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Review Article

Green Analytical Chemistry in Pharmaceutical and Environmental Analysis: A Review

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ABSTRACT

Green Analytical Chemistry (GAC) focuses on developing analytical methodologies that reduce environmental burden while maintaining analytical performance. This review highlights recent advances in sustainable analytical approaches, emphasizing the use of environmentally benign solvents, reduced sample and reagent consumption, and method miniaturization. The discussed strategies demonstrate a substantial decrease in solvent requirements and waste production without compromising accuracy, sensitivity, or reliability. Adoption of green analytical practices across pharmaceutical, environmental, and industrial applications illustrates their potential to support sustainable development objectives. The review further emphasizes the importance of continuous methodological innovation to ensure that analytical chemistry evolves in harmony with global environmental and regulatory expectations.

.INTRODUCTION

Growing environmental awareness has significantly reshaped scientific research, with analytical chemistry facing increasing scrutiny due to its reliance on toxic chemicals, high solvent consumption, and substantial waste generation. Conventional analytical procedures, while effective, often pose risks to human health and the environment. In response to these challenges, Green Analytical Chemistry (GAC) has emerged as an essential discipline aimed at integrating sustainability into analytical method development without compromising analytical quality.

Green Analytical Chemistry promotes strategies such as the replacement of hazardous reagents with safer alternatives, reduction of sample and

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solvent volumes, energy-efficient instrumentation, and methodological miniaturization. Although numerous studies have reported individual green approaches, a holistic assessment of these strategies across pharmaceutical, environmental, and industrial applications remains limited. Therefore, this review focuses on recent innovations and methodological advancements in GAC, highlighting their contribution to improved analytical efficiency and reduced environmental impact. By consolidating current knowledge, this article aims to emphasize the role of GAC in advancing sustainable analytical practices and addressing contemporary environmental and regulatory demands.

Principles of Green Analytical Chemistry

Green Analytical Chemistry (GAC) is based on fundamental principles that aim to reduce the environmental and health hazards associated with analytical practices while ensuring reliable analytical performance. The major principles guiding GAC are as follows:

1. **Safer Reagents**: GAC encourages the use of chemicals that are non-toxic or possess reduced toxicity in comparison to conventional reagents. The substitution of hazardous substances with safer alternatives minimizes risks to analysts and decreases adverse environmental effects [1].
2. **Waste Minimization**: One of the central objectives of GAC is the reduction of waste generated during analytical procedures. This is achieved through optimized sample preparation, reduced reagent volumes, and improved waste management strategies, thereby limiting environmental pollution [1][2].
3. **Energy Efficiency**: The development of analytical methods that require lower energy input is a key principle of GAC. Energy-efficient instrumentation and reduced analysis time contribute to a decreased carbon footprint associated with analytical operations [1].
4. **Real-Time Analysis:** Real-time and in-situ analytical techniques enable immediate measurement without the need for extensive sample collection, storage, or transportation. These approaches help conserve resources and reduce energy consumption linked to sample handling processes [1].
5. **Use of Sustainable Resources**: GAC promotes the utilization of renewable materials and environmentally friendly solvents, particularly those derived from biomass. The adoption of sustainable resources supports the development of greener analytical methodologies and reduces dependence on non-renewable chemicals [1].

Fig.1.The 12 principles of GAC In our approach

Principles of Green Analytical Chemistry

The twelve fundamental principles of Green Analytical Chemistry (GAC) emphasize the development of analytical methods that minimize environmental impact while ensuring analytical efficiency and safety [6].

These principles are summarized as follows:

1. **Preference for Direct Analytical Techniques**: Analytical approaches should enable direct measurement whenever possible, thereby eliminating or minimizing the need for extensive sample pretreatment steps.
2. **Reduction of Sample Quantity and Number**: The use of smaller sample sizes and a reduced number of samples is encouraged to limit material consumption and waste generation.
3. **In-situ Analysis**: Measurements should be carried out at the sampling site to avoid unnecessary sample transportation, storage, and associated resource consumption.
4. **Integration of Analytical Operations**: Combining analytical steps into a single process helps conserve energy and reduces the overall consumption of reagents.
5. **Automation and Miniaturization**: Automated and miniaturized analytical techniques are preferred, as they improve efficiency while decreasing reagent use, analysis time, and waste production.
6. **Avoidance of Derivatization**: Chemical derivatization steps should be minimized or eliminated, as they often require additional reagents and generate extra waste.
7. **Minimization of Analytical Waste**: The formation of large volumes of waste should be prevented, and appropriate waste management strategies should be implemented.
8. **Use of Multi-Analyte or Multi-Parameter Methods**: Analytical methods capable of simultaneous determination of multiple analytes are favored over single-analyte approaches to enhance efficiency.
9. **Reduction of Energy Consumption**: Analytical procedures should be designed to operate with minimal energy requirements,

thereby lowering their environmental footprint.

10. **Preference for Renewable Reagents**: Reagents derived from renewable resources should be selected whenever feasible to support sustainable analytical practices.

11. **Elimination of Toxic Chemicals**: The use of hazardous reagents should be avoided or replaced with less toxic alternatives to reduce risks to both humans and the environment.

12. **Enhancement of Operator Safety**: Analytical methods should be designed to improve laboratory safety by minimizing exposure to hazardous substances and ensuring safe waste handling.

Fig.2.The 12 Principles of green analytical chemistry

History of Green Analytical Chemistry

Table 1: Historical Development of Green Analytical Chemistry

Year / Period	Major Event or Development	Key Contributors / Remarks	Reference No.
Early 1990s	Rising concern regarding environmental contamination and chemical waste	Regulatory authorities and researchers begin emphasizing environmentally responsible chemistry	7
1998	Introduction of the 12 Principles of Green Chemistry	Paul T. Anastas and John C. Warner publish *Green Chemistry: Theory and Practice*	7
Early 2000s	Awareness of waste generation in analytical laboratories	Identification of the need to green analytical instrumentation and sample preparation techniques	8
2000–2006	Formulation of the 12 Principles of Green Analytical Chemistry (GAC)	Koel and Kaljurand establish a structured GAC framework	8
2010 onwards	Advancement of miniaturized and solvent-efficient analytical techniques	Expansion of UHPLC, microextraction methods, and lab-on-chip technologies	9,10
Present day	Broad application of GAC across multiple disciplines	Adoption driven by sustainability goals and stricter safety regulations	9,10

Scope of Green Analytical Chemistry

Table 2: Scope of Green Analytical Chemistry

Scope Area	Focus and Description	Representative Examples / Techniques	Reference No.
Environmentally Benign Analytical Methods	Replacement of hazardous chemicals with safer and greener alternatives	Water, ethanol, ionic liquids, supercritical CO_2	7,9
Sustainable Sample Preparation	Minimization of solvent use and reduction of toxic waste generation	SPME, ultrasound-assisted extraction, microwave-assisted extraction	8,10
Miniaturized Analytical Approaches	Reduction of sample size and reagent consumption	Microfluidic systems, lab-on-chip platforms	9
Energy and Waste Efficiency	Lower solvent consumption and enhanced analytical efficiency	UHPLC requiring less solvent compared to conventional HPLC	10
Enhanced Laboratory Safety	Reduction of occupational exposure to toxic substances	Safer solvent alternatives and closed analytical systems	7,8
Broad Industrial Applications	Implementation across pharmaceutical, environmental, food, and clinical sectors	Drug quality control, pesticide analysis, water contaminant monitoring	9,10
Contribution to Sustainable Development	Support of global sustainability and environmental protection goals	Sustainable and responsible chemical measurement practices	7,9

Methods in Green Analytical Chemistry

The practical application of Green Analytical Chemistry (GAC) relies on a range of innovative methodologies designed to improve sustainability while maintaining analytical reliability. Key methodological approaches include:

1. Sample Preparation Strategies

Green sample preparation focuses on minimizing environmental impact through the use of safer solvent systems and reduced processing steps. Whenever possible, sample pretreatment is avoided to limit reagent consumption and waste generation. Additionally, alternative extraction techniques are employed to decrease solvent usage and improve overall efficiency [3].

2. Analytical Instrumentation

Advances in analytical instrumentation have enabled the development of portable and on-site analytical devices, reducing dependence on centralized laboratory facilities and extensive sample handling. The integration of automated analytical systems further enhances efficiency, minimizes human error, and reduces resource consumption during analysis [4][6].

3. Quality by Design (QbD) in Method Development

The application of Quality by Design principles in analytical method development ensures method robustness while simultaneously addressing environmental considerations. This systematic approach involves identifying critical method parameters and optimizing them to achieve reliable performance with minimal ecological impact [2].

4. Greenness Assessment Tools

To evaluate the environmental friendliness of analytical methods, various assessment tools are employed. Metrics such as the HPLC-EAT index and the Analytical Method Volume Intensity (AMVI) approach assess greenness based on factors including reagent toxicity, solvent consumption, and waste generation [2].

Sample Preparation Methods in Green Analytical Chemistry

Green Analytical Chemistry (GAC) emphasizes sustainable practices in analytical processes, particularly in sample preparation. This approach aims to reduce the environmental impact associated with traditional methods, which often rely on hazardous solvents and generate significant waste. Here are some key methods of sample preparation that align with GAC principles:

1. Use of Green Solvents:

Replacement of Harmful Solvents: Traditional organic solvents can be replaced with safer alternatives such as water, ethanol, or other biodegradable solvents. This minimizes health risks and environmental contamination [1,3]

Green Extraction Techniques: Techniques like Solid Phase Extraction (SPE) utilize less solvent and can be more efficient than conventional methods [3]

2. Minimization of Sample Preparation Steps:

Omitting Steps Where Possible: Reducing the number of steps in sample preparation not only saves time but also decreases the amount of solvent and reagents used. For instance, direct analysis methods can eliminate the need for extensive sample handling [3,5]

Miniaturization: Implementing miniaturized techniques, such as micro-extraction methods, allows for lower reagent consumption and waste generation while maintaining analytical performance [2,4]

3. Innovative Techniques:

Assisted Extraction Methods: Techniques such as QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) are designed to simplify extraction processes while using minimal solvents [3]

Use of Renewable Resources: Incorporating renewable materials in sample preparation helps reduce reliance on non-renewable resources and aligns with sustainability goals [1]

4. Real-Time Analysis:

In Situ Techniques: Methods that allow for real-time analysis can significantly reduce the need for sample transport and preparation, thus minimizing waste and energy consumption[1,3]

By adopting these green sample preparation methods, laboratories can enhance the sustainability of their analytical processes while ensuring compliance with environmental regulations and improving safety for personnel involved in chemical analysis.

Sample Preparation Methods in Green Analytical Chemistry

Green Analytical Chemistry (GAC) promotes environmentally responsible practices in analytical workflows, with particular emphasis on sustainable sample preparation. Conventional sample preparation techniques often involve toxic solvents and generate substantial chemical waste, raising environmental and health concerns. GAC-oriented approaches aim to minimize these impacts while preserving analytical accuracy and efficiency.

1. Use of Green Solvents

A fundamental strategy in green sample preparation is the replacement of hazardous organic solvents with safer and biodegradable alternatives. Solvents such as water, ethanol, and other environmentally benign media are increasingly preferred to reduce toxicity and environmental pollution [1,3]. In addition, green extraction approaches, including solid-phase extraction (SPE), require lower solvent volumes and often provide enhanced extraction efficiency compared to traditional methods [3].

2. Minimization of Sample Preparation Steps

Reducing the number of sample handling steps is a key objective in GAC. Eliminating unnecessary pretreatment procedures lowers solvent and reagent consumption while improving overall efficiency. Direct analytical techniques, for example, can significantly decrease the need for extensive sample manipulation [3,5]. Furthermore, the adoption of miniaturized sample preparation methods, such as micro-extraction techniques, enables substantial reductions in reagent use and waste generation without compromising analytical performance [2,4].

3. Innovative Sample Preparation Techniques

Modern green methodologies include assisted extraction techniques designed to simplify and accelerate sample preparation. The QuEChERS approach (Quick, Easy, Cheap, Effective, Rugged, and Safe) is widely applied due to its low solvent requirement and operational simplicity [3]. Additionally, the incorporation of renewable materials in sample preparation procedures reduces dependence on non-renewable resources and supports long-term sustainability goals [1].

4. Real-Time and In-Situ Analysis

Real-time and in-situ analytical techniques represent an advanced strategy in green sample preparation. By enabling on-site analysis, these methods reduce the need for sample transportation, storage, and extensive preparation, thereby lowering energy consumption and waste production [1,3].

Overall, the adoption of green sample preparation strategies enhances the sustainability of analytical practices while ensuring regulatory compliance and improving laboratory safety for personnel engaged in chemical analysis.

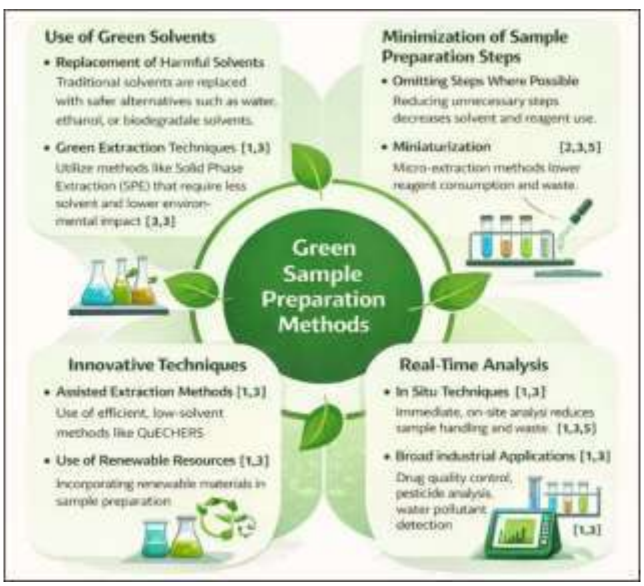

Fig.3. Main Application of GAC

Types of Green Analytical Chemistry Methods [2,3,4]

Green Analytical Chemistry (GAC) includes a range of analytical approaches that are classified according to their methodological strategies and practical applications. These methods aim to reduce environmental impact while ensuring reliable analytical performance.

1. **Green Chromatographic Techniques**: Green chromatography focuses on reducing solvent consumption and replacing hazardous solvents with environmentally friendly alternatives. Techniques such as ultra-high-performance liquid chromatography (UHPLC) and high-performance thin-layer chromatography (HPTLC) are widely employed due to their lower solvent requirements and improved efficiency.
2. **Spectroscopic Techniques**: Spectroscopic methods, including ultraviolet–visible (UV–Vis) spectroscopy, are considered green due to their minimal reagent consumption and reduced waste generation. These techniques often eliminate the need for extensive sample preparation and hazardous chemicals.
3. **Microextraction-Based Methods**: Microextraction techniques, such as solid-phase extraction (SPE) and dispersive liquid–liquid microextraction, are designed to significantly reduce solvent volumes while maintaining sensitivity and analytical accuracy. These approaches are particularly valuable for trace analysis.
4. **Miniaturized Analytical Systems**: The development of compact and portable analytical devices represents an important advancement in GAC. Miniaturized systems operate with smaller sample volumes, consume fewer reagents, and generate less waste, making them suitable for on-site and real-time analysis.

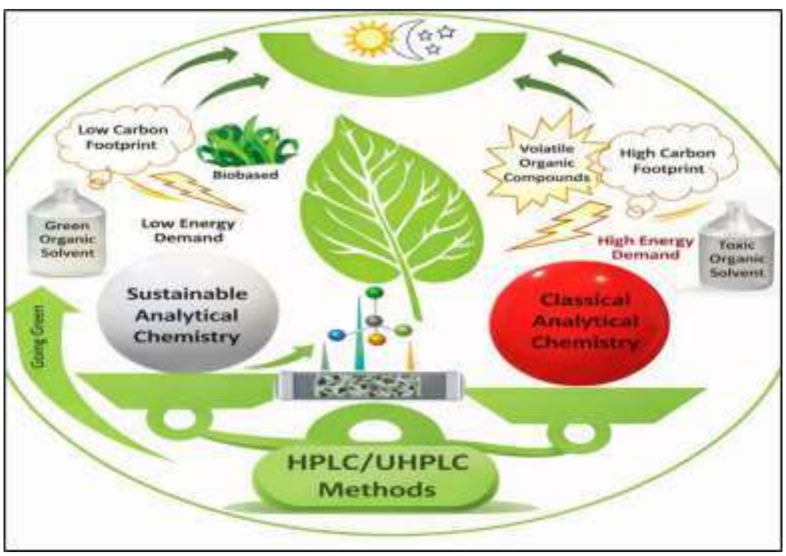

Fig.4. Green Analytical Techniques.

Advantages of Green Chemistry [11]

1. Reduces Waste: Green chemistry helps reduce the production of harmful waste, protecting both the environment and human health.
2. Energy Conservation: It focuses on saving energy, which is important because energy use affects the environment.

3. Faster Reactions: Techniques like solid-state microwave irradiation speed up chemical reactions compared to traditional methods in liquid solutions.

4. Safer and Scalable: Microwave-assisted solvent-free reactions can be done in open containers, reducing high-pressure risks and making it easier to scale up.

5. Proven Methods: Many real-world reactions and the creation of heterocyclic compounds have successfully used solvent-free microwave synthesis.

Disadvantages of Green Chemistry [11]

1. Challenging Goals: Designing chemical products and processes that reduce or eliminate harmful substances is the main goal but also the hardest to achieve.

2. Time and Cost: Transitioning from traditional products to green alternatives can be expensive and time-consuming due to lack of information and alternative materials.

3. Implementation Issues: High costs and uncertainty about what is considered safe make adopting green chemistry difficult.

4. Limited Alternatives: In many cases, there are no known alternative technologies for greener processes.

5. Questions on Effectiveness: Some green chemistry methods, like using certain ionic liquids, may seem environmentally friendly but might still pose risks.

6. Environmental Concerns: Some ionic liquids, although less volatile, are water-soluble and can still reach the biosphere, potentially causing harm.

Software Used in Green Analytical Chemistry (GAC) [12,13,14]

Several software tools have been developed to evaluate the greenness of analytical procedures. Most of these tools use different metrics to measure environmental impact, safety, and energy efficiency.

1. Complex GAPI Software

- Purpose: Assesses the greenness of analytical procedures.
- Developed in: Python (using the Tkinter library for user interface).
- Features: Uses multiple metrics to evaluate the environmental friendliness of a method.

2. Common GAC Metrics and Tools

Table 3: GAC Software tools

Software / Metric	Description	Example Solvent Focus
NEMI (National Environmental Methods Index)	Uses a pictogram divided into 4 parts to indicate waste, toxicity, hazards, and corrosiveness. Green = safe; uncoloured = not safe.	Organic solvents like chloroform, methanol, and acetone
Advanced NEMI	Updated version of NEMI with more detailed evaluation.	Solvents commonly used in HPLC, GC
AGP (Assessment of Green Profile)	Scores the overall greenness of the analytical method.	Water, ethanol, acetone
ChlorTox Scale	Estimates toxicity of chloroform and related chemicals.	Chloroform, dichloromethane

GAPI (Green Analytical Procedure Index)	Graphical representation of environmental impact.	Organic and aqueous solvents
Complex GAPI	Combines multiple metrics for a detailed greenness evaluation.	All standard lab solvents
RGB Model & RGB12 Algorithm	Uses color coding to represent greenness visually.	Water, ethanol, methanol
AGREE / AGREE prep	Numerical scoring system for procedure greenness.	Water, acetonitrile, ethanol
HEXAGON	Multi-criteria evaluation of green analytical methods.	General lab solvents (organic and aqueous)
BAGI (Blue Applicability Grade Index)	Focuses on applicability and environmental safety.	Water-based methods preferred

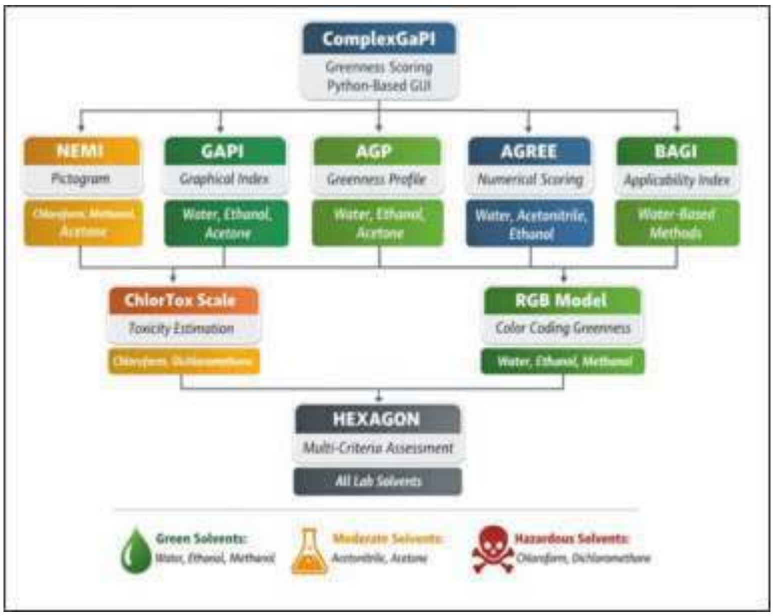

Fig 5: Green Analytical Chemistry Software and Solvent Classification

Types of Solvents

1. Green / Safer Solvents: Water, ethanol, methanol, ethyl acetate
2. Moderate / Traditional Solvents: Acetonitrile, acetone, dichloromethane
3. High-Risk / Toxic Solvents: Chloroform, carbon tetrachloride, benzene

Green analytical chemistry aims to replace hazardous organic solvents with water or ethanol wherever possible. Software like GAPI, ComplexGAPI, or AGREE helps evaluate whether a solvent choice is environmentally friendly.

CONCLUSION

Green chemistry represents a transformative approach in modern chemical and pharmaceutical practices, emphasizing sustainability, safety, and environmental responsibility. By minimizing waste, reducing energy consumption, and promoting the use of safer solvents and renewable materials, green chemistry aligns scientific innovation with ecological preservation. In the analytical domain, Green Analytical Chemistry (GAC) plays a vital role in assessing the environmental impact of laboratory procedures. The development of specialized software tools, such as Complex GAPI, GAPI, AGREE, and HEXAGON, allows researchers to systematically evaluate and improve the greenness of analytical methods. These tools not only facilitate the selection of safer solvents and energy-efficient processes but also encourage adherence to the principles of green chemistry. Overall, integrating green chemistry principles with advanced assessment tools fosters sustainable scientific practices, reduces environmental hazards, and supports the global goal of eco-friendly chemical innovation.

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