Green Analytical Chemistry Approaches for Pharmaceutical Quality Testing

Dr. Sundhararajan R[1], Mr.S.G. Raman*[2], Abdul Haleem. M[3]
Gokul. E. B[3], Haji Mohamed. M[3]

1. **Principal and Professor, Mohamed Sathak AJ College of Pharmacy**
2. **Professor in Charge, Mohamed Sathak AJ College of Pharmacy**
3. **B.Pharm, Final Year Students**

Abstract :

Pharmaceutical quality testing plays a vital role in safeguarding public health by ensuring the safety, efficacy, and purity of medicines. Conventional analytical methods such as HPLC, GC, and spectroscopy, though reliable, rely heavily on toxic solvents, energy-intensive processes, and extensive sample preparation, leading to significant environmental and economic burdens. The emergence of Green Analytical Chemistry (GAC) addresses these challenges by integrating the principles of sustainability, efficiency, and safety into pharmaceutical analysis. This thesis examines the principles and applications of GAC with a focus on greener sample preparation and extraction techniques, greener chromatographic methods, the use of chemometrics, and the integration of Quality by Design (QbD). These approaches collectively reduce solvent consumption, minimize waste generation, and enhance analytical robustness, making pharmaceutical quality control more eco-friendly and cost-effective. The study also explores the challenges that hinder wider implementation and highlights future prospects for integrating green practices into mainstream pharmaceutical laboratories. Findings indicate that adopting GAC not only aligns with global sustainability goals but also provides economic advantages and ensures compliance with evolving regulatory expectations.

Keywords: Pharmaceutical quality testing, Green Analytical Chemistry (GAC), Quality by Design (QbD),chemometrics, greener chromatographic methods

Introduction :

Pharmaceutical quality testing is the foundation of today's healthcare system, ensuring that all drug products entering the marketplace meet established standards of safety, effectiveness, purity, and consistency. Quality testing is key to its ability to detect and measure active pharmaceutical ingredients (APIs), degradation products, impurities, and contaminants that can influence therapeutic results. International regulatory bodies, such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the Indian Pharmacopoeia Commission, have built robust guidelines for analytical method development and validation to ensure high standards of quality assurance [1]. These regulations have brought analytical chemistry into the center of pharmaceutical development, research, and manufacturing. Conventionally, the most widely used analytical methods in pharmaceutical quality control are high-performance liquid chromatography (HPLC), gas chromatography (GC), ultraviolet-visible (UV-Vis) spectroscopy, infrared (IR) spectroscopy, nuclear magnetic resonance (NMR) spectroscopy, and mass spectrometry (MS) [2]. These methods offer high sensitivity, specificity, and accuracy in the detection of pharmaceutical compounds and their impurities. Although they are efficient, these methods have severe disadvantages with respect to the environment and sustainability. Most chromatographic methods use massive amounts of toxic, non-renewable, and expensive-to-dispose-of organic solvents like acetonitrile, methanol, or chloroform [3]. In addition, the methods are usually energy-intensive, involve complicated sample preparation sequences, and produce large laboratory wastes. Consequently, the pharmaceutical industry has come under growing pressure to reduce the ecological impact of its analytical processes.Green Chemistry (GC) is a phenomenon that originated in the 1990s due to increasing consciousness of chemical risks and ecological sustainability. Green Chemistry emphasizes the design of chemical processes and products that minimize or eliminate the use of hazardous chemicals, minimize waste generation, and increase efficiency in general [4]. Based on these tenets, the arena of Green Analytical Chemistry (GAC) has emerged as a niche branch focused on greening analytical practices. As opposed to traditional approaches, GAC aims to reduce the usage of solvents and reagents, lessen energy expenditure, substitute dangerous chemicals with cleaner alternatives, and promote the utilization of renewable materials [5].

Principles of Green Analytical Chemistry

The 12 principles of green chemistry provide a foundational framework for designing chemical processes and products that prioritize environmental and human health. When applied to analytical techniques, these principles drive the development of methodologies that are safer, more efficient, and environmentally benign. Figure 3.1 shows the 12 principles of Green Analytical Chemistry (GAC), highlighting key strategies such as waste prevention, atom economy, safer chemicals, energy efficiency, and real-time analysis, which collectively guide the development of sustainable and environmentally conscious analytical techniques. Waste prevention, the first principle,

emphasizes designing analytical processes that avoid generating waste rather than managing it after the fact, a critical consideration in high-throughput laboratories. Atom economy, another key principle, ensures that chemical reactions used in analytical processes maximize the incorporation of all starting materials into the final product, reducing by-products and inefficiencies. Less hazardous chemical syntheses and designing safer chemicals focus on minimizing toxicity in reagents and solvents used during analysis, protecting both analysts and the environment. The principle of safer solvents and auxiliaries is particularly relevant to analytical chemistry, as it encourages the use of non-toxic, biodegradable, or less harmful solvents, such as water, ionic liquids, or supercritical carbon dioxide, reducing reliance on hazardous organic solvents.

Figure 3- 1: The 12 principles of Green Analytical Chemistry (GAC)

Energy efficiency is another critical aspect, urging the development of techniques that operate under milder conditions, such as room temperature and pressure, to lower energy consumption. This is exemplified in the use of alternative energy sources, such as microwave-assisted or ultrasound-assisted methods, to accelerate processes without excessive energy inputs. The principle of renewable feedstocks encourages the replacement of finite resources with renewable ones, such as bio-based solvents or reagents derived from natural materials. Reducing derivatives, which minimizes the need for temporary chemical modifications like protection or deprotection steps, ensures analytical methods are streamlined and resource-efficient. Catalysis, a cornerstone principle, promotes the use of catalytic reagents over stoichiometric ones in analytical methods, enhancing selectivity and reducing material use while minimizing environmental impacts. The principle of design for degradation ensures that chemicals and materials used in analytical processes decompose into harmless products at the end of their lifecycle, preventing persistent environmental contamination. Real-time analysis for pollution prevention is particularly significant in analytical chemistry, advocating for methodologies that monitor and control processes in real-time to prevent hazardous by-products before they form. Finally,

inherently safer chemistry for accident prevention underlines the need to design processes with minimized risk of accidents, explosions, or hazardous releases, ensuring a safer working environment. Together, these principles provide a comprehensive strategy for reimagining analytical chemistry to meet the demands of sustainability, safety, and environmental responsibility. By embedding these principles into the development of analytical techniques, the discipline not only aligns with green chemistry's ethos but also actively contributes to reducing the ecological footprint of scientific research and industrial processes.

Green Analytical Techniques in Pharmaceutical Quality Testing

The advancement of Green Analytical Chemistry has led to the development of several innovative approaches that minimize environmental impact while ensuring reliable pharmaceutical quality testing. Among these, greener sample preparation and extraction techniques focus on reducing solvent and reagent use through miniaturization and the application of eco-friendly solvents. Greener chromatographic techniques emphasize replacing hazardous solvents with safer alternatives, adopting methods such as UPLC, SFC, and micellar chromatography to improve efficiency and sustainability. In parallel, chemometrics has emerged as a powerful tool for data analysis, enabling the optimization of experimental design, reduction of unnecessary trials, and improved interpretation of complex datasets. Finally, the integration of Quality by Design (QbD) principles with green practices ensures robust, reproducible, and environmentally conscious analytical methods. Collectively, these strategies provide a sustainable framework for modern pharmaceutical quality control, aligning scientific rigor with ecological responsibility.

Greener sample preparation and extraction techniques

The optimal sample preparation is the absence of any preparation [54]. This idea may be applicable given the heightened sensitivity of contemporary instruments, rendering the sample enrichment phase unnecessary in numerous instances, allowing for direct use of samples without pretreatment. The uncertainty of measurement is the paramount quantity that characterizes the quality of measurements. Uncertainty fundamentally influences decisions derived from the measurement outcome [55]. By omitting sample pretreatment and analyzing samples immediately, more accurate results will be achieved, as the uncertainty linked to the preceding procedure would be entirely eliminated. A common application of this approach is the quantification of residual solvents in pharmaceutical goods utilizing a gas chromatography (GC) system with headspace injection, or the analysis of pesticide residues in water samples by liquid chromatography–mass spectrometry (LC–MS). Solid-phase extraction (SPE). Solid-phase extraction (SPE) is regarded as a critical method for sample purification and preconcentration. It enhances productivity, prolongs column longevity and instrument availability, and selectively enriches the target solutes with a minimal volume of organic solvent.

Should solid-phase extraction (SPE) be implemented as a substitute for liquid–liquid extraction, numerous advantages would ensue, including cost reduction, increased throughput, and diminished solvent and waste generation.

Solid phase microextraction (SPME). SPME offers numerous advantages in sample preparation, including enhanced reliability, selectivity, and sensitivity, while also decreasing analytical costs and duration. This procedure is quite straightforward. It is presently utilized as an extraction and preconcentration phase preceding MS analysis. SPME integrates sampling with sample preparation, rendering it appropriate for on-site analysis and process monitoring. Table 4.1 enumerates several uses in pharmaceutical quality control.

Table 4- 1: Examples of SFME applications in analysis of pharmaceuticals

Analyte, matrix	Method	Technique
Volatiles in biological fluids	Application of head-space SPME for the analysis of volatile metabolites	GC–MS
Solvents in pharmaceutical products	Determination of residual solvents in pharmaceuticals with automated SPME	GC–FID
Components in drugs	Analysis of components in crude drugs by headspace SPME method	GC
Residual solvents in pharmaceutical samples	Headspace SPME method optimization for residual solvent analysis	GC
Verapamil	Verapamil drug metabolism studies by automated in-tube solid phase microextraction	LC–MS
Trends	New trends in sample preparation for clinical and pharmaceutical analysis	LC–MS

Sampling in the gas phase. This approach employs inert gasses for extraction, categorizing it as an environmentally friendly method. A variety of techniques exist for volatile substances, including static headspace (SHS), in-tube extraction (ITEX), dynamic headspace (DHS), purge and trap (P&T), and headspace sorptive extraction (HSSE). Semivolatile analysis may be conducted using extractions at elevated temperatures, thereafter trapping the solutes on a sorbent or cryotrap for concentration prior to injection.

Greener chromatographic techniques

Micellar Liquid Chromatography (MLC). Micelles were initially utilized in HPLC by Armstrong and Henry in 1980 [56]. This methodology was presented in multiple articles as a more

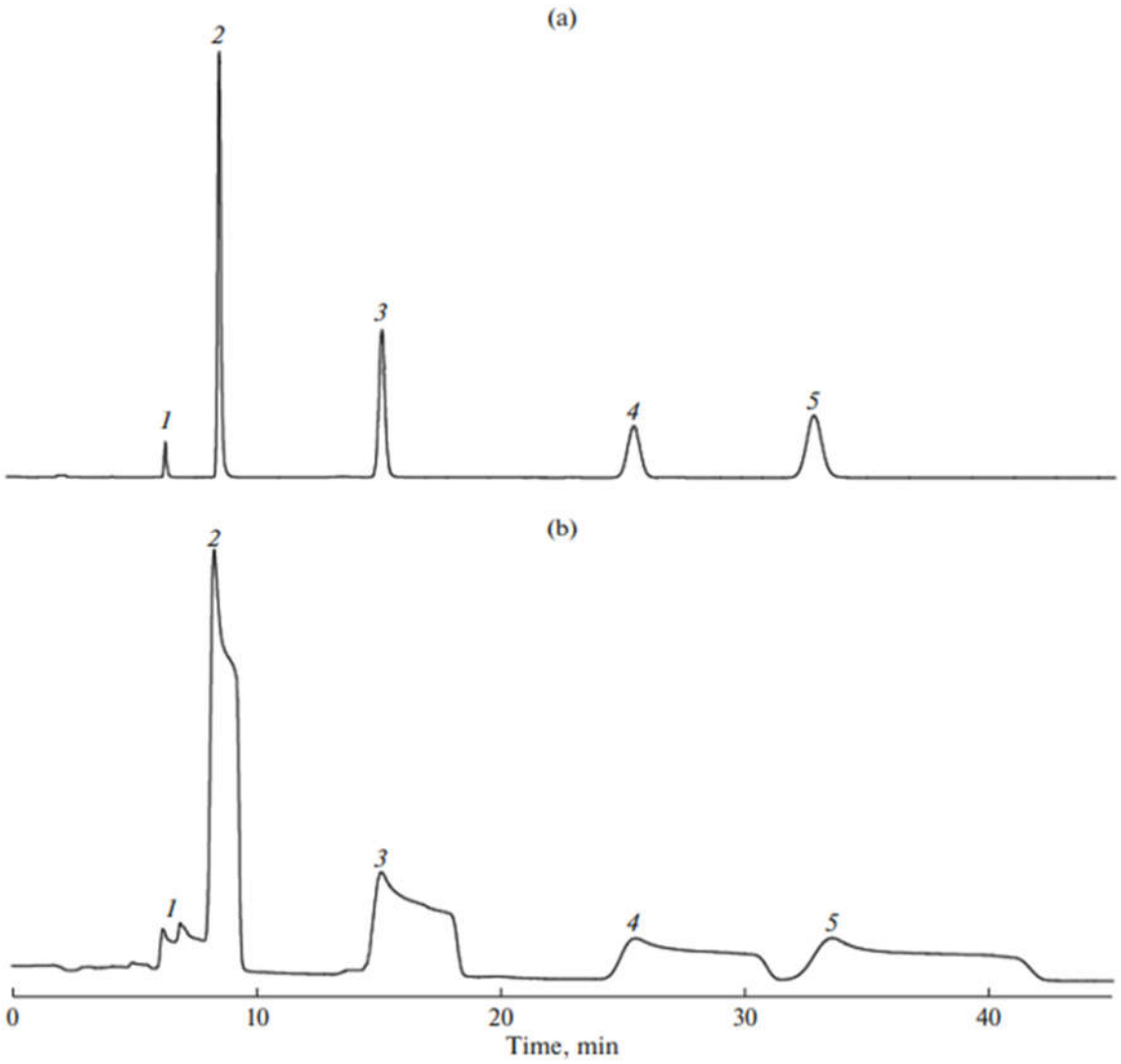

Figure 4- 1: Peaks deformation due to temperature mismatch (without preheating of mobile phase). (a)—with preheating of mobile phase at 60°C, (b)—without preheating of mobile phase; 1—uracil, 2—caffeine, 3—phenol, 4—acetophenone, 5—propylparaben.

environmentally sustainable chromatographic method in pharmaceutical testing [57][58]. The incorporation of micelles into the mobile phase creates a pseudo-stationary phase, allowing solutes to partition and so diminishing or obviating the necessity for organic modifiers. Solvents like ethanol and isopropanol, regarded as less harmful than methanol and acetonitrile, are typically employed in low concentrations in micellar chromatography techniques to enhance separation efficiency. These modifiers, together the increase in temperature, are incorporated to enhance the wetting of the stationary phase by the micellar aqueous mobile phase, facilitate mass transfer between the micelles and the stationary phase, and optimize mass transfer within the stationary phase. In MLC, three partition coefficients must be considered. The solute will distribute between the water and the stationary phase (KSW), between water and the micelles (KMW), and between micelles and the stationary phase (KSM). Guermouche et al. [59] computed the capacity factor as follows: $1/k\not\subset=\left[n\left(KMW-1\right)/\left(fKSW\right)\right]c_m+1/\left(fKSW\right)$ In this context, $k\not\subset$ denotes the capacity factor of the solute, f represents the phase volume ratio (stationary phase volume to mobile phase volume), n indicates the molar volume of the surfactant, and cm signifies the concentration of micelles in the mobile phase (total surfactant concentration minus critical micelle concentration).

Supercritical fluid high-performance liquid chromatography (SFC). SFC has been advancing for the fast separation of intricate mixtures, particularly in preparative applications, including the purification of chiral, botanical, and other medicinal chemicals. The method is deemed "green" as the primary constituent of the mobile phase is carbon dioxide, which returns to its gaseous form once the supercritical conditions are absent at the detector output. A small particle column is unsuitable for SFC as the pressure across the column diminishes its efficiency [61]. In contemporary supercritical fluid chromatography (SFC), polar modifiers are used due to the comparatively nonpolar nature of supercritical carbon dioxide. This results in the mobile phase attaining a sub-critical state, whereby pressure does not significantly alter the elution capacity, and the correlation between efficiency and particle size is reinstated.

Optimization of GC. Probably more than 90% of the present GC instruments run with helium as carrier gas, meanwhile the supply of helium has become a challenge, so many labs are now considering the use of hydrogen as the carrier gas of choice. The linear velocity of a carrier gas has an effect similar to the column temperature on the separation of compounds, as higher linear velocity accelerates the analysis but reduces the separation efficiency. The linear velocity is influenced by column dimensions, pressure drop and viscosity of the carrier gas. Generally the gas viscosity increases with temperature, but the viscosity of hydrogen is influenced less by temperature than the viscosity of helium and nitrogen. Therefore, it is easier to maintain

higher linear velocities with hydrogen, which results in shorter analysis times, particularly at high temperatures [62]. This advantage could be explained by van Deemter plot in Fig. 4.2. Another important approach is changing the capillary column dimensions. If column internal diameter is decreased along with length, the same resolution can be maintained, or, in some cases, actually increased due to increasing efficiency of the column. GC capillary column with reduced dimension is useful in reducing analysis time and the cost of the column itself. Another important aspect related to the GC columns is the phase ratio which expresses the ratio of the gas volume to the stationary phase volume in a column and depends on the column diameter and its film thickness as follows:

$$The\ phase\ ratio(\beta) = column\ radius(\mu m)/2 \times film\ thickness(\mu m)$$

The selection of columns with varying β values should be based on the application; specifically, columns with β values below 100 are appropriate for highly volatile and low molecular weight chemicals, whilst those with β values over 400 are good for high molecular weight compounds and trace analysis. The utilization of hydrogen as a carrier gas, in conjunction with narrower capillary columns, will lead to a reduction in analysis time.

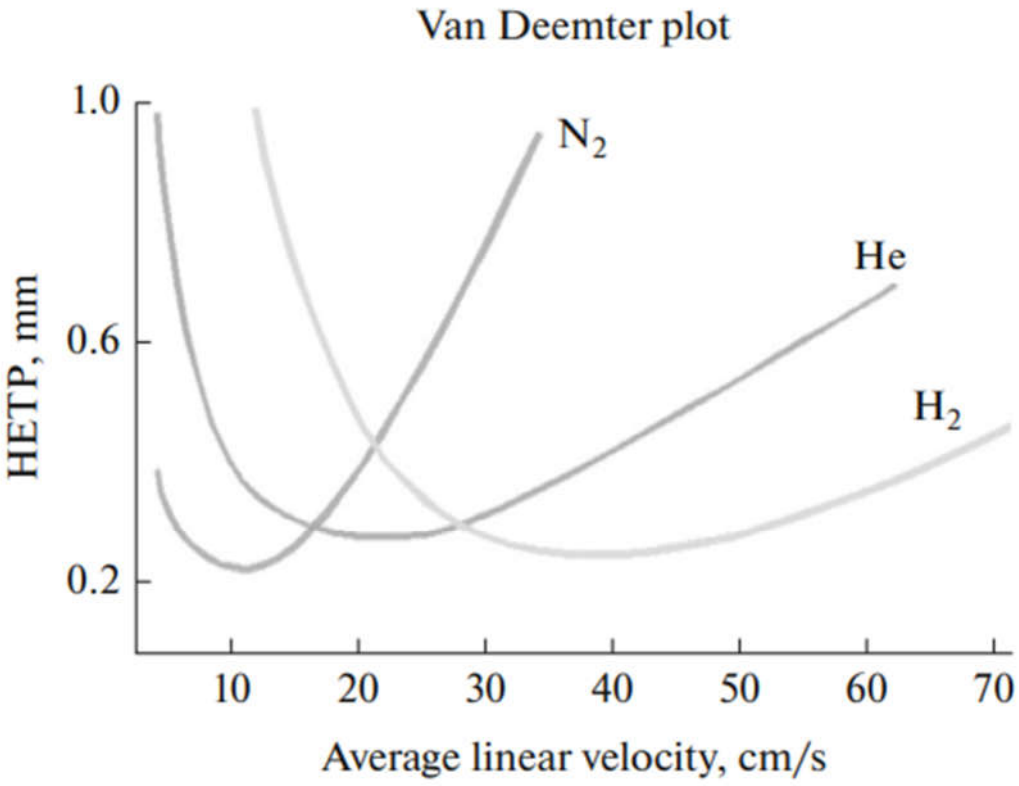

Figure 4- 2: The effect of average linear velocity on column efficiency using three different gases. Hydrogen offers the fastest optimal velocity.

Chemometrics

The greater the quantity of information acquired within a specified timeframe, the more environmentally sustainable the process becomes. Chemometrics, a hallmark of contemporary analytical chemistry [63], optimally enhances the information derived from samples. The initial aim of chemometrics was to enhance data processing; nevertheless, it currently serves as a superior tool to minimize reliance on external calibrations and specialized methods for assessing the qualities or constituents of a sample. Chemometrics is crucial for the advancement of non-invasive or distant sensing methodologies to enhance and extract data from direct measurements. Employing environmentally friendly analytical methods, such as near-infrared spectroscopy, remote sensing, or image analysis, enables direct sample analysis without pretreatment, resulting in a significant reduction in chemical usage, energy consumption, and analysis duration. Process analytical technology (PAT) refers to systems designed for the analysis and control of manufacturing processes, utilizing timely measurements of critical quality and performance attributes of raw and in-process materials and products to ensure high product quality upon completion of manufacturing. Process Analytical Technology (PAT) encompasses a scientifically grounded design process that determines essential metrics of product quality and the major process variables influencing them. Various spectroscopic approaches are employed for the implementation of PAT in the real-time monitoring of pharmaceutical

operations. Near-infrared spectroscopy (NIRS) has emerged as a highly regarded analytical tool within the pharmaceutical sector. It is a quick, non-invasive method that necessitates little to no sample preparation. The NIR area encompasses the wavelength range of 4000–12500 cm–1. In this range, absorption bands primarily correspond to overtones and combinations of basic vibrations [64]. NIRS is the predominant technology employed for PAT in the pharmaceutical sector. Numerous qualitative and quantitative applications of NIRS have been documented across production processes, encompassing the qualitative and quantitative assessment of active ingredients and excipients in both pure forms and medicinal products, as well as crystallinity and moisture content [65]. Ensuring blending homogeneity during the manufacturing of pharmaceutical medicinal products, particularly in low-strength formulations, can be regulated by Near-Infrared Spectroscopy (NIRS) [66]. Various chemometric approaches are employed to handle NIRS data, hence simplifying the spectrum information, which is essential for deriving valuable analytical insights [67].

Challenges & Future Prospects

Despite its numerous advantages, the pharmaceutical industry faces hurdles and constraints in the implementation of Green Analytical Chemistry (GAC). The challenges may stem from the sector's technological and operational attributes, in addition to financial and legal limitations. Comprehending these problems is crucial for the effective integration of sustainable practices within pharmaceutical operations. The initial financial barrier may deter industries from adopting sustainable practices, particularly if the economic return is ambiguous or postponed. Transitioning to more ecologically sustainable analytical technologies typically necessitates a substantial initial investment in new equipment, eco-friendly chemicals, and solvents, which may be costlier than conventional alternatives. Moreover, the use of innovative, eco-friendly techniques may necessitate protracted regulatory approval and validation procedures to confirm compliance with pharmaceutical product safety standards. Regulatory bodies like the FDA or EMA may impose stringent regulations on conventional testing methodologies, despite the fact that GAC principles promote sustainable practices. Moreover, transitioning to more environmentally friendly analytical methods (e.g., SFC in lieu of HPLC) necessitates capital investment that may be impractical for smaller pharmaceutical companies. The lack of regulatory permission may impede broader adoption, perhaps delaying or obstructing the transition to more sustainable practices and methodologies.

Numerous conventional analytical methods, such as spectroscopy and chromatography, currently lack entirely eco-friendly alternatives. They cannot concurrently guarantee environmental sustainability while attaining the sensitivity, precision, and robustness necessary for high-quality pharmaceutical analysis. For example, substituting methods such as gas chromatography (GC) or high-performance liquid chromatography (HPLC), which depend on conventional solvents, may pose challenges in certain

domains of drug quality control and stability assessment. The absence of eco-friendly alternatives to various methods obstructs the extensive implementation of GAC principles in pharmaceutical testing. Eco-friendlier green chemicals, reagents, and solvents may be costlier and more difficult to get than their traditional equivalents. In certain locations or markets, green alternatives may be challenging to find or nonexistent. Multinational pharmaceutical businesses may encounter obstacles due to the scarcity of environmentally friendly products in certain areas. Moreover, the higher cost of green products may dissuade smaller firms from transitioning. A significant issue in the pharmaceutical industry is the possibility that environmentally friendly procedures may not match traditional methods for sensitivity, selectivity, and accuracy.

The trade-off between performance and sustainability is a significant challenge in pharmaceutical analysis, where precision is critical (such as in quality control, stability testing, and drug development). Pharmaceutical businesses may be reluctant to adopt environmentally friendly practices due to concerns about meeting the stringent requirements of specificity and precision necessary for quality control and medication development. Widespread use of GAC necessitates a proficient staff capable of comprehending and implementing sustainable concepts in analytical methodologies. Currently, there is a scarcity of educational and training programs expressly dedicated to GAC, especially in the realm of pharmacological analysis. Staff personnel may be inadequately prepared to use GAC principles effectively due to insufficient specialized training, perhaps resulting in inappropriate or inefficient implementation of sustainable practices.
Green metrics such as GAPI, AGREE, AES, and Analytical Eco-Scale are intended to assess the environmental impact of analytical processes; nevertheless, they can be difficult to utilize and understand. Pharmaceutical businesses may lack the resources or proficiency to consistently employ these indicators. It presents difficulties in assessing the environmental impact of their activities, particularly when multiple variables are included (e.g., solvent selection, waste management, energy use). The evaluation of the long-term viability of certain systems is subjective and intricate, perhaps leading to confusion or misuse of these indicators. Businesses may have challenges in implementing these KPIs throughout their whole process portfolio.

Future Prospects

As the concepts of green chemistry evolve, green measurements will likewise become increasingly sophisticated. Novel criteria may arise to evaluate not only the environmental friendliness of analytical procedures but also their sustainability over the full drug development lifecycle. In the forthcoming years, green analytical technologies will increasingly be integrated into normal pharmaceutical practices. More environmentally friendly alternatives to traditional methods, like MAE, SFC, and green solvents, will be

increasingly utilized in pharmaceutical discovery, quality assurance, and stability testing. Consequently, an increasing number of regulatory authorities will embrace these indicators, facilitating the standardization of greener pharmaceutical definitions and ensuring their consistent use across the sector. By improving the efficacy, cost-effectiveness, and ecological sustainability of analytical processes, GAC has the capacity to fundamentally revolutionize the pharmaceutical sector.

The utilization of GAC in pharmaceutical analysis yields numerous advantages, including diminished waste, decreased solvent usage, energy conservation, and improved safety, all of which substantially advance the industry's sustainability objectives. It also corresponds with worldwide trends favoring greener and more sustainable methods across several industries. Progress in analytical tools will significantly influence GAC's future inside the pharmaceutical sector. Emerging technologies that utilize reduced energy, produce minimal waste, and incorporate environmentally benign compounds will soon be accessible. Miniaturizing instruments and creating portable analytical devices will enhance analytical efficiency and diminish environmental effect. In the future, GAC in the pharmaceutical sector will involve increased collaboration among academic institutions, pharmaceutical businesses, regulatory authorities, and organizations focused on green chemistry. Through the exchange of best practices and expertise, the pharmaceutical sector may collaborate to address issues associated with GAC implementation and expedite the shift towards more environmentally sustainable operations. As governmental and regulatory bodies recognize the significance of sustainability, it is probable that more supportive legislation will be established to promote the implementation of green analytical procedures. Regulatory agencies like the FDA and EMA may amend their recommendations to expressly incorporate green chemistry concepts, so facilitating more transparent avenues for the endorsement of environmentally sustainable practices.

Conclusion

The transition from conventional analytical methods to greener approaches is both a necessity and an opportunity for the pharmaceutical industry. This thesis has demonstrated how Green Analytical Chemistry provides sustainable solutions for pharmaceutical quality testing by focusing on eco-friendly sample preparation, solvent reduction in chromatographic techniques, advanced data analysis through chemometrics, and robust method development under Quality by Design frameworks. While challenges such as high initial costs, limited regulatory guidance, and training requirements remain, the benefits of adopting greener methods are substantial, including reduced waste, lower carbon footprint, improved safety, and long-term cost savings. Future progress will depend on greater

collaboration among academia, industry, and regulatory bodies, alongside advancements in green solvents, instrumentation, and analytical metrics. Ultimately, the integration of GAC into pharmaceutical laboratories represents a transformative step toward achieving reliable quality assurance that is not only scientifically rigorous but also environmentally responsible.

References

[1] U.S. Food and Drug Administration, *Guidance for Industry: Q2(R2) Validation of Analytical Procedures*, FDA, 2022.

[2] D. A. Skoog, D. M. West, F. J. Holler, and S. R. Crouch, *Fundamentals of Analytical Chemistry*, 9th ed. Belmont, CA: Brooks/Cole, 2014.

[3] M. Armenta, S. Garrigues, and M. de la Guardia, "Green Analytical Chemistry," *TrAC Trends in Analytical Chemistry*, vol. 116, pp. 248–259, 2019.

[4] J. Płotka-Wasylka, "A new tool for the evaluation of the analytical procedure: Green Analytical Procedure Index," *Talanta*, vol. 181, pp. 204–209, 2018.

[5] A. Gałuszka, Z. M. Migaszewski, and J. Namieśnik, "The 12 principles of green analytical chemistry and the SIGNIFICANCE mnemonic of green analytical practices," *TrAC Trends in Analytical Chemistry*, vol. 50, pp. 78–84, 2013.

[6] T. Kaur, "Green Analytical Chemistry in Pharmaceuticals: Eco-Friendly Approaches to Drug Testing," *International Journal of Pharmaceutical Sciences and Research*, vol. 12, no. 8, pp. 4212–4219, 2021.

[7] De Gruyter Review, "Green chemistry and its implementation in pharmaceutical analysis," *Reviews in Analytical Chemistry*, vol. 42, no. 1, pp. 1–12, 2023.

[8] I. Eldin, M. Abdel-Rehim, and R. B. Cassells, "Green analytical chemistry: Opportunities for pharmaceutical quality control," *Analytical Methods*, vol. 8, no. 36, pp. 6570–6580, 2016.

[9] S. Saroj, R. Verma, and V. Singh, "Green Analytical Chemistry and Quality by Design: A Combined Approach for Eco-Friendly Method Development," *Current Pharmaceutical Analysis*, vol. 14, no. 5, pp. 475–482, 2018.

[10] Wojnowski, W., Tobiszewski, M., Pena-Pereira, F., & Psillakis, E. (2022). Green analytical chemistry metrics: A review. Talanta, 238, 123046.

[11] Pena-Pereira, F., Wojnowski, W., & Tobiszewski, M. (2020). AGREE—Analytical GREEnness metric approach and software. Analytical Chemistry, 92(14), 10076-10082.

[12] Kumar, A., Singh, R., & Sharma, P. (2023). Green chemistry and its implementation in pharmaceutical analysis. Reviews in Analytical Chemistry, 42(1), 20230069.

[13] Hassan, M. A., Abdelkawy, M., & Abdelaleem, E. A. (2024). Green analytical chemistry-based spectrophotometric techniques for ternary component analysis of pain relievers. Future Journal of Pharmaceutical Sciences, 10, 64.

[14] Ahmed, S., Rizk, M., & El-Enany, N. (2024). Recent application of green analytical chemistry: eco-friendly approaches for pharmaceutical analysis. Future Journal of Pharmaceutical Sciences, 10, 78.