A comparative evaluation of analytical green metrics for microextraction techniques based on polymeric and gel membranes as solid support

Samira Sedehi [a], Hadi Tabani [b,**], Farzaneh Dorabadizare [a], Stig Pedersen-Bjergaard [c], María Ramos-Payán [d,*]

[a] *Department of Analytical Chemistry and Pollutants, Shahid Beheshti University, G. C., Evin, Tehran, 1983963113, Iran*
[b] *Department of Environmental Geology, Research Institute of Applied Sciences (ACECR), Shahid Beheshti University, Tehran, Iran*
[c] *Department of Pharmacy, University of Oslo, P.O Box 1068 Blindern, 0316, Oslo, Norway*
[d] *Department of Analytical Chemistry, Faculty of Chemistry, University of Seville, c/Prof. García González s/n, 41012, Seville, Spain*

A R T I C L E   I N F O

A B S T R A C T

Sample preparation plays a pivotal role in chemical analysis, serving to isolate target analytes from diverse matrices and enhance measurement selectivity and sensitivity. This review examines microextraction's eco-friendliness versus tradition, focusing on LPME and EME systems for acidic compounds. Different solid supports (polymeric and gel membranes) implemented in different configurations are evaluated. These innovative techniques reduce the consumption of chemicals and offer enhanced environmental safety. To determine the greenness of these techniques, we employ three widely recognized metrics: Analytical Eco-Scale, Green Analytical Procedure Index (GAPI), and Analytical GREEnness (AGREE). Our comparative analysis provides insights into the strengths and weaknesses of these metrics and offers a holistic perspective on the greenness of microextraction techniques. This review contributes to the ongoing efforts in Green Analytical Chemistry by facilitating the selection of environmentally benign sample preparation methods, thus promoting sustainable laboratory practices, and minimizing adverse environmental impacts.

1. Introduction

Sample preparation is an indispensable step that precedes chemical analysis, which is carried out to isolate analytes of interest from a wide variety of matrices. This is primarily due to the need to make the target analytes more suitable for measurement and to improve selectivity and sensitivity [1]. Typical sample pretreatment methods include liquid-liquid extraction (LLE) and solid-phase extraction (SPE). The former involves the partitioning of analytes into immiscible solvents [2], whereas the latter involves the distribution of analytes between the solid packing material and the liquid mobile phase [3]. Conventional liquid-liquid extraction (LLE) is burdened by the substantial utilization of toxic organic solvents, resulting in a notable environmental impact. Moreover, this method entails labor-intensive procedures with multiple steps, making it time-consuming. Although SPE takes less time than LLE, it requires column equilibrium and elution with toxic solvents, which makes this method environmentally hazardous [4].

Modern sample preparation strategies aim to develop eco-friendly techniques that utilize fewer toxic solvents and mitigate the drawbacks of traditional methods. A set of methodologies has been devised to create more efficient techniques that eliminate interference by preconcentrating small amounts of analytes [5] and miniaturizing extraction methods. Liquid-phase microextraction (LPME) can be considered a miniaturized version of LLE that uses fewer chemicals and provides a greener approach [6]. The miniaturization in this system has been shown to significantly enhance extraction efficiency, making it compatible with different types of SLMs [7]. Recent advancements in the sample pretreatment process involve utilizing membranes to enhance the cleanup and monitoring of analytes using solventless or solvent-minimized extraction techniques. Two membrane-based techniques that have received significant attention are hollow fiber liquid phase microextraction (HF-LPME) [8–11] and electromembrane extraction (EME) [12,13]. In the HF-LPME process, the target analyte in the donor solution is extracted into the organic layer on the walls of the hollow fiber before moving on to the acceptor phase inside the lumen of the hollow fiber [14]. Although HF-LPME is a popular alternative to LLE,

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01	Minimal sample size and minimal number of samples are goals.
02	Direct analytical techniques should be applied to avoid sample treatment.
03	In situ measurements should be performed.
04	Integration of analytical processes and operations saves energy and reduces the use of reagents.
05	Automated and miniaturized methods should be selected.
06	Derivatization should be avoided.
07	Generation of a large volume of analytical waste should be avoided and proper management of analytical waste should be provided.
08	Multi-analyte or multi-parameter methods are preferred versus methods using one analyte at a time.
09	The use of energy should be minimized.
10	Reagents obtained from renewable source should be preferred.
11	Toxic reagents should be eliminated or replaced.
12	The safety of the operator should be increased.

Fig. 1. 12 Green Analytical Chemistry (GAC) principles. (For interpretation of the references to color/color in this figure legend, the reader is referred to the Web version of this article.)

long extraction times (30–120 min) make this method less desirable because only passive diffusion transports analytes across the membrane [9]. In contrast, EME has resolved this issue by applying a voltage across the membrane, thereby facilitating mass transfer based on electrokinetic migration [12]. Furthermore, researchers explored using microfluidic devices and biopolymer-based membranes in HF-LPME and EME systems to enhance their environmental safety. The microfluidic-chip format scale down the methods and offers substantial economic and environmental advantages because it consumes less sample and solvent [15–18] and biopolymer-based membranes promote biodegradability and cost-effectiveness for the entire extraction set-up [10]. Recently, integrating biopolymers into microfluidic devices offers the potential for greener procedures by reducing the reliance on toxic solvents and enhancing the sustainability of analytical processes [19,20].

Evaluating the greenness of a technique using dedicated metrics is of high importance [21], and the main objective of the present work is to assess and compare the degree of greenness of polypropylene hollow fiber, gel, and microfluidic chips LPME and EME techniques in order to provide qualitative and quantitative data for a group of acidic compounds.

Green Analytical Chemistry (GAC) aims to develop environmentally benign methodologies that minimize the side effects of laboratory practices. GAC applies 12 principles (Fig. 1) to determine whether an analytical method is green [22]. Various metrics have been developed to evaluate the impact of different parameters on the greenness of a particular analytical procedure [23]. In this review, the green characteristics of six different configurations in microextraction techniques were evaluated using three metrics: Analytical Eco-Scale [24], Green Analytical Procedure Index (GAPI) [21], and Analytical GREEnness (AGREE) [25]. The microextraction methods were selected for hollow-fiber configuration, flat membranes and miniaturized microfluidic systems and both LPME and EME techniques were evaluated for these configurations. We specifically selected three that stand out for their comprehensive and flexible characteristics, distinguishing them as preferred choice over others.

The Analytical Eco-Scale is a tool that subtracts penalty points (PPs) from a base of 100, with higher scores indicating greater sustainability [26]. This was selected to provide us with an objective assessment of the eco-efficiency of analytical procedures by indicating the extent of non-green characteristics. GAPI provides a comprehensive overview of the entire analytical method [27] from sample collection to final determination. Each stage of the analytical procedure is represented by a pentagram using three different colors reflecting the greenness of the method: high, medium, and low [28]. In terms of greenness assessment,

Table 1
Comparative analysis of advantages and disadvantages based on Analytical Eco-Scale, GAPI, and AGREE for evaluating the green character of analytical procedures.

Method	Analyzing criteria	Advantage	Disadvantage	Output	Greenness profile	Ref.
Analytical Eco-Scale	- Hazards - Reagents - Energy - Waste	- Simplicity of use - The number of chemicals and the amount of waste is calculated semi-quantitatively - Provides quantitative information about the environmental impact of analytical methods - Analytical approaches can be compared easily	- Does not contain any information about the structure of hazards - Inability to discriminate between micro- and macro-scales of method applications - Prior to preparing the sample, the synthesis part is not taken into consideration	Number (100 – PPs)	x > 75: excellent green analysis 75 < x < 50: acceptable green analysis X < 50: poor green analysis	[22, 24, 30]
GAPI	- Collection - Preservation - Transport - Storage - Preparation - Analysis	- Considers how each step of the analytical process is green - Different analytical procedures can easily be compared	- Do not contain any information about the structure of hazards - Prior to preparing the sample, the synthesis part is not taken into consideration	Pictogram (5 Pentagrams)	Green: low environmental impacts Yellow: medium environmental impact Red: high environmental impact	[22, 30]
AGREE	12 Principles of GAC	- Availability of freeware software - Inclusiveness to cover all the principles of GAC - The assessment results are easy to understand and informative	- Do not contain any information about the structure of hazards - Prior to preparing the sample, the synthesis part is not taken into consideration	Clock-like Pictogram (score range: 0–1)	x > 0.6: a green method	[22, 30]

AGREE is the most recent tool [29] based on software that converts each of the 12 principles of GAC into a 0–1 scale [25]. The software presents a comprehensive and adaptable assessment framework for evaluating the environmental sustainability of analytical procedures. Providing numerical assessments and highlighting areas amenable to improvement. Table 1 presents a comparison of the advantages and disadvantages of each tool. PPs provide a holistic understanding of the ecological impact associated with a method, while three-colored pictograms, as presented in GAPI and AGREE, elucidate the entire process. Furthermore, AGREE stands out as an exceptional metric due to being an automated tool for evaluation of analytical methods.

2. Miniaturized extraction

Using miniaturized extraction techniques, analytes of interest can be extracted with minimum extraction volumes or at low concentrations from a variety of matrices. The following sections examine membrane-based microextraction techniques in two distinct groups, HF-LPME and EME, which are further divided into three subcategories based on the type of membrane used, namely polypropylene, agarose gel, and microfluidic chip.

2.1. Hollow fiber liquid phase microextraction (HF-LPME)

Through the advancement of different LPME formats, the process is becoming more environmentally friendly and the drawbacks are being overcome [4]. There are several LPME modes, but recently the membrane-based strategy has garnered a lot of attention. The most popular material for HF-LPME is polypropylene hollow fiber, but other recently developed membranes, like agarose gel and microfluidic chips, will also be covered further below.

2.1.1. Polypropylene-LPME

It is predominantly polypropylene that is used as a polymeric membrane in HF-LPME. An organic solvent, supported liquid membrane, is immobilized in the pores of this porous hollow fiber and the analytes presented in the sample (donor) solution are transferred into the acceptor solution in the lumen of the hollow fiber. In other words, the organic phase is protected by the polypropylene hollow fiber. It is possible to conduct HF-LPME in a two-phase or a three-phase mode during the extraction and preconcentration steps. In two-phase HF-LPME, the organic phase and acceptor solution are identical; however, in three-phase mode, porous hollow fiber is submerged in an aqueous solution containing two distinct immiscible phases [31]. The disposable nature of this membrane eliminates sample carryover, and the simultaneous cleanup and preconcentration of extracts mean that no additional steps are required prior to analysis. The extracted samples can be directly injected into the chromatographic system, as was the case with a group of acidic compounds analyzed using an HPLC/MS-MS system in conjunction with earlier HF-LPME techniques [32]. Due to the high selectivity and sensitivity of HF-LPME in this study, salicylic acid, ibuprofen, and diclofenac were cleanly extracted from wastewater samples, allowing for direct injection into the chromatographic system. Among the materials used for hollow fibers, polypropylene (PP) is commonly employed due to its favorable mechanical properties and chemical resistance. However, from an environmental perspective, polypropylene is not considered a green material [7]. To enhance the sustainability of microextraction methods, there is a growing interest in exploring alternative materials for hollow fibers that are derived from renewable sources, biodegradable, and produced through eco-friendly processes.2.1.2. Agarose Gel-LPME.

In response to the need for more environmentally friendly processes, gel membranes were developed, and agarose, a polysaccharide derived from seaweed, can create a biodegradable hydrophilic gel for use in LPME. During liquid phase microextraction, the green membrane can function as either an agarose film [33] or a solvent-impregnated agarose

gel disc [34]. Those systems work under stagnant conditions and the gel membranes used are disposables. Offering high enrichment factors for the target analytes made it a versatile method that can easily be adopted for various compounds like organic pollutants.

2.1.2. Microfluidic chip LPME

The combination of microfluidic chips with LPME has been emerged recently. The sample and acceptor solutions are injected into the microchip and the analytes are transferred according to the passive diffusion [15]. The LPME-chip is a highly effective mode to extract a wide range of compounds.

Hollow fiber LPME systems have demonstrated high selectivity and good enrichment in traditional non-miniaturized setups. The aqueous acceptor phase can be analyzed directly using liquid chromatography, electrophoresis, and related techniques without the need for evaporation and reconstitution. The miniaturization of LPME in microfluidic systems has brought advantages in terms of accelerating mass transfer through passive diffusion, thanks to the miniaturization of the channels, as diffusion distances are very short. In recent years, there has been an evolution in microfluidic systems based on LPME, employing different geometries [17,18], or even replacing traditional toxic solvents with natural eutectic solvents [19]. There are two operational modes known in microfluidic systems [16], namely double-flow and semi-continuous systems, which determine improvements in extraction efficiencies or enrichment factors, respectively. Therefore, the aim is to analyze how the degree of greenness in different operational modes affects the analysis of acidic compounds using three different metrics, and whether the recent introduction of natural membranes is relevant in the microfluidic field.

2.2. Electromembrane extraction (EME)

Since the electric field acts as a driving force, EME offers more effective mass transfer across the SLM than HF-LPME. This method involves charging the analytes of interest, which then migrate from the sample through the SLM and into the acceptor solution [35]. Similar to HF-LPME, various membranes have been developed for this method, such as polypropylene, agarose gel, and microfluidic chips. These will be discussed in more detail below'.

2.2.1. Polypropylene-EME

The polypropylene hollow fiber functions as a container for the acceptor solution in the EME methodology, with its porous wall serving to immobilize the artificial liquid membrane, much akin to its role in HF-LPME. However, a noteworthy distinction arises from the presence of electrodes within the hollow fiber and the donor solution in the EME methodology, constituting crucial elements that set it apart. These electrodes play a pivotal role in enhancing the extraction process by generating an electric field, thereby propelling analytes from the donor solution through the liquid membrane and into the acceptor solution. General disadvantages of EME, regardless of the type of membrane, includes cases where the current is high, which may cause drifting pH, bubble formation, and limited stability of the extraction system. The choice of organic solvent as the SLM in electromembrane systems must meet the requirement of being conductive, regardless of the geometry or device used, in contrast to the LPME technique. EME is not suitable for neutral compounds, but the use of ionic carriers, such as di(2-ethylhexyl) phosphoric acid (DEHP), can enable the extraction of these substances.

This distinctive configuration engenders an efficient and selective extraction of target compounds, finding applications in diverse fields such as environmental analysis and pharmaceutical research. An illustrative example involves the extraction of a group of acidic drugs from human plasma, as demonstrated in a study evaluating various SLMs to optimize recovery [36]. As part of ongoing scientific efforts, there is a concerted push to minimize the reliance on organic solvents during the
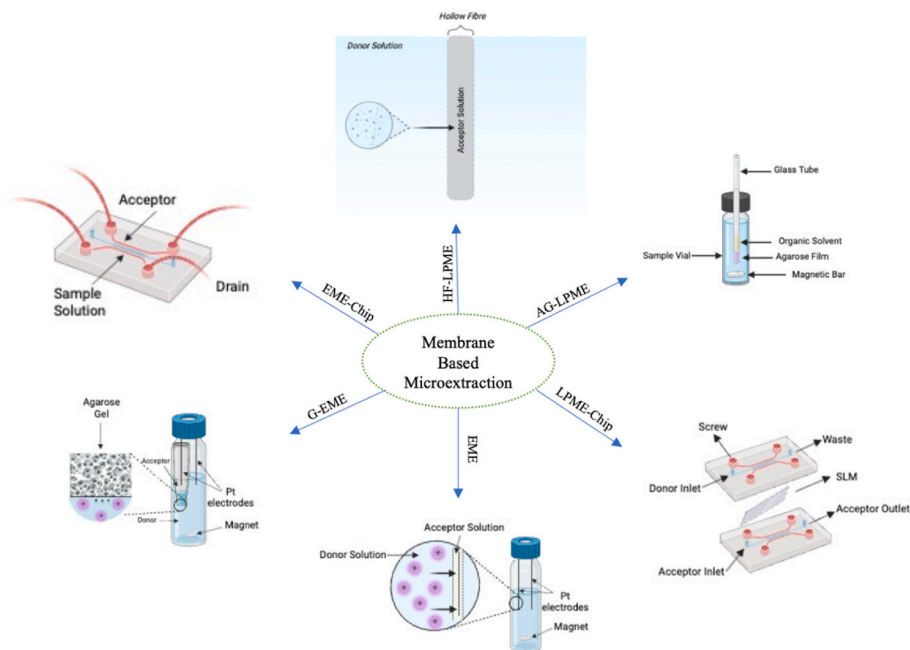
Fig. 2. A schematic illustration of six membrane-based techniques (created with bioRender.com).

extraction process, and in some instances, to develop solventless methodologies. This drive stems from a commitment to reduce environmental impact and enhance the overall sustainability of extraction processes.

2.2.2. Agarose gel- EME

Taking advantage of biopolymers rather than organic solvents, G-EME offers a more environmentally friendly approach that does not result in any water/organic interface and reduces the risk of environmental pollution and waste generation [36–40]. In one study, agarose gel was used to extract a group of polar acidic compounds from fruit juices [37]. The target analytes entered the acceptor solution after passing through the agarose gel membrane. The suggested method is simple to use, and since no organic solvent was used throughout the entire process, it is also quite environmentally friendly due to the agarose gel's green attributes. Under optimized conditions, the result of this study was quite fascinating, and the degree of greenness of this method will be further discussed. On the other hand, Gel-EME, is favorable for polar analytes and no carrier is required, compared to traditional EME using polypropylene. Also, the use of organic solvent is eliminated. However, gel-EME may be complicated by electro-endosmosis which changes the volume of the sample and acceptor during extraction. Also, gel-EME provides less selectivity.

2.2.3. Microfluidic Chip-EME

Microfluidic chips have been used to increase the efficiency and sustainability of extraction with a significant reduction in the use of organic solvents compared to the conventional EME setup. Using microfluidic chips also lessens waste production and enables continuous extraction, further enhancing sustainability in chemical analysis. Combination of EME with microfluidic system not only scale down the EME method but also improve the extractability of various compounds in biological matrices. Ramos-Payan et al. developed a method for the simultaneous extraction of acidic and basic drugs based on an EME on chip system [41]. It was created to carry out two EME extractions in a reusable device at once. In general, advantages of EME includes rapid extraction, selectivity based on the electrical field, efficient sample cleanup, and aqueous acceptors. Also, the devices used in EME are low price. Microfluidic chip EME provides very rapid extractions, and extractions can be performed from very small sample volumes. The use of

Table 2
The PPs to calculate analytical Eco-Scale [24].

	Reagents	Sub-total PP	Total PP
Amount	<10 mL (g)	1	Amount PP * Hazard PP
	10–100 mL (g)	2	
	>100 mL (g)	3	
Hazard (#of pictograms*signal word)	None	0	
	Less severe hazard	1	
	More severe hazard	2	
Reagent	Number of pictograms	Signal word	PPs
Formic Acid	3	Danger	6
Methanol	3	Danger	6
Acetone	2	Danger	4
1-Octanol	1	Warning	1
1-Butanol	3	Danger	6
1-Heptanol	1	Warning	1
1-Dodecanol	2	Warning	2
Ethanol	2	Danger	4
HCl	2	Danger	4
NaOH	1	Danger	2
NaH$_2$PO$_4$	1	Danger	2

organic solvent is only 2–3 μL per sample, and systems are robust. However, microfluidic chip EME requires specialized equipment such as syringe pumps, and are less suited for parallel extraction of multiple samples. In microfluidic chip EME, the extraction device is normally used for multiple extractions. This is an advantage in terms of sustainability, but carryover may be an issue. Using EME in microfluidic systems offers significant green advantages over traditional EME setups. The miniaturization inherent in microfluidic EME results in the consumption of much smaller volumes of solvents and reagents, significantly reducing chemical waste and environmental impact. Additionally, the miniaturized channels in microfluidic systems require much lower voltages for effective extraction, leading to lower energy consumption. These benefits make microfluidic EME a more sustainable and eco-friendly alternative compared to conventional EME methods.
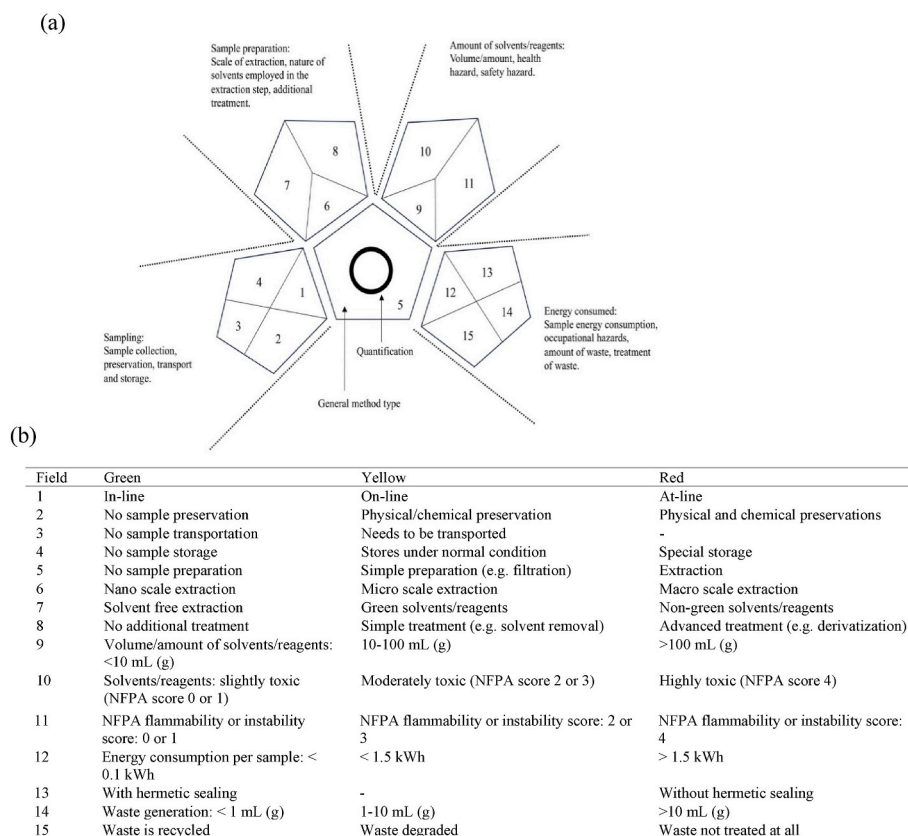
(a)

(b)

Field	Green	Yellow	Red
1	In-line	On-line	At-line
2	No sample preservation	Physical/chemical preservation	Physical and chemical preservations
3	No sample transportation	Needs to be transported	-
4	No sample storage	Stores under normal condition	Special storage
5	No sample preparation	Simple preparation (e.g. filtration)	Extraction
6	Nano scale extraction	Micro scale extraction	Macro scale extraction
7	Solvent free extraction	Green solvents/reagents	Non-green solvents/reagents
8	No additional treatment	Simple treatment (e.g. solvent removal)	Advanced treatment (e.g. derivatization)
9	Volume/amount of solvents/reagents: <10 mL (g)	10-100 mL (g)	>100 mL (g)
10	Solvents/reagents: slightly toxic (NFPA score 0 or 1)	Moderately toxic (NFPA score 2 or 3)	Highly toxic (NFPA score 4)
11	NFPA flammability or instability score: 0 or 1	NFPA flammability or instability score: 2 or 3	NFPA flammability or instability score: 4
12	Energy consumption per sample: < 0.1 kWh	< 1.5 kWh	> 1.5 kWh
13	With hermetic sealing	-	Without hermetic sealing
14	Waste generation: < 1 mL (g)	1-10 mL (g)	>10 mL (g)
15	Waste is recycled	Waste degraded	Waste not treated at all

Fig. 3. (a) Description of pictograms used in Green Analytical Procedure Index (GAPI) and (b) Color of each field in GAPI [22].

For better understanding, Fig. 2 shows a schematic representation of each of these membrane microextraction techniques.

3. Greenness evaluation

Assessing the green character of analytical methodologies is undeniably of high importance from the GAC point of view. There are several tools that can be used for this aim and the most popular ones are Analytical Eco-Scale, Green Analytical Procedure Index (GAPI) and Analytical GREEnneess (AGREE) Metric.

3.1. Analytical Eco-Scale

The Analytical Eco-Scale is a valuable semi-quantitative tool that allows us to test the environmental friendliness of a method. It achieves this by assigning penalty points to various aspects: (i) reagents are evaluated based on their quantity and potential hazards, and (ii) instruments are assessed in terms of their energy consumption, occupational hazards, and waste generation [24]. Table 2 summarizes the PPs to calculate analytical Eco-Scale. A higher score indicates a greener approach.

3.2. Green Analytical Procedure Index (GAPI)

GAPI provides a comprehensive evaluation of the environmental impact of an analytical methodology, covering all stages from sample collection to final determination. The level of "greenness" in an analytical method is directly proportional to the number of stages involved. The more steps there are, the less environmentally friendly the methodology becomes. It is evident that less eco-friendly methodologies consume more energy and generate larger amounts of waste. The stages in every analytical procedure typically include: (i) sample collection, (ii) preservation, (iii) transportation, (iv) sample preparation, and (v)

determination and quantification. There is a pictogram to classify the degree of greenness in each step which is used color coding to visually represent environmental impact of each stage [21]. The central pentagram denotes whether it was used for qualification or both qualification and quantification (Fig. 3). Recognizing sample preparation as the core of any analytical procedure, microextraction plays a crucial role in making this process more environmentally sustainable.

3.3. Analytical GREEnneess (AGREE)

Another newly introduced tool is AGREE which assess methods according to the 12 GAC principles (Fig. 1). Each principle is converted to a numerical value ranging from 0 to 1 and represented by a color [25]. The availability of a free application for this metric system makes it even more appealing to compare a group of membrane-based microextraction methodologies in this study. The aforementioned metric tools have assessed and evaluated the environmental sustainability profile of various membrane-based microextraction techniques, pinpointing the most eco-friendly options among both established and recently developed methods. The Analytical Eco Scale provides a numerical representation of a method's greenness, giving a quick overview of its environmental impact. Pictograms delve into each step, offering qualitative insights for a more detailed understanding. AGREE, on the other hand, offers a comprehensive overview by considering both qualitative and quantitative aspects. Clearly, recycling waste is a crucial consideration, as it has a significant impact on the green index. The combination of solvent-free extraction with chip-based approaches and miniaturized chromatography systems can reduce waste generation throughout the entire system in the future. Table 3 offers a comprehensive summary of six membrane-based microextraction techniques, showcasing their eco-friendly characteristics when it comes to extracting various acidic compounds.

The variations in the green indices of the Eco-Scale, GAPI, and

Table 3

Evaluation of green index of selected membrane-based analytical methodologies.

Ref	Analyte	Matrix	Method	Eco-Scale		GAPI	AGREE
[32]	Acidic drug compounds	Wastewater	HF-LPME	Reagents	PPs		0.43
				Formic acid	6		
				Methanol	6		
				Acetone	4		
				Instruments			
				HPLC-MS	2		
				Occupational hazard	3		
				Waste	8		
				Total PPs	29		
				Score	71		
[34]	Polycyclic aromatic hydrocarbons	Water	AG-LPME	Reagents	PPs		0.49
				Acetonitrile	4		
				Methanol	6		
				Ethanol	4		
				Acetone	4		
				1-Octanol	1		
				Instruments			
				GC-MS	2		
				Heat	2		
				Occupational hazard	3		
				Waste	8		
				Total PPs	34		
				Score	66		
[15]	Polycyclic aromatic hydrocarbons	Water	LPME-Chip	Reagents	PPs		0.47
				Methanol	6		
				1-Butanol	6		
				Instruments			
				HPLC-UV	1		
				Occupational hazard	0		
				Waste	6		
				Total PPs	19		
				Score	81		
[35]	Acidic drug compounds	Human plasma	EME	Reagents	PPs		0.55
				Methanol	12		
				Formic Acid	12		
				1-Heptanol	1		
				Instruments			
				HPLC-UV	1		
				Occupational hazard	0		
				Waste	8		
				Total PPs	34		
				Score	66		
[37]	Acidic compounds	Fruit juices	G-EME	Reagents	PPs		0.58
				HCl	4		
				NaOH	2		
				NaH_2PO_4	2		
				Acetonitrile	8		
				Instruments			
				HPLC-UV	1		
				Heat	2		
				Occupational hazard	0		
				Waste	8		
				Total PPs	27		
				Score	73		
[42]	Acidic drug compounds	Human plasma	EME-Chip	Reagents	PPs		0.56
				1-dodecanol	2		
				Formic Acid	6		
				Methanol	6		
				Instruments			
				HPLC-UV	1		
				Occupational hazard	0		
				Waste	6		
				Total PPs	21		
				Score	79		
[17]			LPME-Chip	Reagents	PPs		0.63
				Dihexylether	1		
				Methanol	6		
				Formic acid	6		
				Instruments			
				HPLC-UV	1		
				Occupational hazard	0		
				Waste	6		
				Total PPs	20		
				Score	80		

Table 3 (*continued*)

Ref	Analyte	Matrix	Method	Eco-Scale		GAPI	AGREE
[18]			LPME-Chip	Reagents	PPs		
				Tributyl phosphate	2		
				Methanol	6		
				Formic acid	6		0.62
				Instruments			
				HPLC-UV	1		
				Occupational hazard	0		
				Waste	6		
				Total PPs	21		
				Score	79		
[19]			LPME-Chip	Reagents	PPs		
				Camphor	2		
				Methanol	6		
				Formic acid	6		0.69
				Instruments			
				HPLC-UV	1		
				Occupational hazard	0		
				Waste	6		
				Total PPs	21		
				Score	79		

AGREE can be attributed to the distinct features and criteria each tool considers when evaluating the greenness of analytical methodologies. The analytical Eco-Scale, for instance, serves as a tool to evaluate the environmental impact of analytical methods by factors such as the quantity of reagents and energy utilized by the instrument. It also considers whether the produced waste recycled or not [43]. By integrating the Eco-Scale with other metrices like AGREE, researchers are better equipped to assess the environmental impact of a method. GAPI, on the other hand, evaluates 15 factors of an analytical procedure, ranging from sample preparation to the utilization of reagents and solvents [44]. Due to the qualitative nature of this technique, combination of that with AGREE and Eco-scale yields a more comprehensive understanding of the entire technique. Ultimately, AGREE provides a software to facilitate evaluation of each method, based on 12 principles of green analytical chemistry, which are then transformed into a 0–1 scale [45].

4. Conclusions and outlooks

Recent endeavors to advance membrane-based microextraction techniques highlight the necessity of minimizing the environmental impact associated with the utilization of organic solvents. This underscores the significance of incorporating eco-friendly practices into analytical approaches. The greenness of six microextraction processes, which were obtained from two primary extraction techniques (LPME and EME), has been evaluated for a diverse set of acidic compounds. This assessment was conducted using three metrics tools: Analytical Eco-Scale, GAPI and AGREE. Based on the results (Table 3), it is worth noting that LPME-Chip and EME-Chip demonstrate the highest Analytical Eco-Scale Score in their respective categories, whereas AG-LPME and G-EME achieve the highest AGREE Score. However, it is worth noting that differences in the AGREE metric are observed for LPME-chip in different geometries and natural solvents. The use of natural eutectic solvents (DESs) in microfluidics [19] shows a higher number of green fields (0.69) compared to microfluidic systems with the same operational mode in double-flow (0.63) [17] using traditional toxic solvents, demonstrating the ecological improvement with DESs. On the other hand, no significant difference was observed between double-flow [17] and semi-continuous geometries [18], with AGREE metric values of 0.63 and 0.62, respectively. The slight decrease in green points in semi-continuous systems can be attributed to higher sample consumption. Furthermore, G-EME has the greatest number of green fields compared to the other GAPI pictograms. These findings collectively reinforce the pivotal role of environmentally conscious microextraction methodologies in advancing sustainable analytical practices.

CRediT authorship contribution statement

Samira Sedehi: Writing – original draft, Visualization, Investigation. **Hadi Tabani:** Writing – original draft, Visualization. **Farzaneh Dorabadizare:** Writing – original draft, Visualization, Investigation. **Stig Pedersen-Bjergaard:** Writing – original draft. **María Ramos-Payán:** Writing – review & editing, Visualization, Supervision, Project administration.

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.

Data availability

Data will be made available on request.

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