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Green Analytical Chemistry: A Critical Review of Eco-friendly Techniques

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ABSTRACT:

Green Analytical Chemistry (GAC) is a newly developed branch of science that applies the concepts of green chemistry to analytical methods with the focus of reducing the negative consequences to the environment and human health. GAC reduces the use of harmful reagents, saves energy, and avoids the production of dangerous wastes. GAC must be in compliance with the 12 principles of green chemistry that defines frameworks for developing green and eco-friendly analytical procedures which must prioritize the prevention of waste, and the use of energy and solvent. Green Analytical Chemistry (GAC) is supported with the endorsement of non-conventional techniques such as microwave and ultrasound-assisted methods that increase the speed of reactions and decrease energy expenditure. Non-intrusive monitoring of processes in real time together with some chemometric techniques yield optimal resource utilization in the context of performing and acquiring results through analyses of processes. This review showcases the development from lowering the volume of solvent for sample pre-treatment to alternative direct analytical methods that do not require solvents or reagents to overpower the sample. NEMI, AES, and GAPI were developed as tools to evaluating the greenness of analytical methods.

Keywords: Green Analytical Chemistry, Eco-friendly Techniques

INTRODUCTION

The concept of Green Analytical Chemistry (GAC) has been established in the literature for over 20 years. The fundamental principles of GAC have been well discussed in articles published in 1999 by Anastas, 2006 by Koel and Kaljurand, and 2008 by Armenta et al., presenting and further building on the idea of implementing green chemistry in analytical procedures. The most important assumptions of GAC were formulated in 2013 by Gałuszka et al[1].

Green Analytical Chemistry (GAC) is an evolving discipline that integrates the principles of green chemistry into analytical methodologies, aiming to reduce the environmental and human health impacts traditionally associated with chemical analysis [2]. By minimizing the use of toxic reagents, reducing energy consumption, and preventing the generation of hazardous waste, GAC seeks to align analytical processes with the overarching goals of sustainability. The foundation of GAC lies in the 12 principles of green chemistry, which provide a comprehensive framework for designing and implementing environmentally benign analytical techniques [3]. These principles emphasize waste prevention, the use of renewable feedstocks, energy efficiency, atom economy, and the avoidance of hazardous substances, all of which are central to reimagining the role of analytical chemistry in today's environmental and industrial landscape.

Although sustainability is a growing priority, the increasing global energy consumption and expanding trade in organic solvents highlight the complexities of achieving a full transition to greener alternatives. Nevertheless, GAC continues to play a pivotal role in advancing cleaner production practices and promoting sustainable scientific research. Analytical chemistry, traditionally reliant on resource-intensive methods and harmful solvents, has faced growing scrutiny for its environmental footprint. GAC addresses these concerns by transforming analytical workflows through the incorporation of green solvents, such as water, ionic liquids, and supercritical fluids, which replace volatile organic compounds (VOCs) and reduce toxicity. Furthermore, GAC embraces energy-efficient techniques, such as microwave-assisted and ultrasound-assisted methodologies, to enhance reaction rates and reduce the energy demands of analytical processes. These innovations not only lower operational costs but also contribute to the broader goals of reducing greenhouse gas emissions and mitigating climate change [4]. The role of GAC extends beyond its immediate environmental benefits, as it fosters a more holistic approach to chemical analysis. By prioritizing the real-time, in-process monitoring of reactions, GAC enables industries to detect and address inefficiencies or hazardous by-products before they escalate, thus preventing pollution at its source. The adoption of chemometric tools further enhances the precision and efficiency of these methods, enabling robust data analysis while minimizing resource use. This shift towards proactive rather than reactive approaches highlight the transformative potential of GAC in redefining traditional paradigms in analytical chemistry [5].

Principles and Framework

The 12 principles of green chemistry provide a foundational framework for designing chemical processes and products that prioritize environmental and human health. When applied to analytical techniques, these principles drive the development of methodologies that are safer, more efficient, and environmentally benign. Figure 1 shows the 12 principles of Green Analytical Chemistry (GAC), highlighting key strategies such as waste prevention, atom economy, safer chemicals, energy efficiency, and real-time analysis, which collectively guide the development of sustainable and environmentally conscious analytical techniques. Waste prevention, the first principle, emphasizes designing analytical processes that avoid generating waste rather than managing it after the fact, a critical consideration in high-throughput laboratories. Atom economy, another key principle, ensures that chemical reactions used in analytical processes maximize the incorporation of all starting materials into the final product, reducing by-products and inefficiencies. Less hazardous chemical syntheses and designing safer chemicals focus on minimizing toxicity in reagents and solvents used during analysis, protecting both analysts and the environment. The principle of safer solvents and auxiliaries is particularly relevant to analytical chemistry, as it encourages the use of non-toxic, biodegradable, or less harmful solvents, such as water, ionic liquids, or supercritical carbon dioxide, reducing reliance on hazardous organic solvents. Energy efficiency is another critical aspect, urging the development of techniques that operate under milder conditions, such as room temperature and pressure, to lower energy consumption. This is exemplified in the use of alternative energy sources, such as microwave-assisted or ultrasound-assisted methods, to accelerate processes without excessive energy inputs. The principle of renewable feedstocks encourages the replacement of finite resources with renewable ones, such as bio-based solvents or reagents derived from natural materials. Reducing derivatives, which minimizes the need for temporary chemical modifications like protection or deprotection steps, ensures analytical methods are streamlined and resource-efficient. Catalysis, a cornerstone principle, promotes the use of catalytic reagents over stoichiometric ones in analytical methods, enhancing selectivity and reducing material use while minimizing environmental impacts. The principle of design for degradation ensures that chemicals and materials used in analytical processes decompose into harmless products at the end of their lifecycle, preventing persistent environmental contamination. Real-time analysis for pollution prevention is particularly significant in analytical chemistry, advocating for methodologies that monitor and control processes in real-time to prevent hazardous by-products before they form. Finally, inherently safer chemistry for accident prevention underlines the need to design processes with minimized risk of accidents, explosions, or hazardous releases, ensuring a safer working environment. Together, these principles provide a comprehensive strategy for reimagining analytical chemistry to meet the demands of sustainability, safety, and environmental responsibility. By embedding these principles into the development of analytical techniques, the discipline not only aligns with green chemistry's ethos but also actively contributes to reducing the ecological footprint of scientific research and industrial processes [6].

Milestones in Green Analytical Chemistry

The adverse environmental impact of analytical methodologies has been reduced in three different ways:

i) reduction of the number of solvents required in sample pre-treatment;

ii) reduction in the amount and the toxicity of solvents and reagents employed in the measurement step, especially by automation and miniaturization; and,

iii) development of alternative direct analytical methodologies not requiring solvents or reagents [7].

Figure 1: The 12 principles of green Analytical chemistry [6].

Scope

- Fundamental developments facilitating green analytical chemistry technologies/methods
- Development of eco designed sensors and biosensors
- Reuse of the devices to reduce waste
- Alternative solvents, replacing hazardous compounds, solventless extraction techniques
- Miniaturization, making it possible to reduce dramatically the amounts of reagents consumed and wastes generated.
- Reducing or avoiding side effects of analytical methods
- Reducing time and energy
- Environmentally friendly sample preparation techniques
- On-site analytical instrument development and sampling protocols
- Fully or partially automated techniques to perform the analysis of environmental and biological samples parameters, in an accurate, safe, fast, and efficient way.
- Flow cells
- Green physicochemical and structural analysis,
- Green Chemistry Education
- New strategies of assuring quality in analytical chemistry by following the goals of sustainable development, developing assessment methods and validation standards [8].

Principles of green analytical chemistry (GAC) and green sample preparation (GSP) Throughout the next decade, the general concepts relating to green analytical chemistry were steadily developed and published. This culminated in the publication of the 12 principles of green analytical chemistry (GAC) in 2013 by Galuszka, Migaszewski, and Namiesnik. The GAC principles are simply a refined collection of general concepts developed over many years, into a concise format that has, in one form or another, been used to develop several methods to determine the relative “greenness” of analytical methods for sampling, preparation, and analysis. Recently, the 12 principles have been subject to a re-examination to focus more directly on green analytical sample preparation. A

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comparison of the 12 principles of green analytical chemistry (GAC) and the 10 principles of green sample preparation (GSP) is shown in Fig. 2[9].

Figure 2: Principles of green analytical chemistry (GAC) and green sample preparation (GSP)[9]

Figure 3 includes the steps involved in developing and implementing a green microextraction-based method, beginning with sample collection and continuing to implementing method automation. Each step is directly related to the choice for the microextraction technique (SPME or LPME), which in turn is determined by the requirements of the sample collection, transport, preparation, instrumentation for separation and detection, and finally possibility of automation.

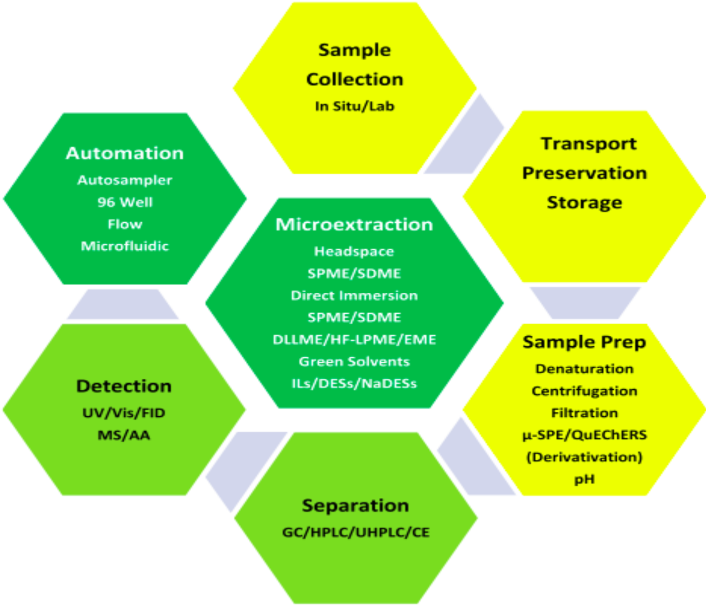

Figure 3: Steps involved in developing and implementing a GAC/GSP compliant method: Colour coding indicates the degree of "greenness" associated with each step and where particular emphasis needs to be taken to ensure GAC or GSP compliance, ranging from most to least compliance-dark green>light green>yellow [9].

The White Analytical Chemistry principles:

To formulate the 12 WAC principles, we propose to synthesize the 12 known GAC principles into 4 overarching "green" rules covering the most important and mutually independent aspects of GAC (G1-G4). These 4 principles are then joined by the 4 "red" principles (R1-R4) and 4 "blue" principles (B1-B4) relating to analytical efficiency and practical/economic criteria, respectively, to compose the 12 WAC principles in total. It is worth emphasizing at the beginning that, according to the WAC concept, all colours and principles are equally important, to maintain the idea of sustainability. However, the actual usefulness and functionality of a method may be determined only by certain principles that are crucial in a given specific case and related circumstances, e.g. by LOD and cost-efficiency. Therefore, each principle should be considered during the method evaluation, but the most important ones for a specific application should be assessed more severely, adequately to the requirements. The overall compliance of the method with the proposed rules is expressed by a quantitative parameter called "whiteness", which is the simplified measure of how the method fits the planned application[10].

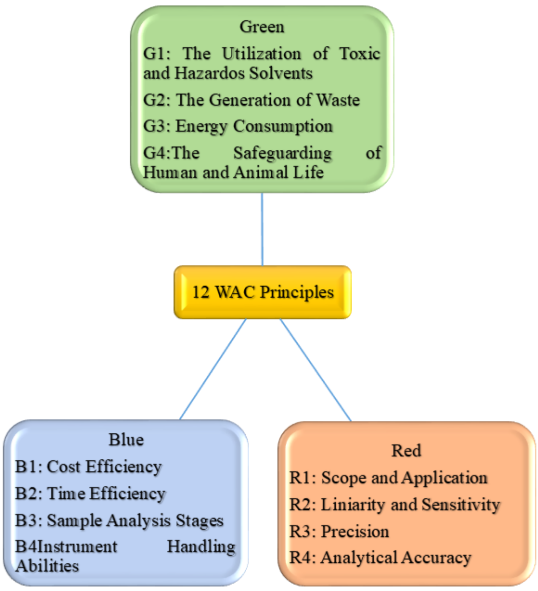

Figure 4: 12 White Analytical Chemistry principles

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TOOLS OF GREEN ANALYTICAL CHEMISTRY:

1. National Environmental Method Index (NEMI)

This tool is industrialized by the methods and data comparability board (MDCB). It has the biggest ecological analytical database. The NEMI has free database access through www.nemi.gov (accessed on 14 February 2021) for environmental methods. This tool was fully described by Keith et al. in 2007, who stated that the NEMI is expressed by a circle called the greenness profile, which is divided into 4 equal parts, as shown in Figure 5. The first part of the circle expresses PBT, which is the abbreviation of three items: persistent, bio accumulative, and toxic. The second part expresses the hazardous aspect. The third and the fourth parts express the corrosiveness and the waste, respectively. Each part may take a green colour, which reflects the greenness of the method, or may take a blank colour, which reflects the lack of greenness. The greenness profile takes into consideration many important factors, such as compounds with specific properties, pH, and waste amount. Following that, the analyst may simply visually compare the greenness of different analytical techniques to evaluate the greenness and eco-friendliness degree of each one [11-12].

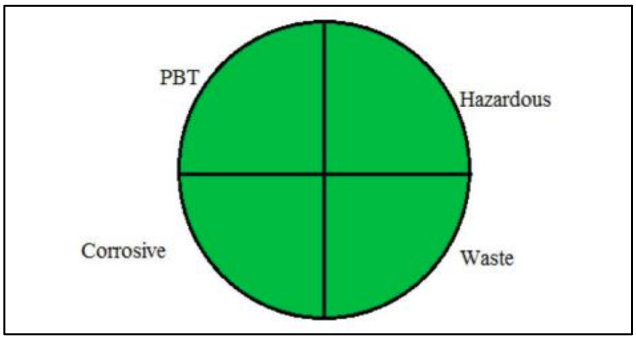

Figure 5: National Environmental Method Index

2. Analytical eco-scale/eco-scale assessment (AES/ESA)

AES was proposed in 2012 as a semi-quantitative tool because it integrates descriptive and numerical data and the obtained results enable researchers to make a reasonable estimation of the method's greenness profile. When assessing the greenness with AES, the score calculation starts with a 100-point scale and is subtracted from 100 with certain penalty points. 100 points represent the ideal greenness, and the penalty points are created based on the parameters, such as solvent/reagent amount, energy consumption, waste amount, etc. If the total score is higher than 75, it suggests that the method has excellent greenness. A total score between 50 and 75 indicates that the method's greenness is acceptable. If the total score is lower than 50, the method's greenness is inadequate. The main advantages of the AES tool are ease of use, quantitative information on the environmental impacts, and evaluation of various environmental impacts. Although it appears to give decisive results, it may have difficulty distinguishing details of the analytical procedures. Additionally, the total AES score cannot be regarded as truly indicative of the cause of negative impacts; therefore, it becomes hard to determine the points that need improvement in the process. However, AES is an improvement over previously developed tool. AES tool is considered the most widely used tool with GAPI and AGREE.

3. Green analytical Procedure Index (GAPI)

GAPI is an integrative tool that evaluates a method's sustainability, from sampling to determination. It was first proposed in 2018, and the results of the GAPI assessment are demonstrated as a pictogram consisting of four additional pentagons surrounding a centre pentagon. They are related to five parameters: method's general type, sample handling, sample preparation, solvents/reagents, and instrumentation. According to the evaluation results, the pictogram contains red, yellow, and green colours. In total, fifteen different criteria are assessed with GAPI. The main advantage of this tool is that it is a simple tool that includes many different parameters of an analytical method. Even though it overcomes the significant disadvantages of the NEMI tool, giving qualitative results and providing a complex representation are the drawbacks of GAPI [13].

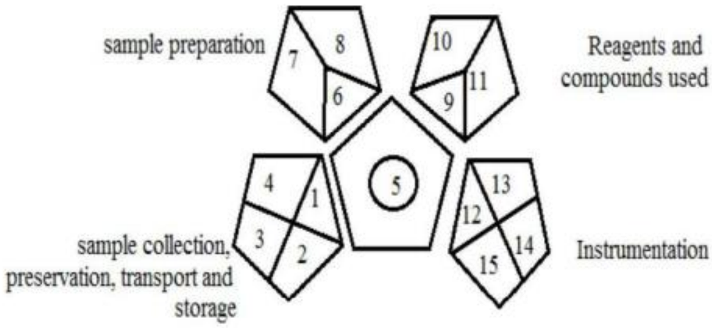

Figure 6: Green analytical Procedure Index pictogram with description

4. Analytical Greenness metric (AGREE)

AGREE tool was first introduced by Pena-Pereira et al. in 2020, and its evaluation criteria are based on twelve principles of green analytical chemistry [14]. The program AGREE tool is free to access online, and it has twelve windows to consider each principle. The result is a pictogram with 12 sections around it, associated with each parameter, and a circle in the middle, giving the final score between 0 and 1. It is also possible to interpret the results with colours such as red, yellow, and green tones in the pictogram. In the final score scale, 0 indicates un-satisfactory, and 1 indicates satisfactory.

The most important advantages of the AGREE tool can be listed as follows:

- It is more comprehensive as it includes all the principles of green analytical chemistry.
- It is more flexible as it allows users to make some modifications.
- It allows easy analysis of the positive and negative aspects of the method thanks to the detailed pictogram.
- It gives both qualitative and quantitative results.
- The software is easy to use and gives fast results.

The most significant disadvantage of the tool is that the reason for the weight of each section is not specified. The AGREE tool is one of the most widely used tools for greenness evaluation today [15-16].

4. The Blue Applicability Grade Index (BAGI)

BAGI was introduced by Natalia Manousi, et al. in 2023 as a novel metric for assessing the practicality of analytical methods within the framework of White Analytical Chemistry WAC. Unlike traditional green metrics that focus on environmental impact, BAGI centers on ten key attributes crucial for method applicability. These include the type of analysis, the capability to determine multiple analytes simultaneously, the required analytical techniques and instrumentation, the number of samples that can be simultaneously treated, sample preparation, throughput in samples per hour, choice of reagents and materials, necessity for preconcentration, degree of automation, and sample size requirement. Table 1 shows the main attributes, and score points of the BAGI index. The BAGI metric tool provides two types of outcomes: a pictogram and a numerical score. The overall assessment is represented as an asteroid pictogram with a number in its center Fig. 7. The color gradient of the pictogram indicates how well the method meets the set criteria: dark blue signifies high compliance, blue indicates medium compliance, light blue suggests low compliance, and white denotes no compliance. The number inside the BAGI pictogram represents the overall score of the analytical method, ranging from 25 to 100. A score of 25 corresponds to the lowest level of applicability, while a score of 100 indicates excellent performance.

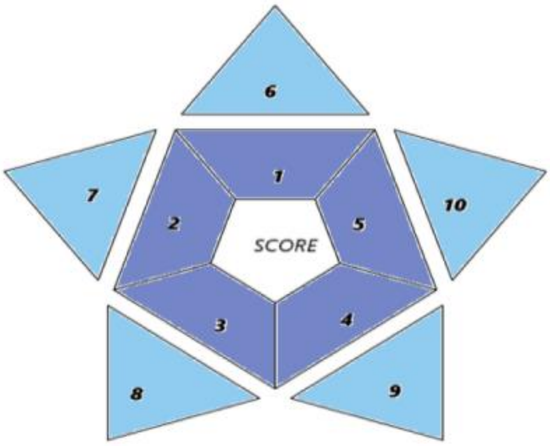

Figure 7: The Blue Applicability Grade Index

Table 1: Score points of BAGI index.

1	Type of analysis
2	Multi- or sin single element analysis
3	Analytical technique
4	Simultaneous sample preparation
5	Sample preparation
6	Samples per h (sample preparation+analysis time)
7	Reagents and materials
8	Preconcentration
9	Automation degree
10	Amount of sample

5. Green certificate modified Eco scale

The Green Certificate modified Eco-Scale, follows a similar calculation method to the Analytical Eco-Scale. It is based on subtracting penalty points corresponding to the amounts of solvents used and wastes generated. Additionally, the eco-scale value is categorized into different classes, ranging from A (green) to G (red), providing a clearer visual representation of the method's environmental impact Fig. 8[17].

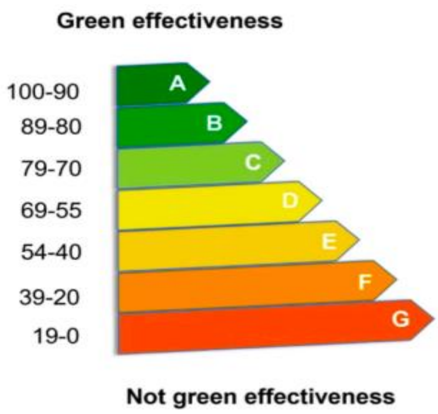

Figure 8: The green certificate modified eco-scale [16].

6. The Chloroform-oriented Toxicity Estimation Scale (ChlorTox Scale)

The Chloroform-oriented Toxicity Estimation Scale (ChlorTox Scale) is a greenness indicator aimed at estimating the chemical risk of a laboratory method/ procedure in a comprehensive yet simple way [18].

The key assumption is to refer to the reference substance which we selected for this purpose – chloroform. It is a well-known and thoroughly tested chemical substance in terms of toxicity and safety, which poses many potential hazards of various nature to the user and the environment, therefore it requires the use of adequate personal protective equipment, hazard prevention and detailed characterization in readily available risk assessment sheets. In addition, chloroform is offered by many different manufacturers, and thus there are many different sources of data on its properties in the form of safety data sheets, which are regularly updated. The basis of our approach is to estimate the overall chemical hazard for the substance-of-interest (CH_{sub}), and refer it to the overall chemical hazard posed by the standard – chloroform (CH_{CHCl3}). Secondly, it is required to reliably calculate and consider the mass of the substance-of interest needed for a single analysis/measurement (m_{sub}):

$$\text{ChlorTox} = CH_{sub} / CH_{CHCl3} \cdot m_{sub} \quad \ldots\ldots(1)$$

Where the ChlorTox value, expressed in the mass of chloroform [g], reflects a degree of chemical risk associated with the substance-of-interest, taking into account its properties (hazards) and the amount used. CH_{sub}/CH_{CHCl3} represents a relative hazard of using the assessed substance in relation to chloroform, assuming the same mass-to-volume concentration of both chemicals. The ChlorTox values characterizing different substances can be added together to express the total chemical risk predicted for the whole method (Total ChlorTox)[19].

Conclusion:

As environmental concerns and sustainability goals continue to shape the future of science and industry, Green Analytical Chemistry emerges as a vital discipline in driving this transformation. By embedding eco-friendly principles into the core of analytical practices, GAC not only minimizes the ecological impact of chemical analysis but also enhances the efficiency, safety, and relevance of modern methodologies. The development of standardized assessment tools and the adoption of innovative green technologies further empower researchers and industries to make informed, responsible choices. Looking ahead, the continued evolution of GAC will be essential in ensuring that scientific progress aligns with the global imperative for sustainability, making it not just a scientific necessity, but a moral and environmental obligation.

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