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Green and Sustainable Analytical Techniques in Pharmaceutical Sciences: Innovations in Eco-Friendly Drug Analysis

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Abstract

The growing emphasis on environmental protection and sustainable industrial practices has significantly transformed pharmaceutical research and quality control, leading to the development of Green Analytical Chemistry (GAC). Traditional analytical methods employed in pharmaceutical laboratories often rely heavily on toxic organic solvents, energy-intensive instrumentation, and extensive sample preparation procedures, resulting in substantial chemical waste and environmental burden. Green analytical techniques aim to address these concerns by minimizing hazardous reagent consumption, reducing waste generation, lowering energy requirements, and improving operator safety while maintaining analytical accuracy and reliability. Recent innovations, including ultra-high-performance liquid chromatography, supercritical fluid chromatography, capillary electrophoresis, microextraction methods, microfluidic devices, and ambient spectroscopic techniques, have emerged as promising alternatives to conventional analytical platforms. The integration of artificial intelligence, automation, and digital analytical workflows further enhances sustainability by optimizing experimental conditions and reducing unnecessary resource utilization. In addition, several green assessment tools, such as the Analytical Eco-Scale, Green Analytical Procedure Index (GAPI), AGREE metric, and ComplexGAPI, have been developed to quantitatively evaluate the environmental performance of analytical procedures. These advancements support the pharmaceutical industry's transition toward environmentally responsible manufacturing and quality assurance practices. Despite challenges related to regulatory acceptance, method validation, and implementation costs, green analytical chemistry continues to evolve rapidly, driven by global sustainability initiatives and stricter environmental regulations. This review discusses the fundamental principles, recent technological developments, pharmaceutical applications, current limitations, and future prospects of green and sustainable analytical techniques, highlighting their growing importance in eco-friendly drug analysis and sustainable healthcare systems.

Keywords: Green analytical chemistry; Sustainable pharmaceutical analysis; Eco-friendly drug analysis; Green chromatography; Pharmaceutical quality control.

1. Introduction

Pharmaceutical analysis occupies a central role throughout the lifecycle of a medicinal product, encompassing drug discovery, formulation development, manufacturing, quality control, stability testing, bioanalysis, and post-marketing surveillance. The reliability and precision of analytical methodologies directly

influence the safety, efficacy, and quality of pharmaceutical products delivered to patients. However, conventional analytical laboratories often generate considerable environmental burdens due to the extensive use of toxic solvents, hazardous chemicals, disposable consumables, and energy-intensive instrumentation [1].

High-performance liquid chromatography (HPLC), gas chromatography (GC), and classical extraction techniques remain indispensable tools in pharmaceutical analysis, yet these methods typically consume large quantities of organic solvents such as acetonitrile, methanol, dichloromethane, and hexane. These chemicals not only contribute to laboratory waste but also pose occupational health hazards and increase disposal costs [2]. The pharmaceutical sector, therefore, faces increasing pressure to adopt analytical methodologies that align with the principles of sustainable development while maintaining stringent quality standards.

The concept of Green Chemistry was formally introduced by Paul Anastas and John Warner in 1998 through the establishment of twelve guiding principles aimed at reducing or eliminating hazardous substances in chemical processes [3]. Building upon this foundation, Green Analytical Chemistry (GAC) emerged as a specialized discipline dedicated to minimizing the environmental footprint of analytical operations. Unlike traditional analytical approaches that focus solely on accuracy and sensitivity, GAC seeks to balance analytical performance with environmental responsibility.

Green analytical chemistry encompasses the entire analytical workflow, including sample collection, transportation, preparation, separation, detection, data analysis, and waste disposal. The primary objectives are to reduce solvent consumption, minimize sample sizes, replace hazardous reagents with environmentally benign alternatives, simplify sample preparation, and lower energy requirements [4]. Modern technological innovations have enabled the development of highly efficient analytical methods that achieve these goals without compromising analytical robustness.

Sample preparation often represents the most environmentally demanding stage of pharmaceutical analysis, accounting for a substantial proportion of solvent consumption and waste generation. Conventional liquid-liquid extraction procedures may require several hundred milliliters of toxic solvents per sample. In contrast, emerging green extraction technologies such as solid-phase microextraction (SPME), stir-bar sorptive extraction (SBSE), and dispersive liquid-liquid microextraction (DLLME) drastically reduce solvent usage while improving extraction efficiency [5].

Similarly, chromatographic science has undergone substantial transformation through the introduction of ultra-high-performance liquid chromatography (UHPLC) and supercritical fluid chromatography (SFC). UHPLC systems employ columns packed with sub-2 μm particles, enabling faster analyses with reduced mobile phase consumption. Supercritical fluid chromatography utilizes carbon dioxide as the principal mobile phase, significantly lowering dependence on hazardous organic solvents [6].

Spectroscopic methods have also gained prominence as inherently green analytical tools. Near-infrared (NIR), Fourier transform infrared (FTIR), Raman, and UV-visible spectroscopy often require little or no sample preparation, enabling rapid, non-destructive pharmaceutical analysis with minimal waste generation. The increasing availability of portable spectroscopic instruments further supports real-time process monitoring and in-line quality control applications [7].

Miniaturization represents another major advancement in sustainable pharmaceutical analysis. Microfluidic devices and lab-on-a-chip systems integrate multiple analytical functions into compact platforms that operate using microliter or nanoliter sample volumes. These technologies substantially reduce reagent consumption, shorten analysis times, and facilitate automation while maintaining exceptional analytical sensitivity [8].

Artificial intelligence (AI) and machine learning have recently emerged as powerful tools for enhancing the sustainability of analytical laboratories. AI-driven algorithms can optimize chromatographic conditions, predict analyte behavior, reduce experimental iterations, and facilitate predictive maintenance of analytical instruments. Such digital innovations decrease resource consumption while improving laboratory efficiency and reproducibility [9].

An equally important aspect of green analytical chemistry is the objective evaluation of method sustainability. Various assessment metrics have been developed to compare analytical procedures based on their environmental impacts. The Analytical Eco-Scale assigns penalty points according to reagent hazards, energy consumption, and waste generation, whereas the Green Analytical Procedure Index (GAPI) and AGREE metrics provide comprehensive visual and numerical evaluations of analytical greenness [10].

The pharmaceutical industry has increasingly embraced sustainable analytical practices due to several driving factors. Regulatory agencies worldwide are encouraging environmentally responsible manufacturing and quality assurance systems. Corporate sustainability initiatives, economic considerations related to solvent procurement and waste disposal, and growing public awareness of environmental stewardship have further accelerated the adoption of green technologies [11].

Despite these advancements, several challenges remain. The initial capital investment required for modern green instrumentation may be substantial, and many laboratories continue to rely on established

conventional methods validated over decades of use. Regulatory harmonization regarding green analytical validation is still evolving, and standardized global guidelines remain limited [12].

Nevertheless, the trajectory of pharmaceutical analysis clearly points toward greater integration of environmentally sustainable methodologies. Future analytical laboratories are expected to combine miniaturized instrumentation, renewable energy systems, artificial intelligence, automation, and advanced green solvents into highly efficient, low-impact analytical ecosystems. Such developments will contribute not only to environmental conservation but also to improved laboratory safety, operational efficiency, and long-term economic sustainability.

This review comprehensively examines the principles, recent technological innovations, applications, assessment metrics, challenges, and future prospects of green and sustainable analytical techniques in pharmaceutical sciences, emphasizing their pivotal role in shaping the future of eco-friendly drug analysis.

2. Principles of Green Analytical Chemistry

Green Analytical Chemistry (GAC) represents the application of green chemistry principles to analytical science with the objective of minimizing the environmental impact associated with chemical analysis while preserving analytical performance [1]. Unlike conventional analytical methodologies, which primarily focus on sensitivity, selectivity, and precision, green analytical approaches integrate environmental sustainability into every stage of the analytical process [2].

The foundation of GAC is based upon reducing the ecological footprint of analytical operations by minimizing sample size, simplifying sample preparation, lowering reagent consumption, replacing toxic chemicals with environmentally benign alternatives, and reducing waste generation [1,3]. The analytical workflow, from sample collection to final data processing, is carefully optimized to maximize efficiency while reducing environmental burden.

One of the fundamental principles of green analytical chemistry is waste prevention rather than waste treatment. Conventional pharmaceutical laboratories may generate several liters of hazardous organic waste daily due to chromatographic analyses and extraction procedures [4]. Green analytical methods seek to prevent this waste at its source by redesigning analytical protocols to consume fewer materials.

Another important principle is the minimization of sample preparation. Sample preparation often accounts for the largest proportion of solvent consumption in pharmaceutical analysis [5]. Direct analytical methods or procedures requiring minimal pretreatment are therefore strongly encouraged. Spectroscopic methods such as near-infrared spectroscopy and Raman spectroscopy allow direct analysis of pharmaceutical formulations without extensive extraction or derivatization steps, thereby significantly reducing chemical usage [6].

The selection of safer solvents and reagents also forms a cornerstone of GAC. Organic solvents such as chloroform, benzene, dichloromethane, and acetonitrile are associated with toxicity, volatility, and disposal challenges [7]. Green analytical chemistry promotes the use of water, ethanol, supercritical carbon dioxide, ionic liquids, and deep eutectic solvents as environmentally preferable alternatives [8].

Energy efficiency has become increasingly relevant in sustainable analytical laboratories. Modern green laboratories employ energy-efficient instrumentation, automated shutdown systems, miniaturized devices, and optimized workflows to reduce power requirements without compromising productivity [9].

Miniaturization is another defining characteristic of green analytical chemistry. Microfluidic platforms, lab-on-a-chip devices, and capillary-based separation techniques drastically reduce reagent and sample volumes while simultaneously improving analytical throughput [10].

Automation and digitalization further contribute to analytical sustainability. Artificial intelligence-assisted analytical optimization reduces experimental iterations and unnecessary reagent consumption while improving method robustness and reproducibility [11].

Real-time and in-process monitoring represent additional principles of green analytical chemistry. Process Analytical Technology (PAT) enables continuous monitoring of pharmaceutical manufacturing using non-destructive spectroscopic tools, reducing the need for repeated offline sampling and laboratory testing [12].

The overall objective of GAC is to establish a balanced relationship between analytical quality and environmental responsibility. Rather than viewing sustainability as a limitation, green analytical chemistry demonstrates that environmentally conscious methodologies can often provide superior analytical performance, lower operating costs, and improved laboratory safety [1,4].

3. Evolution of Sustainable Analytical Methods

The historical development of pharmaceutical analytical methods has been largely driven by the need for greater sensitivity, selectivity, accuracy, and throughput. Classical analytical procedures, including titrimetry, gravimetry, and colorimetric assays, were initially considered adequate for pharmaceutical quality control.

However, these methods often required substantial quantities of reagents and generated considerable chemical waste, making them less compatible with modern sustainability goals [13,14].

The introduction of chromatographic techniques during the second half of the twentieth century revolutionized pharmaceutical analysis. High-performance liquid chromatography (HPLC) and gas chromatography (GC) provided remarkable improvements in analytical precision and sensitivity. Nevertheless, their widespread application was accompanied by intensive consumption of hazardous organic solvents such as acetonitrile, methanol, tetrahydrofuran, and dichloromethane, resulting in increased operational costs and environmental concerns [15,16].

Growing awareness regarding environmental protection during the 1990s encouraged researchers to reconsider traditional laboratory practices. The publication of the twelve principles of green chemistry by Anastas and Warner established a scientific framework for designing environmentally benign chemical processes and subsequently inspired the development of Green Analytical Chemistry (GAC) [1]. Analytical scientists began focusing not only on analytical performance but also on reducing solvent usage, minimizing waste generation, and improving laboratory safety.

The first generation of sustainable analytical methods concentrated primarily on reducing solvent consumption in chromatographic systems. The development of narrow-bore and microbore HPLC columns significantly lowered mobile phase requirements while maintaining separation efficiency [17]. Later, advances in stationary phase technology enabled the introduction of ultra-high-performance liquid chromatography (UHPLC), which employs sub-2 μm particle columns capable of achieving faster analyses with substantially lower solvent volumes [18].

Parallel developments occurred in sample preparation technologies. Conventional liquid-liquid extraction procedures, often requiring large volumes of toxic solvents, gradually gave way to more sustainable alternatives such as solid-phase extraction (SPE). Continuous improvements eventually led to the emergence of solvent-free or solvent-minimized techniques, including solid-phase microextraction (SPME), stir-bar sorptive extraction (SBSE), and dispersive liquid-liquid microextraction (DLLME), all of which substantially decreased chemical waste generation [19,20].

Supercritical fluid chromatography (SFC) represented another milestone in sustainable pharmaceutical analysis. By utilizing supercritical carbon dioxide as the primary mobile phase, SFC dramatically reduced the need for hazardous organic solvents while offering excellent chromatographic performance, particularly for chiral compounds and nonpolar analytes [21].

The advancement of spectroscopic technologies further accelerated the transition toward green pharmaceutical analysis. Near-infrared (NIR), Raman, and Fourier transform infrared (FTIR) spectroscopy permit rapid, non-destructive analysis with minimal or no sample preparation. These methods are increasingly incorporated into pharmaceutical manufacturing under Process Analytical Technology (PAT) frameworks for real-time quality monitoring [22].

Recent developments have introduced miniaturized analytical systems, including microfluidic devices and lab-on-a-chip platforms. These technologies integrate multiple analytical operations into compact devices that consume only microliter or nanoliter quantities of reagents while providing rapid and highly sensitive analyses [23].

The latest stage in the evolution of sustainable analytical methods involves the integration of artificial intelligence, machine learning, robotics, and laboratory automation. AI-driven analytical optimization enables prediction of chromatographic behavior, automated method development, and reduction of experimental redundancy, thereby conserving both time and resources [24]. These digital innovations are expected to play an increasingly important role in establishing fully sustainable pharmaceutical laboratories.

4. Green Sample Preparation Techniques

Sample preparation constitutes one of the most critical stages of pharmaceutical analysis and is often responsible for the majority of solvent consumption and laboratory waste generation. Conventional extraction methods typically require multiple handling steps and large volumes of organic solvents, contributing substantially to environmental pollution and occupational exposure risks [25]. Consequently, the development of environmentally friendly sample preparation techniques has become a major focus of green analytical chemistry.

Green sample preparation strategies seek to simplify analytical workflows while minimizing reagent consumption, reducing waste production, shortening extraction times, and improving analytical sensitivity. These approaches frequently combine extraction, concentration, and sample introduction into a single operation, thereby enhancing overall analytical efficiency [26].

4.1 Solid-Phase Microextraction (SPME)

Solid-phase microextraction is one of the most widely adopted green extraction techniques in pharmaceutical and biomedical analysis. The method utilizes a fused silica fiber coated with a sorbent material

that selectively adsorbs target analytes directly from liquid or gaseous samples. Following extraction, the fiber is transferred directly to the analytical instrument for thermal or solvent desorption [27].

Unlike conventional liquid-liquid extraction, SPME eliminates the need for large volumes of organic solvents. The integration of sampling, extraction, concentration, and injection into a single step significantly reduces sample handling errors and shortens analytical time [28]. Applications of SPME in pharmaceutical sciences include residual solvent determination, impurity profiling, drug stability assessment, and therapeutic drug monitoring.

The environmentally friendly characteristics of SPME have led to its widespread adoption in quality control laboratories where rapid, reproducible, and sustainable analytical procedures are increasingly required [29].

4.2 Stir-Bar Sorptive Extraction (SBSE)

Stir-bar sorptive extraction was developed as an extension of microextraction technology to provide higher extraction capacities and improved analytical sensitivity. In SBSE, a magnetic stir bar coated with a polymeric sorbent is immersed directly into the sample solution, allowing analytes to partition into the sorbent phase during stirring [30].

Because SBSE requires little or no organic solvent, it significantly reduces chemical waste generation while offering excellent extraction recoveries. The technique is particularly useful for trace-level pharmaceutical contaminants, biological fluid analysis, and environmental monitoring of active pharmaceutical ingredients [31].

SBSE also offers operational simplicity, high reproducibility, and compatibility with various chromatographic and spectroscopic detection systems, making it an attractive green alternative to traditional extraction methods.

4.3 Dispersive Liquid-Liquid Microextraction (DLLME)

Dispersive liquid-liquid microextraction represents a miniaturized version of classical liquid-liquid extraction. The technique involves the rapid injection of a small quantity of extraction solvent and disperser solvent into an aqueous sample, producing a cloudy solution composed of fine extraction solvent droplets [32].

The extremely large contact surface area between the extraction solvent and sample matrix enables rapid equilibrium and highly efficient analyte extraction. Typically, only microliter volumes of extraction solvent are required, reducing solvent consumption by several orders of magnitude compared with conventional methods [33].

DLLME has found widespread application in pharmaceutical bioanalysis, environmental monitoring, forensic toxicology, and determination of trace pharmaceutical residues in biological matrices. The technique combines high enrichment factors with excellent reproducibility and environmental compatibility.

4.4 QuEChERS Method

The QuEChERS method, representing "Quick, Easy, Cheap, Effective, Rugged, and Safe," was initially developed for pesticide residue analysis but has since become a valuable tool in pharmaceutical and biomedical research [34].

The procedure combines salting-out extraction with dispersive solid-phase cleanup, allowing efficient analyte isolation while consuming relatively small quantities of extraction solvents. Compared with traditional extraction methods, QuEChERS significantly reduces analysis time, labor requirements, and waste generation [35].

In pharmaceutical sciences, QuEChERS has been successfully applied for the determination of drug residues in biological fluids, food products, herbal medicines, and environmental samples. Its operational simplicity and low environmental impact make it highly suitable for high-throughput analytical laboratories.

4.5 Solid-Phase Extraction (SPE)

Solid-phase extraction remains one of the most versatile and widely employed sample preparation techniques in pharmaceutical analysis. Although SPE predates many modern green technologies, advances in sorbent materials and cartridge design have substantially enhanced its environmental sustainability [36].

SPE generally requires much smaller solvent volumes than classical liquid-liquid extraction while providing superior selectivity and analyte recovery. The introduction of reusable sorbents, molecularly imprinted polymers, nanostructured adsorbents, and magnetic nanoparticles has further reduced waste generation and improved extraction efficiency [37].

Modern SPE methodologies support applications ranging from impurity profiling and pharmacokinetic studies to therapeutic drug monitoring and environmental surveillance of pharmaceutical pollutants. Their

compatibility with automated platforms also contributes to improved laboratory sustainability by reducing manual intervention and reagent wastage.

Collectively, green sample preparation technologies demonstrate that environmentally responsible analytical methods can simultaneously enhance analytical performance, reduce operational costs, and minimize ecological impact. Their continued advancement is expected to play a pivotal role in the future development of sustainable pharmaceutical analysis.

5. Eco-Friendly Chromatographic Techniques

Chromatographic methods constitute the backbone of pharmaceutical analysis owing to their exceptional sensitivity, selectivity, and versatility. However, conventional chromatographic systems, particularly traditional high-performance liquid chromatography (HPLC), consume large quantities of organic solvents and generate significant volumes of hazardous waste. A typical pharmaceutical quality control laboratory may use several hundred liters of acetonitrile and methanol annually, contributing substantially to environmental pollution and operational expenses [38,39]. Green analytical chemistry seeks to overcome these challenges by developing chromatographic methods that reduce solvent consumption, shorten analysis time, and improve energy efficiency without compromising analytical performance.

5.1 Ultra-High-Performance Liquid Chromatography (UHPLC)

Ultra-high-performance liquid chromatography represents one of the most successful innovations in sustainable pharmaceutical analysis. UHPLC employs columns packed with particles smaller than 2 µm, allowing faster and more efficient separations under elevated operating pressures [40]. Compared with conventional HPLC, UHPLC can reduce solvent consumption by approximately 60–80% while simultaneously decreasing analysis time and improving chromatographic resolution [41].

The reduced mobile phase requirements of UHPLC directly translate into lower hazardous waste generation and reduced costs associated with solvent procurement and disposal. Furthermore, shorter run times decrease instrument energy consumption and increase sample throughput, making UHPLC an economically and environmentally attractive alternative for pharmaceutical quality control laboratories [42].

UHPLC has found widespread applications in assay determination, impurity profiling, dissolution testing, bioanalytical studies, stability-indicating methods, and pharmacokinetic investigations. Its compatibility with advanced detection systems, including tandem mass spectrometry, further enhances its utility in modern pharmaceutical research [43].

5.2 Supercritical Fluid Chromatography (SFC)

Supercritical fluid chromatography has emerged as one of the greenest chromatographic technologies available for pharmaceutical analysis. The technique utilizes supercritical carbon dioxide as the principal mobile phase, supplemented by relatively small amounts of organic modifiers such as methanol or ethanol [44].

Carbon dioxide possesses several characteristics that make it an environmentally favorable solvent. It is inexpensive, non-flammable, readily available, and can be recycled within analytical systems. Since carbon dioxide rapidly evaporates following separation, the volume of hazardous liquid waste generated is substantially lower than that associated with conventional liquid chromatography [45].

SFC offers rapid analysis, high separation efficiency, and excellent performance for the resolution of chiral compounds, lipophilic drugs, natural products, and pharmaceutical impurities. The pharmaceutical industry increasingly employs SFC for enantiomeric purity testing, impurity profiling, and preparative purification due to its environmental and economic advantages [46].

In addition to reducing solvent consumption, SFC generally operates at lower temperatures than gas chromatography, thereby preserving thermally labile pharmaceutical compounds and expanding its analytical applicability.

5.3 Micellar Liquid Chromatography (MLC)

Micellar liquid chromatography is an alternative chromatographic approach in which aqueous surfactant solutions replace a substantial portion of conventional organic mobile phases. Surfactants such as sodium dodecyl sulfate form micelles that facilitate analyte partitioning and separation while significantly reducing the need for toxic solvents [47].

The replacement of large quantities of organic solvents with predominantly aqueous mobile phases decreases laboratory hazards and minimizes waste disposal requirements. MLC has been successfully applied for the simultaneous estimation of multiple pharmaceutical compounds, impurity analysis, and biological sample analysis [48].

Another advantage of MLC lies in its ability to directly analyze complex biological matrices with minimal sample preparation, further contributing to the sustainability of the overall analytical workflow.

5.4 Capillary Liquid Chromatography and Nano-LC

The progressive miniaturization of chromatographic systems has given rise to capillary liquid chromatography and nano-liquid chromatography techniques. These methods employ extremely narrow columns operating at very low flow rates, often in the nanoliter per minute range [49].

The drastic reduction in mobile phase consumption results in significantly lower solvent waste generation and improved compatibility with sensitive detectors such as mass spectrometers. Nano-LC has become particularly valuable in pharmaceutical proteomics, metabolomics, and peptide drug analysis due to its high sensitivity and minimal sample requirements [50].

Miniaturized chromatographic systems also contribute to reduced energy consumption and lower operational costs, reinforcing their role within sustainable pharmaceutical laboratories.

5.5 Green Mobile Phases and Alternative Solvents

An important aspect of sustainable chromatography involves replacing hazardous solvents with environmentally benign alternatives. Acetonitrile shortages experienced globally during the past decade further highlighted the importance of developing greener mobile phases [51].

Water remains the ideal green solvent due to its non-toxic and non-flammable nature. Advances in stationary phase technology have enabled greater utilization of highly aqueous mobile phases without compromising chromatographic performance. Ethanol has also emerged as an attractive substitute for methanol and acetonitrile because of its lower toxicity and renewable production sources [52].

Superheated water chromatography utilizes pressurized water at elevated temperatures as the sole mobile phase, eliminating the need for organic solvents altogether. Similarly, ionic liquids and deep eutectic solvents have gained attention as novel green solvents capable of improving chromatographic selectivity while reducing environmental impact [53].

The adoption of alternative solvents contributes not only to environmental sustainability but also to improved laboratory safety and reduced solvent disposal costs.

6. Green Spectroscopic and Electroanalytical Techniques

Spectroscopic methods inherently possess several characteristics that align well with the principles of green analytical chemistry. Unlike chromatographic techniques, many spectroscopic analyses require little or no sample preparation and consume minimal quantities of reagents or solvents. Their non-destructive nature further enhances their environmental compatibility by preserving samples for additional testing if required [54].

6.1 UV-Visible Spectroscopy

UV-visible spectroscopy remains one of the simplest and most widely utilized analytical techniques in pharmaceutical sciences. Direct spectrophotometric methods frequently eliminate the need for extensive extraction procedures, significantly reducing solvent consumption and waste generation [55].

Modern diode-array spectrophotometers provide rapid multi-wavelength analysis with excellent precision and sensitivity. The technique is extensively employed for assay determination, dissolution testing, content uniformity evaluation, and stability studies of pharmaceutical formulations.

Derivative spectroscopy and chemometric-assisted UV analysis further improve selectivity, allowing simultaneous estimation of multiple components without chromatographic separation [56]. Such approaches simplify analytical workflows and enhance laboratory sustainability.

6.2 Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy has become an indispensable green analytical tool due to its ability to provide rapid molecular fingerprinting without requiring chemical reagents. Samples are typically analyzed directly in solid or liquid form, eliminating the need for extraction or derivatization [57].

The pharmaceutical industry widely employs FTIR spectroscopy for raw material identification, excipient compatibility studies, counterfeit drug detection, and process monitoring. The introduction of attenuated total reflectance (ATR) accessories has further simplified sample handling by allowing direct surface analysis with virtually no sample preparation [58].

Portable FTIR instruments also facilitate on-site quality control and field analysis, reducing transportation requirements and associated environmental impacts.

6.3 Near-Infrared (NIR) Spectroscopy

Near-infrared spectroscopy has gained substantial importance within pharmaceutical manufacturing due to its non-destructive and reagent-free nature. NIR instruments can analyze powders, granules, tablets, and capsules directly through packaging materials, minimizing sample handling and contamination risks [59].

NIR spectroscopy forms an integral component of Process Analytical Technology (PAT) initiatives, enabling real-time monitoring of blending, granulation, drying, and tablet compression processes. Continuous in-line monitoring reduces the need for repetitive laboratory testing and decreases overall material consumption [60].

The combination of NIR spectroscopy with chemometric algorithms further enhances analytical accuracy while supporting automated process control.

6.4 Raman Spectroscopy

Raman spectroscopy complements infrared techniques by providing highly specific molecular information with minimal sample preparation. The method is particularly valuable for pharmaceutical polymorph identification, counterfeit medicine detection, and raw material verification [61].

Portable Raman spectrometers enable rapid field-based analysis without requiring reagents or consumables. Their application in pharmaceutical supply chain monitoring has expanded significantly, contributing to safer and more sustainable quality assurance practices [62].

The non-invasive nature of Raman spectroscopy allows direct analysis through transparent packaging materials, eliminating unnecessary sample manipulation.

Table 1. Comparison of Conventional and Green Analytical Techniques Used in Pharmaceutical Sciences

Analytical Process	**Conventional Approach**	**Green Alternative**	**Major Environmental Benefit**
Sample Preparation	Liquid-Liquid Extraction (LLE)	Solid-Phase Microextraction (SPME)	Eliminates or minimizes organic solvents
Sample Cleanup	Conventional SPE with large solvent volumes	QuEChERS / Miniaturized SPE	Lower solvent consumption and waste
Chromatography	Conventional HPLC	UHPLC	60–80% reduction in solvent use
Separation Technique	Normal-phase chromatography	Supercritical Fluid Chromatography (SFC)	Carbon dioxide replaces hazardous solvents
Detection	Wet chemical assays	FTIR / Raman / NIR Spectroscopy	Non-destructive and reagent-free
Bioanalysis	Classical extraction methods	DLLME / SBSE	Microliter solvent consumption
Process Monitoring	Offline laboratory analysis	Process Analytical Technology (PAT)	Reduced sampling and material wastage
Method Development	Trial-and-error optimization	AI-assisted optimization	Fewer experimental runs
Quality Control	Batch-wise destructive testing	In-line spectroscopic monitoring	Reduced sample destruction
Environmental Assessment	No standardized evaluation	Eco-Scale, GAPI, AGREE	Quantitative greenness assessment

Table 1. Comparison of conventional pharmaceutical analytical methods with sustainable green alternatives and their principal environmental advantages.

Table 2. Green Analytical Assessment Metrics Used for Evaluating Pharmaceutical Analytical Methods

Green Metric Tool	Primary Purpose	Key Evaluation Parameters	Output Format	Major Advantages
Analytical Eco-	Quantitative assessment	Reagent toxicity, solvent	Numerical	Simple, easy to

Scale	of method greenness	consumption, energy usage, waste generation	score (0–100)	calculate, widely accepted
GAPI (Green Analytical Procedure Index)	Holistic evaluation of the entire analytical procedure	Sample collection, preparation, reagents, instrumentation, waste	Color-coded pentagram diagram	Visual representation of environmental impact
AGREE (Analytical GREEnness Metric)	Comprehensive evaluation based on the 12 principles of Green Analytical Chemistry	Waste prevention, miniaturization, automation, reagent safety, energy efficiency	Circular pictogram with score (0–1)	Integrates all GAC principles into a single metric
ComplexGAPI	Expanded lifecycle assessment of analytical methods	Reagent production, transportation, sample preparation, analytical process,		

Conclusion

Green and sustainable analytical techniques have become an essential component of modern pharmaceutical sciences, offering environmentally responsible alternatives to conventional analytical methods. Traditional pharmaceutical analyses often involve the extensive use of hazardous organic solvents, energy-intensive instrumentation, and complex sample preparation procedures, leading to significant chemical waste and increased operational costs. The adoption of green analytical chemistry principles addresses these concerns by promoting solvent reduction, waste minimization, energy efficiency, and safer laboratory practices without compromising analytical quality.

Technological advancements such as ultra-high-performance liquid chromatography, supercritical fluid chromatography, capillary electrophoresis, green sample preparation methods, and non-destructive spectroscopic techniques have significantly improved the sustainability of pharmaceutical analysis. Furthermore, the integration of artificial intelligence, automation, and microfluidic platforms has enhanced analytical efficiency while reducing resource consumption and human intervention.

The implementation of green assessment metrics has also enabled objective evaluation of the environmental performance of analytical methods, encouraging continuous improvement and innovation. Although challenges related to regulatory acceptance, standardization, and initial investment remain, the long-term environmental, economic, and operational benefits strongly support the widespread adoption of sustainable analytical practices. Ultimately, green analytical chemistry represents a progressive and indispensable approach for achieving safer, cost-effective, and environmentally conscious pharmaceutical analysis.

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