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Application of the click analytical chemistry index for the assessment of endocrine-disrupting chemicals in cosmetics and personal care products

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ABSTRACT

Cosmetics and personal care products often contain parabens, phthalates, and bisphenols, compounds used as preservatives or plasticizers that may also migrate from packaging materials into the product. Their potential endocrine-disrupting effects have prompted stricter regulations and concentration limits. Given their occurrence and the complexity of cosmetic matrices, several extraction and chromatographic techniques have been developed to ensure reliable quantification. In this review, representative methods published from 2018 to 2025 focused on the determination of these compounds were evaluated using the click analytical chemistry index (CACI), a recently developed color-coded tool that integrates analytical performance, environmental impact, cost, and applicability within a single framework. CACI allows an objective and balanced comparison of analytical methods, emphasizing practicality and real-world feasibility. The obtained CACI scores ranged from 57 to 80, suggesting that the evaluated methodologies can be categorized as acceptable (50–75%) or highly practical (>75%). It is expected that the use of CACI will promote the development of more sustainable, practical, and user-oriented analytical strategies for the evaluation of chromatographic methods, not only for endocrine-disrupting chemicals in cosmetics and personal care products, but also for other substances of interest.

1. Introduction

Cosmetic and personal care products (PCPs) are used daily by millions of consumers worldwide [1]. These formulations include a wide variety of items such as creams, shampoos, perfumes, make-up, and sunscreens. Their continuous application on skin and hair has created a direct and recurrent route of human exposure to numerous chemicals. Although most compounds are added to improve product stability, appearance, or sensory properties, several of them have raised concern due to their potential interference with hormonal systems [2]. In particular, endocrine-disrupting chemicals (EDCs) are substances capable of altering the normal function of hormones. They can imitate or block hormonal signals and disturb physiological processes controlled by the endocrine system. Long-term exposure to EDCs has been associated with reproductive disorders, thyroid dysfunction, metabolic alterations, and developmental problems. Even small concentrations, particularly during pregnancy or early life, can produce measurable biological effects [3].

Among the wide group of EDCs, bisphenols, parabens, and phthalates are commonly detected in PCPs and cosmetics [4]. Parabens are synthetic esters derived from *p*-hydroxybenzoic acid and are widely used as preservatives to inhibit microbial growth. They can be absorbed through the skin and have shown estrogen-like activity [5]. Phthalates, a group of diesters of phthalic acid, are used as solvents, fixatives, or plasticizers to improve texture and fragrance retention. Several phthalates are known to interfere with androgen and thyroid hormone regulation [6]. Bisphenols, particularly bisphenol A (BPA), are applied in the production of plastic containers and coatings used in packaging. These materials can release bisphenols into cosmetic formulations, resulting in dermal or oral exposure. Structural analogues such as bisphenol S (BPS) and bisphenol F (BPF) have replaced BPA in some applications, but their safety profile remains uncertain [7,8]. It should be noted that

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regulations vary significantly between regions. The European Union [9] restricts or bans several parabens, phthalates, and bisphenols in cosmetic formulations, whereas the United States follows a more permissive approach [10]. Such regulatory divergence highlights the need for reliable analytical methodologies capable of detecting EDCs at trace levels and ensuring product safety.

The chemical complexity of cosmetic matrices presents analytical challenges as well. Ingredients with varying polarity, viscosity, and solubility can interfere with the extraction and quantification of target compounds. Sample preparation therefore plays a decisive role in isolating analytes from these heterogeneous mixtures [11]. Conventional methods such as solid-phase extraction, liquid-liquid extraction, and solid-liquid extraction are effective, but require large volumes of organic solvents and generate considerable waste [12]. To reduce environmental impact, modern analytical chemistry promotes approaches aligned with the principles of green analytical chemistry [13] and green sample preparation [14]. These principles recommend minimizing solvent use, shortening experimental time, and introducing miniaturized techniques that reduce cost and waste. Sorbent- and solvent-based microextraction techniques, including solid-phase microextraction, dispersive liquid-liquid microextraction, and fabric phase sorptive extraction, have been developed as more sustainable alternatives to conventional procedures [15,16]. Moreover, although targeted approaches based on liquid chromatography (LC) coupled with diode array detection (DAD) or mass spectrometry (MS), as well as gas chromatography (GC) coupled with flame ionization detection (FID) or MS, are employed for the determination of these compounds [12], emerging non-target methods have gained attention for the assessment of complex cosmetic matrices. An example of a non-target approach is high-performance thin-layer chromatography (HPTLC) coupled with planar hazard-related bioassays, which has been proposed as a promising effect-directed analysis strategy [17]. This technique enables cost-efficient, fast, and sustainable non-target safety screening of PCPs.

In recent years, several tools have been designed to assess the environmental performance and operational efficiency of analytical methods. Following the conceptual framework of white analytical chemistry, these evaluation systems are often grouped into color-based categories: red tools focus on analytical performance, green tools assess environmental sustainability, blue tools examine practicality and applicability, while others address specific aspects [18]. To date, only one study has considered both sample preparation and analysis for the evaluation of green and blue characteristics of EDC in PCPs and cosmetics [19]. However, no previous work has attempted a broader assessment that combines all dimensions simultaneously. To address this limitation, the click analytical chemistry index (CACI), recently developed by Mansour et al [20], is applied in this review to evaluate analytical methodologies for the determination of EDC in cosmetics and PCPs. It integrates these complementary aspects to deliver a comprehensive and balanced evaluation of how analytical methods meet current expectations for sustainability, efficiency, and methodological transparency.

2. The basis of the click analytical chemistry index

Building upon the color scale-based in WAC, click analytical chemistry (CAC) introduces an additional layer of simplicity and modularity, drawing inspiration from the principles of click chemistry [21]. Just as click reactions transformed organic synthesis through reliability, speed, and efficiency, CAC adapts these ideas to the analytical context. It promotes analytical procedures that are practical, fast, and accessible, encouraging the design of methods that are both operationally straightforward and scientifically robust. In this sense, a new tool called "click analytical chemistry index (CACI)" was developed to represent the translation of CAC's conceptual foundation into a quantitative and visual evaluation system, allowing researchers to assess analytical methods in a structured and objective way. It complements existing chemistry tools by focusing on applicability and user-friendliness, two dimensions often overlooked in conventional assessments [20].

As described by Mansour et al [20], CACI is a color-coded and point-based framework developed to evaluate analytical methods through independent yet complementary parameters. The tool is structured around 12 questions organized into 8 categories (or criteria). Each parameter reflects a practical or analytical dimension, and together they form an integrated picture of the method's overall performance. The color scheme of CACI follows a three-tier scale: (a) colored: optimal performance or full compliance with the criterion; (b) gray section: intermediate or acceptable performance; (c) black section: limited or poor performance. Each parameter is assigned a score from 1 to 3 (except analysis time, which ranges from 0 to 6) according to defined criteria. The sum of these scores yields a global index value, which can be visualized through radar plots or color wheels for quick interpretation [20]. The evaluated parameters, including sample size, sample preparation, feasibility, application, portability, automation, sensitivity and sample analysis time, are summarized in Table 1. Applications with a CACI score between 50% and 75% are considered acceptable in terms of practicality. A score of 75% or higher indicates a method that is highly practical, while a score below 50% suggests that the method lacks practical utility.

3. Case studies

Cosmetics and PCPs represent chemically complex matrices that combine aqueous and lipid phases, pigments, stabilizers, and fragrances. Analytical methods targeting EDCs within these matrices must therefore balance selectivity, sensitivity, and operational feasibility. Traditional green metrics primarily emphasize solvent use and waste generation, yet they do not capture the practical challenges involved in routine analysis such as the need for reproducible, low-cost, and rapid protocols that can be applied to different product types. Applying CACI to the study of EDCs in cosmetics addresses this limitation by integrating analytical, environmental, and practical dimensions into a single framework. The index helps to identify methods that are not only environmentally responsible but also feasible for regular laboratory implementation and potential field adaptation. This multidimensional evaluation is particularly valuable when comparing methods involving microextraction, chromatographic separation, and mass spectrometric detection, as it allows a balanced interpretation of trade-offs between performance and sustainability.

The implementation of CACI followed a sequence of steps: (a) method selection, which involves the identification of representative analytical works for EDC determination in cosmetics and PCPs; (b) parameter assignment, referring to the extraction of experimental details related to the CACI attributes; (c) scoring, where each parameter is evaluated according to the CACI scoring guide and the resulting points are compiled into a spreadsheet or entered into the open-access CACI software (available at bit.ly/CACI2025) [20]; (d) color coding and visualization, in which the software automatically generates a pictogram that summarizes each parameter's score, providing an immediate visual overview of the method's balance among performance, practicality, and sustainability; and (e) comparative analysis, where the CACI profiles of different methods are compared to identify those offering optimal analytical performance with minimal resource consumption and greater user applicability.

For this review, analytical methods for the determination of EDCs in cosmetics and PCPs published between 2018 and 2025 were selected using Scopus and Web of Science as databases. The literature search was conducted using relevant keywords such as cosmetics, personal care products, endocrine-disrupting chemicals, parabens, phthalates, bisphenols, sample preparation, extraction, microextraction, and chromatography. Only peer-reviewed articles published in English were considered. Studies were included if they reported analytical methods for EDC determination in cosmetic or PCP matrices and provided

Table 1
Main features of CACI metric. For further details, check the original article [20].

#	Criterion	Question	Options
1	Sample Size	What is the required sample size (in mL or g)?	< 1
			2
			1–10
2	Sample preparation	What level of sample preparation is required?	No sample preparation
			Minimal sample preparation
			Conventional sample preparation
3	Feasibility	a) Are the chemicals and reagents readily available?	Commercially available
			Not commercially available but easily synthesized
			Not commercially available, laborious synthesis
		b) Are the required instruments available in laboratories?	All equipment available in regular analytical labs
			One special equipment required
			More than one special equipment required
		c) What is the total cost of analysis per sample?	< $10 per sample
			$10-$100 per sample
			> $100 per sample
4	Application	a) What is the application type of the method?	Quantitative
			Semi-quantitative
			Qualitative
		b) How many analytes can be tested?	> 3 analytes
			2–3 analytes
			Only one analyte
		c) How many matrices can be tested?	> 3 matrices
			2–3 matrices
			Only one matrix
5	Portability	How portable is the method's instrumentation?	Portable
			Miniaturized but not portable
			Not portable nor miniaturized
6	Automation	What is the level of automation of this method?	Automatic
			Semi-automatic
			Manual
7	Sensitivity	What is the method's sensitivity level?	≤ 1% of target concentration
			≤ 10% of target concentration
			> 10% of target concentration
8	Sample analysis time	How long does the sample analysis take (in minutes)?	≤ 5
			≤ 10
			≤ 20
			≤ 30
			≤ 60
			≤ 90
			≤ 120
			< 180
			180–300
			> 300

sufficient experimental detail to allow CACI evaluation. Review articles, conference abstracts, and studies lacking relevant methodological information were excluded. All selected articles were screened to ensure their relevance and consistency with the scope of this review. Each selected study was analyzed using the CACI scoring system to generate individual profiles as reported in Table 2. The obtained CACI scores ranged from 57 to 80, suggesting that the evaluated methodologies can be categorized as acceptable or highly practical (see Fig. 1).

4. Discussion

4.1. Sample size

This parameter evaluates the total amount of sample (in mL or g) required to perform an analytical procedure, including all preparation and processing steps [20]. It serves as a key indicator of a method's practicality, cost-effectiveness, and environmental footprint. Methods that require very small quantities of sample (<1 mL or g) receive the highest score, as they promote resource conservation, reduce waste generation, and streamline workflow efficiency. Intermediate scores are assigned to methods using 1–10 mL or g, reflecting moderate practicality and compatibility with standard laboratory operations. Methods demanding large sample amounts (>10 mL or g) score lowest, as they tend to increase reagent consumption, analysis time, and storage requirements. As shown in Fig. 2A, most studies achieved the maximum score of 3 points for this parameter, indicating a general trend toward miniaturized analytical protocols. This finding reflects the widespread implementation of microextraction and microscale analysis techniques, which require <1 mL or g of sample.

4.2. Sample preparation

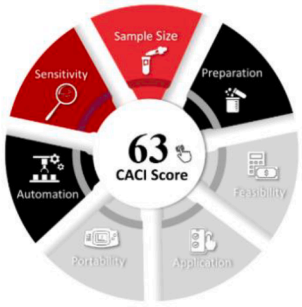
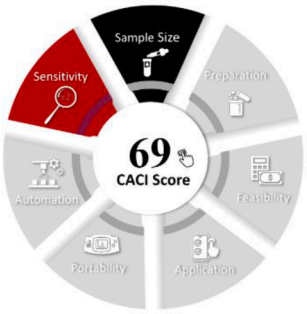
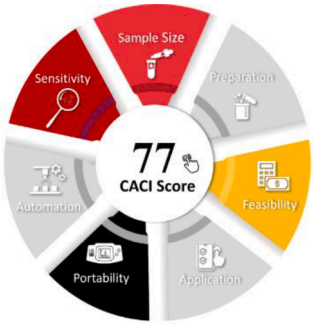
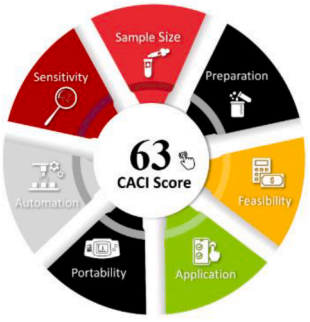
Attribute #2 assesses the complexity and extent of sample handling required before analysis. Methods that eliminate the need for sample preparation receive the highest score, as they reduce analysis time, minimize resource consumption, and lower the risk of procedural errors. Methods requiring minimal preparation, such as dilution, filtration, or simple microextraction steps, are awarded intermediate scores, reflecting acceptable practicality and moderate workload. Conversely, conventional procedures involving multiple extraction or derivatization steps are assigned the lowest score, as they demand more time, reagents, and manual effort.

The results obtained for the sample preparation criterion (see Fig. 2B) showed that none of the evaluated analytical methods achieved the maximum score, indicating that complete elimination of sample preparation remains uncommon in current studies on EDC in cosmetics and PCPs. Some of the analyzed methods obtained 2 points, since they involve minimal sample preparation such as dilution, filtration, or simplified microextraction steps. Z. Khesina et al [22] developed a fast sample preparation method based on microextraction by packed sorbent to determine parabens in cosmetics. They used minimal sample preparation (~ 6 min) considering 1 min of conditioning, 2 min of sample loading, 0.5 min of washing, 0.5 min of elution and 2 min washing between samples. However, a significant number of studies scored 1 point, corresponding to conventional sample preparation approaches involving multiple steps or extended processing times [23]. While these approaches may be effective, they demand longer processing times and greater solvent consumption, limiting their suitability for routine or high-throughput analysis. The distribution of scores highlights a gradual transition toward simpler and more sustainable preparation techniques, although the complete integration of direct analysis remains an area for future methodological improvement.

4.3. Feasibility

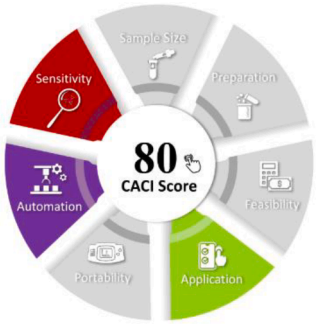
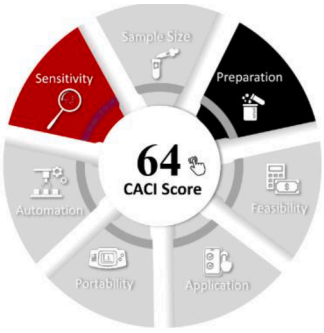
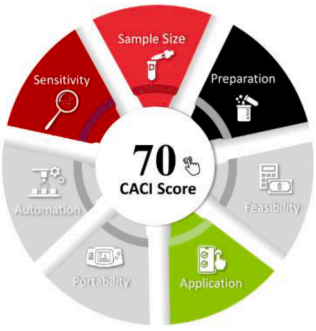
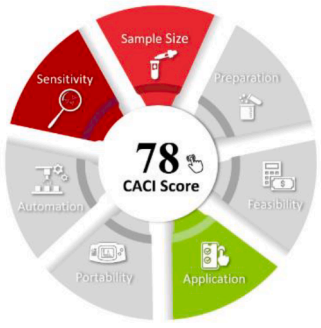
Attribute #3 evaluates the practical accessibility of analytical methods by considering three key aspects: (a) availability of chemicals and reagents, (b) availability of required instrumentation, and (c) total cost of analysis per sample. Together, these factors determine whether a method can be realistically implemented across laboratories with different resource levels. The first aspect, availability of chemicals and

Table 2
Application of the CACI tool for the determination of endocrine-disrupting chemicals in personal care products and cosmetics. In the pictograms, each segment corresponds to a specific criterion and the color-coded reflects the performance level (bright, gray, or black).

#	Sample	Analyte	Sample prep.	Instrument	CACI pictogram	Method practicality	Ref.
1	Cosmetics	Parabens	DI-TFME	UHPLC-UV/Vis		63 (Acceptable)	[38]
2	Micellar cosmetics	Parabens, UV filters	μ-dSPE	UHPLC-UV/Vis		69 (Acceptable)	[39]
3	Facial tonic, shampoo, hair conditioner, body cream	Parabens	UAE	HPLC-ECD		77 (Highly practical)	[40]
4	Facial tonics, hair sprays, mouthwashes, shampoos, hair conditioners, body creams	Antimicrobial agents	Dilution with ultrapure water or UAE	HPLC-DAD-FLD		74 (Acceptable)	[26]
5	Toothpastes, shampoos, bath gels, body lotions, hand sanitizers, hand lotions, facial cleansers, sunscreens, masks, lipsticks, hair sprays	Parabens	UAE	HPLC-MS/MS		63 (Acceptable)	[23]

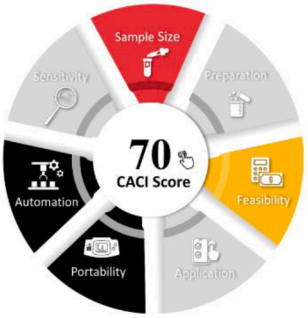
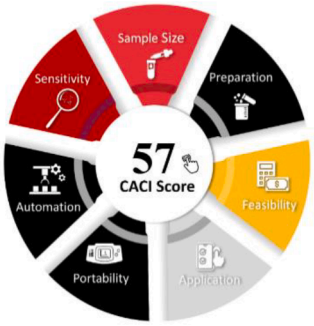
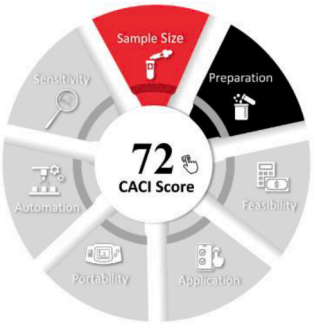
(*continued on next page*)

Table 2 (*continued*)

#	Sample	Analyte	Sample prep.	Instrument	CACI pictogram	Method practicality	Ref.
6	Shampoo, hair mask, hair spray, hair balm, hair mousse, hair lotion	Parabens	MEPS	HPLC-UV		80 (Highly practical)	[22]
7	Candy rod, soybean milk powder, lipstick	Parabens, flavors	SBSE	HPLC-PDA		64 (Acceptable)	[41]
8	Rose water, hair serum, deodorant, cream	Parabens	FPSE	HPLC-UV		70 (Acceptable)	[42]
9	Shampoos, hair conditioning, creams	Parabens	DLLME	UPLC-UV		78 (Highly practical)	[43]
10	Mouthwash, lidocaine gel, aloe vera, skin tonic	Parabens	DLLME	HPLC-DAD		64 (Acceptable)	[44]

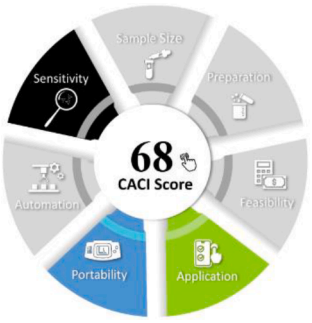
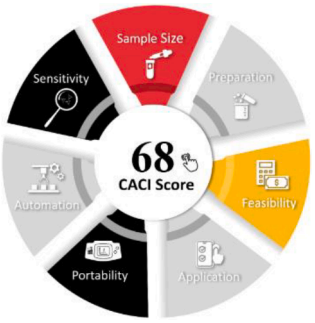
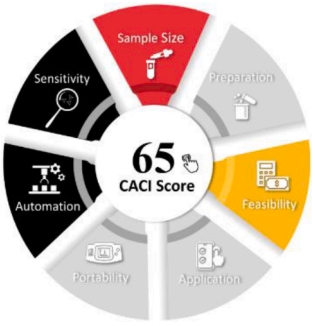
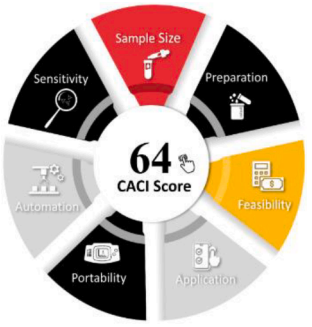
(*continued on next page*)

Table 2 (*continued*)

#	Sample	Analyte	Sample prep.	Instrument	CACI pictogram	Method practicality	Ref.
11	Perfumes	Phthalates	Dilution in ethanol	GC–MS		70 (Acceptable)	[45]
12	Nail polish, lipsticks, baby care products	Phthalates	d-SPE	HPLC-DAD		57 (Acceptable)	[25]
13	Baby shampoo	Phthalates	d-SPE	HPLC-DAD		72 (Acceptable)	[46]
14	Cosmetic cream, lipstick	Phthalates	SPME	GC-FID		71 (Acceptable)	[47]
15	Haircare products	Phthalates, parabens, triclosan	Dissolution, vortex, centrifugation	LC-PDA		62 (Acceptable)	[4]

(*continued on next page*)

Table 2 (*continued*)

#	Sample	Analyte	Sample prep.	Instrument	CACI pictogram	Method practicality	Ref.
16	Rubbing alcohol, contact lens cleaner, saline solution, eye cleaner, antibacterial disinfectant liquid	Phthalates	SPME	GC-FID		68 (Acceptable)	[28]
17	Baby diapers	Bisphenols and derivatives	UASE	LC-MS/MS		68 (Acceptable)	[27]
18	Face, body, and skin moisturizers, lipsticks	Plasticizer, bisphenol	μ-MSPD	GC–MS		65 (Acceptable)	[48]
19	Face cream, body lotion, shampoo, conditioner, body wash, face serum, hair serum, face mask, face water, sunscreen, lipsticks, foundation, toner, face wash, face gel, primer, bactericidal solution	Bisphenols, parabens	USE	UPLC-TQMS		64 (Acceptable)	[49]

DI-TFME, direct immersion thin film microextraction; DLLME, dispersive liquid–liquid microextraction; FPSE, fabric phase sorptive extraction; GC-FID, gas chromatography–flame ionization detector; GC–MS, gas chromatography–mass spectrometry; HPLC-DAD, high-performance liquid chromatography–diode array detector; HPLC-DAD-FLD, high-performance liquid chromatography–diode array detector–fluorescence detector; HPLC-ECD, high-performance liquid chromatography–electrochemical detector; HPLC-MS/MS, high-performance liquid chromatography–tandem mass spectrometry; HPLC-PDA, high-performance liquid chromatography–photodiode array detector; HPLC-UV, high-performance liquid chromatography–ultraviolet detector; LC-MS/MS, liquid chromatography–tandem mass spectrometry; LC-PDA, liquid chromatography–photodiode array detector; MEPS, microextraction by packed sorbent; SBSE, stir bar sorptive extraction; SPME, solid-phase microextraction; UAE, ultrasound-assisted extraction; UASE, ultrasound-assisted solvent extraction; UHPLC-UV/Vis, ultra-high-performance liquid chromatography–ultraviolet/visible detector; UPLC-TQMS, ultra-performance liquid chromatography–triple quadrupole mass spectrometry; UPLC-UV, ultra-performance liquid chromatography–ultraviolet detector; USE, ultrasonic solvent extraction; μ-dSPE, micro dispersive solid-phase extraction; μ-MSPD, micro matrix solid-phase dispersion. For more detailed information on the use and application of CACI, the reader is referred to the original article [20].

reagents, reflects how easily the components required for the analysis can be obtained. Methods using commercially available reagents are considered the most feasible, as they facilitate reproducibility and reduce implementation barriers. If reagents are not commercially available but can be synthesized through simple procedures, feasibility remains moderate. However, methods requiring laborious synthesis of reagents significantly reduce accessibility and are therefore less practical. The second aspect, availability of instruments, assesses whether the analytical equipment needed is standard or specialized. Techniques that can be performed using common laboratory instruments are rated as highly feasible. Methods requiring one specialized instrument are moderately feasible, while those depending on multiple non-standard instruments are less accessible, particularly in smaller or resource-limited facilities. The third aspect, total cost of analysis per sample, measures the economic feasibility of a method. Costs below $10 per sample are considered ideal for routine analysis, while those between $10 and $100 are acceptable for specialized or low-frequency applications. Methods exceeding $100 per sample are regarded as less practical for widespread adoption.

For chemical and reagent availability (see Fig. 2C), most analytical methods achieved high scores (2–3 points), indicating that most reagents employed for EDC determination are commercially available or easily synthesized. A small fraction of studies received lower scores, reflecting reliance on complex or non-standard reagents that could hinder reproducibility. Regarding instrument availability (see Fig. 2D), the results show that nearly all methods utilize standard laboratory equipment which are accessible in most laboratories. Cost per sample (see Fig. 2E) scored consistently high (3 points) for all evaluated methods, suggesting that the analyses are generally cost-effective, requiring limited reagent quantities and low operational expenses. Importantly, these costs are calculated based solely on reagents, solvents, and consumables, excluding equipment depreciation or infrastructure expenses. The cost per sample for CACI is calculated by summing the costs of all reagents, solvents, and consumables required for the analysis of a single sample [20]. Although estimating the total cost of analysis per sample is a fundamental aspect of assessing feasibility, it can be challenging and time-consuming in practical applications. As previously described, this estimation requires accounting for all reagents, solvents, and consumables used per sample and multiplying their quantities by the corresponding unit prices. However, these prices can vary depending on several factors, including the supplier, geographical region, purchasing volume, and even market fluctuations in the cost of chemical products. Additional differences may arise from laboratory agreements or institutional discounts, as well as variations in reagent purity or packaging size. Accordingly, the cost score assigned in a CACI assessment should be interpreted as an estimate, and its objectivity can be influenced by the specific sources and assumptions used for pricing.

4.4. Applications

The fourth attribute evaluates the scope and analytical versatility of a method through three complementary aspects: (a) What is the application type of the method? (b) How many analytes can be tested? and (c) How many matrices can be tested? The first aspect, application type, distinguishes between qualitative, semi-quantitative, and quantitative methods. Quantitative techniques, which provide precise numerical data for accurate decision-making and quality control, receive the highest score. Semi-quantitative methods, although less precise, remain valuable for rapid screening or preliminary assessments and therefore score moderately. Qualitative methods, which only indicate the presence or absence of analytes, are less informative and consequently score lowest. The second aspect, number of analytes tested, highlights the analytical capacity and efficiency of a method. Techniques capable of simultaneously determining more than three analytes demonstrate superior practicality and resource optimization, earning the highest score. The third aspect, number of matrices tested, measures the method's adaptability to diverse sample types. Methods applicable to more than three matrices are regarded as broadly useful and universally adaptable, while those that can analyze two to three matrices are moderately versatile. In contrast, methods limited to a single matrix are less flexible and score lowest [20].

In application type (see Fig. 2F), every evaluated method obtained the highest score, confirming that the procedures currently used for EDC analysis in cosmetics and PCPs are quantitative. This indicates a preference for methods capable of producing accurate numerical data that can support validation and compliance studies, a need that extends beyond regulatory purposes. Researchers and health authorities are also increasingly focused on quantifying these compounds because of their potential cumulative and long-term effects on human health [24]. Even at trace concentrations, continuous exposure to these chemicals may result in bioaccumulation and subtle hormonal disruptions over time [3]. Hence, quantitative information is not only crucial for meeting safety requirements but also for evaluating chronic exposure risks, defining reliable toxicological limits, and promoting the development of safer product formulations. For number of analytes tested (see Fig. 2G), most methods also reached the maximum value, emphasizing the growing implementation of multi-residue strategies that allow the simultaneous determination of several compounds in a single run. Only one study determined three phthalate esters (dimethyl phthalate, di-butyl phthalate and benzyl butyl phthalate) from cosmetics and baby care products [25]. Number of matrices tested (see Fig. 2H) showed greater variability, as some methods demonstrated broad applicability across diverse product types. For example, Abad-Gil et al [26], studied paraben-, isothiazolinone- and alcohol-type preservatives in facial tonics, mouthwashes, shampoos, hair sprays, hair conditioners or body creams. In contrast, Chabowska et al [27] assessed the exposure risk of infants and newborns to bisphenols and their derivatives originating from diapers. This uneven distribution suggests that, although the analytical field is advancing toward more universal and flexible methods, certain techniques remain matrix-dependent.

4.5. Portability

The portability attribute considers the mobility and operational flexibility of analytical methods, emphasizing their potential for in-field or on-site applications. Portable systems, such as handheld devices, are awarded the highest score (3 points) because they allow rapid, real-time analysis. Miniaturized but non-portable instruments, which still require a fixed setup but occupy less space and often consume fewer resources, are moderately valued (2 points) for their balance between precision and partial mobility. Large-scale benchtop systems, including LC-MS or GC–MS platforms, though powerful, receive the lowest score (1 point) due to their lack of portability and dependence on complex infrastructure.

In the reviewed studies most of them achieved intermediate scores (2 points), corresponding to miniaturized but non-portable techniques (see Fig. 2I). This trend reflects the predominance of compact benchtop instruments, such as chromatographic or spectrometric systems which, while reducing size and resource consumption, still require a fixed laboratory setup. Only one method achieved the maximum score (3 points), as it was based on a portable and novel 3D-printed solid-phase microextraction device equipped with a silver-polyaniline-coated pencil lead for the extraction of phthalate esters in cosmeceutical products [28]. Although miniaturization continues to progress, true portability remains limited, likely due to the high sensitivity and selectivity demands that still require sophisticated instrumentation. Chromatographic techniques inherently depend on complex systems involving precise temperature control, pressurized gas or solvent delivery, and sensitive detectors such as mass spectrometers. Consequently, while portable sensors and microextraction devices are promising tools for preliminary screening, chromatographic methods remain indispensable

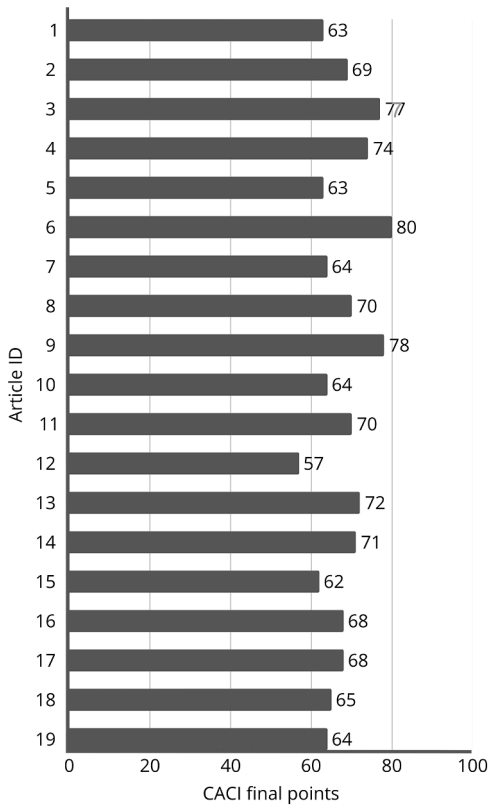


Fig. 1. CACI final points correspond to the analytical methods evaluated for the determination of endocrine-disrupting chemicals in cosmetics and personal care products. Scores below 50% suggest limited practical applicability; scores between 50% and 75% represent acceptable practicality, while values above 75% indicate highly practical methods.

for confirmatory and regulatory analyses.

4.6. Automation

The automation attribute in CACI assesses how much an analytical method operates without manual intervention. Fully automated methods, which perform all steps independently, score 3 points for ensuring speed, consistency, and minimal human error. Semi-automated procedures, combining manual and automated stages, receive 2 points, while manual methods, dependent entirely on the operator, obtain 1 point due to higher variability and workload.

As shown in Fig. 2J, most analytical methods are semi-automated. These methods typically combine automated data acquisition or instrument control with manual steps during sample preparation or calibration. Only one study achieved 3 points, as it employed an automated microextraction by packed sorbent coupled with HPLC-UV for the quantitative determination of parabens in cosmetics [22]. Despite progress toward automation, the full implementation of automated systems in chromatographic and sample preparation workflows remains limited, mainly due to cost and instrument complexity.

4.7. Sensitivity

Sensitivity attribute considers how effectively a method can detect and quantify very low concentrations of analytes with accuracy and precision. Methods capable of detecting ≤1% of the target concentration receive the highest score (3 points), as they enable early detection of contaminants and ensure compliance with regulatory limits. Those detecting ≤10% score 2 points, while methods with detection limits >10% obtain 1 point, since they are less suitable for trace-level determinations. Sensitivity is particularly important in the analysis of EDCs, which are usually found at very low levels in complex cosmetic matrices. Achieving these detection limits typically requires advanced chromatographic systems coupled with mass spectrometry. However, such techniques often involve higher operational costs and instrument complexity, making them less accessible to some laboratories.

The results displayed in Fig. 2K indicate that most analytical methods achieved high sensitivity, with many reaching the maximum score of 3 points, corresponding to detection limits ≤1% of the target concentration. It is important to note that the sensitivity of an analytical method must comply with regulatory requirements, meaning that the limit of quantitation (LOQ) should be well below the maximum permissible limit established by legislation. When estimating this parameter, researchers must consider both the LOQ and the target concentration, which can vary depending on the analyte, country-specific regulations, and the application area (e.g., environmental, cosmetic, or food analysis). In this context, sensitivity can be calculated as the ratio between the LOQ and the target concentration, expressed as a percentage, providing both parameters in the same units. To clarify these differences and guide researchers, the authors of CACI have included a supplementary table, which summarizes representative target concentrations according to the sample type and analytical purpose [20].

4.8. Analysis time

The last attribute evaluates the overall duration required to complete both sample preparation and instrumental analysis. Shorter processing times are preferred because they improve laboratory efficiency and reduce energy consumption. Methods capable of finishing the entire procedure in ≤5 min receive the maximum score (6 points), as they align with the principles of rapid and streamlined analytical workflows promoted by CACI. The achievement of near-instantaneous results remains challenging, as it requires the seamless integration of highly efficient sample preparation and analytical processes without compromising accuracy or reliability. Methods taking 10–20 min remain acceptable but slightly less ideal, while those exceeding 60–90 min become less practical for routine or high-throughput applications. Instruments such as spectrophotometers, colorimeters, and point-of-care devices often meet these criteria due to their minimal preparation steps and nearly instantaneous measurements. Conversely, chromatographic systems, despite offering superior selectivity and sensitivity, tend to require longer running times and conditioning periods, reducing their overall time efficiency.

The results displayed in Fig. 2L show a moderate distribution of analysis times. Most studies scored between 3.0 and 4.5 points, indicating total analysis times typically ranging from 10 to 30 min. These durations are acceptable within most analytical workflows, particularly when high selectivity or multi-analyte capabilities justify slightly longer runs. Only one study reached the lowest score (0 points), corresponding to procedures exceeding 300 min [23]. In this study, the sample preparation was notably lengthy, requiring overnight equilibration at room temperature, 30 min of ultrasonic extraction, and 20 min of centrifugation. These extremely long methods are the least preferred, as they are highly inefficient, consume more resources, and often involve complex sample preparation steps. Notably, none of the methods achieved the maximum score of 6 points, confirming that ultrafast (<5 min) analytical protocols remain uncommon or perhaps still unrealistic today for the determination of EDC in PCPs and cosmetics. This limitation is attributed to the complexity of some chromatographic separations. Future progress in this area should focus on integrating high-throughput strategies and miniaturized separation systems to reduce total analysis time without compromising analytical performance.

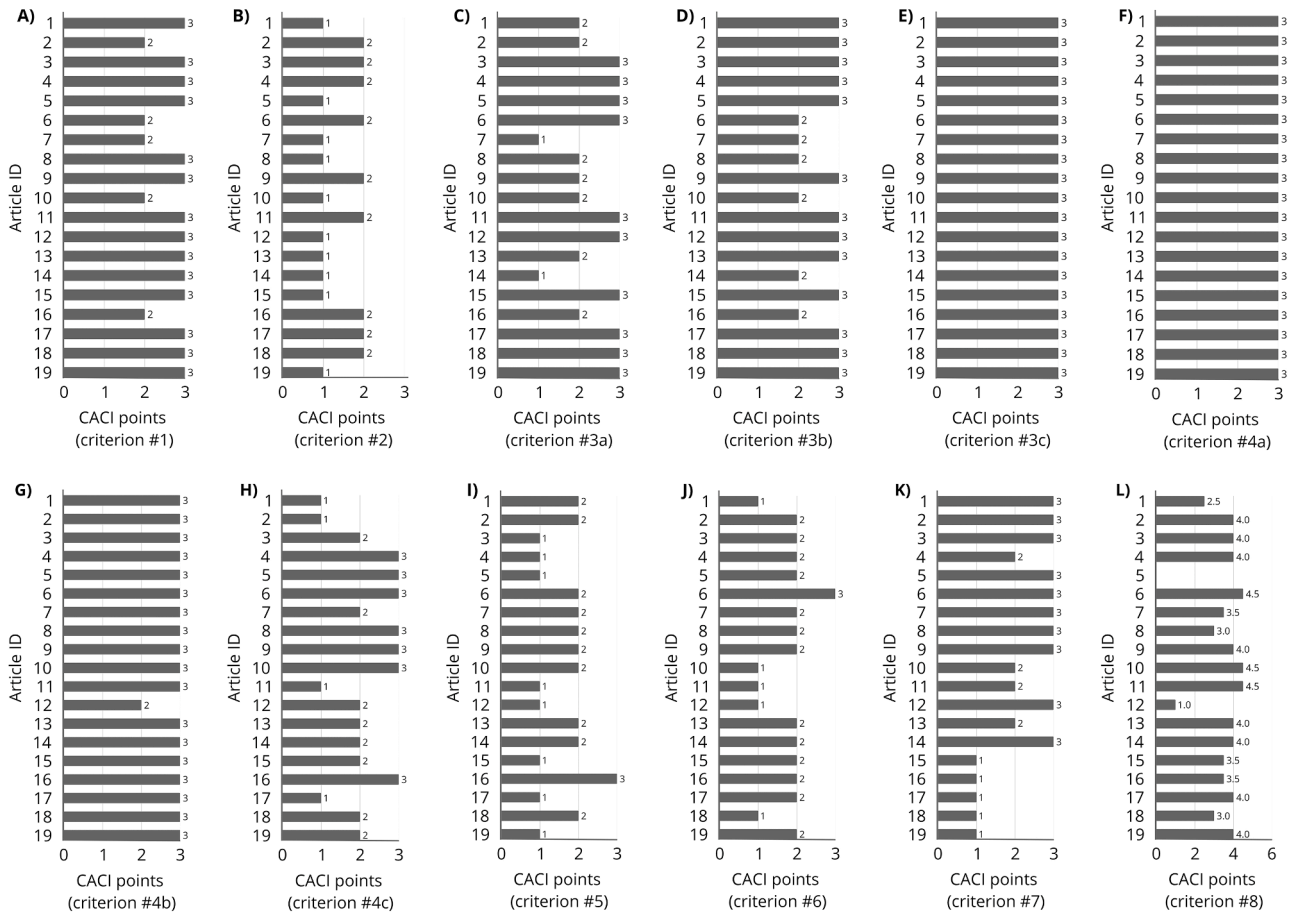


Fig. 2. CACI scores correspond to the analytical methods evaluated for the determination of endocrine-disrupting chemicals in cosmetics and personal care products. A) Based on criterion #1 (sample size). "What is the required sample size (in mL or g)?"; B) Based on criterion #2 (sample preparation). "What level of sample preparation is required?"; C) Based on criterion #3a (feasibility). "Are the chemicals and reagents readily available?"; D) Based on criterion #3b (feasibility). "Are the required instruments available in laboratories?"; E) Based on criterion #3c (feasibility). "What is the total cost of analysis per sample?"; F) Based on criterion #4a (application). "What is the application type of the method?"; G) Based on criterion #4b (application). "How many analytes can be tested?"; H) Based on criterion #4c (application). "How many matrices can be tested?"; I) Based on criterion #5 (portability). "How portable is the method's instrumentation?"; J) Based on criterion #6 (automation). "What is the level of automation of this method?"; K) Based on criterion #7 (sensitivity). "What is the method's sensitivity level?"; L) Based on criterion #8 (sample analysis time). "How long does the sample analysis take (in minutes)?". For further details about CACI points check the original article [20].

5. Comparison with other metrics

The development of analytical metrics has expanded notably, leading to the creation of numerous tools designed to evaluate, quantify, and measure various dimensions of analytical methods [29,30]. Researchers have increasingly combined several of these tools to obtain a more integrated assessment of their methodologies. For instance, M. Abdel-Monem conducted a detailed multi-criteria sustainability evaluation using eight different metrics, which demonstrated the method's high level of greenness, practicality, analytical performance, and innovation [31]. Similarly, A. El-Deen and K. Shimizu analyzed their procedures through comparable criteria and complemented their assessment with the GLANCE tool, which offered a concise visual summary of the method's main strengths, limitations, and overall performance, thereby improving transparency and comprehension for readers [32]. Many of these metrics assess similar parameters, whereas others have refined over time to address emerging analytical needs [33]. Moreover, a few guidelines and recommendations have been proposed to standardize their development, use and interpretation [34–37]. Each metric, however, has specific strengths and limitations that influence its applicability, making it particularly relevant to compare CACI with other tools (see Table 3).

The comparative analysis highlights that CACI offers a broader and more integrative framework than previously established metrics (see Table 3). Its main strength lies in combining performance, environmental sustainability, cost, and applicability within a single, color-coded platform. Unlike many greenness-focused tools, CACI incorporates practical dimensions such as analysis cost, matrix versatility, automation, and portability. This multidimensional structure makes it particularly suitable for modern analytical contexts involving miniaturized or field-deployable systems. Nevertheless, certain parameters, such as the cost per sample, are difficult to estimate objectively because market prices can vary and may also depend on the source consulted. In addition, the sensitivity attribute is challenging to assess, as the information required for its evaluation is often not reported in published studies. Despite these main constraints, CACI is a new and versatile tool that has received growing attention from the scientific community and can bridge the gap between theoretical assessment and practical applicability, contributing to a more balanced evaluation of analytical methods.

6. Perspectives and limitations

The continuous progress of analytical chemistry suggests that many more evaluation metrics will be developed soon. As society and technological challenges move forward, the tools that guide decision-making must also adapt. Metrics cannot remain static since they require periodic revision to incorporate new methodological and sustainability-driven advances. This dynamic nature calls for frameworks that are

adaptable, transparent, and capable of reflecting the complexity of modern analytical practice. A flexible and continuously updated system ensures that analytical chemistry remains aligned with broader societal and scientific priorities. A holistic and multichromatic perspective is a must for the next generation of analytical assessment tools. The combination of complementary indices offers an opportunity to build hybrid models that integrate greenness, analytical performance, and applicability into a single evaluative structure. Tools designed with this philosophy should be adaptable to the specific needs of each context while maintaining clear, consistent, and reproducible algorithms. Ideally, the incorporation of artificial intelligence could enhance these systems by allowing users to input details of their analytical procedures and obtain a comprehensive evaluation covering innovation, performance, sustainability, and operational simplicity.

Beyond their evaluative purpose, current analytical tools should also serve an educational function. The inclusion of didactic resources would make them valuable for students and early-career researchers seeking to understand how analytical assessments are performed and interpreted. In a broader sense, frameworks like CACI could support regulatory agencies in comparing analytical methods for monitoring purposes, thereby promoting transparency and informed decision-making in areas such as chemical safety and green compliance. As summarized in Table 4, current analytical methodologies still present several limitations, but also opportunities for improvement aligned with CACI principles. It is important to note that achieving a balanced performance across all CACI criteria remains a challenging task, as optimizing one parameter may often compromise another. In this sense, it is evident that all analytical methods present both strengths and weaknesses, and the goal should not be to maximize a single parameter, but to reach an optimal compromise.

It is important to note that the application of metric tools such as CACI is not universally transferable to all types of analytical methodologies. The use of these frameworks requires the availability of a minimum set of experimental and methodological information to address the evaluation criteria. When such information is not reported or the method is not designed to generate these parameters, certain studies may be excluded from the assessment. Recent developments in analytical metrics have started to address this limitation by incorporating flexible scoring options such as “not applicable” or “not studied”, allowing a more adaptable evaluation. In this sense, although the present review is focused on LC- and GC-based methodologies, the application and further adaptation of tools to alternative approaches, including for example HPTLC-bioassay systems [17], should be encouraged.

From an application perspective, the fast expansion of new cosmetics and PCPs market further reinforces the need for improved analytical methods. These products are used daily and in large quantities, often involving prolonged skin contact and complex chemical formulations. The increasing diversity of product types, including skincare, haircare, sunscreens, and fragrances, has led to a rise in the number of ingredients and potential contaminants present in these matrices. As a result, analytical methods must adapt not only to ensure quantification, but also to deal with high sample throughput, diverse formulations, and stricter regulatory requirements.

Another limitation is the long analysis time associated with chromatographic methods. As shown in this review, none of the evaluated methodologies achieved ultrafast analysis conditions, showing that time efficiency remains an unresolved challenge. Reducing total analysis time through the optimization of both sample preparation and chromatographic separation is therefore critical, particularly for routine and high-throughput applications. In addition to target EDCs, cosmetic formulations may contain intentionally added substances and non-intentionally added compounds, including impurities, degradation products, and by-products formed during manufacturing. This chemical complexity highlights the need to move beyond targeted approaches towards screening works.

Table 3
Strengths and limitations of some of the most used analytical tools.

Metric	Strengths	Limitations
Analytical Eco-Scale [50]	Simple quantitative system; allows fast estimation of method greenness using penalty points	Focused only on environmental aspects; excludes practicality, cost, and applicability criteria
AGREE [51]	Visual, easy-to-interpret circular output; provides comprehensive greenness assessment based on GAC principles	Limited to environmental impact; does not address cost, or applicability
AGREEprep [52]	Evaluates the greenness of sample preparation procedures; consistent with AGREE methodology	Restricted to the sample preparation step; lacks evaluation of method practicality and cost
ComplexMoGAPI [53]	Expanded greenness assessment covering more analytical steps	Still limited to sustainability aspects; excludes parameters like sensitivity, applicability, or operational feasibility
RGB 12 [18]	Introduce a multidimensional color-based model	Practicality not explicitly evaluated; lacks detailed criteria such as cost per sample or matrix versatility
BAGI [54]	Focus on method applicability and user practicality; simple and visual	Omits parameters such as analysis cost, applicability to multiple matrices, and treatment of semi-quantitative methods
CACI [20]	Provide an objective evaluation of real-world applicability and efficiency	Some parameters (e.g., cost per sample, sensitivity) may be difficult to assess objectively due to lack of consistent reporting or data availability

AGREE, analytical greenness metric; AGREEprep, analytical greenness metric for sample preparation; BAGI, blue applicability grade index; CACI, click analytical chemistry index; ComplexMoGAPI, complex modified green analytical procedure index; RGB 12, red-green-blue model.

Moreover, although we focused on the application of CACI to the determination of EDCs in cosmetics and PCPs, its use should be extended to other analytes and matrices to better understand how analytical methods are changing over time. The long-term impact of such progress depends on maintaining open-access, community-driven platforms, expanding databases, and improving visualization tools to strengthen the collective advancement of analytical chemistry.

7. Conclusions

The determination of EDCs in cosmetics and PCPs remains a demanding task due to their trace concentrations and complex sample matrices. The increasing focus on sustainability has encouraged the use of greener solvents, innovative sorbents, and miniaturized extraction techniques. However, evaluating the overall feasibility and practicality of analytical methods continues to be a major challenge that has not yet been fully addressed. CACI fills this gap as a new and user-friendly metric specifically designed to evaluate the feasibility of analytical methods. It provides both a tool and software solution to assess and compare analytical procedures, integrating performance, environmental impact, cost, and applicability. Through its color-coded and modular framework, CACI promotes the development of sustainable, practical, and effective techniques while ensuring clarity and reproducibility in method evaluation. When applied to the determination of EDCs in cosmetics and PCPs, the CACI scores (57–80), indicated that the evaluated methodologies can be considered acceptable or highly practical. It is expected that its continued application will inspire the design of analytical methods that are more sustainable, efficient, and aligned with current and future demands of analytical science.

Table 4
Summary of current limitations and CACI-oriented improvement strategies for analytical methods applied to EDC determination in cosmetics and personal care products.

CACI criterion	Current limitations identified	Proposed improvements
Sample preparation	Multi-step procedures (extraction, clean-up, solvent exchange) still increase time, solvent use, and variability	Use of microextraction techniques or simplified workflows to reduce handling steps and improve reproducibility
Analysis time	Some methods require long total times due to extended preparation steps or chromatographic runs	Adoption of faster analytical strategies, including high-throughput and miniaturized systems
Portability	Strong dependence on laboratory-based instrumentation (LC-MS, GC–MS) limits on-site analysis	Development of portable or miniaturized devices for rapid screening applications
Automation	Partial automation with manual sample preparation steps increases operator dependency	Implementation of fully or semi-automated workflows to improve consistency and throughput
Feasibility (chemicals & reagents)	Use of significant volumes of organic solvents reduces sustainability	Replacement with greener solvents or reduction of solvent consumption
Applications (matrix scope)	Some methods are limited to specific cosmetic matrices	Development of multi-matrix methods to improve versatility
Feasibility (cost per sample)	Cost estimation is often unclear or not reported, reducing comparability	Standardized reporting of reagent and consumable costs per sample
Sensitivity	In some cases, sensitivity is not clearly linked to regulatory limits	Optimization of detection and calibration to ensure compliance and reliability

Declaration of use of AI-Assisted technologies

The authors employed ChatGPT (GPT-4, OpenAI) to assist with language refinement. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

CRediT authorship contribution statement

Adrián Fuente-Ballesteros: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Ana Jano:** Writing – original draft, Visualization, Methodology, Investigation. **Jorge A. Custodio-Mendoza:** Writing – review & editing, Visualization, Conceptualization. **Victoria Samanidou:** Writing – review & editing, Validation, Conceptualization. **Fotouh R. Mansour:** Writing – review & editing, Visualization, Conceptualization. **Ana M. Ares:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Conceptualization. **José Bernal:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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