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# Determination of geosmin and 2-methylisoborneol in water and wine samples by ultrasound-assisted dispersive liquid–liquid microextraction coupled to gas chromatography–mass spectrometry

Carol Cortada [a], Lorena Vidal [b,*], Antonio Canals [b,*]

[a] Labaqua S.A., C/Dracma 16-18, Pol. Ind. Las Atalayas, 03114 Alicante, Spain
[b] Departamento de Química Analítica, Nutrición y Bromatología e Instituto Universitario de Materiales, Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain

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ABSTRACT

A fast, simple and environmentally friendly ultrasound-assisted dispersive liquid–liquid microextraction (USADLLME) procedure has been developed to preconcentrate geosmin and 2-methylisoborneol (MIB) from water and wine samples prior to quantification by gas chromatography–mass spectrometry (GC–MS). A two-stage multivariate optimization approach was developed by means of a Plackett–Burman design for screening and selecting the significant variables involved in the USADLLME procedure, which was later optimized by means of a circumscribed central composite design. The optimum conditions were: solvent volume, 8 μL; solvent type: tetrachloroethylene; sample volume, 12 mL; centrifugation speed, 2300 rpm; extraction temperature 20 °C; extraction time, 3 min; and centrifugation time, 3 min. Under the optimized experimental conditions the method gave good levels of repeatability with coefficient of variation under 11% ($n = 10$). Limits of detection were 2 and 9 ng $L^{-1}$ for geosmin and MIB, respectively. Calculated calibration curves gave high levels of linearity with correlation coefficient values of 0.9988 and 0.9994 for geosmin and MIB, respectively. Finally, the proposed method was applied to the analysis of two water (reservoir and tap) samples and three wine (red, rose and white) samples. The samples were previously analyzed and confirmed free of target analytes. Recovery values ranged between 70 and 113% at two spiking levels (0.25 μg $L^{-1}$ and 30 ng $L^{-1}$) showing that the matrix had a negligible effect upon extraction. Only red wine showed a noticeable matrix effect (70–72% recovery). Similar conclusions have been obtained from an uncertainty budget evaluation study.



## 1. Introduction

The flowering of green–blue algae occurs in surface waters by eutrophication processes. Metabolites are produced in the degradation of these algae which are responsible for musty and earthy odours in tap water [1]. It has also been found that certain bacteria of the Actinomyces kind produce this typical smell [2]. These metabolites are geosmin and 2-methylisoborneol (MIB), among others, and their odours are perceptible at low levels, between 4 and 10 ng $L^{-1}$ for geosmin, and between 9 and 42 ng $L^{-1}$ for MIB [3].

In addition, geosmin and MIB are also responsible for some unwanted aromas in wine. When grapes have been attacked by one of the filamentous fungi producing geosmin or MIB, wine can also submit earthy aromas characteristic of these molecules, and their odours are perceptible from 50 to 55 ng $L^{-1}$ levels [4]. Although, these compounds present an unknown health hazard, their concentration beyond the threshold levels produce the rejection of the consumer.

A rapid, selective, and sensitive analytical method for monitoring residues of these odorant compounds is therefore required. However, a preconcentration step is usually necessary in order to meet these demands. Among the extraction/enrichment techniques, closed loop-stripping analysis (CLSA) and some of its modified versions have been the most frequently used method for geosmin and MIB analysis [5,6]. Also, liquid–liquid extraction (LLE) [7–9], solid phase extraction (SPE) [7], solid phase microextraction (SPME) [4,10–13], purge and trap (PT) [3], stir bar sorptive extraction (SBSE) [14], and recently headspace single drop microextraction (SDME) [15] have been developed.

All of the above mentioned techniques present some drawbacks. CLSA, PT, SPME and SBSE use expensive materials, are time-consuming and usually have carryover effects. Furthermore, SPME and SBSE have long-time sorbent conditioning. On the other hand, LLE and SPE use large amounts of potentially toxic and normally expensive organic solvents, are time-consuming and the high

* Corresponding authors. Tel.: +34 96 5909790; fax: +34 96 5909790.
*E-mail addresses:* lorena.vidal@ua.es (L. Vidal), a.canals@ua.es (A. Canals).

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manipulation of the sample can lead to undesirable contaminations. In the case of SDME fast stirring speed and air bubbles cause a drop instability and tend to break up the organic drop, and equilibrium could not be attained after a long time in most cases. For these reasons, other new extraction techniques need to be developed.

Dispersive liquid–liquid microextraction (DLLME) is a recent extraction technique [16], which eliminates all the problems described above, whereby a small droplet of extractant is disrupted on many microdroplets by the action of a disperser solvent. The increase of surface favours the exchange of analyte between phases, and hence speed up the extraction process. However, a large disperser volume is used, which decreases the partition coefficient of analytes in the extractant solvent. Recently, ultrasound energy has been used to assist the dispersion [17–25]. The use of ultrasound energy to disrupt the extractant phase reduces the consumption of organic solvent because the disperser solvent is not needed, being ultrasound-assisted dispersive liquid–liquid microextraction (USADLLME) a more environmentally friendly technique. However, this fact led most of the published works to use a higher volume of extractant phase (40–100 μL) than with DLLME or SDME (5–10 μL).

The aim of this paper is to develop a fast, inexpensive and environmentally friendly sample preparation method based on ultrasound energy to assist the dispersion of a few microlitres of extractant solvent used for the preconcentration of geosmin and MIB in water and wine samples before the quantification by GC–MS. The optimization of the extraction conditions has been done using experimental design and uncertainty budget has been used for establishing confidence as a more realistic approach to the regulatory environment [26]. Good figures of merit have been obtained and the analytical method has been validated and applied to water and wine samples.

## 2. Experimental

### 2.1. Chemicals and samples

Geosmin and MIB were obtained from Dr. Ehrenstorfer (Agsburg, Germany). Tetrachloroethylene, bromoform and methanol were pesticide-grade and were obtained from Sigma–Aldrich (St. Louis, MO, USA). De-ionized water was prepared on a water purification system (Gradient A10) supplied by Millipore (Billerica, MA, USA). Stock standard solutions of 1 mg $L^{-1}$ and 10 μg $L^{-1}$ of target compounds were prepared in methanol. Working solutions were prepared by dilution of standard stock solution in water. In order to eliminate volatilisation losses, all aqueous working solutions were freshly prepared before each extraction. All solutions were stored in the dark at 4 °C.

The recovery studies were carried out using reservoir water (Seville, Spain), tap water (Murcia, Spain), red wine (Eroski, Spain), and rose and white wine (Casón Histórico, Ciudad Real, Spain). Samples were also stored in the dark at 4 °C. Initial analysis confirmed that they were free of target analytes.

### 2.2. Ultrasound-assisted dispersive liquid–liquid microextraction (USADLLME)

12 mL of sample was placed in a 20 mL glass test tube with a conical bottom and 8 μL of tetrachloroethylene as extraction solvent was dropped into the sample solution. The mixture was sonicated in an ultrasonic bath (Ultrasons-H, Selecta, Spain) for 3 min and subsequently centrifugated for 3 min at 2300 rpm in a centrifuge table (GS-6R of Bekman, Fullerton, CA, USA). Finally, 2 μL of the extractant phase deposited at the bottom of the test tube was manually injected into the GC–MS system for analysis.

### 2.3. GC–MS determination

All analyses were carried-out on a Varian 3800-Saturn 2000 Gas Chromatography/Mass Spectrometer system (Walnut Creek, CA, USA) equipped with a Meta.X5 Tecknokroma column (30 m × 0.25 mm, 1.0 μm) (Barcelona, Spain). The mass spectrometer employed was an ion trap (20 μA) with 0.82 s of scan time. The injector was maintained at 250 °C and operated in the splitless mode with the split closed for 0.75 min. Helium (>99.999% pure) was used as the carrier gas at a flow rate of 1.0 mL $min^{-1}$. The column oven was initially set at 50 °C for 1 min, then programmed at 10 °C $min^{-1}$ to 180 °C where it was held for 2 min, followed by a 4 °C $min^{-1}$ ramp to 200 °C and held for 4 min. The interface temperature was set at 200 °C and the detector voltage at 4 V. A 10 min solvent cut time was allowed for all analyses. The base peak ion and two other significant ions of each analyte were chosen as the quantifying ions. The base peaks ion ($m/z$) for the target analytes were 112 and 95 for geosmin and MIB, respectively. Prior to quantification, the identification of target compounds was based on their mass spectra and GC retention times. Fig. 1 shows a typical chromatogram of a standard solution spiked at 10 μg $L^{-1}$ of both target analytes after USADLLME.

### 2.4. Data handling and processing

Experimental design matrices were constructed and the results were evaluated using the Statgraphics Statistical Computer Package "Statgraphics Plus 5.1".

## 3. Results and discussion

### 3.1. Study of experimental factors involved in USADLLME

#### 3.1.1. Solvent extraction study

The selection of an appropriate extraction solvent is very critical for developing an efficient dispersive liquid–liquid microextraction. Generally, extraction solvent used in USADLLME procedures must fulfill the following requirements: it should have a higher density than water, a low solubility in water, high extraction capability of the target analytes, and additionally it should be easily dispersed in water during sonication. Based on these facts, two solvents including bromoform and tetrachloroethylene were tested as potential acceptor phases. The extraction solvent should also have good chromatographic behaviour during the course of chromatographic separation. Bromoform presented problems overlapping the peak of geosmin, and areas of MIB were less than those obtained with tetrachloroethylene. Hence, tetrachloroethylene was chosen for the next optimization procedure as the extractant phase.

#### 3.1.2. Study of other experimental factors by multivariate optimization

Different factors can affect the extraction yield in the USADLLME procedure and in most cases they are correlated. Therefore, their optimization through a multivariate approach is recommended. However, some of them might not have a significant effect and they can, thus, be obviated. In this respect, a screening study, prior to the optimization, is helpful in order to assess the significant factors involved in the analytical system under study.

In this case, based on the literature and the previous experience of our group [27,28], the influence of six factors, namely sample volume, solvent volume, extraction temperature, extraction time, centrifugation speed and centrifugation time were studied in order to maximize the extraction yield in the USADLLME procedure.

If a large number of factors are involved, reduced factorial designs are employed for screening. A particular type of those designs is the Plackett–Burman design [29] which assumes that the

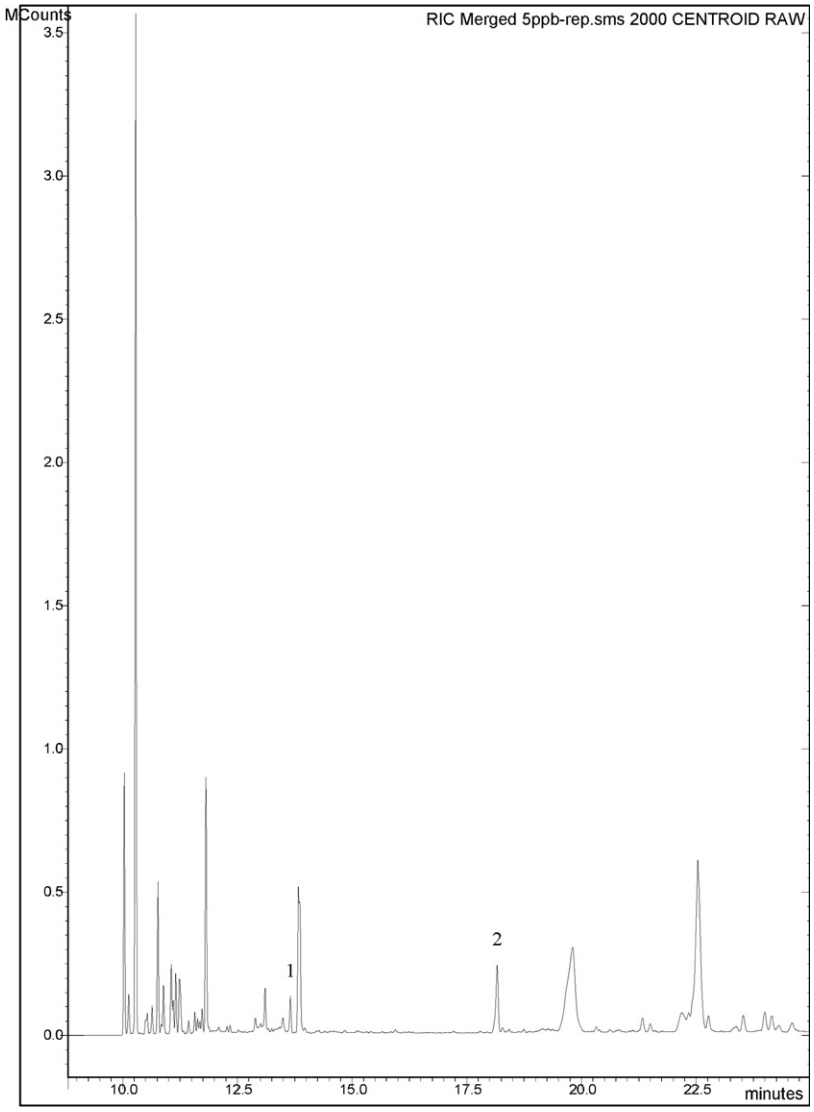


**Fig. 1.** Typical chromatogram of a standard solution (10 μg $L^{-1}$) subject to the USADLLME–GC–MS procedure. (1) MIB; (2) geosmin.

interactions can be completely ignored and so the main effects are only calculated with a reduced number of experiments. A saturated Plackett–Burman matrix was employed because of the large number of factors to be tested. A matrix with 11 factors (six real factors and five dummy factors) was used. The effects of dummy factors were used for the estimation of the experimental error used in the statistical interpretation [30,31].

For each factor two levels were considered (Table 1). The matrix of the Plackett–Burman design was composed of 12 experiments. The experiments were randomly carried out in order to nullify the effect of extraneous or nuisance factors using standard solutions of 10 μg $L^{-1}$ and evaluating the GC peak area of both analytes on each experiment.

**Table 1**
Experimental factors and levels studied on the Plackett–Burman design.

| Factors | Level | |
|---|---|---|
| | Low (−1) | High (+1) |
| Sample volume (mL) | 5 | 10 |
| Solvent volume (μL) | 20 | 50 |
| Extraction temperature (°C) | 20 | 50 |
| Extraction time (min) | 1 | 3 |
| Centrifugation speed (rpm) | 1500 | 2300 |
| Centrifugation time (min) | 3 | 6 |

An ANOVA test was used to evaluate the data and statistically significant effects were determined using a *t*-test with a 95% probability [30,31] and visualized using main effects Pareto charts (Fig. 2).

According to the results, sample and solvent volume were the most significant factors for both target analytes showing a positive and negative effect, respectively.

Pareto charts also reveal that centrifugation speed appeared as a non-significant effect showing a negative sign for both analytes. Despite this value, in this study 2300 rpm was used because sometimes the sedimentation with 1500 rpm was poor.

Extraction temperature appeared to have a positive non-significant effect upon extraction. This result is according to an increased temperature enhancing the diffusion transference. Despite this value, room temperature was chosen because it is easier to control and handle with the ultrasonic bath used. Extraction time appeared to have a negative non-significant effect for geosmin and a positive non-significant effect for MIB, therefore, 3 min were chosen as a compromise value for both analytes. Finally, centrifugation time appeared to have a non-significant negative effect for both analytes and 3 min were chosen.

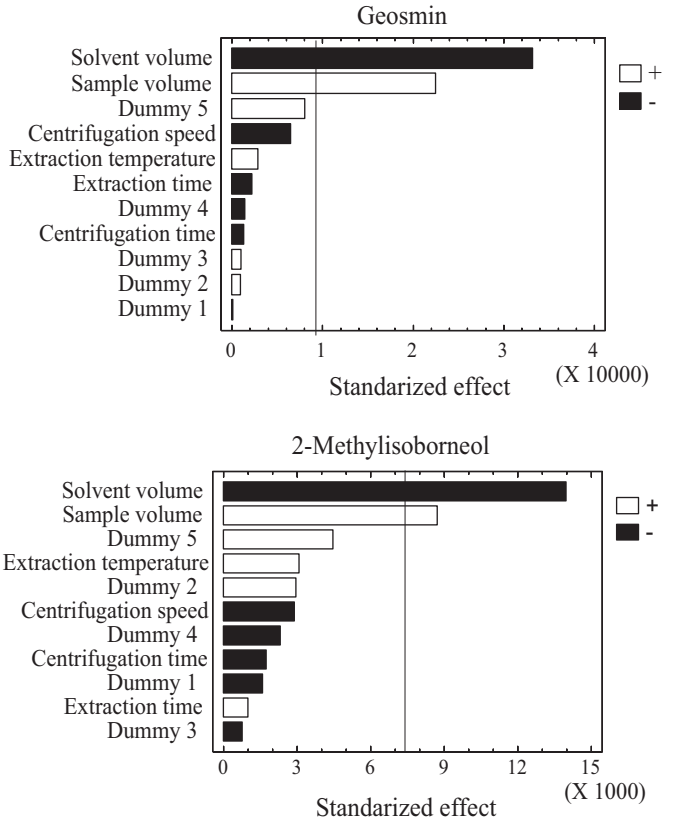


**Fig. 2.** Pareto charts of the main effects obtained from the Plackett–Burman design.

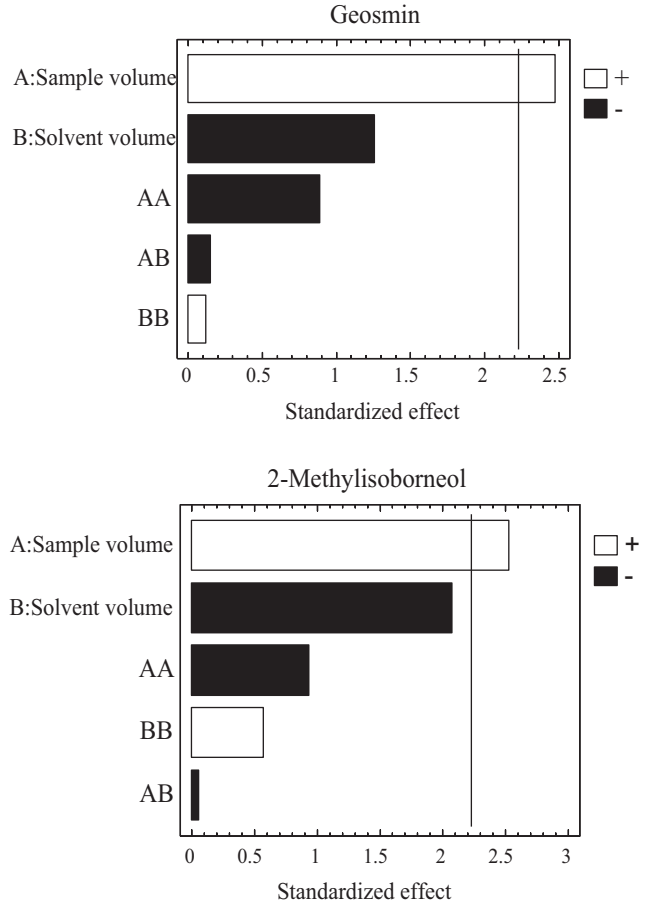


**Fig. 3.** Pareto charts of the main effects obtained from the circumscribed central composite design.

Overall, the results of this first screening study revealed that four factors could be established, centrifugation speed at 2300 rpm, extraction temperature at 20 °C, extraction time at 3 min and centrifugation time at 3 min for the following optimization.

The second study was concerned with optimizing the significant factors in order to obtain the best response. Different experimental designs can be found in the literature, many of them are based on the so-called response surface designs. Box–Wilson or central composite design (CCD) is one of the most used response surface designs, which is constructed by several superimposed designs. It consists of a factorial design ($2^k$) augmented with ($2k$) star points, where $k$ is the number of factors to be optimized, and with a central point, which can be run $n$ times [29]. A circumscribed central composite design (CCCD) was employed, where the star points were located at $\pm\alpha$ from the centre of the experimental domain, which was situated at 0. In order to establish the rotatability of the experimental design, $n$ was set at 2 and $\alpha = \sqrt[4]{2^k}$ [29]. Therefore, the overall matrix of CCCD design involved 16 experiments.

In this study, the two factors considered were: sample volume and solvent volume. The low (−1), central (0), and high (+1) levels of these factors, as well as the location of their star points (±1.414), are given in Table 2.

**Table 2**
Experimental factors and levels studied on the circumscribed central composite design (CCCD).

| Factors | Level | | | Star points ($\alpha$ = 1.414) | |
|---|---|---|---|---|---|
| | Low (−1) | Central (0) | High (+1) | −$\alpha$ | +$\alpha$ |
| Sample volume (mL) | 5.0 | 8.0 | 11.0 | 3.8 | 12 |
| Solvent volume (μL) | 15 | 20 | 25 | 8 | 32 |

The data obtained were evaluated by ANOVA test, and the effects were visualized using Pareto charts (Fig. 3). As can be seen, sample volume is significant showing a positive effect, whilst solvent volume shows a non-significant negative effect upon extraction. Indeed, increasing the sample volume results in an increase in the total amount of analyte extracted, reaching a maximum at 12 mL (+1.414). Solvent volume shows a negative effect, reaching a maximum at 8 μL (−1.414). This negative effect could be attributed to a dilution effect.

Overall, summarizing the results of screening and optimization studies yield the following optimum experimental conditions: sample volume, 12 mL; solvent volume, 8 μL; extraction tempera-

**Table 3**
Main method parameters for the determination of geosmin and MIB in water samples using the optimized USADLLME–GC–MS method.

| Analyte | Correlation coefficient ($r$)[a] | CV (%)[b] | LOD (ng L$^{-1}$)[c] | LOQ (ng L$^{-1}$)[d] |
|---|---|---|---|---|
| Geosmin | 0.9988 | 10.4 | 2 | 7 |
| MIB | 0.9994 | 10.1 | 9 | 30 |

[a] Working range: geosmin: 0.01–1 μg L$^{-1}$ (number of standards = 5; number of repetitions = 3 for each level); MIB: 0.05–1 μg L$^{-1}$ (number of standards = 4; number of repetitions = 3 for each level).
[b] Coefficients of variation (CVs) were calculated for ten replicate analyses at 1 μg L$^{-1}$ spiking level.
[c] Limits of detection (LODs) were calculated for a three signal to noise ratio (S/N = 3).
[d] Limits of quantification (LOQs) were calculated for a ten signal to noise ratio (S/N = 10).

**Table 4**
Comparison of different methods of analysis for the determination of geosmin and MIB.

| Preconcentration method[a] | Linear range (ng L$^{-1}$) | | LOD (ng L$^{-1}$) | | CV (%) | | Solvent extraction (volume) | Extraction time (min) | Sample volume (mL) | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|
| | Geosmin | MIB | Geosmin | MIB | Geosmin | MIB | | | | |
| PT | 10–200 | 10–200 | 2 | 1 | 7.9 | 6.4 | – | 30 | 25 | [3] |
| LLE | 1–500 | 1–500 | 0.1 | 0.1 | 6.3 | 6.9 | Pentane (1 mL) | 30 | 250 | [9] |
| SPME | 10–30,000 | 10–30,000 | 10 | 10 | 7.8 | 11.9 | – | 15 | 6 | [10] |
| SBSE | 0.5–100 | 0.5–100 | 0.15 | 0.33 | 3.7 | 9.2 | – | 20 | 5 | [14] |
| SDME | 5–900 | – | 0.8–3.3 | – | <5 | – | 1-Octanol (2 μL) | 15 | 5 | [15] |
| USADLLME | 10–1000 | 50–1000 | 2 | 9 | 10.4 | 10.1 | Tetrachloroethylene (8 μL) | 3 | 12 | This work |

[a] In all cases GC–MS has been used for separation and quantification.

**Table 5**
Recovery study of geosmin and MIB in different water and wine samples using the proposed USADLLME–GC–MS method at 0.25 μg L$^{-1}$ spiking level.

| Analyte | Found concentration ± $U$ ($k$ = 2)[a] μg L$^{-1}$ (recovery ± CV, %)[b] | | | | |
|---|---|---|---|---|---|
| | Red wine | Rose wine | White wine | Reservoir water | Tap water |
| Geosmin | 0.18 ± 0.03 (72 ± 7) | 0.28 ± 0.05 (112 ± 7) | 0.24 ± 0.06 (96 ± 11) | 0.20 ± 0.04 (80 ± 7) | 0.22 ± 0.06 (88 ± 11) |
| MIB | 0.18 ± 0.04 (72 ± 7) | 0.23 ± 0.05 (92 ± 9) | 0.19 ± 0.06 (76 ± 14) | 0.23 ± 0.03 (92 ± 2) | 0.28 ± 0.05 (113 ± 8) |

[a] $U$ = expanded uncertainty with a coverage factor $k$ = 2, corresponding to a level of confidence of 95%.
[b] Four replicate analyses.

**Table 6**
Recovery study of geosmin and MIB in different water and wine samples using the proposed USADLLME–GC–MS method at 30 ng L$^{-1}$ spiking level.

| Analyte | Found concentration ± $U$ ($k$ = 2)[a] ng L$^{-1}$ (recovery ± CV, %)[b] | | | | |
|---|---|---|---|---|---|
| | Red wine | Rose wine | White wine | Reservoir water | Tap water |
| Geosmin | 21 ± 9 (71 ± 18) | 22 ± 8 (73 ± 14) | 26 ± 9 (87 ± 16) | 22 ± 9 (73 ± 18) | 23 ± 8 (78 ± 16) |
| MIB | 21 ± 19 (70 ± 12) | 22 ± 19 (73 ± 11) | 25 ± 20 (85 ± 15) | 28 ± 21 (85 ± 20) | 25 ± 20 (73 ± 18) |

[a] $U$ = expanded uncertainty with a coverage factor $k$ = 2, corresponding to a level of confidence of 95%.
[b] Four replicate analyses.

ture, 20 °C; extraction time, 3 min; centrifugation speed, 2300 rpm; and centrifugation time, 3 min.

### 3.2. Analytical figures of merit

A calibration study was performed by spiking pure aqueous samples with analytes over the concentration range of 0.01–1 μg L$^{-1}$ and 0.05–1 μg L$^{-1}$ for geosmin and MIB, respectively. The calculated calibration curves gave a high level of linearity for both target analytes with correlation coefficients ($r$) 0.9988 and 0.9994 for geosmin and MIB, respectively, as shown in Table 3. The repeatability of the proposed method, expressed as coefficient of variation (CV), evaluated by extracting and analyzing ten consecutive aqueous samples spiked at 1 μg L$^{-1}$ with each target analyte, was found to be lower than 11%. The limits of detection (LODs) for both target analytes were determined according to a signal-to-noise-ratio (S/N) of three and the limits of quantification (LOQs) as ten times the above mentioned ratio. As can be seen in Table 3 the LODs and LOQs values were found to be 2 and 7 ng L$^{-1}$ for geosmin and 9 and 30 ng L$^{-1}$ for MIB, respectively. Comparison of the USADLLME method developed in this work with other methods of analysis is shown in Table 4. As a compromise between LOD values, extraction time and sample volume USADLLME–GC–MS seems the best option for the analysis of geosmin and MIB. SBSE and PT show lower detection limits but these sample preparation methodologies are more expensive, time consuming and show carry-over problems. In addition, the odour threshold is higher than the LOD values obtained by USADLLME–GC–MS.

### 3.3. Samples analysis

Water (reservoir and tap) and wine (red, rose and white) samples were extracted using the ultrasound-assisted dispersive liquid–liquid microextraction developed method and the extracts were analyzed by GC–MS. Four replicates of water and wine samples were spiked at 0.25 and 0.03 μg L$^{-1}$ with both target analytes and were extracted under the optimized experimental conditions. The preliminary analysis showed that samples were free of geosmin and MIB.

The results for each set of experiments are summarized in Tables 5 and 6. Recovery values range between 72 and 113% at 0.25 μg L$^{-1}$, and between 70 and 87% at 0.03 μg L$^{-1}$, being the lowest for red wine (70–72%).

Expanded uncertainty values were also calculated based on Ref. [32]. Uncertainty of measurement is a component of uncertainty in all individual steps of an analytical procedure. Hence it is necessary to determinate the sources and types of uncertainty for all these steps. Estimation of uncertainty leads to better measurement reliability, renders data from inter-laboratory studies comparable, and helps to assess the statistical significance of the difference between the measurement and a relevant reference value [26,32]. Expanded uncertainty is also included in Tables 5 and 6 (see supplementary content). From the expanded uncertainty values obtained, at 0.25 μg L$^{-1}$ spiking level, a systematic error is concluded for geosmin and MIB on a red wine sample, and for geosmin on a reservoir water sample since reference (spiked) value is not included into the found concentration ± expanded uncertainty intervals. For samples spiked at 0.03 μg L$^{-1}$, no systematic error is concluded for geosmin. Nevertheless, conclusions for MIB cannot be obtained from the expanded uncertainty values obtained since the spiking level is the LOQ value for this analyte.

## 4. Conclusions

A new sample preparation methodology has been developed, based on the use of ultrasound energy to assist the dispersion of

organic extractant on a liquid–liquid microextraction, to preconcentrate geosmin and MIB from water and wine samples before the quantification by GC–MS. Microextraction methodology proposed is environmentally friendly, faster, cheaper and easier to handle than those previously studied for the same purpose. LOD values obtained satisfy the consumer requirements for these analytes on water and wine samples. Therefore, the suggested analytical method (USADLLME–GC–MS) can be an excellent alternative for laboratories which perform routine analysis of these compounds in these kinds of samples.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.chroma.2010.11.007.

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