstream flow in the lungs. The lung lobes were dissected, and the amount of BaP deposited in the lung tissues was analyzed. The bioavailability of the inhaled particle-phase BaP was dose-dependent and was approximately 100% under sub-saturation dosing regimens. It has been noted by the U.S. Food and Drug

Table 1
Measurements of the SVOC bioaccessibility *via* inhalation.

Reference	SVOC	Vapor pressure (Pa)	Particle	Particle size (μm)	SVOC content (ng/mg particle)	Synthetic lung medium	Leaching temperature (°C)	Leaching time	Extraction medium	Extraction temperature (°C)	Extraction time	Agitation	Analytical instrument	Bioaccessibility
(Bevan and Yonda, 1985)	BaP	7.3×10^{-7}	Woodstove particle	NA	1.5 ± 0.1	Phospholipid vesicles	37	18 h	Ethyl acetate	50	NA	Bath-type sonicator	HPLC	25%
(Gerde et al., 2001)	BaP	7.3×10^{-7}	Diesel soot	1.3 ± 0.2	14,500	1-octanol (120 μg particle in 17 ml liquid)	37	20 s	1-octanol	37	8 min	Two-bladed impeller (15 mm diameter, 12 mm height, 400 rpm)	HPLC	36%
(Ewing et al., 2006)	BaP	7.3×10^{-7}	Silica	3.5	1300 ± 60	1-octanol (100 mg particle in 17 ml 1-octanol)	37	5 min	1-octanol	37	NA	Stirring	HPLC	> 85%
(Bevan and Yonda, 1985)	BkF	1.3×10^{-7}	Woodstove particle	NA	0.22 ± 0.02	Phospholipid vesicles	37	18 h	Ethyl acetate	50	NA	Bath-type sonicator	HPLC	68%
(Borm et al., 2005)	Phe	1.6×10^{-2}	Diesel or carbon black particle	NA	0.001–191	Dipalmitoylphosphatidylcholine (3–60 mg particle in 3 ml saline)	37	24 h	Tertiary butylmethyl ether	NA	60 s	Shaking water bath	HPLC	< 1.2%
(Borm et al., 2005)	Pyr	6.0×10^{-4}	Diesel or carbon black particle	NA	0.001–191	Dipalmitoylphosphatidylcholine (3–60 mg particle in 3 ml saline)	37	24 h	Tertiary butylmethyl ether	NA	60 s	Shaking water bath	HPLC	< 0.4%
(Borm et al., 2005)	Ant	8.7×10^{-4}	Diesel or carbon black particle	NA	0.001–191	Dipalmitoylphosphatidylcholine (3–60 mg particle in 3 ml saline)	37	24 h	Tertiary butylmethyl ether	NA	60 s	Shaking water bath	HPLC	< 1%
(Borm et al., 2005)	Chr	8.3×10^{-7}	Diesel or carbon black particle	NA	0.001–191	Dipalmitoylphosphatidylcholine (3–60 mg particle in 3 ml saline)	37	24 h	Tertiary butylmethyl ether	NA	60 s	Shaking water bath	HPLC	< 1.3%
(Borm et al., 2005)	Flu	1.2×10^{-3}	Diesel or carbon black particle	NA	0.001–191	Dipalmitoylphosphatidylcholine (3–60 mg particle in 3 ml saline)	37	24 h	Tertiary butylmethyl ether	NA	60 s	Shaking water bath	HPLC	< 1.3%

BaP: benzo[*a*]pyrene, BkF: benzo[*k*]fluoranthene, Phe: phenanthrene, Pyr: pyrene, Ant: anthracene, Chr: chrysene, Flu: fluoranthene, NA: not available, HPLC: high-performance liquid chromatography. Vapor pressures were calculated at 25 °C using the EPI Suite program developed by the U.S. Environmental Protection Agency.

Table 2
Measurements of the SVOC bioavailability *via* inhalation.

Reference	SVOC	Vapor pressure (Pa)	Particle	Particle diameter (μm)	SVOC content (ng/mg particle)	Animal	Method	Exposure time	Biological endpoints	Sampling period	Analytical instrument	Bioavailability
(Nessel et al., 1992)	TCDD	2.0×10^{-7}	Soil	< 20	72.2 ppm	Female Sprague-Dawley rats (200–250 g)	*In vivo*	1, 7, or 28 d	Liver tissue	After exposure	GC–MS	100%
(Gardiner et al., 1992)	Pyr	6.0×10^{-4}	Carbon black	NA	8 mg/m^3	Humans	*In vivo*	5 d	Urine	After exposure	HPLC	0.3 μmol 1-hydroxy-pyrene per molcreatinine
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	200 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Blood	After exposure	HPLC	2.5 ± 0.7 μg/g blood
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	200 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Lung	After exposure	HPLC	1.6 ± 0.4 μg/g organ
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	350 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Blood	After exposure	HPLC	5.4 ± 0.9 μg/g blood
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	350 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Lung	After exposure	HPLC	4.7 ± 0.7 μg/g organ
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	500 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Blood	After exposure	HPLC	12.1 ± 1.4 μg/g blood
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	500 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Lung	After exposure	HPLC	9.4 ± 1.8 μg/g organ
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	650 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Blood	After exposure	HPLC	19.2 ± 3.1 μg/g blood
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	650 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Lung	After exposure	HPLC	14.8 ± 2.4 μg/g organ
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	800 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Blood	After exposure	HPLC	23.4 ± 4.4 μg/g blood
(Withey et al., 1992)	Pyr	6.0×10^{-4}	Micro-condensation aerosol	1.6–2.7	800 mg/m^3	Pregnant Wistar rats (250–300 g)	*In vivo*	95 min	Lung	After exposure	HPLC	14.8 ± 1.9 μg/g organ
(Fouchécourt et al., 1999)	Pyr	6.0×10^{-4}	Coke plant soil	< 10	54	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	327 ng/g organ
(Withey et al., 1993)	BaP	7.3×10^{-7}	Micro-condensation aerosol	0.61–0.88	200 mg/m^3	Pregnant Wistar rats (250–350 g)	*In vivo*	95 min	Blood	After exposure	HPLC	2.7 μg/g blood
(Withey et al., 1993)	BaP	7.3×10^{-7}	Micro-condensation aerosol	0.61–0.88	350 mg/m^3	Pregnant Wistar rats (250–350 g)	*In vivo*	95 min	Blood	After exposure	HPLC	4.4 μg/g blood
(Withey et al., 1993)	BaP	7.3×10^{-7}	Micro-condensation aerosol	0.61–0.88	500 mg/m^3	Pregnant Wistar rats (250–350 g)	*In vivo*	95 min	Blood	After exposure	HPLC	13.7 μg/g blood
(Withey et al., 1993)	BaP	7.3×10^{-7}	Micro-condensation aerosol	0.61–0.88	650 mg/m^3	Pregnant Wistar rats (250–350 g)	*In vivo*	95 min	Blood	After exposure	HPLC	18.8 μg/g blood
(Withey et al., 1993)	BaP	7.3×10^{-7}	Micro-condensation aerosol	0.61–0.88	800 mg/m^3	Pregnant Wistar rats (250–350 g)	*In vivo*	95 min	Blood	After exposure	HPLC	21.9 μg/g blood

(*continued on next page*)

Table 2 (*continued*)

Reference	SVOC	Vapor pressure (Pa)	Particle	Particle diameter (μm)	SVOC content (ng/mg particle)	Animal	Method	Exposure time	Biological endpoints	Sampling period	Analytical instrument	Bioavailability
(Gøtze et al., 1994)	BaP	7.3×10^{-7}	Urban air particle	NA	NA	Male Sprague-Dawley rats (350 g)	*In vivo*	NA	Lung tissue	After exposure	HPLC	29–60%
(Fouchécourt et al., 1999)	BaP	7.3×10^{-7}	Coke plant soil	< 10	21	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	648 ng/g organ
(Gerde et al., 2001)	BaP	7.3×10^{-7}	Diesel soot	1.3 ± 0.2	14,500	1-year-old beagle dogs	*In vivo*	4–5 s	Blood	Within 1 h after exposure	HPLC	18% in 4.3 min, 36% in 5.6 months
(Ramesh et al., 2001)	BaP	7.3×10^{-7}	Carbon black	NA	0.1–2.5 mg/m^3	10-week-old male and female F344 rats	*In vivo*	4 h	Blood and lung tissue	0.5–4 h after exposure	HPLC	65% in 2 h
(Ramesh et al., 2002)	BaP	7.3×10^{-7}	Carbon black	NA	100 μg/m^3	8-week-old male Fisher-344 rats (200 g)	*In vivo*	4 d	Lung tissue	Within 72 h after exposure	Reverse-phase HPLC and fluorescence detector	25%
(Ewing et al., 2006)	BaP	7.3×10^{-7}	Silica	3.5	1300 ± 60	Female Sprague-Dawley rats (325 ± 19 g)	*Ex vivo*	1 min	Lung tissue	After exposure	HPLC	95–100%
(Fouchécourt et al., 1999)	Flu	1.2×10^{-3}	Coke plant soil	< 10	78	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	284 ng/g organ
(Fouchécourt et al., 1999)	BbF	6.7×10^{-5}	Coke plant soil	< 10	39	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	BkF	1.3×10^{-7}	Coke plant soil	< 10	14	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	BgP	1.3×10^{-8}	Coke plant soil	< 10	12	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	IP	4.0×10^{-8}	Coke plant soil	< 10	15	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	Phe	1.6×10^{-2}	Coke plant soil	< 10	97	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	Ace	2.9×10^{-1}	Coke plant soil	< 10	141	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	Ant	8.7×10^{-4}	Coke plant soil	< 10	33	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	Chr	8.3×10^{-7}	Coke plant soil	< 10	< 0.1	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	BaA	4.1×10^{-5}	Coke plant soil	< 10	2	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ
(Fouchécourt et al., 1999)	DaA	1.3×10^{-7}	Coke plant soil	< 10	3	Male adult Sprague-Dawley rats (200-220 g)	*In vivo*	88 ± 2 h	Lung tissue	After exposure	HPLC	< 40 ng/g organ

TCDD: 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, Flu: fluoranthene, BbF: benzo[*b*]fluoranthene, BkF: benzo[*k*]fluoranthene, BaP: benzo[*a*]pyrene, BgP: benzo[*g, h, i*]perylene, IP: Indeno[1,2,3,-c,d]pyrene, Phe: phenanthrene, Ace: acenaphthene, Ant: anthracene, Pyr: pyrene, Chr: chrysene, BaA: benzo[*a*]anthracene, DaA: dibenz[*a,h*]anthracene, NA: not available, GC–MS: gas chromatography–mass spectrometry, HPLC: high-performance liquid chromatography. Vapor pressures were calculated at 25 °C using the EPI Suite program developed by the U.S. Environmental Protection Agency.

Administration and other associations that data from unrestrained animals that are chronically instrumented for telemetry are preferable to data from restrained animals (U.S. Food and Drug Administration, 2001).

The results reported in Table 2 suggest that the bioavailability following an inhalation exposure to particle-phase SVOCs depends on the content of SVOCs on the carrier particles as well as the substrate and diameter of the particles. The ratio of the SVOC concentration in the organs or blood to the SVOC content in the particles increases with the SVOC content in the particles. The exposed subject, exposure protocol, dosing regimen, and sampling method differ from one study to another, resulting in difficulties in interpreting and comparing the results. Some test conditions, such as stuffing particles down the lung and remaining apneic after exposure, differ from normal breathing. Although animal tests are often considered relevant to human exposure assessment, the translation of animal data to equivalent human data remains challenging (Kastury et al., 2017). Moreover, animal testing raises ethical concerns. As a conclusion, data on bioaccessibility and bioavailability *via* inhalation are available only for very few SVOCs.

3. Modeling of SVOC bioaccessibility and bioavailability following inhalation

The modeling approaches to address the bioaccessibility and bioavailability of compounds *via* inhalation are shown in Fig. 1. For inhaled compounds in the gas phase, the deposition rate along the respiratory tract (the GD mechanism) should be considered. Inhaled compounds in the particle phase may evaporate into the gas phase and then deposit together with the other inhaled gas-phase compounds (the EGD mechanism), or they may be retained in the particles. The compounds in the deposited particles may transfer into the mucus of the respiratory tract *via* evaporated gas deposition (the PDEGD mechanism) or diffusion (the PDD mechanism). The fraction of an inhaled compound that is deposited along the respiratory tract due to the four abovementioned mechanisms is the bioaccessible fraction. Models addressing each of the four mechanisms were reviewed. The models on the inhaled gas- and particle-phase compounds are presented in Sections 3.1 and 3.2, respectively. The fraction of a bioaccessible compound that can transfer across the tissue to reach the blood circulation is defined as being bioavailable. Models addressing this mass transfer process were reviewed and are presented in Section 3.3. Overall, forty-four articles have been found on the modeling of the bioaccessibility and bioavailability *via* inhalation; twenty-nine of them were published after the year 2000, and six of them were published over the past five years.

3.1. Deposition of inhaled gas-phase compounds

No specific model has been developed to address the deposition of inhaled gas-phase SVOCs along the respiratory tract, *i.e.*, the GD mechanism. Some mass transfer models did not target any specific compound (Davies, 1985; Kimbell et al., 1997). Other models were originally developed for formaldehyde, ozone, chlorine, or VOCs (Bush et al., 2001; Kepler et al., 1998; Padaki et al., 2009).

Davies considered inhaled gas-phase compounds absorbed in the respiratory tract through the diffusion of the gas molecules to the surface of the airway and assumed a tube shape of the respiratory tract (Davies, 1985). Therefore, the dynamic concentration of the inhaled compounds along the respiratory tract depends on the geometry and diffusion coefficient of the tube, and the flow rate of the inhaled gas. Moreover, the absorption of the inhaled gas into the fluid of the respiratory tract depends on the physicochemical properties of the inhaled compounds, particularly the octanol/water partition coefficient and water solubility (Nielsen et al., 2008). Compounds that are very soluble in water absorb rapidly into the fluid of the upper airways and can reach the deeper airways and lungs after the diffusion of the inhaled compounds into upper airways reaches equilibrium (Davies, 1985).

Although the human respiratory tract is three-dimensional, it is difficult to specify the air velocity everywhere within the respiratory tract (Miller et al., 1985). Therefore, a one-dimensional airway was assumed to simplify the three-dimensional equation of continuity to simulate the concentrations of inhaled gas-phase ozone and chlorine along the respiratory tract (Bush et al., 2001; Miller et al., 1985). The radial flux of the inhaled gas towards the mucus of an airway was considered, and the one-dimensional mass transport along the airway was described as

$$\frac{\partial \overline{C}}{\partial t} + \overline{U}\frac{\partial \overline{C}}{\partial x} = D\frac{\partial^2 \overline{C}}{\partial x^2} - \frac{2}{R}k_g(\overline{C} - C_R) \quad (1)$$

where t is the time, x is the distance along the x-axis, $\overline{C}$ is the average airway concentration of the compound at x and t, R is the airway radius, $\overline{U}$ is the average air velocity through the cross section of the airway, D is the effective dispersion coefficient, k_g is the gas-phase mass transfer coefficient, and C_R is the concentration of the compound in the gas phase immediately adjacent to the mucus. Since SVOCs are different from ozone and chlorine, the mass transfer parameters, *e.g.*, D and k_g, should be determined for each SVOC, and the one-dimensional model should be modified accordingly to simulate the gas-phase SVOC deposition.

Although the one-dimensional model may be reasonable for the lower respiratory tract, it is not valid in nasal passages due to the shape of the nasal passages and the airflow patterns. Thus, Kimbell et al. developed a three-dimensional computational fluid dynamics (CFD) model that incorporated airflow patterns and the diffusion of the inhaled gas to quantify the delivery of a compound to a rat's nasal passages (Kimbell et al., 1997, 1993). Kepler et al. used this method to model the nasal absorption of formaldehyde in rhesus monkeys and concluded that the total nasal wall uptake of formaldehyde was 90% (Kepler et al., 1998). This value may vary among SVOCs since they are generally much less soluble in water than formaldehyde. Moreover, the use of the one-dimensional model is restricted to symmetrically branched airways, and the mass transfer parameters are applied to idealized geometric and flow conditions (Keshavarzi et al., 2009). To overcome these disadvantages, CFD technology has been used to construct three-dimensional airway models (Padaki et al., 2009; Taylor et al., 2007).

Combining the CFD nasal model and the one-dimensional airway model, dynamic models of the whole respiratory system were developed (Overton et al., 2001; Schroeter et al., 2013). Human respiratory tracts were divided into 24 generations (the division point where one airway branches into multiple airways) from the trachea to the alveolar sacs, and in each generation, one-dimensional symmetrically branched airways were constructed. The absorption of inhaled gas-phase formaldehyde and hexamethylene diisocyanate was analyzed using nasal-airway models. These models may be used to predict the absorption of SVOCs along the human respiratory tract if some characteristic parameters, *e.g.*, the dispersion and overall mass transfer coefficients of the SVOCs, are determined.

In conclusion, the abovementioned models were all developed originally for general compounds or specific compounds, such as ozone and formaldehyde; none were developed particularly for SVOCs. Therefore, the mass transfer parameters for SVOCs need to be determined before using the models. Three limitations of the abovementioned models may be addressed in the future. First, a respiratory cycle includes both inhalation and exhalation. Inhaled compounds are absorbed in the fluid of the respiratory tract, but 30% of them may desorb during exhalation (Medinsky and Bond, 2001), *i.e.*, the washin-washout effect (Johanson, 1991). This bi-directional transport of inhaled gas-phase compounds between the inhaled air flow and the airway tissue has not been well characterized. Thus, the amount of inhaled compounds that is bioaccessible or bioavailable may be overestimated. Second, in the abovementioned models, only nasal inhalation was considered, while oral inhalation was neglected. In real life, a fraction of air may be inhaled through the mouth, especially by

children, the elderly, and people with diseases or performing physical activities. Finally, the properties of the airway mucus and alveolar surfactant have not been considered in the models. Thus, the fate of the inhaled SVOCs in the mucus and surfactant has not been modeled. SVOC concentrations in airway and alveolar tissues may decrease with time due to the fate of SVOCs, which may enhance the mass transfer of SVOCs from the inhaled airflow to the respiratory tract.

3.2. Deposition of inhaled particle-phase compounds

While GD is the direct deposition of the inhaled gas-phase compounds along the respiratory tract, EGD, PDEGD, and PDD are associated with the deposition of the inhaled particle-phase compounds along the respiratory tract and the desorption of the compounds from the inhaled particles to the fluid of the respiratory tract (Fig.1).

3.2.1. Particle deposition along the respiratory tract

The deposition of inhaled particles along the respiratory tract has been well modeled in past decades. Mechanisms of particle deposition include inertial impaction, sedimentation, diffusion, interception, and electrostatic precipitation, which are related to the particle's momentum, gravity, size, shape, and electrostatic charges, respectively (Carvalho et al., 2011). The existing models can be generally classified into five categories. First, the typical-path lung models (Schum and Yeh, 1980; Yeh and Schum, 1980) consider the dynamic deposition of particles in anatomical respiratory tracts. Respiratory tracts are divided into a number of generations, *e.g.*, 25 generations for humans (Yeh and Schum, 1980), and in each generation, all the airways are assumed to have the same geometric parameters. Second, considering the variation in the geometric parameters of airways in the same generation, stochastic models incorporating Monte Carlo simulation were developed (Koblinger and Hofmann, 1990, 1985) in which the geometric parameters of airways are randomly selected in accordance with their distributions in each generation. Third, to simplify the calculation of the stochastic models, multiple-path models use a number of structurally different airways derived from the stochastic model to represent the geometry of the airways (Asgharian et al., 2010, 2001). Moreover, with the development of computational technologies, the dynamic deposition of inhaled particles can be modeled in 3-dimensional respiratory tracts using the computational fluid-particle dynamics (CFPD) method (Koullapis et al., 2017). Finally, empirical models of the steady-state deposition of particles for the general population were developed based on *in vivo* tests of the particle deposition in human airways (Cheng et al., 1996) and lungs (Asgharian et al., 1995). A number of individuals should be measured to reduce the variability in an empirical model. Models of the deposition of inhaled particles in the human respiratory tract have been reviewed and presented elsewhere (Hofmann, 2011; Sturm, 2012). Therefore, we do not present detailed models of particle deposition in the present review.

The deposited fraction of inhaled particles is size-dependent. Inhaled ultrafine particles can efficiently deposit in the respiratory tract during spontaneous breathing. For particles < 100 nm in diameter, the mean deposited fraction for the total respiratory tract is 0.66 by particle number and 0.58 by particle mass concentration for healthy people at rest (Daigle et al., 2003). Swift et al. used radon progeny aerosols for a deposition study and found that the nasal deposition rate can be > 95% for particles < 1 nm in diameter (Swift et al., 1992). Moreover, nasally deposited ultrafine particles can subsequently translocate *via* the olfactory nerve and accumulate in the olfactory bulb of the brain (Mistry et al., 2009; Oberdörster et al., 2004; Peters et al., 2006).

3.2.2. Desorption of particle-phase compounds into airway fluid

The desorption rate of the particle-phase compounds in the respiratory tract depends on the gas/particle and liquid/particle partition coefficients (Pankow, 2001). For small-molecule compounds with high volatility, *e.g.*, nicotine in tobacco smoke, the fraction deposited into the respiratory tract due to the EGD mechanism is much larger than that due to the PDEGD and PDD mechanisms (Pankow, 2001). This process can be simplified by compound deposition in a denuder tube (Liu et al., 2017) and described as (Lipowicz and Piadé, 2004)

$$2v\left(1-\frac{r^2}{R^2}\right)(1-\varnothing)\frac{\partial C_g}{\partial x}=\frac{D}{r}(1-\varnothing)\frac{\partial}{\partial r}\left(r\frac{\partial C_g}{\partial r}\right)-2\pi NDdF(C_g-C_{eq}) \tag{2}$$

$$2v\left(1-\frac{r^2}{R^2}\right)\varnothing\frac{\partial C_p}{\partial x}=2\pi NDdF(C_g-C_{eq}) \tag{3}$$

where v is the air flow velocity, C_g and C_p are the gas- and particle-phase concentrations of the inhaled compound, respectively, C_{eq} is the gas-phase concentration if the equilibrium partitioning of the inhaled compound between the gas and particle phases is reached, r and x are the radial and axial dimensions, respectively, R is the tube radius, N is the particle number concentration, D is the gas diffusion coefficient, d is the particle diameter, ϕ is the volume fraction of particles, and F is the Fuchs-Sutugin correction factor. A major limitation of the model is that deposition of particle-phase compounds is neglected in the model because the EGD mechanism is the dominant deposition mechanism for small-molecule compounds with high volatility. However, the EGD mechanism may not be dominant compared to the PDEGD and PDD mechanisms for SVOCs due to their low volatility.

Therefore, Liu et al. took into account the dynamic partitioning of inhaled SVOCs between the gas and particle phases in the human head, tracheobronchial, and alveolar regions and developed a model to address the SVOC deposition associated with the GD, EGD, and PDEGD mechanisms (Liu et al., 2017). The model considered both inhalation and exhalation. During inhalation, the concentrations of the gas- and particle-phase SVOCs in the airflow of a region are described as

$$V_1\frac{dC_{g1}}{dt}=Q(C_{g0}-C_{g1})+h_{m1}A_1\left(\frac{C_{s1}}{K_{s1}}-C_{g1}\right)+\frac{V_1v_tC_{mp1}A_p}{V_p\rho_p}\left(\frac{C_{sp1}\rho_p}{C_{mp1}K_p}-C_{g1}\right) \tag{4}$$

$$V_1\frac{dC_{sp1}}{dt}=Q(C_{sp0}-C_{sp1})-Q\frac{D_1C_{mpout}}{C_{mp1}}C_{sp1}+\frac{V_1v_tC_{mp1}A_p}{V_p\rho_p}\left(C_{g1}-\frac{C_{sp1}\rho_p}{C_{mp1}K_p}\right) \tag{5}$$

$$V_1\frac{dC_{mp1}}{dt}=Q(C_{mp0}-C_{mp1})-QD_1C_{mpout} \tag{6}$$

where V_1 and V_p are the volumes of the present region and of a single particle, respectively, C_{g1} and C_{g0} are the gas-phase SVOC concentrations in the present and previous regions, respectively, t is the time, Q is the breathing rate, h_{m1} is the mass transfer coefficient over the surface of the respiratory tract, A_1 and A_p are the surface areas of the present region and of a single particle, respectively, C_{s1} and C_{sp1} are the SVOC concentrations in the present region in the airway wall and particle phase, respectively, K_{s1} is the gas-mucus partition coefficient, v_t is the mass transfer coefficient around the inhaled particles, C_{mp0} and C_{mp1} are the particle mass concentrations in the present and previous regions, respectively, ρ_p is the particle density, C_{sp0} is the particle-phase SVOC concentration in the previous region, D_1 is the deposition fraction of the inhaled particles in the present region, and C_{mpout} is the particle mass concentration of the inhaled particles.

The results show that most of the gas-phase SVOCs are deposited (the GD mechanism) in the head region, while the particle-phase SVOCs travel deeper into the respiratory tract. As the particles go deeper, the SVOC content on the particles decreases due to the evaporation of the particle-phase SVOCs into the gas phase (the EGD mechanism). The evaporation effect is more significant for particles of small size and SVOCs with high volatility. The study provided the gas- and particle-

deposition values in each region, but the bioaccessibility value was not provided because the desorption of SVOCs from deposited particles into the mucus (the PDD mechanism) was not modeled. This model has three limitations. First, the geometry of the respiratory system was largely simplified. For example, the alveolar region was modeled as a sphere. This simplification lacks anatomical support. Second, the SVOC concentrations in the gas and particle phases in each of the three regions were assumed to be uniform. However, due to the complexity of the human respiratory system and the progressive deposition of the inhaled compounds, the gradient of the SVOC concentration in each region may not be neglected. Finally, the model does not consider the mucociliary clearance and alveolar macrophage clearance of particles, which influences the particle mass concentration. Also, the model does not consider the fate of SVOCs in the airway and alveolar walls, which can influence the SVOC concentration in the tissue and the mass transfer of the inhaled SVOCs in the respiratory system.

Desorption of particle-phase compounds from the deposited particles into the respiratory fluid (the PDD mechanism) has rarely been studied. This process depends on the solubility of the compound in the fluid (Gerde and Scholander, 1989) and is associated with energy changes (Risby et al., 1988). Considering a particle as a sphere, the desorption of a particle-phase PAH from the outer surface into an aqueous phase was described by Gerde and Scholander (1989)

$$\frac{C_s(t)}{C_s(t=0)} = 1 - \frac{2D_L C_{Lsat} t}{d_s C_s(t=0)}, \quad \text{for } 0 < t < t_{iso} \tag{7}$$

$$\frac{C_s(t)}{C_s(t=0)} = \frac{K_L C_{Lsat}}{C_s(t=0)} \exp\left\{\frac{-2D_L(t-t_{iso})}{K_L d_s}\right\}, \quad \text{for } t > t_{iso} \tag{8}$$

where C_s is the surface concentration of the PAH on the deposited particles, t is the time, t_{iso} is the time to reach the linear adsorption isotherm of the saturated solution, D_L is the diffusion coefficient of the PAH in the fluid, C_{Lsat} is the saturated PAH concentration in the fluid, d_s is the diameter of the sphere, and K_L is the coefficient of the linear adsorption isotherm in the fluid. Moreover, the desorption of a particle-phase PAH from a pore into an aqueous phase was described by Gerde and Scholander (1989)

$$\frac{dQ}{dt} = \frac{-\pi d_p^2 D_L C_{Lsat}}{4x} \tag{9}$$

where Q is the amount of the PAH in the pore, d_p is the pore diameter, and x is the distance into the pore. When the fluid was water, the PAHs on the outer surface and in the pores of the deposited particles desorbed within 4 s and 10 min, respectively (Gerde and Scholander, 1989). This model should be integrated in a particle-deposition model in future studies to provide a full understanding of SVOC deposition due to the PDD mechanism.

3.3. Mass transfer of inhaled compounds across the tissue

Modeling the mass transfer of inhaled compounds across the epithelium into the blood circulation corresponds to a bioavailability evaluation. Two types of models exist for gas-phase and particle-phase compounds.

For gas-phase compounds, all the studies focused on the exchange of oxygen at the level of the alveolar region. Two geometric structures for the alveolar sac were assumed, *i.e.*, the spherical model (Suresh et al., 2005) and the layered model (Reynolds et al., 2010; Roy and Secomb, 2014). Suresh et al. studied the liquid breathing of human lungs for treating acute lung injuries and developed a spherical model of alveolar gas exchange in partial liquid ventilation (Suresh et al., 2005). The spherical model considers an alveolar sac as a spherical shell with a variable volume encapsulated by a tissue layer and surrounded by a capillary blood compartment (Fig. 2). For the partial liquid ventilation, the volume encapsulated by the tissue is filled with a liquid layer of perfluorocarbon and the inhaled gas (Suresh et al., 2005). For the breathing of a healthy lung, the volume encapsulated by the tissue is filled with only gas (Pavelka and Roth, 2005). The mass transfer in the alveolar tissue was assumed to be driven by diffusion (Suresh et al., 2005). The spherical structure of the alveolar sac has not been validated using measured data because the model describes the mass transfer in a single alveolar sac. An expanded model on the whole alveolar region has not been developed yet. The layered model considers three layers in the alveolar region: the air space, the tissue, and the blood (Fig. 2) (Reynolds et al., 2010; Roy and Secomb, 2014). The mass transfer of compounds across the tissue was assumed to be driven by diffusion. The simplification of the geometric structure compared to the spherical model allows the expansion of the layered model to the whole alveolar region. However, compared to the measured values, the layered model tends to overestimate the concentrations of compounds in the blood (Roy and Secomb, 2014).

For particle-phase compounds, a study on the transport of particle-phase nicotine in the lungs assumed a 3-layer structure of the alveolar region: the airway fluid containing nicotine desorbed from the inhaled particles, the tissue, and the blood (Gowadia and Dunn-Rankin, 2010). The mass transfer of nicotine across the tissue was assumed to be driven by diffusion (Gowadia and Dunn-Rankin, 2010). The mass transfer of the deposited compounds in the mucus through the airway tissue has been modeled in many studies (George and Hlastala, 2011; Tian and Longest, 2010a, 2010b). The compound concentration in the airway tissue (C_t) at any time (t) can be described by the reaction-diffusion equation (Asgharian et al., 2012, 2011; Schroeter et al., 2006)

$$-\frac{\partial C_t}{\partial t} + D_t \frac{\partial^2 C_t}{\partial r^2} = K_f C_t + \frac{V_{max} C_t}{V_t (K_m + C_t)} \tag{10}$$

where D_t is the diffusion coefficient of the compound in the tissue, r is the radial dimension of the tissue, K_f is the first-order rate constant if the reaction of the compound in the tissue initiates, V_t is the tissue volume, and V_{max} and K_m are Michaelis-Menten rate constants. In these models, the permselectivity of the epithelium is not considered, which allows the development of a simplified physical model. However, the errors in the results due to the simplification have never been studied.

4. Perspectives on determining the bioaccessibility and bioavailability of inhaled SVOCs

Many studies have reported the bioaccessibility and bioavailability of SVOCs *via* the ingestion of soil or settled dust (Fang and Stapleton, 2014; He et al., 2016; Quintana et al., 2017; Wang et al., 2013), and the bioaccessibility and bioavailability of PAHs *via* dermal contact have been reviewed and presented elsewhere (Beriro et al., 2016), but the literature on inhalational exposure remains scarce. The existing studies on the bioaccessibility or bioavailability of inhaled SVOCs involved 2,3,7,8-tetrachlorodibenzo-p-dioxin and some PAHs, especially BaP. However, no data are available for the other SVOCs present in indoor environments, such as phthalate esters, flame retardants, and PCBs. Specific experimental conditions known to influence the results are of crucial importance, such as the temperature, agitation, extraction duration, composition of the lung lining fluid, extraction method and solid/liquid ratio in the bioaccessibility tests (Basta and Juhasz, 2014; Stefaniak et al., 2010; Turner, 2011) and in the biological endpoints (blood, tissue or urine) in bioavailability tests. Analytical methods to determine the bioaccessibility and bioavailability differ widely from one study to another (Carbonell-Capella et al., 2014; Wiseman, 2015).

Within modeling, the model developed by Liu et al. focused on SVOCs and considered the deposition of both gas- and particle-phase inhaled SVOCs (Liu et al., 2017), while the model developed by Gerde and Scholander focused on PAH desorption from the deposited particles into the surrounding liquid (the PDD mechanism) (Gerde and Scholander, 1989). Due to these pioneering works, the SVOC deposition associated with the GD, EGD, PDEGD, and PDD mechanisms can be quantitatively predicted under some assumptions and simplifications.

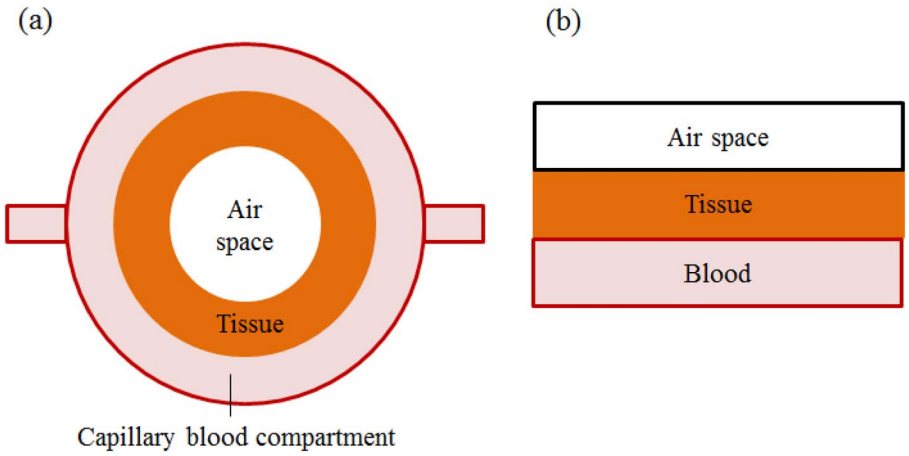

Fig. 2. Schematics of the alveolar sac (a) spherical model (b) layered model.

The other existing models in the literature frequently consider only one phase because they do not focus on modeling SVOCs. A number of parameters should be determined before applying these models to SVOCs. Four mechanisms exist for characterizing gas- and particle-phase SVOC deposition (GD, EGD, PDEGD, and PDD) and estimating the bioaccessibility of the inhaled SVOCs in both gas and particle phases. These mechanisms have not yet been considered together in one model. The following four points may be considered in future modeling approaches for improvements.

First, mass transfer models may be developed for the whole respiratory system or for different regions, *e.g.*, the extrathoracic, tracheobronchial and alveolar regions (Hofmann, 2011). However, for the purpose of bioaccessibility and bioavailability studies, a model considering the whole respiratory system is needed because the concentration of an inhaled compound in one region can interfere with that in another region. Moreover, an empirical model of the deposition of inhaled particles considered both the nasal and oral airways (Cheng et al., 1996), while other models considered nasal inhalation to be the only inlet of air. A calculation of the SVOC bioavailability and bioaccessibility including both the nasal and oral airways may be developed.

Second, the washin-washout effect plays an important role in the respiratory uptake of inhaled compounds (Johanson, 1991). The inhaled compounds absorbed on the surface of the respiratory epithelium may not be able to diffuse across the epithelium by the end of inhalation. For example, the time for nicotine to diffuse across the epithelium differs from one region to another, *e.g.*, 10^{-5} s in the pulmonary region and 0.7 s in the tracheobronchial region (Gowadia and Dunn-Rankin, 2010). A fraction of the inhaled nicotine deposited on the epithelium may be lost in the exhaled breath due to the slow diffusion rate, leading to a reduction in the amount of compound that is bioaccessible or bioavailable. As suggested by Medinsky and Bond, up to 30% of inhaled gas is exhaled (Medinsky and Bond, 2001). For inhaled particles, Heyder suggested that their deposition fraction increases with the particle size, particle density, and respiratory cycle period (Heyder, 2004). The impact of the respiratory cycle period on the availability and accessibility of inhaled SVOCs in the gas and particle phases may be quantified in models.

Third, the mucociliary clearance and alveolar macrophage clearance of inhaled particles may be considered to better address the deposited particle mass concentration along the respiratory tract. The deposition of particle-phase SVOCs may depend on the substrate of the particles, as mentioned above for diesel and silica particles. The properties of the airway mucus, alveolar surfactant, and inhaled particle-phase SVOCs may be considered to characterize the fate of inhaled SVOCs in airway and alveolar tissues to improve the existing mass transfer model.

Finally, a large variation in the deposited amount of inhaled particles exists across individuals, which is influenced by the morphological factors of the airways, distribution factors of inhaled particles, and breathing patterns among human individuals (Cuddihy et al., 1979; Heyder et al., 1982). Hofmann et al. studied the variation among individuals caused by differences in the airway morphology and concluded that the variation in the extrathoracic deposition was a major source of the difference in the total deposition (Hofmann et al., 2002). A variation in the deposition due to variations in the respiratory cycle period and volumetric flow rate of the air also exists within an individual (Cuddihy et al., 1979; Heyder et al., 1982). Although some studies investigated the influence of individuals' biological variability on the deposition of particles, the influence of this variation on the absorption of the inhaled gas and the desorption of the deposited particle-phase SVOCs into the fluid of the respiratory tract has never been studied. This variability may be addressed using probabilistic models that incorporate physical mass transfer models.

5. Conclusion

Bioaccessibility and bioavailability of SVOCs in the gas and particle phases along the human respiratory tract are essential to evaluate the uptake of inhaled SVOCs and to more accurately assess the associated health risks. The existing *in vitro*, *in vivo*, and *ex vivo* methods have been carried out for 2,3,7,8-tetrachlorodibenzo-p-dioxin and a few PAHs. Valid methods should be developed for the quantification of other SVOCs. Regarding the modeling of the SVOC bioaccessibility and bioavailability, we suggest developing modeling approaches based on the whole respiratory system. The model should incorporate mechanisms of the gas- and particle-phase SVOC mass transfer, particle deposition, gas- and particle-phase SVOC absorption to the respiratory tract, and respiratory cycle period. Additionally, the model should account for individual differences, such as the lung morphology and breathing pattern. Lastly, the model and the measurement method of bioaccessibility should be validated using data from *in vivo* studies.

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Human exposure to semi-volatile organic compounds (SVOCs) via dust ingestion: a review of influencing factors

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SUMMARY
Dust ingestion is a non-negligible pathway of human exposure to several SVOCs. To get a better knowledge on this human exposure, a review of the literature was performed on its influencing factors including (1) the fraction of dust that enters the body via hand to mouth contact: dust with particle size < 100 µm was deemed more relevant to human exposure, and (2) the fraction of pollutant released in the digestive tract, i.e. the bioaccessibility of SVOCs: the composition of the matrix, the dust particle size, the physicochemical characteristics of the pollutant, the way the SVOC has contaminated dust, i.e. through adsorption or material abrasion, and the use of Tenax as a sink were among the main determinants.

PRACTICAL IMPLICATIONS
Taking bioaccessibility into account allows a better estimation of the exposure dose via dust ingestion and thus a more accurate human risk assessment. In vitro studies are proxies of bioavailability data and are easier to implement particularly from an ethical point of view.

KEYWORDS
Bioaccessibility, dust particle size

INTRODUCTION
Humans are exposed to a wide range of indoor chemical pollutants including SVOCs, which are suspected of adverse health effects such as reprotoxic and neurotoxic effects (Fournier et al., 2014). Dust ingestion is a non-negligible pathway of human exposure to several SVOCs (Bekö et al., 2015; Tue et al., 2013). To improve this human exposure assessment, it is necessary to consider the fraction of dust that will enter the body via hand to mouth contact and the quantity of pollutants released in the digestive tract. The present work reviews the literature related to the size of ingested dust particles and the bioaccessibility of indoor SVOCs.

DUST PARTICLE SIZE
The size of ingested dust particle is very important, particularly because SVOC concentrations vary significantly with particle size. First, in general, concentration of toxic chemicals in dust increases as particle size decreases (Lewis et al., 1999). Second, studies show that fine particles adhere better to human's hands than larger ones (Cao et al., 2012). The size of dust particles adherent to hands was measured and a particle size distribution of 29 ± 22 µm was

reported (Cao et al., 2013). Furthermore if < 150 µm was considered as skin adherent dust fraction, 86% of this fraction would be in a 9.3-105 µm range (Kefeni and Okonkwo, 2014).

SVOC BIOACCESSILITY IN DUST

Regarding bioaccessibility, most reported methods simulated the gastrointestinal tract, dust being successively submitted to synthetic gastric and intestinal fluid (Yu et al., 2011). The model was sometimes extended to saliva (Ertl and Butte, 2012) or colon (Abdallah et al., 2012) digestion. The presence of food could be considered with the addition of milk powder (Ertl and Butte, 2012). Tenax beads were also used as an adsorption sink to estimate the dynamic absorption of SVOCs (Fang and Stapleton, 2014).

SVOC bioaccessibility is influenced by several factors related to the matrix: the organic carbon content was often associated with a decrease of bioaccessibility, for example for polybrominated diphenyl ethers (PBDEs) (Yu et al., 2012, 2013) or the more hydrophobic organophosphorous flame retardants and phthalate esters, but no effect was noticed on the less hydrophobic ones (He et al., 2015). A decrease of dust particle size (Wang et al., 2013c; Wang et al., 2013b) or an increase of dust pore volumes (Yu et al., 2013) lead to a larger specific surface area which was linked to an increase of SVOC bioaccessibility. Dust aging was tested for flame retardants and showed a decrease of their bioaccessibility for older dust samples (Fang and Stapleton, 2014).

SVOC bioaccessibility was also influenced by factors related to the compound itself. For example, substances with higher octanol-water partition coefficients (K_{ow}) were less bioaccessible (Kang et al., 2012, 2013; Wang et al., 2013a). For PBDEs, congeners that had integrated dust by adsorption were more bioaccessible than BDE 209 whose presence in dust is suspected to originate from material abrasion (Yu et al., 2013), although this origin could not be confirmed (Abdallah et al., 2012). SVOC bioaccessibility was not influenced by the pollutant's concentration (Yu et al., 2011).

Last, SVOC bioaccessibility was positively influenced by parameters of the method itself such as the use of Tenax (Fang and Stapleton, 2014) or milk powder (Ertl and Butte, 2012) and the increase of the concentration of bile in the intestinal solution (He et al., 2015). This emphasizes the need of a physiologically relevant, standardized measurement protocol (Collins et al., 2015).

Overall, measured bioaccessibilities were subject to a large variability, ranging from < 20% for BDE 209 (Yu et al., 2013), polycyclic aromatic hydrocarbons (Kang et al., 2011) or high molecular weight phthalates (Wang et al., 2013d), up to > 60% for OPFRs, low molecular weight PBDEs (Fang and Stapleton, 2014) or tetrabromobisphenol A and hexabromocyclodecanes (Abdallah et al., 2012). This confirms that taking bioaccessibility into account allows a better estimation of the ingested dose, whereas the latter could be overestimated when the studied pollutants are considered 100% bioaccessible.

CONCLUSIONS

Bioaccessibility data are useful for a better quantification of SVOC exposure doses and thus for a better estimation of associated health risks. However more studies are needed to assess SVOC bioaccessibilities, which should be compared to in-vivo studies for validation.

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Bioaccessibility of semi-volatile organic compounds (SVOCs) in settled dust

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Humans are exposed to a wide range of indoor chemical pollutants including semi-volatile organic compounds (SVOCs), which are suspected of adverse health effects such as reprotoxic and neurotoxic effects. Dust ingestion is a non-negligible pathway of human exposure to several of these compounds. To improve this human exposure assessment, it is necessary to consider the bioaccessibility of SVOCs, i.e. the fraction of pollutants released in the digestive tract following the ingestion of dust. The present work reviews the literature for the methods, measured values, and influencing factors related to the bioaccessibility of SVOCs in indoor dust.

Reported bioaccessibility measurement methods simulate the gastrointestinal tract, with dust samples being successively submitted to synthetic gastric and intestinal fluids. Models were sometimes extended to include the role of saliva or colon. Milk proteins, Tenax® beads or Caco-2 cells could also be added for a better physiological relevance.

So far, SVOC bioaccessibility in dust has not been well documented in the scientific literature. However, the available articles show that measured bioaccessibilities ranged from < 20% for bromodiphenylether (BDE) 209, polycyclic aromatic hydrocarbons (PAHs) or high molecular weight phthalates, up to > 60% for organophosphorous flame retardants (OPFRs), low molecular weight polybromodiphenylether (PBDEs), hexabromocyclododecanes or tetrabromobisphenol A.

SVOC bioaccessibility is influenced by several factors related to the matrix. An increase of organic carbon content was often associated with a decrease of bioaccessibility: this was observed for PBDEs or the more hydrophobic OPFRs and phthalate esters, but no effect was noticed on the less hydrophobic ones. A decrease of dust particle size or an increase of dust pore volumes lead to a larger specific surface area which was linked to an increase of bioaccessibility.

SVOC bioaccessibility was also influenced by factors related to the compound itself. For example, substances with higher octanol-water partition coefficients (K_{ow}) were less bioaccessible. For PBDEs, congeners that had integrated dust by adsorption were more bioaccessible than BDE 209 whose presence in dust is suspected to originate from material abrasion. Bioaccessibility was not influenced by the pollutant's concentration.

Bioaccessibility data are useful for a better quantification of SVOC exposure doses, which could otherwise be overestimated when the pollutant's total concentration is considered. However, more studies are needed, which should be compared to in-vivo studies for validation.

ASSESSMENT OF THE ORAL BIOACCESSIBILITY OF SEMI-VOLATILE ORGANIC COMPOUNDS IN INDOOR SETTLED DUST USING A SIMPLIFIED METHOD

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Humans are exposed to a wide range of indoor chemical pollutants including semi-volatile organic compounds (SVOCs), which are suspected of adverse health effects such as reprotoxic and neurotoxic effects. Dust ingestion is a non-negligible pathway of human exposure to several of these compounds including phthalates (Langer et al., 2014), and polybromodiphenylethers (PBDEs) (Bramwell et al., 2016; Fromme et al., 2016). To better assess this human exposure, it is necessary to consider the oral bioaccessibility of SVOCs, i.e. the fraction of pollutants released from the dust matrix in the digestive tract following the ingestion of dust. A few methods for measuring the oral bioaccessibility of SVOCs in dust have been described in the literature (Abdallah et al., 2012; Ertl and Butte, 2012; Quintana et al., 2016) but they were never applied on a large number of samples because of their complexity.

In this context, a simple method for the extraction of the bioaccessible fraction of SVOCs was proposed. This method is an in vitro simulation of the gastric and intestinal stages of human digestion, in the presence of an adsorbent (Tenax®) to simulate the dynamics of the digestion. The ratio between dust and digestive fluid was 1/200. The pH, temperature, and incubation times were those of the human body (Figure 1).

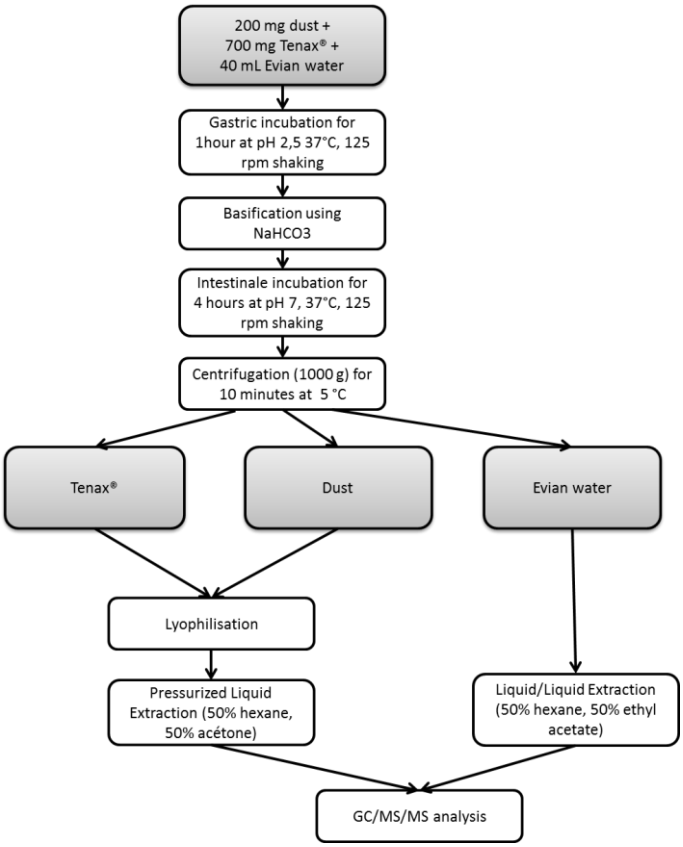

Figure 1: synoptic of the bioaccessibility measurement method

This method was used to produce bioaccessibility data for the SVOCs present in the dust reference material SRM 2585, analyzed in triplicates.

Measured bioaccessibilities (in %) ranged from 25 to 76, 37 to 83, 27 to 78, 23 to 95, and 0 to 39 for pyrethroids, PAHs, PCBs, phthalates and PBDEs, respectively. These results are comparable to those already reported in the literature for PCBs and phtalates (3 to 92 % and 1 to 81 %, respectively), however they were higher in the literature for PBDEs (11 to 71 %) and lower for PAHs (2 to 17 %) (Raffy et al., 2016).

A decreasing trend was observed between the bioaccessibility of SVOCs and their octanol-water coefficient partition (Kow), as shown in Figure 2 below (r^2=0.6).

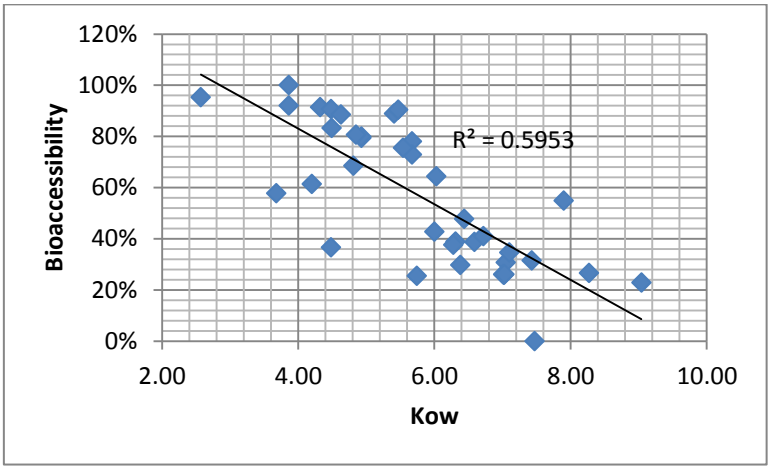

Figure 2: bioaccessibility as a function of the SVOC's Kow

These results are preliminary and the measurements method still needs to be optimized then compared to the few available in-vivo data, using rats for PBDEs (Huwe et al., 2008) and using piglets for phthalates (Plichta and Fromme, 2016).

Following development and validation of the simplified method, bioaccessibility will be assessed for school dust samples within a national survey in order to help filling the gap between contamination data and children's exposure to SVOCs in indoor dust.

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Characterisation of human exposure to semivolatile organic compounds (SVOCs) through indoor dust ingestion: measurement of SVOC bioaccessibility

G. RAFFY [abc], F. MERCIER [abc], P. GLORENNEC [ab], C. MANDIN [de], B. LE BOT [abc]

Context & Objectives

Semi-volatile organic compounds (SVOCs) are suspected of adverse health effects. Indoor dust ingestion has been shown to be a non-negligible pathway of human exposure to several SVOCs. To improve this human exposure assessment, it is necessary to consider the fraction of dust that will enter the body via hand to mouth contact and the amount of SVOC released in the gastrointestinal tract and available for absorption, i.e. the SVOC bioaccessibility.

SVOC settled dust contamination

Size of ingested dust particles

SVOC bioaccessibility

Human exposure

How to measure SVOCs in settled dust to better estimate human exposure by dust ingestion ?

Methodology

1. Substances of interest : how are chemicals incorporated to dust ?

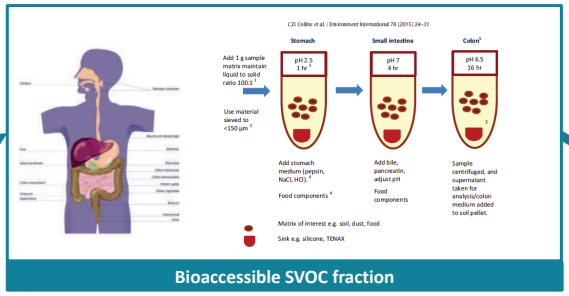
Mainly through volatilization and condensation on dust particles (human activities)	Mainly through abrasion (materials wear and tear)
Pesticides: lindane, permethrine **Polycyclic aromatic hydrocarbons (PAHs):** fluorene, phenanthrene, anthracene, fluoranthene, pyrene and benzo(a)anthracene	**Phthalates:** diethylphthalate, diisobutylphtahlate, dibutylphthalate and butylbenzylphthalate **Flame retardants :** Tributlyphosphate, polybromodiphenylethers 47, 85, 99, 100 and 153

2. Measurement strategy

Call for Proposals

Vacuumed settled dust

Sieving



Bioaccessible SVOC fraction

TD-GC-MS/MS

Total SVOC concentration

A global measurement strategy including a simple and reliable extraction method of the bioaccessible SVOC fraction will be proposed . This method will reproduce the digestion process in-vitro. It will be based on previous developments related to bioaccessible lead carried out by the LERES (Le Bot et al., 2010, 2011). It will be validated by comparison (n=30) to simulations of the gastro-intestinal tract where dust is successively submitted to synthetic saliva, gastric, duodenal and bile fluids (Collins et al., 2015). SVOC bioaccessibility (%) will be calculated from the ratio between bioaccessible SVOC fraction and total SVOC concentration.

3. Implementation on settled dust samples

Settled dust samples are being collected since June 2013 in 600 classrooms representative of French schools within a nationwide survey by the indoor air quality observatory (OQAI). The total SVOC concentration is being measured for all samples. A subsample of 60 samples will be selected based on their contamination profil and used for the implementation of the bioaccessibility assessment method.

Expected results & perspectives

Scientific articles:
- Review of SVOC bioaccessibility and its influencing factors in dust
- Development and validation of the measurement strategy
- Description and determinants of SVOC bioaccessibility within 60 classrooms

Output for the scientific community :
- Better estimation of SVOC exposure through dust ingestion
- Useful for epidemiologic studies & risk assessments

Le Bot 2010 *Eur. J. Mineral.* 22 651–657 ; Le Bot 2011 *J. Environ. Sci. Heal. Part A* 46 63–69 ; Collins 2015 *Environ. Int* 78, 24–31

Bioaccessibility of semivolatile organic compounds (SVOCs) in settled dust

Gaëlle RAFFY [abc], Fabien MERCIER [abc], Philippe GLORENNEC [ab], Corinne MANDIN [de], Barbara LE BOT [abc]

Context

Semi-volatile organic compounds (SVOCs) are suspected of adverse health effects. Indoor dust ingestion is a non-negligible pathway of human exposure to several SVOCs. To improve this human exposure assessment, it is necessary to consider the bioaccessibility of SVOCs, i.e. the quantity of pollutants released in the digestive tract following the ingestion of dust. This poster reviews the literature related to the bioaccessibility of SVOCs in indoor dust.

SVOC settled dust contamination

Dust ingestion rate → Size of ingested dust particles → SVOC bioaccessibility

Human exposure

Bioaccessibility vs. bioavailability:
SVOC bioavailability: percentage of SVOC that becomes available (reaches the systemic circulation) ; difficult to measure due to ethical and cost issues.
SVOC bioaccessibility: percentage of SVOC released into the gastrointestinal tract and available for absorption ; can be used as a proxy of bioavailability to characterize exposure to SVOCs by dust ingestion.

In-vitro evaluation methods

Saliva fluid dissolution: aqueous solution of salts, proteins (mucin, α-amylase), urea, uric acid, at pH 6.5, T = 37°C, for 0.5 hour [2,15].

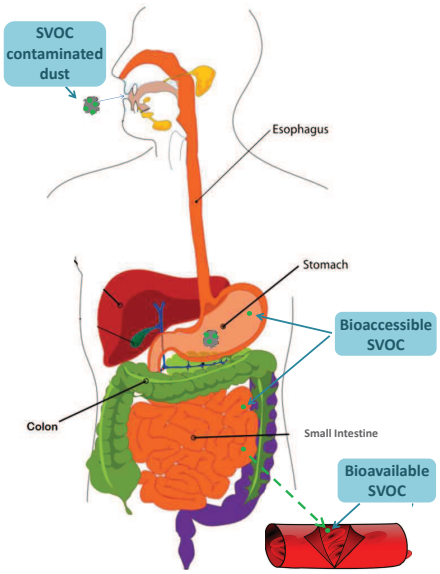
Gastric fluid dissolution: aqueous solution of **pepsin**, salts, urea[2], albumin[2], mucin[16], glucids[2]or other food components[7] at pH < 2.5, T = 37°C, for 1 to 2 hours.
=> Use of Tenax[7,23]: simulation of the dynamic absorption during digestion.

Intestinal fluid dissolution: aqueous solution of **pancreatin**, **bile**, salts, urea[2], albumine[2], lipase[2,7] and food components[7] at 6.5<pH<8, T = 37°C for 4 to 7 hours.
=> Bile concentration: from 0.23[15] to 6.7[10-12,17-20] g/L (0.23 to 2.2 g/L in humans[13])

Colon fluid dissolution [1,7]: aqueous solution of salts, mucin, cystein hydrochloride[16], bile, haemin and food components at T=37°c for 8 to 16 hours.

Ratio between solution (mL) and dust (mg): from 20 to 133 for gastric fluid, and from 37 to 300 for intestinal fluid ; recommended values from 100[3] to 200[21].

Use of Caco-2 cells[4]: simulation of the transport through intestinal cells, a step towards bioavailability.



Conclusion & prospects

15 scientific articles investigated the bioaccessibility of SVOC in dust (2011-2016): measured bioaccessibilities ranged from < 20% (PAHs) to > 60% (OPFRs).
This wide range shows that **bioaccessibilities should be considered for a better quantification of SVOC exposure doses**:

- Beneficial for health risk assessment studies
- Beneficial for epidemiological associations between environmental exposures and health outcomes

SVOC bioaccessibility in dust is influenced by factors related to the matrix and the SVOC itself : these factors could be used in prediction models.
SVOC bioaccessibility is also influenced by factors related to the measurement method : these factors need to be mastered and harmonized to enable better inter-study results comparison.

More studies are still needed:

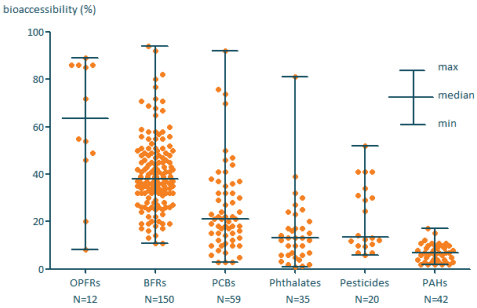
- **covering a larger range of SVOCs**
- **using an *in-vitro* method, which should be physiologically relevant, harmonized[3], and validated against *in-vivo* studies.**

Influencing parameters

Factor related to the matrix characteristics:	Effect on SVOC bioaccessibility:
Dust organic content ↗	↘ (tri- to hepta-BDEs[23], PBDE[22], fipronil[15], and the more hydrophobic OPFRs and PAEs[9]) → (FRs[7], OCPs[18], and the less hydrophobic OPFRs and PAEs[9])
Dust particle size ↗	↘ (PAHs[19], PBDEs[23], OCPs[18])
Factor related to SVOC characteristics:	**Effect on SVOC bioaccessibility:**
K_{OW} ↗	↘ (PCBs[12,17], PBDEs[1], PAEs[11], PAHs[10]) → (PBDEs[22])
SVOC content in dust ↗	→ (PBDEs[21,22])
How the SVOC integrated dust (sorption → abrasion)	↘ (PBDEs[23]) → (PBDEs[1])
Factor related to the bioaccessibility measurement method:	**Effect on SVOC bioaccessibility:**
Presence of Tenax®	↗ (OPFRs[7,9], PBDEs[7])
Presence of food	↗ (pesticides and PCBs[6])
Bile concentration ↗	↗ (OPFRs + PAEs[9], PCBs [12], PBDEs[21])

BDE: bromodiphenylether, FR: flame retardant, K_{OW}: octanol water partition coefficient, OPFR: organophosphorus flame retardant, OCP: organochlorine pesticide, PAE: phthalate ester, PAH: polycyclic aromatic hydrocarbon, PBDE: polybromodiphenylether, PCB: polychlorinated biphenyl

Measured SVOC Bioaccessibilities



SVOC bioaccessibilities measured in dust and reported in the literature are shown in this graph with orange dots, which represent the median value for one compound in one study.

BFR: brominated flame retardant, OPFR: organophosphorus flame retardant, PAH: polycyclic aromatic hydrocarbon, PCB: polychlorinated biphenyl

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> JOURNEE DES DOCTORANTS
> CSTB - PARIS

Evaluation de la bioaccessibilité orale des COSV contenus dans les poussières des bâtiments

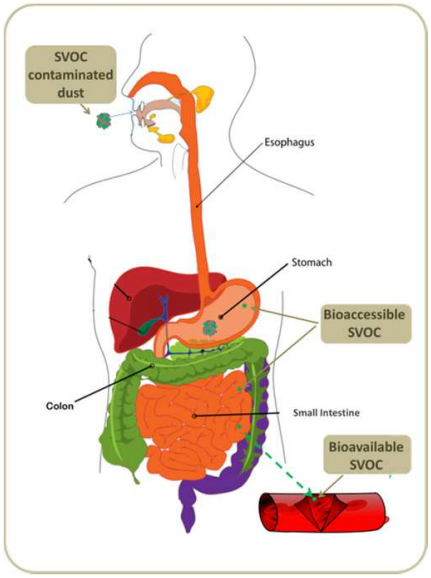
Gaëlle Raffy

04-10-2016

CONTEXTE ET OBJECTIFS

Contexte

> Les COSV (composés organiques semi-volatils) sont suspectés d 'effets néfastes pour la santé (effets cancérogènes, reprotoxiques et neurotoxiques).
> Les concentrations de COSV retrouvées dans les poussières des logements et des écoles sont sujettes à préoccupation.
> L'ingestion de poussières est une voie d'exposition non négligeable à certains COSV, et les enfants, du fait de contacts sol-main-bouche fréquents sont tout particulièrement concernés.
> Seule la fraction bioaccessible des COSV, définie comme la fraction de polluant libérée dans le tractus gastro-intestinal et disponible à l'absorption, est responsable de l'exposition humaine par ingestion poussière.



Objectif

> Evaluation de la bioaccessibilité orale des COSV contenus dans les poussières des bâtiments :
  – Revue de la littérature scientifique du domaine
  – Développement et validation d'une méthode simple de mesure de la bioaccessibilité des COSV dans les poussières.
  – Production de données de bioaccessibilité pour plusieurs familles de COSV (phtalates, pesticides organochlorés et pyréthrinoïdes, hydrocarbures aromatiques polycycliques (HAP), retardateurs de flamme bromés et organophosphorés).

PRINCIPAUX RÉSULTATS

ANALYSE DE LA LITTÉRATURE SCIENTIFIQUE :

1. **Bioaccessibilité des COSV dans les poussières documentée dans seulement 16 articles scientifiques (2011-2016)**
2. **Forte variabilité des bioaccessibilités mesurées varient de < 20% à > 60% => intérêt de prendre la bioaccessibilité en compte pour mieux quantifier les doses d'exposition, et ainsi mieux caractériser les risques pour la santé.**
3. **Bioaccessibilité des COSV influencée par des paramètres relatifs à la nature de la poussière (teneur en matière organique, taille des particules) et aux caractéristiques des COSV (K_{OW}, voie d'intégration dans la poussière) : ces facteurs pourraient être utilisés dans des modèles de prédiction de la bioaccessibilité.**
4. **Bioaccessibilité des COSV aussi influencée par des facteurs relatifs à la méthode de mesure (inclusion d'un adsorbant, concentration biliaire) : ces facteurs doivent être maîtrisés et harmonisés pour permettre de meilleures comparaisons inter-laboratoires.**

ETAT D'AVANCEMENT

Revue de la littérature scientifique

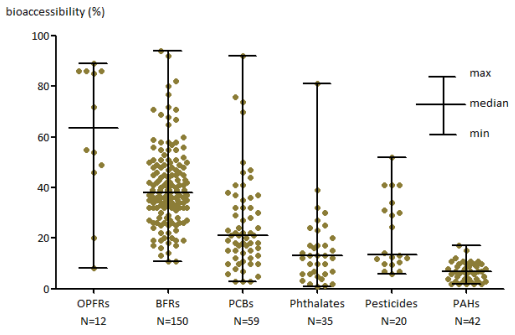
Les méthodes d'évaluation de la bioaccessibilité sont des simulations *in-vitro* de la digestion :

> Compartiment salivaire : pH 6,5, T = 37°C, durée = 0,5 hour .
> Compartiment gastrique : pepsine, composés alimentaires, pH < 2,5, T = 37°C, durée 1 à 2 heures.
> Compartiment intestinal : pancreatine, bile, composés alimentaires, 6,5<pH<8, T = 37°C, durée 4 à 7 heures.
  => Ajout d'un adsorbant (Tenax®) pour simuler la dynamique de l'absorption pendant la digestion
  => Concentration biliaire : de 0,23 à 6,7g/L (de 0,23 à 2,2 g/L chez l'homme)
> Colon : composés alimentaires, T=37°C, durée 8 à 16 heures.
> Utilisation de cellules Caco-2 pour simuler le transport à travers la paroi intestinale.

La bioaccessibilité des COSV est influencée par des paramètres propres à la matrice, à la nature du COSV, et à la méthode de mesure :

Factor related to the matrix characteristics:	Effect on SVOC bioaccessibility
Dust organic content ↗	↘ (PBDEs, fipronil, and the more hydrophobic OPFRs and PAEs) → (FRs, OCPs, PBDEs, and the less hydrophobic OPFRs and PAEs)
Dust particle ↗	↘ (PAHs, PBDEs, OCPs)
Factor related to SVOC characteristics:	**Effect on SVOC bioaccessibility**
K_{OW} ↗	↘ (PCBs, PBDEs, PAEs, PAHs) → (PBDEs)
SVOC content in dust ↗	→ (PBDEs)
How the SVOC got in dust (sorption → abrasion)	↘ (PBDEs and HBCDs) → (PBDEs)
Factor related to the bioaccessibility measurement method:	**Effect on SVOC bioaccessibility**
Presence of tenax	↗ (OPFRs, PBDEs)
Presence of food	↗ (pesticides and PCBs)
Bile concentration ↗	↗ (OPFRs + PAEs, PCBs , PBDEs)

Les bioaccessibilités mesurées dans la littérature varient de < 20% (PAHs) à > 60% (OPFRs) :



BFR: brominated flame retardant, OPFR: organophosphorus flame retardant, PAH: polycyclic aromatic hydrocarbon, PCB: polychlorobiphenyl

Chaque point représente la valeur médiane de la bioaccessibilité d'un COSV dans une étude.

CONCLUSION ET PERSPECTIVES

1. **Les connaissances sur la bioaccessibilité des COSV sont fragmentaires. Des études complémentaires sont nécessaires, couvrant de plus nombreux COSV et utilisant une méthode harmonisée et validée.**
2. **Ce projet de thèse vise ainsi à documenter la bioaccessibilité d'une vingtaine de COSV dans 60 échantillons de poussières de la Campagne Nationale Ecole (OQAI).**

Encadrement – Barbara Le Bot, directrice, EHESP ; Corinne Mandin, co-directrice, CSTB
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Assessment of the oral bioaccessibility of semi-volatile organic compounds (SVOCs) in indoor settled dust

Gaëlle RAFFY [abc], Corinne MANDIN [de], Barbara LE BOT [abc]

Context & Objectives

Semi-volatile organic compounds (SVOCs) are suspected of adverse health effects. Indoor dust ingestion is a non-negligible pathway of human exposure to several SVOCs. To improve this human exposure assessment, it is necessary to consider the oral bioaccessibility of SVOCs, i.e. the quantity of pollutants released in the digestive tract following the ingestion of dust.

SVOC settled dust contamination

Dust ingestion rate → Size of ingested dust particles → SVOC bioaccessibility

Human exposure

Bioaccessibility vs. bioavailability

SVOC bioavailability: percentage of SVOC that becomes available (reaches the systemic circulation) ; difficult to measure due to ethical and cost issues.

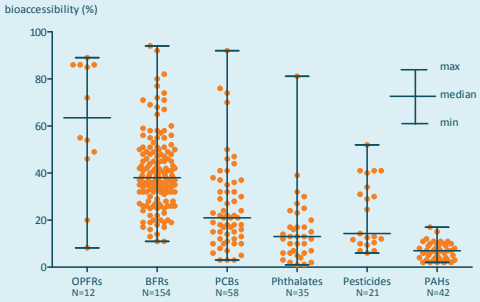
SVOC bioaccessibility: percentage of SVOC released into the gastrointestinal tract and available for absorption ; can be used as a proxy of bioavailability to characterize exposure to SVOCs by dust ingestion.

Review of the scientific literature

- 16 publications between 2011 to 2016
- Large variability of SVOC bioaccessibities, according to the substance, the dust characteristics, and the measurement method used
- Measurement methods long and difficult to implement ; need for harmonization[1] and simplification

Objectives of the PhD project:

- **To develop a simple method for measuring the bioaccessibility of SVOCs in settled dust**
- **To generate bioaccessibility data for the SVOCs mainly found in indoor settled dust**



SVOC bioaccessibilities measured in dust and reported in the literature are shown in this graph with orange dots, which represent the median value for one compound in one study[2]

BFR: brominated flame retardant
OPFR: organophosphorus flame retardant
PAH: polycyclic aromatic hydrocarbon
PCB: polychlorinated biphenyl

Methodology

In vitro evaluation method

Reference method[3]:

Stomach: aqueous solution of pepsin, salts, and food components , incubation at pH =2.5, T = 37°C, for 1,5 hours

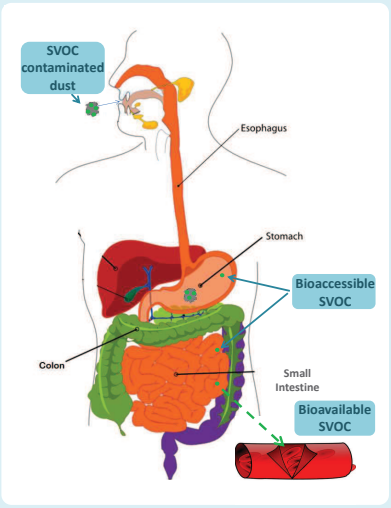
Small Intestine: aqueous solution of pancreatin, bile, lipase and food components, incubation at pH 6.5, T = 37°C for 4 hours

Colon: aqueous solution of salts, mucin, cystein hydrochloride, bile, haemin and food components , incubation at T=37°c for 16 hours

Addition of Tenax as an adsorbent in all compartments for simulating the dynamic absorption during digestion.

➔ **Simplified method (only stomach and gastric compartment, adsorbent, minimum reagents, physiologically relevant pH and T°C)**

Analytical technique: gas chromatography coupled to tandem mass spectrometry (GC/MS/MS) after liquid/liquid or pressurized liquid extraction



Selected SVOC

Selection upon 3 filters:
- Hierarchisation based on toxicity[4]
- Analytical feasibility in multi-residue analysis[5]
- High content in school settled dust[6]

Organochlorine pesticide	Lindane
Pyrethroids	cyfluthrin, cypermethrin, deltamethrin, tetramethrin and permethrin
Polycyclic Aromatic Hydrocarbons (PAHs)	fluorene, phenanthrene, anthracene, fluoranthene, pyrene et benzo(a)pyrene
Phthalates	DEP, DiBP, DBP, BBP, DEHP et DiNP
Brominated Flame retardants	BDE 47, 85, 99, 100 et 153
Organophosphorus Flame Retardant	Tributylphosphate

Selected dust samples

Settled dust from the French national school campaign (French Indoor Air Quality Observatory (OQAI) 2013-2017)

- SVOC content higher in school dust than in house dust, particularly for phthalates[6,7]
- Children more exposed than adults because of their behavior and the immaturity of their systems
- Up to 200 samples available
- Nationwide representativeness

Expected results & Prospects

Simplified method, easy to implement on a large scale study

Documentation on the bioaccessibility of SVOCs for up to 200 school settled dust

➔**better quantification of SVOC exposure doses:**

- **Beneficial for health risk assessment studies**
- **Beneficial for epidemiological associations between environmental exposures and health outcomes**

Further studies needed:

- ***In-vivo* validation of the method**
- **Measurement of pulmonary bioaccessibility for a better evaluation of human exposure *via* inhalation of dust particles.**

References

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> 6th Day of the Young Researchers of Irset

> 11-01-2018

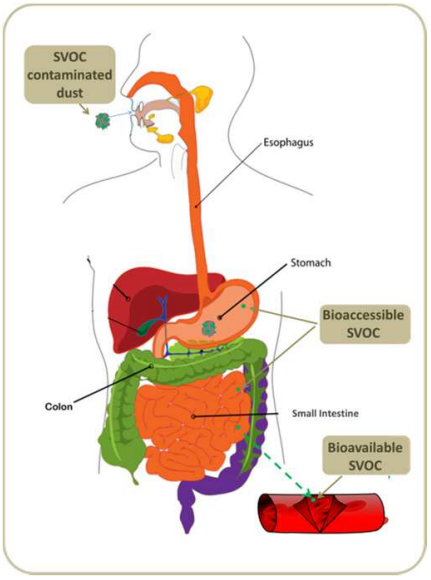
ASSESSMENT OF THE ORAL BIOACCESSIBILITY OF SEMI-VOLATILE ORGANIC COMPOUNDS (SVOCs) IN INDOOR SETTLED DUST USING A SIMPLIFIED METHOD

Gaëlle Raffy

CONTEXT AND OBJECTIVES

Context

- SVOCs (semi-volatile organic compounds) are suspected of having adverse health effects (carcinogenic, reprotoxic and neurotoxic effects).
- The concentrations of SVOCs found in indoor settled dust are subject to concern.
- Dust ingestion is a non-negligible exposure pathway for some SVOCs. Children, because of frequent hand-to-mouth contact, are particularly concerned.
- Only the bioaccessible fraction of SVOCs, defined as the fraction of pollutant released into the gastrointestinal tract and available for absorption, is responsible for human exposure by dust ingestion.



Objectives

- Evaluation of the oral bioaccessibility of SVOCs in indoor settled dust:
  - Review of the scientific literature.
  - Development and validation of a simple method for measuring the bioaccessibility of SVOCs in dust.
  - Production of bioaccessibility data for several SVOC families (organochlorine and organophosphorus pesticides, pyrethroids, polycyclic aromatic hydrocarbons (PAHs), polychlorobiphenyls (PCBs), phthalates and polybromodiphenylethers (PBDEs).

MAIN RESULTS

ON THE SIMPLIFIED MEASUREMENT METHOD

1. **Repeatable method for the analysis of dust, Tenax and liquid. Majority of CVs <20%, all <33%** (except dieldrin and oxadiazon in dust).
2. **Mass balance between 80 and 120% of the contamination value** (except cypermethrin and g-HCH)

Liquid + Tenax® + Dust = Contamination value

3. **Less than 5% of COSVs bioaccessible in liquid phase ➔ liquid analysis could be avoided**
4. **Bioavailable concentration of PBDE measured in-vivo in rats for SRM2585 ➔ aim: to obtain greater bioaccessible concentrations.**

SVOC	Bioaccessible SVOC in SRM2585	Bioavailable SVOC in SRM2585 In vivo study on rats (all tissues)*
BDE47	39%	69.4 ± 11.4 %
BDE100	26%	78.4 ± 7.6 %
BDE99	26%	43.7 ± 5.2 %
BDE85	35%	39.3 ± 10.2 %
BDE153	0%	73.1 ± 9.1 %

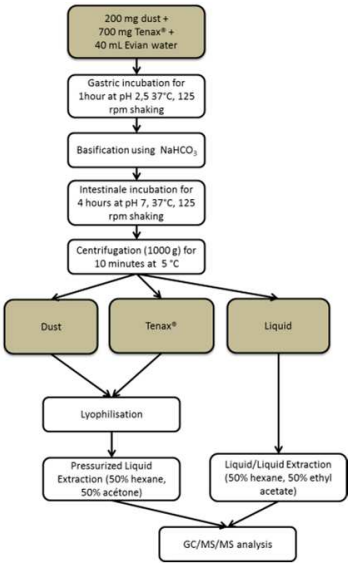
*Huwe et al., 2008. Environ. Sci. Technol. 42, 2694–2700

STATE OF PROGRESS

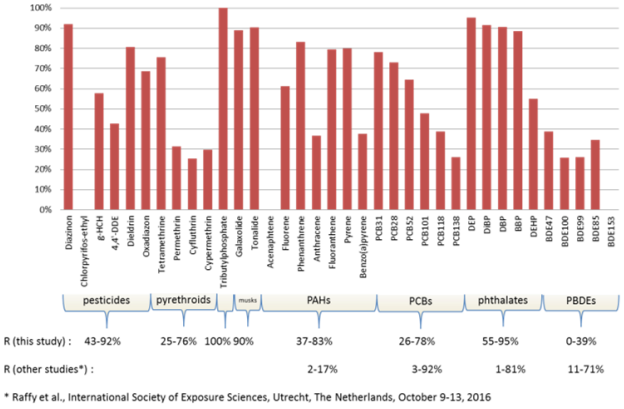
36 substances of interest

Famille chimique	COSV
OP	Diazinon
	Chlorpyrifos-ethyl
OC	g-HCH
	4,4'-DDE
	Dieldrin
Oxadiazolone	Oxadiazon
Pyrethroid	Tetramethrine
	Permethrin
	Cyfluthrin
	Cypermethrin
OPFR	Tributylphosphate
PAH	Acenaphtene
	Fluorene
	Phenanthrene
	Anthracene
	Fluoranthene
	Pyrene
	Benzo(a)pyrene
Musk	Galaxolide
	Tonalide
PCB	PCB31
	PCB28
	PCB52
	PCB101
	PCB118
	PCB138
Phthalate	DEP
	DiBP
	DBP
	BBP
	DEHP
PBDE	BDE47
	BDE100
	BDE99
	BDE85
	BDE153

Simplified measurement method



Bioaccessible SVOC ratio (R, %) in the standard reference material SRM 2585



* Raffy et al., International Society of Exposure Sciences, Utrecht, The Netherlands, October 9-13, 2016

CONCLUSION AND PROSPECTS

1. **Proposal of a simple and robust method to measure the SVOC bioaccessibility in many dust samples.**
2. **Need to improve and validate the simplified method using in-vivo testing.**
3. **This project will document the bioaccessibility of about 30 SVOCs in 30 dust samples from the National School Campaign (CSTB/OQAI).**
4. **This project is the first step towards a better evaluation of human exposure to SVOCs in dust and particles, considering their oral, pulmonary and dermal bioaccessibility**

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> ISES Europe 2018
> Dortmund (DE)
> 19-20 June 2018

ASSESSMENT OF THE ORAL BIOACCESSIBILITY OF SEMI-VOLATILE ORGANIC COMPOUNDS (SVOCs) IN INDOOR SETTLED DUST USING A SIMPLIFIED METHOD

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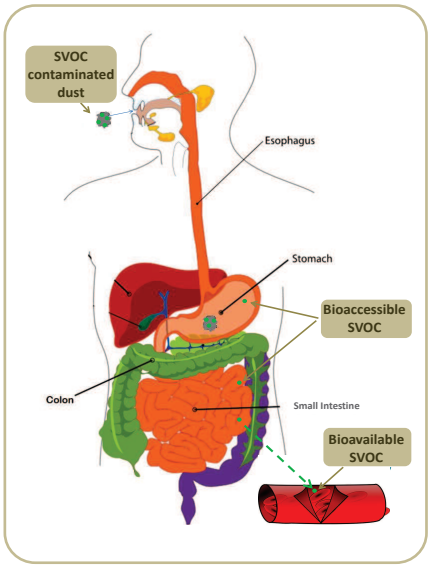
CONTEXT

- SVOCs are suspected of having adverse health effects (carcinogenic, reprotoxic and neurotoxic effects).
- The concentrations of SVOCs in indoor settled dust are subject to concern.
- Dust ingestion is a non-negligible exposure pathway for some SVOCs. Children, because of frequent hand-to-mouth contact, are particularly concerned.
- Only the bioaccessible fraction of SVOCs, defined as the fraction of pollutant released into the gastrointestinal tract and available for absorption, is responsible for human exposure by dust ingestion.
- To date, measurement methods have never been applied on many samples due to their complexity, hence the need for a simplified method

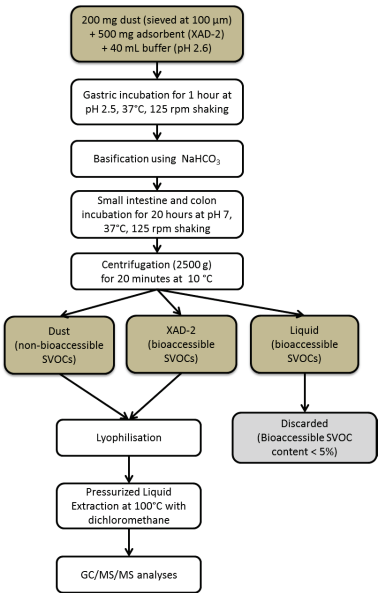


MATERIAL & METHOD

39 substances of interest

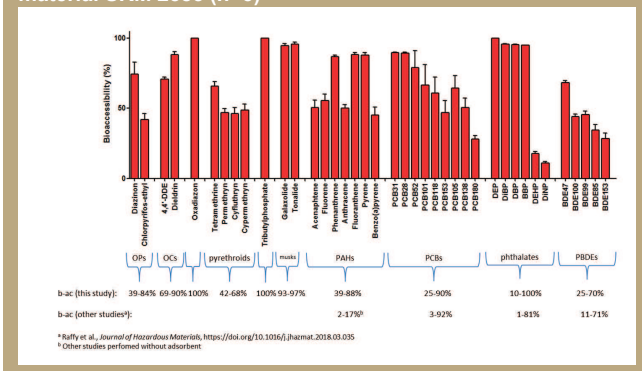
Chemical family	SVOC
Organophosphorus pesticides (OPs)	Diazinon
	Chlorpyrifos-ethyl
Organochlorinated pesticides (OCs)	4,4'-DDE
	Dieldrin
Oxadiazolones	Oxadiazon
Pyrethroids	Tetramethrin
	Permethrin
	Cyfluthrin
	Cypermethrin
Organophosphorus flame retardants	Tributylphosphate
Musks	Galaxolide
	Tonalide
Polycylic aromatic hydrocarbons (PAHs)	Acenaphtene
	Fluorene
	Phenanthrene
	Anthracene
	Fluoranthene
	Pyrene
	Benzo(a)pyrene
Polychloro-biphenyls (PCBs)	PCB28
	PCB31
	PCB52
	PCB101
	PCB105
	PCB118
	PCB138
	PCB153
	PCB180
Phthalates	DEP
	DiBP
	DBP
	BBP
	DEHP
	DiNP
Polybromo-diphenyl ethers (PBDEs)	BDE47
	BDE100
	BDE99
	BDE85
	BDE153

Simplified measurement method

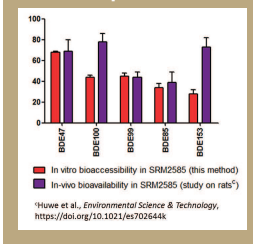


RESULTS

Bioaccessible SVOC ratio (b-ac, %) in the standard reference material SRM 2585 (n=3)



In-vitro / in-vivo data comparison



CONCLUSION

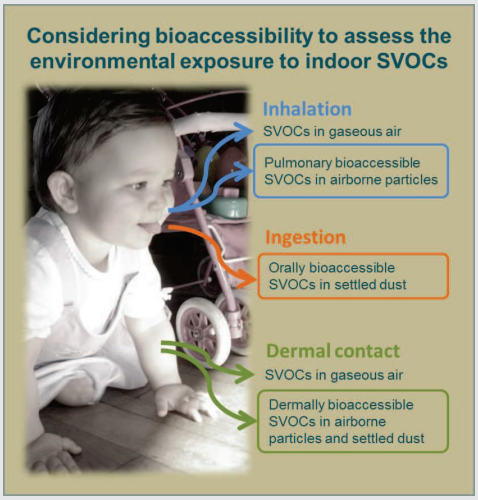
Proposal of a simple and robust method to measure the SVOC bioaccessibility in many dust samples.

Need to improve and validate the simplified method using in-vivo testing.

EUROPEAN PROSPECTS

⇒ **Working towards a better evaluation of human exposure to SVOCs in dust and airborne particles, considering their oral, pulmonary and dermal bioaccessibility**

⇒ **Need to establish partnership for the production of in-vivo data to validate the in-vitro methods**



Titre : Exposition humaine aux composés organiques semi-volatils (COSV) en environnement intérieur par ingestion de poussières : évaluation de la bioaccessibilité orale des COSV

Mots clés : qualité de l'air intérieur ; écoles ; exposition humaine ; ingestion de poussière ; biodisponibilité ; polluant.

Résumé : La qualité de l'environnement intérieur est aujourd'hui un sujet de préoccupation majeur en santé publique. Les populations passent près de 90 % de leur temps en environnement intérieur où elles sont exposées à des polluants comme les composés organiques semi-volatils (COSV) suspectés d'effets néfastes pour la santé. L'ingestion de poussières est une voie d'exposition non négligeable à certains de ces COSV, en particulier chez les enfants. Pour caractériser cette exposition, il est nécessaire de prendre en compte la bioaccessibilité orale des COSV, définie comme la fraction de polluant libérée dans le tractus gastro-intestinal et disponible à l'absorption. Dans ce contexte, les objectifs de cette thèse sont de (i) développer et valider une méthode simple à mettre en œuvre pour la mesure de la bioaccessibilité orale des COSV dans les poussières et (ii) produire des données de bioaccessibilité pour des COSV d'intérêt sanitaire. Cette thèse sur articles est constituée de trois chapitres : un contexte scientifique, qui présente les sources et la toxicité des COSV, puis décrit leur présence dans l'air et les poussières des écoles, avant d'aborder les différentes voies d'exposition humaine ; un état de l'art sur la bioaccessibilité orale des COSV dans les poussières ; la proposition d'une méthode simplifiée pour la mesure de cette bioaccessibilité, sa validation et son application à de premiers échantillons. Ces travaux se concluent sur un contexte plus large que l'ingestion en établissant des perspectives considérant également la bioaccessibilité par inhalation et par contact cutané, afin de caractériser de manière globale l'exposition aux COSV en environnement intérieur.

Title : Human exposure to semi-volatile organic compounds (SVOCs) in indoor environments by dust ingestion: evaluation of SVOCs' oral bioaccessibility

Keywords: indoor air quality; school; human exposure; dust ingestion; bioavailability; pollutant.

Abstract: The quality of indoor environments is now a major public health concern. People spend nearly 90% of their time indoors where they are exposed to pollutants such as semi-volatile organic compounds (SVOCs) suspected of adverse health effects. Dust ingestion is a significant route of exposure to some of these SVOCs, especially for children. To characterize this exposure, it is necessary to consider the oral bioaccessibility of SVOCs, defined as the fraction of pollutant released into the gastrointestinal tract and available for absorption. In this context, the objectives of this PhD thesis are to (i) develop and validate a simple method for measuring the oral bioaccessibility of SVOCs in indoor dust and (ii) produce bioaccessibility data for SVOCs of health interest This article-based thesis consists of three chapters: a scientific context, which presents the sources and toxicity of SVOCs, then describes their presence in school air and dust, before addressing the different routes of human exposure; a state of the art on the oral bioaccessibility of SVOCs in dust; and the proposal of a simplified method for measuring this bioaccessibility, its validation, and its application to first samples. This work concludes on a broader context than ingestion by establishing perspectives that also consider inhalation and dermal bioaccessibility, in order to characterize the overall exposure to COSV in indoor environments.

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