



Analytical Testing of Cosmetics

Cosmetic products may contain ingredients that could pose health risks. In addition to a long list of completely banned substances such as hormones, cosmetics must not contain harmful substances whose concentration cannot exceed certain limits. The precise analysis and monitoring of all ingredients ensures the quality and safety of cosmetic products. In this whitepaper, you can find an overview of the most common active ingredients and harmful substances in cosmetics (pp. 2-3), a brief summary of sample preparation methods for the complex matrices of cosmetic products (pp. 4-6), and recent case studies on the analysis of different substance classes (pp. 7-8).

Active ingredients and harmful substances in cosmetics

Antioxidants

Antioxidants inhibit radical propagation reactions, reactions with oxygen or the reduction of active oxygen species in cosmetics. Antioxidants are intended to protect the product, but not the skin, from oxidative damage caused by UV radiation or singlet oxygen generation.^[1] One important class is tocopherols, which is used for its antioxidant and anti-inflammatory effects.^[2]

Acids

The pH value of the skin is between pH 4.0 and 6.5^[3]. If this is altered, the acid mantle of the skin will be impaired. If the pH value is not within the normal range, it can be maintained or restored by adding certain acids to cosmetics.^[4] Lactic acids, aloe vera, allantoin, hyaluronic acid, panthenol or urea, for example, are used for regulation.^[5]

Botanicals

Plant ingredients were among the first cosmetics and their use has always attracted interest. Today, many consumers prefer products made with natural ingredients. Essential oils derived from plants are also often added as preservatives.^[6]

Colorants

Color is used in cosmetic products for several reasons: Adding color to a product makes it more attractive and increases consumer acceptance; tinting helps to hide discoloration caused by the use of a particular ingredient or by age. There is a difference between organic colorants, inorganic colorants and nacreous pigments.^[1]

Emulsifiers

Emulsifiers have the ability to bind components such as water and oil as two phases of an emulsion in a chemically stable way. Unfortunately, the emulsifiers also continue to emulsify in the skin, causing harm. There they bind lipids in the protective layer of the skin and dissolve them. When they come into contact with water later, they are washed out of the skin. This makes the

protective layer porous. In addition, emulsifiers are fatty acids that are often produced from industrially processed then refined palm oil.

Formaldehyde

Formaldehyde is one of the preservatives that may be present in products that are rinsed off after brief contact with the skin. However, if they remain on the skin, they can cause adverse reactions.

Fragrances

Fragrances are used in cosmetics to cover up unpleasant odors or to add a special something. These chemical substances stimulate our senses. They can be produced synthetically or used in the form of essential oils if they come from nature. However, there are people who react to even the smallest traces with irritation.^[7]

Inorganic salts

Potassium, amine and sodium salts are used to make fatty acids more soluble in water, in shaving creams and sprays for example, to produce a foam with the desired consistency and rinsing properties.^[1]

Lipids

Lipids are used as plasticizers, lubricants, adhesives, hardeners or binders for the manufacturing of compressed powders. They are also used as shining agents.^[1]

Metals

Aluminum is used, for example, to block the channels leading to the surface of the skin by protein denaturation. In this way it acts as an antiperspirant.^[1] However, certain metals used in cosmetics, such as nickel, cobalt, chromium and palladium can accumulate in the skin, leading to allergic contact dermatitis^[8]. Other metals, such as mercury, lead, cadmium, and aluminum, can enter the bloodstream through the skin and be transported to various organs where they accumulate and produce toxic effects.^[9]

Microbial contamination

Due to the existence of the protective layer of the skin and its various defense mechanisms, cosmetics generally do not have to be aseptic. In such cases, (what cases – it doesn't make sense) there is a significantly increased risk of infection from the use of microbiologically contaminated cosmetics. Microbiological contamination of cosmetic products can occur at three stages: either during manufacture or filling, or when the product is used by the consumer. In the first case, it is the responsibility of the manufacturer to ensure proper microbial preservation of the cosmetic product, also in order to enhance the product's shelf life. It holds responsibility for ensuring consumer safety and maintaining the quality of the product at the level foreseen in the specification.^[10]

Mineral oil

Mineral oils have been used for many decades in skin and lip care cosmetic products due to their skin tolerance, their high protective and cleansing performance and broad viscosity options.^[11] A distinction is made between mineral oil saturated hydrocarbons and mineral oil aromatic hydrocarbons.

Mineral waxes

Waxes serve as barriers against water loss. They are often used to provide the texture and hardness in sticky products.^[12]

Pesticide residues

Pesticides such as fungicides, herbicides, insecticides and others are applied at various times during the growing season or during subsequent storage of a wide variety of crops. However, the numerous active substances degrade at different rates, so they can be introduced into a product via contaminated plant raw materials. Depending on their type and composition, plant protection products can be harmful to health.^[13, 14]

Peroxides

Peroxides have an antibacterial effect and serve as bleaching agents. However, in too high doses, they are very harmful to the health. If significant amounts of hydrogen peroxide is topically applied it can penetrate the epidermis or mucous membranes and cause rapid spontaneous or enzyme-catalyzed degradation to water and oxygen in the underlying tissue. This can lead to the formation of small gas bubbles and bleaching of the exposed tissue. The formation of larger amounts of gaseous oxygen can lead to the detachment of cell layers and rupture of tissues and organs. Locally formed oxygen is carried away by the blood. However, the increase in oxygen content in the blood leads to a hyperbaric reaction. ^[15]

Preservatives

Various microorganisms can survive and multiply on unpreserved cosmetic products. Preservatives are routinely added to all preparations that can support microbial growth. Choosing a preservative for a particular product is difficult. Formaldehyde, for example, is one of those preservatives that should be rinsed off shortly after skin contact, as it can otherwise cause undesirable reactions. ^[1]

Plasticizers

Microplastics such as phthalates are contained in peelings as abrasive bodies. They ultimately end up in the environment via waste water where they can cause problems. ^[16]

(Residual) solvents

Solvents can be added to cosmetics to help dissolve the components used in cosmetic preparations. Water is the most common solvent and is the continuous phase in most suspensions and water/oil emulsions. Solvents used in cosmetics include acetone, denatured alcohol, butoxyethanol (ethylene glycol monobutyl ether), diethylene glycol, dimethyl isosorbide, ethyl acetate, heptane, isopropyl alcohol, mineral alcohol, polyethylene glycol, propylene glycol,

toluene and tricaprin (glyceryl tri-n-decanoate). The selection of solvents for the use in cosmetics is a complex task due to odor, as well as topical and inhalation toxicity. ^[1]

Retinol

Retinol is a fat-soluble vitamin and is used in cosmetics to reduce skin wrinkles. Excessive intake can lead to acute or chronic symptoms of hypervitaminosis. ^[17]

Surfactants

Substances commonly classified as surfactants or tensides are required in a variety of cosmetics. Prolonged contact with anionic surfactants may cause some swelling of the skin. Although this is a temporary phenomenon, the skin in this swollen state allows permeation of topically applied substances. Nonionic surfactants as a group are generally considered mild, even under exaggerated conditions. The more hydrophobic nonionic surfactants, those that are water dispersible (not water soluble), can improve transdermal passage. Amphoteric surfactants as a group have a favorable safety profile. Finally, cationic surfactants are generally considered

more irritating than the anionic surfactants, but there is insufficient evidence to draw generalized conclusions. ^[1]

UV-filters

UVA and UVB can lead to an acute sunburn and in the long-term also to wrinkling, actinic keratosis or carcinomas. The use of UV light absorbing substances is accepted worldwide in order to protect the skin and body from UV radiation damage and trauma. These colorless organic substances are raised to a higher energy level when they absorb UV light. It is also possible to deflect UV radiation by physically blocking the radiation with an opaque makeup product. Titanium dioxide with a small particle size can reflect UV light without causing the undesirable brightening effect on the skin. ^[1]

Whitening agent

Whitening agents are often used to cover pigmentation and for other aesthetic reasons. However, the substances very often have a toxic effect. ^[18]





Sample preparation techniques for cosmetic analysis

Cosmetic products often consist of a long list of ingredients, including potentially harmful substances. The identification and precise quantification of these substances is crucial to ensure that they are within the authorized concentrations for cosmetics. Additionally, there are more than 1,200 prohibited substances, including hormones, glucocorticoids, and antibiotics [19].

Taking this to account, sample preparation is a crucial step for cosmetic analysis to effectively extract or separate the analyte from complex matrix in order to make the extract

more compatible with the subsequent determination and quantification. This section will give an overview of the most important techniques for the extraction or separation of analytes from cosmetic products.

Solid-phase extraction (SPE)

SPE is a packed-bed extraction system, and it is based on trapping of the analytes on or in a suitable sorbent when liquid sample passes through the sorbent bed (cartridges, precolumns, or disks). Interfering substances are removed from the sorbent by a washing solvent, and analytes adsorbed are desorbed using a suitable eluting solution. Thus, SPE can be used for purification and concentration of extracts obtained after sample dilution and sonication.

SPE has been widely used for cosmetic analysis. Compared with liquid-liquid extraction (LLE) and solid-liquid extraction (SLE), SPE uses much smaller volumes of organic solvents and obtains cleaner extracts. But SPE still is a time-consuming and multistep technique, and may cause analyte loss. The

highly viscous sample and suspended particles are likely to lead to SPE column clogging, this requires additional steps such as dilution, filtration, or centrifugation before loading sample. In addition, the extraction of samples containing the concentrated analytes may result in carryover problems. In this case, a serial dilution of sample is required and the one-off SPE cartridge is used.

Solid-phase microextraction (SPME)

SPME techniques can be used to minimize the matrix effects caused by coextracted interfering substances in LLE. The syringe-like fiber is the most commonly used pattern of SPME, and its extraction phase is coated on a fiber or a wire support. The fiber coating is an essential component affecting extraction efficiency and selectivity.

The SPME procedures used poly(methacrylic acid-co-ethylene glycol dimethacrylate) monolithic microextraction (PMME) [20, 21], and polyaniline-coated SBA-15 nanocomposite [22] as coatings were combined with LC to determine nitroanilines [23], phthalate esters [24],



and parabens^[25] in various kinds of products including sun block, lotion, perfume, remover, and hair dyes. These materials provided high sensitivity and good recovery^[26, 27].

Certain commercial fibers used organic polymers as coatings, such as polydimethylsiloxane (PDMS), PDMSdivinylbenzene, carboxen-PDMS, and divinylbenzene-carboxen-PDMS. They were employed to extract paraben, triclosan, benzoate, bronidox, and antioxidants from diverse types of cosmetics^[28, 29].

Headspace (HS)-SPME using a commercial polymer coating was employed to extract preservatives and antioxidants in creams with good recovery^[30].

Matrix solid-phase dispersion (MSPD)

The most common types of cosmetics involve solid, colloid, and emulsified products, which are required to dissolve or disperse into solution before using SPE and SPME. This introduces additional steps and increases the use of organic solvents. MSPD can simplify the operation and avoid the formation of an emulsion associated with the conventional LLE and SLE. It integrates extraction and clean-up processes in one step, leading to elimination of matrix interference and low consumption of solvents. The solid support materials used are similar to those used in SPE, and the ratio of sample-to-solid material generally ranges from 0.25 to 1. Sometimes a drying agent (anhydrous sodium sulfate) is required to absorb moisture from sample matrix. The most suitable elution solvents include methanol, acetonitrile, ethyl acetate, acetone, hexane, and their mixtures.

A miniaturized MSPD approach coupled with GC-MS and GC-MS/MS was proposed for the analysis of 25 fragrance allergens and 13 preservatives in cosmetic products^[31]. This micro-MSPD method only used 0.1 g sample and 1 mL ethyl acetate or hexane/acetone (1:1, v/v), which may reduce the cost and

consumption of organic solvents.

MSPD combined with ultrasound-assisted extraction was employed to extract nine intermediates in hair dyes^[32]. In this process, hair dye matrices were dispersed by neutral alumina, analytes were transferred into methyl sulfonic acid (MSA) solutions from matrices, and liposoluble substances were effectively removed by n-hexane, while certain interfering components were retained on dispersing sorbents.

MSPD has been employed to isolate fragrance allergens^[33, 34], preservatives^[35], isothiazolinone biocides^[36], plasticizers, polycyclic musks, and nitromusks^[37] from various types of cosmetics. MSPD involves too much manual operation, and thus its application is restricted in batch analysis of the samples.

Single-drop microextraction (SDME)

SDME utilizes a droplet of solvent as extraction phase to pick up a small fraction of analytes from an aqueous sample and the migration of matrix substances is largely checked. The extract obtained is much cleaner than that of classical LLE. Several factors

Equipment for sample preparation and analysis of cosmetics

Robust and accurate equipment is a prerequisite for any of the methods described herein. On the dedicated Cosmetics & Personal Care resource site, you can find an overview of all Sartorius products that is designed for the effective development and testing of cosmetics and personal care products, including syringe filters, balances, pipettes, ultrapure water systems and a wide range of membranes for specific filtration applications.

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influencing extraction efficiency should be experimentally optimized, which include volume ratio of aqueous-to-vial, salting-out, application of temperature, stirring of the sample, and analyte derivatization^[38].

In cosmetic manufacture process, certain solvents (e.g. ethanol, glycerin, propyleneglycol) are usually employed to dissolve water-immiscible raw materials. The monitoring of residual solvent in cosmetics is essential for the safety of cosmetics. HS-SDME and HS-SPME are preferred methods for the extraction of volatile solvents due to their high enrichment factors and without matrix effects.

SDME is suitably used to extract relatively nonpolar or semi-volatile ingredients from diverse cosmetics, and it has





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been proved to be a simple and feasible approach ^[39].

A three-phase direct immersion SDME was used to isolate parabens from cosmetics with isooctane/1-octanol and sodium hydroxide solution ^[40]. In this approach, a drop of sodium hydroxide (acceptor) was suspended at the tip of a microsyringe and completely immersed in organic phase to back-extract parabens. The extract obtained was detected by HPLC–UV without matrix interference.

Solidification of floating organic drop microextraction (SFOD)

SFOD is a recent mode of liquid-phase microextraction (LPME) based on the same principle as SDME, which uses small volumes of organic solvents with the melting point close to room temperature. The stability of microdrop is largely improved because the organic drop is deposited on the surface of an aqueous sample. After a scheduled extraction time, the sample vial is cooled in ice bath to make extractant solidification, facilitating convenient collection. SFOD coupled with ultrasound-assisted

emulsification microextraction can enhance extraction efficiency and cut down operation time.

SFOD frequently used low-toxicity solvents as extractants, such as 2-dodecanol, 1-undecanol and supramolecular solvents, and a small volume of solvent (30–50 L) was large enough for an effective extraction technique ^[41]. This approach was established for the isolation of parabens and allergenic fragrance substances from gel, toilette, cologne, perfume, and bodymilks ^[42, 43].

Dispersive liquid–liquid microextraction (DLLME)

DLLME is a simple, fast, and inexpensive LPME. When a small volume of mixture of water-immiscible solvent (extractant) and water-soluble solvent (disperser)

is rapidly injected into an aqueous sample, a cloudy solution is formed. The extraction equilibrium is quickly attained due to the considerably large surface area between the microdrop and aqueous sample. After centrifugation, the extract is collected for instrumental analysis. The extraction performance of DLLME is mainly affected by the nature of extraction solvent.

Cosmetic products generally contain various types of surfactants, which are beneficial for dispersing extraction solvent to give rise to a cloudy solution, facilitating the extraction of analytes. DLLME shows high extraction efficiency and consumes small quantities of solvents and extraction time.

FURTHER READ

This text is a short version of the following comprehensive review article:

Zhong, Z. and Li, G. (2017), Current trends in sample preparation for cosmetic analysis. *J. Sep. Sci.*, 40: 152-169; DOI 10.1002/jssc.201600367.

Cosmetic analysis methods

There is a large number of analytical methods for the testing of cosmetics, depending on the product type and which compound classes are to be detected. Amongst the most common methods for the analysis of cosmetic products are gas chromatography (GC) and liquid chromatography (LC) in combination with UV or mass spectrometric detection. Here you can find some recent examples of the application of GC-MS/MS and HPLC-MS/MS for the determination and quantification of limonene oxidation products and UV filters, respectively.

Case study

Quantification of volatile limonene oxidation products through GC-MS/MS

While limonene is present in many essential oils and gives various cosmetic products a lemony scent, its oxidation products are undesirable due to the sometimes unpleasant odors. Bryan Eigenbrodt and co-workers developed a solid-phase microextraction GC-MS/MS method that allows the automated quantification of volatile limonene oxidation products in encapsulated orange oil ^[43].

Methods

Samples of fresh and aged orange oil, respectively, in carbohydrate-based encapsulations, as well as unflavored encapsulations were used in the form of coarse powder. 20-500 mg of the samples were weighted into headspace vials and used for an automated SPME sample preparation using water as solvent.

GC-MS and GC-MS/MS were performed in both electron ionization (EI) and chemical ionization (CI) mode, using helium as carrier gas, ammonia or methane as chemical reagent gas, and argon as the collision-induced dissociation gas. The mass spectrometer's auto sampler was upgraded to the automated SPME system.

Results and discussion

The researchers revealed that the sensitivity of full scan GC-MS is not sufficient for the quantification of the major volatile oxidation products of limonene,

which are cis- and trans-limonene oxide, carvone, and cis- and trans-carveol. In order to optimize the MS parameters for selectivity and sensitivity, they carefully examined different MS modes, including four ionization methods in combination with single ion monitoring (SIM) and multiple reaction monitoring (MRM). Through this investigation they could show that MRM and SIM are equally suited for all analytes as there is no matrix interference. For all target substances both EI and positive CI (PCI) with ammonia as reagent gas give the best results, with lowest detected concentrations of 1 ppb for carvone and 10 ppb for the other oxidation products.

Another focus of the described study was the optimization of the SPME sampling conditions, namely fibre coating, temperature and time, to achieve addi-

tional sensitivity. Comparison of four different fibre coatings – carboxen/PDMS, PDMS, polyacrylate, and DVB/Carboxen/PDMS – showed that polyacrylate is the best material for the investigated volatile limonene oxidation products. A design of experiments (DOE) was used for the optimization of SPME sampling time and temperature due to the potential interaction of these parameters. As carvone and both carveols could be detected with five to 50 times higher signal-to-noise compared to the limonene oxides, the researchers focused on the optimization of the conditions for the latter. Whereas this approach suggested that the best combinations for cis- and trans-limonene oxide are 35 °C and 20 min or 45 °C and 30 min, a closer examination indicated that oxidation of limonene takes place at 45 °C. Accordingly, they concluded that the first combination is the best condition for SPME sampling with regards to sensitivity, selectivity and reproducibility.

Conclusion

The research team presents the development of a headspace SPME GC-MS/MS method with high sensitivity and selectivity for the analysis of five major volatile oxidation product of the commonly used terpene limonene.





Case study

Determination of organic UV filters in sunscreen cosmetics by HPLC–ESI-MS/MS

A team of Chinese scientists developed a methodology to simultaneously separate and determine 15 UV filters that are commonly used in commercially available sunscreen products [44]. They used high-performance liquid chromatography (HPLC) coupled with triple quadrupole mass spectrometry (MS).

Sample Preparation

The author's method starts with a different sample preparation. Previous publications used a single solvent like methanol to extract the UV filters. The matrices in this study are water- and grease-based, namely lotion, emulsion, cream, and lipstick. For the first three classes, extraction with 80% aqueous methanol solution gave the best results. The lipstick sample, as it is wax-based, prompted the addition of tetrahydrofuran in the extraction process. The sample is mixed with a tetrahydrofuran solution containing 0.2% ammonium hydroxide solution added to disperse the sample. The mixture is then shaken for one minute. Then 6 mL of 80% aqueous methanol solution are added, the tube

is again vortexed for one minute, put under sonication for 10 minutes and finally centrifuged at 12,000 g for 10 minutes. A part of the supernatant liquid is taken and evaporated to dryness under a Nitrogen stream. The sample is then reconstituted with one mL methanol and filtered.

HPLC separation and ESI-MS detection

As the UV filters are known for their high hydrophobicity, the separation is carried out as reversed-phase liquid chromatography (RPLC). As mobile phases, two mixtures were tested: methanol-water and acetonitrile-water. For this study, methanol gave the best peak resolution.

As most of the compounds were analyzed with the positive mode of the ESI (ESI+), the authors added 0.05%, 0.1%, and 0.2% aqueous formic acid solution. The largest improvement of peak shapes and mass responses were seen with the 0.1% aqueous formic acid solution. For the compounds analyzed with ESI- mode, 0.1% aqueous ammo-

nium hydroxide solution was found to give the biggest improvement for peak shapes and mass responses.

Within the MS/MS parameter optimization, the spectra of the 12 UV filters analyzed by ESI+ were dominated by the protonated molecular ions. The three UV filters analyzed by ESI- yielded spectra with the deprotonated molecular ion as dominant peak. These pseudomolecular ions were used as precursor ions for fragmentation in the SRM mode. The qualitative determination was based on retention time and two confirmation product ions for each UV filter. Comparison with control samples showed an acceptable tolerance for the retention times ($\pm 2.5\%$) and of $\pm 20\text{--}30\%$ for the relative ion abundance.

Conclusion

The method presented in this publication, ultrasound assisted extraction followed by HPLC-MS/MS, is suitable for routine analysis and quality control of sunscreen cosmetics.

References

- [1] "Cosmetics" in ECT 1st ed., pp. 545–562 by F. E. Wall, Consulting Chemist; in ECT 2nd ed., Vol. 6, pp. 346–375 by H. Isacoff, International Flavors and Fragrances (U.S.); in ECT 3rd ed., Vol. 7, pp. 143–176, by H. Isacoff, International Flavors and Fragrances, Inc.; in ECT 4th ed., vol. 8, pp. 572–619, by Martin M. Rieger, M & A. Rieger Associates; in ECT 5th ed., vol. 7, 820–865, by Martin M. Rieger, M & A. Rieger, Associates.
- [2] Mudgil, P. and Kamal-Eldin, A. (2021). Tocopherols and Tocotrienols in Fats and Oils. In Bailey's Industrial Oil and Fat Products, F. Shahidi (Ed.). <https://doi.org/10.1002/047167849X.bio093>
- [3] <https://www.chemie.uni-hamburg.de/institute/bc/arbeitsgruppen/kerscher/forschung/ph-metrie.html>
- [4] Jacobi, O. (1954), Der Säuremantel der Haut in der Kosmetik. *Fette, Seifen, Anstrichm.*, 56: 928–932. <https://doi.org/10.1002/lipi.19540561110>
- [5] <https://olionatura.de/basiswissen/konservierung/den-ph-wert-kontrollieren/>
- [6] L. L. Schramm, Emulsions, Foams, and Suspensions: Fundamentals and Applications, Wiley-VCH, Weinheim, 2005, Chapt. 15.
- [7] vgl. <https://www.hsm-biolab.de/2018/03/01/duftstoffe-in-der-kosmetik-wie-schaedlich-sind-sie/>
- [8] Thyssen, J. P., Menne, T., Metal allergy—a review on ex-posures, penetration, genetics, prevalence, and clinical implications. *Chem. Res. Toxicol.* 2010, 23, 309–318.
- [9] Centers for Disease Control and Prevention, Mercury exposure among household users and nonusers of skin-lightening creams produced in Mexico, California and Virginia. *Morb. Mort. Wkly. Rep.* 2012, 61, 33–36.
- [10] Michalek, I., John, S. and Caetano dos Santos, F. (2019), Microbiological contamination of cosmetic products – observations from Europe, 2005–2018. *J Eur Acad Dermatol Venereol*, 33: 2151–2157. <https://doi.org/10.1111/jdv.15728>
- [11] Chuberre, B., Araviiskaia, E., Bieber, T. and Barbaud, A. (2019), Mineral oils and waxes in cosmetics: an overview mainly based on the current European regulations and the safety profile of these compounds. *J Eur Acad Dermatol Venereol*, 33: 5–14. <https://doi.org/10.1111/jdv.15946>
- [12] Fridd P, editor. *Natural Ingredients in Cosmetics II*. Dorset: Micelle Press, 1996. p. 61.
- [13] <https://www.bav-institut.de/de/news/Pestizidruueckstaende-in-kosmetischen-Mitteln>
- [14] <https://www.cosmacon.de/glossary/pflanzenschutzmittel/>
- [15] Goor, G., Glenneberg, J., Jacobi, S., Dadabhoy, J. and Candido, E. (2021). Hydrogen Peroxide. In *Ullmann's Encyclopedia of Industrial Chemistry*. https://doi.org/10.1002/14356007.a13_443.pub3
- [16] Pörschke, S. and Eloo, C. (2016), Ersatz von Mikroplastik in kosmetischen Produkten. *Chemie Ingenieur Technik*, 88: 874–880. <https://doi.org/10.1002/cite.201500156>
- [17] Nau, H. and Stahl, W. (2012). Vitamin A und Carotinoide. In *Vitamine und Spurenelemente* (eds H. Dunkelberg, T. Gebel and A. Hartwig). <https://doi.org/10.1002/9783527653058.ch1>
- [18] https://www.researchgate.net/publication/305618053_cosmetics_Overview_of_Skin_Whitening_Agents_Drugs_and_Cosmetic_Products
- [19] Zhong, Z. and Li, G. (2017), Current trends in sample preparation for cosmetic analysis. *J. Sep. Sci.*, 40: 152–169; DOI 10.1002/jssc.201600367.
- [20] Xiao, P. F., Bao, C. L., Jia, Q., Su, R., Zhou, W. H., Jia, J. B., *J. Sep. Sci.* 2011, 34, 675–680.
- [21] Su, R.Y., Zhao, X. W., Li, Z. Y., Jia, Q., Liu, P., Jia, J. B., *Anal. Chim. Acta* 2010, 676, 103–108.
- [22] Ara, K. M., Pandidan, S., Aliakbari, A., Raofie, F., Amini, M. M., *J. Sep. Sci.* 2015, 38, 1213–1224.
- [23] Xiao, P. F., Bao, C. L., Jia, Q., Su, R., Zhou, W. H., Jia, J. B., *J. Sep. Sci.* 2011, 34, 675–680.
- [24] Su, R.Y., Zhao, X. W., Li, Z. Y., Jia, Q., Liu, P., Jia, J. B., *Anal. Chim. Acta* 2010, 676, 103–108.
- [25] Ara, K. M., Pandidan, S., Aliakbari, A., Raofie, F., Amini, M. M., *J. Sep. Sci.* 2015, 38, 1213–1224.
- [26] Melo, L. P., Queiroz, M. E. C., *J. Sep. Sci.* 2010, 33, 1849–1855.
- [27] Moliner-Martinez, Y., Herraiz-Hernandez, R., Verdu-Andres, J., Molins-Legua, C., Campins-Falco, P., *Recent Trends Anal. Chem.* 2015, 71, 205–213.
- [28] Alvarez-Rivera, G., Llompart, M., Garcia-Jares, C., Lores, M., *J. Chromatogr. A* 2015, 1390, 1–12.
- [29] Fernandez-Alvarez, M., Lamas, J. P., Sanchez-Prado, L., Llompart, M., Garcia-Jares, C., Lores, M., *J. Chromatogr. A* 2010, 1217, 6634–6639.
- [30] Yang, T. J., Tsai, F. J., Chen, C. Y., Yang, T. C. C., Lee, M. R., *Anal. Chim. Acta* 2010, 668, 188–194.
- [31] Celeiro, M., Guerra, E., Lamas, J. P., Lores, M., Garcia-Jares, C., Llompart, M., *J. Chromatogr. A* 2014, 1344, 1–14.
- [32] Zhong, Z. X., Li, G. K., Wu, Y. H., Luo, Z. B., Zhu, B. H., *Anal. Chim. Acta* 2012, 752, 53–61.
- [33] Sanchez-Prado, L., Lamas, J. P., Alvarez-Rivera, G., Lores, M., Garcia-Jares, C., Llompart, M., *J. Chromatogr. A* 2011, 1218, 5055–5062.
- [34] Sanchez-Prado, L., Alvarez-Rivera, G., Lamas, J. P., Llompart, M., Lores, M., Garcia-Jares, C., *Anal. Methods* 2013, 5, 416–427.
- [35] Sanchez-Prado, L., Alvarez-Rivera, G., Lamas, J. P., Lores, M., Garcia-Jares, C., Llompart, M., *Anal. Bioanal. Chem.* 2011, 401, 3293–3304.
- [36] Capriotti, A. L., Cavaliere, C., Fatrizia, F., Samperi, R., Stampaciacchiere, S., Ventura, S., Lagana, A., *TrAC Trends Anal. Chem.* 2015, 71, 186–193.
- [37] Llompart, M., Celeiro, M., Lamas, J. P., Sanchez-Prado, L., Lores, M., Garcia-Jares, C., *J. Chromatogr. A* 2013, 1293, 10–19.
- [38] Jain, A., Verma, K. K., *Anal. Chim. Acta* 2011, 706, 37–65.
- [39] Saraji, M., Mirmahdih, S., *J. Sep. Sci.* 2009, 32, 988–995.
- [40] Jain, A., Soni, S., Verma, K. K., *J. Liq. Chromatogr. R. T.* 2015, 38, 82–91.
- [41] Kamarei, F., Ebrahimzadeh, H., Yamini, Y., *Microchem. J.* 2011, 99, 26–33.
- [42] Perez-Outeiral, J., Millan, E., Garcia-Arrona, R., *J. Sep. Sci.* 2015, 38, 1561–1569.
- [43] Liu, Q., Shi, J., Sun, J., Wang, T., Zeng, L., Zhu, N., *Anal. Chim. Acta* 2011, 708, 61–68.
- [44] Emberger, ME, Lin, J, Pika, J, Christ, I, Eigenbrodt, B. *Flavour Fragr J.* 2019; 34: 52– 62.
- [45] Meng, X., Ma, Q., Bai, H., Wang, Z., Han, C. and Wang, C. (2017), *Int J Cosmet Sci*, 39: 386–392.