WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 15, 1890-1906. Review Article ISSN 2277–7105

GREEN ANALYTICAL CHEMISTRY APPROACHES IN PHARMACEUTICAL ANALYSIS

Gumma Sai Tejaswi[1], Gajula Lohitha[1], Jonnalagadda Suneela[1], Arudala Likhitha[1], Koganti Aasritha[1], T. Sreenu[2], P. Srinivasa Babu[3], P. Siva Krishna*[1]

[1,2]Department of Pharmaceutical Analysis, Vignan Pharmacy College, Vadlamudi, Guntur, 522213, Andhra Pradesh, India.

[3]Department of Pharmaceutics, Vignan Pharmacy College, Vadlamudi, Guntur, 522213, Andhra Pradesh, India.

Article Received on 05 July 2026,
Article Revised on 25 July 2026,
Article Published on 01 August 2026,

https://doi.org/10.5281/zenodo.21772722

***Corresponding Author**

P. Siva Krishna

Department of Pharmaceutical Analysis, Vignan Pharmacy College, Vadlamudi, Guntur, 522213, Andhra Pradesh, India.

How to cite this Article: Gumma Sai Tejaswi[1], Gajula Lohitha[1], Jonnalagadda Suneela[1], Arudala Likhitha[1], Koganti Aasritha[1], T. Sreenu[2], P. Srinivasa Babu[3], P. Siva Krishna*[1] (2026). Green Analytical Chemistry Approaches In Pharmaceutical Analysis. World Journal of Pharmaceutical Research, 15(15), 1890–1906.

ABSTRACT

Green Analytical Chemistry (GAC) is increasingly seen as an indispensable methodology in the analysis of pharmaceuticals and the environment, being the first choice of methods that are safe and economically viable to the environment without affecting accuracy or compliance with regulations. Here, we are offering a detailed discussion on the GAC principles and their significance in the pharmaceutical quality control. It points out the negative aspects of the classic analytical methods such as the large use of solvents, the dangerous chemicals involved, and the long processing times; thus, it is their turn to seek greener means. Among the main green techniques, the authors mention the preparation of samples in the micro-scale and without any solvent, the employment of green solvents like supercritical carbon dioxide, deep eutectic solvents, and the solvents derived from plants, plus the progress in the area of Ultra High-Performance Liquid Chromatography (UHPLC), Supercritical Fluid Chromatography (SFC), Fourier Transform Infrared Spectroscopy (FTIR), Near Infrared (NIR), and Raman spectroscopy. The contribution of microfluidics, automation, and the new generation portable analytical devices in the reduction of waste and the improvement of the efficiency is also included in the discussion. Moreover, the paper describes the eco-friendliness assessment tools which are most commonly used Analytical Eco-Scale, NEMI,

GAPI, and AGREE—to check the environmental impact of the analytical processes. The practical examples show the successful GAC application in the pharmaceutical method development and validation.

KEYWORDS: Green analytical chemistry, environmentally friendly, green solvents, green extraction techniques.

INTRODUCTION

Green chemistry (GC) has received global attention in recent decades owing to its role in promoting sustainable practices in laboratories and industries. Green analytical chemistry (GAC) has emerged as a new approach to mitigate the adverse effects of analytical activities on the environment, human safety, and human health. To effectively implement GAC, it is crucial to adopt key measures. These measures include the use of less toxic solventless extraction techniques, the miniaturization of sample processing technologies, and the application of environmentally friendly detection instruments. In labs and business, the idea of green chemistry has evolved into a tool for advancing sustainable development. The twelve principles of green chemistry are the basis of guidance addressed to individuals who want to follow the green chemistry trend. They give a framework for measures that can be performed to make chemical products and processes more ecologically friendly. These acts are designed by scientists representing different disciplines of chemistry, for example, organic synthesis, chemical engineering, or analytical chemistry. The majority of initiatives to make chemical processes more environmentally friendly focus on the need to employ safer, less hazardous, and more benign solvents, or to eliminate solvents altogether, and to use less reagents and auxiliaries.[1-3]

One of the challenges in green chemistry is the evaluation of the greenness of chemical processes. It is well known that the processes that cannot be measured cannot be controlled. In green, control chemistry should be understood as a possibility to select the greenest option. Progress and by using measurement techniques, we may assess how environmentally conscious current solutions are in comparison to freshly developed ones. various elements characterized by a varying amount of complexity are currently employed in evaluation of environmental effect of chemical processes. This article's goal is to evaluate several methods for assessing the environmental impact of chemical processes. There will be a discussion of several quantitative, comparative, and semi-quantitative evaluation techniques.

The crucial requirement to evaluate toxins for safety and public health reasons has encouraged developments in analytical techniques but it is equally important to guarantee that these technologies themselves do not contribute to environmental harm. Recognized professionals in green chemistry, such Paul Anastas and John Charles Warner, have contributed significantly to this subject, emphasizing the necessity of environmentally friendly procedures that limit waste and dangerous compounds, introducing the 12 principles of green chemistry. A sustainable society depends on creating chemical products and processes that promote human and environmental health from the outset. Green chemistry is a science that aims to minimize the negative environmental effects of chemical production and usage. In the work of S. Armenta et al., the early milestones of Green Analytical Chemistry can be found, high lighting significant developments such as reducing solvent consumption, minimizing toxicity through automation and downsizing, and the invention of solvent-free procedures.[4,5]

The use of experimental design in the creation and improvement of chromatographic techniques has recently become a major concern in accordance with the principles of green analytical chemistry. In order to achieve the separation of drugs in combination or the presence of their degradation products and impurities, the ability of experimental design to simultaneously analyse multiple variables and their effects qualifies it as an economical and environmentally friendly approach. This is because it reduces the number of experiments and, consequently, the consumption of solvents.

The increasing need for green and eco-friendly scientific practices has consequently resulted in the fast rise of Green Analytical Chemistry (GAC) to be one of the key areas of modern drug analysis. The classic scientific methods regularly use solvents that are dangerous to the environment and human health, require a lot of energy and produce a huge amount of chemical waste. Besides, these methods are often subjected to accidents and diseases affecting the workers who handle such chemicals. Green Analytical Chemistry has come up with a nice way through which the entire analytical processes are redesigned to be eco-friendly, economically viable, and technologically advanced.

Principles of Green Analytical Chemistry

In our approach, the 12 principles of GAC are as follows:

1. Direct analytical techniques should be applied to avoid sample treatment.
2. Minimal sample size and minimal number of samples are goals.

3. In situ measurements should be performed.
4. Integration of analytical processes and operations saves energy and reduces the use of reagents.
5. Automated and miniaturized methods should be selected.
6. Derivatization should be avoided.
7. Generation of a large volume of analytical waste should be avoided and proper management of analytical waste should be provided.
8. Multi-analyte or multi-parameter methods are preferred versus methods using one analyte at a time.
9. The use of energy should be minimized.
10. Reagents obtained from renewable source should be preferred.
11. Toxic reagents should be eliminated or replaced.
12. The safety of the operator should be increased.

Together, these principles provide a framework for designing analytical methods that are efficient, safe, and sustainable.[6,9]

Greener Organic Solvents in Analytical Chemistry

The perfect zero-solvent system would be the most eco-friendly choice in analytical chemistry, but the use of solvents could not be entirely eliminated since they are needed for dissolving samples, efficient extraction, and separation. Thus, in accordance with green chemistry concepts, less harmful substitutes have been introduced to replace the usual volatile, flammable, and toxic organic solvents. Solvent Selection Guides (SSGs) play a significant role in pointing out the eco-friendly and safer solvent systems, mainly concentrating on amphiphilic solvents, ionic liquids (ILs), and deep eutectic solvents (DESs). These green solvents are gaining popularity in sample preparation as well as in chromatographic techniques.

1. Alternative Solvents for Sample Preparation

Amongst the various solvents water helds the title of the most sustainable and least toxic one. However, its water extraction techniques have been reduced to subcritical water extraction (SWE), micellar extraction, and hydrotropic extraction. Therefore, Natural Deep Eutectic Solvent (NADESs) formed through the hydrogen-bonding of natural substances bear the characteristics of being biodegradable and recyclable.

Bio-based solvents that are ethanol, ethyl acetate, lactic acid esters, succinic acid derivatives, and furfural-based solvents are not only renewable but also non-toxic and healthier alternatives. Low-temperature extraction with supercritical CO_2 is one of the most popular methods used today offering excellent environmental profiles without leaving any residue behind. Other methods employing liquefied gases (dimethyl ether, propane, butane) as well as supercritical fluids can also produce similar results.

2. Greener Mobile Phases in Chromatography

Methanol and acetonitrile are the most common solvents in reversed-phase liquid chromatography, but less toxic and more environmentally friendly solvents such as ethanol, acetone, and ethyl acetate are becoming the preferred options. Acetone has similar separation efficiency as acetonitrile and is the better choice from an environmental perspective. The use of water-rich mobile phases, high-temperature LC, and polymer-based stationary phases (such as polyethylene glycol) are also among the approaches that significantly contribute to reducing the consumption of organic solvents. In the normal-phase systems designed for nonpolar analytes, the use of green solvents such as cyclopentyl methyl ether, hexamethyldisiloxane, isopentyl acetate, and 2-methyltetrahydrofuran has been successful.

Green Chromatographic Techniques

Pharmaceutical analysis still counts chromatography among its most favored analytical methods and yet at the same time it is not uncommon for chromatography to depend on the heavy use of organic solvents consistently throughout the processes, such as acetonitrile, methanol, or hexane, for example. Green chromatographic techniques focus on lessening the influence of the environment through the especially solvent consumption cut down, toxic solvent replacement with non-toxic ones, increasing method efficiency, and the adoption of advanced technologies that are environment-friendly. The technological development in these methods has allowed for the conservation of analytical performance while the ecological footprint of chromatographic workflows has been significantly reduced.

Green Sample Preparation Techniques

Sample preparation is the most time-consuming step in many methodologies, especially those used for complicated matrices. In order to make this step more benign, various approaches including miniaturization, simplification and automation of extraction procedures have been adopted. Following is an overview of the most common green sample preparation methods focusing mostly on organic analytes.

1. Solid Phase Extraction (SPE)

One of the most popular methods for sample preparation is SPE. In SPE, the solutes are adsorbed onto the column after an aqueous sample is run through a brief column filled with an appropriate solid sorbent. Afterwards, modest volumes of organic solvents of high elution strength are utilized to recover the analytes from the sorbent, which leads to their enrichment. Solid phase extraction produces minimal waste and uses minimal solvent. As a result, it is considered an eco-friendly practice. Despite this method's advantages, there are a few possible drawbacks that should be taken into account to prevent ineffective analyte extraction. The non-uniformity of the packing material bed is one of the problems, which could result in a loss of efficiency.

The non-uniformity of the packing material bed is one of the problems, which could result in a loss of efficiency. One safe solution to this issue is to utilize commercial cartridges. In addition, limited selectivity of some traditional sorbents may lead to insufficient retention of extremely polar molecules. Another difficulty is the competition between the analytes and the sample matrix for retention, which can substantially impair analyte recovery. Consequently, careful optimization of the method is required to ensure effective extraction of analytes.

- Quenchers Extraction Methodology
- Microextraction by Packed Sorbent (MEPS)
- Stir-Bar Sorptive Extraction (SBSE)
- Solid Phase Nano extraction (SPNE)

2. Liquid-Phase Microextraction Techniques (LPME)

LPME techniques use a small volume of an organic solvent (typically 1–100 μL) to extract the analytes. The major modes of LPME are single drop microextraction (SDME), hollow fiber liquid-phase microextraction (HF-LPME) and dispersive liquid-liquid microextraction (DLLME).

- Single Drop Microextraction (SDME)
- Hollow Fiber Liquid-Phase Microextraction (HF-LPME)
  - Two-phase hollow fiber LPME.
  - Three-phase hollow fiber LPME.
- Dispersive Liquid-Liquid Microextraction (DLLME)

3. Membrane Extraction

These procedures utilize nonporous membranes that can be a solid or a liquid, and which are fixed between two other phases, usually liquid, but sometimes gaseous.

- Supported Liquid Membrane Extraction (SLME)
- Microporous Membrane Liquid–Liquid Extraction (MMLLE)
- Membrane Extraction with a Sorbent Interface (MESI)
- Membrane Assisted Solvent Extraction (MASE)
- Green Agarose Gel Electro-Membrane Extraction
- Micro dialysis Sampling
- Thin-Film Microextraction (TFME).

4. Green Alternatives to Extraction Solvents

- Subcritical Water Extraction (SWE)
- Supercritical Fluid Extraction (SFE)
- Ionic Liquids (ILs)
- Deep Eutectic Solvents (DES)
- Surfactants and Hydrotropes
- Bioderived (Agro) Solvents

Spectroscopic Green Techniques

Spectroscopic techniques are essential tools for characterizing chemical reactions and products in green chemistry. These techniques provide valuable information about the molecular structure, composition, and properties of the reaction mixture.

➢ NMR spectroscopy in Green Chemistry

Nuclear Magnetic Resonance (NMR) spectroscopy is a strong tool for structure elucidation and reaction monitoring in green chemistry. NMR spectroscopy can provide extensive information about the molecular structure, dynamics, and interactions of molecules in the reaction mixture. The use of NMR spectroscopy in green chemistry offers various advantages, including:

- **Non-destructive analysis:** NMR spectroscopy is a non-destructive technique, which means that the sample is not damaged or eaten during the analysis.

- **High sensitivity:** Modern NMR spectrometers offer high sensitivity, allowing for the identification of minuscule levels of contaminants or byproducts.
- **Quantitative analysis**: NMR spectroscopy can yield quantitative data regarding the reaction mixture's composition.

➢ **IR Spectroscopy for Monitoring Reactions**

Another popular method in green chemistry for tracking reactions and locating functional groups is infrared (IR) spectroscopy. IR spectroscopy can provide information about the molecular structure and composition of the reaction mixture, allowing for the identification of potential difficulties and the adjustment of reaction conditions.

Some of the advantages of IR spectroscopy in green chemistry include

- **Fast analysis:** IR spectroscopy is a quick technique, allowing for real-time monitoring of processes.
- **Non-destructive analysis:** IR spectroscopy is a non-destructive technique, which means that the sample is not damaged or eaten during the analysis.
- **In situ analysis:** IR spectroscopy can be utilized for in situ analysis, which enables real-time reaction monitoring.

➢ **Raman Spectroscopy for Analyzing Complex Mixtures**

Raman spectroscopy is a complementary technique to IR spectroscopy, providing information about the molecular structure and composition of the reaction mixture. Raman spectroscopy is particularly useful for analyzing complex mixtures, as it can provide detailed information about the molecular structure and interactions of molecules in the mixture.

Raman spectroscopy has several benefits in green chemistry, such as:

High sensitivity: Raman spectroscopy can identify small levels of contaminants or by products.

- **Non-destructive analysis:** Raman spectroscopy is a non-destructive technique, which means that the sample is not damaged or consumed during the analysis.
- **In situ analysis:** Real-time reaction monitoring is possible with Raman spectroscopy.[10-15]

Green Solvents

Green solvents are environmentally friendly chemical solvents that are used as a part of green chemistry. They came to prominence in 2015, when the UN defined a new sustainability-focused development plan based on 17 sustainable development goals, recognizing the need for green chemistry and green solvents for a more sustainable future. Green solvents are developed as more environmentally friendly solvents, derived from the processing of agricultural crops or otherwise sustainable methods as alternatives to petrochemical solvents. Some of the expected characteristics of green solvents include ease of recycling, ease of biodegradation, and low toxicity.

Examples

- **Water**

Although not an organic solvent, water is an attractive solvent because it its non-toxic and renewable. It is a useful solvent in many industrial processes. Traditional organic solvents can sometimes be replaced by aqueous preparations. Water-based coatings have largely replaced standard petroleum-based paints for the construction industry; however, solvent-based anti-corrosion paints remain among the most used today.

Supercritical water (SCW) is obtained at a temperature of 374.2 °C and a pressure of 22.05 MPa. It behaves as a dense gas with a dissolving power equivalent to that of organic solvents of low polarity. However, the solubility of inorganic salts in SCW is radically reduced. SCW is used as a reaction medium, especially in oxidation processes for the destruction of toxic substances such as those found in industrial aqueous effluents. The use of supercritical water has two main technical challenges, namely corrosion and salt deposition.

- **Supercritical carbon dioxide**

Supercritical carbon dioxide (CO_2) is the most commonly used supercritical fluid because of its relatively easy to use. Temperatures above 31 °C and pressures above 7.38 MPa are sufficient to obtain supercriticality, at which point it behaves as a good nonpolar solvent.

- **Alcohols and esters**

Ethanol is used in toiletries, cosmetics, some cleaners and coatings.

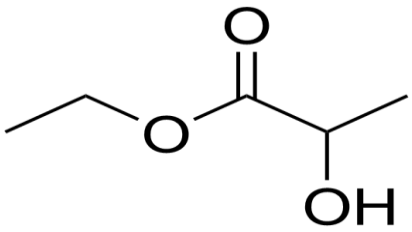

Fig. 1: Ethyl lactate.

Bioethanol, made industrially by fermentation of sugars, starch, and cellulose is widely available. Biobutanol (butyl alcohol, various isomers) is also produced by fermentation of sugars. Tetrahydrofurfuryl alcohol (THFA) is a specialty solvent that may be obtained from hemicellulose.

Ethyl lactate, made from lactic acid obtained from corn starch, is notably used as a mixture with other solvents in some paint strippers and cleaners. Ethyl lactate has replaced solvents such as toluene, acetone, and xylene in some applications.

- **Lipid-derived solvents**

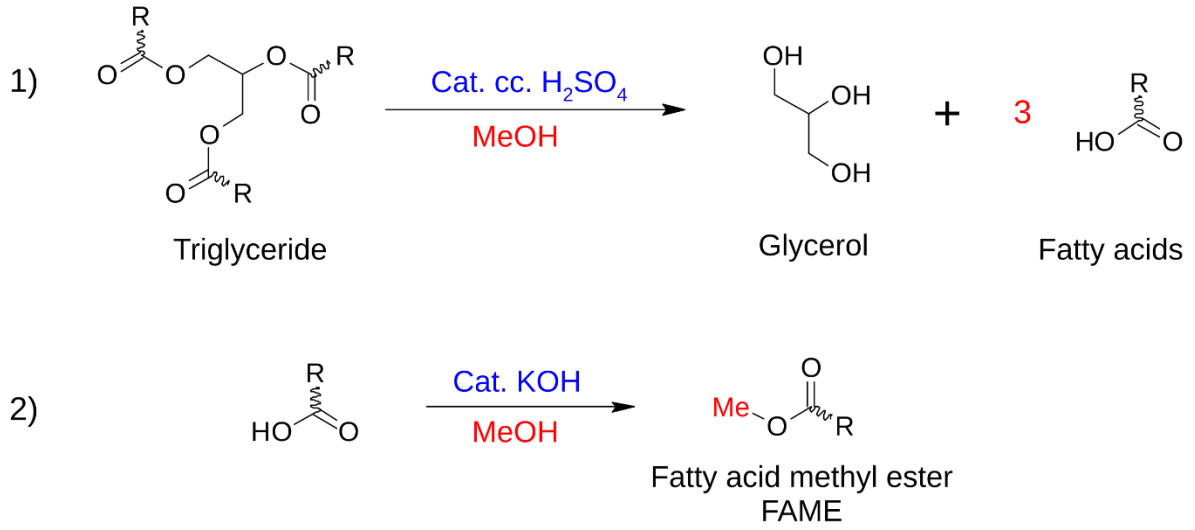

Fig. 2: Fatty acid methyl ester synthesis.

Lipids (triglycerides) themselves can be used as solvents, but are mostly hydrolysed to fatty acids and glycerol (glycerin). Fatty acids can be esterified with an alcohol to give fatty acid esters, e.g., FAMEs (fatty acid methyl esters) if the esterification is performed with methanol. Usually derived from natural gas or petroleum, the methanol used to produce FAMEs can also be obtained by other routes, including gasification of biomass and household hazardous

waste. Glycerol from lipid hydrolysis can be used as a solvent in synthetic chemistry, as can some of its derivatives.

- **Deep eutectic solvents**

Deep eutectic solvents (DES) have low melting points, can be cheap, safe and useful in industries. One example is octyl ammonium bromide/decanoic acid (molar ratio of [1:2]) has a lower density compared to water of 0.8889 $g.cm^{-3}$, up to 1.4851 $g.cm^{-3}$ for choline chloride/trifluoroacetamide [1:2]. Their miscibility is also composition-dependent.

A mixture whose melting point is lower than that of the constituents is called an eutectic mixture. Many such mixtures can be used as solvents, especially when the melting-point depression is very large, hence the term deep eutectic solvent (DES). One of the most commonly used substances to obtain DES is the ammonium salt choline chloride. Smith, Abbott, and Ryder report that a mixture of urea (melting point: 133 °C) and choline chloride (melting point: 302 °C) in a 2:1 molar ratio has a melting point of 12 °C.

Natural deep eutectic solvents (NADES) are also a research area relevant to green chemistry, being easy to produce from two low-cost and well-known ecotoxicity components, a hydrogen-bond acceptor, and a hydrogen-bond donor.

- **Terpenes**

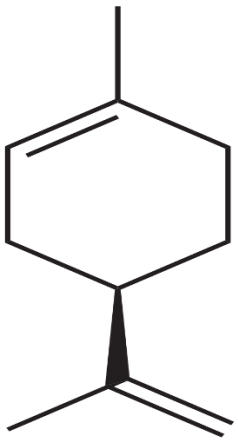

Fig. 3: D-Limonene.

Solvents in a diverse class of natural substances called terpenes are obtained by extraction from certain parts of plants. All terpenes are structurally presented as multiples of isoprene with the gross formula $(C_5H_8)_n$.

- D-limonene, a monoterpene, is one of the best known solvents in this class, as is turpentine.
- D-limonene is extracted from citrus peels while turpentine is obtained from pine trees (sap, stump) and as a by-product of the Kraft paper-making process (Sell, 2006).
- Turpentine is a mixture of terpenes whose composition varies according to its origin and production method. In Canada and the United States, a range of mass concentrations of 40 to 65% α-pinene, 20 to 35% β-pinene, and 2 to 20% d-limonene are found.
- α-pinene can replace n-hexane for the extraction of vegetable oil, and as a substitute solvent for extracting molecules such as carotenoids used as food additives.

  Turpentine, formerly used as a solvent in organic coatings, is now largely replaced by petroleum hydrocarbons. Nowadays, it is mainly used as a source of its constituents, including α-pinene and β-pinene.

➢ **Ionic liquids**

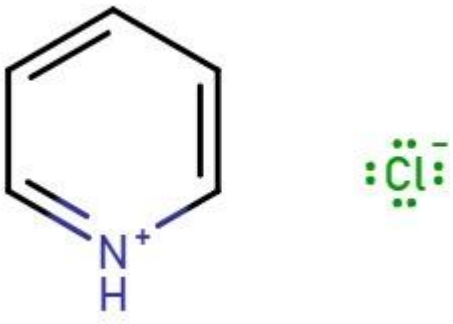

Fig. 4: Pyridinium chloride.

Ionic liquids are molten organic salts that are generally fluid at room temperature. Frequently used cationic liquids, include imidazolium, pyridinium, ammonium and phosphonium. Anionic liquids include halides, tetrafluoroborate, hexafluorophosphate, and nitrate. Bubalo et al. (2015) argue that ionic liquids are non-flammable, and chemically, electrochemically and thermally stable. These properties allow for ionic liquids to be used as green solvents, as their low volatility limits VOC emissions compared to conventional solvents. The ecotoxicity and poor degradability of ionic liquids has been recognized in the past because the resources typically used for their production are non-renewable, as is the case for imidazole and halogenated alkanes (derived from petroleum). Ionic liquids produced from renewable and biodegradable materials have recently emerged, but their availability is low because of high production costs.[16,21]

- **Switchable solvents**

Bubbling CO_2 into water or an organic solvent results in changes to certain properties of the liquid such as its polarity, ionic strength, and hydrophilicity. This allows an organic solvent to form a homogeneous mixture with the otherwise immiscible water. This process is reversible, and was developed by Jessop et al. (2012) for potential uses in synthetic chemistry, extraction and separation of various substances. The degree of how green switchable solvents are is measured by the energy and material savings it provides; thus, one of the advantages of switchable solvents is the potential reuse of solvent and water in post-process applications.

- **Solvents from waste materials**

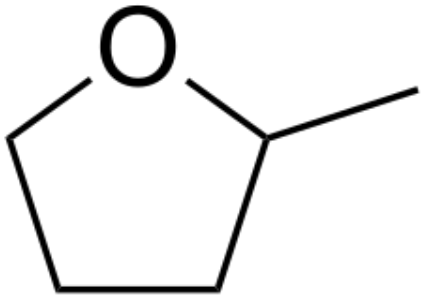

Fig. 5: 2. Methyltetrahydrofuran.

First-generation biorefineries exploit food-based substances such as starch and vegetable oils. For example, corn grain is used to make ethanol. Second-generation biorefineries use residues or wastes generated by various industries as feedstock for the manufacture of their solvents. 2-Methyltetrahydrofuran, derived from lignocellulosic waste, would have the potential to replace tetrahydrofuran, toluene, DCM, and diethyl ether in some applications. Levulinic acid esters from the same source would have the potential to replace DCM in paint cleaners and strippers.

Used cooking oils can be used to produce FAMEs. Glycerol, obtained as a by-product of the synthesis of these, can in turn be used to produce various solvents such as 2,2-dimethyl-1,3-dioxolane-4-methanol, usable as a solvent in the formulation of inks and cleaners.

Fusel oil, an isomeric mixture of amyl alcohol, is a by-product of ethanol production from sugars. Green solvents derived from fusel oil such as isoamyl acetate or isoamyl methyl carbonate could be obtained. When these green solvents are used to manufacture nail

polishes, VOC emissions report a minimum reduction of 68% compared to the emissions caused by using traditional solvents.

- **Petrochemical solvents with green characteristics**

Due to the high price of new sustainable solvents, in 2017, Clark et al. listed twenty-five solvents that are currently considered acceptable to replace hazardous solvents, even if they are derived from petrochemicals.

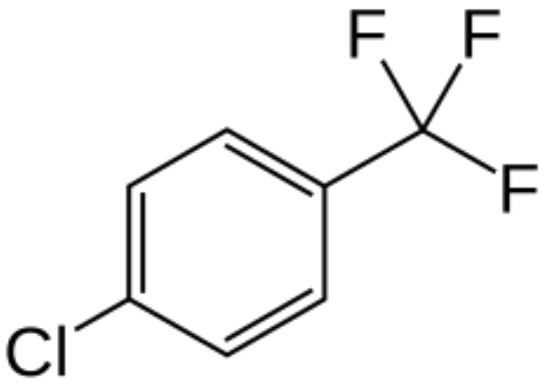

Fig. 6: Parachlorobenzotrifluoride (PCBTF).

These include propylene carbonate and dibasic esters (DBEs). Propylene carbonate and DBEs have been the subject of monographs on solvent substitution. Propylene carbonate and two DBEs are considered green in the manufacturer GlaxoSmithKline's (GSK) Solvent Sustainability Guide, which is used in the pharmaceutical industry. Propylene carbonate can be produced from renewable resources, but DBEs that have appeared on the market in recent years are obtained as by-products of the synthesis of polyamides, derived from petroleum. Other petrochemical solvents are variously referred to as green solvents, such as halogenated hydrocarbons like parachlorobenzotrifluoride, which has been used since the early 1990s in paints to replace smog-forming solvents.

Siloxanes are compounds known in industry in the form of polymers (silicones, R-SiO-R'), for their thermal stability and elastic and non-stick properties. The early 1990s saw the emergence of low molecular weight siloxanes (methyl siloxanes), which can be used as solvents in precision cleaning, replacing stratospheric ozone-depleting solvents.

A final category of petrochemical solvents that qualify as green involves polymeric solvents. The International Union of Pure and Applied Chemistry defines the term "polymer solvent" as "a polymer that acts as a solvent for low-molecular weight compounds". In industrial

chemistry, polyethylene glycols (PEGs, $H(OCH_2CH_2)_nOH$) are one of the most widely used polymeric solvent families. PEGs, with molecular weights below 600 Da, are viscous liquids at room temperature, while heavier PEGs are waxy solids.

Soluble in water and readily biodegradable, liquid PEGs have the advantage of negligible volatility (< 0.01 mmHg or < 1.3 Pa at 20 °C). PEGs are synthesized from ethylene glycol and ethylene oxide, both of which are petrochemical-derived molecules, though ethylene glycol from renewable sources (cellulose) is commercially available.[21,24]

CONCLUSION

Green Analytical Chemistry is the revolutionary method of pharmaceutical analysis that can be considered as a new eco-friendly approach to traditional methods which generally involve the use of solvents, and are therefore hazardous and burdensome to the environment. GAC reduces greatly the waste, the toxicity, and energy use with the help of integrating the eco-friendly sample preparation methods, the green solvents, the advanced chromatographic and the spectroscopic methods, and the miniaturized analytical platforms, while also keeping the accuracy and the compliance of the analysis with the regulations. The use of greenness assessment tools like Eco-Scale, NEMI, GAPI, and AGREE guarantees analytical procedures are assessed based on the environmental impact systematically. Challenges such as technical issues, industry reluctance, and economic concerns still exist even though the pros are crystal clear. On the other hand, fast development in microfluidics, automation, robotics, and artificial intelligence is inviting wider use of GAC in pharmaceutical research and quality control. The world is putting more and more emphasis on sustainability and it's no longer a choice but a necessity to integrate green analytical methods for the responsible development of pharmaceuticals. GAC, in general, is leading to a future where the analysis of pharmaceuticals will be done to the highest standard, and the ecological footprint will be reduced, safety will be improved, and operational efficiency will be the main feature.

REFERENCES

1. Tobiszewski, Marek. "Analytical chemistry with biosolvents." *Analytical and bioanalytical chemistry*, 2019; 411(19): 4359-4364, https://doi:10.1007/s00216-019-01732-2.
2. Yin, Lei et al. "Green analytical chemistry metrics for evaluating the greenness of analytical procedures." *Journal of pharmaceutical analysis*, 2024; 14(11): 101013. https://doi:10.1016/j.jpha.2024.101013

3. Gullifa, G et al. "Portable NIR spectroscopy: the route to green analytical chemistry." *Frontiers in chemistry,* 25 Sep. 2023; 11: 1214825. https://doi:10.3389/fchem.2023.1214825
4. Gama, Mariana R et al. "An overview of the Brazilian contributions to Green Analytical Chemistry." *Anais da Academia Brasileira de Ciencias*, 2019; 91(1): e20180294. https://doi:10.1590/0001-3765201920180294
5. Elsheikh, Soha G et al. "Green analytical chemistry and experimental design: a combined approach for the analysis of zonisamide." *BMC chemistry,* 17 Apr. 2023; 17(1): 38., https://doi:10.1186/s13065-023-00942-1
6. Tobiszewski, Marek et al. "Green Chemistry Metrics with Special Reference to Green Analytical Chemistry." *Molecules (Basel, Switzerland)* 12 Jun. 2015; 20(6): 10928-46., https://doi:10.3390/molecules200610928
7. Miladinović, Saša M. "Green analytical chemistry: integrating sustainability into undergraduate education." *Analytical and bioanalytical chemistry*, 2025; 417(4): 665-673. https://doi:10.1007/s00216-024-05680-4
8. Silva, Javier et al. "Should we think about green or white analytical chemistry? Case study: Accelerated sample preparation using an ultrasonic bath for the simultaneous determination of Mn and Fe in beef." *Heliyon.,* 13 Oct. 2023; 9(10): e20967, https://doi:10.1016/j.heliyon.2023.e20967
9. Tobiszewski, Marek. "Analytical chemistry with biosolvents." *Analytical and bioanalytical chemistry*, 2019; 411(19): 4359-4364. https://doi:10.1007/s00216-019-01732-2
10. Parhi, Pankaj Kumar. "Editorial: Separation and analytical chemistry." *Frontiers in chemistry,* 2 Nov. 2023; 11: 1298452. https://doi:10.3389/fchem.2023.1298452
11. Parhi, Pankaj Kumar. "Editorial: Separation and analytical chemistry." *Frontiers in chemistry*, 2 Nov. 2023; 11: 1298452. https://doi:10.3389/fchem.2023.1298452
12. Wang, Joseph. "Real-time electrochemical monitoring: toward green analytical chemistry." *Accounts of chemical research,* 2 Nov. 2023; 35(9): 811-6. https://doi:10.1021/ar010066e
13. Périno, Sandrine et al. "Downscaling of Industrial Turbo-Distillation to Laboratory Turbo-Clevenger for Extraction of Essential Oils. Application of Concepts of Green Analytical Chemistry." *Molecules (Basel, Switzerland),* 27 Jul. 2019; 24(15): 2734., https://doi:10.3390/molecules24152734

14. Vanga, Mohan Goud et al. "Integrating green analytical chemistry and analytical quality by design: an innovative approach for RP-UPLC method development of ensifentrine in bulk and inhalation formulations." *BMC chemistry*, 15 Mar. 2025; 19(1): 70., https://doi:10.1186/s13065-025-01448-8
15. Cutillas, Víctor et al. "Green analytical approaches for contaminants: Sustainable alternatives to conventional chromatographic methods." *Journal of chromatography, A* 2005; 1750: 465921. https://doi:10.1016/j.chroma.2025.465921
16. Agnieszka Gałuszka, Zdzisław Migaszewski, The 12 principles of green analytical chemistry and the SIGNIFICANCE mnemonic of green analytical practices, TrAC Trends in Analytical Chemistry, 2013; 50: 78-84, ISSN 0165-9936, https://doi.org/10.1016/j.trac.2013.04.010.
17. Aly, Alshymaa A, and Tadeusz Górecki. "Green Approaches to Sample Preparation Based on Extraction Techniques." *Molecules (Basel, Switzerland*, 9 Apr. 2020; 25(7): 1719., https://doi:10.3390/molecules25071719
18. Dulaurent S., El Balkhi S., Poncelet L., Gaulier J.-M., Marquet P., Saint-Marcoux F. QuEChERS sample preparation prior to LC-MS/MS determination of opiates, amphetamines, and cocaine metabolites in whole blood. Anal. Bioanal. Chem., 2016; 408: 1467–1474. https://doi:10.1007/s00216-015-9248-3.
19. Mehta, M., Mehta, D. & Mashru, R. Recent application of green analytical chemistry: eco-friendly approaches for pharmaceutical analysis. *Futur J Pharm Sci*., 2024; **10**(24). https://doi.org/10.1186/s43094-024-00658-6
20. Keith LH, Gron LU, Young JL (2007) Green analytical methodologies. Chem Rev., 107(6): 2695–2708. https://doi.org/10.1021/cr068359e
21. Ibanez E, Cifuentes A (2020) Moving forward to greener extraction techniques. TrAC Trends Anal Chem., 122: 115698. https://doi.org/10. 1016/j.trac.2019.115698
22. Płotka-Wasylka J (2018) A new tool for the evaluation of the analytical procedure: green analytical procedure index. Talanta, 181: 204–209. https://doi.org/10.1016/j.talanta.2018.01.013
23. Khataei, Mohammad Mahdi et al. "A review of green solvent extraction techniques and their use in antibiotic residue analysis." *Journal of pharmaceutical and biomedical analysis*, 2022; 209: 114487. https://doi:10.1016/j.jpba.2021.114487
24. https://www.numberanalytics.com/blog/green-chemistry-characterization-techniques.