Master in Bioengineering – Specialization in Biological Engineering

Occurrence and human exposure to siloxanes by inhalation

Dissertation for the master's degree in Bioengineering

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ABSTRACT

The production and consumption of siloxanes, specifically volatile melylsiloxanes (VMSs), has been increasing significantly over the past 30 years. As a result of their properties recognized as unique, these compounds are applied in multiple areas, such as personal care, cleaning, food, and transport, among others. Due to the volatile nature of VMSs, they are released into the atmosphere during their manufacture and/or during the use of products that contain them in their formulations. It is in debate if the presence of VMSs can compromise air quality and, consequently, pose some danger to human health, since there is an exposure to these compounds through inhalation, especially in closed environments. In fact, some VMSs have already manifested harmful effects on the health of laboratory animals.

Since the information available so far in the literature is still limited, the three main aims of this dissertation were to analyze different VMSs (L3-L5 and D3-D6) in the air of several indoor environments, identify potential sources of contamination, and estimate the human inhalation exposure to these chemicals in different scenarios. For that, three 14-day sampling campaigns were carried out using passive air samplers comprising XAD-2 as sorbent. Then, the VMSs were extracted through a solid-liquid extraction procedure with n-hexane and quantified by gas chromatography coupled to a mass spectrometer detector (GC-MS).

The highest levels of total VMSs were detected in a private bedroom (14095.47 ± 402.73 ng/day) being D5 the prevalent congener, which is likely related with the patterns of use of personal care products, where D5 also predominates. Two outdoor locations were also chosen as background checks and had, as expected registered the lowest total values, particularly the remote area (1.19 ± 0.19 ng/day). The individual concentration of cyclic VMSs (cVMSs) ranged between 0.39 ± 0.01 to 13340.60 ± 465.94 ng/day, whilst the linear VMSs (lVMSs) ranged between 0.02 ± 0.00 to 597.48 ± 26.05 ng/day, a higher incidence of cVMSs over lVMSs was verified in all the environments studied. Regarding the estimation of the human exposure, women are apparently more susceptible to higher inhalation doses than men, due to their physiology. The highest exposure levels estimated were found for hairdressers (1200.95 ± 47.36 ng/kg bw·day ng/kg bw·day), and the lowest in the laboratory (8.98 ± 0.87ng/kg bw·day ng/kg bw·day). More than 50% of the inhaled doses occur at home, highlighting the importance of our daily routine in the exposure to these compounds and its changes in extreme situations like the current pandemic (an increase of 42% of the daily exposure to VMSs). Furthermore, the estimated exposure by ingestion of dust contaminated by VMSs (60.41 ± 3.17 µg/kg bw·day) was shown to be higher than inhalation (4.92 ± 0.48 µg/kg bw·day) for babies.

Keywords: siloxanes; atmospheric pollution; passive air sampling; indoor environments; human exposure

RESUMO

O consumo e produção de siloxanos, nomeadamente, volátil melilsiloxanos (VMSs), tem vindo a aumentar significativamente ao longo dos últimos 30 anos. Devido as suas propriedades reconhecidas como únicas estes compostos são aplicados em múltiplas áreas, como beleza, cuidado pessoal, alimentação, transportes, entre outras. Dada a natureza volátil destes compostos, estes são libertados para a atmosfera durante o seu processo de produção e/ou durante o uso de produtos que os contenham na sua formulação. Suspeita-se que a contaminação do ar por VMSs possa comprometer a sua qualidade**,** podendo representar algum perigo para a saúde humana, através da sua inalação, principalmente em ambientes fechados. Para além disso alguns destes compostos já mostraram ser prejudiciais para saúde de animais de laboratório.

Dado que as informações disponíveis na literatura são muito limitadas, os principais objetivos desta dissertação foram a análise desta classe de siloxanos (L3-L5 e D3-D6) no ar de vários ambientes internos, identificar potencias fontes de contaminação, e calcular a exposição humana através da inalação destes compostos em diferentes cenários. Para isso, foram realizadas três amostragens com uma duração de 14 dias cada, recorrendo-se a uma amostragem de ar passiva, utilizando-se XAD-2 como sorbente. De seguida, os VMSs foram extraídos através de uma extração sólido-líquido, e quantificados por cromatografia gasosa associado a um detetor de massa (GC-MS).

Verificou-se que os níveis mais elevados de VMSs foram encontrados num quarto privado (14095.47 ± 468.86 ng/day), onde o D5 foi o VMSs detetado com mais frequência, o que está associado ao uso de produtos de higiene. Adicionalmente, dois locais ao ar livre foram escolhidos como verificação de antecedentes, e como esperado a menor concentração de tVMSs foi detetada numa área remota (1.19 ± 0.27 ng/day). A concentração individual de cVMSs variou entre 0.39 ± 0.01 e 13340.60 ± 465.94 ng/dia, enquanto a de lVMSs variou entre 0.02 ± 0.00 e 597.48 ± 26.05 ng/dia, sendo registada uma maior incidência de cVMSs do que lVMSs nos diferentes ambientes estudados. Concluiu-se também que as mulheres estão mais suscetíveis as maiores doses de inalação do que os homens, devia às suas características fisiológicas, os maiores níveis de exposição humana estimados foram detetados para trabalhadores de um cabeleiro (1200.95 ± 45.01 ng/kg bw·day), e os menores para trabalhadores de um laboratório (8.98 ± 0.69 ng/kg bw·day). Em casa é onde se verifica ocorrer mais de 50% da exposição diária, evidenciando a importância da nossa rotina diária na exposição a estes compostos e suas alterações em situações extremas como a atual pandemia (aumento de 42% da exposição diária aos VMSs). Para além disso, a exposição por ingestão de poeira contaminada por VMSs (60.41 ± 3.17 μg/kg bw·day) mostrou ser mais elevada do que a sua inalação (4.92 ± 0.47 μg/kg bw·day) para babes.

Palavras-chave: siloxanos; poluição atmosférica; amostragem passiva de ar; ambientes internos; exposição humana

DECLARATION

I declare, under oath, that this work is original and that all non-original contributions were properly referenced with the source identification.

Eu declaro, sob compromisso de honra, que este trabalho é original e que todas as contribuições não originais foram devidamente referenciadas com identificação da fonte.

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Ana Catarina Pires Rodrigues

INDEX

LIST OF FIGURES

LIST OF TABLES

NOMENCLATURE

AAs – Active air sampler

APCI-MS/MS - Atmospheric pressure chemical ionization tandem mass spectrometry

C_{air} - Concentration in the air

cVMSs- Cyclic volatile methylsiloxanes

D3 - Hexamethylcyclotrisiloxane

D4 - Octamethylcyclotetrasiloxane

D5 - Decamethylcyclopentasiloxane

D6 - Dodecamethylcyclohexasiloxane

ECHA- European Chemicals Agency

$ED_{inhalation}$ - daily inhalation exposure

GC-MS - Gas chromatography-mass spectrometry

IR - Inhalation rate

L2 - Hexamethyldisiloxane

L3 - Octamethyltrisiloxane

L4 - Decamethyltetrasiloxane

L5 - Dodecamethyltetrasiloxane

lVMSs - Linear volatile methylsiloxanes

LDH - lactate dehydrogenase

LH - luteinizing hormone

LOD - Limit of detection

LOQ - Limit of quantification

LRAT - long-range atmospheric transport

tVMSs - Total volatile methylsiloxanes

OECD - Organization for Economic Cooperation and Development

PBT- persistent, bioaccumlative and toxic

PCPs - Personal care products

PDMSs - Polydimethylsiloxanes

PLE - Pressurized liquid extraction

PUF - Polyurethane foam

REACH - Registration, Evaluation, Authorization, and Restriction of Chemicals

SCCS- Scientific Committee on Consumer Safety

SIP - Sorbent-impregnated polyurethane foam disks

SLE - Solid-liquid extraction

SVHC - Substances of Very High Concern

TD-GC/MSD - Thermal desorption and gas chromatography-mass spectrometry

V_{room} - Volume of the room

vPvB - Very persistent and very bioaccumulative compounds

XAD - Polystyrene−divinylbenzene copolymeric resin

USA- United Sates of America

UV- Ultraviolet radiation

(γ-GT) - gamma-glutamyl transferase

1. INTRODUCTION

1.1 Context

Siloxanes, often described as silicones, are man-made chemicals with a backbone of intercalated atoms of silicon (Si) and oxygen (O) bonded to functional groups, mainly, methyl, ethyl, or phenyl groups (Gaj & Pakuluk, 2015). These chemicals are classified into several classes, the major ones being volatile methyl siloxanes (VMSs), polydimethylsiloxanes (PDMSs), and functionalized siloxanes (Ru & Ku, 2015). Their chemical structure defines a range of physicochemical properties that are recognized as unique from their viscosity to hydrophobicity (Homem & Ratola, 2020). For that reason, they are valuable for many different industries, such as cosmetics, paper, silicone, food, and personal care products (PCPs), among others. As a result of their wide application, more than ten million tons of siloxanes are manufactured each year, which led to their inclusion on the list of high production volume chemicals by OECD (Organization for Economic Cooperation and Development) (Mojsiewicz-Pieńkowska & Krenczkowska, 2018).

VMSs are characterized by their low molecular weight and high vapor pressure, being mainly emitted to the atmosphere during production and usage, whereas the non-volatilized fraction of VMSs is discarded in wastewater and landfills (Li et al., 2020a). Their fate, when released into the atmosphere, has been studied over the last few years. Until now, it is known that they are likely to undergo long-range atmospheric transport (Genualdi et al., 2011; Krogseth et al., 2012), their concentrations on air are affected by seasonal trends (Ratola et al., 2016), and high concentrations in air are significantly related to the population density and the usage of PCPs (Buser et al., 2013).

Furthermore, worries have been raised about VMSs toxic and accumulative behavior in the environment and human health. A few studies reported harmful effects of VMSs in laboratory animals, ranging from lungs inflammation to significant reduction in fertility, increasing the awareness about siloxane's hazards among the scientific community (Dekant & Klaunig, 2016; Lu et al., 2010; Meeks et al., 2007; Quinn et al., 2007). Besides, people are exposed to VMSs by different routes, the main ones are dermal (through the application of personal care and cosmetic products in the skin) and inhalation (by breathing contaminated air, especially indoor air) (Homem & Ratola, 2020). Since we spend 90 % of the time in different indoor environments breathing air contaminated with VMSs (Guo et al., 2020), it is extremely important to know the toxicity and human exposure to these chemicals, and whether or not they pose any risk to human health.

1.2 Problem

VMSs are present in many everyday products, such as moisturizing creams, body lotions, shampoos, makeup, conditioners, cleaning agents, foams, food, among others (Capela et al., 2016; Gaj & Pakuluk, 2015). During the production, application, and disposal of these products, VMSs tend to be released into the air due to their volatile character, rising their concentrations on the environment. However, the major problem arises in indoor atmospheres, where the levels of these compounds are relatively high, promoting greater human exposure by inhalation (Homem & Ratola, 2020). Despite this, only a few studies have monitored the presence of VMSs indoors, and some potentially harmful environments (such as perfumeries and dentist clinics) have not been described in the literature. Furthermore, the lack of information on these chemicals' toxicity in humans is a concern among the scientific community. Even though some studies have been carried out in rats, which demonstrated that the exposure to these chemicals harmed their health (Dekant & Klaunig, 2016), almost no information is available on the exposure and effects on the human body, being necessary to do more research on this subject.

1.3 Goals

The main goals of this master dissertation are to measure and quantify the levels and spatial variation of linear (L3-L5) and cyclic (D3-D6) VMSs in several indoor and outdoor environments, (some of them never studied before), identify potential sources of contamination, and estimate the human exposure via inhalation to these compounds.

To accomplish the proposed goals, passive sampling of VMSs using amberlite XAD-2 polymeric sorbent (XAD-PAS) was performed in each environment studied. After a solid-liquid extraction of VMSs from the XAD-2 using n-hexane as a solvent, VMSs were quantified by gas chromatography coupled to mass spectrometry (GC-MS) in order to obtain the profile and trends of the studied compounds. The human exposure through inhalation was estimated taking into consideration the concentration of VMSs, the inhalation rate, the time of exposure, and physiological parameters.

1.4 Outline of the work

This work is structured in five chapters. The first chapter (Introduction) presents the theme of the dissertation and the main problem, as well as the objectives defined to help face the problem. The second (State of the Art) reports an overview of the current knowledge existent in the scientific community about siloxanes, with a focus on their chemical and physical properties, applications, human exposure, threat to human health and environment, legislation, indoor and outdoor concentrations. Chapter 3 (Material and Methods) gives detailed information about the strategy, equipment and analytical methods used to perform the present work. Then, the fourth chapter (Results

and Discussion) is divided according to the main project goals (VMSs concentrations in the different environments; Potential sources of contamination; Human exposure to D4 and D5). The fifth chapter (Conclusions; Limitations and Future Recommendations) presents the concluding remarks by assessing where the project goals were accomplished and suggests some future assignments to complement this dissertation. Additionally, supplementary information to the main dissertation can be found in the Appendices.

2. STATE OF THE ART

2.1 Siloxanes overview

Siloxanes are chemical compounds intensively used in many daily products. They can be described as substrates of silicone polymers, composed by interconnections of silicon atoms (Si) and oxygen (O), where Si atoms are connected to several functional groups (methyl, ethyl, phenyl, and vinyl groups, or hydrogen atoms) (Gaj & Pakuluk, 2015). The chemical and physical properties of siloxanes vary according to these functional groups, alongside with cross- linking density, length of the Si–O backbone and molecular weight (Zuber et al., 2019). There is a great variety of these compounds, most remarkably the polydimethylsiloxanes (PDMS), functionalized siloxanes, and volatile methyl siloxanes (VMSs) (Ru & Ku, 2015). In this latter group the chemical bonds lead to the formation of linear or cyclic structures, being expressed as L_n when the structure is linear and D_n when it is cyclic, indicating the subscripted "n" the number of Si atoms present in the chemical structure (Capela et al., 2016; Gaj & Pakuluk, 2015) as shown in Figure 1.

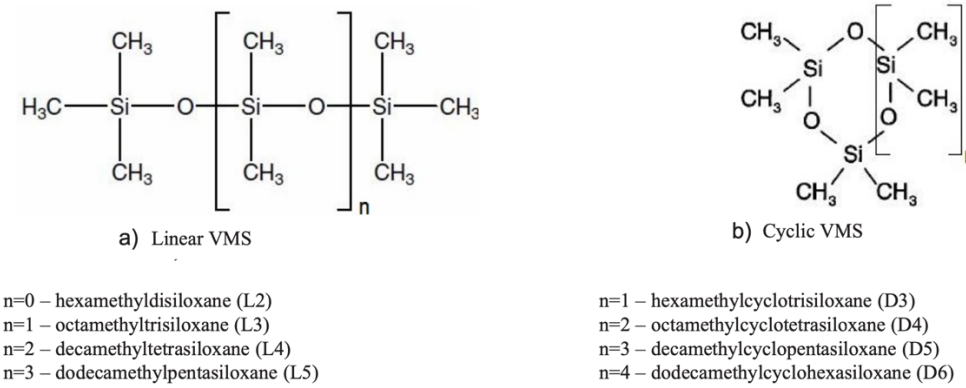

Figure 1. Representation of the chemical structure of cyclic (left) and linear (right) methylsiloxanes (source: Gaj et al. 2015).

In general, siloxanes are colorless, odorless, have low chemical reactivity, are stable, resistant to oxidation, UV radiation, temperature (-100 to 250 ºC), atmospheric conditions, and degradation. Also, they have unique flexibility, durability, high spreadability, power to permeate in water vapor and oxygen, are biocompatible (they have the ability to be occluded in the skin without causing irritation), and do not promote the growth of microorganisms (Mojsiewicz-Pieńkowska & Krenczkowska, 2018). VMSs containing from 2 to 6 Si atoms are also characterized by their low surface tension, viscosity, molecular weight, and high vapor pressure (Wang et al., 2013).

Due to the exclusive properties of siloxanes, these compounds are applied in many different areas, such as beauty, personal care, medical, food, paper, oral health, paint, electricity, textile, cleaning agents, furniture, rubber products, car and ship manufacturing (Gaj & Pakuluk, 2015; Mojsiewicz-Pieńkowska & Krenczkowska, 2018; Homem & Ratola, 2020). In the beauty/cosmetic

and PCPs industry, siloxanes, mostly cyclic VMSs (D4, D5 and D6), are used as emollients, humectants, solvents and antiperspirants, in make-up, shampoos, hair conditioners, coloring treatments, masks, perfumes, sunscreens, body lotion, face gel, toothpaste, moisturizing creams, and deodorants (Capela et al., 2016; Horii & Kannan, 2008; King et al., 2020). They are also reported to occur in dermal medic products and medical devices. For instance, siloxanes are present in ointments against pathogens and for treatments of scars, gels for keloids, emollients for atopic dermatitis products against lice, prostheses, catheters, medical device lubrication, transdermal drug delivery system and implants (Mojsiewicz-Pieńkowska & Krenczkowska, 2018). In the food industry, siloxanes work as additives like anti-foaming agents, in oral health as molds, in electricity as insulation, in the paper industry as defoamers during pulp making, in car and ship manufacturing as silicone rubbers, lubricants, plastic additives, coating and adhesives (Global Silicones Council 2020a; Homem & Ratola, 2020; Zuber et al., 2019)

Recently, VMSs were classified as emerging environmental contaminants. The increase of data amount, as well as improvements in analytical methods were the keys to this deliberation (Ru & Ku, 2015). The term “emerging contaminants” is broadly accepted by the scientific literature. It refers to those natural or anthropogenic chemicals foreign to a specific environment and having the capability to be distributed to other locations with pernicious effects on human health or to the ecosystem itself (Barroso et al., 2019). There are some special properties of the siloxanes that leaded to this categorization, such as low biodegradability, lipophilicity, and their capacity to spread and transportation, which can promote their bioaccumulation (Homem & Ratola, 2020). Also, toxic effects in animal were verified for certain VMSs (D4 and D5) (Lu et al., 2010). The VMSs can be released into the environment during their manufacture, use, and disposal, with more than 90% freed to the atmosphere, and the remaining discharged to the wastewater and landfills (Li et al., 2020a; Li et al., 2020b).

2.2 Main routes of human exposure to siloxanes

People are exposed to siloxanes throughout vital actions, such as breathing, eating, and drinking water. Actually, siloxanes are present in water and food, and even though VMSs have extremely low solubility in water, L2 and D3 can be found in this matrix (Homem & Ratola, 2020). However, the main routes of exposure are the dermal application of PCPs and inhalation. As stated earlier, cyclic VMSs are the major subclass of siloxanes present in PCPs formulation. During the application of these products, VMSs are absorbed through skin (1% of absorption) and released into the air, rising their concentrations. This phenomenon is especially intense in indoor environments, where inhalation is considered to be a significant pathway of human exposure to VMSs (Tran et al., 2019; Homem & Ratola, 2020). Furthermore, users tend to use more than one PCP at the same time, being exposed to

the same substance through different routes and sources (Biesterbos et al., 2015). Over the past few years, the human exposure to VMSs through dermal and inhalation pathways have been matter of study. Table 1 presents a summary of the daily intake of siloxanes from dermal and inhalation exposure, depending on the state of life and gender.

Researchers demonstrated that the daily exposure to VMSs through inhalation is greater in environments where PCPs are frequently used such as beauty salons and homes (Tran & Kannan, 2015). D5 is the siloxane with higher contribution to the daily inhalation exposure, due to its multiple applications, especially in PCPs (Capela et al., 2016; Tran & Kannan, 2015). The groups with highest levels of exposure are infants and children, due to the different inhalation rates that are directly related with physiological parameters (*e.g.*, lung volume), body growth and weight. Even though adults inhale greater amounts of air than infants and children, the volume of air that passes through infants and children lungs is twice the volume of the adults, when resting (EPA, 2011).

In order to determine the daily intake of VMSs through inhalation, a few models can be found in the literature. All of them are based in three fundamental variables: the concentration of VMSs in the air (C_{air}) expressed in ng/m^3, the inhalation rate (IR) in m^3/day, and the body weight (BW) in kg. However, more complex models add supplementary variables, such as the time of exposure (ET), and the volume of the room (V_{room}). The daily exposure via inhalation ($ED_{inhalation}$) in ng/kg bw·day can be calculated by using the following equations (Tran et al., 2017, 2018; Tran & Kannan, 2015;Tran et al., 2019; Sha et al., 2018; Capela et al., 2016):

$$ED_{inhalation} = \frac{C_{air} \times IR}{BW} \quad \textbf{Equation 1}$$

$$ED_{inhalation} = \frac{C_{air} \times IR \times ET}{BW} \quad \textbf{Equation 2}$$

$$ED_{inhalation} = \frac{C_{air} \times IR \times V_{room}}{BW} \quad \textbf{Equation 3}$$

$$ED_{inhalation} = \frac{\frac{C_{air}}{V_{room}} \times IR \times ET}{BW} \quad \textbf{Equation 4}$$

Apart from inhalation exposure, previous studies analyzing VMSs and other chemical compounds have calculated the average daily dose ($ADD_{inhalation}$) in ng/kg bw·day using the following equation (Gungormus et al., 2014; Téllez Tovar & Rodríguez Susa, 2020;Guo et al., 2020):

$$ADD_{inhalation} = \frac{C_{air} \times IR \times ET \times EF \times ED}{BW \times AT} \quad \textbf{Equation 5}$$

where, EF represents the frequency of exposure in days/year, ED the duration of exposure in years, and AT the average exposure time in days.

In an assay carried out in Albany, USA, the daily inhalation exposure to cyclic and linear siloxanes (D3-D7, L3-L11) was estimated in homes, offices, hair salons, and public places for

different stages of life: infants, toddlers, children, teenagers, and adults, applying Equation 3. The outcome reveled that the most problematic environments were salons, and the mean values from the indoors settings studied were 3.18 μg/kg·bw/day for infants, 1.59 μg/kg·bw/day for toddlers, 0.34 μg/kg·bw/day for teenagers, and 0.27 μg/kg·bw/day for adults. Moreover, D5 was the VMSs that contributed to the highest daily exposures (Tran & Kannan, 2015).

In Vietnam, the human inhalation exposure doses to VMSs (D3-D6, L2-L5) were predicted for homes, cars, kindergartens, offices, hair salons, and homes, using Equation 1, for infants, toddlers, children, teenagers, and adults. The maximum $ED_{inhalation}$ was detected in hair salons and homes, being the principal sources of exposure PCPs and furniture. The total $ED_{inhalation}$ were 352 ng/kg bw·day, 219 ng/kg bw·day 188 ng/kg bw·day, 132 ng/kg bw·day, 95.9 ng/kg bw·day, for infants, toddlers, children, teenagers, and adults, respectively (Tran et al., 2017). Another report in Vietnam, estimated the inhalation of cyclic VMSs (D4, D5, and D6) of women and men who worked at the hair salon for a period of 8 hours per day, using Equation 2. The results demonstrated that the inhalation for women was higher than for men, resulting in exposure doses of 103 and 79.5 ng/kg bw·day, respectively (Tran et al., 2018). In a third study in Vietnam, the inhalation exposure doses of adults, children, and university subjects (*e.g.*, laboratory staff, researchers, and students) to cyclic VMSs (D4, D5, D6) was calculated for offices and laboratories. Among the siloxanes studied, D5 was the one with higher exposure levels. Also, children were the group with highest exposures doses: 60.8, 112, and 80 ng/kg bw·day for D4, D5 and D6, respectively (Anh et al., 2020).

Despite equations 1-5 are the most frequently used to calculate exposure, some studies implemented different indicators. Pieri et al., (2013) calculated the average daily intake inhalation (μg/day) for UK and Italy citizens (children and adults) based in their everyday life habits. For that, the total amount of VMSs inhaled daily (working days) for each activity, such as sleeping (bedroom), showering (bathroom), working (office, supermarket, kindergarten), shopping (supermarket), lounge (living room), among other activities, was calculated using the following equation:

$$I_{act} = B \times C \times T \qquad \textbf{Equation 6}$$

where, I_{act} is the mass of VMSs inhaled per day (μg/day), B is the breathing rate (m^3/day), C is the total concentration of VMSs in each atmosphere studied (μg/m^3), and T represents time of the activity. The sum of all I_{act} for each activity provide the VMSs inhaled daily. The highest exposures were obtained for UK children and adults with 3188 and 1875 μg/day, respectively, while the levels of exposure in Italy for adults were 1563 μg/day, and 1251 μg/day for children. The environments that had a greater influence in the exposure levels were the bedrooms in Italy, that represented 60% of the VMSs inhaled daily, and in UK 50% of the of the exposure take place in working places.

Table 1. Summary of the human daily exposure through dermal and inhalation pathways.

Pathways	Source	Siloxanes	Daily exposure	Units	Groups	Country	Reference
Dermal	PCPs.	D4-7, L4-14	307	mg/day	Women	USA	(Horii & Kannan, 2008)
Dermal	PCPs.	D4-7, L4-14	0.3-1250	mg/day	Adults	China	(Lu et al., 2011)
Inhalation	Bathroom, bedroom, living room, offices, and public places.	D3-6, L2-5	3188	μg/day	Children	UK	(Pieri et al., 2013)
			1875	μg/day	Adults		
		D3-6, L2-5	1563	μg/day	Children	Italy	
			1261	μg/day	Adults		
Inhalation	Homes, offices, laboratories, schools, salons, and public places.	D3-7 L3-11	3.18	μg/kg bw·day	Infants	USA	(Tran & Kannan, 2015)
			1.59	μg/kg bw·day	Toddlers		
			0.76	μg/kg bw·day	Children		
			0.34	μg/kg bw·day	Teenagers		
			0.27	μg/kg bw·day	Adults		
Inhalation	Homes, laboratories, offices, hair salons, cars, and kindergartens.	D4-6, L4-9	352	ng/kg bw·day	Infants	Vietnam	(Tran et al., 2017)
			219	ng/kg bw·day	Toddlers		
			188	ng/kg bw·day	Children		
			132	ng/kg bw·day	Teenagers		
			95.6	ng/kg bw·day	Adults		
Inhalation	Hair salons.	D4-6	103	ng/kg bw·day	Women	Vietnam	(Tran et al., 2018)
			79.5	ng/kg bw·day	Men		

Table 1 (continuation). Summary of the human daily exposure through dermal and inhalation pathways.

Pathways	Source	Siloxanes	Daily exposure	Units	Groups	Country	Reference
Inhalation	Office and laboratories.	D4	20.8	ng/kg bw·day	Adults	Vietnam	(Anh et al., 2020)
			60.8	ng/kg bw·day	Children		
		D5	33.9	ng/kg bw·day	Adults		
			112	ng/kg bw·day	Children		
		D6	23.4	ng/kg bw·day	Adults		
			80	ng/kg bw·day	Children		

2.3 Siloxanes as a threat to human health and the environment

The use of siloxanes in consumer products is considered to be safe by the Scientific Committee on Consumer Safety (SCCS) (Homem & Ratola, 2020). However, the potential toxic behavior of VMSs, precisely of D4 and D5, has raised some concerns. Recently, a few studies have been performed exposing rats to different concentrations of D4 and D5 through inhalation to understand if it could induce any side effects. In Table 2 is represented a summary of studies carried out about the siloxane's harmful effects in rats.

Klykken et al. (1999), exposed groups of Fischer 344 rats to a whole-body vapor inhalation at different concentrations of D5 (0, 10, 25, 75, and 160 ppm), 6 hours per day, for 28 days. The results indicated that D5 had no immunosuppressive and humoral action under these conditions. However, some harmful effects were verified. At the concentration of 160 ppm, male rats developed a significant increase in lung weight and a slight increase liver weight, whereas female rats observed a significant increase of liver weight. An increase of cell proliferation of the nasal cavity occurred in both sexes, but only became harshness at 160 ppm. Also, a prevalence and severity submucosal inflammation (females), and an increase of alveolar macrophage accumulation in the lung (males) was verified. After the exposure processes, the rats followed a recovery period of 14 days, and at the end of this period, neither liver nor lungs weigh increased. However, the increase in cell proliferation of the nasal cavity kept occurring for females subject to 160 ppm, and there was no recovery of the alveolar macrophage accumulation in the lung. These results suggests that D5 promotes pulmonary inflammatory reaction.

Burns-Naas et al. (2002) followed a 3-month nose-only inhalation exposure program, in order to study D5 subchronic toxicity. For that, Fischer 344 rats were exposed 6 hours per day, 5 days a week

for 3 months to D5 vapor (26 and 86 ppm; 20/sex/group), mixed vapor/aerosol of D5 (224 ppm; 30/sex/group), or control air (0 ppm; 30/sex/group). This resulted in a slight increase of the lung and liver weight in both sexes at 224 ppm. A decrease in cholesterol and an increase in serum glucose levels was verified for male rats only. Females suffer a noteworthy rise of gamma-glutamyl transferase (γ-GT) at 224 ppm, suggesting an alteration in the good function of the liver. Both sexes had a diminution of the lactate dehydrogenase (LDH) levels, however, the decrease was more drastic in females (86 and 224 ppm). In addition, a severe increase in alveolar macrophage accumulation and interstitial inflammation of the lungs occurred for males and females at the highest concentration. After a recovery period of 1 month, there was no alteration in the lung and liver weight, the males recovered from the alteration in cholesterol and serum glucose levels. However, γ-GT levels increased, and there was no recovery of levels of LDH, alveolar macrophage accumulation, and interstitial inflammation of the lungs.

Quinn et al. (2007), studied the influence that D4 may have in the pre-ovulatory luteinizing hormone (LH) surge in Sprague-Dawley rats, conducting an experiment divided in two phases. In the first, groups of non-cannulated rats were exposed by whole-body vapor inhalation on their third diestrus days to 0 (24 females/group), 700 (22 females/group) or 900 (27 females/group) ppm of D4, 6 hours per day on diestrus days 1 and 2, and for 2.5 h on the day of proestrus. In the second part of the experience, groups of cannulated animals were exposed to 0, 700, or 900 ppm of D4, for 6 hours per day for 3 days, from their third diestrus day 1 through proestrus. During the first phase, a significant reduction in body weight was observed at both concentrations' studies, while in the second phase only the group exposed to 900 ppm experienced body weight reduction. Plasma LH levels suffered a decrease in peak LH concentrations, but only significant at 900 ppm, which led to a failed in ovulation. In another study, female rats (24 females/group), were exposed to 70, 300, 500, or 700 ppm of D4 for 28 days prior to mating, and through mating and gestation until gestation day, in order to evaluate the effects of D4 in the female rat reproductive cycle, which resulted in a suppression or delay of LH at 700 and 900 ppm, blocking ovulation (Meeks et al., 2007).

Even though these studies have been performed in laboratory animals to understand the potential harms of D4 and D5, until this moment, it is not known the potential damages on human health, but there are indications that inhalation of VMSs could compromise the proper functioning of the respiratory tract. King et al. (2020) exposed human lung cells A549 to byproducts of D5, which led to a decrease in their viability. This outcome leaves us to believe that air quality has a significant impact on the quality of human life, being necessary to study this matter in detail.

In terms of environmental pollution, the worries are focused on their persistence and accumulation in the aquatic environment. But due to their extensive manufacture, use, and volatile nature, VMSs

have also been detected in the worldwide environment at significant concentrations, namely in soil, air, sediment, wastewater, and sludge (Wang et al., 2013).

Table 2. Summary of results from key toxicity studies on VMSs using inhalation and ingestion as routes of exposure in animals.

Pathways	VMS	Animal	Experimental conditions	Side Effects	Reference
Inhalation	D5	Fischer 344 rats	Whole body vapor inhalation to 0, 10, 25, 75 and 160 ppm, 6h per day, 7 days per week for 28 days.	Increase of liver (reversible) and lung weight, and alveolar accumulation at 160 ppm; Morphological alterations in nasal cavity at > 10 ppm.	(Klykken et al., 1999)
Inhalation	D5	Fischer 344 rats	Nose inhalation to 0, 26, 46, 86, and 224 ppm, 6h per day, 5 days per week for 3 months.	Increase gamma glutamyl transferase (γ-GT) at 224 ppm; Decrease in serum lactate dehydrogenase (LDH) at 86 and 224 ppm (female); Increase of lung weights, macrophage accumulation and interstitial inflammation in the lungs at 224 ppm.	(Burns-Naas et al., 2002)
Inhalation	D4	Sprague - Dawley rats	Whole body vapor inhalation to 0, 700 and 900 ppm, 6h per day for 3 days.	Body weight reduction at 900 ppm; Reduced the pre-ovulatory LH surge at 700 and 900 ppm.	(Quinn et al., 2007)
Inhalation	D4	Sprague - Dawley rats	Whole body vapor inhalation to 700 ppm, during the overall phase of the reproductive cycle.	Significant reduction in fertility.	(Meeks et al., 2007)
Inhalation	D5	Fischer 344 rats	6 months, 1 and 2 years of vapor inhalation to 0, 10, 40 and 160 ppm, 6h per day, 5 days per week.	Uterine tumor after 2 years of exposure.	(Dekant & Klaunig, 2016)
Oral	D5	Sprague - Dawley rats	Oral exposure of 0, 100, 330 and 1000 mg/kg bw, 5 days per week for 90 days.	Increase of liver weight, without histopathological changes at all doses.	
			Oral exposure of 0, 25, 100, 400 and 1600 mg/kg bw, 5 days per week for 28 days.	Increase of liver weight at > 100 mg/kg.	

2.4 Legislation

Even though VMSs are considered safe by the industry and have low chemical reactivity, their possible toxic behavior, bioaccumulation, and persistence in the environment led to the implementation of some restrictions by the European Union, regarding the use of D4 and D5 in wash-off cosmetic products under REACH (Registration, Evaluation, Authorization, and Restriction of Chemicals) in May 2017 (Global Silicones Council, 2020a). In this new limitation, the concentration of D4 and D5 must be lower than 0.1% (w/w) in wash-off cosmetic products, being compulsory for all companies from January 31, 2020. Moreover, the European Commission has the intention to add D6 in this restriction and implement a new one for leave-on PCPs for consumer and professional applications. However, the European Chemicals Agency (ECHA) proposed exemptions for certain industrial and professional uses of D4, D5 and D6, in sealants, protective coating, dental impressions and prosthetic devices (Global Silicones Council, 2020a). In addition, in 2018 ECHA decided that the cyclic VMSs D4, D5 and D6 should be added on the Candidate List of Substances of Very High Concern (SVHC). According to the standards set out in REACH, D4 fulfill the standards of a substance that is very persistent, bioaccumlative and toxic (PBT), while D5 and D6 complete the requirements to be considered very persistent and very bioaccumulative compounds (vPvB) (Global Silicones Council, 2020b).

As we have seen, VMSs are potentially pernicious to humans and the environment. However, as far as their environmental levels remain unknown, it is not yet possible to evaluate it. Therefore, sampling, extraction, and quantification of these compounds should be the first step to assess their risks.

2.5 Sampling, extraction, and quantification of VMS from air

The sampling techniques available to collected VMSs from the air can be divided into passive and active. Passive sampling is a low-cost process that occurs when the air naturally passes through a sorbent, capturing the VMSs present in the air with a characteristic sampling rate. Theoretically, at the beginning of this sampling technique the uptake of the chemical on the sorbent is linear, then starts to accumulate developing a curvilinear behavior until an equilibrium is reached (Sha et al., 2018). The sampling rate at which the compounds are collected from the air is a variable influenced by the sorbent, VMSs congeners, and atmospheric conditions. This technique can be performed by using sorbent-impregnated polyurethane foam disks (SIP), polyurethane foam (PUF), amberlite XAD-2, a hydrophobic copolymer of styrene-divinylbenzene resin, filled in mesh cylinders placed in passive air samplers (XAD-PAS), and Tenax-filled thermal desorption tubes (Okan et al., 2021).

Active sampling uses a pump to pull the air through the sorbent at constant airflow, leading to more accurate concentrations, in the way that the volume of the air that passes over the sorbent is

controlled and known. In this type of sampling, tubes can be filled with a sorbent, such as Tenax TA, or with a combination of sorbents (silica gel, carbon-sieve, and charcoal, Tenax TA/carbon-sieve or Tenax GR/ graphitised carbon black). Solid phase extraction (SPE) cartridges with Isolute ENV +, PUF, SIP, XAD-PAS, and active air samplers (AAS) are also used in active this type of sampling (Ahrens et al., 2014; Companioni-Damas et al., 2014).

In order to extract the samples collected, several methods such as Soxhlet**,** pressurized liquid extraction (PLE), and solid-liquid extraction (SLE) are often performed (Barroso et al., 2019; Ramos et al., 2016). The main advantage of Soxhlet extraction is that it generates a continuous interaction between the solvent and the sample, which makes it a very reproducible extraction process. The main drawbacks are the higher consumption of solvents and the extraction time compared to other methods. PLE requires a low volume of solvents, being more environmentally friendly, and less time-consuming. However, at the same time, is a process that uses high pressures and high temperatures, involving expensive equipment and maintenance (Ramos et al., 2016). Solid-liquid extraction is a simple practice that allows good recovery, although there is a higher consumption of the solvent (Krogseth et al., 2012).

To quantify the concentration of VMSs after extraction, gas chromatography is the method of choice, preferably in combination with mass spectrometry detection (GC-MS) (Ru & Ku, 2015). However, thermal desorption and gas chromatography-mass spectrometry (TD-GC/MSD) is used when a combination of several sorbents in a tube was used for sampling the VMSs from the air (Companioni-Damas et al., 2014). Also, quantifying VMSs directly from the air is possible by using atmospheric pressure chemical ionization tandem mass spectrometry (APCI-MS/MS). This technique has the advantage of not needing an extraction or a prior chromatographic separation. However, it is barely used due to its higher detection limits in comparison with other quantification methods (Ahrens et al., 2014; Badjagbo et al., 2009).

Active sampling of VMSs (resorting to PUF), followed by SLE extraction (shaking PUF plugs with DCM and n-hexane), and GC-MS, has been used as a methodology to obtain and quantify VMSs from the indoor air. Several studies have resort to this method, as the LODs tend to be low (0.06-0.83 ng/m^3), and the recovery percentages high (73.4-112%) (Anh et al., 2020; Tran et al., 2017, 2018; Tran & Kannan, 2015). Passive sampling, using SIP, trailed by Soxhlet extraction, and GC-MS, was also previously applied to measure the VMSs from indoor and outdoor air (Genualdi et al., 2011; Ratola et al., 2016; Sha et al., 2018). This method allows good LODs (0.001-7.1 ng/m^3), and the recovery percentages can vary between 20-100% outdoors (Genualdi et al., 2011). However, in a study indoors the recovery percentage was only 58 ± 25%, and the LOQs varied between 20 - 42 ng/m^3 (Sha et al., 2018). Another technique typically used to quantify the amounts of VMSs in outdoor and outdoor air is using active sampling (SPE cartridges with Isolute ENV+), SLE (n-hexane

used as solvent), and GC-MS. This method was applied in several studies, and demonstrate low LODs (0.43-0.83 ng/m^3), and recoveries percentages that can array between 99% to 110% for cVMSs (Buser et al., 2013; Krogseth et al., 2013; Li et al., 2020c; Yucuis et al., 2013). A practice using passive sampling (XAD-PAS), SLE extraction (with n-hexane), and GC-MS has been also depicting by Krogseth et al., (2012) to obtain VMSs concentrations from the outdoor air This process showed to have LOQs that varied from 10.7 ng/m^3 to 25 ng/m^3, and good recovery percentages (78 ± 16 -110 ± 23%). Analyzing the performance of the methods applied in previous studies, the majority confirmed to be reliable and accurate, demonstrating good recoveries percentages (typically should be between 80% and 120%), and low LODs. These last two parameters are of extreme importance, since some environments, especially outdoor (remote zones), tend to have very low concentrations of VMSs

2.6 VMSs in outdoor air

Data related to VMSs emissions and concentrations outdoors is limited, even though these compounds are nowadays considered in some air quality monitoring programs. However, in the last years, a few studies have been made all over the world with the aimed of measuring the concentration of VMSs outdoor. A summary of the studies made so far is shown in Table 3.

Several studies have demonstrated that VMSs are present in higher quantities in metropolitan areas than in rural areas, conforming those VMSs concentrations increase with population density. In Switzerland, Buser et al., (2013) monitored the levels of cVMSs (D5 and D6) in the city center and background of Zurich. The outcome indicated that the highest concentrations registered were in the city center with a range between 100-650 ng/m^3 for D5 and 10-79 ng/m^3 for D6. In the Zurich background, the levels were among 45-160 ng/m^3 for D5 and 7-16 ng/m^3 for D6. Yucuis et al. (2013) developed an assay in areas with varying population densities, including downtown Chicago, Cedar Rapids, and West Branch (USA). The results demonstrated that the concentrations of cVMSs (D4-D6) increased alongside population density. Consequently, downtown Chicago displayed the peak concentration of 280 ng/m^3, while Cedar Rapids and West Branch recorded a maximum concentration of 73 ng/m^3 and 29 ng/m^3 respectively.

VMSs are predicted to have a high transportation capacity, undergoing long-range atmospheric transport (LRAT), and their amounts are considered to vary according to the season. In this regard, Krogseth et al. (2013) analyzed, in summer and winter, the air of Zeppelin observatory in the remote artic in order to evaluate the cVMSs (D3-D6) LRAT capacity. The results confirmed the presence of D5 and D6 in the Arctic atmosphere, validating their high transportation capability theory. In summer, the average concentrations were 0.73 ± 0.31 ng/m^3 for D5 and 0.23 ± 0.17 ng/m^3 for D6, whereas in winter the levels of D5 were 2.94 ± 0.46 ng/m^3 for D5 and 0.45 ± 0.18 ng/m^3 for D6. According to the authors, these results proved that cVMSs have the power to undergo long-range atmospheric

transport. Also, the presence of VMSs is higher in winter, which can be due to an increase of hydroxyl radical in the air during summer, resulting in the higher degradation of VMSs. In Portugal, Ratola et al. (2016) investigated the levels, trends, and behavior of VMSs in different environments such as urban, industrial, remote and beach areas during summer and winter. The total concentration of VMSs ranged between 0.6 to 7.8 ng/m^3, with maximum concentrations recorded during summer. Urban areas showed a higher predominance of VMSs, followed by industrial areas, beaches, and remote areas. Furthermore, cyclic VMSs were present in higher quantity than linear, especially D5 and D6. These results, showed a dominance of VMSs during summer over winter can be related to the increase of PCPs use directly associated to the bathing season (where the consumption of sunscreens and after sun creams rises), confirmed the increase of concentrations alongside population density, and the frequency of cVMSs over lVMSs.

Usually, the concentrations of cyclic VMSs tend to be higher than linear VMSs. For instance, Kierkegaard & McLachlan (2013) monitored the levels of cVMSs (D3-D6), and lVMSs (L3-L6) in Tystberga, a Sweden city. The outcomes indicated that the concentration of cVMSs (0.42-28 ng/m^3) were found to be up to 4 orders of magnitude higher than lVMSs (0.003- 0.54 ng/m^3). The same outcome was observed in in Barcelona by Companioni-Damas et al. (2014) where the levels of cyclic cVMSs (D3- D6) and lVMSs (L2- L5) varied from 2.2 to 439 ng/m^3 and 6 to 22 ng/m^3, respectively.

The information available demonstrates that the amounts of VMSs are typically more abundant in inhabited areas than in remote regions, owing to population density and industrial activities (Buser et al., 2013). Furthermore, the seasonal variations impact VMSs concentrations (Ratola et al., 2016). Thus, summer causes an increase in cosmetic use (for example sunscreen, or/and body lotion) but presents a higher concentration of hydroxyl radicals in the air, which contributes to the transformation of VMSs in subproducts (Alton & Browne, 2020). VMSs proved to have high transportation capacity, explaining their presence in locations where their occurrence was not expected such as the Arctic (Krogseth et al., 2013; Genualdi et al., 2011). Usually, cVMSs appear to be 2–4 times more concentrated than linear VMSs, with D5 as the prevalent VMS. The lower volatility of linear VMSs when compared with their cyclic counterparts, alongside with the extensive use of D5 on a variety of products (particularly PCPs and cosmetics) helps to explain why linear VMSs tend to appear in smaller amounts than D5.

Table 3. Summary of scientific studies reporting concentrations (ng/m3) of VMSs in outdoor air from different locations, and respective extraction and quantification methods.

Country	Location	Method overview	VMS Concentration (ng/m^3)									Reference
			L2	L3	L4	L5	L6	D3	D4	D5	D6	
China	Industrial area, Guangzhou (n=8)	Not specified	-	-	-	-	-	1.9×10^3-9.3×10^3	6.4×10^3 - 2.05×10^4	-	-	(Wang et al., 2001)
	Industrial area, Macau (n=8)		-	-	-	-	-	2.1×10^3-5.8×10^3	8×10^2- 4.3×10^3	-	-	
Czech Republic	Remote area, Kosetice	**Passive sampling** SIP[b] **Soxhlet extraction** **Quantification** GC-MS[c]	-	n.d.[a]	0.034	n.d.[a]	-	25	9.3	8.2	1.7	(Genualdi et al., 2011)
Canada	Polar region, Alert (NU) (n=20)		-	n.d. [a]	n.d.[a]	n.d.[a]	-	10	12	0.58	0.31	
	Remote area, Bratt's (Lake) (n=20)		-	n.d.[a]	0.024	0.028	-	17	2.6	1.0	0.31	
	Urban area, Whistler (BC) (n=20)		-	0.016	0.067	0.044	-	117	45	6.4	1.5	
	Urban area, Downsview (ON) (n=20)		-	0.12	0.66	0.45	-	18	11	55	6.2	
	Remote area, Fraserdale (ON) (n=20)		-	n.d.[a]	n.d.[a]	n.d.[a]	-	15	5.4	1.9	0.41	
	Beach area, Ucluelet (BC) (n=20)		-	n.d. [a]	n.d. [a]	0.001	-	81	44	7.3	1.2	
	Remote area, Sable Island NS (n=20)		-	n.d.[a]	n.d. [a]	n.d.[a]	-	-	-	-	-	
UK	Tudor Hill (n=20)		-	n.d.[a]	0.063	n.d.	-	3.8	3.8	7.3	0.69	
Iceland	Remote area, Storhofdi (n=20)		-	n.d.[a]	n.d.[a]	n.d.[a]	-	0.72	0.94	0.14	0.40	
Norway	Polar area, Ny-Alesund (n=20)		-	n.d.[a]	n.d.[a]	n.d.[a]	-	17	16	4.0	0.54	
Ireland	Coast area, Malin Head (n=20)		-	n.d.[a]	0.073	0.043	-	11	6.2	15	1.9	
France	Urban area, Paris (n=20)		-	0.029	0.057	0.12	-	30	50	280	53	
Australia	Coast area, Cape Grim (n=20)		-	n.d.[a]	n.d.[a]	n.d.[a]	-	0.45	1.2	n.d.[a]	n.d.[a]	

[a]Non detected; [b] sorbent-impregnated polyurethane foam disks; [c] Gas chromatography-mass spectrometry detector; [d] polystyrene−divinylbenzene copolymeric resin; [e] Thermal desorption- gas chromatography- mass spectrometry detector

Table 3 (continuation). Summary of scientific studies reporting concentrations (ng/m^3) of VMSs in outdoor air from different locations, and respective extraction and quantification methods.

Country	Location	Method overview	VMS Concentration (ng/m^3)									Reference
			L2	L3	L4	L5	L6	D3	D4	D5	D6	
USA	Coast area, Point Reyes (CA) (n=20)	**Passive sampling** SIP[b] **Soxhlet extraction** **Quantification** GC-MS[c]	-	0.011	0.046	0.030	-	6.0	4.2	6.5	0.57	(Genualdi et al., 2011)
	Urban area, Sydney (FL) (n=20)		-	n.d.[a]	0.16	0.081	-	0.65	5.4	82	4.0	
	Urban area, Barrow (AL) (n=20)		-	n.d.[a]	n.d.[a]	n.d.[a]	-	0.53	0.66	0.30	0.13	
	Semi urban area, Hilo (HI) (n=20)		-	0.019	0.019	n.d.[a]	-	32	24	6.5	4.5	
	Urban area, Groton (CT) (n=20)		-	0.013	0.34	0.52	-	-	3.9	96	12	
Canada	Urban area (n=17), Toronto	**Passive sampling-** XAD[d] sorbent **Solvent extraction** n-hexane **Quantification-** GC-MS[c]	-	1.8	1.2	0.5	-	24.2	93.5	65.9	-	(Krogseth et al., 2012)
Switzerland	Urban area, Zurich (n=25)	**Active sampling -**cartridges containing Isolute ENV+ sorbent **Solvent extraction** n-hexane **Quantification-** GC-MS[c]	-	-	-	-	-	-	-	100-650	10-79	(Buser et al., 2013)
	Remote area, Uetliberg (n=25)		-	-	-	-	-	-	-	45-160	7-16	
Norway	Zeppelin Observatory Summer (n= not specified)	**Active sampling -**Polyethylene cartridges- Isolute ENV+ sorbent **Solvent extraction** n-hexane **Quantification-** GC-MS[c]	-	-	-	-	-	n.d.[a]	n.d.[a]	1.26-0.22	0.71-0.10	(Krogseth et al., 2013)
	Zeppelin Observatory winter (n= not specified)		-	-	-	-	-	n.d.[a]	n.d.[a]	2.23-3.86	0.20-0.82	
USA	Downtown Chicago (n=16)	**Active sampling-** Polyethylene Cartridge – Isolute ENV + sorbent **Solvent extraction** n-hexane **Quantification-** GC-MS[c]	-	-	-	-	-	-	18-190	100-1100	n.d.-50	(Yucuis et al., 2013)
	Cedar Rapids (n=4)		-	-	-	-	-	-	5.1-37	22-65	3.3-9.3	
	West Branch (n=5)		-	-	-	-	-	-	5.6-14	10-29	<1.4 – 2.3	

[a]Non detected; [b] sorbent-impregnated polyurethane foam disks; [c] Gas chromatography-mass spectrometry detector; [d] polystyrene−divinylbenzene copolymeric resin; [e] Thermal desorption- gas chromatography- mass spectrometry detector

Table 3 (continuation). Summary of scientific studies reporting concentrations (ng/m^3) of VMSs in outdoor air from different locations, and respective extraction and quantification methods.

Country	Location	Method overview	VMS Concentration (ng/m^3)									Reference
			L2	L3	L4	L5	L6	D3	D4	D5	D6	
Sweden	Remote area, Tystberga (n=82)	**Active sampling** Polyethylene Cartridge - Isolute ENV + sorbent **Solvent extraction** n-hexane **Quantification-** GC-MS[c]	-	0.056-0.54	0.012-0.048	<0.003-0.033	<0.008-0.080	0.42-2.4	1.8-8.0	5.6-28	0.48-2.7	(Kierkegaard & McLachlan, 2013)
Spain	Urban area, Barcelona (n= not specified)	**Passive sampling-** Polyethylene Cartridge - Isolute ENV + sorbent **Solvent extraction** n-hexane **Quantification-** GC-MS[c]	12-22	14- 16	16 - 17	6.0 - 8	-	2.2–5.0	73 - 79	375-439	45 - 60	(Companioni-Damas et al., 2014)
Canada	Semi urban meteorological station, Toronto (n=70)	**Active air sampling-** high volume active air samplers (HV-AAS) **Pressurized liquid extraction** **Quantification** GC-MS[c]	-	0.2-4.9	0.4-65	0.7-4.8	-	0.5-4.7	2.8-77	15-247	1.9-22	(Ahrens et al., 2014)
		Passive sampling SIP[b] **Pressurized liquid extraction** **Quantification** GC-MS[c]		1.1-2.2	1.1-3.6	1.2-2.9	-	0.7-2.9	9.3-35	89-168	8.0-20	
Portugal	urban, industrial, remote and beach areas (n= not specified)	**Passive sampling** SIP[b] **Soxhlet extration** **Quantification** GC-MS[c]	$\sum$ VMS 0.6 – 7.8									(Ratola et al., 2016).
Spain	Urban areas (n= not specified)	**Active sampling** glass multi-sorbent cartridge tubes (Carbotrap, Carbopack X and Carboxen sorbent **Quantification** – TD-GC/MSD[e]	3-125	0.3-35	n.d.[a] - 12	n.d.[a]-3	-	39-1166	9-676	7-1942	16-68	(E. Gallego et al., 2017)
	Urban area hot spot (n= not specified)		6	7	4	18	-	1358	642	14914	449	

[a] Non detected; [b] sorbent-impregnated polyurethane foam disks; [c] Gas chromatography-mass spectrometry detector; [d] polystyrene−divinylbenzene copolymeric resin; [e] Thermal desorption- gas chromatography- mass spectrometry detector

2.7 VMSs in indoor environments

Since most of our everyday life is spent indoors, human health has become very susceptible to the quality of air indoors. The presence of harmful chemicals within this environment implies a higher exposure risk when compared to others. Consequently, several studies have been conducted measuring the concentrations of VMSs in different indoor environments. In Table 4 is a summary of the studies made so far on the presence of VMSs in the air of different indoor locations.

Li et al. (2020c) assessed the concentrations of cVMSs (D3-D6) in a student house of the University of China in order to understand their patterns in terms of the use of PCPs. A significant difference between the concentrations obtained in male and female dormitories was verifed, particulary of D5, indicating a larger use of PCPs by female students. The concentrations found in the females' dorms were 190 ng/m^3 for D3, 460 ng/m^3 for D4, 37000 ng/m^3 for D5, and 670 ng/m^3 for D6, whereas in the males the maximum were 55 ng/m^3, 95 ng/m^3, 4400 ng/m^3, 26 ng/m^3, for D3, D4, D5 and D6, respectively. This study suggests that the patterns of PCPs usage have a massive impact in the VMSs concentrations in the air, and that these products are major source of their presence in indoor air.

In order to clarify the disparity between the distribution and concentrations of cVMSs (D4-D6) indoors and outdoors, Anh et al. (2020) conducted an air sampling in chemistry laboratories, offices, and homes of a metropolitan area in Hanoi (Vietnam). The results indicated that the levels of the cVMSs captured from the air were significantly higher indoors than outdoors. From the indoor locations, the concentrations detected in the chemistry laboratories were 8.6 ng/m^3 for D4, 8.96 ng/m^3 for D5, and 24.1 ng/m^3 for D6, in offices 22.9 ng/m^3 for D4, 64.7 ng/m^3 for D5, and 31.8 ng/m^3 for D6, and in homes 73.7 ng/m^3, 97.3 ng/m^3 and 65.1 ng/m^3 for D4, D5, and D6 respectively. In the outdoors of these rooms the concentrations ranged between 2.15 (laboratory) -17.1 (homes) ng/m^3 for D4, 2.36 (laboratory)-25 (homes) ng/m^3 for D5, and 7.52 (laboratory)-18.3 (homes) ng/m^3 for D6. From this survey, it is possible to verify that the concentrations in the closed atmosphere are clearly higher than outdoors, which, in the case of VMSs, encompass a higher potential harmful health effect. The study also pointed out the abundance of D5 at homes and offices, and of D6 in the chemistry laboratories, indication possible different sources of VMSs.

The occurrence of cVMSs in hair salons suggest that these locations are likely to be a potential environment for high human exposure to siloxanes. To understand the relationship between the use of siloxanes in commercial hair care products and their distribution in environments, Tran et al. (2018) measured the concetrations of (D4-D6) in the air of hair salons from Hanoi city (Vietnam). The outcome results in a total range concentration of the three compounds from 415 ng/m^3 to 2610

ng/m^3, with D5 prevailing. This information confirms that hair salons are environments with high levels of cVMSs, which is mainly due to hair care products.

Sha et al. (2018) studied the levels of cVMSs (D4-D6) of several different enviorenments, such as dining areas, lecture rooms, offices, and homes from Sweden. The sum of cVMS concentrations reached between 900-2600 ng/m^3 for dining areas, 110-620 ng/m^3 for laboratories, 830-2600 ng/m^3 for lecture rooms, 550-3600 ng/m^3 of offices, and 570-3600 ng/m^3 for homes. Tran et al. (2017) collected indoor air samples and analyzed the concentrations of lVMSs (L4-L6), and cVMSs (D3-D6) from cars, hair salons, homes, laboratories, kindergartens, and offices. The results showed a range of 1.91-1500 ng/m^3 for cVMSs and 21.8-817 ng/m^3 for lVMSs, which indicates that cyclic are more frequent than linear VMS. In addition, the highest average concentrations were found in the hair salons from Hanoi city. Moreover, the concentrations of siloxanes in air collected from homes in Hanoi were higher than those from other smaller cities, confirming that the urban pressure can also be an important factor for the presence of VMSs in indoor air. In Europe, Pieri et al. (2013) confirmed the occurrence of lVMSs and cVMSs in the air of bathrooms, supermarkets, living rooms, bedrooms, and offices from United Kingdom and Italy. The amounts of cVMSs were again higher than lVMSs and the individual concentrations of these compounds peaked in bathrooms and bedrooms, likely due to the higher use of personal care products in these places. And in America, Tran & Kannan (2015) studied the distibution of linear and cyclic VMSs in laboratories, homes, schools, hair salons and public places from USA. The mean concentrations of total VMSs ranged from 249 ng/m^3 in laboratories to 6210 ng/m^3 in hair salons.

The literature allows to conclude that, as expected, indoor air concentrations tend to be much higher than outdoors, with cVMSs also more abundant than lVMSs. D5 is the most frequent VMS, mainly due to its many applications, especially in PCPs, and. The environments with high concentrations of these compounds are the ones where PCPs and hair care products are usually applied, such as bedrooms, bathrooms, and hair salons. The concentrations of VMSs can vary substantially from different settings, which may be owing to differences in interior furnishings and specific use patterns of consumer products, for example, cleaning agents and cosmetic products. However, there are still many indoor environments that have not been tested and that could present different VMS profiles.

Table 4. Summary of scientific studies reporting concentrations (ng/m3) of VMSs in indoor air from different locations, and respective extraction and quantification methods.

Country	Method overview	Sampling room	VMS Concentration VMS (ng/m^3)									Reference
			L2	L3	L4	L5	L6	D3	D4	D5	D6	
China	**Active sampling** SPE[a] cartridge and ENV+ **Solvent extraction** n-hexane **Quantification-** GC-MS[b]	Female dormitories (n=12)	-	-	-	-	-	22-190	130-460	7.3×10^3-3.7×10^4	200-670	(Li et al., 2020b)
		Male dormitories (n=12)	-	-	-	-	-	15 -55	34-95	130-4.4×10^4	5.0-26	
Vietnam	**Passive sampling** – PUF[c] **Solvent extraction** **Quantification-**not specified	Laboratories (n =16)	-	-	-	-	-	-	8.60	8.96	24.1	(Anh et al., 2020)
		Offices (n=8)	-	-	-	-	-	-	22.9	64.7	31.8	
		Homes (n =14)	-	-	-	-	-	-	73.7	97.3	65.1	
China	**Active sampling** SPE [a]cartridge and ENV+ **Solvent extraction** **Quantification-** GC-MS[b]		$\sum$ Cyclic VMS									(Guo et al., 2020)
		Factory housing (n=25)	2.4×10^5- 5.0×10^5									
		Girls' college dormitories (n=40)	1.0×10^5- 1.8×10^5									
Vietnam	**Active sampling** PUF[c] **Solvent extraction** **Quantification-** GC-MS[b]	Hair salon (n=24)	-	-	-	-	-	-	86.9 - 605	148 - 1.57×10^3	93.9 - 479	(Tran et al., 2018)
Sweden	**Passive sampling** SIP **Solvent extraction** **Quantification-** GC-MS[b]	Dining area (n=3)	-	-	-	-	-	-	1.4×10^5 - 1.9×10^5	6.4×10^5 – 2.1×10^6	1.4×10^5 – 5.7×10^5	(Sha et al., 2018)
		Laboratories (n=3)	-	-	-	-	-	-	<3.1×10^4 - 7.3×10^4	8.6×10^4 -4.9×10^5	2.9×10^4 -1.1×10^5	
		Lecture rooms (n=3)	-	-	-	-	-	-	4.3×10^4 - 2.3×10^5	6.1×10^5 -2.0×10^6	1.4×10^5 -1.9×10^5	
		Offices (n=8)	-	-	-	-	-	-	5.1×10^4 - 4.7×10^5	3.6×10^5 -1.7×10^6	9.0×10^4 -1.5×10^6	
		Homes (n=9)	-	-	-	-	-	-	9.7×10^4 - 4.6×10^5	2.7×10^5 -2.3×10^5	1.4×10^5 -1.9×10^5	
		Computer room (n=1)	-	-	-	-	-	-	1.1×10^5	9.0×10^5	2.6×10^4	

[a] Polyurethane foam disks;[b] Gas chromatography-mass spectrometry detector; [c] polyurethane foam disks;[d] Dichloromethane; [e] Non detected

Table 4 (continuation). Summary of scientific studies reporting concentrations (ng/m^3) of VMSs in indoor air from different locations, and respective extraction and quantification methods.

Country	Method overview	Sampling room	VMS Concentration VMS (ng/m^3)									Reference
			L2	L3	L4	L5	L6	D3	D4	D5	D6	
Vietnam	**Active sampling** PUF[c] **Solvent extraction –** DCM[d] and n-hexane **Quantification-** GC-MS[b]	Homes HN (n=19)	-	-	n.d.[e] - 42.7	2.10-36.4	n.d.[e]-124	n.d.[e] - 43.5	n.d.[e]-218	318-683	6.07-339	(Tran et al., 2017)
		Cars HN (n=8)	-	-	n.d.[e]-70.2	3.64-50.1	21.5-135	n.d.[e] -19.4	2.04-58.1	3.20-100	8.89-335	
		Kindergartens HN	-	-	n.d.[e] - 118	4.05-84.4	5.75-125	n.d.[e] - 10.6	3.64-19.5	6.17-85.7	n.d.[e] - 46.7	
		Laboratories HN (n= 19)	-	-	n.d.[e] - 86.3	n.d.[e] - 55.9	n.d.-76.2	n.d.[e] -16.8	n.d.[e] - 62.3	0.75- 53.0	n.d.[e] - 128	
		Offices HN (n=9)	-	-	n.d.[e] - 61.5	n.d.[e] - 294	n.d.-129	1.11-11.6	1.31-24.0	9.76-167	n.d. [e] - 15.8	
		Hair salons HN (n=13)	-	-	12.6-100	3.68-77.9	11.1-68.8	3.92-30.1	20.1-662	53.0-675	14.7-580	
		Homes BN (n=8)	-	-	3.39-185	n.d.[e] - 88.3	12.5-86.5	n.d.[e] -11.8	n.d.[e] - 151.9	n.d.[e] -41.7	n.d.[e] - 52.9	
		Homes TB (n=6)	-	-	n.d.[e] - 12.0	n.d.[e] - 7.33	n.d.[e]-24.4	n.d.[e] -6.41	n.d.[e] - 29.1	n.d.[e] -63.7	1.42-42.8	
		Homes TQ (n=8)	-	-	n.d.[e] - 20.3	n.d.[e] - 43.5	n.d.[e]-56.2	n.d.[e] -8.31	n.d.[e] - 17.9	n.d.[e] -16.9	n.d.[e] - 54.4	
USA	**Active sampling** PUF **Solvent extraction-** DCM[d] and n-hexane **Quantification**-GC-MS[b]	Homes (n=20)	-	n.d.[e] - 5.62	n.d.[e] - 8.39	n.d.[e] - 106	n.d.[e]-191	3.46-68.6	4.37-210	18-800.12	7.91-240	(Tran & Kannan, 2015)
		Laboratories (n=13)	-	n.d.[e] - 53.5	n.d.[e] - 3.68	n.d.[e] - 38.8	n.d.[e]-92.3	3.76-61.3	5.27-87.5	15.8-163	4.68-11	
		Schools (n=6)	-	n.d.[e]	n.d.[e] - 2.45	n.d.[e] - 3.55	n.d.[e]-40.3	6.25-20.2	12.8-245	111-1.02×10^3	10.4-136	
		Offices (n=7)	-	n.d.[e] - 1.29	n.d.[e]	n.d.[e] - 49.2	n.d.[e] - 13.7	1.96- 5.99	0.06-7.8	6.36-92.5	3.09-30.7	

[a] Polyurethane foam disks;[b] Gas chromatography-mass spectrometry detector; [c] polyurethane foam disks;[d] Dichloromethane; [e] Non detected

Table 4 (continuation). Summary of scientific studies reporting concentrations (ng/m^3) of VMSs in indoor air from different locations, and respective extraction and quantification methods.

Country	Method overview	Sampling room	VMS Concentration VMS (ng/m^3)									Reference
			L2	L3	L4	L5	L6	D3	D4	D5	D6	
USA	**Active sampling** PUF **Solvent extraction-** DCM[d] and n-hexane **Quantification**-GC-MS[b]	Hair salons (n=6)	-	n.d.[e] - 2.65	n.d.[e] -8.87	1.68 -28.3	7.12 - 150	6.34- 16.1	193 - 722	375- 3.71×10^3	121-885	(Tran & Kannan, 2015)
		Public places (n=8)	-	n.d.[e] - 2.96	n.d.[e] - 5.69	n.d.[e] -31.8	4.77 - 424	12.6-43.2	34.3 - 501	236 – 2.42×10^3	4.1-283	
Italy	**Active sampling-** not specified **Extraction-** not specified **Quantification-** not specified	Bathroom (n=15)	n.d.[e] - 1.3×10^4	n.d.[e] - 5.4×10^3	n.d.[e] - 8.5×10^3	n.d.[e] - 9.8×10^3	-	1.3×10^3 - 3.5×10^6	1.9×10^3- 2.7×10^4	3.8×10^3 - 3.0×10^5	n.d.[e]- 7.9×10^4	(Pieri et al., 2013)
		Boy bedroom (n=6)	n.d.[e] - 4.4×10^3	n.d.[e]	n.d.[e]	n.d.[e] - 1.4×10^3	-	230 - 1.4×10^5	740 - 3.5×10^4	2.5×10^3 – 3.5×10^4	n.d.[e] - 6.2×10^3	
		Girl bedroom (n=5)	n.d.[e] - 9.6×10^3	n.d.[e]	n.d.[e]- 3.7×10^3	n.d.[e] - 1.2×10^3	-	390 - 1.4×10^5	720 - 7.3×10^4	n.d. [e] - 5.1×10^4	n.d.[e] - 1.8×10^4	
		Living room (n=5)	n.d.[e] - 1.1×10^4	n.d.[e]	n.d.[e] - 760	n.d.[e] - 1.6×10^3	-	510 – 8.2×10^3	2.1×10^3- 2.2×10^4	8.4×10^3 - 7.9×10^4	n.d.[e] - 1.8×10^5	
		Adult bedroom (n=9)	n.d.[e] - 3.9×10^3	n.d.[e]	n.d.[e] - 4.8×10^3	n.d.[e]	-	n.d.[e] - 2.5×10^5	n.d.[e] - 6.0×10^4	1.7×10^3- 7.3×10^4	n.d.[e] - 1.2×10^5	
		Supermarket (n=2)	n.d.[e]	n.d.[e]	n.d.[e]	n.d.[e]	-	3.3×10^3 - 4.5×10^3	5.2×10^3	4.5×10^4 - 6.2×10^4	1.3×10^4- 3.1×10^4	
		Office (n=5)	n.d.[e] - 4.3×10^3	n.d.[e] – 420	n.d.[e] - 580	n.d.[e] - 830	-	850 - 5.5×10^3	940 - 5.2×10^3	4.4×10^3 - 1.1×10^3	n.d.[e]	
UK		Bathroom (n=9)	n.d. [e] - 1.3×10^4	n.d.[e]	n.d.[e] - 8.5×10^3	n.d.[e] - 3.4×10^3	-	1.3×10^3 - 3.5×10^5	2.3×10^3- 2.7×10^5	3.8×10^3 - 3.0×10^4	1.4×10^3- 7.9×10^4	
		Boy bedroom (n=5)	n.d.[e]	n.d.[e] - 4.6×10^4	n.d.[e]	n.d.[e]	-	2.9×10^2 - 8.0×10^3	3.8×10^3- 1.5×10^4	9.0×10^4 - 2.90×10^5	5.3×10^3- 6.5×10^4	

[a] Polyurethane foam disks;[b] Gas chromatography-mass spectrometry detector; [c] polyurethane foam disks;[d] Dichloromethane; [e] Non detected

Table 4 (continuation). Summary of scientific studies reporting concentrations (ng/m^3) of VMSs in indoor air from different locations, and respective extraction and quantification methods.

Country	Method overview	Sampling room	VMS Concentration VMS (ng/m^3)									Reference
			L2	L3	L4	L5	L6	D3	D4	D5	D6	
UK	**Active sampling-** not specified **Extraction-** not specified **Quantification-** not specified	Girl bedroom (n=5)	n.d.[e] - 1.5×10^4	n.d.[e] - 4.0×10^4	n.d.[e]	n.d.[e]	-	220- 2.67×10^5	n.d.[e] -6.2×10^4	3.2×10^3 - 1.7×10^5	470 - 3.1×10^4	(Pieri et al., 2013)
		Living room (n=5)	n.d.[e] - 9.3×10^4	n.d.[e] - 7.1×10^4	n.d.[e] - 2.5×10^4	n.d.[e] - 2.2×10^3	-	3.1×10^3 - 2.7×10^5	3.1×10^4 – 1.6×10^5	5.1×10^3 - 3.2×10^4	7.8×10^4- 5.0×10^5	
		Adult room (n=1)	n.d.[e]	n.d.[e]	n.d.[e]	n.d.[e]	-	1.2×10^3	1.9×10^3	4.5×10^4	5.4×10^3	
		Kindergarten (n=1)	1.8×10^4	1.6×10^4	7.5×10^3	n.d.[e]	-	1.4×10^4	1.7×10^4	2.7×10^5	4.3×10^3	
		Supermarket (n=3)	n.d.[e] - 6.3×10^4	n.d.[e] - 5.2×10^4	n.d.[e] - 2.3×10^4	n.d.[e] - 2.3×10^3	-	4.7×10^3- 3.4×10^4	3.5×10^3- 1.2×10^4	1.1×10^5 - 4.4×10^5	4.2×10^3- 1.3×10^4	
		Office (n=4)	n.d.[e] - 4.2×10^3	n.d.[e] - 710	n.d.[e] - 5.9×10^3	n.d.[e] - 1.4×10^3	-	2.7×10^3- 1.6×10^4	3.5×10^3- 2.0×10^4	2.4×10^3- 1.7×10^5	40- 1.5×10^4	

[a] Polyurethane foam disks;[b] Gas chromatography-mass spectrometry detector; [c] polyurethane foam disks;[d] Dichloromethane; [e] Non detected

3. MATERIALS AND METHODS

3.1 Standards and chemicals

Three linear volatile methylsiloxanes (lVMSs) (octamethyltrisoloxane (L3), decamethyltetrasiloxane (L4), and dodecamethylpentasiloxane (L5)) and four cyclic volatile methylsiloxanes (cVMSs) (hexamethylcyclotrisiloxane (D3), octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5), and dodecamethylcyclohexasiloxane (D6)) were analyzed. Standards of all the aforementioned analytes, as well as the compound used as internal standard, "tetrakis (trimethylsilyloxy) silane" (M4Q), were obtained from Sigma-Aldrich (St. Louis, MO, USA) with a purity > 97%. All solutions were stored and preserved at -20ºC and protected from light. To perform the solid-liquid extraction, n-hexane (VWR, Darmstadt, Germany) was used as a solvent with analytical purity of ≥ 95%. To clean-up the XAD-2 resin before its use, a mixture of n-hexane-dichloromethane (1:1) was used, using dichloromethane provided by VWR (Darmstadt, Germany) with a purity of ≥ 99.8%.

3.2 XAD amberlite preparation

To prepare the hydrophobic copolymer of styrene-divinylbenzene resin (XAD-2) (Supelco, Bellefonte PA, USA) for the sampling process, 200 g of humid sorbent were weighed, and then dried in a muffle (Nabertherm, Lilienthal, Germany) at 100 °C for 24 h. After dried, the sorbent (100 g) was cleaned with a 250 mL mixture of n-hexane-dichloromethane (1:1), in a 500 mL separation funnel, which was shaken by hand for 10 minutes. Afterwards, the solvent was collected for further shipping to the hazardous waste handling provided by EcoFEUP (as all other waste produced during the course of this work), and the process was repeated twice. Before filling up the XAD-2 in the separation funnel, baked glass wool was inserted inside to avoid losses of the sorbent. Finally, the XAD-2 was dried in a laminar flow hood overnight.

3.3 Passive air sampling

The sampling of indoor and outdoor air in this work was done using two aluminum mesh cylinders (10 cm long, 2 cm diameter) filled with approximately 10 g of XAD-2 resin protected with a stainless-steel cover case in each location (Figure 2). Cylinders and metal cases were custom-made, based on the study by Krogseth et al. (2012). In addition, for the baby room, besides using this type of sampler, two samples were taken by exposing 10 g of XAD-2 directly to the air (the XAD-2 was placed in Petri dishes that remained open during the sampling period). The sampling period took an average of 14 days. After the sampling, the mesh cylinders were wrapped in aluminum foil and stored in the freezer at -20 ºC until analysis.

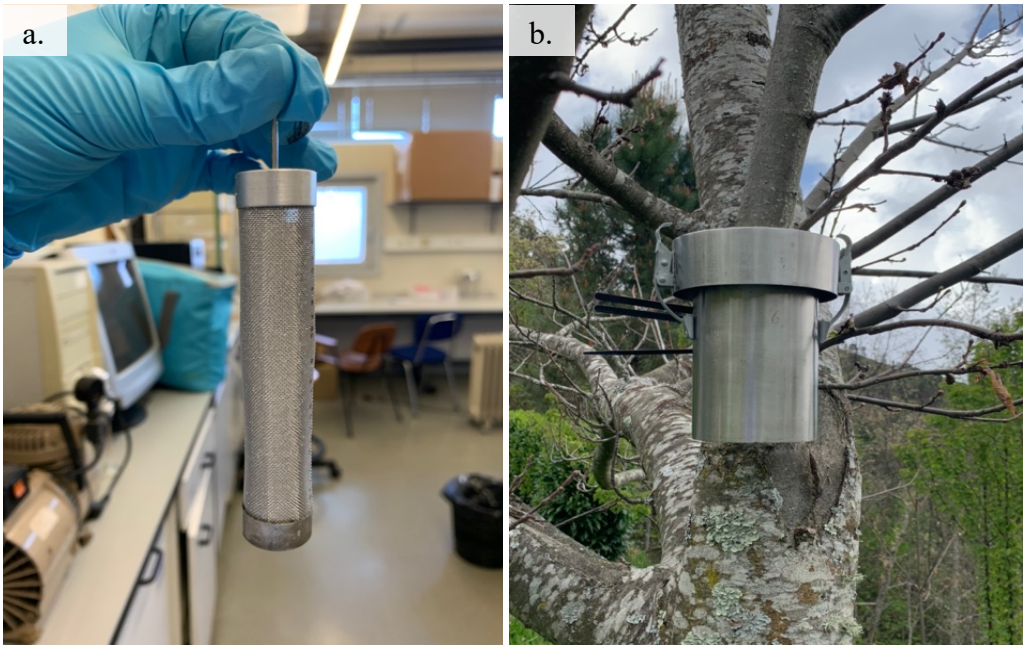

Figure 2. Passive air sampling devices: a) Aluminum mesh cylinder; b) Two mesh cylinders protected by a stainless-steel cover case.

3.4 Sampling sites

The sampling strategy was divided in three campaigns and conducted indoors and outdoors in three different cities: Aveiro, Vila Real, and Porto. A 1st and 2nd sampling campaign were performed in a bedroom, boat workshop, car, hair salon, laboratory (E-201) living room, office (E-319), stationery store, and rooftop (outdoor). A 3rd sampling campaign was undertaken in different locations: baby room, car workshop, dental clinic, laboratory (E-106), paint store, pharmacy, perfumery, restaurant, reprography at FEUP, and remote outdoor location. In the 1st sampling campaign, all the activities performed in these environments occurred under normal circumstances, even considering some restrictions due to the pandemic. However, some changes happened during the second sampling campaign. To begin with, the location of the boat workshop changed. The hair salon was closed to the public due to the quarantine, although still used by the owner to practice technical works, the living room user spent less time at home. In addition, this campaign was conducted during the Easter break reducing considerably the people attendance at FEUP, where the laboratory (E-201), office (E-319), and stationery store are located. The sampling conditions in the remaining settings remained the same.

Overall, indoor air sampling was conducted in 15 different environments, and outdoor in 2 different areas (urban and remote area, to serve as VMS background levels). These locations were chosen in order to clarify the profile of VMSs in their atmospheres, potential sources of contamination, and human exposure in these environments. To the best of our knowledge, the air of some of these rooms (boat workshop, dental clinics, paint warehouses, pharmacies, perfumeries,

restaurants, reprographies, and stationery stores) has never been studied. A total of 51 samples were collected, duplicates and one field blank were deployed in each sampling point. The field blank consisted in exposing the mesh cylinder filed with XAD-2 to the atmosphere of the location of sampling during the time the deployment of the material took place (about 5 to 7 minutes), to remove the background level of VMSs caused by transportation and manipulation from the XAD. All the locations and sampling data are displayed in Table A1 in the Appendix A1.

3.5 Sample extraction and instrumental analysis

For the extraction, the XAD-2 resin sorbent was transferred from the mesh cylinder to a 100 mL separation funnel, and 50 µL of internal standard containing 250 ng of M4Q were spiked. Then, 30 mL of n-hexane were added, and the slurry was hand-shaken for 5 minutes. The extract was later drained to a 60 mL amber vial. This protocol was repeated twice with the addition of 10 mL of n-hexane, till having a final volume of approximately 50 mL. Before filling the funnel with XAD-2 sorbent, glass wool was inserted inside to retain the sorbent, and the funnel with the glass wool was washed three times with n-hexane. The internal standard was added with a 100 µL microsyringe (Hamilton, Reno, USA) previously rinsed with acetone and hexane. This extraction procedure was adapted from Krogseth et al. (2012) due to its simplicity good recovery results and low LODs.

After the extraction was finished, the volume of the extract was reduced to 1 mL with a gentle nitrogen stream (Linde, Maia, Portugal), and transferred to 1.5 mL GC-MS vials. The 60 mL amber vials were subsequently rinsed three times with hexane to gather possible sample traces that may be left inside. If more than 1 mL were reached after rinsing, the volume was carefully reduced under the nitrogen stream. The vials were sealed with parafilm and stored in the freezer at -20 ºC until quantification analysis. Figure 3represents the main steps of the extraction and quantification method.

The quantification was performed by a Varian 240 gas chromatography with detection by mass spectrometry (GC-MS). 1 µL of the extracts was injected and the target analytes were separated on a DB-5 column (30 m, 0.25 mm inner diameter, 0.25 µm film, J&W Agilent, Palo Alto CA, USA) and quantified using the Internal Standard method, considering the following temperature program: 35 °C (5 min), 95 °C at 10 °C min^{-1}, 140 °C at 5 °C min^{-1} and 300 °C at 35 °C min^{-1} (5.5 min) - total time of analysis of 30 min. One microliter was injected in spitless mode (200 °C) followed by a 100:1 split after 1 min. Temperatures of manifold, ion trap and transfer line were 50, 200 and 250 °C, respectively (all the GC-MS handling process was done by the researcher Sánchez-Soberón).

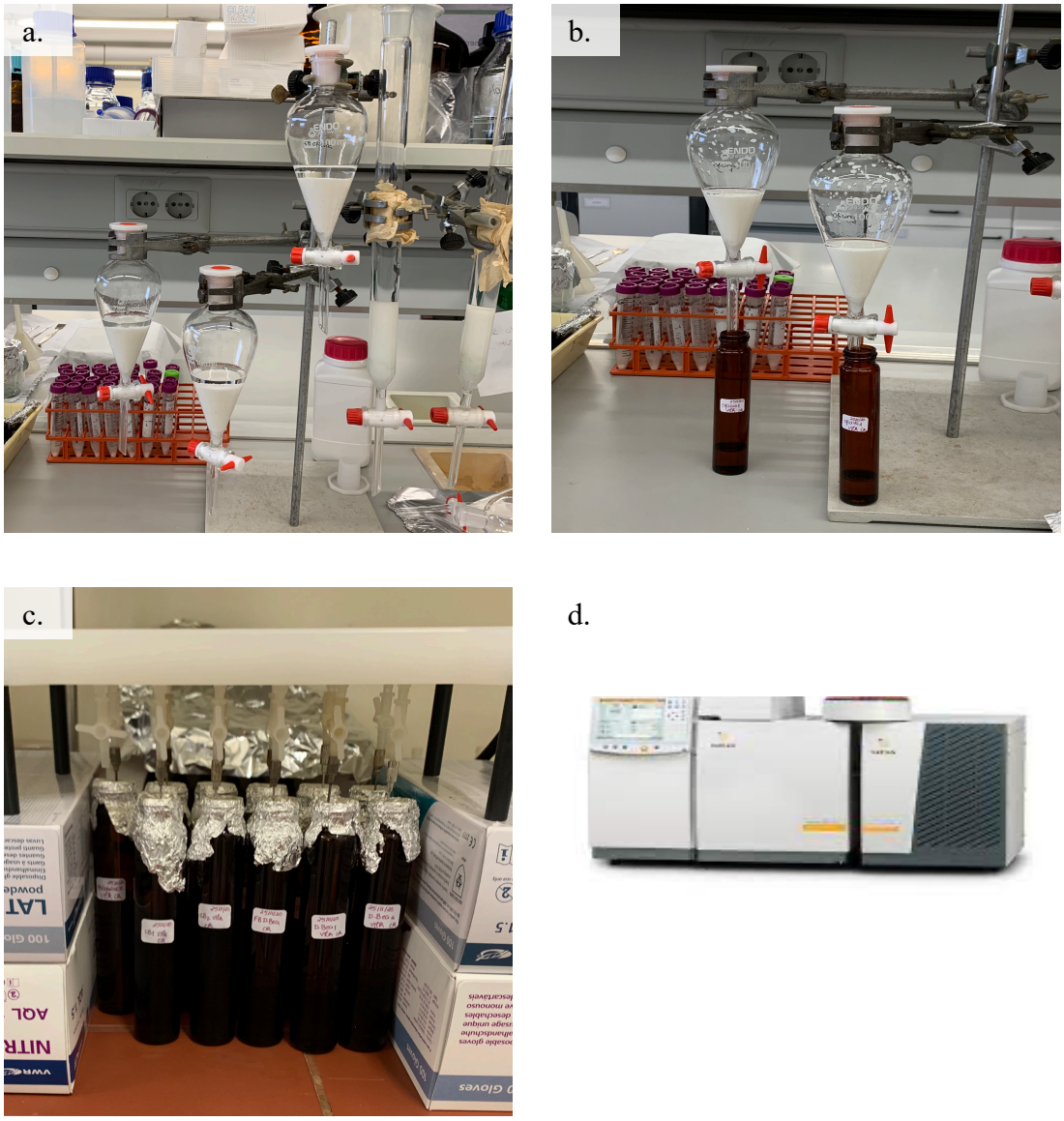

Figure 3. Main steps of the analytical protocol: Solid-liquid extraction (a and b), volume redaction through a stream of nitrogen (c), and quantification process (d).

3.6 Quality Assurance/Quality Control

In order to prevent and/or reduce any cross contamination during the sampling and extraction process, the use of products containing siloxanes in the laboratory was avoided, especially PCPs, by the researchers and cleaning detergents. Two laboratory blanks were prepared for each day of extractions to detect any external contamination, and a field blank was also performed in each site to uncover any source of contamination from the processes of sample manipulation and transportation.

The detection (LOD) and quantification limits (LOQ) were estimated by multiplying by three or ten respectively the concentration to signal-to-noise ratio from the least concentrated standard of the calibration curve. The LOD and LOQ calculated for each target VMSs can be found in Table A6 of the Appendices A2.

The needles used to reduce the volume with nitrogen were submerged in acetone and taken to the ultrasound bath for 10 min. The rest of the material used was washed with a VMS-free detergent, and rinsed with water, distilled water, and acetone. After washing, this material was placed to dry in an WTC Binder 7200 E115 oven (Tuttlingen, Germany). All ungraded glassware (amber vials, beakers, GC-MS injection vials, Pasteur pipettes and separation funnels), and aluminum foil used in the extraction method were placed in the furnace (Nabertherm, Lilienthal, Germany) at 400 ºC for 4 h before used, in order to eliminate possible residues/contaminants in the material.

3.7 Calculation of VMSs air concentrations

First, the mass (ng) in 1 µL was obtained by comparing the relative areas of each VMSs to M4Q with the calibration curve (the calibration curves and their respective parameters are detailed in the Appendice A2). Then, to estimate the concentration in the XAD-2 (ng/day), the mass previously calculated was multiplied 1000 µL, which correspond to the mass in 1 mL of sample, and divided by the time of sampling, 14 days.

To estimate the concentration in the ng/m^3 (C_{air}), the following equation was applied:

$$C_{air} = \frac{M}{R \times t} \quad \textbf{Equation 7}$$

where, M represents the mass (ng) of the siloxane intended to be analyzed, R (m^3/day) is the passive sampling rate of XAD-PAS, and t (day) the time of the sampling campaign. The values of the Rs were obtained from Krogseth et al. (2012). However, they are not ideal since were obtained for outdoor conditions, which tipically tend to be higher due to the differences in atmospheric conditions (*e.g.*, wind speed). Nevertheless, they were applied since there was no other information regarding the R for the type of sampler used and the compounds analyzed in this work. The concentration in the air (ng/m^3) of the target siloxanes are displyed in Table A7 of th Appendice A2.

3.8 Inhalation and dust ingestion exposure estimation

To estimate the $ED_{inhalation}$ (ng/kg bw·day) the following equation, applied in previous studies, was used (Anh et al., 2020; Tran et al., 2018):

$$ED_{inhalation} = \frac{C_{air} \times IR \times ET}{BW} \quad \textbf{Equation 8}$$

Where C_{air} (ng/m^3) represents the concentration of siloxanes in the air, IR (m^3/day) the inhalation rate, ET (unitless) stands for the time of exposure, and BW (kg) the individual body weight. Some parameters used were adopted from the US EPA and reformed to Portuguese habits (EPA, 2011; Lopes & Coelho, 2002; Perista, 2016). The parameters are presented in Table 5.

The exposure thought dust ingestion ($ED_{dust\ ingestion}$) in mg/kg bw·day was estimated for babies in the baby room using the following equation adapted from (Tran et al., 2019):

$$ED_{dust\ ingestion} = \frac{C_{dust} \times f_{ingestion\ rate}}{BW} \quad \textbf{Equation 9}$$

where, C_{dust} (mg/day) stands for the concentration of the VMS, $f_{ingestion\ rate}$ (mg/day) the ingestion rate, and BW (kg) the individual body weight. The C_{dust} was estimated only for baby room, where, in addition to the air sampling technique used, two open Petri dishes with 10 g of XAD were used to sample VMSs. The difference between the concentrations found in the Petri dishes and the mesh cylinders was considered to be the input of dust (the sampling of VMSs using mesh cylinders and Petri dishes was made at the same time). The parameters were adopted from the US EPA (EPA, 2011). The parameters are displayed in Table 5.

Table 5. Exposure data (inhalation rates, body weight, exposure time, and dust ingestion rate).

Inhalation rates (m^3/day)			**References**
Adults		16	(EPA, 2011)
Babies (2 years old)		5.1	
Sleeping (adults and baby)		6.6	
Body weight (kg)			
Adult		65	(EPA, 2011)
Adult	Men	75	
	Women	56	
Babies (2 years old)		10	
Time of inhalation exposure (h/h)			
First and second case scenario	Workplace	8/24	(Lopes & Coelho, 2002; Perista, 2016)
Third case scenario	Bedroom	8/24 (sleeping) + 2/24 (getting ready for the day and for bed)	
	Living room	2/24	
	Car	1/24	
	Workplace	8/24	
	Restaurant	2/24	
	Outdoors	1/24	
Fourth case scenario	Bedroom	8/24 (sleeping) + 4/24 (getting ready for the day and for bed)	
	Living room	10/24	
	Outdoors	2/24	
Fifth case scenario	Baby room	14/24 (sleeping) + 4/24 (activities)	
Dust ingestion rate (mg/day)			(EPA, 2011)
Babies (2 years old)		60	

4. RESULTS AND DISCUSSION

4.1 VMSs concentrations in different environments

4.1.1 Concentrations of VMSs in the first and second sampling campaigns

As mentioned earlier, two sampling campaigns were conducted in the bedroom, boat workshop, car, hair salon, living room, laboratory (E-201), office (E-319), and stationery store environments. Also, a sample outdoors (rooftop) was done to assess the background presence of VMSs. In addition, some parameters were modified in the second sampling campaign that are specified in section 3.2 of the Materials and Methods

Table 6 displays the concentrations of the VMSs studied in both sampling campaigns. Analyzing Table 6, linear and cyclic VMSs were detected in all air samples collected. However, the cyclic ones appeared in remarkable higher levels than lVMSs. This disparity was also confirmed by several studies, and it is directly related to the intense use of cVMSs (D3-D6) in personal care products (Li et al., 2020c; Pieri et al., 2013; Tran & Kannan, 2015). In the 1st sampling, the indoors concentrations ranged between 34.69 ± 4.91 ng/day and 14095.47 ± 468.86 ng/day. In the bedroom was where the highest total VMS (tVMS) concentration was detected (14095.47 ± 468.86 ng/day), followed by the hair salon (6877.39 ± 240.38 ng/day), living room (656.59 ± 67.13 ng/day), car (357.50 ± 8.88 ng/day), stationery store (301.97 ± 21.20 ng/day), office (E-319) (247.22 ± 10.89 ng/day), laboratory (E-201) (58.19 ± 3.85 ng/day), rooftop (50.75 ± 1.70 ng/day) (outdoor), and boat workshop (34.69 ± 4.91 ng/day). On the other hand, in the 2nd sampling, the maximum tVMSs concentration recorded indoors was 12791.08 ± 1329.94 ng/day, and the lowest concentration was 67.55 ± 4.12 ng/day. The bedroom screened 12791.08 ± 1329.94 ng/day, the hair salon 5318.75 ± 67.28 ng/day, the car 906.03 ng/day, the living room 200.66 ± 1.49 ng/day, the boat workshop 149.61 ± 14.31 ng/day, the laboratory (E-201) 78.86 ± 10.77 ng/day, the stationery store 80.49 ± 12.89 ng/day, the office (E-319) 67.55 ± 7.15 ng/day, and the rooftop 56.87 ± 4.35 ng/day (outdoor).

Comparing the concentrations obtained from the first and second sampling, it is possible to observe the effects of the alterations on the sampling conditions in the tVMSs concentrations. The boat workshop exhibited a noteworthy increase in the tVMSs concentrations from 34.69 ± 4.91 to 149.61 ± 14.31 ng/day. This increase could be promoted due to the location changes, and alterations in working schemes could influence the achieved results. The hair salon showed a drop from 6877.39 ± 240.38 to 5318.75 ± 67.28 ng/day. Even though the hair salon was closed to the public, the owner carried out technical procedures for practice with her family members. Therefore, some difference between the tVMSs concentrations was expected, but not a remarkable one. The living room, office (E-319), and stationery store revealed a notable decrease of tVMSs concentrations from 656.59 ± 67.13 to 200.66 ± 1.49 ng/day, 247.22 ± 10.89 to 67.55 ± 4.12 ng/day, and 301.97 ± 21.20 to 80.49

± 12.89 ng/day, respectively. These outcomes demonstrate that occupancy has a major impact on the tVMSs concentrations since the reduction of people influx resulted in an important decrease in the tVMSs concentrations.

The bedroom, car, and laboratory (E-201) were the only indoor environments where the sampling conditions remained similar in both sampling campaigns. Even though the second sampling campaign occurred during spring break, the attendance at the laboratory remained the same. Regarding the tVMSs concentrations in the bedroom, those experience a minor variation from 14095.47 ± 468.86 to 12791.08 ± 1329.94 ng/day, which shows consistency of the obtained results. While in the car, the levels were detected at 357.50 ± 8.88 ng/day (first sampling), and 906.03 ng/day (second sampling), this increase was not expected. However, the temperature inside the car was higher during the second sampling, which could lead to higher volatilization of the VMSs in the car, and consequentially increase the tVMSs concentrations. But to obtain more reliable results a 3rd sampling should be made. The laboratory exhibited an increase in the tVMSs concentrations from 58.19 ± 3.85 to 78.86 ± 10.77 ng/day, which could be due to the increase of the staff members. In this case, it is important to emphasize that siloxanes are matter of study in this laboratory, and to prevent any cross-contamination of samples the use of products that contained siloxanes in their composition is avoided by the researchers. Therefore, the tVMSs concentrations in this location were expected to be lower than the majority of the other setting studied, which was verified.

From all the locations studied in both campaigns, the environments where VMSs were detected in highest levels were in the private bedroom and in the hair salon. These results are in agreement with the ones found in literature, settings where the use of PCPs is very frequent are likely to have high concentrations of VMSs in their atmospheres. Furthermore, the lowest concentrations were recorded outdoor (rooftop), which also is in line with the results in previous studies, indoors are prospective to possess higher concentrations of VMSs than outdoors (Gallego et al., 2020; Li et al., 2020b).

Table 6. VMSs concentrations (ng/day) and respective standard deviation (ng/day) in the first and second sampling.

Concentrations (ng/day)									
1st sampling									
Siloxane	**Bedroom (n=2)**	**Boat workshop (n=2)**	**Car (n=2)**	**Hair salon (n=2)**	**Laboratory (E-201) (n=2)**	**Living room (n=2)**	**Office (E-319) (n=2)**	**Stationery store (n=2)**	**Rooftop (n=2)**
D3	266.37 ± 2.65	2.59 ± 0.65	222.78 ± 7.46	118.64 ± 7.05	13.63 ± 2.59	119.01 ± 14.91	92.08 ± 1.88	22.90 ± 1.98	4.16 ± 0.40
D4	139.18 ± 14.16	10.39 ± 2.34	88.66 ± 4.74	102.33 ± 12.37	10.53 ± 1.09	77.63 ± 12.96	44.85 ± 1.26	19.96 ± 1.91	1.35 ± 0.38
D5	13340.60 ± 465.94	18.18 ± 4.18	17.24 ± 0.10	6518.40 ± 239.58	28.28 ± 2.61	432.79 ± 64.05	93.28 ± 10.67	209.41 ± 21.01	41.74 ± 1.61
D6	335.43 ± 50.21	3.15 ± 0.84	19.22 ± 0.81	58.51 ± 6.73	4.01 ± 0.38	25.11 ± 3.81	13.34 ± 1.09	39.15 ± 1.91	1.39 ± 0.08
L3	1.24 ± 0.07	n.d.[a]	0.17 ± 0.00	74.67 ± 10.78	0.78 ± 0.06	0.38 ± 0.03	0.80 ± 0.05	7.52 ± 0.24	1.13 ± 0.03
L4	1.12 ± 0.08	n.d.[a]	0.99 ± 0.11	0.43 ± 0.02	0.33 ± 0.01	n.d.[a]	0.34 ± 0.01	0.71 ± 0.01	0.35 ± 0.01
L5	11.51 ± 1.47	0.39 ± 0.03	8.45 ± 0.25	2.59 ± 0.27	0.63 ± 0.05	1.66 ± 0.32	2.53 ± 0.15	2.33 ± 0.06	0.62 ± 0.04
Total	14095.47 ± 468.86	34.69 ± 4.91	357.50 ± 8.88	6877.39 ± 240.34	58.19 ± 3.85	656.59 ± 67.13	247.22 ± 10.89	301.97 ± 21.20	50.75 ± 1.70
2nd sampling									
Siloxane	**Bedroom (n=2)**	**Boat workshop (n=2)**	**Car (n=1)**	**Hair salon (n=2)**	**Laboratory (E-106) (n=2)**	**Living room (n=2)**	**Office (E-319) (n=2)**	**Stationery store (n=2)**	**Rooftop (n=2)**
D3	174.29 ± 20.23	2.85 ± 0.86	447.65	76.76 ± 9.36	16.72 ± 2.21	64.08 ± 2.83	30.97 ± 3.07	9.09 ± 2.38	4.42 ± 0.53
D4	210.75 ± 25.17	7.15 ± 1.94	262.38	96.94 ± 12.47	17.78 ± 3.16	56.97 ± 0.35	17.57 ± 1.79	12.79 ± 4.29	7.55 ± 0.28
D5	11686.87 ± 1328.52	28.28 ± 9.72	41.08	4993.55 ± 64.11	36.26 ± 10.03	70.57 ± 1.12	14.72 ± 2.08	40.71 ± 11.57	41.49 ± 4.29
D6	314.18 ± 47.40	111.20 ± 10.29	144.74	96.16 ± 11.79	7.07 ± 0.67	6.59 ± 1.07	3.92 ± 0.07	16.53 ± 2.84	1.81 ± 0.45
L3	69.29 ± 2.34	n.d.[a]	n.d.[a]	53.45 ± 5.76	0.75 ± 0.08	1.50 ± 0.02	n.d.[a]	0.55 ± 0.06	0.79 ± 0.02
L4	164.99 ± 3.40	0.07 ± 0.01	1.00	0.27 ± 0.03	0.28 ± 0.03	0.23 ± 0.03	0.09 ± 0.09	0.22 ± 0.01	0.35 ± 0.03
L5	170.71 ± 21.27	0.06 ± 0.05	9.18	1.28 ± 0.18	1.21 ± 0.35	0.72 ± 0.02	0.27 ± 0.27	0.59 ± 0.18	0.45 ± 0.02
Total	12791.08 ± 1329.94	149.61 ± 14.31	906.03	5318.75 ± 67.28	78.86 ± 10.77	200.66 ± 1.49	67.55 ± 4.12	80.49 ± 12.89	56.87 ± 4.35

[a] Non detected

4.1.2 Concentrations of VMSs in the third sampling campaign

The third sampling campaign occurred in the indoor of a baby room, car workshop, dentist, laboratory E-106, paint store, perfumery, reprography, restaurant. In addition, outdoor air was collected in a remote area. Analyzing Table 7, the tVMSs levels indoor varied between 15.03 ± 7.33 ng/day to 6093.48 ± 560.69 ng/day. The baby room recorded the higher tVMSs concentration with 6093.48 ± 560.69 ng/day, followed by the perfumery (2408.88 ± 43.08 ng/day), dentist (1874.69 ± 149.11 ng/day), pharmacy (686.61 ± 34.11 ng/day), laboratory (E-106) (529.17 ± 78.40 ng/day), restaurant (404.53 ± 32.20 ng/day), reprography (199.61 ± 30.58 ng/day), paint store (105.74 ± 21.27 ng/day), and car workshop (15.03 ± 7.33 ng/day). While in the remote area only a tVMSs concentration of 1.19± 0.27 ng/day was detected, the presence of VMSs air contamination in this location confirms their transportation capability that was demonstrated in the aforementioned studies (Genualdi et al., 2011; Krogseth et al., 2012).

Some of these results obtained were not anticipated. The car workshop registered a minimal tVMSs concentration, this lowest concentration was not predictable.

In a previous study, VMSs were found in the air of automobile plants and in shell paint/polish at high levels (Xu et al., 2015). This may signal the presence of VMSs in formulations used in the car workshop. Nevertheless, the volume of this facility is over 1500 m^3, which could promote the VMSs dilution in the air. In addition, the paint store also registered tVMSs concentration that was not estimated, as Xu et al. (2015) detected the presence of VMSs in a paint plant. However, the paint pots were closed most of the time, which may have influenced the VMSs emission from the paints.

Table 7. VMSs concentrations (ng/day) and respective standard deviation (ng/day) in the third sampling.

Concentrations (ng/day)										
	3rd sampling									
Siloxane	**Baby room (n=2)**	**Car workshop (n=2)**	**Dentist (n=2)**	**Laboratory (E-106) (n=2)**	**Paint store (n=2)**	**Perfumery (n=2)**	**Pharmacy (n=2)**	**Reprography (n=2)**	**Restaurant (n=2)**	**Remote area (n=2)**
D3	47.03 ± 8.58	n.d.[a]	165.23 ± 18.78	197.35 ± 6.96	17.48 ± 0.82	14.49 ± 1.17	17.04 ± 2.96	23.63 ± 7.71	144.49 ± 25.05	0.39 ± 0.01
D4	67.11 ± 12.94	4.54 ± 1.20	246.69 ± 38.74	147.67 ± 5.12	24.22 ± 0.45	17.81 ± 0.49	22.18 ± 1.10	30.71 ± 2.38	85.29 ± 13.43	0.74 ± 0.19
D5	5806.28 ± 559.86	9.09 ± 7.03	1349.53 ± 142.15	138.55 ± 77.90	43.56 ± 12.32	1228.48 ± 33.29	467.76 ± 30.86	126.65 ± 28.40	81.64 ± 13.29	n.d.[a]
D6	141.82 ± 25.77	1.21 ± 1.66	97.93 ± 13.10	37.77 ± 2.09	14.17 ± 12.3	69.53 ± 2.20	160.99 ± 14.11	17.36 ± 7.97	10.86 ± 1.02	n.d.[a]
L3	n.d.[a]	n.d.[a]	7.21 ± 1.29	4.00 ± 0.07	6.06 ± 0.10	328.78 ± 7.53	13.94 ± 1.34	0.59 ± 0.06	18.13 ± 3.16	0.03 ± 0.00
L4	n.d.[a]	0.17 ± 0.00	3.98 ± 0.73	5.06 ± 0.11	n.d.[a]	597.58 ± 26.05	n.d.[a]	n.d.[a]	41.40 ± 6.29	0.02 ± 0.00
L5	31.24 ± 4.88	0.03 ± 0.03	4.13 ± 0.43	2.76 ± 0.26	0.25 ± 0.13	152.22 ± 2.38	4.70 ± 0.31	0.67 ± 0.28	22.73 ± 2.88	n.d.[a]
Total	6093.48 ± 560.69	15.03 ± 7.33	1874.69 ± 149.11	529.17 ± 78.40	105.74 ± 21.27	2408.88 ± 43.08	686.61 ± 34.11	199.61 ± 30.58	404.53 ± 32.30	1.19 ± 0.27

[a] Non detected

4.2 VMSs profiles and potential source of contamination

4.2.1 First and second sampling campaigns

The VMSs spatial variation of all settings in the first and second sampling is shown in Figure 4. As shown in Figure 4, the prevalent VMS was D5 for most of the locations regardless of the sampling period, except for the boat workshop (2nd sampling), car, living room (2nd sampling), and office (2nd sampling). This predominance has also been detected in several previous studies and it is due to the high concentrations of this compound in personal care products (Li et al., 2020b; Pieri et al., 2013; Tran & Kannan, 2015). Comparing the VMSs profiles obtained from the 1st to the 2nd sampling it is possible to recognize a certain consistency in some of the indoor atmospheres studied. The VMSs distribution obtained from the two sampling periods in the bedroom, hair salon, car, laboratory, and rooftop air persisted very similar. The air of the boat workshop, living room, office, and stationery store exhibited significant variances in the profiles between the first and second sampling. These last results are mostly connected with the changes in the location (boat workshop), and the people influx (living room, office, and stationery store). They also suggest different sources of contamination.

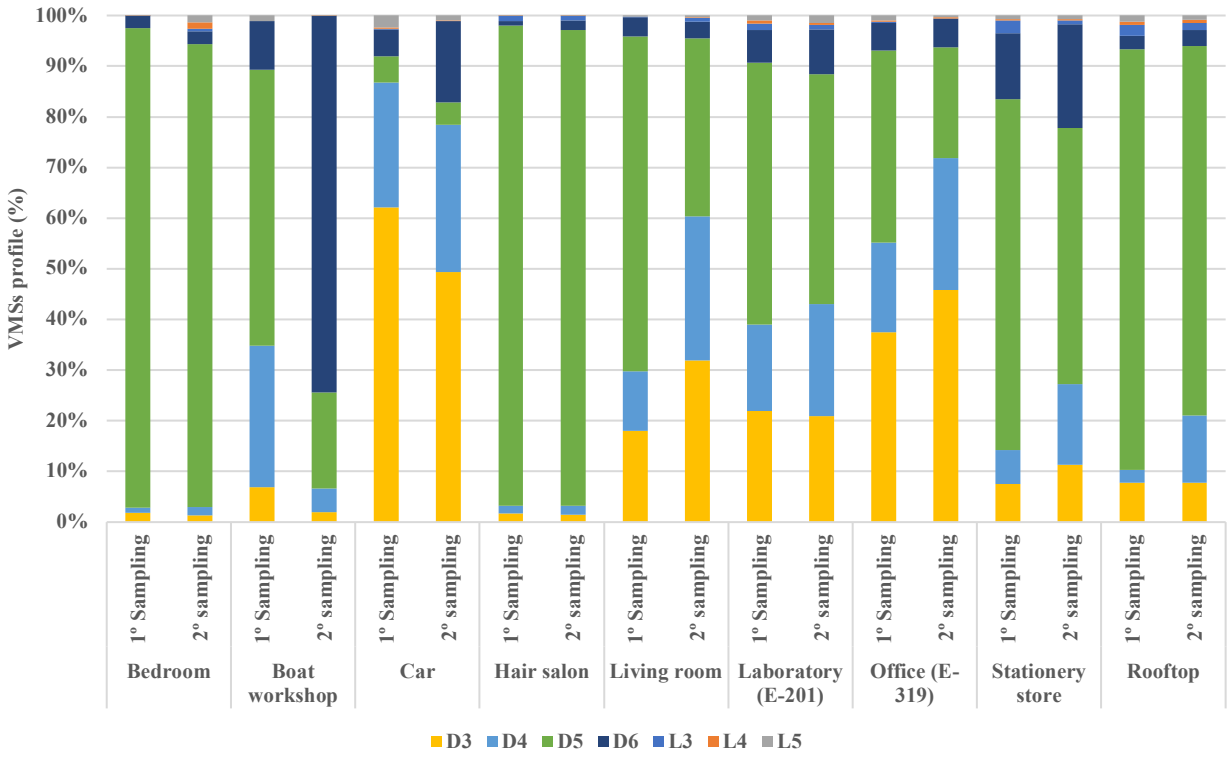

Figure 4. VMSs profile variation of the different locations in the first and second samplings.

Considering Figure 4, D5 represents 95% of the tVMs in the first sampling of the bedroom, and the remaining 5% were distributed among the others cVMSs (D3, D4, and D6). This prevalence is mostly due to the patterns of use of PCPs in this location. Cyclic and linear VMSs are commonly used in these types of products. However, cyclic are frequently detected, while linear are barely found (Capela et al., 2016). In the second sampling, the VMSs distribution persisted very similar, with D5 representing the largest percentage of VMSs (91%). Nevertheless, lVMSs appeared with a percentage of 1% each. Antiperspirant, make-up, facial creams, and sunscreen were the major sources of VMSs contamination in this environment. However, during the second sampling, the application of sunscreen was higher, which could be responsible for the appearance of lVMSs since Guo et al., (2021) have detected linear methylsiloxanes in sun protection products.

The boat workshop was the location that developed major disparities in the siloxane's distribution (Figure 4). In the first sampling campaign, D5 contributed 54% for the tVMS captured, followed by D4 with 28%, D6 with 10%, D3 with 7%, and L5 with 1%. Whilst in the second, D6 represented 74% of the tVMS, D5 19%, D4 5%, and D3 2%. The change in the location of the boat workshop, as well as the position of the sampler, could be the key for the turn of the results obtained in the 2nd sampling. In addition, PDMs and modified PDMs have multiple applications in the transportation industry being applied in ship manufactory. They can be applied in many usages, such as adhesives, coatings, lubricants, plastic additives, resins, sealants, and silicone rubber (Homem & Ratola, 2020). When into degradation processes, VMSs can be hydrolyzed into lower molecular weight products like VMSs, which contributes to their release into the environment by volatilization over time (Stevens, 1998). This last phenomenon can explain the presence of these compounds in this environment.

D3 was the dominant siloxane studied in both samplings in the car (Figure 4). In the first sampling with a percentage of 62%, and in the second sampling with 49%. It is known that siloxanes are used in car manufactory, being D3 one of the most volatile compounds studied it is predicted to volatilize first than the others, which may be the reason to its predominance over the remaining VMSs (Homem & Ratola, 2020). Also, a slight rise of the other VMSs, D4 from 25% to 29%, D6 from 6% to 16%, and a drop of L5 from 2% to 1% was observed, possibly related to the release over the time of the most volatile to the less volatile. Nevertheless, it is important to mention that this car was brand new, has never been used and stayed locked inside a garage during the sampling periods, excluding thus the existence of external VMSs contamination.

In the hair salon, the VMSs profile remained similar between the two sampling periods. D5 was the most frequent siloxane, contributing to 95% of the tVMSs in the first sampling, and 94% in the second (Figure 4). Several studies had reported the presence of cyclic VMSs (D3-D6) in hair care products (Dudzina et al., 2014; Tran et al., 2018; Wang et al., 2009). Thus, D5 is the cVMSs found

in greater levels in shampoos (28.8 μg/g), hair conditioners (6.4 mg/g) hair gels (88.4 μg/g) and hair mousses (11.4 μg/g), hair sprays (0.02 mg/g), among others which explains the predominance of D5 in the VMSs profile (Dudzina et al., 2014; Lu et al., 2011; Tran et al., 2018; Wang et al., 2009). The other cVMSs represented a minimal fraction of tVMSs

From the first to the second sampling in the living room from a private house, several differences in the siloxane's distribution were verified (Figure 4). D5 represented 66% of the tVMSs in the 1st sampling, whereas in the 2nd only stand for 36%. D3 and D4 increased from 18% to 32%, and from 12% to 29%, respectively. These variations were directly influenced by the occupancy of the room: the owner spent no time in the living room during the second period of sampling, which led to a decrease in the pattern of use of products containing siloxanes, especially PCPs. Nevertheless, the user makes an effort to use products free of siloxanes, but only a few alternatives are available in the market, indicating that the dominance of D5 in the 1st sampling may be due to the use of PCPs. In addition, assays had demonstrated the presence of D4 in high concentrations in household cleaning products (*e.g.*, furniture polish) and decoration material (Horii & Kannan, 2008). By keeping the same cleaning pattern while decreasing the occupation of this room, it is expected to find differences in VMSs profile.

The siloxanes distributions in the laboratory persisted very similar between the two sampling periods (Figure 4). In the 1st sampling, the dominant compound was D5 with 52% of the tVMSs, followed by D4 with 17%, D3 with 22%, D6 with 9%, and lVMSs with 1% each. In the 2nd sampling, D5 was also dominant with 46%, followed by D4 with 22%, D3 with 21%, D6 with 9%, and L5 with 2%. In this laboratory, siloxanes are matter of study, and to prevent any cross-contamination of samples the use of products that contained siloxanes in their composition is avoided by the researchers. However, other sources of VMSs can be present in this location. The use of softeners in the cleaning processes of the clothes contained high concentrations of D5 which work as softener (Tran et al., 2019). Consequently, to the use of softeners, during the usage of those clothes, D5 can be released into the air. Another potential source of contaminations can be the coating furniture, and electrical/electronic devices used in this environment (Zuber et al., 2019).

By analyzing Figure 4, it is possible to verify the alterations in the VMSs spatial distribution in the Office (E-319). In 1st sampling, D3 and D5 were the predominant siloxanes with a percentage of 38% each, followed by D4 (18%), D6 (5%), and L5 (1%). These results may be due to the use of PCPs by the works (D5, D4, and D6), the occurrence of siloxanes in coating furniture, cleaning agents (D4), and electric devices (Horii & Kannan, 2008; Zuber et al., 2019). In the 2nd sampling, D3 (46%) was the main VMSs present in the air, followed by D4 (26%), D5 (22%), and D6 (6%). Since during the 2nd sampling the attendance decreased, the concentration of D5 was also reduced due to the decline of PCPs use. Under these circumstances, D3 overcame D5, which suggests its presence in coating

furniture and electric devices, or the presence of PDMS that were hydrolyzed in VMSs (Homem & Ratola, 2020; Horii & Kannan, 2008; Zuber et al., 2019).

In the stationery store, D5 was the siloxane found in highest concentrations. Contributing with 69% and 51% for the tVMSs concentrations, D6 with 13% and 21%, D4 with 7% and 16%, D3 with 8%, and 11%, in the first and second sampling, respectively. L5 represented only 1% of the tVMSs in both, and L3 2% in the 1st sampling only. In addition to the VMSs applications in PCPs, they are also applied as defoamers during the processes of manufacturing pulp and paper, and as additives in food industry (Homem & Ratola, 2020). As this stationery store, in addition to office supplies, sells food, drinks, and PCPs, all of them can be potential sources of contamination in this atmosphere. Nevertheless, PCPs are also used by customers and workers, which, according to our results, could have a major impact in the D5 frequency.

As expected, the VMSs profile in the rooftop remained very similar (Figure 4). D5 was the siloxane found with highest percentage in both sampling (83% in the 1st, and 74% in 2nd sampling). This rooftop is located in building E of FEUP, where ventilation output from fume hoods and air conditioning systems is also located. Therefore, the VMSs present in this outdoor may be owing to the process of ventilation from the building as well as and due to the use of PCPs by the students in the campus.

4.2.2 Third sampling campaign

The distribution profile of VMSs from the third sampling is shown in Figure 5. Considering the Figure 5, D5 was the predominant VMS in most of the locations, including the baby room, car workshop, dentist, paint store, perfumery, pharmacy, and reprography. Whilst D3 was the most frequent in the Laboratory (E-106) and restaurant, and D4 was the prevalent in the remote area.

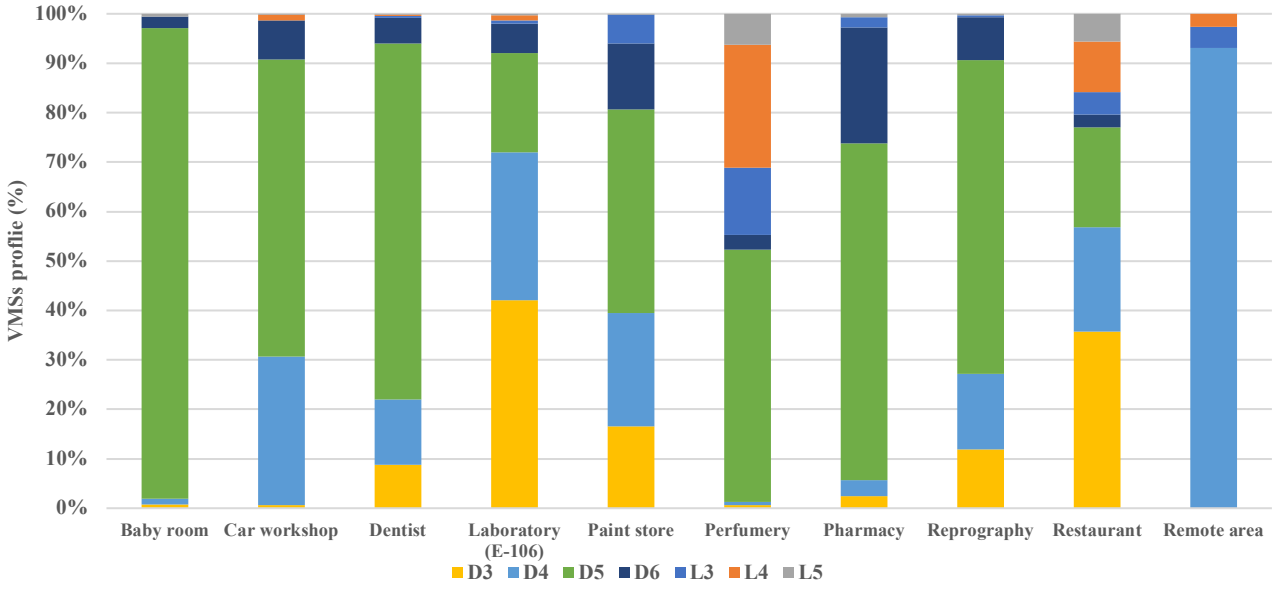

Figure 5. VMSs profile variation of the different locations in the third sampling campaign.

Regarding the VMSs spatial distribution in the baby room, D5 was the most recurrent VMSs in this atmosphere (Figure 5), with an incidence of 95%. While D6 represented 2% of the tVMSs, and D3, D4, and L5 1%. The application of cVMSs (especially, D5) on multiple baby care products (baby lotions, creams and, diaper creams), pacifiers, teethers, silicone nipples, soft rubber toys, and hard toys, may suggest these products as sources of contamination (Xu et al., 2017; Zhang et al., 2012).

In the car workshop, D5 (60%) and D4 (30%) were the main siloxanes detected (Figure 4), suggesting their presence in the specific products used in the car workshop. In fact, Xu et al., (2015), detected the presence of VMSs in the air of automobile plants (D4 in higher concentrations), and in shell paint/polish, D5 (487 μg/g) and D6 (367 μg/g) in higher levels. Thus, suggest the presence of specific products used in the car workshop that contained VMSs in their formulations.

Once again, D5 was the siloxane with a higher incidence. In the dentist, D5 standing for 72% of the tVMSs, D4 for 13%, D3 for 9%, D6 for 5%, and L5 for 1%. The prevalence of D5 is directly related to the use of PCPs by the workers and customers, and household products. Nevertheless, sealants, impression materials, coating furniture, and electrical devices present in this establishment can also contribute to VMSs levels in this location (Global Silicones Council 2020a; Horii & Kannan, 2008; Zuber et al., 2019).

Laboratory (E-106) is the location where the process of sample quantification by GC-MS takes place. In this environment, the most prevalent VMS was D3 (42%), followed by D4 (30%), D5 (20%), D6 (6%), L3, and L4 (1%) (Figure 5).VMSs are present in GC instruments, electronic devices, and furniture coatings that are common in this type of laboratory and are likely to be the major sources of contaminations. Nevertheless, VMSs emissions from the vials filled with the samples can occur during the quantification processes.

The distribution profile of VMSs in the Paint store is represented in Figure 5 and shows the upper frequency of D5 (41%), followed by D4 (23%), D3 (17%), D6 (13%), and L3 (6%). These results are in agreement with Xu et al. (2015), that reported that D5 and D4 are the VMSs present in the highest concentrations during the paint production process, suggesting the presence of VMSs in paints.

In the perfumery, D5 represented 51% of the tVMSs, L4 25%, L3 14%, L5 6%, D6 3%, and D4 1%. In this store, besides perfumes, make-up products, facial creams, sunscreems, and body lotions were also for sale, contributing to VMSs potential source of contaminations. As stated earlier, several studies had measured the concentrations of VMSs in make up, face creams, sunscreens, and body lotions, displaying cVMSs (especially D5) greater concentrations than lVMSs (Capela et al., 2016; Dudzina et al., 2014; Horii & Kannan, 2008; Lu et al., 2011; Wang et al., 2009). However, in this particular case, the lVMS represented 45% of the tVMSs, which suggests that lVMSs may be present in perfumes.

In regard to the distribution of VMSs in the pharmacy, D5 and D6 were the predominant compounds (68% and 23% of tVMSs respectively). The remaining VMSs were found in small percentages (i.e.< 5%). Until this moment, the direct application of VMSs in pharmaceutical formulations is not reported, to the best of our knowledge. However, PDMSs function as coating, antiflatulence, antifoaming, emollients agents in pharmaceutical products. For instance, PDMSs are used in syringes for drug delivery, capsules, drops, chewable tablets, emulsions, and suspensions (Malmstrøm, 2019; Mojsiewicz-Pieńkowska, 2012). As mentioned earlier, the hydrolysis process of PDMSs could also lead to the formation of VMSs, explaining VMSs presence in this pharmacy atmosphere. In addition to pharmaceutical goods, PCPs are also sold (although in another area) and used by workers in the pharmacy, promoting the presence of D5.

In the reprography, D5 had the highest contribution to this result (64%) to the tVMS concentration, followed by D4 (15%), D3 (12%), and D6 (9%), as exhibited in Figure 5. VMSs are used during the process of pulp making as defoamers (Homem & Ratola, 2020). In fact, Xu et al. (2016) discovered the presence of cVMSs (D3-D6) in water and soil samples collected from the producing processes of one papermaking factory, suggesting the presence of cVMS in paper. Thus, along with the use of PCPs from customers and workers, paper is likely to be a source of air contamination in this environment. Nevertheless, inks cloud also be an important/potential source of contamination.

The cVMS represented 80% of tVMS (D3 36%, D4 21%, D5 20%, and D6 3%), while lVMS count for 20% of tVMSs (L5 10%, L4, 6%., and L3 4%) in the restaurant (Figure 5). The presence of these man-made compounds in the restaurant air is in line with the study of (Fromme et al., 2019)In this study, the concentration of several siloxanes, including cVMSs (D3-D6), were quantified in air and in cakes while baking with silicone and metal molds. The results confirmed the presence of all cVMSs, with the highest incidence of D5 in the air and cake samples, suggesting the presence of cVMSs in cookware and its migration to food. Therefore, the main source of VMSs contamination are probably the cookware, food, and the PCPs used by workers and customers. In addition, the prevalence of D3 in this envornment could be triggered by the higher temperatures reached during the cooking process, since D3 is one of the most volatile siloxanes studied. Nevertheless, PDMSs are used as antifoaming agents in food. During the degradation process, these compounds can generate VMSs, contributing to their presence in this environment (Homem & Ratola, 2020).

D4 was the most common siloxane (93%), followed by L3 (4%) and L4 (3%) in the remote area (Figure 5). Althought low, this concentration confirmed the transportation capability of VMSs in the air, as demonstrated in previous studies (Genualdi et al., 2011; Krogseth et al., 2012).

4.3 Human exposure to D4 and D5 by inhalation

As stated earlier, the concerns about the toxic effects of D4 and D5 in human health have been increasing in the past few years. Therefore, human exposure to these compounds was estimated for several different scenarios. In the first scenario, it was considered the human inhalation exposure for 8 hours (h) of work in several different locations. In the second scenario, it was reviewed if the gender has implications in the inhalation exposure, considering the time at work (8 h), the workplaces were chosen according to the results obtained in the first scenario (hair salon, and laboratory (E-201). In the third scenario, it was calculated the inhalation exposure during a whole day of a worker in the hair salon and in the laboratory. For that, 10 h were considered to be spent in the bedroom (8 h sleeping, and 2 h to get ready for the day and for sleep), 8 h at work, 2 h at the restaurant, 1 h in the car driving, 1 h in the outdoors, and 2 h lounging in the living room. The fourth scenario was regarding the increase of the inhalation exposure doses during the pandemic. Considering the daily routine of a worker to the laboratory (equal to the third scenario), and its changes due to the pandemic (telework) (8h sleeping, 4 h at the bedroom getting ready for the day and for bed, 10 h at the living room, and 2 h outdoors). Finally, the exposure was also estimated for a two-year-old baby to these cVMSs though inhalation (18 h in the baby room (14 h sleeping, 4 h playing) and dust ingestion in his baby room. Furthermore, the additional paraments (inhalation rate and body weight) used to calculate the exposers are represented in Table 5 of Section 3.8 in Materials and Methods

4.3.1 First scenario: exposure by inhalation in different workplaces

In Table 8 are presented the human exposures (adults) for 8h work in several locations. The results showed that the workers at the hair salon are the ones exposed to greatest levels of the total cVMSs studied (1200.95 ± 45.01 ng/kg bw·day) while the ones working at the laboratory (E-201) are exposed to the lowest levels (8.98 ± 0.69 ng/kg bw·day). The workers at the perfumery are exposed to 302.11 ± 9.10 ng/kg bw·day, at the dentist to 288.91 ± 26.46 ng/kg bw·day, at the pharmacy to 87.77 ± 5.51 ng/kg bw·day, at the stationery store to 44.81 ± 4.11 ng/kg bw·day, at the office (E-319) to 32.24 ± 2.22 ng/kg bw·day, and at the paint store 12.50 ± 3.86 to ng/kg bw·day. As expected from results in section 4.2, D5 is the siloxane with the highest levels of human exposure. These results are in line with the ones found in the literature, the inhalation exposures doses are higher in locations where the use of PCPs is constantly being used (Tran et al., 2017, 2018). Being the workers at the hair salon, and at perfumery, the ones that are susceptible to greater exposure doses.

Table 8. The estimated human exposure by inhalation (ng/kg bw·day) to D4 and D5 in different workplaces and respective standard deviation (ng/kg bw·day).

Siloxane	Dentist	Hair salon	Laboratory (E-201)	Office (E-319)	Paint store	Perfumery	Pharmacy	Stationery store
D4	48.19 ± 7.57	19.99 ± 2.42	2.06 ± 0.21	8.53 ± 0.32	4.73 ± 0.09	4.72 ± 0.13	4.33 ± 0.22	3.90 ± 0.37
D5	240.72 ± 24.36	1180.96 ± 44.98	6.92 ± 0.66	23.71 ± 2.19	7.77 ± 3.77	297.39 ± 8.06	83.44 ± 5.51	40.91 ± 4.09
Total	288.91 ± 26.46	1200.95 ± 45.01	8.98 ± 0.69	32.24 ± 2.22	12.50 ± 3.86	302.11 ± 9.10	87.77 ± 5.51	44.81 ± 4.11

4.3.2 Second scenario: exposure by inhalation difference between gender

Another scenario of study was calculated regarding gender. The inhalation exposure dose was estimated for men and women workers at the hair saon and at the laboratory (E-201) (Table 9). The outcome showed that inhalation exposure for women was higher than for men, being the daily exposure for women working at the hair salon 1393.96 ± 52.24 ng/kg bw·day, and for men 1040.82 ± 39.00 ng/kg bw·day, while in the laboratory the exposure was 10.42 ± 0.80 ng/kg bw·day for women, and 7.78 ± 0.60 ng/kg bw·day for men. Tran et al., (2018), also concluded that women are more susceptible to higher inhalations exposure doses than men. This is highly due to physiologic characteristics (weight).

Table 9. Estimated daily inhalation exposure (ng/kg bw·day) to cVMSs (D4+D5) and respective standard deviation (ng/kg bw·day) for women and men working at the laboratory (E-201) and at the hair salon.

	Men	Women
Laboratory	7.78 ± 0.60	10.42 ± 0.80
Hair salon	1040.82 ± 39.00	1393.96 ± 52.24

4.3.3 Third case scenario: exposure by inhalation during an entire day

The daily exposure was estimated for a whole day (adult) of a worker at the hair salon and at the laboratory, considering the time at home, working, eating, driving, and spent outdoors. Analyzing Table 10, the highest daily exposure concentration was obtained for the worker at the hair salon, with 2851.10 ± 69.95 ng/kg bw·day. The locations that had the greater contributions for this outcome were the home (bedroom (1610.94 ± 53.42 ng/kg bw·day) and living room (26.55 ± 3.49 ng/kg bw·day) and the working place. While the locations with minor influence were the outdoors (0.99 ± 0.05 ng/kg bw·day) and the car (4.53 ± 0.16 ng/kg bw·day). In the case of the worker at the laboratory, the total daily exposure was 1659.80 ± 53.42 ng/kg bw·day. On the contrary to the worker at the hair salon, the workplace had not a major influence on the total daily exposure. However, at

home was where the majority of the exposure occurred. In addition, the high levels of exposure in the bedroom demonstrate that the patterns of use of personal products have a major impact on the human exposure to siloxanes, being necessary to find suitable alternatives to these compounds. These results are in agreement with the ones obtained from Pieri et al., (2013), which demonstrate that homes and working places are the environments where most of the inhalation exposure occurs.

Table 10. The estimated human exposure by inhalation (ng/kg bw·day) of cVMS (D4+D5) and respective standard deviation (ng/kg bw·day) of an entire day of worker at the hair salon and at the laboratory.

		Worker at the laboratory	Worker at the hair salon
Home	**Bedroom**	1610.94 ± 53.42	1610.94 ± 53.42
	Living room	26.55 ± 3.49	26.55 ± 3.49
Car		4.53 ± 0.16	4.53 ± 0.16
Workplace		8.98 ± 0.69	1200.95 ± 45.01
Restaurant		7.81 ± 0.88	7.81 ± 0.88
Outdoors		0.99 ± 0.05	0.99 ± 0.05
Total		1659.80 ± 53.55	2851.10 ± 69.95

4.3.4 Fourth case scenario: pandemic effect in the exposure by inhalation

As discussed in the previous scenario, at home is where more than 50% of the total inhalation exposure occurs. Therefore, a fourth scenario was considered. Due to the pandemic (covid-19) lived in the current and yesteryear, people have the civic duty to spend more time at home. A routine of a normal worker at the laboratory with no restrictions, and a routine the same worker but in telework was considered. As Figure 6 indicates, the daily inhalation exposure registered a noteworthy increase from 1659.80 ± 53.55 to 2353.60 ± 75.61 ng/kg bw·day, which is equivalent to a 42% increase in exposure. This outcome suggests that with pandemic people are exposed to greater concentrations of VMSs through inhalation.

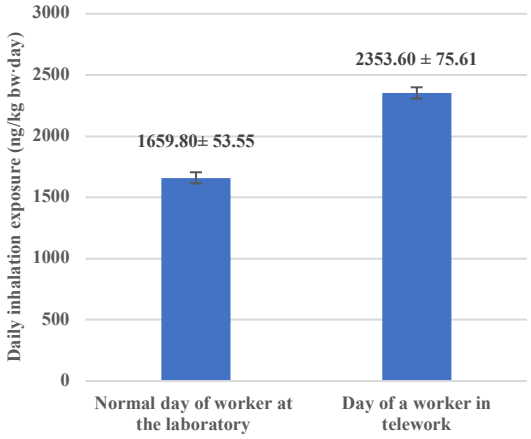

Figure 6. Estimated daily exposure by inhalation of adults to siloxanes (D4+D5) and respective standard deviation for (a) worker at the laboratory and (b) during telework (due to the current pandemic).

4.3.5 Fifth case scenario: Inhalation vs Dust ingestion exposure to cVMSs

The exposure was estimated for a two-year-old baby cVMSs (D4 and D5) through inhalation and dust ingestion in his baby room. In this case, it was necessary to obtain the concentrations (ng/day) of VMSs in the dust, the methodology used to collect the dust is mentioned in Section 3.8 of the Materials and Method. The concentrations obtained in the dust are displayed in Table 11, the tVMSs concentration obtained in the dust was 11070.31 ± 528.47 ng/day, and as expected from the results obtained in the section 4.2.2, D5 was de most frequent siloxane, with a concentration of 10659.99 ± 528.42 ng/day, representing 93% of the tVMSs.

Table 11. Estimated VMSs concentrations (ng/day) in dust from the baby room and respective standard deviation (ng/day).

Siloxane	Baby room (Petri dishes (n=2))
D3	97.53 ± 0.94
D4	155.81 ± 0.07
D5	10659.99 ± 528.42
D6	331.79 ± 6.12
L3	114.42 ± 1.78
L4	0.74 ± 0.01
L5	77.21 ± 1.20
Total	11070.31 ± 528.47

Analyzing Table 12, the levels of exposure dose to dust ingestion showed to be higher than inhalation, with a dust ingestion daily dose of 60.41 ± 3.17 µg/kg bw·day and a daily inhalation dose of 4.92 ± 0.47 µg/kg bw·day.

Table 12. Estimated inhalation and dust ingestion (µg/kg bw·day) of VMSs (D4 and D5) and respective standard deviation (µg/kg bw·day) for a 2-years-old baby.

Siloxane	Inhalation	Dust ingestion
D4	0.06 ± 0.01	0.94 ± 0.00
D5	4.82 ± 0.47	59.48 ± 3.17
Total	4.92 ± 0.47	60.41 ± 3.17

5. CONCLUSIONS

Given the extreme use of volatile methylsiloxanes (VMSs) in several industries and their release into the atmosphere, scientists have been studying its implication on air quality. Although siloxanes are, at the moment, considered safe by the scientific community, some studies have reported harmful effects of VMSs in rats and human lung cells when exposed to D4 and D5, and bioproducts of D5, respectively.

The main aims of this dissertation were to study the occurrence of cyclic (D3-D6) and linear (L3-L5) VMSs in the atmosphere of several environments (indoor and outdoor), measure and quantify their levels and distribution, and estimate the human exposure by inhalation to these man-made compounds. From the multiple settings analyzed, the private bedroom was the one that possessed an atmosphere with a higher presence of VMSs (concentration range from to 14095 $\pm$ 468.86 ng/day), and the remote area was the location where the lowest concentration of VMSs was detected (1.19 $\pm$ 0.69ng/day). These results confirmed that indoor air imposes a higher risk than outdoor air. Within indoor environments, a factor that has a major influence on the levels of these compounds in the air is occupancy. The results obtained suggest that the greater the number of people influx, the greater concentration of VMSs in the air, as the living room, office (E-319) and stationery store showed a decrease of tVMSs concentrations from 656.59 ± 67.13 to 200.66 ± 1.49 ng/day, 247.22 ± 10.89 to 67.55 ± 4.12 ng/day, and 301.97 ± 21.20 to 80.49 ± 12.89 ng/day, respectively, when a reduction of people influx occurred. Among the VMSs investigated, cVMSs appeared in several superior orders of magnitude than lVMSs. D5 was the one that appeared with a higher frequency, which seems to be directly related to its application on personal care products. However, in some environments, D3 was predominant (car and restaurant). This can be due to its proprieties, being one of the most volatile siloxanes studied, and also suggest the presence of materials used in these settings, such as in coatings, plastic additives, resins, and silicone rubber of the car, and cookware present in the restaurant. In addition, the settings: boat workshop, dental clinics, paint stores, pharmacies, perfumeries, restaurants, reprographies, and stationery stores have never been study in the past and the results demonstrated that VMSs are present in all of them, being the perfumery the environment with greater amounts of VMSs (2408.88 $\pm$ 43.08 ng/day), and the paint store the lowest (105.74 $\pm$ 21.27 ng\day). These results demonstrate that VMSs are present in a variety of environments. Therefore, in the future, the legislation regarding their concentration and composition in various products for human consumption may be more rigorous than it is today.

The human inhalation exposure to siloxanes was greater for workers at the hair salon, and women are more susceptible than men due to their physiologic characteristics (*e.g.*, weight). Our daily routine also plays a key role in human exposure by inhalation to VMSs since half of our day is likely to be spent at home. As a result of the pandemic, people are exposed to higher concentrations of VMSs,

since the majority of the day is spent at home. Furthermore, in babies, exposure by dust ingestion of cVMSs (60.41 ± 3.17 µg/kg bw·day) showed to be more dangerous than inhalation exposure (4.92 ± 0.48 µg/kg bw·day).

5.1 LIMITATIONS AND FUTURE RECOMMENDATIONS

Despite the good results obtained, it is important to bear in mind that our study presented some limitations. As a result of using passive air sampling, it was not possible to quantify the passive sampling rate. Therefore, in future studies, the application of active sampling could overcome this issue, as the flux of air is controlled by a pump. Furthermore, a new sampling campaign should be done in the locations where only one sampling campaign occurred, to obtain more reliable results. In addition, a new sampling needed to be made in the car, as was verified the noteworthy increase of the tVMS concentration, and the sampling conditions were practically the same from the first to the second sampling campaign.

Few studies have been made regarding human exposure to siloxanes through inhalation. As this project proved, VMSs can reach high concentrations, especially indoors where personal care products are constantly being used. In that matter, it would be important to explore indoor locations where the concentrations are predicted to be high, such as in heavy silicone-using industries, estimate the workers' inhalation and dust ingestion exposure, as well as the potential long-term impacts to their health in, specifically to the respiratory system. For that, groups of human lung cells A549 could be exposed to several concentrations of VMSs during different periods of time and measure the viability of the cells through their metabolic activity. Moreover, reference doses are needed to evaluate the risk assessment to VMSs. Nevertheless, environmentally friendly, non-potentially toxic, and equally good alternatives to these compounds must be found in the near future, in order to reduce their emissions to the air and their subsequent inhalation.

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APPENDICES

A1. Locations and data of sampling

Table A1. Sampling locations and time periods.

Sampling location	1st sampling	2nd sampling	3rd sampling
Baby room	16/04/2021 – 30/04/2021	-	-
Bedroom	27/10/2020 – 10/11/2020	23/03/2021 – 06/04/2021	-
Boat workshop	27/10/2020 – 10/11/2020	18/03/2021 – 02/04/2021	-
Car	27/10/2020 – 10/11/2020	15/03/2021 – 29/03/2021	-
Car workshop	-	-	16/04/2021 – 30/04/2021
Dental clinic	-	-	20/04/2021-04/05/2021
Hair salon	27/10/2020 – 10/11/2020	01/03/2021 – 15/02/2021	-
Laboratory E-201 at FEUP	27/10/2020 – 10/11/2020	23/03/2021 – 06/04/2021	-
Laboratory E-103 at FEUP			09/04/2021 – 23/04/2021
Living room	27/10/2020 – 10/11/2020	01/03/2021 – 15/02/2021	-
Office E-319 at FEUP	27/10/2020 – 10/11/2020	23/03/2021 – 06/04/2021	-
Paint store	-	-	09/04/2021 – 23/04/2021
Pharmacy	-	-	03/05/2021 – 17/05/2021
Perfumery	-	-	05/05/2021 – 19/04/2021
Remote area	-	-	09/04/2021 – 23/04/2021
Restaurant	-	-	20/04/2021 – 04/05/2021
Reprography	-	-	20/04/2021 – 04/05/2021
Rooftop at FEUP	27/10/2020 – 10/11/2020	23/03/2021 – 06/04/2021	-
Stationery store	27/10/2020 – 10/11/2020	23/03/2021 – 06/04/2021	-

A2. Quantification of the volatile methyl siloxanes

To quantify the samples, it was necessary to build a calibration curve for each VMS that was intended to be analyzed (D3, D4, D5, D6, L3, L4, and L5). For this, 11 standards of siloxanes were prepared and injected with increasing known concentrations (0.001 to 1.5 ng/μL), with the addition of an internal standard, M4Q (0.25 ng/μL) in the GC-MS. Next, individual calibration curves were constructed for each siloxane (Figure A1), relating the ratio between the siloxane peak area and the M4Q peak area with the siloxane concentration in ng/μL (quantitation by the internal standard method). Since all the extracts were concentrated with a stream of nitrogen to a final volume of 1 mL, the final concentration obtained with the calibration curves was multiplied by 1000 μL, to obtain the mass (ng) of each siloxane in the samples.

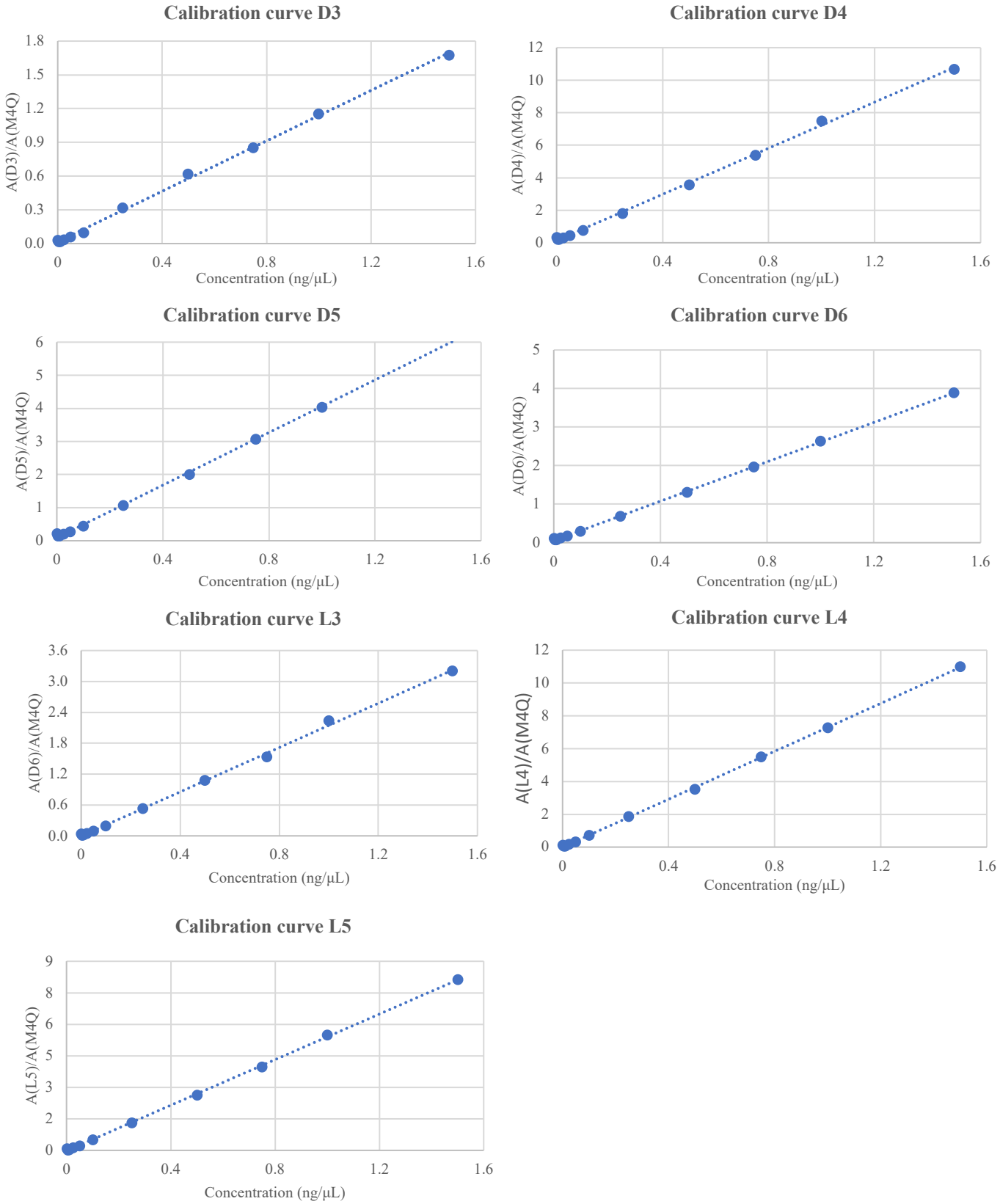

Figure A1. Individual calibration curves for the quantification of VMSs (D3, D4, D5, D6, L3, L4, L5) in GC-MS (1stsampling).

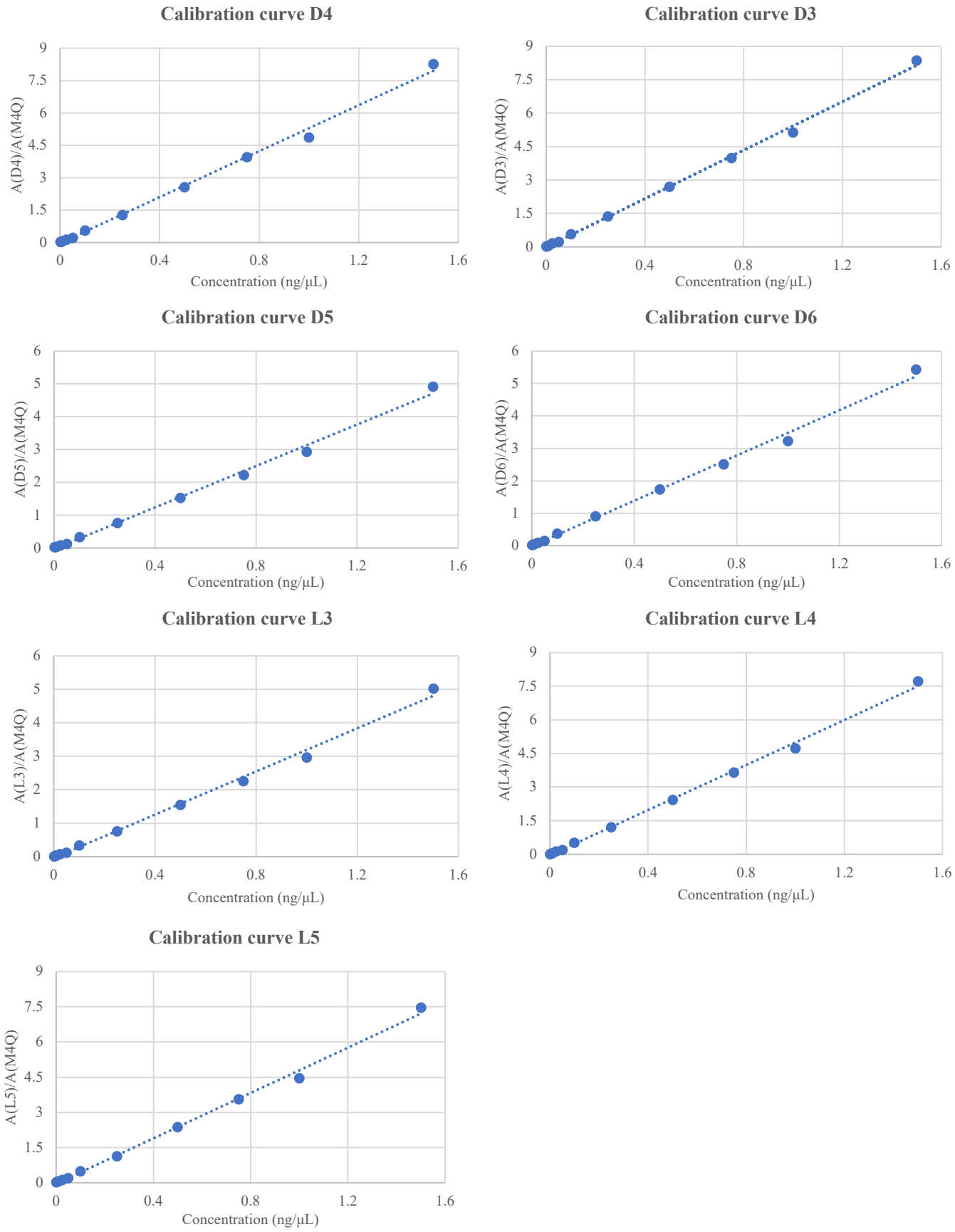

Figure A2. Individual calibration curves for the quantification of VMSs (D3, D4, D5, D6, L3, L4, L5) in GC-MS (2nd sampling).

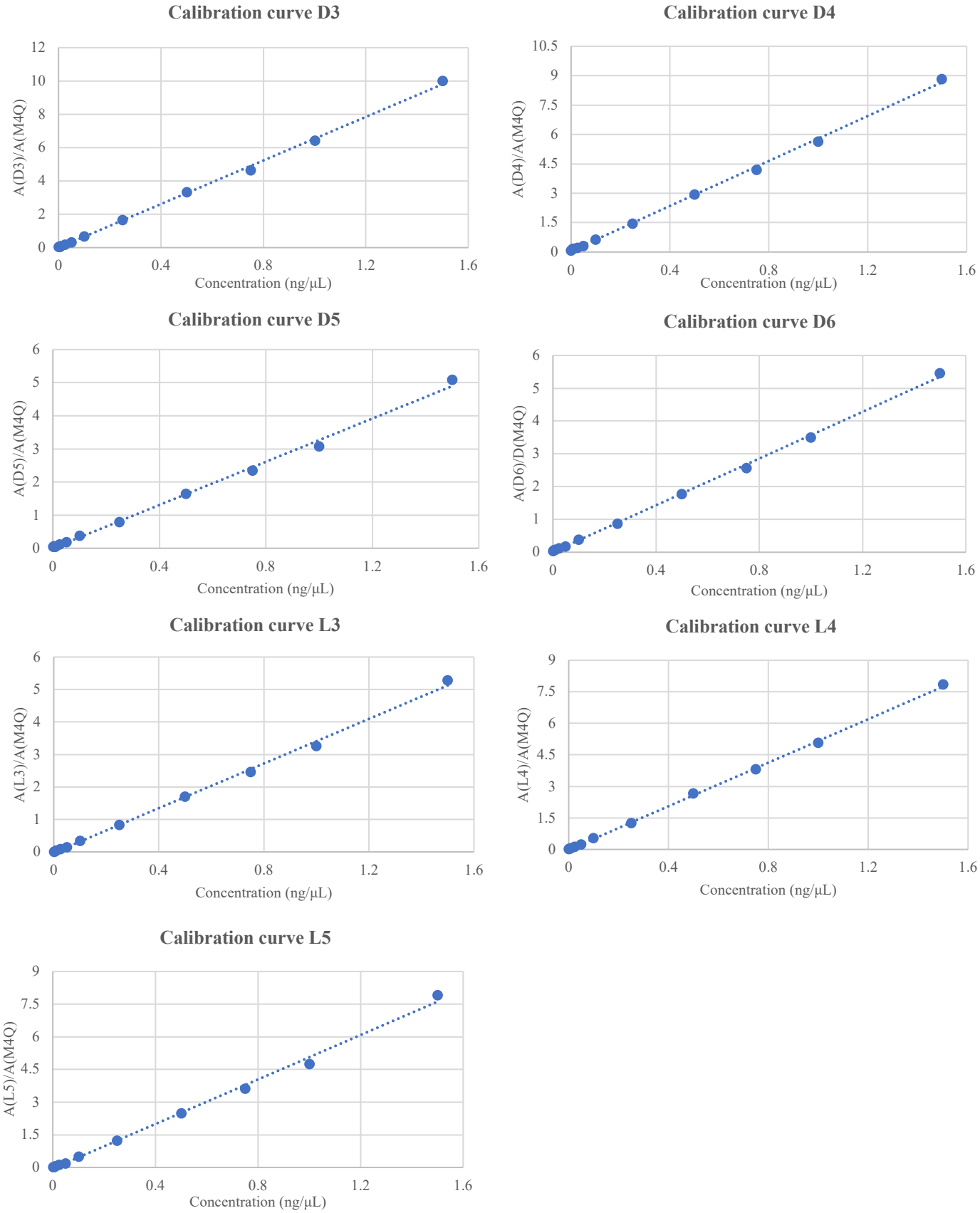

Figure A3. Individual calibration curves for the quantification of VMSs (D3, D4, D5, D6, L3, L4, L5) in GC-MS (3rdsampling).

The equation of each calibration curves and respective uncertainties were calculated and are accessible in Table A2. The equation of the calibration curve was obtained by the following linear regression:

$$\frac{A_{siloxane\ peak}}{A_{M4Q\ peak}} = (a \pm t_{sa}) \times C_{siloxame} \left(\frac{ng}{\mu l}\right) + (b \pm t_{sb}). \quad \textbf{Equation A1}$$

where, a represents the slope, b the $\frac{A_{siloxane\ peak}}{A_{M4Q\ peak}}$ intercept, and t_{sa} and t_{sb} the respective associated uncertainties.

Table A2. Slope values (a), ordinate at origin (b) and respective associated uncertainties (tsa, tsb), and coefficient of determination of the calibration lines for each of the siloxanes.

Calibration curves parameters and associated uncertainties (1st sampling quantification)

Siloxane	D3	D4	D5	D6	L3	L4	L5
a	1.121	7.090	3.972	2.553	2.151	7.301	5.424
t_{sa}	0.008	0.047	0.019	0.009	0.015	0.023	0.021
b	0.017	0.142	0.091	0.056	-0.005	-0.004	-0.021
t_{sb}	0.005	0.029	0.001	0.125	0.163	0.014	0.013
R^2	0.999	0.999	0.999	0.999	0.999	0.999	0.999

Calibration curves parameters and associated uncertainties (2nd sampling quantification)

Siloxane	D3	D4	D5	D6	L3	L4	L5
a	5.437	5.320	3.155	3.485	3.226	5.025	4.830
t_{sa}	0.045	0.485	0.038	0.204	0.041	0.045	0.164
b	-0.010	-0.024	-0.024	-0.009	-0.036	-0.036	-0.040
t_{sb}	0.028	0.297	0.001	0.125	0.025	0.233	0.031
R^2	0.998	0.996	0.996	0.996	0.995	0.998	0.998

Calibration curves parameters and associated uncertainties (3rd sampling quantification)

Siloxane	D3	D4	D5	D6	L3	L4	L4
a	6.537	5.738	3.262	3.560	3.434	5.175	5.111
t_{sa}	0.042	0.002	0.296	0.021	0.028	0.020	0.010
b	-0.0002	0.056	0.002	0.010	-0.027	0.014	-0.049
t_{sb}	0.026	0.0003	0.178	0.013	0.017	0.012	0.034
R^2	0.999	0.999	0.997	0.999	0.998	0.99	0.997

For the application of the calibration curves, it was necessary to validate them. For that several parameters had to be fulfilled, such as the calibration curve must contain at least 5 points, the concentration range between the least and the most concentrated standard have to differ at least a factor of 10, the correlation coefficient (r) has to be greater than 0.995, the relative standard deviation of the slope has to be less than 5% and the error range of the intercept has to contain the origin (b-Sb <0< b+Sb). As the Table A3 indicates, most of the requirements meet, except for the confidence interval of the ordinate at the origin contains the origin itself (b-sb <0< b+sb). This parameter may not be satisfied due to the baseline noise detected in the chromatogram, as well as the existence of possible cross contamination caused by the components of the GC-MS, for example the column, which separate siloxanes in its composition. Nevertheless, the calibration curves were considered valid for the present study.

Table A3. Parameters for validation of calibration lines of the 1st sampling. NOTE: in red are pointed out the cases where the parameters are not fulfilled.

Siloxane	Concentration difference of a factor of 10	Correlation Coefficient	Number of standards	Slope relative standard deviation (%)	$\frac{A_{siloxane\ peak}}{A_{M4Q\ peak}}$ interception
D3		0.999 > 0.995		0.38	0.014 < 0 > 0.019
D4		0.999 > 0.995		0.36	0.126 < 0 > 0.158
D5		0.999 > 0.995		0.26	0.089 < 0 > 0.091
D6	120	0.999 > 0.995	11>5	0.19	-0.012 < 0 > 0.125
L3		0.999 > 0.995		0.38	-0.094 < 0 > 0.084
L4		0.999 > 0.995		0.17	-0.012 < 0 > 0.003
L5		0.999 > 0.995		0.21	-0.028 < 0 > -0.014

Table A4. Parameters for validation of calibration lines of the 2nd sampling. NOTE: in red are pointed out the cases where the parameters are not fulfilled.

Siloxane	Concentration difference of a factor of 10	Correlation Coefficient	Number of standards	Slope relative standard deviation (%)	$\frac{A_{siloxane\ peak}}{A_{M4Q\ peak}}$ interception
D3		0.999 > 0.995		0.45	-0.024 < 0 > 0.005
D4		0.998 > 0.995		4.97	-0.185 < 0 > 0.138
D5		0.998 > 0.995		0.66	-0.025 < 0 > -0.023
D6	120	0.984 > 0.995	11>5	3.19	-0.076 < 0 > 0.059
L3		0.998 > 0.995		0.69	-0.049 < 0 > -0.022
L4		0.999 > 0.995		0.48	-0.166 < 0 > 0.446
L5		0.998 > 0.995		1.85	-0.057 < 0 > -0.023

Table A5. Parameters for validation of calibration lines of the 3rd sampling. NOTE: in red are pointed out the cases where the parameters are not fulfilled.

Siloxane	Concentration difference of a factor of 10	Correlation Coefficient	Number of standards	Slope relative standard deviation (%)	$\frac{A_{siloxane\ peak}}{A_{M4Q\ peak}}$ interception
D3		0.999 > 0.995		0.35	-0.014 < 0 > 0.014
D4		0.999 > 0.995		0.61	0.044 < 0 > 0.067
D5		0.998 > 0.995		4.95	-4.949 < 0 > 4.953
D6	120	0.999 > 0.995	11>5	0.33	0.003 < 0 > 0.017
L3		0.999 > 0.995		0.44	-0.035 < 0 > -0.018
L4		0.999 > 0.995		0.21	-0.020 < 0 > 0.007
L5		0.998 > 0.995		0.11	-0.068 < 0 > -0.031

Table A6. Detection limits (LODs), and quantification limits (LOQs).

Quantification of the 1st sampling samples							
Siloxane	**D3**	**D4**	**D5**	**D6**	**L3**	**L4**	**L5**
LOD (ng/mL)	1.07	9.14	161.39	6.22	1.28	4.25	3.38
LOQ (ng/mL)	3.56	30.48	537.96	20.72	4.28	14.16	11.92
Quantification of the 2nd sampling samples							
Siloxane	**D3**	**D4**	**D5**	**D6**	**L3**	**L4**	**L5**
LOD (ng/mL)	0.26	0.20	12.41	0.34	0.10	4.28	3.28
LOQ (ng/mL)	0.88	0.68	41.36	1.12	0.32	14.28	10.68
Quantification of the 3rd sampling samples							
Siloxane	**D3**	**D4**	**D5**	**D6**	**L3**	**L4**	**L5**
LOD (ng/mL)	0.3	0.78	41.46	0.82	0.14	12.50	6.72
LOQ (ng/mL)	1	2.6	138.2	2.72	0.48	41.68	22.4

Table A7. VMSs concentrations (ng/m^3) in the 1st, 2nd and 3rd sampling, and respective standard deviation (ng/m^3). NOTE.: D3 and D6 were not calculated due to absence of sampling rates.

Concentrations (ng/m^3)									
1st sampling									
Siloxane	**Bedroom (n=2)**	**Boat workshop (n=2)**	**Car (n=2)**	**Hair salon (n=2)**	**Laboratory (E-201) (n=2)**	**Living room**	**Office (E-319) (n=2)**	**Stationery store (n=2)**	**Rooftop (n=2)**
D4	331.37 ± 33.72	24.73 ± 5.57	211.10 ± 11.29	243.65 ± 29.45	25.06 ± 2.59	184.84 ± 30.85	103.93 ± 3.89	47.52 ± 4.56	3.21 ± 0.91
D5	29001.31 ± 1012.92	39.51 ± 9.09	37.47 ± 0.21	14170.44 ± 520.82	61.48 ± 5.67	940.86 ± 139.14	194.07 ± 23.20	455.25 ± 45.67	90.73 ± 3.49
L3	2.53 ± 0.13	n.d.[a]	0.35 ± 0.00	152.38 ± 22.01	1.59 ± 0.13	0.78 ± 0.07	1.64 ± 0.11	15.34 ± 0.49	2.31 ± 0.05
L4	2.23 ± 0.16	n.d.[a]	1.97 ± 0.23	0.87 ± 0.04	0.65 ± 0.01	n.d.[a]	0.60 ± 0.02	1.43 ± 0.03	0.70 ± 0.02
L5	23.48 ± 3.00	0.80 ± 0.06	17.25 ± 0.52	5.29 ± 0.05	1.29 ± 0.10	3.38 ± 0.43	5.16 ± 0.30	4.75 ± 0.12	1.27 ± 0.08
2nd sampling									
Siloxane	**Bedroom (n=2)**	**Boat workshop (n=2)**	**Car (n=1)**	**Hair salon (n=2)**	**Laboratory (E-201) (n=2)**	**Living room (n=2)**	**Office (E-319) (n=2)**	**Stationery store (n=2)**	**Rooftop (n=2)**
D4	501.79 ± 59.92	17.03 ± 4.62	624.23	230.82 ± 29.70	42.32 ± 7.53	135.65 ± 0.83	41.84 ± 4.27	30.45 ± 10.21	17.98 ± 0.66
D5	25406.24 ± 2888.09	62.48 ± 21.12	38.45	10856.28 ± 139.38	78.83 ± 21.81	153.41 ± 2.42	32.01 ± 4.52	88.51 ± 25.15	90.19 ± 9.32
L3	141.40 ± 4.78	n.d.[a]	n.d.[a]	109.08 ± 11.75	1.54 ± 0.17	3.06 ± 0.04	n.d.[a]	1.12 ± 0.11	1.62 ± 0.04
L4	330.00 ± 6.81	0.13 ± 0.03	2.09	0.54 ± 0.06	0.55 ± 0.05	0.47 ± 0.05	n.d.[a]	0.45 ± 0.02	0.70 ± 0.05
L5	348.38 ± 44.40	0.13 ± 0.09	18.70	2.62 ± 0.37	2.47 ± 0.72	1.47 ± 0.04	0.55 ± 0.09	1.21 ± 0.38	0.92 ± 0.04

[a] non detected

Table A7 (continuation). VMSs concentrations (ng/m^3) in the 1st, 2nd and 3rd sampling, and respective standard deviation (ng/m^3). NOTE.: D3 and D6 were not calculated due to absence of sampling rates.

	3rd sampling									
Siloxane	**Baby room (n=2)**	**Car workshop (n=2)**	**Dentist (n=2)**	**Laboratory (E-106) (n=2)**	**Paint store (n=2)**	**Perfumery (n=2)**	**Pharmacy (n=2)**	**Reprography (n=2)**	**Restaurant (n=2)**	**Remote area (n=2)**
D4	159.79 ± 30.92	10.81 ± 2.87	587.35 ± 92.23	303.92 ± 12.19	57.67 ± 1.95	42.41 ± 1.18	52.80 ± 2.62	73.12 ± 5.68	203.06 ± 31.98	1.76 ± 0.45
D5	12622.35 ± 1217.09	19.75 ± 15.29	2933.77 ± 309.93	185.98.77 ± 169.34	94.70 ± 0.97	3138.37 ± 589.14	1016.88 ± 67.09	275.34 ± 61.73	177.47 ± 28.89	n.d.
L3	n.d.[a]	0.48 ± 0.08	14.07 ± 2.62	6.44 ± 0.15	11.13 ± 25.15	788.85 ± 151.33	28.44 ± 2.74	1.20 ± 0.11	36.99 ± 6.44	0.07 ± 0.01
L4	n.d.[a]	n.d.[a]	7.76 ± 1.47	8.69 ± 0.22	n.d.[a]	1402.00 ± 240.42	n.d.[a]	0.57 ± 0.15	82.57 ± 12.58	0.04 ± 0.00
L5	63.75 ± 9.05	0.05 ± 0.07	8.42 ± 0.88	2.97 ± 0.52	0.51 ± 0.31	366.73 ± 84.18	9.59 ± 0.64	1.37 ± 0.57	46.38 ± 5.87	n.d.[a]

[a] non detected