REVIEW ARTICLE

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

Exploring the Critical Role of Green Chemistry in Enhancing Sustainability and Efficiency in Pharmaceutical Analytical Testing: Using Chromatographic, Spectrophotometric and Microextraction Techniques

Aziza E Mostafa [a], Ahmed F Mohammed [a, *], Ghada M Hadad [a], Randa A Abdel Salam [a], Mohamed A Abdelshakour [b]

[a] Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Suez Canal University, Ismailia, Egypt; [b] Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Sohag University, Sohag, Egypt.

Received: 26. 11. 2024

Revised: 13. 12. 2024

Accepted: 15. 12. 2024

*Corresponding Author:

Tel: +201092714982

E-mail address:

dr.ahmed.fathi1558@gmail.com
pgs.14210119@pharm.suez.edu.eg.

Abstract

Integrating the green chemistry principles into chromatographic, spectrophotometric and microextraction techniques concepts not only enhances the environmental sustainability of analytical practices but also aligns with the broader goals of reducing chemical hazards and promoting safer laboratory environments with accurate reliable analysis techniques (Andraos et al., 2022). By focusing on sustainable greener solvents and waste reduction leading to significantly an advancing green chemistry initiative (Tucker et al., 2006). By highlighting the urgent need for greener alternatives, this review focuses on the most common analytical techniques used in pharmaceutical analysis such as chromatographic, spectrophotometric and microextraction techniques (Napolitano et al., 2021; Zhang et al., 2024). It also highlights their ability in utilizing cleaner and less harmful solvents, minimizing or eliminating reagents and other substances, and reducing energy consumption. It also examines a range of organic solvents, including ethanol, and innovative options like water-based or buffer solutions as well as surfactants (Prat et al., 2016). It also assesses the potential of more environmentally friendly solvents such as pure water, ionic liquids (ILs) and supercritical carbon dioxide ($scCO_2$) (Kunz et al., 2016; Nasirpour, et al., 2020). This review also illustrates the integration of green chemistry principles in pharmaceutical analysis, discussing advances in analytical techniques, solvent reduction strategies, challenges, and future perspectives.

Keywords: Chromatography; Spectroscopy; Micro-extraction; Green Chemistry

1. Introduction

The expanding field of green analytical chemistry, with a particular emphasis on sustainable solvents for liquid chromatography which is a widely used technique in pharmaceutical, food, and environmental analysis, it typically relies on large amounts of toxic and non-renewable solvents, which present significant environmental and health hazards (Tucker et al., 2006). The concept of green chemistry emphasizes the design of chemical products and processes to minimize or eliminate hazardous substances throughout their life cycle. Green analytical chemistry (GAC) focuses on improving analytical laboratory practices which could be achieved by reducing environmental impact (Locatelli et al., 2023). In 2022, green sample preparation (GSP) was introduced, adapting GC and GAC principles specifically for sample preparation (Melissa et al., 2024). Chromatographic and spectrophotometric systems have proven invaluable role in analytical chemistry for separating, identifying, and quantifying targeted components in complicated mixtures. They also contribute to many sectors, including pharmaceuticals, food safety, and environmental monitoring. As the use of such techniques continues to grow, particularly with advancements in automation enabling continuous operation, the generation of toxic waste has become an increasingly critical issue to address sustainably (Melissa et al., 2024). The main issue of using such techniques as laboratories in large pharmaceutical companies collectively produce thousands of liters of hazardous waste daily, contributing to an estimated millions of liters of chemical waste globally each year which demands an attention for its environmental implications.

Green chemistry has become a cornerstone in contemporary research, with sustainable development serving as a primary objective for scientists worldwide. Eco- friendly initiatives have increasingly permeated green analytical chemistry (GAC), emphasizing the development of greener methodologies (Venkatesan et al., 2024).

Regarding pharmaceutical analytical techniques, significant progress has been made, with a focus on evaluating greenness using various tools such as the Green Analytical Procedure Index (GAPI), Analytical Eco-Scale, Analytical Method Greenness Score (AMGS), and Analytical Greenness Metric Approach (AGREE), National Environmental Methods Index (NEMI) (Semysim et al.,2024).

2. Pharmaceutical field and green chemistry principles

The pharmaceutical industry in especially in developing countries is facing major challenges in terms of cost and efficiency (Ahmed et al., 2024). Strict environmental regulations have increased production expenses, including the costs associated with proper industrial waste handling. Recent environmental protection laws are pushing industry leaders to identify and adopt innovative, cost-effective, and eco-friendly synthetic methods.

Green chemistry focuses on designing chemical products and processes that reduce or eliminate the use and generation of hazardous substances. That made the pharmaceutical industry gives a great concern about adopting to green chemistry principles to address environmental and economic challenges.

The twelve Principles of Green Chemistry were introduced by Paul Anastas and John Warner "Green Chemistry: Theory and Practice," book (Anastas et al., 2000). This foundational work outlines guidelines for creating safer and more sustainable chemical processes with principles aimed at reducing the environmental impact of chemical processes and products (Ahmed et al., 2024). These principles emphasize reducing waste, minimizing environmental impact, and enhancing efficiency as shown in **Fig. 1** which could be achieved by:

2.1. Prevent Waste: Avoiding waste creation rather than managing it after it is produced.

2.2. Maximize Atom Economy: Ensuring that most materials used in a analysis end up in the final product, minimizing by-products.

2.3. Use Safer Methods: Designing processes to reduce generating harmful and hazardous substances.

2.4. Develop Safer Chemicals: Formulating chemicals to work effectively with minimizing toxicity to human beings and ecosystems.

2.5. Minimize Solvents: Reducing or replacing the use of solvents and auxiliary substances, seeking for safer alternatives when necessary.

2.6. Increase Energy Efficiency: Designing of processes that require less energy and could operate at ambient conditions.

2.7. Use Renewable Resources: Using raw materials from renewable sources like plants, over finite resources like petroleum.

2.8. Reduce Extra Steps: Minimizing unnecessary modifications or intermediate steps which require extra chemicals and produce hazardous waste.
2.9. Utilize Catalysts: Using catalytic agents instead of stoichiometric to help in making the process more efficient with lower waste production.
2.10. Enhance Biodegradability: Designing products that break down into harmless safe materials after the use.
2.11. Monitor Processes in Real Time: Incorporating real-time monitoring as analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
2.12. Promote Safety: Focusing on chemicals and processes that help in minimizing the accident risks, such as explosions or spillage of toxic materials.

3. Chromatographic Analytical Techniques

Chromatography is a widely used analytical technique in pharmaceutical industry analysis, chemical research and environmental monitoring. However, traditional chromatography techniques often involve significant usage of toxic chemicals, high consumption of energy, and waste generation leading to environmental and health risks (Safaei et al., 2014). Integrating the green chemistry principles into liquid chromatography concepts not only enhances the environmental sustainability of analytical practices but also aligns with the broader goals of reducing chemical hazards and promoting safer laboratory environments with accurate reliable analysis techniques (Kalisz et al., 2024). By focusing on sustainable greener solvents and waste reduction, the liquid chromatography can significantly contribute to advancing green chemistry initiatives (Ahmed et al., 2024).

Figure 1. Twelve principles of the green chemistry used in enhancing the greenness of the pharmaceutical analytical techniques.

3.1. Green Chemistry Challenges in Traditional Chromatography

3.1.1. Solvent Usage: Liquid chromatography methods, such as high- performance liquid chromatography (HPLC), may require large volumes of organic non-green solvents such as acetonitrile and methanol as mobile phases (Shaaban et al., 2016). These solvents are categorized as hazardous expensive chemicals which impact on the environmental pollution (Kleiman et al., 2009).

3.1.2. Energy Consumption: Chromatographic techniques especially gas chromatography (GC) relies on high temperatures during the analysis which leads to significant energy consumption.

3.1.3. Waste Generation: It generates considerable waste, especially liquid chromatography. Disposal of the waste further impacts the environment and ecosystem.

3.1.4. Equipment and Resources: Chromatography is considered as large-scale systems which are often resource-intensive in the terms of chemical reagents and operational requirements.

3.2. Green Approaches in Chromatography

The objective of green chemistry is to make chromatographic techniques more sustainable through innovations and modification in techniques, solvents and instrumentation (Płotka et al., 2013).

3.2.1. Reducing Solvent Use

Using recent techniques such as Ultra-High-Performance Liquid Chromatography (UHPLC) reduces solvent consumption by operating with smaller column diameters and higher-pressure systems, aiding in faster separations and smaller volumes of mobile phase. Also using techniques such as Solid-Phase Chromatography Solid-phase extraction (SPE) and solid-phase microextraction (SPME) eliminate the need for large amounts of solvents used in traditional liquid-liquid extraction.

3.2.2. Green Solvents:

Replacing organic solvents with water-based mobile phases or buffer solutions which are green environmentally friendly solvents (Yabré et al., 2018). Ethanol is considering the greenest solvent for replacing such hazardous ones as methanol and acetonitrile (Deineka et al., 2023). They are designed to minimize environmental impact, reduce toxicity and enhance sustainability

Also, Ionic liquids, which are recyclable non-volatile liquid, and supercritical carbon dioxide ($scCO_2$) in supercritical fluid chromatography (SFC) are promising substitutes to traditional organic solvents (Nasirpour et al., 2020).

3.2.3. Miniaturization and Automation

Micro-scale systems, such as capillary chromatography, use minimal solvent amounts with lower waste generation. Automation contributes to reducing errors and ensuring the efficiency of the solvent used (Handlovic et al., 2024).

3.2.4. Energy Efficiency

Green instrumentation designs focus on reducing energy requirements and optimizing operating conditions. Low-temperature alternatives in Gas Chromatography, such as using advanced columns with improved thermal properties, reduce energy consumption.

3.2.5. Key Techniques for Green Chromatography

There are key techniques that plays an important role in the greenness of the methods. For example, Supercritical Fluid Chromatography (SFC) uses supercritical CO_2 as the main mobile phase, which is non-toxic, inexpensive and recyclable (Zuo et al., 2023). This method is widely adopted for chiral separations and pharmaceutical analysis. Also, Hydrophilic Interaction Liquid Chromatography (HILIC) utilizes water-rich mobile phases leading to reduce the need for organic solvents. Another technique such as Solid-Phase Extraction (SPE) SPE reduces solvent usage compared to liquid-liquid extractions and is highly compatible with automated systems.

3.2.6. Challenges and Future Directions

However, the high cost of advanced systems and the scarcity of green solvents, green chromatography offers numerous benefits in the green chemistry. Future research focuses on developing affordable, universally applicable green methods and techniques to overcome such challenges (Ražić et al., 2023). Tailoring the chromatography to green chemistry principles is a vital step toward sustainable analytical practices, aligning with the global push for environmental responsibility in the chemical and pharmaceutical industries

4. Spectroscopy and Green Chemistry

Spectroscopy is a critical and vital analytical tool used in many fields, including pharmaceutical analysis, environmental monitoring, and materials science. It depends on the theory of the interaction of light with matter to study the properties of substances. Traditional spectroscopic techniques often rely on hazardous solvents, chemicals and energy-intensive processes. Integrating green chemistry principles into spectroscopic systems depends on minimizing environmental impact which could be achieved by reducing harmful solvents, improving energy efficiency and minimizing waste generation with taking in consideration maintaining accurate and reliable analytical methods.

4.1. Green Chemistry Principles Applied to Spectroscopy

4.1.1. Hazardous Solvents Reduction

In traditional spectroscopic methods, organic solvents such as chloroform, hexane, or acetone are commonly used. Green chemistry emphasizes replacing these harmful solvents with safer alternatives, such as water, ethanol, or bio-derived solvents.

4.1.2. Energy Efficiency

Spectroscopic techniques require significant energy inputs especially in methods such as UV-Vis or Infrared (IR) spectroscopy that use powerful light sources. Green chemistry promotes the development of low-energy, and efficient systems limited hazardous impact on the environment.

4.1.3. Waste Reduction

Traditional spectroscopy can generate waste from regent’s usage and sample preparation. So, green chemistry seeks to reduce or eliminate these wastes through advanced methods such as miniaturization of instruments and utilizing more sustainable reagents and solvents.

4.1.4. The Simplicity of Sample Preparation

Green chemistry encourages minimizing the use of hazardous organic reagents and simplifying sample preparation. Techniques like solid-phase microextraction (SPME) or using non-toxic solvents in sample preparation are examples of greener alternatives in spectroscopic system.

4.2. Green Approaches in Spectroscopy

4.2.1. UV-Visible Spectroscopy (UV-Vis)

In such techniques we depend on solvent reduction by using safer solvents such as water or bio-based solvents instead of hazardous organic solvents (methanol or acetone) is a significant advancement in UV-Vis spectroscopy. The development of portable smaller spectrophotometers also reduces the need for large quantities of solvents and minimizes waste.

4.2.2. Infrared Spectroscopy (IR)

IR spectroscopy is inherently green as it is a non-destructive technique, meaning it does not require significant amounts of chemicals or reagents. Also, introduction of eco-friendly materials for constructing IR spectrometer instruments such as reusable windows or using biodegradable solvents helps in reducing environmental impacts (Armenta et al., 2008).

4.2.3. Fluorescence Spectroscopy

Green chemistry encourages the use of safer, less toxic fluorophores and reducing the usage of toxic chemical reagents in fluorescence-based analytical methods. New advanced fluorescence systems have been developed with lower energy consumption with often incorporating LED light sources instead of high-intensity lamps.

4.2.4. Raman Spectroscopy

Raman spectroscopy is particularly green because it does not require solvents for analysis, thus minimizing waste (Hu et al., 2023). So, it is considered as non-invasive and solvent free: It’s used for solid, liquid, or gaseous samples making it suitable for eco-friendly analysis in many applications.

4.3. Emerging Green Techniques in Spectroscopy

4.3.1. Green Analytical Chemistry (GAC) Approaches

Green Analytical Chemistry is becoming an essential part of spectroscopy. It involves developing methods that use renewable or green safe solvents and optimize the consumption of energy.

4.3.2. Use of Green Analytical Protocols

Green chemistry protocols encourage the usage of non-toxic solvents such as
ionic liquids, or even supercritical CO_2, to conduct spectroscopic measurements. These alternatives are safer for both the environment and humans (Nasirpour et al., 2020).

4.4. Challenges and Opportunities

While there are significant advancements in making spectroscopic techniques more environmentally friendly, challenges remain such as high initial costs as new green technologies and instruments often require high costs. However green chemistry is essential nowadays, adoption of green methods may be slow due to regulatory requirements for traditional methods, especially in industries like pharmaceuticals.
There is a need for more awareness and education on the benefits of green chemistry in spectroscopy for wider adoption in both academic research field and industry.

5. Microextraction Methods

Microextraction methods are considered as sample preparation techniques used in analytical chemistry to aid in extracting and concentrating analytes from complex matrices like biological matrices using minimal amounts of solvents and reagents.
These methods play a critical role in green chemistry by promoting sustainability through reduced solvent use, minimized waste generation and energy efficiency. By integrating green chemistry principles, microextraction techniques can be made even more environmentally friendly while maintaining high analytical performance.

5.1. Principles of Green Chemistry Applied to Microextraction

Microextraction techniques, such as solid-phase microextraction (SPME) and dispersive liquid-liquid microextraction (DLLME), significantly reduce the use of organic solvents and generate minimal waste (Kokosa et al., 2022). These methods have been particularly impactful in trace-level pharmaceutical analysis. In the context of microextraction, the key green chemistry principles that can be applied include:

5.1.1. Reduction in Solvent Use

Traditional extraction methods often require large volumes of solvents, which are typically toxic and difficult to dispose. Green chemistry advocates for the use of minimal solvents and safer alternatives (e.g., water, biodegradable solvents, or supercritical fluids) in microextraction processes.

5.1.2. Use of Non-toxic Materials

Green microextraction methods favor the use of materials such as ionic liquids, deep eutectic solvents (DES) or environmentally friendly solvents instead of organic solvents like chloroform, methanol and hexane (Nasirpour et al., 2020; Zhang et al., 2024).

5.1.3. Minimization of Energy Consumption

Green chemistry promotes techniques that reduce energy consumption. So, microextraction methods such as solid-phase microextraction (SPME) and liquid-phase microextraction (LPME), which require little to no heating or other energy-intensive procedures compared to conventional extraction methods, are the best tools in green microextraction methods (Tintrop et al., 2023).

5.1.4. Waste Minimization

Green microextraction methods aim to minimize waste generation, which is achieved by reducing the volume of solvents used and using reusable materials for extraction (El-Deen et al., 2023).

5.2. Common Microextraction Methods in Green Chemistry

5.2.1. Solid-Phase Microextraction (SPME)

SPME is a widely used green extraction technique that aid in the extraction of volatile and semi-volatile compounds without the need for large amounts of solvent (Alahmad et al., 2023). The method depends on the use of a solid sorbent, a fiber coated with an adsorbent, to absorb analytes from a sample.
The green aspect in such techniques is SPME typically eliminates the need for solvents or significantly reduces their usage. The extraction

fiber can be reused multiple times which contributes to reducing waste. SPME can be performed at room temperature and requires little or no heating with lower energy consumption

5.2.2. Liquid-Phase Microextraction (LPME)

LPME involves the use of a small volume of solvent for the extraction of analytes from a liquid sample (Kokosa et al., 2023). A variety of LPME techniques exist such as single-drop microextraction (SDME) and hollow fiber liquid-phase microextraction (HF-LPME). One of its green aspects is the minimal solvent use as it uses a very small amount of solvent which reduces the volume of waste generated. It is considered as energy efficient tool as it can be conducted at ambient temperature, reducing the need for energy-intensive heating steps.

5.2.3. Dispersive Liquid-Liquid Microextraction (DLLME)

DLLME is a microextraction technique that involves the rapid dispersion of a water immiscible organic solvent into the aqueous sample using a dispersing agent. This led to creation of a cloudy solution where the analytes partition between two phases (aqueous phase and the organic phase).
DLLME uses only microliter amounts of organic solvents minimizing environmental impact (Kamal et al., 2023). The process produces very little waste. DLLME achieves high extraction efficiency with minimal solvent, making it an environmentally friendly method for complex samples.

5.2.4. Micro-Solid-Phase Extraction (μ-SPE)

μ-SPE is an advancement in solid-phase extraction (SPE) that uses micro-scale sorbent materials for the extraction of analytes from liquid samples. This technique is particularly useful for small-volume samples (Alahmad et al., 2023).
μ-SPE typically requires less solvent than traditional SPE. The sorbent material can often be reused multiple times, contributing to reduced waste. The high surface area of micro-scale sorbents results in efficient extractions, which reduces the need for extensive sample preparation and cleanup.

5.2.5. Supercritical Fluid Microextraction (SFME)

SFME uses supercritical fluids, such as CO_2, as solvents for the extraction of analytes. Supercritical fluids have properties that make them ideal for extraction, as they have high diffusivity and low viscosity.
Supercritical CO_2 is non-toxic which making it a safer alternative to conventional solvents. CO_2 can be reused in many cycles, minimizing waste (Zhang et al., 2024).
SFME can be conducted at moderate temperatures and pressures, reducing energy consumption.

5.3. Benefits of Microextraction in Green Chemistry

Microextraction techniques use much smaller volumes of solvents compared to traditional methods, leading to a significant reduction in the environmental impact of solvent waste. By using less solvent and reusable materials, these methods produce minimal waste, reducing disposal costs and environmental impact (Yahaya et al., 2024).
Many microextraction methods can be performed without heating, thus requiring less energy compared to traditional extraction techniques. They are often less expensive than traditional methods because they use fewer chemicals and are less energy intensive.

5.4. Challenges and Opportunities

While microextraction methods offer many environmental benefits, challenges also exist. Some microextraction techniques require optimization to maximize efficiency and recovery rates for different sample types. Certain methods like SPME may not be suitable for all sample matrices or analytes that limits their application (Ražić et al., 2023).

6. Future Perspectives of Green Chemistry in Pharmaceutical Testing

Analytical chemistry plays a central role in the pharmaceutical industry, particularly in ensuring the quality and safety of drugs. The future of green analytical chemistry in pharmaceuticals will focus on minimizing the environmental impact of testing processes.
The development of alternative, non-toxic reagents for chromatographic and spectroscopic analysis will reduce environmental hazards. Using miniaturized analytical techniques using microfluidics technologies will lead to efficient and sustainable analytical methods with less reagent and energy.
Miniaturized chromatographic techniques (such as micro-liquid chromatography) use smaller sample

volumes and reduce solvent usage, making the analysis of pharmaceutical products more sustainable. Traditional techniques rely heavily on organic solvents, many of which are toxic, expensive and difficult to dispose of safely. In the future, green solvents such as supercritical CO_2, ionic liquids, and water-based systems are expected to replace conventional solvents humans (Nasirpour et al., 2020). Solvent-free processes or the use of minimal solvent quantities will become more widespread as part of efforts to reduce the environmental footprint.

Supercritical Fluids can be used in processes like supercritical fluid extraction (SFE) or supercritical fluid chromatography (SFC), which reduce the need for organic solvents and provide a greener alternative for separating complex mixtures of drug compounds (Zuo et al., 2023).

Green chemistry promotes the principle of minimizing waste and recycling materials. The future of green pharmaceutical testing will likely focus on achieving the lowest amount of waste during the analysis process.

6. Conclusion

The future of green chemistry in the pharmaceutical industry holds promising potential for sustainable and environmentally friendly drug development and manufacturing (Ganesh et al., 2021). By embracing green chemistry principles such as reducing waste, optimizing energy use, using safer materials, and adopting eco-friendly technologies the pharmaceutical sector can not only improve its sustainability but also contribute to a greener future for public health and the environment. These changes are essential for meeting the growing demand for green products while maintaining the efficacy and safety of pharmaceutical drugs.

7. References

Ahmed, M., Abdullah, Eiman, E., Al-Ahmary, K. M., Aftab, F., Sohail, A., Ali, I., 2024. Advances in green liquid chromatography for pharmaceutical analysis: A comprehensive review on analytical greenness to sustainable chemistry approaches. Microchemical Journal, *205*, 111400.

Alahmad, W., Kaya, S. I., Cetinkaya, A., Varanusupakul, P., & Ozkan, S. A., 2023. Green chemistry methods for food analysis: Overview of sample preparation and determination. Advances in Sample Preparation, *5*, 100053.

Anastas, P. T., & Warner, J. C., 2000. *Green Chemistry: Theory and Practice*: Oxford University Press.

Andraos, J., & Matlack, A.S., 2022. Introduction to Green Chemistry (3rd ed.). CRC Press.

Ashley, M. A., Aukland, M. H., Bryan, M. C., Cismesia, M. A., Dutschei, T., Engl, O. D., Zeng, M., 2024. Green Chemistry Articles of Interest to the Pharmaceutical Industry. Organic Process Research & Development, 28(9), 3450-3459.

Deineka, V.I., Oleinits, E.Y., Blinova, I.P. *et al.*, 2023. Replacement of acetonitrile with ethanol in the determination of anthocyanins by reversed-phase high- performance liquid chromatography. Journal of Analytical Chemistry *78*(1), 63-67.

Ganesh, K. N., Zhang, D., Miller, S. J., Rossen, K., Chirik, P. J., Kozlowski, M. C., Voutchkova-Kostal, A. M., 2021. Green Chemistry: A Framework for a Sustainable Future. Organometallics, 40(12), 1801-1805.

Handlovic, T.T., Armstrong.,2024. Strategies and considerations to green analytical separations: a review. Environmental Chemistry Letters, 1-23.

Hu, Y., Huang, S. Y., & Lu, X., 2023. A green analytical method for fish species authentication based on Raman spectroscopy. Green Analytical Chemistry, 4, 100052.

Kamal El-Deen, A., Elmansi, H., Belal, F., & Magdy, G., 2023. Recent advances in dispersion strategies for dispersive liquid–liquid microextraction from green chemistry perspectives. Microchemical Journal, *191*, 108807.

Kalisz, O., Tobiszewski, M., Nowaczyk, A., & Bocian, S., 2024. Exploring the potential of green chemistry in reversed-phase liquid chromatography: A review of sustainable solvents. *TrAC Trends in Analytical Chemistry*, *181*, 118007.

Kleiman, R., Nickle, R., & Schwartz, M., 2009. Medical toxicology and public health—Update on research and activities at the centers for disease control and prevention, and the agency for toxic substances and disease registry. Journal of Medical Toxicology, 5(3), 158-164.

Kokosa, J. M., & Przyjazny, A., 2022. Green microextraction methodologies for sample preparations. Green Analytical Chemistry, 3, 100023.

Kokosa, J. M.., 2023. Principles for developing greener liquid-phase microextraction methods. TrAC Trends in Analytical Chemistry, 167, 117256.

Kunz, W., & Häckl, K., 2016. The hype with ionic liquids as solvents. Chemical Physics Letters, 661, 6-12.

Locatelli, M., Kabir, A., Perrucci, M., Ulusoy, S., Ulusoy, H. I., & Ali, I., 2023. Green profile tools: Current status and future perspectives. Advances in Sample Preparation, 6, 100068.

Napolitano-Tabares, P. I., Negrín-Santamaría, I., Gutiérrez-Serpa, A., & Pino, V., 2021. Recent efforts to increase greenness in chromatography. Current Opinion in Green and Sustainable Chemistry, *32*, 100536.

Nasirpour, N., Mohammadpourfard, M., & Zeinali Heris, S., 2020. Ionic liquids: Promising compounds for sustainable chemical processes and applications. Chemical Engineering Research and Design, 160, 264-300

Prat, D., Wells, A., Hayler, J., Sneddon, H., McElroy, C. R., Abou-Shehada, S., & Dunn, P. J. J. G. C., 2016. CHEM21 selection guide of classical- and less classical-solvents. Green Chemistry Journal, *18*(1), 288-296.

Płotka, J., Tobiszewski, M., Sulej, A. M., Kupska, M., Górecki, T., & Namieśnik, J. , 2013. Green chromatography. Journal of Chromatography A, 1307, 1-20.

Ražić, S., Arsenijević, J., Mračević, S. Đ., Mušović, J., & Trtić-Petrović, T. J. A., 2023. Greener chemistry in analytical sciences: from green solvents to applications in complex matrices. Current challenges and future perspectives: a critical review. Analst, *148*(14), 3130-3152.

Safaei, Z., Bocian, S., & Buszewski, B. J. R. a., 2014. Green chromatography-carbon footprint of columns packed with core–shell materials. RSC Advances,*4*(96), 53915-53920.

Semysim, F. A., Hussain, B. K., Hussien, M. A., Azooz, E. A., & Snigur,.,2024. Assessing the greenness and environmental friendliness of analytical methods: modern a pproaches and recent computational programs. Critical Reviews in Analytical Chemistry, 1- 14.

Shaaban, H. J. A., & chemistry, b., 2016. New insights into liquid chromatography for more eco-friendly analysis of pharmaceuticals. Analytical and Bioanalytical Chemistry, 408, 6929-6944.

Sharma, A., Pal, K., Saini, N., Kumar, S., Bansal, D., & Mona, S. J. N., 2023.

Remediation of contaminants from wastewater using algal nanoparticles via green chemistry approach: an organized review. Nanotechnology *34*(35), 352001.

Tintrop, L. K., Salemi, A., Jochmann, M. A., Engewald, W. R., & Schmidt, T. C., 2023. Improving greenness and sustainability of standard analytical methods by microextraction techniques: A critical review. Analytica Chimica Acta, 1271, 341468.

Tucker, J. L., 2006. Green Chemistry, a Pharmaceutical Perspective. Organic Process Research & Development, *10*(2), 315-319.

Venkatesan, K., Sundarababu, J., & Anandan, S. S., 2024. The recent developments of green and sustainable chemistry in multidimensional way: current trends and challenges. Green Chemistry Letters and Reviews, *17*(1), 2312848.

Yabré M, Ferey L, Somé IT, Gaudin K., 2018. Greening reversed-phase liquid chromatography methods using alternative solvents for pharmaceutical analysis. Molecules, *23*(5), 1065.

Yahaya, N., Mohamed, A. H., Miskam, M., Abdul Keyon, A. S., Loh, S. H., Mohamad Zain, N. N., & Sajid, M., 2024. Green analytical chemistry metrics for evaluation of microextraction methods: Fascinating or essential tools in real-world applications? TrAC Trends in Analytical Chemistry, *172*, 117587.

Zhang, Y., Chen, M., Li, L., Lv, Y., & Ma, Q., 2024. Recent advances in microextraction techniques using sustainable green solvents for mass spectrometry analysis. *TrAC* Trends in Analytical Chemistry, *170*, 117412.

Zuo, J., Geng, S., Kong, Y., Ma, P., Fan, Z., Zhang, Y., & Dong, A., 2023. Current progress in natural deep eutectic solvents for the extraction of active components from plants. Critical Reviews in Analytical Chemistry, *53*(1), 177-198.