



Fabric phase sorptive extraction as a sustainable sample preparation procedure to determine synthetic musks in water

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ABSTRACT

A rapid sample preparation fabric phase sorptive extraction (FPSE) methodology followed by gas chromatography coupled to tandem mass spectrometry is proposed for the first time to determine 12 synthetic musks including nitro-, polycyclic and macrocyclic musk in environmental water and wastewater. An asymmetric screening design of experiments was used to evaluate the influence of nine parameters affecting FPSE in only 16 experiments. The factors included the sol-gel sorbent coating, stirring mode (both extraction and desorption), extraction and desorption time, salting-out effect, sample volume, type of solvent, and desorption solvent volume. The selected conditions imply the use of the sol-gel PDMS sorbent coating, 15 min extraction by ultrasound energy employing 10 mL of sample and 0.5 mL of ethanol as desorption solvent during 5 min. Accuracy and precision were assessed in different real water samples. Matrix effects were evaluated performing recovery studies in several aqueous matrices: river, sea, spring, laundry washing place, and wastewater at different concentration levels (0.1, 2, 10 $\mu\text{g L}^{-1}$) demonstrating method accuracy (results ranged between 82 and 110%) and good precision (relative standard deviation, RSD < 12% in all cases). Limits of detection (LODs) were below 8 ng L^{-1} for the analyzed synthetic musks. As extraction was quantitative (exhaustive extraction), calibration was carried out using solvent standards without the need of repeating the extraction step, which is required in most microextraction methods, improving sample throughput, and reducing costs. Finally, the analysis of real contaminated samples revealed the presence of 11 out of the 12 target synthetic musks at concentrations up to 30 $\mu\text{g L}^{-1}$, three of them banned in cosmetic regulation (musk tibetene, ambrette, and moskene). The developed FPSE based methodology uses low volume (0.5 mL) of a Generally Recognized as Safe (GRAS) solvent (ethanol), as well as minimum energy and time consumption, demonstrating to be a sustainable alternative to detect these microcontaminants in environmental waters and wastewaters.

1. Introduction

Fragrances are used to create pleasant scents and make products more attractive to consumers. They are extensively employed in household (e.g. laundry and dishwashing detergents) and personal care products (PCPs, e.g. cosmetics) of daily use [1]. However, their massive use implies that a large number of these products continuously get into the environment, principally through municipal sewage discharges [2,3]. Some constituents of these products have become a concern due to

their bioaccumulation and potential ecotoxicological effects, such as synthetic musks. In addition, they can induce carcinogenetic (nitro-musks) and cause endocrine disruption [4,5]. Musk fragrances can be classified in polycyclic, nitro, macrocyclic and alicyclic musks considering their chemical structure. The nitromusks were the first to be produced but, most of them were forbidden in several consumer products in the 1990 s, such as cosmetics [6], due to their harmful toxicological and environmental effects, related to the presence of a nitroaromatic group in their structure [7,8]. The polycyclic musk fragrances, mainly

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galaxolide and tonalide, are massively used because of their low-cost production, and galaxolide is recognized as a HPVC (high production volume chemical) [9].

Musk fragrances are considered hazardous for the environment. They have been found in water, as well as other environmental compartments such as sludge, soil, sediments, and air, being tonalide and galaxolide the most frequently found (up to mg L^{-1}). In addition, several forbidden nitromusks are still detected [10,11], showing their persistence in the environment.

The improvement of analytical methodologies able to determine trace levels of these emerging pollutants in the environment, including water bodies, is needed. Because of its pervasiveness, their analysis is a challenge and sample preparation is an essential step, influencing the reliability, accuracy, cost, and time of analysis [12,13].

The main technique to extract musks from water samples has been solid-phase extraction (SPE) [10,14] but, in last years' trends in sample preparation are moving towards the substitution of conventional extraction techniques by miniaturized and microextraction procedures in consonance with green sample preparation (GSP) principles and green analytical chemistry (GAC) [15,16]. Different miniaturized techniques have been suggested for these PCPs extraction, including stir bar sorptive extraction (SBSE), single drop microextraction (SDME), ultrasound-assisted emulsification microextraction (USAEME), solid-phase microextraction (SPME), or dispersive microextraction (DLLME) [10,17–21]. The new approaches provide important benefits in comparison with classical techniques, but they also present some drawbacks as the non-exhaustive extraction which requires the inclusion of the extraction step for calibration purposes, a long extraction time in some cases (SBSE) or the difficulties achieving a stable and reproducible extraction phase (SDME).

Fabric phase sorptive extraction (FPSE) was introduced a few years ago as a pioneering sample preparation approach [22]. It combines SPE (exhaustive extraction) and SPME (equilibrium extraction), in a unique step. FPSE is the sorbent-based sorptive extraction techniques that employs a permeable substrate to speed up the extraction equilibrium, increasing the primary contact surface area (PCSA) for a rapid analyte-sorbent interaction, thus, reducing the extraction time. This permeability, in combination with the porous sponge-type structure of sol-gel sorbent coating, favors high sorbent loading on the substrate [23,24]. Other advantages of FPSE include its suitability for directly exposing the sample solution over a wide pH interval (1–12), direct desorption with an organic solvent or mixtures and a large variety of sol-gel coating formulations and combinations, that can be tailored depending on the chemical and physical properties of the analyzed compounds.

FPSE has been applied to extract different organic analytes from water samples, such as pesticides, fungicides, polycyclic aromatic hydrocarbons (PAHs), hormones, pharmaceuticals, and PCPs including parabens, UV filters, and antimicrobials [22,25–31]. However, to our knowledge, it has not been used for the extraction of synthetic musk fragrances.

The aim of this research is the development of an accurate and sensitive method based on FPSE followed by GC-MS/MS to analyzed 12 synthetic musks in environmental waters. The most influential experimental parameters affecting FPSE are optimized by experimental design and, after the method validation, it was performed on different water matrices, proving its convenience to determine trace levels of this type of ubiquitous PCPs.

2. Materials and methods

2.1. Chemicals and materials

In Table S1, the 12 target synthetic musks, CAS numbers, octanol/water partition coefficients ($\log K_{OW}$), retention times, MS/MS transitions, and collision energies are shown. Ethyl acetate, ethyl lactate, acetone, acetonitrile, and ethanol were purchased from Sigma-Aldrich

Chemie GmbH (Germany) and ultrapure water MS grade was supplied by Scharlab (Spain). The FPSE membranes coated with sol-gel sorbent were manufactured at Florida International University in Miami, Florida, USA and generously provided by Prof. Kabir. Their preparation and characterization is described elsewhere [32,33]. Four different FPSE membranes were tested, coated with sol-gel i) Carbowax 20 M (CW 20 M), ii) tetrahydrofuran (THF), iii) polydimethylsiloxane (PDMS), and iv) poly(caprolactone-dimethylsiloxane-caprolactone) block copolymer (PCAP-PDMS-CAP). All of them were cut into 2×2.5 cm, providing an extraction surface area of 5 cm^2 on each side. Individual stock solutions of each studied musk fragrance were prepared in hexane (musk ambrette, $2412 \mu\text{g mL}^{-1}$; musk xylene, $1369 \mu\text{g mL}^{-1}$; musk moskene, $3708 \mu\text{g mL}^{-1}$; musk tibetene, $3254 \mu\text{g mL}^{-1}$; musk ketone, $3346 \mu\text{g mL}^{-1}$; cashmeran, $3662 \mu\text{g mL}^{-1}$; celestolide, $1008 \mu\text{g mL}^{-1}$; phantolide, $908 \mu\text{g mL}^{-1}$; galaxolide, $7916 \mu\text{g mL}^{-1}$; and tonalide, $6707 \mu\text{g mL}^{-1}$), acetone (traseolide, $528 \mu\text{g mL}^{-1}$), and isooctane (ambrettolide, $36793 \mu\text{g mL}^{-1}$). Ethanol or acetone were used in the preparation of the dilutions and/or mixtures for the calibration studies or sample fortification solutions, respectively. Solutions were stored at $-20 \text{ }^\circ\text{C}$ protected from light.

2.2. Sampling

Different water samples such as wastewater, bath water, seawater, spring water, laundry water, river water, laundry washing place water, swimming pool water, washing machine water, and mop water were collected. The samples were kept away from light at $4 \text{ }^\circ\text{C}$ until analysis. Sampling details are provided in Table S2.

2.3. FPSE procedure

To remove any undesirable impurities from the fabrication procedure, the sol-gel PDMS coated FPSE membrane was conditioned under the optimized conditions (see section 3). This membrane was immersed into 2 mL of acetonitrile:methanol (1:1) during 5 min, then into 2 mL of ethanol for 5 min and finally into 2 mL of ultrapure water during 5 min to eliminate organic solvents residues. Thereafter, the membrane (sol-gel PDMS, optimum phase) was placed in a 20 mL glass vial containing 10 mL of water sample. The vial was encapsulated with an aluminum cap furnished with PTFE and immersed into an ultrasound bath (50 kHz) for 15 min, under controlled temperature ($25 \text{ }^\circ\text{C}$). Then, the membrane was taken out from the vial and placed on a watch glass to air-dry at room temperature. Once it was dry, it was immersed in 0.5 mL of ethanol under ultrasound energy for 5 min. Finally, the organic extract was filtered ($0.45 \mu\text{m}$ PTFE) and injected in the GC-MS/MS instrument. For each extraction, a new FPSE device was used since slightly lower extraction efficiency (between 5 and 10% depending on the compound) was observed (results not shown).

2.4. GC-MS/MS analysis

Chromatographic analysis was carried out employing a Thermo Scientific Trace 1310 instrument with a triple quadrupole mass spectrometer (TSQ 8000) working in Selected Reaction Monitoring (SRM) acquisition mode. The specific operational conditions are included in Table S3.

2.5. Statistical analysis

Statistical analysis was performed using the Microsoft Excel® software and the experimental design was performed by NemrodW® statistical software (LPRAI, Marseille, France).

3. Results and discussion

3.1. Chromatographic analysis

The chromatographic GC–MS/MS conditions for the determination of the target synthetic musks was previously developed by the authors [34,35]. MS/MS conditions were optimized using the semi-automated selected reaction monitoring (auto SRM) tool implemented in the TSQ8000 GC–MS/MS software. This process allowed the selection of two or three transitions for each compound according to ion abundance achieving a high selectivity. The most intense transition was used for quantification purposes, whereas the second and the third ones were employed for identification/confirmation purposes. The chromatographic conditions have been previously described in section 2.4.

3.2. Optimization of the FPSE procedure

Several experimental parameters critically affecting the FPSE process have been evaluated: the FPSE membrane, the desorption solvent and volume, the stirring mode (both extraction and desorption), the extraction time and the desorption time, the salting out effect, and the sample volume. The FPSE membrane size (2.5 cm × 2.0 cm) and the extraction temperature (25 °C) were kept constant, based on previous studies [26,27].

3.2.1. Preliminary experiments

3.2.1.1. Selecting a sol–gel sorbent-coated FPSE membrane. It is well known that the sorption efficiency depends on the sorbent material and the analytes' physicochemical characteristics. In FPSE, the extraction efficiency is due to intermolecular interactions between the analytes and the sol–gel based functional phase (dipole–dipole interactions, London dispersion, and hydrogen bonding) [24,33]. Since the studied synthetic musks present wide variety of polarity (log K_{OW} between 2.1 and 5.9, see Table S1), several sorbent coatings of different characteristics were tested: PDMS, non-polar, for which the London dispersion interactions were predominant; PCAP-PDMS-CAP and THF, both with intermediate polarity, with hydrogen bonding and London dispersion; and CW 20 M, a polar sorbent, with dipole–dipole interactions and hydrogen bonding. Trials were performed with 10 mL of ultrapure water fortified at $2 \mu\text{g L}^{-1}$ and extraction was done under magnetic agitation to speed up the extraction procedure (20 min). The desorption was carried out by vortex stirring for 3 min using 1 mL of ethyl acetate.

Fig. 1 displays the obtained results. Upon observation, the responses were similar regardless the sol–gel sorbent coating employed for most analytes. However, the most polar sol gel, CW 20 M, offered slightly lower responses for most of the target synthetic musks. Also, the PCAP-PDMS-CAP showed the lowest chromatographic areas in some cases,

such as cashmeran, whose signals were almost 2 times lower than those achieved with the other coatings. As regards to the differences between PDMS and THF, the differences in extraction efficiency were not significant. Therefore, both sol–gel sorbent coatings, PDMS and THF, were included in the optimization study employing an experimental design.

3.2.2. Optimization by design of experiments

An asymmetric screening design 2732/16 was done to evaluate the effect of nine FPSE factors in only 16 experiments. The design generation and evaluation were carried out using NemrodW® software (see section 2.5). The nine experimental parameters are shown in Table S4. Seven of them were studied at two levels: b1, sol–gel sorbent coated FPSE membranes (PDMS, THF); b2, extraction agitation (magnetic stirring and ultrasounds); b3, desorption agitation (vortex stirring and ultrasounds); b4, extraction time (15, 30 min); b5, desorption time (2, 5 min); b6, salting-out effect (0, 15% salt) and b7, sample volume (10, 20 mL). Two factors were studied at three levels: b8, desorption solvent (ethyl acetate, ethanol, ethyl lactate) and b9, volume of desorption solvent (0.5, 1, 1.5 mL). This assay was done with spiked water ($2 \mu\text{g L}^{-1}$ of each analyte). Results were plotted in Total Effect and Delta Weight plots. The Delta Weights graph studies the differences in the signal (peak area), when varying the level for a certain parameter. The size of the bars is related to the increase (bars going rightwards) or decrease (bars going leftwards) of the effect when shifting from one to another factor level. When the bars surpass the dotted reference line, there is a notable statistical significance regarding the response of level effect. Moreover, to determine an optimal factor level, Total Effect graphs were employed when there is not statistical significance. In this case, the magnitude of the bars corresponds to the impact each variable level exerts on analytical response. The ANOVA analysis shows that some factors were statistically significant ($p < 0.05$). As an example, Fig. 2 displays the Total Effect plots (Fig. 2a, 2b and 2c) and Delta Weight plots (Fig. 2d, 2e and 2f) for ambrettolide, celestolide, and musk xylene, respectively. The sol–gel sorbent coating (b1) and the salting-out effect (b6) were statistically significant for six analytes. PDMS phase and no salt addition achieved the best extraction results for all the studied fragrances. Sample volume (b7) was statistically significant for celestolide, phantolide, and galaxolide and the use of 10 mL of sample was the ideal goal for all the analytes. The stirring mode (b2 and b3) was statistically significant for xylene and ultrasounds stirring is more favorable for both extraction and desorption steps, in all cases. The usage of ethanol as desorption solvent (b8) was almost statistically significant for xylene and tonalide. It is important to note that only GRAS solvents were considered in this work to obtain a green and sustainable methodology. The use of ethanol as well as ethyl acetate, provided good peak shape for all analytes in comparison with ethyl lactate. Hence, the selection of ethanol as extraction solvent was not only based on the chromatographic response but also on the peak shape obtained. As an example, in

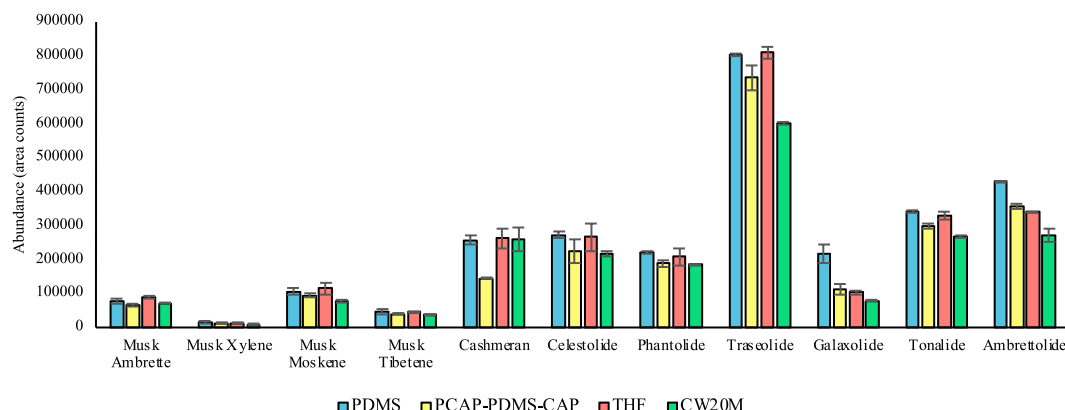


Fig. 1. Effect on the chromatographic abundance (area counts) for the FPSE sol–gel sorbent coating.

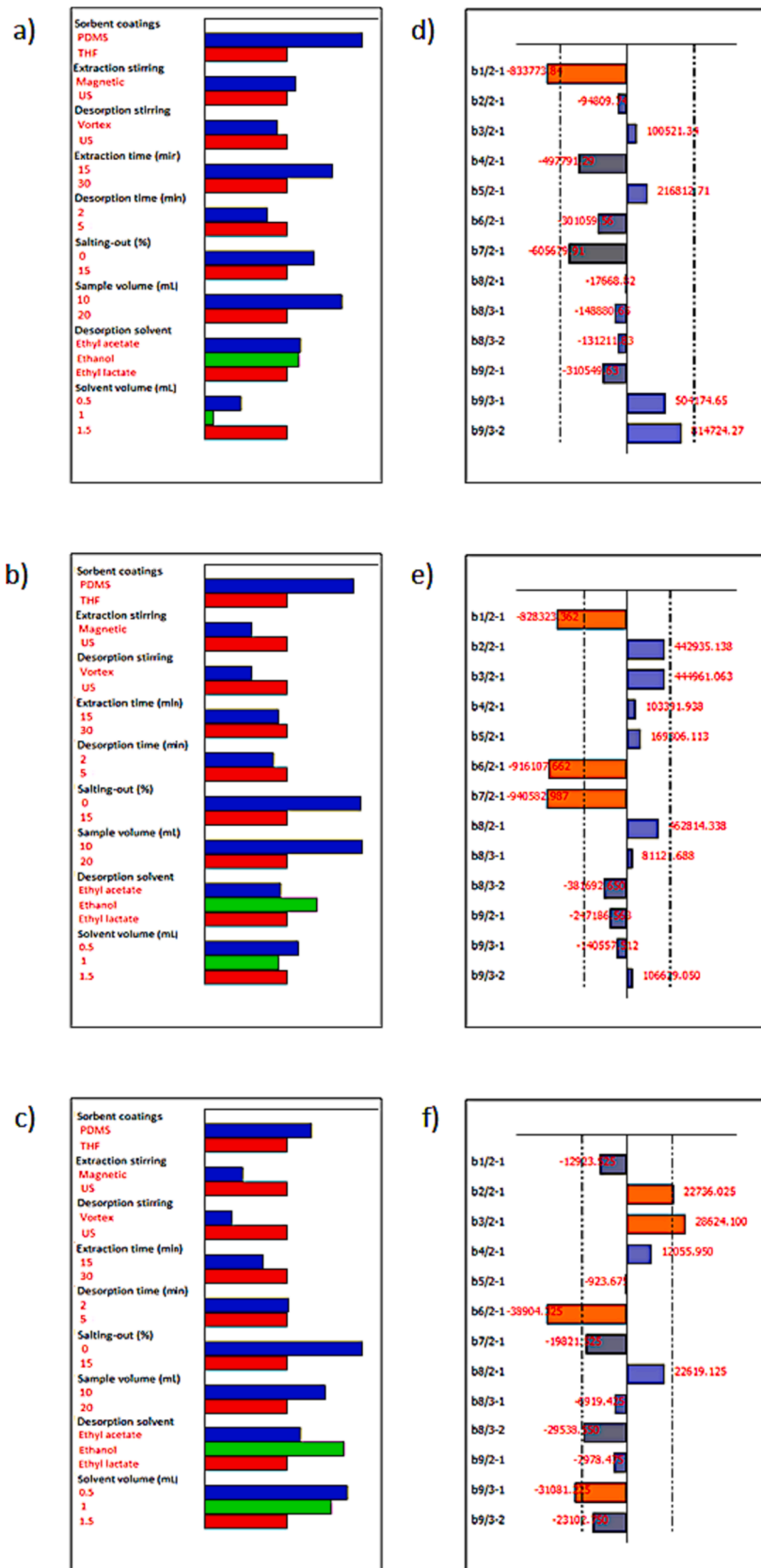


Fig. 2. Total Effect plots for: a) ambrettolide, b) celestolide and c) musk xylene; and Delta Weight plots for: d) ambrettolide, e) celestolide and f) musk xylene.

Fig. S2 is shown the difference of phantolide peak shape for the three tested extraction solvents in a solution at $20 \mu\text{g L}^{-1}$. As can be seen, the use of ethyl lactate (Fig. S2b) highly affects the chromatographic peak shape, showing worst shape, whereas standard prepared in ethyl acetate (Fig. S2a) and ethanol (Fig. S2c) showed, in both cases, satisfactory peak resolution. Volume of desorption solvent (b9) was not statistically significant, but 0.5 mL produced the best responses, except for ambrettolide for which a volume of 1.5 mL was the best option. Only for ambrettolide the extraction time (b4) was statistically significant and to reduce the analysis time, 15 min was enough to perform the extraction step for all the compounds. Finally, desorption time (b5) was not statistically significant, but 5 min was selected to ensure desorption of all analytes. In Fig. S1, the Delta Weight plots and Total Effect plots of the other studied compounds (musk ambrette, musk moskene, musk tibetene, musk ketone, cashmeran, phantolide, traseolide, galaxolide, and tonalide) are shown.

To sum up, the selected optimal conditions according to the preliminary studies and the experimental design imply the use of the sol-gel PDMS coating, performing extraction under ultrasound energy for 15 min employing 10 mL of water sample without salt, and carrying out the desorption by ultrasounds during 5 min with 0.5 mL of ethanol.

3.3. Performance of the FPSE-GC-MS/MS methodology

The method accuracy, linearity, precision, limits of detection (LOD) and quantification (LOQ) were assessed and it is included in Table 1. Calibration experiments involved using standard solutions that contain the 12 target synthetic musks in ethanol, covering a broad range of concentrations (0.5 to $1000 \mu\text{g L}^{-1}$ with 11 levels, particular concentration ranges for each target analyte are presented in Table 1). Good linearity (coefficients of determination, $R^2 > 0.9904$) was obtained for all analytes. Inter-day and intra-day precision were favorable with relative standard deviation, $RSD < 9\%$ and $RSD < 5\%$, respectively (Table 1).

FPSE-GC-MS/MS accuracy was assessed in real samples by recovery studies employing different water matrices such as river water, seawater, spring water, wastewater, and laundry washing place water at three different concentrations (10 , 2 , and $0.1 \mu\text{g L}^{-1}$). Procedure blanks were done daily. In the cases the compounds were found in the blanks, they were taken into account while evaluating the responses (galaxolide, celestolide, and phantolide). The method precision, repeatability, and reproducibility, were also evaluated, showing RSD values lower than 8%

Table 1
Method performance.

Synthetic musks	Linearity		Precision, RSD (%)		FPSE-GC-MS/MS				
	R^2	Linear range ($\mu\text{g L}^{-1}$)	Intra-day (n = 6) ^a	Inter-day (n = 6) ^b	Mean recoveries, %	Precision, RSD (%) ^c		LOD (ng L^{-1})	LOQ (ng L^{-1})
						Repeatability	Reproducibility		
Nitromusks									
Musk Ambrette	0.992	0.5–1000	3.3	4.0	98.5 ± 2.9	2.5	4.2	1.1	3.9
Musk Xylene	0.995	2–1000	1.0	8.1	90.6 ± 6.5	3.3	9.8	7.3	24
Musk Moskene	0.990	1–1000	0.91	4.5	93.9 ± 6.4	3.7	5.4	2.2	7.2
Musk Tibetene	0.994	1–1000	2.2	6.2	87.9 ± 5.2	1.4	7.5	6.2	21
Musk Ketone	0.992	1–1000	1.7	8.9	85.9 ± 6.3	6.2	8.8	3.9	13
Polycyclic musks									
Cashmeran	0.999	2–1000	0.68	3.9	98.0 ± 2.0	2.1	6.1	7.7	26
Celestolide	0.996	1–1000	2.8	7.4	86.7 ± 6.3	8.7	11	4.7	16
Phantolide	0.996	1–1000	2.5	5.1	82.6 ± 4.8	7.5	8.4	2.3	7.6
Traseolide	0.995	2–1000	0.99	6.7	110.2 ± 6.2	7.8	8.5	5.3	17
Galaxolide	0.997	0.5–1000	4.4	8.0	82.2 ± 4.7	6.5	7.6	0.6	2.1
Tonalide	0.997	2–1000	1.5	6.8	106.0 ± 4.6	4.3	6.3	6.1	20
Macrocyclic musks									
Ambrettolide	0.997	0.5–1000	1.5	5.6	83.4 ± 7.6	6.2	7.4	3.2	11

^a $20 \mu\text{g L}^{-1}$.

^{b,c} $2 \mu\text{g L}^{-1}$.

and 11%, respectively.

Mean recovery values obtained for ultrapure water at the three spiked concentrations are shown in Table 1. In all experiments, the recovery values were calculated as the ratio of concentration found/added considering the responses (peak area) obtained for each analyte. In those cases, the compound was found in the non-spiked samples, the response was subtracted. In all cases, they were quantitative with average values ranging between 82% and 110% and RSD values were less than 12%. Fig. 3 displays the individual recoveries in the spiked water matrices (sea, river, laundry, spring, ultrapure and wastewater), at different concentration levels. Results obtained for the waters fortified at $0.1 \mu\text{g L}^{-1}$ are shown in Fig. 3a, and at $2 \mu\text{g L}^{-1}$ and $10 \mu\text{g L}^{-1}$ are depicted in Fig. 3b. In general, a good accuracy of the method was achieved, with recovery values between 75 and 120% for most compounds and RSD values about 5%. Only 3 of the 96 recovery values which correspond with the wastewater sample, were slightly lower. These results allow the use of external calibration with standards made in ethanol, since satisfactory recoveries were obtained. In addition, as can be seen in Fig. 3, the responses were similar for the different water samples to those obtained for ultrapure water, demonstrating the absence of matrix effects (excluding 3 of the 12 compounds in the wastewater sample).

The LODs and LOQs were determined based on the concentration of the compound that resulted in a signal-to-noise ratio of 3 and 10, respectively. For galaxolide, celestolide, and phantoline (detected on blanks), the LODs and LOQs were determined by calculating the average analyte concentration that produced a response equivalent to the blank plus 3 and 10 times the standard deviation, respectively. LODs and LOQs are displayed in Table 1, showing lower than 7 ng L^{-1} for LODs and than 26 ng L^{-1} for LOQs, in most cases. In summary, the FPSE-GC-MS/MS method is a sustainable and high throughput alternative to detect trace levels of musks fragrances in a large variety of water matrices.

3.4. Greenness and comparison with other methodologies

As it was commented, in recent years the development of extraction methodologies fulfilling GAC and GSP principles is increasing. These procedures include the usage of safe solvents, reagents, and materials minimizing the experimental steps and reducing waste generation and energy consumption, allowing high sample throughput. Very recently, a metric tool, AGREEPrep [36] was proposed for evaluating the greenness of sample preparation. The sustainability of FPSE methodology developed in this study to extract musks from water was calculated and results

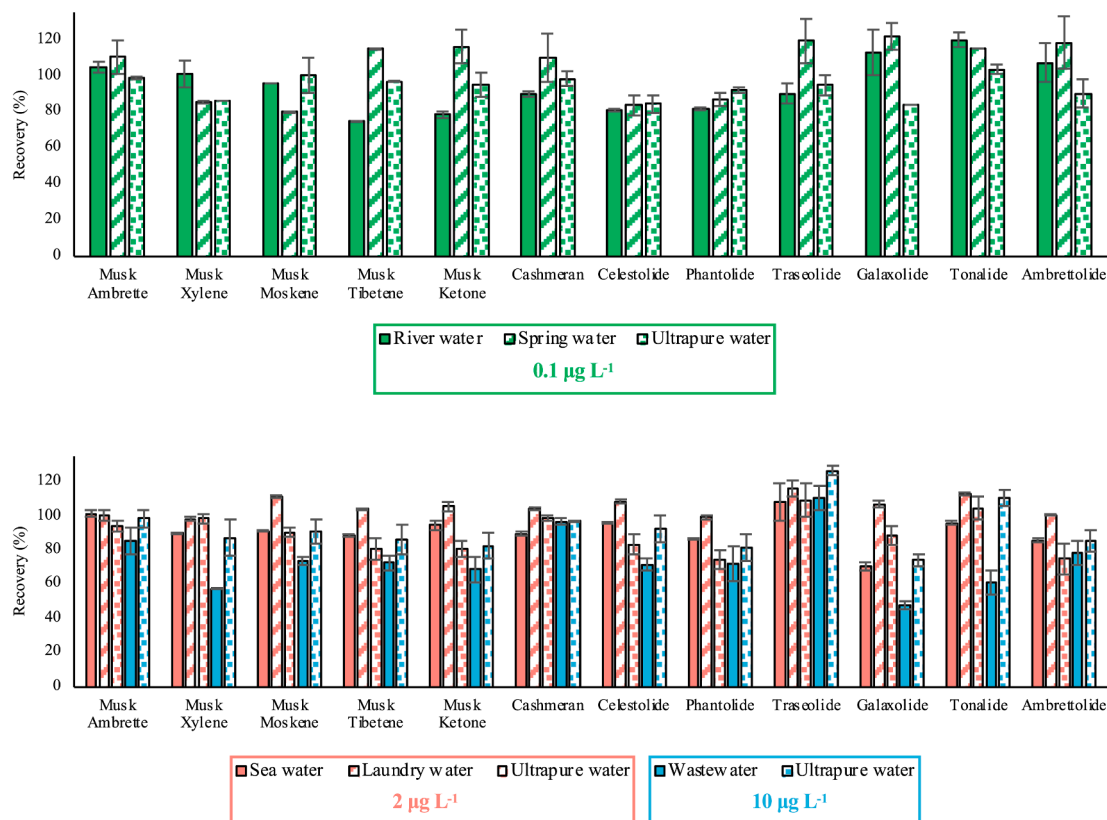


Fig. 3. Recoveries obtained for: a) river water, spring water, and ultrapure water fortified at $0.1 \mu\text{g L}^{-1}$; b) seawater, laundry washing place water, and ultrapure water fortified at $2 \mu\text{g L}^{-1}$; and wastewater and ultrapure water fortified at $10 \mu\text{g L}^{-1}$.

are displayed in Fig. 4. As can be seen, a value of 0.72 was obtained, demonstrating the greenness of the proposed FPSE method.

In Table 2, a comparative between the developed FPSE method and other reported microextraction based methodologies such as SBSE, SDME, SPME, DLLME, or USAEME [17–21] is displayed. As can be seen, the proposed methodology achieves LODs lower or similar than the other techniques, exhibiting its suitability for the analysis of musk fragrances at trace levels. In addition, extraction time is similar than other methodologies such as DLLME [20] and USAEME [21] but much lower than SDME (45 min) [19] and SBSE (4 h) [18]. One of the outstanding advantages of FPSE is the suitability of external calibration without the need of including the extraction step, increasing throughput, and reducing procedure time.

3.5. Application to real samples

The suitability of the method was also demonstrated through the analysis of a wide variety of real contaminated water samples, such as seawater, wastewater, swimming pool water, river water, spring water, laundry water, laundry washing place water, bath water, washing machine water, and mop water. Concentrations of the synthetic musks are shown in Table 3.

All the target synthetic musks were detected in the samples excluding musk xylene. Galaxolide was found in all samples ($0.2 - 30 \mu\text{g L}^{-1}$) which is quite logical because of it is the most frequently used in cosmetics and household and cleaning products [8]. Ambrettolide was found in 7 samples, and the other target fragrances were detected in 20–50% of the samples.

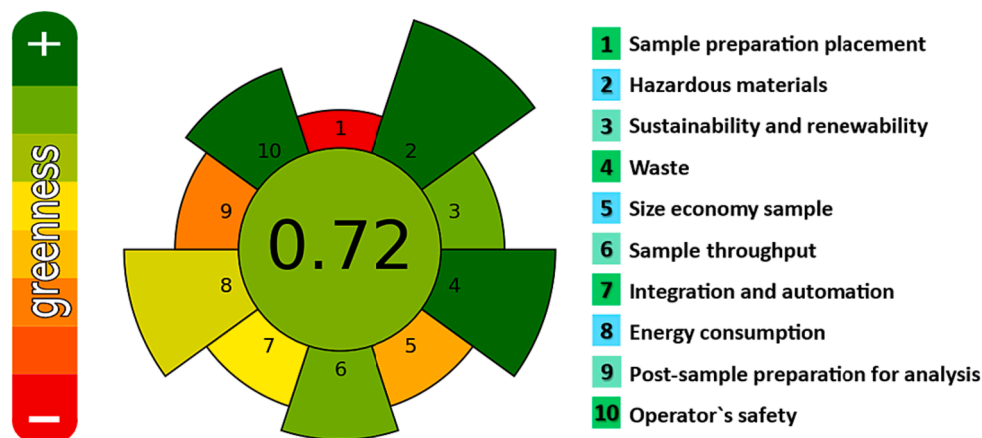

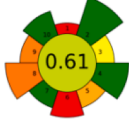


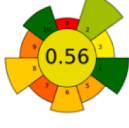



Fig. 4. Evaluation of the degree of greenness. Pictogram obtained for FPSE under the optimized conditions.

Table 2
Comparison between the proposed method and other methodologies reported in the literature to determine synthetic musks.

Number of musks	Water matrix	Extraction technique	Analysis	Sample volume (mL)	Extraction time (min)	Recovery (%)	LOD (ng L ⁻¹)	AGREEPrep [36]	Ref
4	River, tap, sea, wastewater	SBSE	GC-MS	30	240	84–108	19–41		[18]
9	Wastewater	SDME	GC-MS	10	45	np	10–30		[19]
6	Wastewater	SPME	GC-MS	10	25	np	0.1–46		[17]
8	Tap, river, sea, wastewater	DLLME	GC-MS/MS	6	15	80–120	0.1–20		[20]
8	Swimming pool, sea, wastewater	USAEME	GC-MS	10	13	78–114	9–29		[21]
12	River, sea, spring, laundry, well, swimming pool, washing machine, mop, wastewater	FPSE	GC-MS/MS	10	15	82–110	0.6–7.7		This work

np: Not provided.

Concerning the number of fragrances per sample, 8 out of the 12 compounds were presented in the laundry water (see SRM reconstructed chromatogram in Fig. 5) at concentrations between 0.052 and 30 $\mu\text{g L}^{-1}$, followed by a wastewater where 7 musks were detected at concentrations between 0.06 and 0.35 $\mu\text{g L}^{-1}$. This behavior can be expected, as fragrances, including synthetic musks, are added as ingredients in many consumer products being the final fate urban wastewaters where they are not efficiently removed. Two nitro musks, tibetene and moskene, both forbidden in cosmetics due to their adverse effects [6], were found in the wastewater sample at levels below 0.1 $\mu\text{g L}^{-1}$, demonstrating their

persistence in this type of water matrix. Musk ambrette is also banned by the European Cosmetic Regulation and it was detected in two real water samples, laundry water and seawater at 0.071 $\mu\text{g L}^{-1}$ and 0.049 $\mu\text{g L}^{-1}$, respectively. In the other analyzed waters, between 1 and 5 musks were found at concentrations between 0.03 and 25 $\mu\text{g L}^{-1}$. These levels are in accordance with the literature [10] and demonstrate that synthetic musks enter the aquatic environment through residual waters and bathing waters (rivers and beaches), as well as indirect discharges, such as domestic water (bathing, washing machine, etc.).

Table 3
Real sample analysis: concentrations ($\mu\text{g L}^{-1}$) of the synthetic musks.

Synthetic musks	Bath water	Laundry water	Swimming pool water	River water	Mop water	Laundry washing place water	Washing machine water	Seawater	Wastewater	Spring water
Nitromusks										
Musk Ambrette		0.071					0.049			
Musk Moskene									0.091	
Musk Tibetene									0.067	
Musk Ketone	0.11	11					0.19			
Polycyclic musks										
Cashmeran		0.59					0.21			
Celestolide		0.052							0.090	
Phantolide									0.070	
Traseolide	0.58	0.39								
Galaxolide	25	30	0.52	0.24	0.25	0.22	1.1	0.24	0.35	1.0
Tonalide	0.88	3.0	0.21				0.26		0.31	
Macrocyclic musks										
Ambrettolide	0.24	0.90		0.024	0.27	0.035		0.22	0.21	

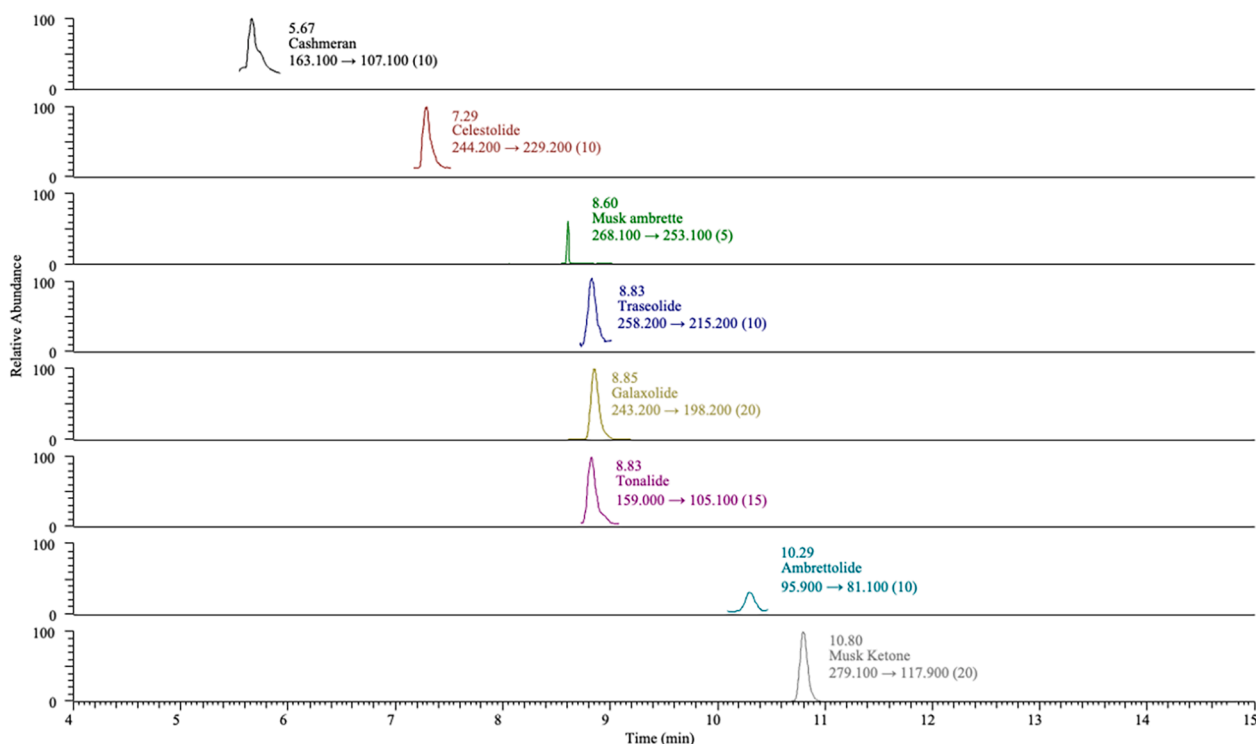


Fig. 5. SRM reconstructed chromatogram of a real water sample (laundry water) containing 8 compounds from the 12 studied synthetic musks (see concentration in Table 3).

4. Conclusions

FPSE-GC-MS/MS has proven to be an appropriated microextraction alternative for the concurrent determination of 12 synthetic musks in water samples. The major critical factors affecting the effectiveness of FPSE have been optimized to obtain the highest possible extraction efficiency. Upon optimization, the methodology was validated, showing good accuracy, precision, and linearity. No interferences from the sample matrix were detected during the recovery studies carried out on six distinct water matrices (ultrapure water, wastewater, river water, seawater, spring water, and laundry washing place water) at 3 different concentration levels. LODs and LOQs were relatively low, at levels down to the ng L^{-1} . The presence of 11 out of the 12 synthetic musks, including some forbidden in cosmetics products, at concentrations up to

$30 \mu\text{g L}^{-1}$ was shown. This work demonstrates the FPSE potential as an effective technique for extracting organic compounds, including PCPs, from diverse water samples.

CRediT authorship contribution statement

Ana Castiñeira-Landeira: Investigation. **Lua Vazquez:** Investigation. **Antonia M. Carro:** Conceptualization, Supervision. **Maria Celeiro:** Investigation, Supervision. **Abuzar Kabir:** Supervision, Conceptualization. **Kenneth G. Furton:** Conceptualization, Supervision. **Thierry Dagnac:** Resources, Investigation. **Maria Llompart:** Conceptualization, Investigation, Methodology.

Declaration of Competing Interest

Authors assert that they do not possess any recognizable competing financial or personal interests that may be supposed to impact the outcome of this research article.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.microc.2023.109542>.

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