Sample Preparation for Cosmetics Analysis

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Traditional cosmetics sample preparation techniques involve liquid–liquid extraction (LLE) and solid–liquid extraction (SLE). In last years, modern sample extraction techniques are advancing towards fast sample processing, easy automatization, as well as a reduction in organic solvent volumes, in agreement with the green chemistry principles in two ways (i) the miniaturization of conventional procedures allowing a reduction of the solvents and reagents consumption and (ii) the development and application of sorbent- and liquid-based microextraction technologies to obtain a high analyte enrichment, avoiding or significantly reducing the use of organic solvents.

sample preparation | microextraction techniques | miniaturization | cosmetics | personal care products

1. Introduction

The use of cosmetics and personal care products is increasing worldwide, and Europe is a key market for the cosmetics industry. In fact, the European cosmetic market generated more than EUR 120,000 billion in 2019. The Regulation 1223/2009 [1] includes the definition of cosmetic, and establishes rules to be complied with by any cosmetic product made placed on the market, to ‘ensure the functioning of the internal market and a high level of protection of human health’. For this purpose, it provides a ‘List of substances prohibited in cosmetic products’ (Annex II) which currently involves more than 1400 chemical compounds. On the other hand, Annex III lists the substances allowed for their use as cosmetic ingredients, although most of them present restrictions in terms of maximum permitted concentration depending on the use of the final product or the product type. Besides, different positive lists of substances for several ingredient families, such as colorants, preservatives, and UV filters (Annexes IV, V and VI, respectively) are included [2]. It is important to note that, although the Regulation 1223/2009 entered into force in 2013, it is continuously revised and updated (with more than 60 amendments since its entry into force).

From the point of view of their composition, cosmetics are very complex, with variable matrices formed by a high number of substances from highly lipophilic to moderately polar, or exhibiting basic, acidic, or neutral properties. In addition, it is quite frequent that technical mixtures containing impurities or unknown or banned/unexpected compounds that can be formed by the reaction of compounds become present in the formulation under particular exposition conditions [3].

In recent years, several reviews covering this topic have been published [2][4][3][5][6][7] , most of them focused on specific types of cosmetics ingredients such as fragrances, preservatives or dyes since they are the most common compounds present in the formulations [2][8][9]. Regarding the reported sample preparation methodology for cosmetics analysis, traditional liquid–liquid extraction (LLE) and solid–liquid extraction (SLE) are still employed, although the use of advanced techniques such as ultrasound-assisted extraction (UAE), solid phase extraction (SPE), matrix solid-phase dispersion (MSPD) or pressurized liquid extraction (PLE) is growing. In recent years, green analytical chemistry (GAC) principles have been increasingly implemented for cosmetics analysis through the miniaturization of classical extraction procedures, as well as the substitution of hazardous chemicals and solvents by environmentally friendly alternatives, as the main objective is to improve their environmental friendliness without compromising method performance [10][11][12].

Due to the capability of several compounds present in cosmetics, such as UV filters or some plasticizers, to absorb light in the UV-Vis spectrum, diode-array detector (DAD) was the preferred detection method after LC separation. However, due to its low specificity, which complicates quantifying multiple compounds in complex sample matrices, such as cosmetics, the combination of GC or LC with mass spectrometry (MS) or tandem mass spectrometry (MS/MS) detection became the most suitable option. This approach improves the analytical selectivity and sensibility, allowing the detection of the target analytes at trace levels, which is especially important to identify the impurities and banned compounds. In recent years, the use of high-resolution mass spectrometry (HRMS), mainly based on QTOF detection, has started to play a more important role for multitarget analysis.

2. Sample Preparation Strategies for Cosmetics Analysis

Traditional cosmetics sample preparation techniques involve liquid–liquid extraction (LLE) and solid–liquid extraction (SLE). However, the main drawback of SLE and LLE is their high organic solvent (hundreds of mL) and time consumption. On the other hand, modern sample extraction techniques are advancing towards fast sample processing, easy automatization, as well as a reduction in organic solvent volumes, in agreement with the green chemistry principles. In this way, ultrasound-assisted extraction (UAE), solid-phase extraction (SPE), pressurized liquid extraction (PLE) and matrix solid-phase dispersion (MSPD) are techniques that can be considered environmentally friendly, as most of them easily miniaturized.

One of the most employed nowadays is MSPD. In comparison with other extraction techniques that use high pressure such as PLE, or the application of supplementary energy like UAE, MSPD extraction is performed at ambient conditions, being not necessary any special equipment. In addition, the possibility of performing extraction and an *in-situ* clean up, reduce the sample preparation time, also decreasing the required amount of solvent. MSPD was introduced in 1989 by Barker et al. for the determination of drug residues in animal tissue [13]. Since then, it has attracted growing interest for its versatility and possibility of application to a broad range of solid, semisolid, or viscous matrices. The general procedure consists on the direct mechanical blending of the sample (with a dispersant agent) in a mortar until the obtention of an homogeneous and dispersed material that is transferred to a cartridge and compressed. Analytes elution is performed by passing through the column the correspondent solvent by gravity or vacuum assisted.

MSPD first application to cosmetics samples was in 2011 to determine fragrance allergens and multiclass preservatives (parabens, bromine derivatives and antioxidants) in rinse-off and leave-on cosmetics [14][15] and in baby care products [16] before GC-MS analysis. The most critical experimental parameters such as dispersant, elution solvent and volume were optimized by DoE (design of experiments) to obtain the highest extraction efficiency. In all cases, the experimental conditions involved the use of 0.5 g of sample, 2 g of Florisil® as dispersant agent and elution was accomplished with 5 mL of hexane/acetone (1:1, v/v). For preservatives determination, the MSPD obtained extracts were derivatized employing anhydride acetic to improve the chromatographic analysis of those containing hydroxyl groups such as parabens. The acetylation procedure was also optimized to obtain a quantitative reaction yield in a short time (10 min) [15]. Other preservatives family, isothiazolinones, were also successfully extracted from cosmetic matrices by MSPD. In this case, methanol resulted as the optimal elution solvent, and analysis was performed LC-MS/MS [17]. In all cases, quantitative recoveries and LODs at the low ng g^{-1}, were obtained, well below the legal requirements for those restricted compounds.

In order to reduce sample and solvent consumption, a miniaturization of the classical MSPD, µMSPD, was proposed for the first time in 2013 for the simultaneous analysis of plasticizers (phthalates and adipates) and synthetic musks in cosmetics and personal care products [18]. Later, µMSPD has been successfully applied for the determination of other cosmetic ingredients including dyes, fragrances, preservatives [19][20][21][22][23][24] as well as for the multianalyte determination of a high number of allowed and restricted ingredients, and banned compounds such as glucocorticoids [25][26]. Recently, this miniaturized approach has been also applied to extract impurities or unexpected compounds, such as polycyclic aromatic hydrocarbons (PAHs), fungicides, nitrosamines, or alkylphenol ethoxylates (APEOs) from cosmetics formulations. In this case, analysis was performed by GC-MS or LC-MS/MS, depending on the chemical properties of the target analytes. In general, obtained LODs were at the very low ng g^{-1} concentration levels, showing that the combination of µMSPD with chromatography and mass spectrometry detection is a suitable option to determine trace levels of impurities and banned compounds with different chemical nature [27].

It is important to highlight that the use of the µMSPD approach allows a reduction of the extraction costs since it employs disposable common laboratory use material such as pipette tips or glass Pasteur pipettes. The substitution of the classical plastic MSPD cartridges by glass material is a very suitable and low-cost option for the determination of ubiquitous compounds such as plasticizers, reducing possible interferences during sample preparation. Other advantages of the µMSPD in comparison with classical MSPD is the reduction of the sample amount, reagents, and organic solvents consumption. In most cases, satisfactory results were achieved employing only between 0.05-0.1 g of sample. Regarding elution solvent, ethyl acetate showed the highest extraction efficiency for most of the target compounds before GC analysis, whereas MeOH were the preferred elution solvent for µMSPD extractions before LC analysis. The use of green solvents such as supramolecular solvents (SUPRASs) has been also recently reported to extract parabens from cosmetics [24], constituting an environmentally friendly alternative to classical organic solvents.

On the other hand, microextraction techniques involve the use of a small volume of the extraction phase in relation to the sample volume. Although microextraction techniques could not be exhaustive procedures compared with classical ones, they have the advantage of being almost solvent-free and therefore, more sustainable and easily implemented that are key factors in the current developments for cosmetics analysis. The most relevant sample preparation developments for cosmetics analysis are based on liquid-phase (liquid-liquid microextraction (LLME), dispersive liquid-liquid microextraction (DLLME), ultrasound-assisted emulsification microextraction (USAEME)) and sorbent-phase (solid-phase microextraction (SPME), fabric-phase sorptive extraction (FPSE), stir bar sorptive dispersive microextraction (SBSDME)) microextraction techniques.

3. Future Trends and Directions

In recent years, great efforts have been made to develop robust and reliable analytical methodologies for cosmetics analysis. In this way, sample preparation plays an essential role. Due to the high number of chemical compounds co-existing in these formulations, the development of automated and fast procedures for the simultaneous extraction of a high number of analytes in a single step is necessary. Extraction procedures such as SLE, LLE, UAE, SPE, PLE or MSPD are still in use for cosmetics analysis. However, the trends moving towards miniaturization allow reducing sample, solvent, and time consumption. The improvements made in terms of the miniaturization and portability of extraction devices greatly facilitate the implementation of these techniques in control laboratories and in the performance of in situ analysis. Regarding microextraction techniques, to date, SPME has been the most employed for its simplicity, non-organic solvent use and high analytes' enrichment. In addition, the variety of commercially available fibre coatings is constantly growing, which are opening up the range for further applications in the cosmetics analysis field. However, the application of recently developed techniques such as FPSE or SBSDME, that have mainly been applied to environmental analysis, in the field of cosmetics is generating growing interest. The development of new sorbent materials such as MWCNTs, LDHs or MIP-based coatings will continue being of particular interest to these approaches. Further directions of research should also consist of developing analytical tools to evaluate the presence of non-expected compounds, such as those of botanical origin, since the presence of cosmetics containing ingredients of natural origin is growing, assessing the stability of these compounds and evaluating the potential by-products formed by photodegradation.

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