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Miniaturized Sample Preparation Methods to Simultaneously Determine the Levels of Glycols, Glycol Ethers and Their Acetates in Cosmetics

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Abstract: Two environmentally friendly methodologies based on ultrasound-assisted extraction (UAE) and micro-matrix solid-phase dispersion (μMSPD) followed by gas chromatography-mass spectrometry (GC-MS) analysis are proposed for the first time for the simultaneous analysis of 17 glycols, glycol ethers, and their acetates in cosmetics. These sample preparation approaches result in efficient and low-cost extraction while employing small amounts of sample, with a low consumption of reagents and organic solvents. The use of a highly polar column allows for the direct analysis of the obtained extracts by GC-MS without a previous derivatization step, drastically reducing the sample preparation time and residues and thus complying with green analytical chemistry (GAC) principles. Both the UAE and μMSPD methodologies were validated in terms of linearity, accuracy, and precision, providing satisfactory results. LODs were found to be lower than 0.75 μg g^{-1}, allowing the determination of trace levels of the forbidden target compounds. Finally, the validated methodologies were applied to real cosmetics and personal care products, showing suitability, and providing a reliable and useful tool for cosmetics control laboratories.

Keywords: glycol ethers; glycol ether acetates; glycols; sample preparation; green chemistry; micro-matrix solid-phase dispersion; ultrasound-assisted extraction; gas chromatography; mass spectrometry

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1. Introduction

Glycol ethers are chemical compounds that exhibit the solubility characteristics of both ethers and alcohols. Therefore, they are soluble in water as well as in many organic solvents [1]. These features lead to their wide application in both organic and water-based products. Typically, glycol ethers are categorized as ethylene oxide-based glycol ethers (e-series) and propylene oxide-based glycol ethers (p-series). P-series glycol ethers are usually employed in aerosol paints and adhesives, whereas the e-series derivatives are mainly found in pharmaceutical and cosmetic products, and are used as a low-cost replacement for fatty acid isopropyl esters [2].

Their physicochemical characteristics convert glycol ethers into effective solvents and viscosity-reducing agents in cosmetics and personal care products, serving as coupling agents promoting the miscibility of aqueous and organic phases. However, their legal requirements as cosmetic ingredients are very different according to European Regulation EC No 1223/2009 [3]. The presence of several glycol ethers and their derived acetates is permitted in these products (Annex III of Regulation EC No 1223/2009) [3], although the maximum allowed concentration in the final product depends on the type of cosmetics and the area of application. On the other hand, extensive scientific evidence has shown that lower-molecular-weight e-series glycol ethers and their acetates have toxic effects

on reproduction [4]. Among them, ethylene glycol monoethyl ether (EGEE) and its acetate, ethylene glycol monoethyl ether acetate (EGEEA), stand out, and have both been classified as being toxic for reproduction and teratogenic [5]. Other congeners such as ethylene glycol monomethyl ether (EGME) and ethylene glycol monomethyl ether acetate (EGMEA) are efficiently absorbed via dermal penetration. EGMEA is rapidly converted to EGME in the body, with both compounds being hazardous for human health [4,6]. Therefore, their presence in the final cosmetic product is forbidden (Annex II of the Cosmetics Regulation) [3].

Glycols are the main glycol ether precursors. Several, such as ethylene glycol (ETG) or tetramethylene glycol (TMG), are allowed as ingredients in cosmetics, while the presence of traces of diethylene glycol (DEG) is also permitted when technically unavoidable during the manufacturing of cosmetic products.

Thus, the development of an analytical methodology that can detect maximum concentrations in order to fulfill legal requirements and can also be used to identify trace levels of forbidden glycol ethers and their derivatives in cosmetics is mandatory to ensure consumer health. Official methodologies available focus on a limited number of compounds to be determined in materials that differ from cosmetic matrices. Additionally, these methodologies are usually based on the use of gas chromatography (GC) with a flame ionization detector (FID) and relative retention times. An example is the method published by the European Pharmacopoeia that is indicated as a reference method for the identification of just two glycol ethers (ETG and DEG) in ethoxylated substances. In 2010, Environment Canada (EC) published a reference method based on gas chromatography-mass spectrometry (GC-MS) for the analysis of 2-butoxyethanol (ethylene glycol butyl ether) and 11 other glycol ethers in selected products (automotive and household cleaners, paints, paint strippers and solvents) not including cosmetics.

To the best of our knowledge, only two works in the literature have been reported to determine some target compounds in cosmetic products [7,8]. In both cases, solid-liquid extraction (SLE) was employed for extraction, although sequential steps as well as further procedures such as clean-up or derivatization were required, resulting in laborious experimental procedures involving high solvent and time consumption.

In recent years, green analytical chemistry (GAC) principles have been implemented in cosmetics analysis, with the substitution of hazardous chemicals and solvents with environmentally friendly alternatives and the miniaturization of classical extraction procedures [9,10]. In this way, the inclusion of ultrasound energy (which is environmentally friendly with low energy consumption) to assist solvent extraction allows for a reduction in the extraction time, resulting in a high extraction yield. Another advantage of using ultrasound assisted extraction (UAE) is the lower cost of instrumentation and its compatibility with any solvent.

A miniaturization of classical matrix solid-phase dispersion (known as micro-MSPD (μMSPD)) using disposable low-cost material also constitutes a suitable alternative to classical extraction procedures. The main advantage of μMSPD is that a small sample size (0.1 g) and low organic solvent consumption (1 mL) are required. In addition, the inclusion of an in situ cleaning step during the extraction procedure avoids the need for further clean-up steps such as SPE, drastically reducing the extraction time and possible analyte losses. The combination of UAE- and μMSPD-based methodologies with GC-MS has been successfully employed for the analysis of both allowed cosmetic ingredients as well as trace levels of banned or unexpected compounds, showing suitability for application to complex matrices such as cosmetic formulations [11–13]. However, UAE and μMSPD have never been applied to determine the content of glycol ethers and derived compounds in cosmetics as effective alternatives to classical SLE methodologies.

The main goal of this work is the validation of two miniaturized and environmentally friendly methodologies based on UAE and μMSPD followed by GC-MS analysis to simultaneously analyze 17 compounds, including glycols, glycol ethers, and their acetates in leave-on and rinse-off cosmetics.

2. Materials and Methods

2.1. Chemicals, Reagents, and Materials

The 17 target compounds, their CAS numbers, and EU regulation requirements in cosmetics are summarized in Table 1. Methanol was supplied by Sigma-Aldrich Chemie GmbH (Steinheim, Germany) and acetone was provided by Fluka Analytical (Steinheim, Germany). Anhydrous sodium sulfate, Na_2SO_4 (99%) was obtained from Panreac (Barcelona, Spain). Florisil® (60–100 µm mesh) and glass wool were purchased form Supelco Analytical (Bellefonte, PA, USA). All reagents were of analytical grade.

Table 1. Target compounds. Suppliers, CAS number, and current EU restrictions in cosmetics.

Acronym	Common Name	CAS	EU Restrictions [3]
	Glycols		
ETG [a]	Ethylene glycol	107-21-1	Allowed as a humectant, solvent, and for viscosity control
DEG [a]	Diethylene glycol	111-46-6	Forbidden, except as traces in ingredients (0.1%)
TMG [a]	Tetramethylene glycol	110-63-4	Allowed as solvent
	Glycol ethers		
EGME [a]	Ethylene glycol monomethyl ether	109-86-4	Forbidden
EGDME [a]	Ethylene glycol dimethyl ether	110-71-4	Forbidden
EGEE [a]	Ethylene glycol monoethyl ether	110-80-5	Forbidden
EGBE [b]	Ethylene glycol monobutyl ether	111-76-2	Forbidden in aerosol dispensers (sprays); 4% (oxidative hair dyes); 2% (non-oxidative hair dyes)
DEGME [a]	Diethylene glycol monomethyl ether	111-77-3	Forbidden
DEGDME [a]	Diethylene glycol dimethyl ether	111-96-6	Forbidden
DEGEE [b]	Diethylene glycol monoethyl ether	111-90-0	Forbidden in eye and oral products; 7% (oxidative hair dyes); 5% (non-oxidative hair dyes); 10% (other leave-on products); 2.6% (other non-spray products); 2.6% (sprays: fine fragrance, hair sprays, antiperspirants, deodorants). In all cases, ETG $\leq$ 0.1%.
DEGBE [b]	Diethylene glycol monobutyl ether	112-34-5	Forbidden in aerosol dispensers (sprays); 9% (solvent in hair dye products)
PGME [a]	Propylene glycol monomethyl ether	1589-47-5	Forbidden
TEGDME [a]	Triethylene glycol dimethyl ether	112-49-2	Forbidden
	Glycol ether acetates		
EGMEA [a]	Ethylene glycol monomethyl ether acetate	110-49-6	Forbidden
EGEEA [a]	Ethylene glycol monoethyl ether acetate	111-15-9	Forbidden
PGMEA [a]	Propylene glycol monomethyl ether acetate	108-65-6	Allowed as solvent
iPGMEAb [a]	Isopropylene glycol monomethyl ether acetate	70657-70-4	Forbidden

[a] Sigma-Aldrich Chemis (Darmstard, Germany) [b] Tokio Chemical Industry (TCI, Tokyo, Japan).

Individual stock solutions for each compound (about 20 mg mL^{-1}) were prepared in methanol. Further dilutions and mixtures were prepared in methanol (calibration curve) or in acetone (spike solutions). For the daily evaluation of the GC-MS instrument, a methanolic solution containing the 17 target compounds at 1 µg mL^{-1} was employed. Diluted solutions were prepared weekly. All solutions were stored protected from light at −20 °C.

2.2. Cosmetic Samples

Two cosmetic samples, a moisturizing hand cream (leave-on) and a shower gel (rinse-off), were selected to validate the proposed methodology. The absence of the target compounds was verified to avoid overestimation in the results.

Different samples were also selected to show the suitability of the proposed methodology, including a liquid soap, a solid soap, and a body milk intended for children. All products were purchased in local markets. They were kept in their original containers and protected from light at room temperature until their use.

2.3. UAE Procedure

The experimental UAE procedure was adapted from that previously optimized by the authors for the determination of fragrances, preservatives, and musks in cosmetics [11]. Briefly, 0.1 g of the cosmetics sample was weighted into a 10 mL glass vial and 2 mL of methanol was added. The vial was sealed with an aluminum cap furnished with polytetrafluoroethylene (PTFE), and introduced in an ultrasound bath (J Selecta (Barcelona, Spain)) for 10 min at 50 kHz and 25 °C. Afterwards, the obtained extract was diluted 1:5 v/v with methanol, filtered through 0.22 µm PTFE filters, and analyzed using GC-MS.

2.4. Micro-MSPD Procedure

The µMSPD procedure was adapted from that previously optimized by the authors for the extraction of fragrances, UV filters, or preservatives from cosmetic and personal care products [12,13]. Briefly, 0.1 g of the cosmetics sample was weighted into a 10 mL glass vial. Then, the sample was gently blended with 0.2 g of Na_2SO_4 (drying agent), and 0.4 g of Florisil® (dispersing agent) into the vial, using a glass rod, until a homogeneous mixture was obtained. The mixture was then transferred into a glass Pasteur pipette (150 mm), which contained a small amount of glass wool at the bottom and about 0.1 g of Florisil® to obtain a high fractionation degree and an in situ clean-up step. Finally, a small amount of glass wool was placed on the top to compress the mixture. Elution with methanol was carried out by gravity flow, collecting 1 mL of extract in a volumetric flask. The obtained extracts were diluted 1:10 (v/v) in methanol, filtered, and analyzed by GC-MS. Figure 1 illustrates the UAE and µMSPD experimental procedures.

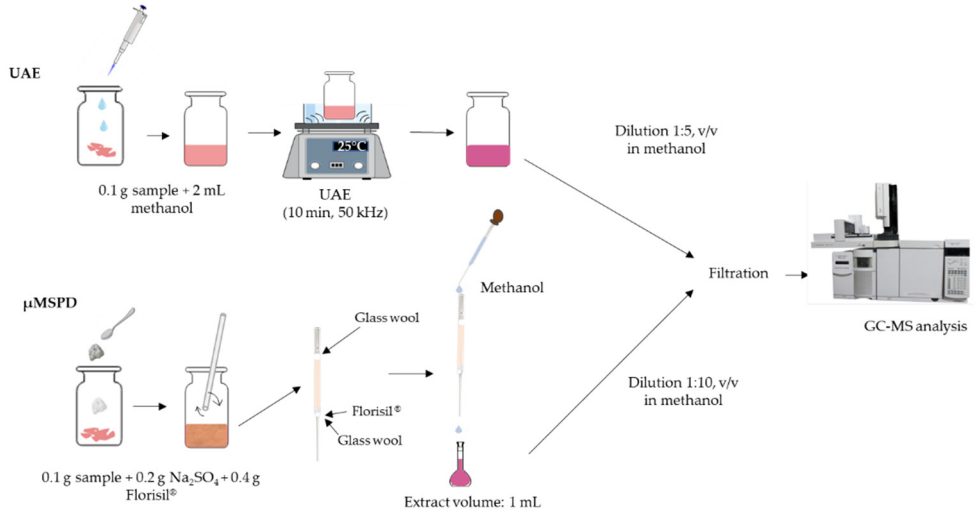

Figure 1. Schematic representation of the UAE and µMSPD experimental procedures.

For the recovery studies, the sample was spiked with 50 µL of an acetonic solution containing the target compounds at 200 µg mL^{-1}, and the corresponding procedure described above was carried out. Blanks were daily processed to evaluate the presence of the target compounds during the experimental procedure.

2.5. GC-MS Analysis

The GC-MS analysis was performed using an Agilent 7890A coupled to an Agilent 5975C inert mass spectra detector (MSD) with a triple-axis detector and an Agilent 7693 autosampler from Agilent Technologies (Palo Alto, CA, USA). The separation was achieved employing a J&W Scientific DB-WAX 128-7052 (50 m × 0.20 mm i.d., 0.2 µm film thickness) column obtained from Agilent Technologies. The chromatographic ramp ranged from 40 °C (held 1 min) to 240 °C at 8 °C min^{-1}. The total run time was 29 min. Helium (purity 99.999%) was employed as carrier gas at a constant flow of 0.8 mL min^{-1}. The sample volume was 1 µL, and the injector temperature was set at 240 °C. The mass spectrometer detector (MSD) was operated in the electron impact (EI) ionization positive mode (+70 eV). The temperature of the ion source was 150 °C and the transfer line temperature were set at 240 °C. The selected ion monitoring (SIM) acquisition mode was employed, monitoring 3 or 4 mass/charge (*m/z)* fragments for each compound for an unequivocal identification.

2.6. Analytical Quality Parameters

The proposed UAE- and µ-MSPD-GC-MS methodologies were validated in terms of linearity, precision, and accuracy. Calibration standards were prepared in methanol, covering a concentration range between 2 and 2000 µg L^{-1} with 9 levels and 3 replicates per level. The instrumental method precision was evaluated within a day (n = 3), and among days (n = 6) for all the calibration concentration levels. To assess the accuracy of the proposed methodology, recovery studies were carried out employing two cosmetics samples: a leave-on moisturizing hand cream and a rinse-off shower gel. The samples were spiked at 100 µg g^{-1} with all compounds (equivalent to 1 µg g^{-1} in the injected extracts). The spiked samples were extracted by UAE and µMSPD in triplicate and analyzed by GC-MS. Limits of detection (LODs) were calculated as the compound concentration giving a signal-to-noise ratio of 3 (S/N = 3), employing samples spiked with the target compounds.

3. Results and Discussion

3.1. Chromatographic Separation

The target compounds were formed by glycol units, alkyl ethers, or acetates that provide them certain polarity. Due to their unique amphiphilic structures, their simultaneous determination supposes a challenge from an analytical point of view. Liquid chromatography (LC) and GC are the most commonly employed separation techniques. However, in most cases, a previous derivation step is implemented to improve chromatographic response [14,15]. As is well known, derivatization procedures have several drawbacks, in addition to being tedious and time consuming. A very suitable alternative to directly analyzing extracted glycol ethers and their derivatives by GC is the use of a high-polarity chromatographic column packed with polyethylene glycol (PEG). The incorporation of the oxygen group in the backbone creates a phase with a high selectivity for polar analytes, such as those analyzed in this work, allowing satisfactory analyte separation and peak resolution [16,17].

Since the objective of this work was to develop a sensitive analytical methodology able to detect even trace levels of the forbidden target compounds, mass spectrometry (MS) in the SIM mode was employed. The retention times for the 17 target compounds and selected quantification and identification MS ions are summarized in Table 2.

Table 2. Retention time, quantification, and identification of MS ions for the 17 target compounds.

Compounds	Retention Time (Min)	Quantification *m/z* Ion	Identification *m/z* Ions
Glycols			
ETG	17.06	31	33, 43, 62
DEG	21.97	75	45, 76
TMG	21.18	71	44, 57

Table 2. *Cont.*

Compounds	Retention Time (Min)	Quantification *m/z* Ion	Identification *m/z* Ions
Glycol ethers			
EGME	9.91	45	58, 76
EGDME	7.16	60	45, 90
EGEE	10.59	59	45, 72
EGBE	13.57	57	87, 100
DEGME	16.57	59	58, 90
DEGDME	12.32	59	58, 89
DEGEE	17.04	59	72, 104
DEGBE	19.56	57	75, 87, 100
PGME	10.32	59	60, 75
TEGDME	18.52	103	59, 89, 133
Glycol ether acetates			
EGMEA	10.99	58	43, 73
EGEEA	11.64	72	59, 87
PGMEA	10.49	43	72, 87
iPGMEA	10.96	59	43, 72

Figure 2 provides the obtained chromatogram for the 17 target compounds, showing good separation and complete identification in less than 22 min.

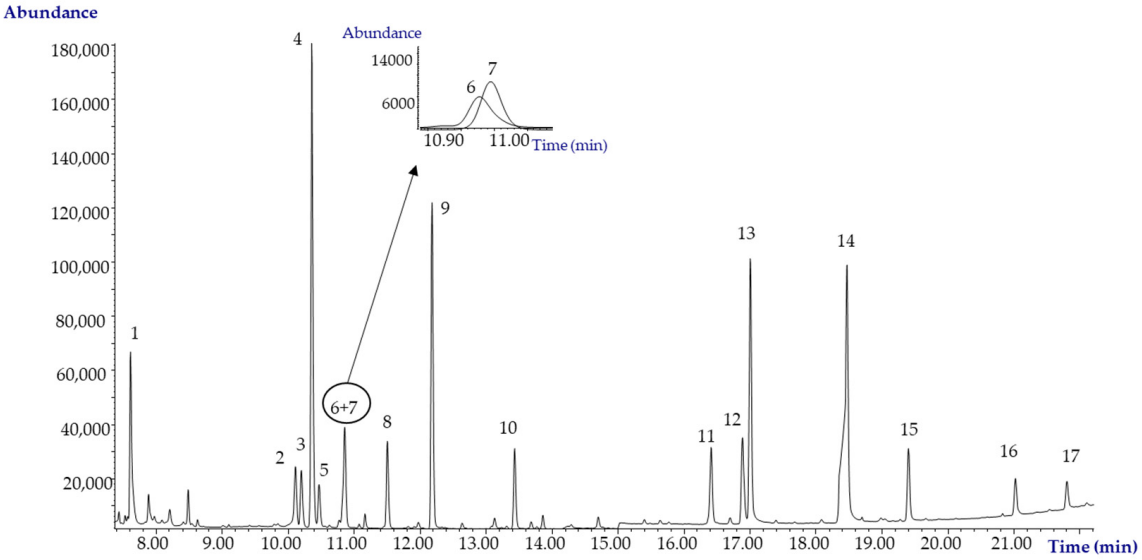

Figure 2. Total ion chromatogram (TIC) for a standard solution containing the 17 target compounds at 1 μg mL^{-1} prepared in methanol. Codes: 1: EGDME; 2: EGME; 3: PGME; 4: PGMEA; 5: EGEE; 6: iPGMEA; 7: EGMEA; 8: EGEEA; 9: DEGDME; 10: EGBE; 11: DEGME; 12: DEGEE; 13: ETG; 14: TEGDME; 15: DEGBE; 16: TMG; 17: DEG.

3.2. UAE and μMSPD-GC-MS Performance

In both cases, the UAE- and μMSPD-GC-MS methodologies were deeply validated in terms of linearity, repeatability, reproducibility, and accuracy. Limits of detection (LODs) were also calculated. The GC-MS method exhibited a direct proportional relationship between the amount of each analyte and its chromatographic response, with coefficients of determination (R^2) higher than 0.9935 in all cases, as can be seen in Table 3.

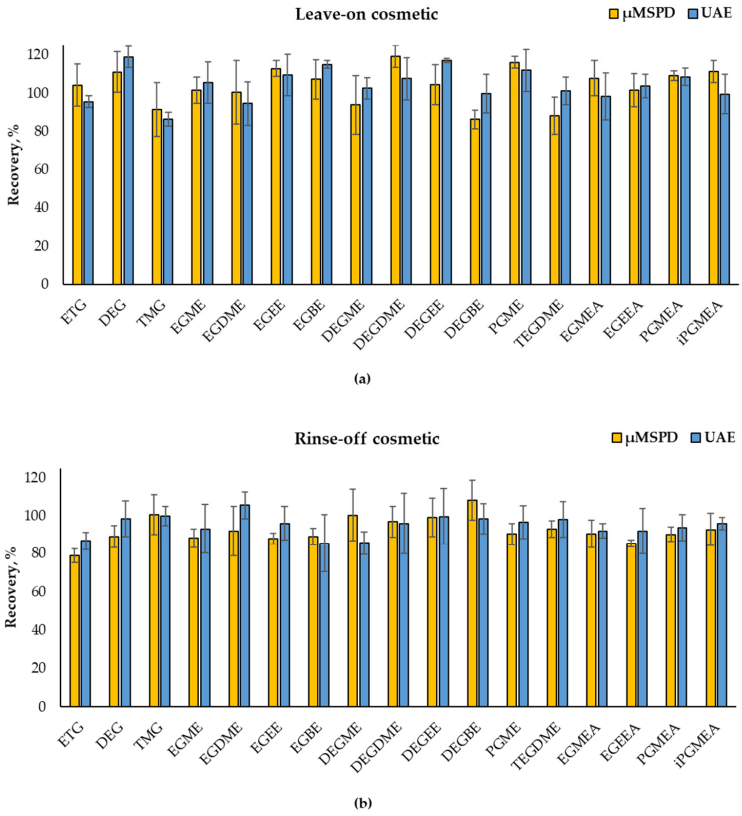

Figure 3. Individual recovery values (%) for the UAE- and µMSPD-GC-MS methodologies for: (**a**) leave-on and (**b**) rinse off cosmetics samples.

Table 3. UAE- and µMSPD-GC-MS performance. Linearity, accuracy, precision, and LODs.

Compounds	Linearity		Precision, RSD %		Recovery, % [a]		LODs (µg g^{-1}) [b]	
	Linear Range (µg L^{-1})	R^2	Intra-Day	Inter-Day	UAE	µMSPD	UAE	µMSPD
Glycols								
ETG	2–2000	0.9987	9.1	7.7	91 ± 6	92 ± 18	0.20	0.10
DEG	2–2000	0.9992	4.6	3.9	109 ± 14	100 ± 16	0.30	0.40
TMG	2–2000	0.9999	2.2	14	93 ± 10	96 ± 7	0.45	0.40
Glycol ethers								
EGME	2–2000	0.9941	6.5	4.9	99 ± 9	95 ± 9	0.19	0.10
EGDME	5–2000	0.9992	8.0	8.1	100 ± 8	96 ± 6	0.43	0.44
EGEE	2–2000	0.9947	0.8	0.7	103 ± 10	101 ± 18	0.25	0.21
EGBE	2–2000	0.9977	4.2	3.0	100 ± 20	98 ± 13	0.25	0.14
DEGME	2–2000	0.9991	4.2	6.4	94 ± 12	97 ± 5	0.75	0.38
DEGDME	2–2000	0.9952	4.0	3.3	102 ± 8	108 ± 16	0.07	0.03
DEGEE	5–2000	0.9984	3.6	3.1	108 ± 12	102 ± 4	0.75	0.43
DEGBE	5–2000	0.9988	0.1	5.6	99 ± 1	97 ± 15	0.50	0.30
PGME	2–2000	0.9959	8.0	5.8	104 ± 11	103 ± 18	0.25	0.11
TEGDME	2–2000	0.9991	13	9.4	100 ± 2	91 ± 4	0.30	0.31
Glycol ether acetates								
EGMEA	5–2000	0.9955	0.6	3.3	95 ± 4	99 ± 12	0.55	0.25
EGEEA	5–2000	0.9980	9.8	7.2	98 ± 8	94 ± 11	0.60	0.33
PGMEA	2–2000	0.9935	3.6	2.7	101 ± 10	100 ± 13	0.20	0.08
iPGMEA	2–2000	0.9947	2.5	2.6	98 ± 3	102 ± 13	0.15	0.08

[a] Mean recovery values for leave-on and rinse-off spiked samples. Individual recoveries are depicted in Figure 3. [b] LODs calculated for the leave-on sample.

Instrumental method precision was also evaluated. Relative standard deviation (RSD) values for 100 μg L^{-1} are shown in Table 3. In all cases, the RSD values were lower than 13% and 14% for repeatability and reproducibility, respectively, with mean values of about 5%. The mean recovery values obtained after performing extraction by UAE and μMSPD are summarized in Table 3 (see experimental procedure in Section 2.4). As can be seen, good accuracy and precision were achieved, with mean recovery values between 91% and 108% and relative standard deviation (RSD) values lower than 18%. The individual recovery values for each sample type and extraction technique are depicted in Figure 3. In all cases recoveries ranged between 79% and 116%. The LODs for the leave-on sample are depicted in Table 3, and ranged between 0.07 and 0.75 μg g^{-1} for UAE. For μMSPD they were slightly lower, at between 0.03 and 0.44 μg g^{-1}. This could be attributed to the fact that μMSPD includes an in situ clean-up step that provides cleaner extracts than UAE. In any case, obtained LODs were well below the Cosmetics Regulation requirements, allowing the detection of trace levels of the considered compounds.

3.3. Comparison with Other Methodologies

Since few works have been reported with regard to the identification of glycol ethers in cosmetics [7,8], the proposed methodologies were also compared with those applied to household and cleansing products [17,18]. As it is shown in Table 4, few of the target compounds considered in this work have been simultaneously analyzed. Besides, several of the reported sample preparation methodologies include a derivatization step, resulting in experimental procedure times of up to 3 h.

Table 4. A comparison of the proposed UAE- and μMSPD-GC-MS methodologies with other reported methods for the analysis of glycol ethers in cosmetics and household products.

Analytes	Matrix	Extraction Technique	Extraction Time	Analysis	Recovery (%)	LODs (μg g^{-1})	Year	Ref.
10 glycol ethers and their acetates	Cosmetics (0.5 g)	SLE	19 min	GC-MS	80–105	0.09–0.59	2018	[7]
EGME	Cosmetics (0.1 g)	SLE + derivatization	>3 h	HPLC-UV [a]	84–89	0.6–7.6	1999	[8]
12 glycols, glycol ethers, and their acetates	Household water-based sprays (0.5 mL)	SPE	-	GC-MS	42–103	0.04–1.3	2017	[17]
6 glycol ethers	Household cleaning products, detergents (2 g)	QuEChERS [b]	5 min	GC-MS	89–115	0.01–1	2016	[18]
17 glycols, glycol ethers, and their acetates	Cosmetics (0.1 g)	μMSPD, UAE	10 min	GC-MS	79–116	0.03–0.75	2021	This work

[a] HPLC-UV: High-performance liquid chromatography with ultraviolet detection. [b] QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe.

Compared with other analytical methodologies based on GC-MS, the proposed UAE and μMSPD-GC-MS methods present lower LODs (up to one order of magnitude for some compounds) than those reported for the analysis of glycol ethers in cosmetics, and similar or even lower values than those reported for household products, which are usually more simple water-based matrices than cosmetics. Other advantages of the proposed procedures include the fact that small amounts of sample (0.1 g) and only 1–2 mL of organic solvent (methanol) are required. Besides, for μMSPD, the inclusion of an in situ clean-up step

allows a high fractionation degree, obtaining clean extracts in 10 min that can be directly injected into the chromatographic system without further preparation steps.

3.4. Application to Real Samples

In view of the results, it can be confirmed that both validated procedures (UAE- and μMSPD-GC-MS) are equally suitable for the analysis of target compounds in cosmetic samples. Therefore, as either of them can be applied interchangeably for the analysis of cosmetics, the results obtained by applying the UAE-GC-MS method are given. Samples include leave-on (liquid and solid soaps) and rinse-off (body milk intended for children) products. Results, expressed as μg g^{-1}, are shown in Table 5.

Table 5. Concentration (μg g^{-1}) of the target compounds in the analyzed samples.

Analytes	Liquid Soap	Solid Soap	Body Milk
ETG	9.7 ± 0.8	8.2 ± 1.3	14 ± 3
DEG	7.0 ± 2.7	16 ± 3	15 ± 1
DEGEE	ND	ND	9.4 ± 0.7

ND: not detected.

Only 2 glycols (ETG, DEG) and 1 glycol ether (DEGEE) out of the 17 target compounds were detected in the analyzed samples, with concentrations ranging between 7 and 16 μg g^{-1}. Although the detected compounds were not labeled in the products, they would fulfill with the EU cosmetics regulation requirements. ETG is allowed as an ingredient without maximum concentration restrictions. DEG was found at ultra-trace concentrations in all analyzed samples (the maximum allowed concentration is 1000 μg g^{-1} (0.1% *w*/*w*)). DEGEE, which was only found in the body milk sample, is allowed in leave-on cosmetics up to 100,000 μg g^{-1} (10% *w*/*w*) in the final product.

4. Conclusions

Two fast, easy to use, sustainable, and environmentally friendly methodologies based on UAE and μMSPD are proposed as simple alternatives to classical sample preparation procedures for the analysis of glycols, glycol ethers, and their acetates in leave-on and rinse-off cosmetics. Both procedures involve the use of small amounts of sample (0.1 g), and a low volume (1–2 mL) of organic solvent is required. The use of GC-MS employing a highly polar chromatographic column provides the required chromatographic resolution, selectivity, and analyte sensitivity without the need for prior derivatization.

Both methodologies were successfully validated in terms of linearity, repeatability, and reproducibility. Recovery studies were also performed and were quantitative for leave-on and rinse-off cosmetic matrices. LODs were lower than 0.75 μg g^{-1} for all compounds, allowing the detection of trace levels of the forbidden compounds. Therefore, the combination of UAE and/or μMSPD with GC-MS is presented here as a very suitable tool for cosmetics control laboratories and manufacturers to determine levels of glycols, glycol ethers, and their derivatives in the final products, assuring cosmetics quality, legal compliance, and, above all, consumer and user health and safety.

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