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## Review Article

# Green Analytical Chemistry: Principles, Innovations, and Comprehensive Review of Current Trends

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### ABSTRACT

Green Analytical Chemistry (GAC) represents a transformative paradigm in chemical analysis, dedicated to minimising the environmental footprint and health risks associated with traditional laboratory practices. This report provides a comprehensive overview of GAC, tracing its foundational principles, exploring key methodologies, highlighting recent advancements between 2020 and 2025, and detailing its diverse applications in environmental monitoring, food safety, and pharmaceutical analysis. It also identifies the leading academic journals and conferences that shape the discourse and drive innovation within this field. The evolution of GAC from broad green chemistry concepts to specialised, measurable practices, coupled with advancements in miniaturisation, automation, and the integration of quality-by-design principles, underscores its critical role in fostering sustainable scientific practices and contributing to global environmental and public health objectives.

## INTRODUCTION

### 1. Introduction to Green Analytical Chemistry (GAC)

#### 1.1. Definition and Historical Context

Green Analytical Chemistry (GAC) is fundamentally defined as the strategic design and implementation of analytical procedures aimed at reducing or eliminating the generation and use of

hazardous substances, thereby mitigating adverse effects on human safety, human health, and the environment.<sup>[1]</sup> The emergence of GAC is rooted in a growing global environmental consciousness and increasing regulatory pressures, building upon the broader philosophical tenets of green chemistry.<sup>[1]</sup>

The intellectual foundation for GAC was laid in the 1990s when Paul Anastas and John Warner first postulated the 12 principles of Green

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Chemistry.<sup>[1]</sup> These seminal principles advocated for the minimisation or complete elimination of toxic solvents and waste generation across all chemical processes.<sup>[1]</sup> Recognising the unique demands and challenges inherent in analytical chemistry, these general principles were subsequently adapted. In 2013, Gałuszka, Migaszewski, and Namieśnik revised the original 12 principles to specifically fit the context of Green Analytical Chemistry, providing a more tailored and actionable framework for green analytical practices.<sup>[1]</sup> This adaptation was crucial because, while the initial green chemistry principles offered a broad philosophical direction, analytical chemistry operations involve distinct considerations such as sample preparation, detection limits, and matrix effects.<sup>[1, 2]</sup> The refined GAC principles address these specific nuances, making the guidelines directly applicable and effective for analytical chemists. This tailoring signifies a maturation of the field, moving beyond a general philosophy to provide precise, actionable guidance for daily laboratory work, thereby making "greenness" a practically achievable goal.<sup>[1]</sup>

The overarching aim of GAC is to develop analytical methods that are not only environmentally friendly but also economically viable and socially responsible.<sup>[3]</sup> This pursuit extends beyond mere environmental benefits, implicitly striving towards what is sometimes referred to as "white" analytical chemistry, which seeks a balance between environmental impact reduction and the maintenance of high analytical performance, practicality, and cost-efficiency.<sup>[8]</sup> The field acknowledges that achieving sustainability should not come at the expense of analytical quality or economic feasibility, highlighting the need for a holistic approach where environmental responsibility is seamlessly integrated with practical analytical requirements.

## 1.2. Importance and Relevance in Modern Science

The importance of Green Analytical Chemistry in contemporary science is paramount, driven by an escalating global environmental awareness and the imperative for sustainable development.<sup>[1]</sup> Traditional analytical methods frequently rely on hazardous chemicals, consume significant energy, and generate substantial amounts of toxic waste.<sup>[1]</sup> GAC directly addresses these critical issues by promoting practices that mitigate such adverse impacts.<sup>[1]</sup>

By embracing GAC principles, chemists actively contribute to environmental protection, enhance safety for laboratory personnel by minimising exposure to toxic substances, and can achieve long-term cost efficiencies through reduced consumption of expensive reagents and lower waste disposal costs.<sup>[2]</sup> Furthermore, GAC aligns seamlessly with broader global sustainability objectives, including the United Nations Sustainable Development Goals (SDGs), by actively reducing energy consumption, greenhouse gas emissions, and chemical waste generation in analytical laboratories.<sup>[9]</sup>

A significant characteristic of GAC is its role as a powerful catalyst for innovation. While compliance with environmental regulations is a driving factor, GAC is also recognised as a transformative approach that actively propels scientific and industrial advancement.<sup>[4, 5]</sup> It fosters inventive thinking and encourages the adoption of cutting-edge technologies.<sup>[11]</sup> This dynamic has led to the development of more efficient, safer, and often more cost-effective analytical solutions, exemplified by the integration of artificial intelligence and digital tools for optimising analytical workflows.<sup>[11]</sup> This dual benefit, where environmental responsibility directly stimulates scientific and industrial progress, positions GAC



as a compelling and essential area for continued research and investment. Ongoing research and development in GAC are continuously focused on refining greener sample preparation techniques, advancing analytical instrumentation, and improving data analysis strategies to effectively address current environmental challenges and meet future analytical demands sustainably.<sup>[13]</sup>

## 2. Foundational Principles of Green Analytical Chemistry

### 2.1. The 12 Principles of GAC (adapted from Green Chemistry)

The 12 principles of Green Analytical Chemistry serve as a fundamental framework guiding the incorporation of environmentally sound practices into analytical processes.<sup>6</sup> These principles were adapted explicitly in 2013 by Gałuszka, Migaszewski, and Namieśnik from the original 12 principles of Green Chemistry, initially postulated by Paul Anastas and John Warner.<sup>[1]</sup> The adaptation was critical to address the unique requirements and challenges of analytical procedures, ensuring that the guidelines are directly applicable to laboratory settings.<sup>[1]</sup>

The key principles are outlined in Table 1, emphasizing a holistic approach to minimizing environmental impact:



The creation of a mnemonic, such as "SIGNIFICANCE," for the 12 GAC principles<sup>[6]</sup> highlights a deliberate effort to make these guidelines more accessible, memorable, and actionable for practitioners. This goes beyond mere academic postulation; it serves as a practical tool for implementation and education, indicating a focus on widespread adoption and ease of integration into daily laboratory work.<sup>[6]</sup> The developers recognised the need for a simplified way to internalise and apply complex principles within a busy analytical environment, thereby bridging the gap between theoretical concepts and practical application and fostering a more rapid and effective transition to greener practices.<sup>[6, 9]</sup>

Among these principles, miniaturisation and automation stand out as core pillars. These are not merely individual techniques but are deeply interconnected and mutually reinforcing elements that collectively drive multiple GAC benefits.<sup>[19]</sup> Miniaturisation via microfluidics and microextraction reduces reagent and solvent use, minimises waste, and lowers energy needs in analytics procedures.<sup>[19]</sup> Automation further enhances these efficiencies by improving overall process efficiency, reducing human exposure to hazardous substances, and enabling real-time analysis.<sup>[18]</sup> Miniaturisation and automation reduce environmental impact, improve safety and efficiency, and are key to achieving comprehensive GAC goals.<sup>[18]</sup> This integrated approach points towards a future of highly efficient, low-impact analytical systems that are both environmentally responsible and operationally superior.<sup>[19, 20]</sup>

## 2.2. Key Greenness Assessment Metrics and Tools

For the effective implementation of GAC, it is crucial to develop and employ proper tools and metrics to assess the "greenness" of analytical

assays objectively and to compare different analytical procedures.<sup>[7]</sup> The proliferation and refinement of these GAC metrics are fundamental to the field's advancement. These tools provide an objective and standardised way to quantify environmental impact, enabling researchers and industries to compare the greenness of existing methods with newly developed ones, identify specific areas for improvement within an analytical procedure, and incentivise the development of greener alternatives.<sup>[21]</sup> This capability is vital for demonstrating the verifiable sustainability benefits of GAC methods, which are increasingly essential for regulatory compliance and market trends.<sup>[18]</sup> Widely used GAC metrics include:

- **National Environmental Methods Index (NEMI):** One of the earliest and most recognised tools for evaluating method greenness.<sup>[7]</sup>
- **Analytical Eco-Scale:** A semi-quantitative tool that assigns penalty points to parameters of an analytical process that deviate from an ideal green analysis, considering factors like reagents, energy, and waste.<sup>[7]</sup>
- **Green Analytical Procedure Index (GAPI):** A comprehensive tool that provides a visual representation of the greenness of each step of an analytical procedure, from sampling to final determination.<sup>[7]</sup>
- **Analytical Greenness Metric Approach (AGREE and AGREEprep):** Provides a comprehensive, flexible, and straightforward assessment, often yielding an easily interpretable colored pictogram that highlights the strengths and weaknesses of a method based on the 12 GAC principles.<sup>[14]</sup> AGREEprep focuses explicitly on the sample preparation step.<sup>[15]</sup> The AGREE tool's output is a colored pictogram with twelve segments, automatically colored from red (non-



sustainable) to dark green (sustainable), indicating the method's strengths and weaknesses.<sup>[15]</sup>

- **ChlorTox Scale:** Used for assessing toxicity related to chlorinated solvents.<sup>[17]</sup>
- **Assessment of Green Profile (AGP):** Another metric for evaluating the greenness of analytical methods.<sup>[17]</sup>
- **Analytical Method Greenness Score (AMGS):** Used for assessing the overall greenness of an analytical method.<sup>[17]</sup> Fig. 1-3 represents all the tools.

- These metrics collectively consider various aspects, including the quantity and toxicity of solvents and reagents, the volume of waste generated, energy consumption, the number of procedural steps, and the extent of miniaturisation and automation.<sup>[14]</sup> The development and widespread use of these metrics are not merely academic exercises; they are fundamental enablers for the practical implementation and continuous improvement of GAC across industries, transforming it from a conceptual ideal into a measurable and actionable practice.<sup>[21]</sup>

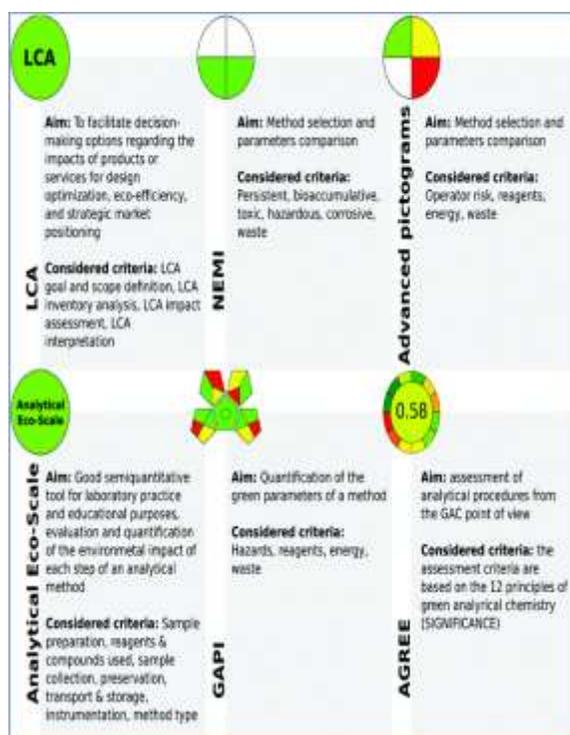


Figure 2 Analysis and comparison of leading metrics used to assess the environmental sustainability of analytical methods<sup>[40]</sup>



Figure 3 Comparison of conventional HPTLC and greener HPTLC methods evaluated using the AGREE tool.<sup>[39]</sup>

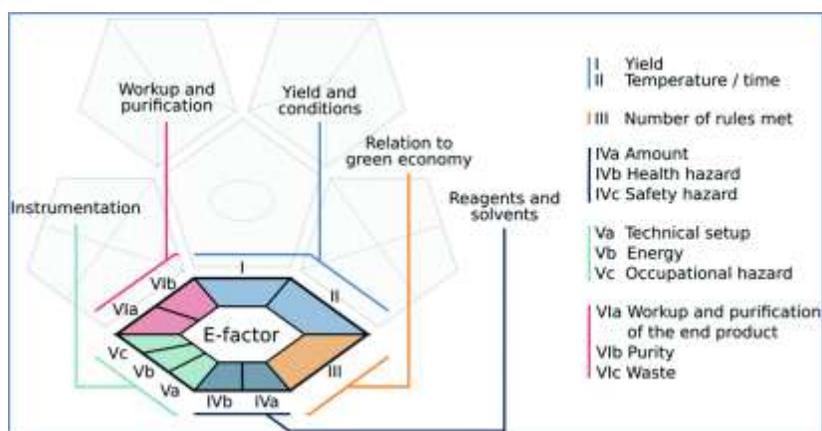


Figure 4 The ComplexGAPI pictogram is shown with the original GAPI version faded in the background, while individual glyphs are grouped and color-coded within hexagonal fields for better visual clarity.<sup>[40]</sup>

Table 1: Key Points of Green Analytical Chemistry Metrics

| Metric Acronym | Full Name   | Key Features/Parameters Considered   | Purpose/Application   |
|----------------|---|--|---|
| NEMI           | National Environmental Methods Index                        | Four-quadrant pictogram based on waste, hazards, energy, and corrosivity. <sup>[7]</sup>                     | Qualitative assessment of method greenness, easy comparison. <sup>[7]</sup>                                 |
| Eco-Scale      | Analytical Eco-Scale  | Assigns penalty points based on reagent amounts, hazards, energy, waste, and instrumentation. <sup>[7]</sup> | Semi-quantitative assessment, provides a numerical score for comparison. <sup>[21]</sup>                    |
| GAPI           | Green Analytical Procedure Index                            | Five-point pictogram evaluating greenness for each step (sampling, preparation, analysis). <sup>[7]</sup>    | Visual, comprehensive assessment of entire analytical procedure. <sup>[14]</sup>                            |
| AGREE          | Analytical Greenness Metric Approach                        | Twelve-segment pictogram based on 12 GAC principles, with numerical scores and color-coding. <sup>[15]</sup> | Comprehensive, flexible, and user-friendly assessment, identifies strengths and weaknesses. <sup>[15]</sup> |
| AGREEprep      | Analytical Greenness Metric Approach for Sample Preparation | Specifically focuses on the greenness of sample preparation steps. <sup>[15]</sup>                           | Detailed assessment of sample preparation, aids in method optimization. <sup>[15]</sup>                     |
| AMGS           | Analytical Method Greenness Score                           | Considers various aspects for overall method greenness. <sup>[17]</sup>                                      | Provides a single score for holistic greenness evaluation. <sup>[17]</sup>                                  |

### 2.3 Analytical GREENness Calculator

The Analytical GREENness Calculator is a digital tool based on the 12 principles of Green Analytical Chemistry. It quantitatively assesses analytical methods by scoring them from 0 to 1 in categories like:

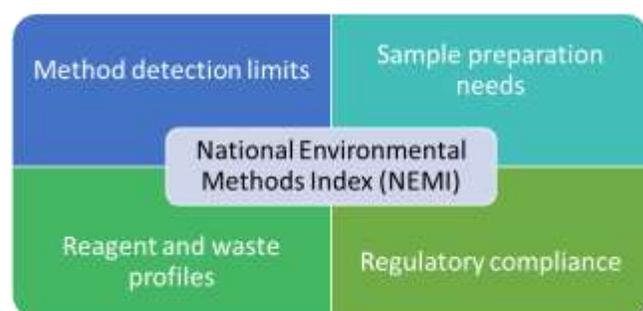


Figure 5 Analytical GREENness Calculator

This score helps laboratories to benchmark their methods and encourages the development of environmentally benign alternatives. The calculator's visual representation simplifies complex data, making it user-friendly for chemists, educators, and regulatory authorities alike.

## 2.4 National Environmental Methods Index (NEMI)

Launched in 2002, the **National Environmental Methods Index (NEMI)** is a searchable database developed by the US Geological Survey (USGS) and the EPA. NEMI offers a platform to compare:



**Figure 6 National Environmental Methods Index (NEMI)**

One of its main strengths lies in the **uniform criteria for comparison**, which was previously lacking in published methods. By presenting a color-coded pictogram indicating compliance with green criteria (e.g., persistence, bioaccumulation, toxicity), NEMI facilitates quick environmental evaluations. [14-16]

## 3. Key Methodologies and Techniques in GAC

### 3.1. Green Solvents and Solvent-Free Approaches

A central objective of Green Analytical Chemistry is the substantial reduction or complete elimination of hazardous substances, with a particular focus on solvents, which often represent the largest volume of hazardous waste in analytical

laboratories.<sup>[1]</sup> This emphasis has driven significant research into alternative solvent systems and solvent-free methodologies.

The evolution of green solvent research signifies a paradigm shift from merely seeking "less hazardous" alternatives to actively pursuing "inherently benign" or "ideal" solvents.<sup>[4]</sup> This deeper commitment aligns with the "Design Safer Chemicals" and "Use Renewable Feedstocks" principles, aiming for solutions that are fundamentally sustainable throughout their lifecycle, rather than just less harmful.<sup>[4]</sup>

Key categories of green solvents include:

- **Water-based solvents:** Water is considered a cornerstone of GAC due to its non-toxic, non-flammable, abundant, and inherently environmentally benign nature. Its use significantly reduces the ecological impact of analytical processes.<sup>[1]</sup>
- **Ionic Liquids (ILs):** These salts remain liquid at room temperature and offer unique advantages such as low volatility, high thermal stability, and tunable properties, making them effective alternatives to traditional volatile organic compounds (VOCs).<sup>[1]</sup>
- **Supercritical Fluids (SCFs):** Supercritical carbon dioxide (CO<sub>2</sub>) is particularly notable in this category. It is non-toxic, non-flammable, and can be easily removed from the final product, making it an ideal solvent for high-efficiency separations and extractions.<sup>[1]</sup>
- **Deep Eutectic Solvents (DESs):** These emerging green alternatives are typically mixtures of a hydrogen bond donor and acceptor, forming a eutectic mixture with a melting point lower than its individual components. They offer tunable properties,

often derived from natural products, and present a promising avenue for sustainable analytical applications.<sup>[16]</sup>

- **Bio-based alternatives:** Solvents derived from renewable biomass sources represent another important development, aligning with the principle of using renewable feedstocks and reducing reliance on petrochemicals.<sup>[10]</sup>
- In parallel with the development of green solvents, solvent-free methods have gained significant traction. Techniques such as Solid-Phase Microextraction (SPME) eliminate the need for harmful solvents entirely, thereby substantially reducing waste generation and potential contamination.<sup>[1]</sup> This represents a direct and impactful way to achieve the goals of GAC.<sup>[22, 23]</sup>

### 3.2. Miniaturisation and Microextraction Techniques

Miniaturisation, encompassing approaches like microfluidics and various microextraction techniques, is a cornerstone strategy in GAC. Its primary benefit lies in significantly reducing reagent and solvent consumption, minimising waste generation, and lowering energy requirements across analytical procedures.<sup>[1]</sup>

Prominent microextraction techniques include:

- **Solid-Phase Microextraction (SPME):** This technique is a leading solvent-free approach that integrates sampling, extraction, and concentration into a single step. It drastically reduces or eliminates solvent use and waste, offering advantages such as enhanced sensitivity and rapid sample preparation.<sup>[1]</sup> SPME has found widespread application in environmental, food, forensic, pharmaceutical, and biomedical analyses, including the extraction of drugs and metabolites from biological samples.<sup>[14]</sup>

- **Liquid-Phase Microextraction (LPME):** This technique utilises very small volumes of solvents, thereby reducing consumption and associated risks.<sup>[1]</sup> A specific variant, Hollow Fibre Liquid-Phase Microextraction (HF-LPME), involves the use of porous hollow fibres to facilitate analyte partitioning.<sup>[27]</sup>
- **Fabric Phase Sorptive Extraction (FPSE):** An innovative technique that simplifies sample preparation and reduces the consumption of hazardous solvents, proving effective in both biological and environmental matrices.<sup>[28]</sup>

Beyond specific techniques, the development of miniaturised and portable analytical devices represents a significant advancement.<sup>[19]</sup> These instruments enable on-site analysis, which minimises the need for sample collection, transport, and extensive laboratory infrastructure.<sup>[19]</sup>

The interplay of miniaturisation, automation, and real-time analysis for holistic greenness is a key development. These techniques are not isolated strategies but form a synergistic ecosystem that maximises green benefits.<sup>[19]</sup> Miniaturisation enables portable devices and on-site analysis, which directly supports real-time analysis for pollution prevention by reducing the need for sample transport and extensive laboratory-based processing.<sup>[10]</sup> Automation further integrates these steps, making the entire workflow more efficient, safer for operators, and less resource-intensive.<sup>[18]</sup> Microfluidic systems, often referred to as "Lab-on-a-chip" devices, exemplify this integration by offering compact size, reduced reagent consumption, and precise control over fluid flow, aligning perfectly with GAC principles for applications such as phosphate and cinnarizine determination.<sup>[19]</sup> This integrated approach represents a fundamental shift from discrete



"green" steps to a holistically designed "green" analytical system, impacting the entire analytical lifecycle from sampling to data generation.<sup>[19]</sup> This trend points towards a future of analytical chemistry characterised by highly integrated, autonomous, and environmentally benign systems, moving analysis closer to the source of the sample and enabling rapid, on-demand insights.<sup>[19]</sup>

### 3.3. Energy-Efficient and Automated Methods

Energy efficiency is a core principle of GAC, as analytical procedures, despite their scale, contribute to overall energy consumption and carbon footprint.<sup>[1]</sup> The field actively encourages the adoption of energy-efficient techniques and instrumentation to reduce environmental impact.<sup>[18]</sup>

The increasing focus on the energy footprint, extending beyond just chemical waste, indicates a maturing understanding of "greenness".<sup>[4]</sup> This holistic view recognises that even chemically "clean" processes can be unsustainable if they are energy-intensive. This pushes for a more comprehensive life cycle assessment approach for analytical methods, where all environmental impacts, from raw material sourcing (including energy) to waste disposal, are considered.<sup>[4]</sup>

Key energy-efficient approaches include:

- **Microwave-assisted techniques:** These methods significantly enhance reaction rates and reduce energy consumption by directly heating the sample and solvent, leading to faster and more efficient analyses.<sup>[1]</sup>
- **Ultrasound-assisted processes:** Similar to microwave techniques, ultrasound provides energy to accelerate reactions and extractions, contributing to reduced analysis times and energy demands.<sup>[17]</sup>

- **Automation:** Beyond its role in safety and efficiency, automation contributes to energy efficiency by optimising process parameters and reducing manual intervention, which can lead to more consistent and less wasteful operations.<sup>[18]</sup>
- **Flow analysis and microfluidics:** These techniques enable continuous-flow systems, which are inherently more energy-efficient and generate less waste compared to traditional batch processes. They allow for precise control over reaction conditions and reagent consumption.<sup>[1]</sup>

### 3.4. Non-Chromatographic and Advanced Spectroscopic Methods

Green Analytical Chemistry actively promotes the development and adoption of techniques that require minimal sample preparation and operate with no or very low solvent consumption.<sup>[1]</sup> This preference for simplified workflows is driven by the desire to reduce waste, save time, and lower costs associated with extensive sample handling and solvent use.<sup>[2]</sup>

The shift towards direct and in-situ analysis for reduced workflow complexity represents a fundamental re-engineering of the analytical workflow itself.<sup>[25]</sup> By reducing sample preparation, derivatisation, and solvent use, these methods cut waste, save time, and lower costs. They create less impactful, more efficient, and rapid analytical processes, ideal for high-throughput and field applications.<sup>[25, 30]</sup>

Key non-chromatographic and advanced spectroscopic methods include:

- **Green Spectroscopic Methods:** Techniques such as UV-Vis, Fourier Transform Infrared (FTIR), and Nuclear Magnetic Resonance (NMR) spectroscopy often require minimal

sample preparation and can be adapted to be solvent-free or utilise green solvents.<sup>[1]</sup> For instance, UV spectrophotometric methods have been developed using eco-friendly diluents like phosphate buffer instead of hazardous organic solvents.<sup>[31, 32]</sup>

- **Electrochemical Methods:** Voltammetry and amperometry are examples of electrochemical techniques that typically use minimal reagents and generate negligible waste, aligning well with GAC principles.<sup>[1]</sup> Electrochemical sensors are increasingly recognised for their alignment with GAC principles, often utilising sustainable materials and enabling in-situ analysis.<sup>[3]</sup>
- **Real-time analysis techniques:** These methods provide immediate data, minimising the need for sample collection, preservation, and transport to a laboratory, thereby preventing pollution at its source.<sup>[1]</sup>

#### 4. Recent Advancements (2020-2025) in GAC Research

The period from 2020 to 2025 has witnessed significant advancements in Green Analytical Chemistry, driven by continuous innovation in methodologies, instrumentation, and applications. These developments reflect a concerted effort to integrate sustainability more deeply into analytical practices.<sup>[11]</sup>

##### 4.1. Innovations in Method Development

Recent GAC innovations from 2020-2025 focus on green solvents, energy efficiency, miniaturised devices, automation, and chemometric tools.<sup>[11]</sup> A key development is the convergence of Analytical Quality by Design (AQbD) and GAC.<sup>[33, 34]</sup> Traditionally, Aqbd ensured robustness, accuracy, and reliability, but now also explicitly considers "greenness" as a core attribute.<sup>[34]</sup> This integration makes environmental sustainability a fundamental

design element from the start.<sup>[35]</sup> The result is methods that are both high-performing and eco-friendly, balancing analytical rigour and environmental care.<sup>[35]</sup> This convergence signals GAC's evolution from principles to a standard practice, especially in industries like pharmaceuticals.

Specific examples of method development innovations include:

- **UV Spectrophotometric Methods:** Development of multicomponent UV spectrophotometric methods based on GAC principles has advanced, notably replacing hazardous solvents like methanol with eco-friendly alternatives such as phosphate buffer (pH 7.8) for pharmaceutical analysis. The greenness of these methods is rigorously evaluated using metrics like NEMI, Eco-Scale, and AGREE.<sup>[32]</sup>
- **UHPLC Methods with Quality by Design (QbD):** The development of robust and environmentally sustainable RP-UPLC methods for the simultaneous estimation of drugs (e.g., Metformin and Remogliflozin) exemplifies the application of AQbD principles.<sup>[36]</sup> These methods consistently demonstrate high sustainability scores when assessed with metrics like Analytical Eco-Score, GAPI, and AGREE.<sup>[37]</sup> Similarly, QbD-assisted green UHPLC methods have been developed and validated for quantifying drugs like Tolvaptan, ensuring both method stability and environmental sustainability.<sup>[38]</sup>
- **Microfluidic Systems for Flow-Based Analysis:** Novel microfluidic systems, like 3D LOC devices, are combined with reverse flow injection analysis (r-FIA) for colourimetric analyte detection (e.g., phosphate in water, cinnarizine in tablets). These compact systems reduce reagent use



and enhance efficiency, aligning well with GAC principles.<sup>[19]</sup>

- **Green Synthesis of Nanoparticles:** Research continues to explore the green synthesis of nanoparticles (e.g., gold, silver, Co<sub>3</sub>O<sub>4</sub>, CdONPs) using plant extracts or other bio-based methods.<sup>[37, 38]</sup> These greenly synthesised materials are then applied in various analytical and environmental contexts, representing a significant advancement in sustainable material development for analytical applications.<sup>[38]</sup>
- **Novel Carbon-Carbon Bond Formation:** Groundbreaking work introduces greener methods for forming carbon-carbon bonds, key in synthesising complex molecules for medicines and chemicals. These innovations skip hazardous steps, using safer, eco-friendly substances like sodium formate, potentially transforming industrial synthesis sustainability.<sup>[36]</sup>

#### 4.2. Progress in Green Sample Preparation

Sample preparation remains a pivotal step in the analytical process, often contributing disproportionately to waste generation and solvent consumption, making it a primary target for greening efforts.<sup>[14]</sup> Significant progress has been made in developing more sustainable sample preparation techniques.<sup>[25]</sup>

The emergence of "The Ten Principles of Green Sample Preparation" highlights increased specialisation within GAC. While general 12 GAC principles guide broadly, sample preparation often poses unique, resource-intensive challenges. Developing dedicated principles shows recognition of their complexities and the need for tailored guidance. The framework clarifies that "green" sample prep isn't about skipping steps but transforming and optimising them with advanced technologies. These methods often outperform

direct analysis, environmentally and analytically. This specialisation signifies GAC's maturity, shifting from broad guidelines to targeted, actionable frameworks for specific stages, fostering more effective green innovations.<sup>[25]</sup>

Key advancements include:

- **Solid-Phase Microextraction (SPME):** SPME continues to be an up-and-coming technique due to its solvent-free nature, which integrates sampling, extraction, and concentration, thereby significantly reducing solvent use and waste. It is widely applied across environmental, food, forensic, pharmaceutical, and biomedical analyses.<sup>[14]</sup>
- **Alternative Solvents for Extraction:** The field of sample preparation is being revolutionised by the adoption of alternative green solvents, including ionic liquids, supercritical fluids (e.g., CO<sub>2</sub>), and deep eutectic solvents.<sup>[1]</sup> Subcritical water extraction (SWE) is also highlighted as a particularly green method due to water's abundance and non-toxic nature.<sup>[27]</sup>
- **Miniaturisation and Automation:** Continuous efforts to miniaturise and automate sample preparation processes, such as the use of micro-pipette tips and integrated flow systems, significantly reduce solvent consumption, analysis time, and manual handling.<sup>[14]</sup>
- **Fabric Phase Sorptive Extraction (FPSE):** This innovative technique simplifies the sample preparation workflow, reduces the consumption of hazardous solvents, and has proven effective in analysing complex biological and environmental matrices.<sup>[28, 29]</sup>

#### 4.3. Developments in Green Analytical Instrumentation



Advances in green analytical instrumentation are pivotal to the continued growth of GAC.<sup>[11]</sup> These developments primarily focus on miniaturised and portable devices, coupled with the sophisticated integration of automation and chemometric tools, all of which significantly enhance efficiency and reduce the environmental footprint of analytical workflows.<sup>[11]</sup>

The rise of "smart" and decentralised analytical systems marks a major shift in analytical chemistry. Portable, miniaturised instruments with real-time analysis enable on-site measurements, reducing sample transport, preservation needs, and environmental impact. Automation and chemometric tools streamline these processes, making them more efficient, reliable, and user-friendly. This shift supports proactive environmental management and quality assurance by allowing immediate intervention and reducing the environmental burden of traditional lab-based methods.<sup>[19]</sup>

Key areas of development include:

- **Microfluidic Systems ("Lab-on-a-chip"):** These systems are a prime example of miniaturised instrumentation, offering compact size, reduced reagent consumption, and precise control over chemical reactions. They are particularly well-suited for green analytical chemistry due to their ability to utilise safer and environmentally friendly reagents and methodologies.<sup>[19]</sup>
- **Electrochemical Sensors:** These sensors are increasingly recognised for their alignment with GAC principles. They often utilise sustainable materials and enable in-situ analysis, thereby minimising sample handling, reagent consumption, and waste generation.<sup>[2]</sup>
- **Energy-Efficient Equipment:** A core GAC principle is the design and use of analytical

equipment that minimises energy consumption, contributing to a reduced carbon footprint for laboratory operations.<sup>[3]</sup>

## 5. Applications of Green Analytical Chemistry

Green Analytical Chemistry has found extensive and impactful applications across various sectors, demonstrating its versatility and critical role in achieving sustainability goals.

### 5.1. Environmental Monitoring and Pollution Prevention

GAC is widely applied in environmental monitoring to accurately detect and quantify pollutants in diverse matrices such as air, water, and soil.<sup>[1]</sup> This application is crucial for understanding environmental health and informing remediation efforts. Green analytical methods are instrumental in identifying and quantifying hazardous substances within waste streams, thereby guiding proper disposal and recycling initiatives.<sup>[2]</sup> Techniques like green chromatography and spectroscopy are routinely employed for contaminant detection.<sup>[2]</sup>

The application of GAC in environmental monitoring, especially through real-time and in situ analysis, marks a key shift from a reactive "clean-up" approach to a proactive "pollution prevention" strategy.<sup>[1]</sup> By providing instant data on pollutant levels and process conditions, GAC allows for rapid intervention before significant environmental harm occurs, or even during the formation of hazardous substances.<sup>[1]</sup> This ability is essential for effective waste management, industrial process control, and ensuring compliance with strict environmental regulations. It makes GAC crucial to achieving Sustainable Development Goals related to clean water, land, and responsible consumption, bringing society



closer to a truly preventative environmental management approach.<sup>[10]</sup>

Specific applications include:

- **Solid-Phase Microextraction (SPME):** Extensively used for extracting trace quantities of pharmaceuticals and pesticides from water and soil matrices, offering a solvent-free and efficient approach.<sup>[14]</sup>
- **Microfluidic Systems:** Valuable tools for environmental monitoring, exemplified by their use in precise phosphate determination in surface water samples.<sup>[19]</sup>
- **Microplastics and Urbanisation Impact:** Research actively addresses the environmental impacts of microplastics and urbanisation on soil health, emphasising the urgent need for sustainable development and effective management strategies through green analytical approaches.<sup>[37]</sup>

## 5.2. Food Safety and Quality Control

Green Analytical Chemistry is indispensable for ensuring the safety and quality of food products, covering a wide range of analyses from pesticides to additives and contaminants<sup>[1]</sup> Green analytical methods are employed to monitor pesticide levels in food, ensuring compliance with safety regulations while simultaneously minimising waste generated during testing.<sup>[3]</sup>

The application of GAC in food safety and quality control directly contributes to consumer trust and the sustainability of the entire food system.<sup>[15]</sup> By enabling greener, more efficient, and often faster analysis of contaminants like pesticides and phthalates<sup>[15]</sup>, GAC helps ensure that food products are safe for consumption while reducing the environmental footprint of testing.<sup>[15]</sup> Furthermore, research into sustainable food packaging materials<sup>[35, 36]</sup> and green extraction

methods for beneficial food components<sup>[24]</sup> demonstrates GAC's broader role in promoting a circular economy and reducing waste throughout the food supply chain.<sup>[24]</sup> This makes GAC a critical enabler for achieving food security and sustainable consumption patterns, directly impacting public health and economic viability within the food industry.<sup>[24]</sup>

Specific applications include:

- **Advanced Analytical Tools:** Techniques such as UPLC-DAD and the electronic tongue are utilised to assess the authenticity, quality, and oxidative stability of various food products.<sup>[24]</sup>
- **Green Extraction of Bioactive Compounds:** Optimising polyphenol extraction methods contributes to greener and more sustainable food processing, recovering valuable compounds with reduced environmental impact.<sup>[24]</sup>
- **Sustainability Assessment:** Greenness assessment tools like AGREE and BAGI are applied to rigorously evaluate the sustainability of analytical procedures, for instance, in the analysis of phthalate residues in edible oils.<sup>[15]</sup>
- **Sustainable Packaging:** Research explores the use of cellulose-based composites for sustainable food packaging and addresses the pervasive issue of microplastics in food products.<sup>[35]</sup>

## 5.3. Pharmaceutical Analysis and Drug Development

Green Analytical Chemistry plays a significant and increasingly critical role throughout the pharmaceutical industry, extending from early drug development stages to quality control and environmental residue analysis.<sup>[1]</sup> The primary aim is to minimise the use of hazardous chemicals and



solvents in drug analysis, thereby ensuring both product safety and environmental protection.<sup>[1]</sup>

The emphasis on GAC in the pharmaceutical sector highlights its critical role across the entire drug lifecycle. From the greener synthesis of active pharmaceutical ingredients (APIs) to rigorous quality control and the analysis of pharmaceutical residues in the environment, GAC aims to minimise both environmental and human health impacts.<sup>[1]</sup> The growing focus on "sustainable medicines use"<sup>[37]</sup> and the development of "climate-neutral pharmaceuticals and manufacturing"<sup>[34]</sup> indicate a profound shift towards a comprehensive sustainability strategy within the industry. This acknowledges the significant environmental footprint associated with drug production and disposal. This makes GAC an integral part of responsible pharmaceutical manufacturing, contributing to public health and environmental protection by ensuring that the medicines society relies on are produced and analysed with minimal ecological harm.<sup>[33]</sup>

Specific applications include:

- **Quality Control:** Implementing green analytical techniques in quality control processes enhances safety, reduces environmental footprints, and ensures the consistent quality of pharmaceutical products.<sup>[3]</sup>
- **Residue Analysis:** Green methods are developed for detecting pharmaceutical residues in environmental samples, enabling a comprehensive assessment of the impact of drugs on ecosystems.<sup>[3]</sup>
- **Drug Discovery and Development:** Solid-Phase Microextraction (SPME) is invaluable for extracting drugs and metabolites from complex biological samples during drug discovery processes.<sup>[24, 26]</sup> Furthermore,

innovative greener chemical methods for forming carbon-carbon bonds are being developed, which are essential for the synthesis of new medicines.<sup>[33]</sup>

- **Stability-Indicating Methods:** The development of Quality by Design (QbD)-assisted green UHPLC methods for quantifying drugs like Tolvaptan ensures both method stability and environmental sustainability throughout the drug's shelf-life.<sup>[38]</sup>
- **Simultaneous Estimation:** Eco-friendly RP-UPLC methods are being developed for the simultaneous estimation of multiple drugs (e.g., Metformin and Remogliflozin) using Analytical Quality by Design (AQbD) principles, enhancing efficiency and greenness in pharmaceutical analysis.<sup>[36]</sup>

## 6. Leading Journals and Conferences in Green Analytical Chemistry

The dissemination of Green Analytical Chemistry research occurs across a diverse range of academic journals, reflecting both its specialised nature and its broad interdisciplinary relevance.<sup>[33]</sup> The wide array of journals publishing GAC research, ranging from highly specialised GAC-specific titles to broader analytical, environmental, and sustainable chemistry journals, highlights two key trends: its inherent interdisciplinarity and its growing specialisation.<sup>[9]</sup> GAC is intrinsically cross-disciplinary, drawing from and contributing to analytical chemistry, environmental science, chemical engineering, and even policy and economics.<sup>[9]</sup> This broad appeal reflects its relevance across various scientific and industrial sectors.<sup>[9]</sup> Concurrently, the existence of journals specifically named "Green Analytical Chemistry" or "Green Chemistry Letters and Reviews"<sup>[9]</sup> signifies that GAC has matured into a distinct and recognised sub-discipline within chemistry,



necessitating dedicated publication venues.<sup>[9]</sup> This publishing landscape suggests a robust and expanding field where researchers have multiple avenues to disseminate their work, fostering rapid advancements and broad impact.<sup>[38, 9]</sup>

## 7. CONCLUSIONS

Green Analytical Chemistry (GAC) is a vital discipline transforming chemical analysis by focusing on sustainable practices. It applies specialised principles to tackle unique analytical challenges and uses metrics for evaluating and improving methods. GAC promotes benign techniques like water and ionic liquids to minimise hazardous waste, while advancements in miniaturisation and automation lead to efficient, real-time measurements. Its applications span environmental monitoring, food safety, and pharmaceuticals, ensuring sustainability in these fields. With a strong community of journals and conferences, GAC fosters collaboration and innovation, playing a crucial role in addressing global environmental challenges while enhancing the effectiveness of analytical chemistry.

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