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Green Analytical Chemistry Approaches In Pharmaceutical Analysis

Ms. AISHWARYA A. KANERKAR[1] ,Ms.PRAJAKTA B. MHASKE[2] ,Dr.VIJAYKUMAR KALE[3],

Dr.MAHESH THAKARE[4],Mr.VAIBHAV NARWADE[5]

Student[1],Assistant Professor[2]
Bachelor of Pharmacy[1],
Kasturi Shikshan Sanstha College of Pharmacy Shikrapur,Pune ,Maharashtra,India[1]

Abstract: A wide range of factors are considered when assessing an analytical method, such as the amount and toxicity of chemicals used, the volume of waste produced, energy consumption, and the degree of automation, miniaturization, and procedural complexity. Sustainability has become a key focus in modern analytical chemistry, with growing emphasis on green and environmentally responsible practices. These approaches promote the use of techniques that generate minimal hazardous waste and encourage safer methods, solvents, and operational strategies. In a sustainable society, chemicals form the basis of products and processes, guided by life-friendly design principles that evaluate whether substances and methods are renewable or harmful, safe or depleting, and persistent or readily degradable.

Keywords : Green Analytical Chemistry, Pharmaceutical Analysis,Sustainable Analytical Methods,Green Chromatography,Supercritical Fluid Chromatography (SFC),Eco-friendly Solvents,Green Sample Preparation,Solid Phase Extraction (SPE),Solid Phase Microextraction (SPME),Ultrasound-Assisted Extraction (UAE),Microwave-Assisted Extraction (MAE),Green Chemistry Principles,Solvent Reduction,Environmental Sustainability in Analysis

I. INTRODUCTION

Green chemistry is a developing scientific approach focused on designing chemical processes and products that limit or completely avoid the use of dangerous substances. Its purpose is to create efficient and environmentally responsible methods that produce very little waste. By prioritizing sustainability and safety, green chemistry plays an important role in advancing modern chemical synthesis.

The central idea of green chemistry is to develop methods that are safer for both people and the environment. Traditional chemical practices often depend on toxic compounds that can harm ecosystems and human health over time, making the shift toward safer alternatives necessary. Green analytical chemistry supports this transition by encouraging the use of modern techniques that are smaller in scale, automated, accurate, and less harmful. These approaches rely on safer reagents, reduce waste generation, and minimize risks linked to conventional analytical methods.

The primary objective of green chemistry is to limit the harmful impact of chemical activities on the environment, public health, and natural resources. This discipline emerged as concerns grew over the environmental and health effects of conventional chemical processes. Its guiding framework is based on twelve key principles introduced by Paul Anastas and John Warner, which emphasize waste prevention, the use of safer materials, and improved efficiency across all stages of chemical design and production.[1,3,6]

II. GREEN DEVELOPMENT

Modern analytical chemistry increasingly relies on automated, instrument-based systems that streamline sample preparation, separation, and detection into a single workflow. In line with green chemistry principles, integrating multiple steps into one platform boosts efficiency, supports high-throughput analysis, and lowers the overall use of energy and materials. Advancements in materials science and miniaturization such as the use of nanomaterials, micro-devices, and micro-scale analytical systems also contribute to greener practices. These innovations help reduce waste, minimize sample volumes, and improve analytical performance. Enhanced computing power and improved data processing tools, especially in sensor-driven technologies, further enable faster and more dependable analyses.Even though the connection is not always clearly highlighted, many newly developed analytical methods naturally align with green chemistry by lowering energy requirements and simplifying operational procedures. However, the consistent and deliberate application of green chemistry principles when designing or selecting analytical methods is still developing.[4]

III.EVOLUTION OF GREEN CHEMISTRY :

Green analytical chemistry (GAC), sometimes described as the analytical branch of green chemistry, has gained significant attention in recent years. Numerous textbooks, research papers, and special journal editions have explored how this field is evolving and how new analytical strategies are being adapted to reduce environmental impact. Among the twelve guiding principles of green chemistry, the concept of monitoring processes in real time to prevent pollution is especially important for analytical work, though all the principles hold value across chemical research and practice.

As a specialized area, GAC aims to make every step of analytical procedures more sustainable. Its approach extends beyond sample preparation to include how data is processed, interpreted, and ultimately used to make decisions. By encouraging safer materials, streamlined workflows, and reduced environmental burden, green analytical chemistry helps shape analytical methods that are both efficient and eco friendly.[5]

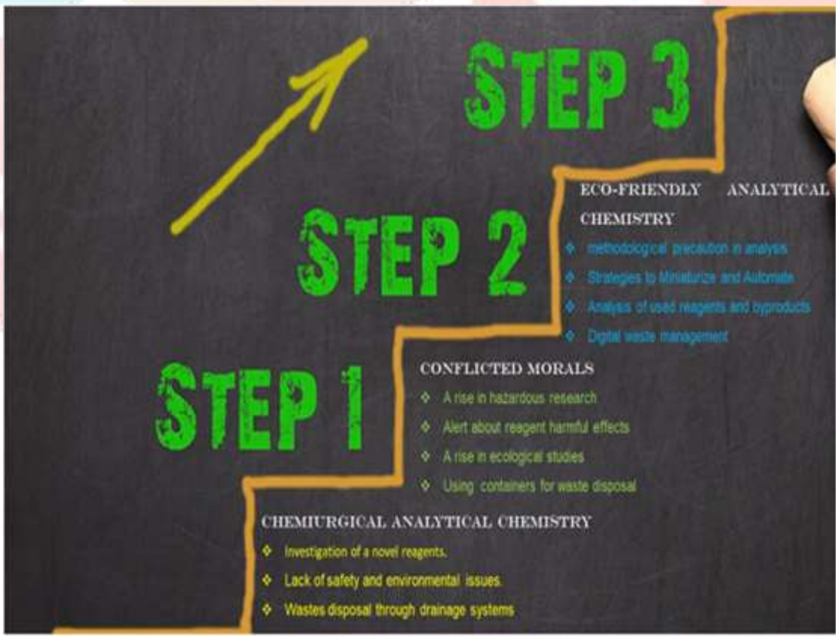

Figure 1: Analytical laboratories' developmental steps toward an ecological mindset.

IV. IMPACT OF GREEN CHEMISTRY ON ENVIRONMENT AND POPULATION:

Minimizing the environmental burden of analytical work requires cutting down the use of water, solvents, and chemical reagents. Green Analytical Chemistry (GAC) focuses on replacing harmful chemicals with safer and more sustainable options. By reducing the amount of toxic waste released, GAC contributes to safer practices, particularly in fields like medical and clinical testing.[11] Conventional analytical procedures have often been associated with contamination and pollution, which highlights the necessity for greener methods. This makes effective waste handling such as proper treatment, disposal, and recycling essential within pharmaceutical laboratories. Although recycling provides clear ecological advantages, it can also involve significant financial costs, which researchers need to balance with practicality.Despite these limitations, recycling is still crucial because it lowers exposure to dangerous substances and helps recover useful materials that would otherwise be lost. However, reuse or recycling must not affect sample quality or compromise the reliability of analytical data. Since pharmaceutical analysis depends on a wide range of chemicals, solvents, and procedures, improper waste management can pose risks to both laboratory workers and the individuals relying on the results.[30]

1.1 GREEN CHROMATOGRAPHIC TECHNIQUE :

Chromatography plays a crucial role in pharmaceutical research, helping scientists separate and analyze various compounds. However, many traditional chromatographic techniques rely heavily on toxic organic solvents, which generate substantial amounts of hazardous waste.Green chromatography aims to address these issues by reducing or eliminating harmful solvents wherever possible. Supercritical Fluid Chromatography (SFC) is one of the leading greener alternatives because it primarily uses carbon dioxide an inexpensive, readily available, and non-toxic fluid as its main mobile phase. Since only small amounts of additional liquid modifiers are required, the overall environmental impact related to CO_2 handling, reuse, and release is considerably lower. This not only makes the technique more sustainable but can also reduce operational expenses when compared to solvent-intensive methods. In sample preparation, SFC offers clear benefits by lowering solvent consumption, cutting down on waste, and reducing the need for extra auxiliary fluids. Despite these strengths, ongoing improvements are still needed, including better control of modifier flow rates, more energy-efficient cooling systems, and enhanced compatibility with mass spectrometric detectors. Even so, SFC remains a highly promising and environmentally conscious option for chromatographic separation and purification.[10]

1.1.1 Supercritical Fluid Chromatography (SFC) –

Supercritical Fluid Chromatography (SFC) primarily uses carbon dioxide in its supercritical state as the mobile phase, which significantly limits the consumption of toxic organic solvents. As a result, it is considered an environmentally friendly technique. SFC is valued for its rapid separation capabilities, excellent efficiency, and the convenience of removing the mobile phase after analysis, making it highly suitable for modern analytical applications.[21]

1.1.2 Ultra-High-Performance Liquid Chromatography (UHPLC)-

Ultra-high-performance liquid chromatography (UHPLC) works under much higher pressures and uses columns filled with extremely small particles. This design enables faster separations while requiring smaller amounts of solvent compared to traditional HPLC, making the technique more efficient and environmentally sustainable.

1.1.3 Capillary Electrophoresis (CE)-

Capillary electrophoresis (CE) is regarded as a green analytical technique because it delivers excellent separation efficiency while using only tiny volumes of electrolyte, which greatly reduces solvent consumption and waste production.

1.1.4 Green Thin-Layer Chromatography (TLC)-

Green thin-layer chromatography (TLC) uses compact plates along with safer, biodegradable solvent mixtures, which lowers overall chemical consumption and helps reduce contact with harmful substances.

2.1 GREENER ORGANIC SOLVENT IN ANALYTICAL CHEMISTRY:

Analytical chemistry is increasingly emphasizing solvent-free techniques because they are considered the most sustainable and environmentally friendly options. However, the complete elimination of solvents is not yet possible, as they are still required for essential steps such as sample preparation and making analytes suitable for measurement. As green chemistry principles continue to shape analytical methods, considerable attention is being given to the development of safer and more eco-friendly solvents to replace traditional organic solvents, which are often volatile, flammable, and toxic. In this context, alternatives such as ionic liquids, deep eutectic solvents, amphiphilic systems, and related substances including alcohols, carboxylic acids, and surfactants are increasingly being explored and selected for analytical applications.Many of these environmentally benign solvents have already found practical use in liquid chromatography, where they act as extraction media, mobile-phase modifiers, pseudo-stationary phases, or as components of the mobile phase during sample preparation.[8]

3.1 GREEN SAMPLE PREPARATION :

3.1.1 Solid Phase Extraction (SPE):

Solid Phase Extraction (SPE) is extensively applied in analytical laboratories as an effective sample-preparation strategy. In this technique, aqueous samples are introduced into a compact cartridge containing a selected solid sorbent that captures the analytes of interest. The retained compounds are subsequently released using very small quantities of a strong elution solvent, allowing simultaneous purification and enrichment of the target species. Due to its low solvent demand and reduced waste generation, SPE is widely recognized as an environmentally sustainable approach.A key advantage of SPE is its compatibility with automation using inexpensive and uncomplicated systems, which increases sample throughput while improving reproducibility and analytical reliability. Nevertheless, extraction efficiency can be compromised if certain practical aspects are overlooked. For example, inconsistencies in sorbent bed structure may negatively influence analyte retention and recovery. The availability of pre-packed commercial SPE cartridges largely addresses issues related to sorbent packing and method consistency. However, some traditional sorbent materials lack sufficient selectivity, particularly when handling highly polar analytes. Additionally, interactions between sample matrix components and the sorbent may compete with analyte binding, leading to reduced recoveries. Therefore, thorough optimization of SPE parameters is crucial to achieve accurate, efficient, and dependable analytical results.[31]

3.1.2 Solid phase microextraction (SPME) :

Solid Phase Microextraction (SPME) is an eco-friendly sample preparation approach that does not require solvents and allows both isolation and enrichment of analytes to occur simultaneously. The method employs a very fine silica-based fiber coated with a selective material that attracts and holds specific compounds of interest. These substances may be absorbed directly from the sample itself or from the vapor phase above it, where they remain on the fiber until analysis. The efficiency of SPME depends on multiple operational factors, including the type of coating applied to the fiber, the movement of the sample during extraction, the length of exposure time, and the chosen working conditions. When coupled with analytical techniques such as HPLC, GC, GC–MS, or LC–MS, SPME offers a reliable and sensitive option for identifying and measuring compounds in food samples and other chemically complex matrices.

3.1.3 Extraction with Microwave Assistance (MAE) :

Microwave-assisted extraction (MAE) is a rapid extraction technique that utilizes microwave energy to enhance the release of target compounds from samples. This method relies on the interaction between microwave radiation and polar molecules, which absorb the energy and generate heat within the system. The rapid internal heating promotes efficient mass transfer, allowing analytes to move more quickly into the surrounding solvent or aqueous phase and thereby improving extraction performance. In laboratory applications, MAE systems typically operate at a frequency of 2.45 GHz, even though microwave radiation spans a broader frequency range. The technique offers several advantages, including fast heating rates, the capability to achieve elevated temperatures, and straightforward operation. However, its effectiveness is strongly influenced by the dielectric properties of the solvent, meaning that solvents with low microwave absorption may limit extraction efficiency for certain sample types.

3.1.4 Ultrasound-Assisted Extraction (UAE):

In recent years, ultrasound has gained significant attention as an extraction tool, mainly because many conventional and alternative techniques suffer from drawbacks such as expensive instrumentation, high energy requirements, and the use of toxic solvents. Ultrasound-assisted extraction (UAE) involves the application of ultrasonic waves during the early stages of sample processing, which enhances mass transfer and improves extraction efficiency. Owing to these advantages, UAE is widely recognized as a cleaner and more sustainable approach.UAE has emerged as a reliable and efficient substitute for traditional extraction methods, particularly in food and allied industries. Compared to several other extraction techniques, ultrasonication is easy to implement, cost-effective, and requires simpler equipment. Furthermore, the application of ultrasound allows for greater flexibility in solvent selection, enabling the use of safer and more environmentally acceptable solvents during the extraction process.[2]

4.1 CHROMATOGRAPHIC METHOD AND THEIR IMPLETATION IN GREEN CHEMISTRY :

Gas chromatography and liquid chromatography are the two main separation methods used for analytical and preparative work. Gas chromatography is mainly employed for compounds that can be vaporized without decomposition. From a sustainability standpoint, this technique is more environmentally friendly because it usually does not require liquid solvents, involves limited sample processing, and relies on carrier gases rather than chemical additives. Helium is often chosen as the carrier gas because it provides reliable separation while being chemically inactive, safe to handle, non flammable, and harmless to users.Liquid chromatography separates substances based on how they distribute between a flowing liquid and a solid surface, which commonly leads to high solvent consumption. Due to this characteristic, applying green chemistry concepts is more difficult in liquid chromatography compared to gas chromatography. Even so, environmentally responsible practices can still be introduced in liquid chromatography by reducing solvent usage and selecting safer operating conditions, which are typically discussed in detail elsewhere.[11]

4.1.1 Reducing the internal diameter of column –

Reducing the MP flow rate can lessen the amount of solvents utilized for separation, and this is achievable when the column's internal diameter is decreased. The flow rate of the MP should be lowered by the square of the column diameter in order to achieve appropriate separations when the internal column diameter is decreased. Since LC is frequently used in conjunction with ultraviolet, fluorescence, and electrospray ionization mass spectrometry (MS) as detectors, decreasing the internal column diameter improves analytical sensitivity by reducing solute dilution in the MP, creating more concentrated bands at the detector, and reducing organic solvent depletion and ultimately organic waste output.

4.1.2 Reducing solvent consumption –

By decreasing the particle size and shortening the column length, chromatographic productivity can be increased while lowering solvent consumption. Ultrahigh-pressure LC can be used to reduce particle size. This reduces analysis time and depletes column diameter and length, which reduces extra-column dispersion and increases MP delivery pressure.ng organic solvent depletion and ultimately organic waste output.

4.1.3 Temperature optimization -

Adjusting the operating temperature can strongly influence sensitivity, separation performance, and compound recognition. While increasing temperature may improve analysis, it has limitations, particularly for heat-sensitive compounds or silica-based chromatographic columns, where temperatures typically should not exceed 60 °C. Despite these limits, modifying temperature is often considered more straightforward than changing the mobile or stationary phase composition or adjusting the pH. When applying temperature control in liquid chromatography, certain practical aspects must be considered. The column must be equipped with accurate thermal regulation, and the mobile phase should be warmed before it reaches the column. In addition, for most detection systems, the eluent should be cooled after exiting the column. These measures help maintain a stable detector response by preventing temperature-related signal fluctuations.[3]

5.1 PRINCIPLE:

Preference for Renewable Resources- Whenever it is practical from both technical and economic perspectives, chemical raw materials should be obtained from renewable sources instead of finite ones. Relying on renewable feedstocks helps reduce environmental damage and limits dependence on exhaustible resources.

Reduction of Derivatization Steps- Chemical processes should avoid unnecessary steps such as protection, deprotection, or temporary structural modifications. These additional steps often increase reagent use and generate extra waste, so minimizing derivatization improves overall process sustainability.

Use of Catalysts- Catalytic systems are favored over reactions that require large, stoichiometric amounts of reagents. Catalysts enhance reaction efficiency and selectivity while lowering energy demand and reducing waste formation.

Design of Environmental Breakdown- Chemical products should be developed in a way that allows them to decompose into non-toxic substances once they have fulfilled their intended purpose. This prevents long-term persistence and accumulation in the environment.

Real-Time Monitoring to Avoid Pollution- Analytical methods should allow continuous, real-time monitoring of chemical processes. Early detection of hazardous intermediates enables corrective action before harmful substances are produced, thereby preventing pollution.

Safer Chemistry to Prevent Accidents- The choice of materials and operating conditions should focus on reducing the risk of accidents such as fires, explosions, or leaks. Using inherently safer chemicals and processes improves both workplace safety and process reliability.

Prevention of Waste Formation- It is more effective to prevent waste at the source than to manage it after production. Chemical processes should be designed to generate as little waste as possible, reducing environmental impact and waste-handling costs.

Maximizing Atom Economy- Synthetic strategies should aim to incorporate the maximum proportion of reactant atoms into the final product. High atom economy minimizes byproduct formation and improves the efficient use of materials.

Development of Less Hazardous Synthesis- Chemical reactions should be planned to use and generate substances that present minimal danger to human health and the environment. Safer reaction pathways reduce overall chemical risk.

Design of Safer Chemical Products- Chemicals should be designed to deliver their intended performance while having the lowest possible toxicity. Creating safer molecules reduces hazards without compromising their functional effectiveness.

Safer Use of Solvents and Auxiliary Materials- Solvents and auxiliary substances should be avoided where possible, and when necessary, environmentally benign alternatives should be chosen. Since these materials significantly influence environmental impact, their careful selection is essential.

Energy-Efficient Process Design- Chemical processes should be optimized to minimize energy consumption. Conducting reactions under mild conditions, such as room temperature and atmospheric pressure, helps reduce both environmental and economic costs.[5]

6.1 ADVANTAGES:

- Reducing hazardous chemical emissions protects lung health and lowers respiratory risks.
- Using safer alternatives (e.g., alcohol instead of water) limits toxic waste release into water systems.
- These practices improve workplace safety by reducing toxic substance use and accident risks.
- Ecosystems, including plants and animals, are safeguarded from harmful pollutants.

- Environmental issues such as ozone depletion, smog, and climate change are mitigated.
- Resource efficiency is enhanced, achieving desired outcomes with fewer materials.[1]

7.1 DISADVANTAGES :

- Cost: Implementing green chemistry can be costly.
- Limited Knowledge: A shortage of information about green chemistry may restrict the availability of alternative technologies and raw materials.
- Skills Gap: There may be a lack of trained personnel with expertise in green chemistry.
- Solvent Availability: Green solvents can be more expensive or harder to obtain than conventional solvents.
- Performance Uncertainty: The efficiency and effectiveness of green technologies and practices may be uncertain, and initial setup costs can be significant.[1]

8.1 APPLICATION :

- Energy Production: Focus on creating sustainable technologies for renewable energy, including solar cells and batteries, and designing catalysts that make energy conversion cleaner and more efficient.
- Water Treatment: Develop environmentally friendly techniques for purifying water and create advanced materials that can efficiently remove pollutants.
- Textile Industry: Encourage eco-conscious alternatives in textile production, such as green dyeing and finishing methods, while supporting sustainable practices in agriculture and food processing.
- Cleaning Products: Formulate household and cleaning products that are safer for the environment through innovative, non-toxic ingredients.
- Waste Management: Apply green chemistry principles to manage hazardous waste by reducing waste production and promoting recycling and safe disposal methods.
- Research and Education: Integrate green chemistry ideas into academic curricula and carry out studies to identify and advance sustainable chemical practices.
- Policy and Regulation: Help shape chemical policies and regulations to support the use of environmentally responsible chemical methods.[1]

Conclusion :

This review provides a detailed guide for researchers, analysts, and industry professionals who are looking to implement innovative, cost-effective, and environmentally sustainable practices in their analytical work. By emphasizing the advantages and practicality of green analytical methods, it encourages their broader adoption across fields like pharmaceuticals, food testing, environmental monitoring, and more.While liquid chromatography remains a cornerstone technique in pharmaceutical quality control, it often generates large amounts of solvent waste and has a considerable environmental footprint. This has driven efforts to develop greener chromatographic approaches that reduce environmental impact while ensuring the safety of analysts.Integrating the principles of green analytical chemistry into method development can help minimize solvent use, reduce waste, and limit exposure to toxic chemicals. Additionally, using tools to assess the environmental impact of chromatographic methods such as evaluating solvent consumption, energy requirements, and waste production can guide the creation of more eco-friendly and sustainable analytical practices.

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