Non-target screening and human risk assessment for adult and child populations of semi-volatile organic compounds in residential indoor dust in Spain

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Abstract

In this work, an analytical strategy based on non-target screening of semi-volatile organic compounds and subsequent risk assessment for adult and child populations has been conducted for the first time in household indoor dust samples in Spain. The methodology was based on a microwave-assisted extraction followed by gas chromatography coupled to high resolution mass spectrometry determination, using a hybrid quadrupole-orbitrap analyzer. The procedure was applied to 19 residential indoor dust samples, collected in different Spanish regions (namely Galicia, La Rioja, Catalunya, the Balearic Islands, and the Valencian Region). From the generated data, 4067 features were obtained, of which 474 compounds were tentatively identified with a high level of identification confidence (probable structure by library spectrum match or confirmed by reference standard), using a restrictive set of identification criteria. Most of the identified chemicals were natural products, metabolites, additives, and substances with industrial applications in the field of foods, cosmetics, pharmaceuticals, pesticides, and plastics. Finally, risk assessment was carried out by applying the threshold of toxicological concern approach, showing that risk to adult and

child populations associated with the presence of the identified substances in the indoor dust was not expected, although the existence of indoor environments with conditions of potential risk cannot be discarded under a worst-case scenario approach.

Keywords: gas chromatography, high resolution mass spectrometry, indoor dust, non-target screening, risk assessment, semi-volatile organic compounds

1. Introduction

Indoor environments have recently raised the concern of scientific community, since it is estimated that people spend around 90% of their time indoors, where the concentrations of some pollutants are often 2 to 5 times higher than typical outdoor concentrations, and modern buildings are characterized to be more thermal and acoustic insulated with lower air exchange rates (U.S. EPA, 2021). Specifically, women and children spend a lot of time in indoor household environment whose air pollution involves particulate matter (PM), inorganic chemical pollutants (such as ozone, carbon monoxide, sulfur dioxide, etc.), organic chemical pollutants (such as toluene, xylene, styrenes, flame retardants compounds, etc.), and other biological pollutants such as moulds (Nardocci et al., 2023). Moreover, different respiratory (lung cancer, chronic obstructive pulmonary disease, etc.) and cardiovascular diseases (coronary heart disease, cerebrovascular accident, etc.) are linked to the exposure to household air pollutants (WHO, 2022). In this way, it is expected that most of the pollutants and organic compounds that are known to be present in the air, especially semi-volatile organic compounds (SVOCs), could be also found in household dust, which acts as a reservoir posing a potential risk to human health. In this regard, human exposure to household dust is mainly produced via inhalation and ingestion (Oomen et al., 2008; Venier et al., 2016), being children at higher risk due to increased hand to mouth transfer (Besis et al., 2021).

Household dust is a complex mixture composed of pollen, PM, dead skin cells, insects, several fibers (both natural and synthetic), and other indoor materials from furnishing and floor (Dubocq et al., 2021). As mentioned, population (especially women and children) spend currently long time in indoor household environments and, as consequences, they are continually exposed to indoor dust. For this reason, a significant number of studies have been performed to demonstrate the presence of different pollutants in this complex matrix (Castro et al., 2019; Zhu et al., 2023). Among the pollutants, polybrominated diphenyl ethers (PBDEs) are commonly used as additive

flame retardants in furniture, carpeting, mattresses, and electronic equipment and they have been widely found in household dust (Regueiro et al., 2006; Yu et al., 2023). Organophosphorus and organobromine flame retardants (usually used as plasticizers) are also known to be found in indoor dust (Cao et al., 2014; Mizouchi et al., 2015) and to produce adverse health effects since they are considered endocrine disrupting chemicals (Cohen et al., 2023; Wua et al., 2020). The esters of benzene-1,2-dicarboxylic acid, commonly known as phthalates, are also used as plasticizers in many domestic and household products, such as polyvinyl chloride (PVC) flooring, cosmetics and personal care products, toys, food packaging, and building materials (Nguyen et al., 2022). The exposure to phthalates is linked to reproductive disorders and they have been found in household dust (Bu et al., 2016; He et al., 2016). Another group of organic pollutants that can be found in indoor household dust are the so-called polycyclic aromatic hydrocarbons (PAHs), whose main emission source is the incomplete combustion of organic matter, mainly from fossil fuels. These pollutants are of concern due to their mutagenic, carcinogenic, and toxic properties (Kim et al., 2022; Mosallaei et al., 2023). Finally, and as expected, main outdoor pollutants can reach indoor environments, thus being a potential source of indoor contamination; for instance, residential areas located near to farming fields are more vulnerable to be exposed to pesticides, which have also been detected in household dust (Mu et al., 2022).

The abovementioned pollutant families, among other relevant substance groups, have been detected and quantified in different targeted studies (Cao et al., 2014; Bu et al., 2016; Mosallaei et al., 2023) dealing with indoor house environments, where the pollutants of major concern that have been studied were flame retardants and plasticizers (Zhu et al., 2023).

For sample treatment, exhaustive extraction techniques using adequate solvents to extract the target analytes, are often required due to the complexity of the indoor dust samples (Gunathilake et al., 2022), such as Soxhlet extraction (SE) (Bu et al., 2016),

accelerated solvent extraction (ASE) (Zuloaga et al., 2000), supercritical fluid extraction (SFE) (Papadopoulos, 2012), ultrasound assisted extraction (UAE) (Wang et al., 2020), or microwave-assisted extraction (MAE) (Besis et al., 2014), which is a useful technique for quick and homogeneous heating of the solvent in contact with the sample matrix to achieve partition of the analytes (Eskilsson and Björklund, 2000). The targeted analytical methodologies preferred to determine organic pollutants are usually based on liquid chromatography (LC) or gas chromatography (GC) coupled to mass spectrometry (MS) or tandem mass spectrometry (MS/MS) (Rostkowski et al., 2019). However, unlike targeted analytical methodologies, where a group of selected analytes are determined, non-target approaches are gaining popularity as useful tools for the discovery and identification of unknown substances and emerging pollutants (Castro et al., 2019; Christia et al., 2021; Miralles et al., 2021). Nowadays, the advantages of high resolution mass spectrometry (HRMS), such as high mass resolving power and high mass accuracy, enable to perform suspect screening analysis as well as non-target analysis to discover and identify new emerging contaminants in complex matrices, such as the indoor dust. In this sense, several studies have been published using hybrid HRMS analyzers such as quadrupole-time of flight (Q-TOF) in USA (Moschet et al., 2018), Spain (Castro et al., 2019), and Belgium (Christia et al., 2021); or Q-Orbitrap in China (Wang et al., 2020) and Canada (Kutarna et al., 2021).

In this context, the main objective of this work is to contribute to the identification of unknown SVOCs and new emerging pollutants that can be present in the household dust from different Spanish regions (namely Galicia, La Rioja, Catalunya, the Balearic Islands, and the Valencian Region), and to contribute to the risk assessment of the potential adverse effects that the exposure to these pollutants by indoor dust ingestion and inhalation can cause to human health for both adults and children.

To the best of our knowledge, this work is addressing for the first time the non-target screening of SVOCs in Spanish residential indoor dust from different Spanish regions using MAE followed by GC-Q-Orbitrap HRMS analysis, and their human risk

assessment for adult and child populations applying the threshold of toxicological concern (TTC) approach (Cramer et al., 1976; Patlewicz et al., 2008) in the assessed sampling locations as well as in a worst-case scenario approach.

2. Materials and methods

2.1. Reagents

High-purity analytical standards of 1,2-diphenoxyethane, 3-methoxyacetophenone, aniline, benzothiazole, benzyl benzoate, benzyl butyl phthalate, benzyl chloride, cedrol, citral, dibutyl phthalate, dicyclohexyl phthalate, dimethyl phthalate, menthol, methyl palmitoleate, octadecanoic acid, o-toluidine, piperine, squalene, terbutryn, tonalid, triphenyl phosphate, and α-methylstyrene, all from Merck KGaA (Darmstadt, Germany), were used to confirm their tentative identification.

Additionally, 22 high-purity analytical standards of pesticides, used as quality control compounds (QCs), were supplied from Merck KGaA (Darmstadt, Germany): aldrin, bifenthrin, chlorpropham, cypermethrin, diazinon, dieldrin, α-endosulfan, β-endosulfan, endosulfan-sulphate, ethyl-chlorpyrifos, ethoprophos, fenitrothion, fipronil, kresoxim-methyl, lambda-cyhalothrin, lindane, malathion, methyl-chlorpyrifos, permethrin, trifluralin, and vinclozolin.

Alkane standard mixtures, C_8-C_{20} and C_{21}-C_{40}, containing 40 mg L^{-1} each in n-hexane, also from Merck KGaA (Darmstadt, Germany), were used to calculate Retention index (RI).

GC-grade acetone, and HPLC-grade n-hexane 99 %, both from VWR International (Radnor, PA, USA), were used as solvents.

2.2. Sampling

Nineteen samples of indoor dust from Spanish residential houses were collected during 2021 and 2022 in: Bunyola (samples 1 and 2), and Inca (sample 3), in the Balearic Islands; Navarrete (sample 4), Munilla (sample 5), Nájera (sample 6), Calahorra (sample 7), Muro (sample 8), Lardero (sample 9), and Logroño (sample 10), in La Rioja; Villagarcía de Arousa (samples 11 and 12), in Pontevedra, Galicia; Barcelona

(sample 13), in Catalunya; and Paterna (samples 14, 15 and 16), and Valencia (samples 17, 18 and 19), in the Valencian Region. For illustrative purposes, a map of the sampling sites in the different Spanish regions is shown in Fig. S1. Dust samples in were collected using a domestic cyclonic vacuum cleaner that collects dust on a built-in cylindrical container, without bags or socks, by aspirating the dust deposited on the floor of the living room and the bedroom. After that, the whole contents of the cylindrical container of the vacuum cleaner were transferred to clean plastic canisters and stored under refrigeration (4 ºC) until analysis.

2.3. Analytical methodology

A diagram of the whole analytical procedure for the non-target screening of SVOCs in residential indoor dust samples is shown in Fig. 1. Briefly, dust samples were sieved to remove foreign objects and then subjected to MAE prior to GC-HRMS analysis. After that, the obtained data were processed for the tentative identification and risk assessment of SVOCs. The detailed analytical procedure is explained in the following subsections.

2.3.1. Sample preparation

The whole contents of the plastic canisters with the collected samples were sieved (<2 mm) to remove tangled hairs, leaves, insects, and other foreign objects prior to MAE. After that, 0.5 g of the sieved dust samples were weighted into 100 mL PTFE extraction vessels and 30 mL of n-hexane:acetone (1:1, *v/v*) solution were added. The MAE was conducted following the extraction conditions published elsewhere (López et al., 2017), using a MARS 5 Digestion Microwave System from CEM Corporation (Matthews, NC, USA). Briefly, the MAE system operated at 1200 W, with the following temperature program: 50 ºC were reached in 5 min from the initial room temperature, and this temperature was then kept for 20 min. After that, the extracts were left to cool to room temperature, filtered, and the extraction vessels were cleaned-up twice with 30 mL of n-hexane:acetone (1:1, *v/v*) solution. The portions were combined in clean glass tubes and the obtained solutions were evaporated to dryness under a gentle nitrogen stream

in a water bath at 35 ºC using a TurboVap 500 evaporator from Zymark (Idstein, Germany), and finally reconstituted with 500 µL of n-hexane. When needed, the reconstituted extracts were filtered through a 0.22 µm membrane disc filter prior to its injection into the GC-HRMS system.

In order to control background contamination and ensure the analytical suitability, procedural blanks and spiked samples, containing 100 ng g^{-1} of QCs, were prepared and analyzed following the same procedure. For that, a standard solution containing 100 ng mL^{-1} of the QCs (see Section 2.1) was prepared in methanol, and 500 µL were added to 0.5 g of the dust sample before the MAE procedure.

2.3.2. GC-HRMS analysis

One microliter of the blanks, spiked samples, and sample extracts obtained from the MAE procedure were injected by duplicate (in splitless mode) into a Trace 1310 GC system coupled to a Q-Exactive GC Orbitrap HRMS mass spectrometer, using a TraceGOLD TG-5MS column (30 m x 0.25 mm, 0.25 µm), all from Thermo Fisher Scientific (Waltham, MA, USA). The inlet temperature was set at 280 °C, and the instrument operated in constant flow mode at 1.2 mL min^{-1} of Helium (He) as carrier gas, using the following oven temperature program: 40 °C, held for 5 min; 5 °C min^{-1} up to 315 °C, held for 10 min. The MS transfer line was set at 300 °C, the electron ionization (EI) source operated at 70 eV, and the ion source temperature was set at 250 °C. The acquisition was performed in full scan (FS) mode with a resolution of 60,000 FWHM and a mass range from 40 to 500 *m/z*.

To perform retention index (RI) calculations, standard n-alkane mixtures, C_8-C_{20} and C_{21}-C_{40}, were also injected in the GC-HRMS system with the same conditions.

2.3.3. Data processing and compound identification

The acquired data were processed using the Compound Discoverer™ 3.3 (CD 3.3) (Thermo Fisher Scientific, 2022), from Thermo Fisher Scientific (Waltham, MA, USA), following the automatic workflow published elsewhere by our research group (Miralles et al., 2021), with some modifications. Briefly, peak picking, alignment of retention time,

deconvolution of EI spectra, tentative identification of unknown compounds (feature annotation) by database searches, and removal of background features were performed. The diagram of the workflow is shown in Fig. S2.

For the tentative identification of the acquired features, the NIST Mass Spectral Library (NIST, 2020), and local database Mass List searches (in this study, the 'Endogenous Metabolites' database, containing 4414 compounds; the 'Extractables and Leachables HRAM' database, containing 1741 compounds; the 'GC Orbitrap Contaminants' library, containing 880 compounds; the 'GC Orbitrap Flavor and Fragrances' database, containing 49 compounds; the 'GC Orbitrap Metabolomics Library', containing 1014 compounds; the 'LipidMaps Structure Database', containing 43400 compounds; the 'Natural Products Atlas', containing 32688 compounds; and a lab-made database containing 667 plastic additives and related substances) were used. A restrictive set of identification criteria was used, including EI spectra match with the NIST Mass Spectral Library, exact mass of annotated fragments, isotopic profiles (found elements), and retention index (RI). The considered parameters for the identification criteria are shown in Table 1. These parameters were calculated and provided automatically by CD 3.3 software; however, a manual revision was required to carefully select the best candidate substances for the acquired features which comply with all the identification criteria.

2.3.4. Risk assessment methodology

For the risk assessment of the identified compounds, the TTC approach was used applying the 'Revised Cramer Decision Tree' (Cramer et al., 1976) using the ToxTree software (Patlewicz et al., 2008), developed by IDEAconsult Ltd. (Sofia, Bulgaria). Briefly, this approach estimates the tolerable daily intake (TDI, mg day^{-1}) for a given substance according to its chemical structure and functional groups, classifying each substance into one class of toxicological hazard or concern: Class I (Low hazard), 1.80 mg day^{-1}; Class II (Intermediate hazard), 0.54 mg day^{-1}; and Class III (High hazard), 0.09 mg day^{-1}, for adult population. These TDI values are applied for an average adult

person of 60 kg body weight, considering default worldwide adult population (both male and female) according to WHO (WHO, 2021). For child population, TDI values should be calculated considering an average body weight of 15 kg, resulting in 0.45 mg day^{-1} for Class I (Low hazard), 0.14 mg day^{-1} for Class II (Intermediate hazard), and 0.02 mg day^{-1} for Class III (High hazard).

This tool can be used as a first approach to carry out the risk assessment of substances without available reference standards, or whose toxicity has not been described, as it only relies on the chemical structure following Cramer rules. In the case of well known substances for which toxicity guidelines or reference toxicological values exist, the reference TDI values could be used. However, the TTC approach lacks efficient tools to assess combined toxicological hazard (cocktail effects), since substances are evaluated individually.

After that, the estimated daily intake (EDI, mg day^{-1}) values were calculated according to the following expression: $EDI = C_i \times D_i$, where C_i is the concentration of a given substance in the indoor dust, and D_i is the total daily intake of indoor dust. In a conservative but realistic estimation, the total daily intake of indoor dust for an average adult person combines the contributions of dust inhalation (0.8 mg day^{-1}) and ingestion (50 mg day^{-1}), as the two main routes of indoor dust exposure, according to the Dutch National Institute for Public Health and the Environment (Oomen et al., 2008). Consequently, a total daily intake of indoor dust (D_i) of 50.8 mg day^{-1} was considered for adult population.

For children, an estimate of dust ingestion of 100 mg day^{-1} was proposed, due to increased hand-to-mouth behaviour, and 2 mg day^{-1} via inhalation (Oomen et al., 2008). Consequently, a total daily intake of indoor dust (D_i) of 102 mg day^{-1} was considered for child population.

The concentration of the identified SVOCs in the indoor dust (C_i) was estimated according to the average response factor (ARF) of the QCs in spiked dust samples, to compensate possible matrix effects and variable extraction recoveries (ILSI, 2015). The

ARF value was calculated as the average ratio between the base peak areas of the QCs and their known spiked concentrations in sample (see Section 2.3.1). From that, the estimated concentrations of the identified substances in the indoor dust (C_i) were semi-quantitatively calculated as the ratio between their base peak area and the obtained ARF value. This semi-quantitative approach using spiked QCs as internal standards is useful to estimate the concentration levels of uncorfirmed substances and substances whose analytical standards are not available, considering matrix effects and extraction efficiencies in the dust samples. However, a quantitative analysis of confirmed analytes in dust would be the most accurate approach for risk assessment.

Finally, TDI and EDI values were compared by means of the hazard quotient (HQ), using the following expression: $HQ = EDI / TDI$. In this sense, a HQ <1 indicates that no risk is expected, whereas a HQ ≥1 indicates potential health risk.

3. Results and Discussion

3.1. System suitability check

Three replicates of a spiked dust sample containing 100 ng g^{-1} of QCs were analyzed under selected conditions at the beginning and at the end of the acquisition sequence. System suitability was evaluated in terms of relative standard deviation (RSD, %) of peak areas and retention times, and exact mass accuracy between replicates. The obtained RSD values were ≤0.1 % for retention times, and ≤20 % for peak areas, thus showing that the system operated steadily during the acquisition sequence. Moreover, high exact mass accuracy was obtained, ΔMass ≤2 ppm in all cases, thus showing that HRMS analyzer provided suitable data. In this sense, the operation parameters of the Q-Orbitrap instrument, including exact mass accuracy, were verified and calibrated when necessary to ensure proper data acquisition.

3.2. Identification of unknown substances

From the generated data, 4067 features were obtained, of which 2342 were filtered out for being also present in the blanks, only detected in one replicate injection of the sample, or not having candidate substances with Total Score ≥90 %. The other 1725

features were thoroughly examined to ensure the selection of the best candidate substances according to the identification criteria (see Table 1). Finally, 474 compounds were tentatively identified with a high level of identification confidence. According to Schymanski's scale (Schymanski et al., 2014), all the tentatively identified substances could be classified into identification confidence level 2a (probable structure by library spectrum match), except those that were later confirmed with their own analytical standards that were classified into identification confidence level 1 (confirmed structure by reference standard).

The list of the tentatively identified SVOCs, including compound name, CAS number, molecular formula, total score (%), ΔRI, toxicological concern according to Cramer rules, and common uses or origins according to PubChem database (NIH, 2004), using EPA Chemical and Products Database (CPDat) and Hazardous Substances Data Bank (HSDB), is shown in Table S1.

Out of the 474 identified SVOCs, most of them were esters (31.4 %), including 24 phthalates and 10 lactones; hydrocarbons (14.4 %); ketones (7.5 %); aldehydes (6.7 %); and alcohols (14.4 %), including 13 phenols. Other functional groups, such as ethers (5.0 %), including 4 furans; carboxylic acids (5.0 %); amides (2.9 %), including 5 lactams; and amines (2.1 %), among others, were also found. Furthermore, a number of substances with halogen atoms in their chemical structure, such as 18 organochlorine, 4 organofluorine, and 3 organobromine compounds, were also identified. Regarding their molecular structure, most of them were aromatic (43.6 %), but also a significant number of linear or branched (37.7 %) and cyclic (18.7 %) compounds were detected.

According to their toxicological hazard assigned through their Cramer class, most of them were classified as low concern substances (57.5 %), followed by high (32.4 %) and intermediate (10.1 %) hazard. Finally, the identified substances were classified by their common uses, application, or sources, most of them having applications in cosmetics (13.8 %), foods (13.7 %), plastics (5.9 %), pharmaceuticals (5.2 %),

pesticides (3.4 %), other industrial applications (20.1 %), metabolites or substances coming from natural sources (20.1 %), or a combination of them, other uses (12.0 %) and unknown (5.9 %). These results are summarized in Fig. 2.

3.3. Confirmation with analytical standards

In order to validate the tentative identification of the unknown substances in the indoor dust, 22 representative substances of the different found chemical families, with commercially available analytical standards, were purchased (see Section 2.1) and analyzed under the same GC-HRMS conditions. For that, multicomponent standard solutions containing 100 ng mL^{-1} of the selected substances were prepared in solvent (n-hexane) and injected together with samples (to ensure retention time consistency) into the GC-HRMS system. In order to confirm the tentative identification of a substance, a good match in retention time (±0.1 min) and MS spectrum (at least 2 matching ions with ΔMass ≤2 ppm) between the peak in the dust samples and in the standard solution was required.

Out of 22 tested substances, 19 of them were confirmed with their analytical standards, thus obtaining an identification accuracy of 86.4 %. These results are summarized in Table S2. In order to increase confidence in these validation results, the confirmed substances were compared with the NORMAN Dataset on European Dust (DSFP, 2023), showing that 18 out of 19 of them (all except octadecanoic acid) have been already reported to be present in European indoor dust. As an example, a comparison between the obtained extracted ion peak (base peak) and EI mass spectrum of triphenyl phosphate in a dust sample and in the standard solution, respectively, is shown in Fig. 3; and those of benzyl butyl phthalate are shown in Fig. S3.

However, the other 3 substances (benzyl chloride, dimethyl phthalate, and dicyclohexyl phthalate) could not be confirmed with their analytical standards, since the retention time and/or MS spectrum match criteria were not fully matched. In the case of dimethyl phthalate and benzyl chloride, a good match in the retention time between samples and analytical standards was obtained, but only one matching ion was found in their

MS spectra, thus the confirmation was not possible. In the case of dicyclohexyl phthalate, although a good MS spectra match was obtained, the retention time between samples and analytical standard showed a difference ±0.5 min, thus it was not possible to confirm. The identification of the other 452 substances, whose analytical standard has not been tested, remains tentative.

3.4. Risk assessment of the identified SVOCs for adult and child population

As explained above, for the semi-quantitative estimation of the concentration of the identified SVOCs in the indoor dust, the ARF was calculated as the average ratio between the base peak areas of QCs and their known spiked concentrations (100 ng g^{-1}) in three replicates of a dust sample, following recent guidelines on risk assessment for unknown and unconfirmed substances (ILSI, 2015). Moreover, the method limit of detection (mLOD) was estimated as the concentration for which a signal-to-noise ratio was equal to three, calculated from the average signal-to-noise ratio of the spiked compounds. The obtained ARF value was $(1.3 \pm 1.1) \times 10^5$ a.u. ng^{-1} g, and the mLOD value was 1.2 ng g^{-1}. From that, the estimated concentrations of the identified SVOCs in the indoor dust samples (C_i) were calculated semi-quantitatively as the ratio between their base peak area and the obtained ARF value. These results are shown in Table S3, the lowest, mean, average, 95th percentile, and highest concentration values are presented.

As can be seen, the average concentrations of the identified substances were ranging from 2 ng g^{-1} (linanool, 3,7-dimethyl decane, 4-methyl-1,1'-biphenyl, or α-ionone, among others) to 102 µg g^{-1} (diisobutyl phthalate), thus showing a wide variability regarding the found concentration levels (5 orders of magnitude). From the estimated concentration values, individual EDI values for the identified SVOCs were calculated in each dust sample. The highest EDI value obtained for each substance among all studied samples (EDI_{max}) ranged from 0.12 ng day^{-1} and 0.24 ng day^{-1} (α-ionone) to 44.1 µg day^{-1} and 88.5 µg day^{-1} (diisobutyl phthalate), for adult and child populations, respectively. Other substances with the highest found EDI_{max} were: bis(2-ethylhexyl)

terephthalate, 2-ethylhexyl-4-methoxycinnamate, squalene, benzyl butyl phthalate, n-hexadecanoic acid, decyl 6-methylhept-2-yl phthalate, tributyl acetylcitrate, and cetyl palmitate. Most of these substances present in industrial applications, mainly as plasticizers, such as phthalates; but also as cosmetic ingredients, thus showing that these are main sources of exposure to chemical substances in indoor environments.

Finally, individual HQ values of the identified substances in each sample were calculated from the EDI values and the TDI values (see Section 2.3.4). For adults, the maximum obtained HQ values for each substance among all samples (HQ_{max}) ranged from 6.8×10^{-8} (β-caryophyllene) to 3.2×10^{-2} (tributyl acetylcitrate), showing no risk (HQ <1) associated to the presence of the identified SVOCs. For child population, the obtained HQ_{max} values ranged from 5.4×10^{-7} (β-caryophyllene) to 0.29 (tributyl acetylcitrate), again showing no risk (HQ <1) associated to the individual presence of the identified SVOCs in dust for children. These results are shown in Table S4.

Furthermore, to consider the combined exposure to SVOCs by indoor dust, the total EDI values (EDI_{total}) for substances with low-Class I (EDI^{I}_{total}), intermediate-Class II (EDI^{II}_{total}), and high-Class III (EDI^{III}_{total}) toxicological hazard were calculated for adult and child population in each sampling location. After that, total HQ values for Class I (HQ^{I}_{total}), Class II (HQ^{II}_{total}), and Class III (HQ^{III}_{total}) substances were also obtained, considering their respective TDI values. The results obtained for adult and child populations are shown in Tables 2 and 3, respectively.

For adults, EDI_{total} values ranged from 0.15 μg day^{-1} (sample 2, Class II substances) to 73 μg day^{-1} (sample 13, Class I substances), showing that the highest EDI was due to the combined exposure to a higher number of low toxicological hazard (Class I) substances. As can be seen, HQ_{total} values ranged from 2.8×10^{-5} (sample 2, Class II substances) to 0.056 (sample 7, Class III sustances), thus showing that no risk was expected (HQ <1) for adults due to combined SVOCs exposure for indoor dust ingestion and inhalation in any of the analyzed samples.

For children, EDI_{total} values ranged from 0.3 μg day^{-1} (sample 2, Class II substances) to 0.15 mg day^{-1} (sample 13, Class I substances), and HQ_{total} values ranged from from 2.1 × 10^{-4} (sample 2, Class II substances) to 0.51 (sample 7, Class III sustances), thus showing that there was not risk (HQ <1) associated with the combined presence of the identified SVOCs, grouped by classes of toxicological hazard, in dust for children.

Finally, a worst-case scenario approach was conducted by considering an indoor environment containing all the identified substances at their maximum found concentration levels in the indoor dust. For adults, the EDI value in this worst-case scenario was obtained as the summation of EDI_{max}, resulting in an estimated total maximum daily intake of SVOCs of 0.14 mg day^{-1}. From that, considering also the TDI for Class III substances (0.09 mg day^{-1}), the HQ value in the worst-case scenario was 1.58, thus showing that the presence of indoor environments with conditions of potential risk (HQ ≥1) to the average adult population can not be discarded. For children, the same worst-case scenario approach resulted in an EDI value of 0.29 mg day^{-1} with a HQ value of 14.3 (considering TDI for Class III, 0.02 mg day^{-1}), thus showing potential risk (HQ ≥1). It should be considered that the estimation of the concentration of SVOCs in the assessed samples also contributes to the uncertainties of the risk assessment procedure (EFSA, 2006). In this sense, more studies regarding the potential mixture toxicity (cocktail effects) using bioassays are needed, since the exposure to a large number of substances with a wide variety of chemical nature and sources in indoor environments is a subject of concern.

4. Conclusions

In this work, the non-target screening and human exposure risk assessment for adult and child populations of SVOCs in 19 residential indoor dust samples in Spain, as a pilot study, by MAE followed by GC-HRMS (Q-Orbitrap) has been conducted for the first time. From the analyzed dust samples, 474 substances were tentatively identified with a high level of identification confidence, according to a restrictive set of identification criteria, and 19 of them were confirmed with their analytical standards,

showing a high level of identification accuracy (86.4 %). According to the results of the risk assessment by applying the TTC approach, risk for adult and child populations associated with the presence of the identified substances in the indoor dust was not expected, although the existence of indoor environments with conditions of potential risk cannot be discarded under a worst-case scenario approach. However, it should be considered that the TTC approach evaluates the individual toxic hazard of a given substance, thus it cannot efficiently assess the potential mixture toxicity (cocktail effects) that could occur when the population is exposed to a large number and variety of substances, which could be assessed in parallel using bioassays.

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Supplementary materials

The following supplementary materials can be downloaded: Table S1: List of the tentatively identified substances; Table S2: Confirmation of 22 tentatively identified substances with analytical standards; Table S3: Estimated concentrations of the identified substances in the analyzed indoor dust samples; Table S4: Risk assessment of the identified substances; Figure S1: Map of the sampling sites in different Spanish regions; Figure S2: Diagram of the Compound Discoverer™ 3.3 workflow; Figure S3: Confirmation of the identity of benzyl butyl phthalate: (a) Base peak (standard); (b) Base peak (sample); (c) MS spectrum (standard); (d) MS spectrum (sample).

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Figure captions

Figure 1. Scheme of the whole proposed procedure for non-target screening of indoor dust.

Figure 2. Distribution of the identified substances according to: (a) functional groups; (b) chemical structure; (c) toxicological hazard; (d) applications and sources.

Figure 3. Confirmation of the identity of triphenyl phosphate: (a) Base peak (standard); (b) Base peak (sample); (c) MS spectrum (standard); (d) MS spectrum (sample).

Table 1. Criteria for the tentative identification of unknown substances.

Parameter	Criteria	Comments
NIST MS Library match (Total score)	≥90 %	Match (Total score) between deconvoluted EI spectrum and NIST Mass Spectral Library, for the proposed substance. Total score is a composite metric that includes contribution from the High resolution filtering score (HRF) and the Search index (SI) score.
Mass accuracy (ΔMass)	≤2 ppm	Exact mass accuracy (ΔMass) for at least 3 annotated ions (matching fragment ions between acquired spectrum and NIST library spectrum).
Isotopic profile match (Found elements)	100 %	Match between found elements according to the acquired isotopic profile in the EI spectrum and the elements present in the molecular formula of the proposed substance.
Retention index (ΔRI)	≤25 units	Retention index absolute difference (ΔRI) between calculated RI and NIST library RI (column type: semi standard non polar). Candidate substances whose RI values were not available in the NIST library were not considered.

Table 2. Risk assessment of total SVOCs in the analyzed indoor dust samples for adult population.

Sample	Class I			Class II			Class III		
	No. of SVOCs	EDI^{I}_{total} [a] (mg day^{-1})	HQ^{I}_{total} [b]	No. of SVOCs	EDI^{II}_{total} [a] (mg day^{-1})	HQ^{II}_{total} [b]	No. of SVOCs	EDI^{III}_{total} [a] (mg day^{-1})	HQ^{III}_{total} [b]
1	154	1.7E-03	9.2E-04	27	1.9E-05	3.5E-05	73	1.9E-04	2.2E-03
2	157	1.2E-03	6.6E-04	26	1.5E-05	2.8E-05	74	3.4E-04	3.8E-03
3	226	2.0E-02	1.1E-02	38	2.0E-04	3.6E-04	108	6.4E-04	7.1E-03
4	192	2.2E-03	1.2E-03	28	2.6E-05	4.8E-05	96	3.3E-04	3.7E-03
5	252	2.7E-02	1.5E-02	47	4.0E-04	7.4E-04	135	2.4E-03	2.7E-02
6	258	3.2E-02	1.8E-02	46	6.6E-04	1.2E-03	142	2.9E-03	3.2E-02
7	253	3.5E-02	1.9E-02	46	3.5E-04	6.5E-04	143	5.1E-03	5.6E-02
8	215	1.1E-02	6.2E-03	38	1.2E-04	2.2E-04	121	2.5E-03	2.8E-02
9	238	1.2E-02	6.8E-03	43	1.9E-04	3.5E-04	128	2.0E-03	2.3E-02
10	235	2.0E-02	1.1E-02	41	2.5E-04	4.6E-04	119	1.0E-03	1.1E-02
11	177	3.3E-03	1.9E-03	33	5.4E-05	1.0E-04	101	2.8E-04	3.1E-03
12	224	1.2E-02	6.6E-03	41	2.1E-04	3.9E-04	126	9.9E-04	1.1E-02
13	235	7.3E-02	4.1E-02	43	2.6E-04	4.9E-04	138	3.8E-03	4.2E-02
14	250	2.7E-02	1.5E-02	43	6.3E-04	1.2E-03	136	1.7E-03	1.9E-02
15	244	1.8E-02	9.8E-03	42	4.0E-04	7.4E-04	127	1.3E-03	1.4E-02
16	248	1.6E-02	9.0E-03	43	2.7E-04	5.1E-04	123	9.9E-04	1.1E-02
17	226	9.8E-03	5.4E-03	41	1.1E-04	2.0E-04	120	9.2E-04	1.0E-02
18	233	1.2E-02	6.8E-03	36	1.0E-04	1.9E-04	120	8.8E-04	9.8E-03
19	217	1.0E-02	5.8E-03	36	1.7E-04	3.1E-04	115	6.5E-04	7.3E-03

[a] Total estimated daily intake (EDI_{total}, mg day^{-1}), as the summation of the EDI of the identified substances assigned to each class of toxicological hazard.
[b] Total hazard quotient (HQ_{total}) calculated as the EDI_{total}/TDI ratio.

Table 3. Risk assessment of total SVOCs in the analyzed indoor dust samples for child population.

Sample	Class I			Class II			Class III		
	No. of SVOCs	EDI^{I}_{total} [a] (mg day^{-1})	HQ^{I}_{total} [b]	No. of SVOCs	EDI^{II}_{total} [a] (mg day^{-1})	HQ^{II}_{total} [b]	No. of SVOCs	EDI^{III}_{total} [a] (mg day^{-1})	HQ^{III}_{total} [b]
1	154	3.3E-03	7.4E-03	27	3.8E-05	2.7E-04	73	3.9E-04	1.9E-02
2	157	2.4E-03	5.3E-03	26	3.0E-05	2.1E-04	74	6.9E-04	3.4E-02
3	226	4.0E-02	8.8E-02	38	3.9E-04	2.8E-03	108	1.3E-03	6.4E-02
4	192	4.4E-03	9.8E-03	28	5.2E-05	3.7E-04	96	6.6E-04	3.3E-02
5	252	5.5E-02	1.2E-01	47	8.0E-04	5.7E-03	135	4.8E-03	2.4E-01
6	258	6.5E-02	1.4E-01	46	1.3E-03	9.5E-03	142	5.8E-03	2.9E-01
7	253	7.0E-02	1.6E-01	46	7.1E-04	5.1E-03	143	1.0E-02	5.1E-01
8	215	2.2E-02	4.9E-02	38	2.4E-04	1.7E-03	121	5.0E-03	2.5E-01
9	238	2.5E-02	5.5E-02	43	3.8E-04	2.7E-03	128	4.1E-03	2.0E-01
10	235	4.0E-02	8.9E-02	41	5.0E-04	3.5E-03	119	2.0E-03	1.0E-01
11	177	6.7E-03	1.5E-02	33	1.1E-04	7.7E-04	101	5.6E-04	2.8E-02
12	224	2.4E-02	5.3E-02	41	4.2E-04	3.0E-03	126	2.0E-03	1.0E-01
13	235	1.5E-01	3.3E-01	43	5.3E-04	3.8E-03	138	7.6E-03	3.8E-01
14	250	5.4E-02	1.2E-01	43	1.3E-03	9.1E-03	136	3.4E-03	1.7E-01
15	244	3.5E-02	7.8E-02	42	8.0E-04	5.7E-03	127	2.5E-03	1.3E-01
16	248	3.2E-02	7.2E-02	43	5.5E-04	3.9E-03	123	2.0E-03	1.0E-01
17	226	2.0E-02	4.4E-02	41	2.1E-04	1.5E-03	120	1.8E-03	9.2E-02
18	233	2.5E-02	5.5E-02	36	2.1E-04	1.5E-03	120	1.8E-03	8.8E-02
19	217	2.1E-02	4.7E-02	36	3.4E-04	2.4E-03	115	1.3E-03	6.6E-02

[a] Total estimated daily intake (EDI_{total}, mg day^{-1}), as the summation of the EDI of the identified substances assigned to each class of toxicological hazard.
[b] Total hazard quotient (HQ_{total}) calculated as the EDI_{total}/TDI ratio.