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Review Article

Green Analytical Chemistry: Principles, Strategies, Tools, And Applications in Sustainable Science

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ABSTRACT

Background: Green Analytical Chemistry (GAC) promotes sustainable analytical practices by reducing the use of hazardous chemicals and limiting environmental effect. It adheres to green chemistry principles, focusing on the use of cleaner solvents, waste reduction, and energy efficiency. Prominent methodologies include solvent minimization, microextraction, and supercritical fluid extraction techniques. Never the less, initial capital expenditures and performance compromises represent notable challenges; Assessment techniques include the Green Analytical Procedure Index (GAPI) and Analytical Greenness Evaluator (AGREE) assist in the evaluation of methodological greenness. GAC endorses environmentally sustainable practices across sectors such as pharmaceuticals and environmental monitoring. Conclusion: Green Analytical Chemistry (GAC) advocates for environmentally sustainable, effective, and

INTRODUCTION

Green Analytical Chemistry

A pivotal paradigm within the chemical domain is the principle of green chemistry, which endeavours to integrate methodologies aligned with sustainable development frameworks. Presently, the principles of green chemistry are widely employed across diverse sectors, including governmental policies, corporate governance, as well as scientific and engineering disciplines. Within the framework of a circular economy, the equilibrium between economic proliferation, sustainability, and ecological conservation is paramount. Thus, it can be postulated that green and sustainable chemistry function as a transformative approach for modifying practices in the design and production of pharmaceuticals. The concept of green processes in chemical reactions has emerged as a contemporary concern among researchers dedicated to enhancing human health, protecting the environment and maintaining safety. Green chemistry focuses on creating ecologically friendly chemical products

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and processes. GAC constitutes a methodology that empowers analysts to incorporate environmental, health, and safety considerations into their assessments. While green chemistry metrics, commonly applied in chemical syntheses, predominantly emphasize product integrity, this paradigm is inadequate for analytical chemistry due to the scarcity of concrete products exhibiting favourable attributes. Hence, GAC requires sophisticated measures to assess the sustainability of the analytical process. In the current context, which directly impacts environmental integrity, the progression of novel technologies has become imperative. The deployment of environmentally compatible chemical agents in various analytical methodologies, notably liquid chromatography techniques, is increasingly prevalent. The paradigms of green analytical chemistry (GAC) and green chemistry originated in the 1990s; however, numerous experimental advancements transpired prior, underscoring that empirical innovations frequently precede theoretical constructs. Collectively, the interval from 1970 to 2007 experienced substantial milestones in minimizing the ecological impact of chemical analysis via innovative methodologies. A sound framework for identifying sustainable chemicals to be integrated into the design of greener analytical techniques can be located within the guidelines pertaining to the evolution of environmentally benign analytical methods. [1-4] **Fig:1**

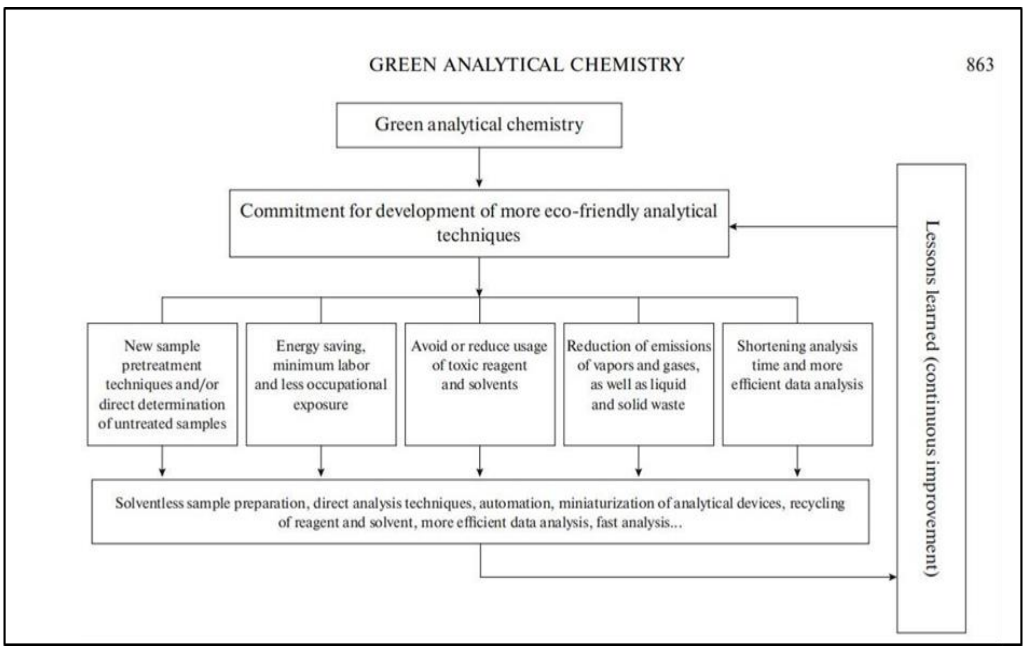

Fig 1: Flow chart of green analytical chemistry

HISTORICAL CONTEXT

The concepts of green analytical chemistry (GAC) and green chemistry originated in the 1990s; however, numerous empirical advancements were realized prior, illustrating that practical innovations often precede theoretical constructs. Overall, the period from 1970 to 2007 witnessed significant progress in reducing the environmental footprint of chemical analysis through innovative methodologies.[5] **Fig:2**

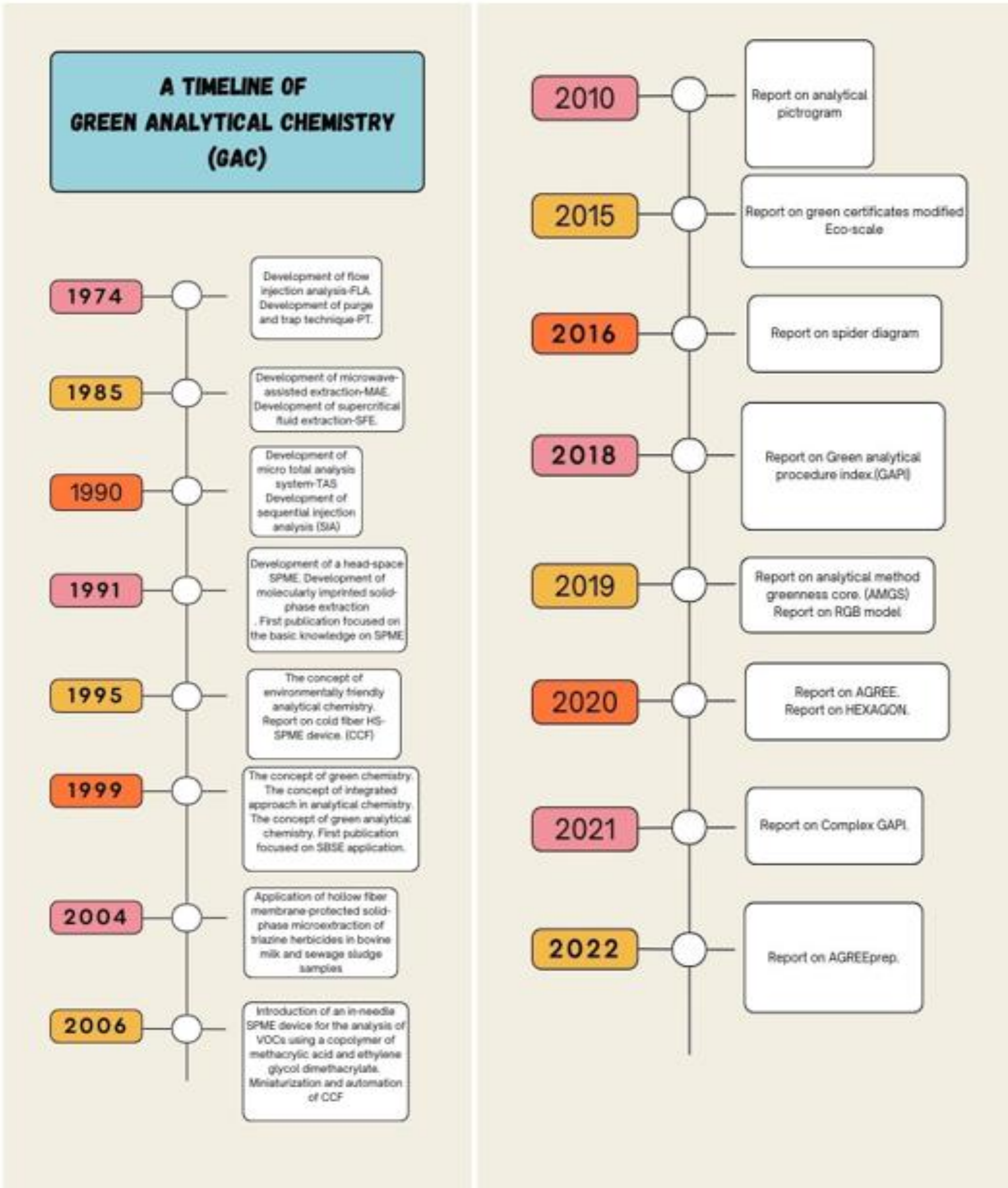

Fig 2: Development of GAC in recent times.[5]

PROGRESS AND MILESTONES:

Three key initiatives have been implemented to reduce the environmental impact of analytical methodologies.

1. Reduction of Solvent Utilization Sample Pre-Treatment: Microwave-assisted extraction (MAE), established in 1975, significantly diminishes solvent consumption and enhances efficiency by utilizing microwave radiation for expedited sample digestion. Automation and Miniaturization: Techniques include solid-phase microextraction (SPME) and dispersive liquid-liquid microextraction (DLLME)decrease the volume and toxicity of solvents employed during the analytical processes.

2. Advancement of Alternative Analytical Methodologies Solvent-Free Techniques:

Supercritical fluid extraction (SFE), emerging in the mid-1980s, utilizes supercritical carbon dioxide (CO2) for compound extraction without the incorporation of organic solvents, although it has yet to fully realize its capabilities in chemical analysis.

SCOPE:

Fundamental advancements enabling environmentally sustainable analytical chemistry methodologies. Development of eco-designed sensors and biosensors. Reutilization of analytical devices to minimize waste generation. Implementation of alternative solvents to supplant hazardous compounds and solvent-free extraction techniques. Minimization strategies facilitate a substantial decrease in reagent consumption and waste production. Mitigation or avoidance of the adverse effects associated with analytical methodologies. Reduction of temporal and energetic expenditure.

Environmentally benign sample preparation methodologies. Fully or partially automated protocols for executing environmental analyses, ensuring precision, safety, rapidity, and efficiency in biological sample parameter assessment. Utilization of flow cells. Green physicochemical and structural analysis. Education in green chemistry. Novel strategies to ensure quality assurance in analytical chemistry consistent with sustainable development objectives, alongside the formulation of assessment methodologies and validation standards.[6]

PRINCIPLES:

In our methodology, the twelve Guidelines for Analytical Chemistry (GAC) principles encompass:

Green analytical chemistry (GAC) encourages analytical chemists to consider environmental, health, and safety concerns during their work.

1. Analytical techniques' greenness is a complex parameter that is difficult to quantify.
2. Green chemistry metric systems, commonly used in chemical synthesis, typically refer to product mass. However, this technique is not suitable for analytical chemistry, which lacks a clear product mass.
3. GAC demands specific parameters to assess the greenness of analytical procedures. Several ways to GAC metrics have been proposed thus far. The first published technique, called the National Environmental Methods Index (NEMI).
4. The metric system is divided into four portions, each reflecting a particular criterion, such as waste generation, reagent persistence, bioaccumulation, hazard, and corrosive conditions. Criteria are evaluated in a binary manner. If a criterion is met, the corresponding part of the pictogram is colored green; otherwise, it remains uncolored. Another metric system, known as the Analytical Eco-Scale.
5. It was subsequently proposed. The Analytical Eco-Scale assigns penalty points for any aspect that diminishes the procedure's greenness. To assess if a technique is green or acceptable, remove points for harmful reagents, waste generation, or high energy demand from a starting score of 100. Multicriteria decision analysis (MCDA) ranks analytical techniques based on multiple criteria simultaneously. If these criteria apply to GAC, MCDA can be used as a GAC metric tool and has proven effective.

6. The Green Analytical Procedures Index was created as another measuring system.

7. It, like NEMI, is based on a pictograph. However, it considers more criteria than NEMI and uses a three-grade scale with a traffic light color system. The latest metric system is the RGB additive color model.

8. This incorporates greenness requirements (green color), analytical performance (red color), and productivity (blue color). The color combination reflects success in each category, making the results easier to read. Each of the metric systems listed above has advantages and, more significantly, problems. The key disadvantage is that just a few assessment criteria are included and treated as non-continuous functions. None of the aforementioned metric systems evaluate analytical techniques based on all 12 principles of GAC. The results may not provide detailed information about the structure of dangers or provide an overly broad overview of the analytical approach. The goal of this project is to create a user-friendly, informative, and sensitive metric tool for evaluating analytical procedures from the GAC perspective. GAPI" is a green analytical chemistry tool that assists in evaluating a method using the "GAC" principles. The pentagon represents five important criteria: overall methodology, sampling procedures, sample processing, chemical components (reagents and solvents), and analytical equipment. Each of these is further classified into around 15 categories to consider. The method's environmental impact was assessed by entering pertinent data into specialized GAPI software. This software employs a straightforward process to evaluate eco-friendliness, using color coded system: red for danger, yellow for moderate, and green for eco-friendliness. [7-8]

Software Tools:

NEMI

The NEMI label has a circular pattern separated into four fields. Figure 2 shows that each field represents a separate feature of the analytical technique and is filled in green if specific requirements are met. The first criteria is that none of the compounds are listed as persistent, bioaccumulative, or poisonous. The second condition stipulates that no chemicals utilized in the method should be on the D, F, P, or U hazardous waste lists. The third condition is that the sample's pH be kept between 2 and 12 to avoid a very corrosive environment throughout the analysis process. Finally, the method must produce fewer than 50 g of trash. The NEMI's user-friendly design makes it an effective instrument for assessing greenness among potential procedure users. The NEMI symbol summarizes a procedure's environmental impact at a glance. NEMI labelling has two main drawbacks: it provides general information and needs a lengthy process to complete. The NEMI sign indicates if each threat is below or above a certain threshold. As a result, it cannot be called semi-quantitative. The second disadvantage is the time-consuming preparation of symbols, especially when using unusual chemicals. It must be verified for every chemical whether it appears on at least one of the limited number of lists.[8] **Fig:3**

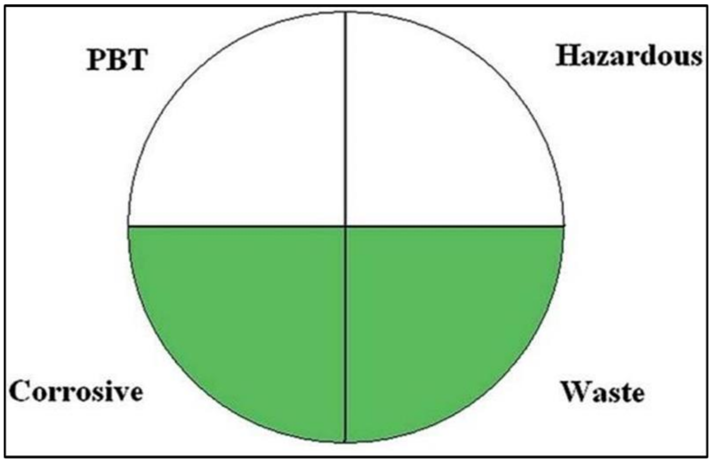

Fig 3: The example of the assessment score with the NEMI procedure.[9]

National Environmental Methods Index (NEMI)

Purpose:

A resource for the evaluation and comparative analysis of analytical methodologies in environmental monitoring.

Features:

A searchable repository of methodologies sourced from diverse regulatory bodies. Capabilities for comparative analysis to ensure data uniformity. Systematic categorization predicated on environmental consequences, emphasizing toxicity and waste production.

Limitations:

Absence of quantitative evaluations of environmental ramifications. Assessing intricate methodologies may necessitate substantial temporal investment.

GAPI

GAPI is a green analytical chemistry device that evaluates methods using the "GAC" principles. The pentagon represents the five major criteria: overall approach, sampling procedures, sample processing, chemical components (reagents and solvents), and analytical equipment. There are around 15 categories to consider, each with its own subcategories. The method's environmental impact was evaluated using specialized GAPI software and related data inputs. The software uses a color-coded system to measure eco-friendliness, with red indicating danger, yellow indicating moderation, and green representing eco-friendliness.[9]

Case Study Example:

This investigation dilineates a chloroform and dodecanol solvent system (30:70%v/v) to extract four antiviral pharmacological agents from aqueous environmental matrices. The agents were then analyzed using high-performance liquid chromatography with ultraviolet detection (HPLC-UV). Key aspects include:

Methodology: Implemented a Hypersil ODS C18 stationary phase with a dual-component mobile phase of acetonitrile and phosphate buffer (50:50, %v/v).

Sample Handling: Environmental samples were procured without chemical preservatives or specialized transport logistics, thereby streamlining the procedure.

Environmental Impact: The protocol employed less than 10 mL of hazardous solvent and necessitated ≤1.5 kWh of energy per sample, denoting minimal environmental waste and energy demand.

Greenness Assessment: The approach achieved a score of 70 on a sustainability index, positioning it as moderately environmentally benign, corroborated by the AGREE framework, which identified a corresponding degree of ecological viability.[10] **Fig:4**

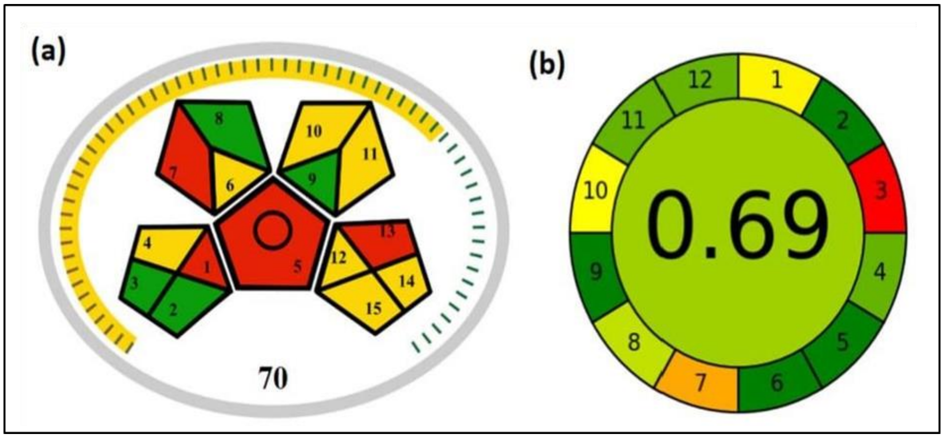

Fig 4: MoGAPI (a) and AGREE (b) assessment scores for the reported method used to determine antiviral in environmental water.[10]

ECO SCALE

The Eco-Scale functions as a pivotal metric in sustainable analytical chemistry. It quantifies the ecological impact of analytical methodologies, assigning a score ranging from 0 to 100, where higher values denote more ecologically benign practices.

The scoring criteria include various parameters:

- Solvent Utilization: Nature and quantity of solvents.
- Reagent Toxicity: Potentially hazardous properties of chemical substances.
- Waste Generation: Quantitative assessment of byproduct volume.
- Energy Consumption: Energy demand for the analytical process.
- Efficiency: Performance effectiveness alongside minimal resource consumption.

The evaluation of organic synthesis strategies in chemistry is predicated upon critical parameters that assess efficacy, safety, and environmental ramifications. Below is a synthesis of primary metrics:

❖ **Key Metrics**

- Atom Economy: Measures the efficiency of reactants in yielding the final product, with cycloaddition reactions achieving 100% atom economy.
- Environmental Factor (E-factor): The waste-to-product mass ratio, instrumental for quantifying waste formation in chemical operations.
- Environmental Quotient (EQ): Enhances the E-factor by accounting for the toxicological

profile of waste constituents, thereby providing a comprehensive analysis of ecological impact.

- Effective Mass Yield: The proportion of the target product to the aggregate of toxic reagents employed, underscoring ecological hazard.
- Mass Intensity: Resource efficiency is measured by the ratio of total process mass to product mass.

❖ **Unified Tools**

- Process Profile: A managerial instrument for evaluating economic parameters pertinent to extensive scale production.
- Life Cycle Analysis (LCA): An assessment methodology examining all phases of a chemical's life cycle to evaluate environmental impacts thoroughly.
- Eco-Scale: An intuitive metric tool that assigns penalty points based on diverse reaction quality variables, yielding a score from 0 to 100 for organic syntheses.
- These metrics and tools collaboratively advocate for sustainable chemistry by prioritizing efficiency and mitigating environmental repercussions.[11]

AGREE

AGREEprep's 10 individual evaluation processes employ a scale of 0 to 1, with extremes representing the worst and best performance. Each criterion is allocated a default weight for the overall score, but assessors can vary these weights to correspond with their analytical goals, as long as they justify the modifications. The overall score, which runs from 0 to 1, is calculated by weighting and combining the scores of each criterion. A score of 1 indicates optimal performance. The AGREEprep software asks for input data for all ten steps of assessment, and when the evaluation is finalized, it generates a round pictogram. This pictogram features a central circle displaying the overall score, as well as ten trapezoidal bars that represent the ten criteria, with lengths proportional to their assigned weights. After evaluation, the color of each element changes, offering an easy means to identify the procedure's weak and strong points and their contribution to the final score.

Subsequently, a detailed discussion of the assessment criteria will illustrate their input values and showcase various aspects of the greenness assessment through case studies.Key Features include:

- Focused Evaluation: Concentrates on sample preparation, delivering a more precise appraisal of its ecological ramifications.
- Comprehensive Assessment: Analyzes factors including solvent selection, waste generation, and energy consumption.
- Strengths and Weaknesses Identification: Aids in pinpointing areas necessitating enhancement in sample preparation practices.
- User-Centric Software: Produces intuitive pictograms facilitating comprehension of environmental impact evaluations.

AGREE preparation enhances the capacity to formulate more sustainable analytical methodologies by providing a clear and implementable framework for assessing sample preparation protocols.

Case study illustration:

The investigation of three distinct methodologies for the detection of polybrominated diphenyl ethers (PBDEs) in soil samples utilizing the AGREE (Analytical GREEnness Metric) framework elucidates critical insights regarding their ecological sustainability and efficacy. Each methodology was assessed against twelve principles, which were assigned equal weight by default, allowing for a comprehensive analysis of their green chemistry attributes.

- **Procedural Overview**

1. SBSE-UAE-HPLC-UV Analytical Methodology

The initial methodology employs stir-bar sorptive extraction (SBSE), succeeded by ultrasound-assisted extraction (UAE) and high-performance liquid chromatography (HPLC) combined with ultraviolet (UV) detection. This protocol necessitates a mere 0.3 grams of soil, rendering it advantageous in terms of sample volume. It encompasses seven distinct analytical phases and operates in a non-automated, offline context, indicating the absence of automated mechanisms. Despite the efficacy of the SBSE-UAE-HPLC-UV method with respect to sample size, it lacks automation and miniaturization, thereby potentially limiting its scalability in high-throughput applications. The methodology yields 21.55 mL of effluent, primarily comprising solvents such as acetone and sodium chloride solutions, and exhibits a throughput of approximately 2.5 samples per hour, due to a desorption duration of merely 20 minutes. Nevertheless, it is imperative to recognize that the liquid chromatography component is energy-intensive, influencing its overall sustainability profile. The Eco-Scale assessment for this methodology is rated at 65.

2. Solvent Extraction-Headspace Solid-Phase Microextraction-Gas Chromatography-Tandem Mass Spectrometry (SE-HS-SPME-GC-MS/MS) Method

The second methodology integrates solvent extraction (SE) with headspace solid-phase microextraction (HS-SPME) and gas chromatography-tandem mass spectrometry (GC-MS/MS). This protocol requires a sample mass of 2 grams and comprises six analytical steps, functioning in an offline configuration. While the methodology lacks automation, it incorporates a compact sample preparation technique that can enhance operational efficiency. The total waste generated is quantified at 10.5 g/mL, encompassing solvents employed during the extraction phase. The throughput for this methodology is constrained, yielding one sample per hour due to the extended HS-SPME extraction duration of 60 minutes. The GC-MS segment is identified as the most energy-demanding component of this workflow. The Eco-Scale index for this method is elevated at 71, indicating a relatively favourable environmental performance compared to the SBSE-based technique.

3. Soxhlet Extraction Coupled with Gas Chromatography-Mass Spectrometry (GC-MS)

The third methodology employs Soxhlet extraction followed by gas chromatography coupled with mass spectrometry (GC-MS). This technique requires a maximum sample mass of 3 grams and encompasses six analytical phases, while operating in an offline configuration. Similar to the preceding methodologies, Soxhlet extraction lacks automation and miniaturization, leading to inefficiencies in processing duration. This method generates a substantial amount of waste, approximately 219 mL or grams, derived from solvents and various compounds, categorizing it as the least environmentally sustainable option among the three evaluated techniques. The throughput is markedly low, estimated at approximately 0.042 samples per hour, owing to the extended extraction duration of 24 hours required for analysis. The Eco-Scale rating for this procedure is a mere 49, reflecting its considerable environmental impact.

Comparative Insights of Different AGREE Approaches.

The AGREE analysis elucidates that while all three methodologies require substantial energy and material resources for the precise isolation and quantification of polybrominated diphenyl ethers (PBDEs), their sustainability metrics exhibit significant variability. The Soxhlet extraction method is identified as the least favourable option due to its considerable waste generation and suboptimal efficiency. Intriguingly, although the SBSE-UAE-HPLC-UV methodology received a lower Eco-Scale rating compared to the SE-HS-SPME-GC-MS/MS methodology, it was evaluated more favourably with respect to green chemistry principles under the AGREE framework. This discrepancy can be attributed to several factors: the sample size reduction necessitated by the SBSE-centric approach, enhancements in analytical efficiency, potential employment of bio-based solvents, and the exclusion of hazardous solvents such as hexane.[12] **Fig:5**

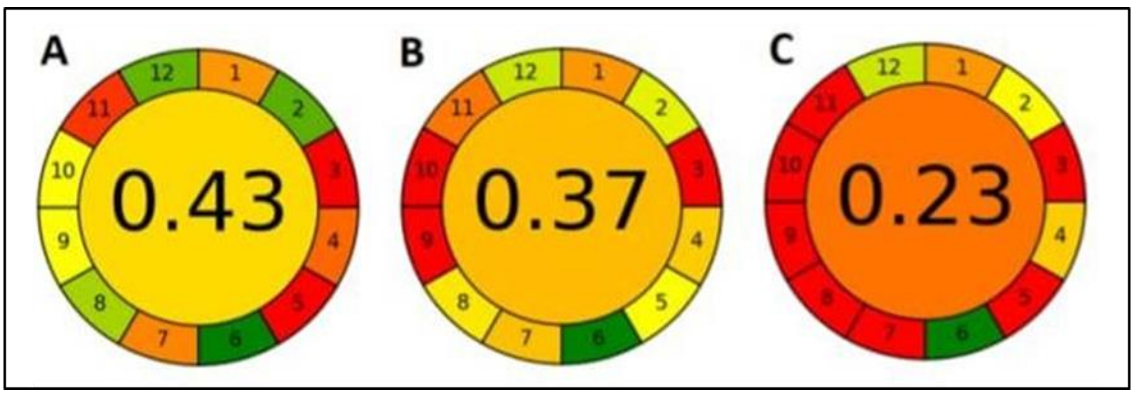

Fig 5: AGREE analytical results for SBSE-UAE-HPLC-UV (A), SE-HS-SPME-GC-MS/MS (B), and Soxhlet extraction using GC-MS (C).[12]

Comparison of evaluation of GAPI and AGREE tools for Proposed methods.

The GAPI and AGREE tools are complementary frameworks for evaluating the greenness of analytical methods based on GAC principles, but differ in their focus, structure, and assessment depth. GAPI (Green Analytical Procedure Index) provides a comprehensive evaluation of the complete analytical process. The assessment covers five main components: methodology, sampling procedures, sample processing, chemical components, and analytical instrumentation. Each of these components is divided into subcategories, totaling approximately 15 criteria. GAPI uses a color-coded pentagon—green indicating eco-friendliness, yellow for moderate impact, and red for hazardous practices. It is particularly user-friendly and visual, making it ideal for quickly identifying problematic areas in a full workflow. For example, in the case study involving DLLME-HPLC-UV for antiviral drug analysis, the GAPI diagram showed the method to be moderately green, with minimal use of hazardous solvents and energy, aligning well with sustainability goals.

On the other hand, AGREE (Analytical GREEnness Metric) focuses more specifically on the sample preparation stage, offering a quantitative, customizable assessment based on ten GAC principles. Unlike GAPI, AGREE generates a numerical score between 0 and 1, reflecting the overall ecological performance. Its circular pictogram includes ten segments, each representing a principle, with color-coded feedback and adjustable weights, enabling a more targeted and diagnostic evaluation. In the case study assessing three soil sample preparation methods for PBDE detection, AGREE clearly distinguished the relative sustainability of the techniques. The SE-HS-SPME-GC-MS/MS method, for instance, scored highest due to its compact preparation, lower waste generation, and favorable energy profile. In contrast, the Soxhlet-GC-MS method, despite its analytical robustness, was rated lowest due to its excessive solvent use, high energy consumption, and extended processing time. In essence, GAPI is better suited for providing an overall view of method sustainability, making it valuable during early method development or comparison of complete analytical workflows. In contrast, AGREE excels at identifying specific strengths and weaknesses in sample preparation, aiding in detailed optimization. When used together, these tools offer a comprehensive and nuanced perspective—GAPI providing the visual macro-level overview, and AGREE delivering the data-driven micro-level insight necessary for advancing green analytical chemistry practices.

STRATEGIES AND CHALLENGES:

Green analytical chemistry (GAC) aims to reduce the use of hazardous compounds while minimizing environmental impact. This field is increasingly relevant in light of escalating concerns regarding sustainability and environmental integrity. The following discourse elucidates pivotal strategies employed within GAC, alongside the challenges encountered in their execution.

Key Strategies in Green Analytical Chemistry

Reduction of Hazardous Solvents

Utilization of Alternative Solvents: Implementing solvents that exhibit lower toxicity or are non-toxic, such as aqueous solutions or ionic liquids, can markedly decrease environmental footprints.

Solvent-Free Techniques: Approaches including solid-phase microextraction (SPME) and headspace analysis substantially reduce or negate solvent utilization.

Miniaturization and Microextraction

Microfluidics: The application of micro-scale apparatus facilitates diminished consumption of reagents and generation of waste.

Miniaturized Sample Preparation: Techniques such as microextraction methods enhance analytical sensitivity while reducing sample volume and solvent usage.

Green Reagents and Materials

Biodegradable Materials: Employing materials capable of natural degradation mitigates long-term ecological impact.

Recyclable and Renewable Resources: The incorporation of resources derived from renewable origins lessens reliance on fossil fuel sources.

Innovative Analytical Techniques

Non-destructive Methods: Techniques such as spectroscopy permit the examination of samples without physical alteration or destruction, thereby reducing waste.

Real-time Monitoring: In situ analysis minimizes the necessity for sample transportation and preprocessing, consequently reducing associated waste generation.

Greenness Assessment Tools

Analytical Eco-Scale: A metric that assesses the environmental consequences of analytical methodologies accounting for variables such as waste production and energy consumption.

AGREE (A Green Analytical Chemistry Metric): A framework for evaluating the sustainability of analytical approaches across multiple dimensions. [13,14]

Challenges in the Implementation of Green Analytical Chemistry

Balancing Performance with Sustainability

Traditional analytical methodologies generally exhibit high sensitivity and specificity, yet frequently rely on hazardous reagents. Transitioning to more environmentally benign alternatives may sometimes compromise these performance metrics.

Regulatory and Compliance Issues

Existing regulations may disproportionately Favor conventional methodologies that adversely impact the ecosystem, thereby impeding the adoption of innovative eco-friendly techniques that fulfil industry standards.

Cost Implications

The initial financial investment for green technologies or reagents may surpass that of traditional approaches, prompting organizations to defer transition despite potential long-term economic benefits.

Limited Awareness and Training

Many chemists may lack formal education in green chemistry principles, leading to an insufficient comprehension of available sustainable alternatives and their corresponding benefits.

Research and Development Needs

Ongoing research is imperative to develop novel sustainable methodologies that provide efficacy comparable to traditional techniques. This requires collaboration among academic entities, industrial sectors, and regulatory bodies. [14,15]

ADVANTAGES:

1. Reduced Environmental Impact

A principal advantage of green analytical methodologies is their efficacy in attenuating ecological degradation. Analytical techniques often include hazardous solvents and chemicals, resulting in large waste generation. In contrast, green analytical methodologies aim to minimize the utilization of toxic chemicals and optimize waste production. For example, eco-conscious techniques frequently employ solvent-free or diminished-solvent methodologies, such as microwave-assisted extraction or supercritical fluid extraction, which incorporate sustainable alternatives. The employment of recyclable materials and environmentally benign reagents further contributes to reduced ecological footprints. This reduction in environmental repercussions is particularly pronounced in sectors characterized by large-scale chemical processes, including pharmaceuticals, food production, and environmental monitoring.

2. Health and Safety Enhancements

Augmentation of Analyst Safety

Green analytical chemistry accentuates the protection of laboratory personnel by significantly decreasing or entirely eliminating the application of toxic and hazardous substances. Numerous traditional analytical strategies necessitate the deployment of dangerous chemicals, which can jeopardize researchers' health through exposure to carcinogens, toxic vapours, or corrosive agents. The transition to non-hazardous solvents and reagents substantially mitigates these health risks.

Example: The implementation of non-toxic solvents such as ethanol or propylene carbonate as substitutes for volatile and carcinogenic solvents like benzene or tetrahydrofuran aids in preventing detrimental exposure to laboratory personnel.

Minimized Toxicity

Green analytical chemistry mitigates the toxicity of chemical analysis processes by substituting hazardous chemicals and solvents with safer alternatives. This is imperative for safeguarding laboratory personnel and preventing deleterious residues from contaminating the environment, consumables, or final products within production processes. A reduction in toxicity facilitates the implementation of safer waste disposal methodologies.

Example: Substituting toxic reagents with less harmful or non-toxic alternatives enhances the sustainability of the entire chemical lifecycle, diminishing potential hazards in both laboratory settings and post-disposal scenarios.[16]

3.Cost Efficiency

Reduction in Reagent Expenditure

Green analytical methodologies are designed to minimize the utilization of expensive or surplus reagents. The adoption of micro-scale methodologies or the optimization of reagent efficiency significantly decreases the overall financial outlay associated with analytical practices. The diminished quantities of chemicals necessitated not only reduce costs but also curtail the volume of chemicals that require procurement, storage, and disposal.

Example: The implementation of miniaturized analytical techniques (e.g., microreactors) or drop-based reaction systems results in reduced reagent demand per analysis, markedly decreasing expenditures compared to conventional bulk methodologies.

Energy and Resource Efficiency

In addition to reductions in reagent costs, environmentally sustainable analytical practices frequently emphasize energy efficiency. Conventional analytical techniques, such as titrations and chromatography, are often characterized by high energy consumption, necessitating elevated temperatures, pressures, or prolonged reaction durations. Green chemistry advocates for energy-efficient methodologies, including solvent-free reactions, processes conducted at ambient temperature, and catalysts that operate under mild conditions. These strategies reduce energy and material demands, yielding financial savings for laboratories and industries.[17]

4. Advancement in Analytical Methodologies

Development of Novel, Sustainable Instrumentation

Green chemistry advocates the development of innovative analytical apparatuses that exhibit enhanced efficacy and environmental compatibility. This includes instruments that exhibit reduced energy consumption or employ less hazardous reagents, along with groundbreaking analytical methodologies focused on minimizing material utilization. Progress in domains such as biosensors, electrochemical methods, and sustainable solvents is facilitating the advancement of sustainable analytical chemistry.

Enabling Sustainable Food Analysis

Green chemistry in food analysis promotes safe and sustainable ways for evaluating food ingredients and pollutants. This is crucial for maintaining the safety and sustainability of food. Eco-friendly methodologies mitigate the ecological footprint of food testing, such as employing non-toxic solvents in chromatography or food extraction.[18]

5. Enhanced Analytical Sensitivity and Precision

Optimized Reagent Utilization

Green analytical chemistry prioritizes ecological sustainability while simultaneously augmenting analytical efficacy. By optimizing reagent utilization, researchers can achieve enhanced precision and sensitivity in quantitative analyses. Techniques such as ultra-sensitive sensors or miniaturized detection systems can reduce the required sample volumes and reagent quantities while maintaining highly accurate and reproducible results.[19]

DISADVANTAGES:

1. Elevated Initial Capital Outlay: A significant barrier to the adoption of green analytical methodologies is the increased initial capital investment for specialized technologies and instrumentation. For instance, techniques such as supercritical fluid extraction (SFE) and microwave-assisted extraction (MAE) demand specialized instrumentation that may incur substantial acquisition and maintenance costs. Furthermore, the requisite training for personnel to competently operate these advanced instruments can also contribute to overall expenses. Laboratories or small enterprises with limited financial resources may deem the initial costs prohibitive, thus complicating the transition to more sustainable methodologies. However, the long-term benefits of reduced waste management, reagent use, and energy conservation make these approaches cost-effective.[16]

2. Restricted Availability of Eco-friendly Reagents and Materials: Notwithstanding significant progress in eco-analytical methodologies, identifying suitable eco-friendly reagents or solvents for each analysis poses a challenge. Due to their efficacy in targeted studies, conventional chemical solvents—such as organic solvents like methanol and hexane—are frequently favored. In particular scenarios, such as high-sensitivity assays or when addressing complex matrices, viable eco-alternatives may not be readily accessible or as effective as traditional reagents. The limited availability of environmentally benign solvents that can replace hazardous chemicals across various analyses constrains the extensive adoption of sustainable methodologies, especially in specialized domains.[17]

3. Complexity and Requirement for Expertise: Eco-analytical methods often incorporate innovative and sophisticated techniques that may require a heightened level of expertise and training. For instance, methodologies such as supercritical fluid chromatography (SFC) or contemporary extraction techniques like pressurized liquid extraction (PLE) may be unfamiliar to laboratory personnel accustomed to conventional methods. The application of these advanced techniques necessitates specialized knowledge, presenting a challenge for laboratories lacking the requisite resources or expertise. This intricacy also suggests that eco-analytical tools may necessitate additional time for optimization and execution, particularly when tailored to specific analytical requirements or sample matrices.[18]

4. Performance Limitations: Despite their numerous advantages, certain green analytical methodologies may exhibit suboptimal performance relative to traditional techniques in specific contexts. For example, eco-sustainable approaches may face limitations in terms of sensitivity, precision, or reliability when analyzing complex matrices or trace amounts of substances. In critical domains such as forensic science, environmental surveillance, or clinical diagnostics, the efficacy of green analytical techniques may still be inferior to that of conventional methodologies. Research initiatives are underway to address these performance barriers and optimize green techniques for broader applicability; however, concerns regarding efficacy may impede the extensive adoption of these sustainable alternatives.[19]

APPLICATION:

1. Electrophoresis: Capillary electrophoresis (CE), particularly capillary zone electrophoresis (CZE), is increasingly recognized as an eco-friendly analytical technique due to reduced solvent and sample consumption, typically requiring only approximately 5 µL for capillary separation and elution. This minimal consumption aligns with green chemistry principles emphasizing waste reduction and safer solvent utilization.

Diminished Sample Volume: Facilitates analysis with small quantities.

Reduced Solvent Utilization: Mitigates chemical waste and economic expenditures.

Enhanced Selectivity and Velocity: Accelerated analysis with superior selectivity relative to high-pressure liquid chromatography (HPLC).

Simplified Instrumentation: Contributes to lower maintenance requirements and user-friendly operation.

Recent advancements are overcoming previous challenges associated with sensitivity and separation robustness, Promoting the use of CE for analyzing complicated materials. Overall, CE presents a sustainable alternative compared to conventional methodologies, fostering environmentally responsible practices in analytical chemistry.

2.Micronization and Microfluidics in Analytical Chemistry: Micronization is a vital technique in analytical chemistry, particularly for handling minuscule sample volumes (sub-microliter). This process diminishes analyte wastage and enhances the efficiency of chemical characterizations. Combinatorial chemistry accelerates these processes through the simultaneous synthesis of diverse compounds, thereby reducing the demand for extensive purification procedures.

Microfluidics and µTAS: Miniaturized total analysis systems (µTAS) consolidate all phases of chemical analysis into compact apparatuses, augmenting selectivity and improving detection thresholds while drastically minimizing waste by 4-5 orders of magnitude relative to traditional methodologies. It necessitates nanoliter or picoliter sample volumes. This facilitates expedited reactions and in situ monitoring of environmental contaminants, aligning with green chemistry principles by reducing ecological impact.

Challenges: A major obstacle is the interfacing of macro-scale processes with micro-scale systems, complicating the transfer of samples and reagents between large and microfluidic platforms. Effective access to this interface is crucial for high-throughput methodologies.

Recent Innovations: Recent advancements encompass a Cross Injection Device employing pressure modulations for efficient sample introduction into capillaries, and a Falling Droplet Sampler that dispenses samples as droplets into a buffer, maintaining a stable liquid head to avoid hydrodynamic pressure discrepancies. These innovations highlight the continuous evolution in microfluidics and combinatorial chemistry, enhancing analytical functions while advocating for sustainable practices.

Ionic Liquid Separation: Ionic liquids (ILs) demonstrate efficacy in liquid-liquid extraction, Specifically, in the removal of sulfur and nitrogenous chemicals from fuels.

3.Alternative Solvents: Supercritical Fluids in Analytical Chemistry. Supercritical fluids (SCFs), predominantly carbon dioxide (CO_2) and water, are increasingly acknowledged as environmentally benign alternatives to traditional organic solvents in analytical chemistry. Their unique properties, including elevated diffusivity and configurability through thermal and pressure modifications, enhance their efficacy for extraction and chromatography.

Advantages of Supercritical Fluid Extraction (SFE) include:

Enhanced Efficiency: Accelerated extraction kinetics relative to traditional methodologies;

Energy Conservation: Removes the necessity for energy-intensive processes like distillation and evaporation;

Reduced Solvent Consumption: Decreases the usage of deleterious organic solvents;

Tunable Physicochemical Properties: Facilitates solubility optimization tailored to specific extraction parameters. Supercritical Fluid Chromatography (SFC) presents remarkable efficacy and adaptability in the separation of various chemical species by integrating attributes of gas and liquid chromatography. Its rapid throughput and environmental benefits when employing CO_2 underscore its significance. Challenges persist, as SCFs face complexities such as technical sophistication, sensitivity to thermal and pressure fluctuations, and diminished effectiveness with highly polar solutes. Future Directions aim to enhance the reliability and integration of supercritical fluid methodologies in laboratory settings by prioritizing the development of standardized protocols and cutting-edge systems, including the online coupling of extraction and separation stages. The potential of SCFs to promote the evolution of greener analytical techniques remains promising.[20]

4.Microextraction Techniques: Solid-phase microextraction (SPME) and liquid-phase microextraction (LPME) present alternatives to conventional solvent-based extraction methodologies, thereby reducing Using fewer organic solvents reduces their environmental impact.Use of Safer Reagents:

Eco-friendly Reagents: Substituting hazardous compounds with safer, environmentally benign alternatives is a core principle. For example, the application of safer reagents such as ionic liquids, characterized by their negligible volatility and lower toxicity, in analytical methodologies.

Energy-Efficient Analytical Techniques: In comparison to traditional methodologies like Soxhlet extraction, microwave-assisted extraction (MAE) and ultrasound-assisted extraction (UAE) are energy-efficient strategies that diminish solvent consumption and energy expenditures.

Miniaturization of Analytical Systems: Lab-on-a-chip (LOC): Miniaturized equipment reduce chemicals, waste, and energy usage, allowing for faster and more effective tests. LOCs are particularly advantageous for environmental surveillance and biomedical applications.

Sustainable Sample Preparation:

Green Sample Preparation Techniques: Approaches employing CO2 instead of conventional solvents, such as supercritical fluid extraction (SFE) or solid-phase extraction (SPE), which necessitate fewer solvents and reagents, align with the objectives of green analytical chemistry.

Sensor-Based and Non-Chemical Methods:

Electrochemical Sensors and Biosensors: These instruments reduce the dependency on hazardous chemicals and mitigate waste generation. For instance, sensors that utilize electrochemical principles for monitoring water quality require minimal reagents and provide instantaneous results while maintaining a minimal environmental impact.

Use of Renewable Energy:

Solar-Powered Analytical Devices: Using renewable energy sources, such as solar energy, in analytical devices mitigates reliance on traditional energy infrastructures, thereby enhancing overall sustainability. [20,27]

CONCLUSION:

Green analytical chemistry (GAC) constitutes an innovative paradigm in the realm of analytical methodologies, emphasizing ecological sustainability and risk mitigation. By integrating green chemistry principles, GAC seeks to minimize the usage of toxic compounds, diminish waste production, and improve energy efficiency within analytical protocols. The implementation of avant-garde techniques such as microextraction, supercritical fluid extraction, and miniaturized analytical systems exemplifies the transition towards sustainable analytical practices. Despite notable advancements and advantages conferred by GAC, several obstacles persist, including the necessity for specialized training, elevated initial capital investment, and potential performance drawbacks when juxtaposed with conventional methodologies. Evaluative tools like the Green Analytical Procedure Index (GAPI) and AGREE metrics help compare and contrast the environmental impact of different analytical techniques. GAC is well-positioned to shape practices in areas such as pharmaceuticals, food safety, and environmental monitoring, given growing concerns about sustainability and ecological health. By nurturing a culture of innovation and interdisciplinary collaboration among researchers, industry experts, and regulatory agencies, GAC can substantially advance the pursuit of a sustainable future in analytical chemistry.

Availability of Data and Material

All the data provided are within the manuscript.

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Authors' contributions

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JP: She is a student at Sigma University she has prepared the manuscript.

KP: She is also a student at Sigma University she has done the formatting.

SS: Suraj Singh, He is completed M.pharm (QA) currently working in Unicure Remedies. He collected the data from various sources.

MD: Dr. Mitali Dalwadi She is completed PhD in Pharmaceutical Science. Although She Reviewed the manuscript.

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