Research Journal of Chemical Sciences ISSN 2231-606X
Vol. **13(2),** 29-39, June **(2023)** *Res. J. Chem. Sci.*

Review paper

Green chemistry aspects in Analytical Chemistry applications

Sudha Tantry and Ajay Kumar*
SABIC Research & Technology Pvt. Ltd, Plot No. 81 to 85, Chikkadunnasandra, Sarjapura - Attibele State Highway, Bengaluru, Karnataka-562125, India
dr.ajay_63@rediffmail.com

Available online at: www.isca.in, www.isca.me
Received 23th October 2022, revised 20th February 2023, accepted 28th April 2023

Abstract

Analytical chemistry, an important branch of chemistry, deals with the analysis of a huge number of samples in different forms for various purposes. Unfortunately, the analytical methods very often contribute to environmental problems. The irony is because many analytical procedures use hazardous and toxic chemicals. Thus the concept of 'green chemistry' needs to be viewed in the context of 'green analytical chemistry' (GAC). The green analytical chemistry emphasizes that the development of any new analytical method/process has to comply with relevant green chemistry principles to reduce the adverse impact of analysis on human health and the environment. This mini-review article outlines various aspects of GAC; concepts of green analysis, green sample preparation, instrumentation, green solvents, and selective green analysis examples. This paper further emphasizes implementing the GAC concept in an analytical laboratory in real sense. This requirement demands; i) appropriate measurements of the environmental impact and greenness of analytical methods/ procedures at each stage, ii) popularization of the existing green chemistry metrics/tools and iii) new software/tool for easy evaluation of the greenness of various parameters of different processes on different scales.

Keywords: Green analytical chemistry; sustainability, matrix; analyte; green solvents.

Introduction

Chemistry has been perfect for improving human life for at least two centuries. This observation is because almost everywhere chemistry is embedded and played a vital role in many fields of applications like chemicals, fossil fuels, energy, building materials, medical, health, textiles, consumer goods, agriculture, and so on.

The rapid growth and need to fulfill the demand of a massive world population has created many constraints. Therefore, chemistry has been exploited to the extent that it has created a threat to human life in terms of environmental damage and pollutions. Environmental chemistry has been developed in response to problems and concerns regarding environmental pollution. Green chemistry could include anything from reducing waste to dispose of it correctly and use of biodegradable materials[1,2].

Segregation and disposal of all the wastes in the best possible ways are the best solutions to save the environment and living beings. Analytical chemistry, which deals with various analyses in a massive variety of samples in different forms and various purposes, is also an important branch[3]. In most of the cases, the chemical analysis uses various reagents or organic solvents. The concept of 'Green Chemistry' need focus on 'Green Analytical Chemistry' (GAC). This article describes the concepts of green analysis, which includes mainly key goals of green analytical chemistry, challenges, greener methods, and process.

Concept of Green Chemistry: In the 1980s, the environment became an important priority for almost all industries. Thus to deal with the challenges posed by chemical industries in terms of environment pollutions, toxicity, health hazards, industrial accidents etc., the green chemistry concept was enabled by strict environmental regulations. The term green chemistry was first used in 1991 by Anastas. P. T, in Environmental Protection Agency (EPA) program. Green chemistry describes 'the design of chemical products and processes which eliminates or minimize the use or generation of hazardous/toxic substances. Table- 1, describes the evolution of green chemistry[1,2].

Green chemistry ensures reducing waste and improving sustainability. Sustainability and green chemistry will go in parallel and are becoming increasingly important in every industry. Green chemistry also referred to as sustainable chemistry, targeted on minimizing the usage and generation of hazardous materials by designing both the products and processes[4-6]. Since chemistry is very vast and each areas of chemistry will have its own ways of defining and designing these processes. Green chemistry is a chemical technique, the environmental chemistry is a discipline, this is the key difference between green chemistry and environmental chemistry. Green chemistry includes the management of waste, which is produced during chemical process. Designing of safe methods, processes, molecules, materials, products, and systems are the main goals of green chemistry.

As shown in Figure-1, Green chemistry is mostly about; i. Reducing the waste at source, ii. Replace many reagents with safe catalysts, iii. More use of nontoxic reagents, iv. Usage of resources from renewable sources, v. Target on improving efficiency, vi. Reduce solvent consumption, design solvent-free systems and use recyclable environment friendly solvents.

Table-1: Green chemistry history.

Year	Activity
1980	Although on the pollution cleanup, the chemical industry and EPA were focused, but chemists are the one to start and major paradigm shift has to begin from them. To prevent the pollution, all scientists have to focus their research in this way to cope up with growing environmental awareness. In each industry, government, forums of both national and international sectors, all need to address the problems and look for preventative solutions.
1990	Green Chemistry phrase started in the scientific field
1991	Green Chemistry was invented by the Chemist Paul Anastas
1995	In the Scientific community Green Chemistry Challenge Award' initiated
1997	Formation of Green Chemistry Institute
1999	The Green Chemistry journal launched
2001	Merging of Green Chemistry Institute and American Chemical Society.

The objective of green chemistry is to make more energy efficient innovative products with reducing waste disposal. Since the sustainability and green chemistry are interlinked, both will have some common goals like; no waste, no toxic chemicals usage, closed and controlled process, low cost and increased growth. Usage of green chemistry methodologies will play a major role to enable this process. All need to ensure that the chemicals which are dangerous to human and environment need to be in control. Green chemistry is based upon twelve principles (Table-2)[7-9]. During the design stage of any methods or processes the concept with the 12 Principles of Green Chemistry has to be considered. Hence, in each stage, the green chemistry approaches will encouraged designing safer products, processes and minimizes the wastes. From the sustainability and environmental aspects, the new techniques are having focus on increased energy efficiency, biodegradable products and the use of renewable resources. From this point of view, now all industries, government bodies etc. are putting effort to achieve this goal and joining hands with the Office of Pollution Prevention and Toxics (OPPT).

Table-2: 12 Principles of Green Chemistry.

S. No.	Principle
1.	**Prevention:** Instead of treating or clean up waste after its generation, better to prevent waste generation in large volume.
2.	**Atom Economy:** The synthetic method has to be designed to consume maximum raw materials/ chemicals/substances during the reaction process.
3.	**Safer Chemical Syntheses**: Both the human health and environment should not be influenced with toxicity or harmful impact from these new designed synthetic methods to produce products/materials.
4.	**Designing Safer Chemicals**: Reduce the toxicity by producing own safer chemical products to conduct their desired functions.
5.	**Safer Solvents and Auxiliaries:** Wherever applicable, no or less use of reagents, chemicals and solvents. In unavoidable circumstances, while using those or after use, try to make them harmless, safe, non-dangerous, non-poisonous, non-toxic.
6.	**Design for Energy Efficiency**: To reduce environmental impact, go with minimum energy requirements consumption for chemical processes. Try to develop and use the methods at ambient conditions.
7.	**Use of Renewable Feedstock's:** Build a mechanism for the renewable process for feedstock or raw material wherever technically practicable, rather than continuously consuming the same.
8.	**Reduce Derivatives:** In the reaction, avoid use blocking groups for protection/de-protection to avoid unnecessary derivatization. Try to modify physical/ chemical processes to avoid additional reagents and waste generation.
9.	**Catalysis:** Instead of stoichiometric processes, select selectively catalyzed processes wherever possible.
10.	**Design for Degradation:** To have better control on harmless degradation products, design the chemical products in advance and prior to the work.
11.	**Real-time analysis for Pollution Prevention**: To control the formation of hazardous substances, develop in-situ / real time process monitoring analytical techniques / methods.
12.	**Inherently Safer Chemistry for Accident Prevention**: In the chemical process, wherever possible, use green and safe chemicals / substances to minimize the hazards and risk for chemical accidents, such as releases, fire, and explosions.

The green analytical practices as explained as per 'significance' mnemonic, green chemistry is a multidisciplinary field, which involves utilization of a set of 12 principles to eliminate or at least reduce the use or generation of hazardous substances in the methods, process, design, manufacturing, and applications. The objective of the green chemistry is to design environmentally friendly chemistry. Green chemistry with sustainable chemistry has been developed rapidly over a time, it still needs further development, it will be one of the most critical research and practice field in the future. As shown in Figure-2, balancing and sustaining the green methods or process in a bigger scale is a challenge to all the industries and organizations. Fast growth of green chemistry is a long-term task, involving collective responsibilities in all the fields. There will be many challenges in the scientific community and all need to understand and resolve suitably to have positive consequences.

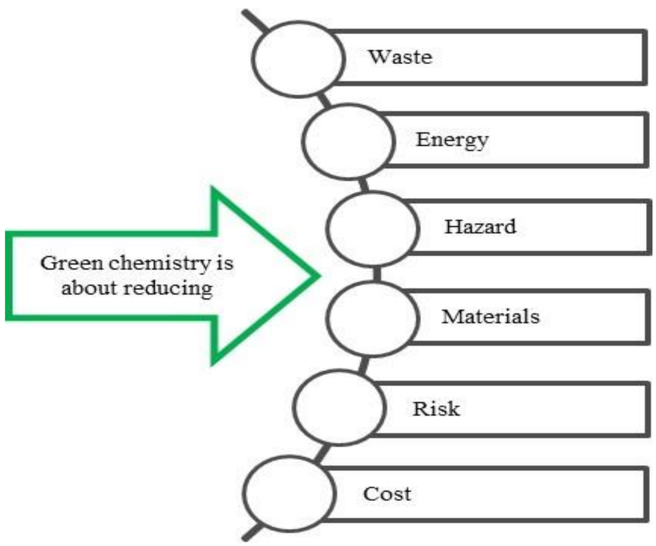

Figure-1: Green chemistry concept.

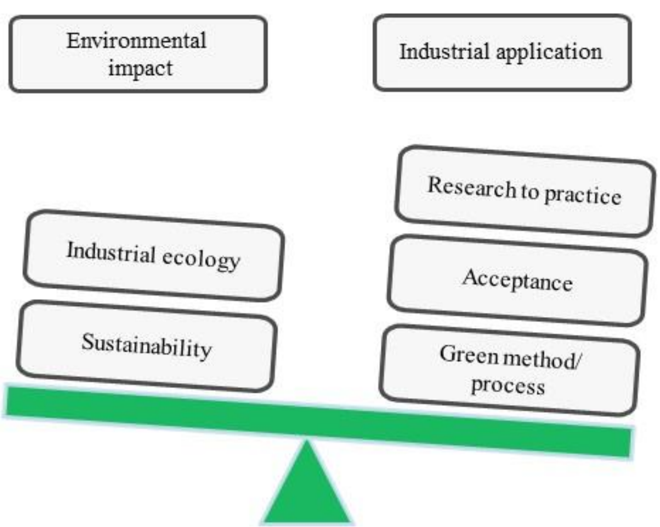

Figure-2: Balancing act on green process and sustainability.

Green analytical chemistry (GAC)

Analytical chemists are routinely working on various methods for analysing variety of samples using multiple techniques. It includes chromatography, spectroscopy and wet analytical and chemical methods. It is unfortunate that many analytical methods / procedures use toxic derivatizing reagents, solvents, hazardous chemicals for sample preparation and analysis. During and after analysis the waste generated will often contribute to environmental problems. The expertise on the instruments and analysis are very important to identify the harmful substances, which will reach the environment. The team efforts are needed from analytical point of view to develop green methods and to avoid or replace the toxic chemicals. Further important concerns on same topic are toxicity evaluation, disposal strategies, neutralization methods, and segregation of hazardous wastes. The concept is shown in Figure-3.

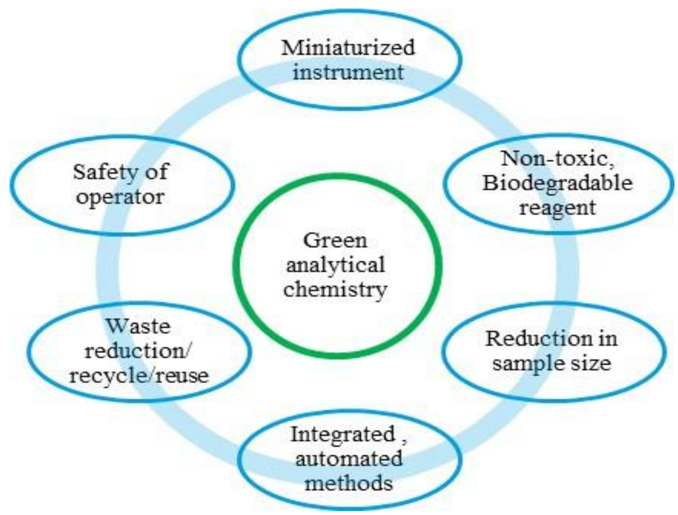

Figure-3: Green analytical chemistry concept.

Thus, GAC is becoming an essential sub-area of green chemistry[10-13]. The goal of green analytical chemistry is to use analytical methods that generate less hazardous waste and more benign to the environment. To achieve this goal, we need to develop either new analytical methodologies or modify the existing methods/techniques. Hence, in chemical laboratories on a large scale set up green chemistry rules need to be introduced on priority. The immediate requirement is to evaluate those analytical methods on their adverse effects on the environment, including various micro pollution aspects along with reagent/ instrument's cost and other analytical parameters.

In spite of the tremendous development of analytical instrumentation, sample preparation is still considered as bottleneck of the analytical process. During sample preparation and analysis, analytical chemists face many challenges like; i. Given the diversity or the breadth of chemical compounds / products, the identification of analytes / impurities is not a straight forward task, ii. Inconsistency of analytes in the investigated media due to time and space, iii. The concentration of impurities is typically very low and hence needs a sensitive method, iv. With the complexity and solubility issues and presence of wide range of analytes, robust composition analysis becomes very challenging and involves the use of multiple techniques. Then method becomes tedious. v. Interferences from compounds, which are having similar chemical structures and properties.

While developing the green methods there may be new challenges or issues with respect to analytical system suitability parameters like; accuracy, precision, robustness, ruggedness, sensitivity and stability. Sometimes it may be very difficult to balance between the analytical method assurance parameters and the green chemistry principles. In few cases, the laboratories may face to meet the performance parameters based on the application field, quantity handled, scale and setups. The 12 green chemistry principles may indirectly responsible for the decrease in performance parameters. The methods maybe evaluated / disagreed by the scientific community, since the aim is to reduce, replace and avoid the toxic chemicals/solvents while developing the method. There will be reduction in sample size, direct analysis without solvents, and fast method with miniaturized instruments, hence the combination of these may be questionable. However, the technical expertise and knowledge while developing the methods for the existing problems and new requirements will run in a right direction and path. Validating the methods using quality check standards using these new green methods/techniques will qualify the methods and overcome all the issues and challenges. The critical challenge is to compromise between the quality of the results and environmental friendliness of analytical methods. To meet the requirements of synthetic chemistry, the twelve principles of green chemistry (Table-2) were designed. However, in analytical, at a given point of time in any single method, only combination of few of these can be directly applied as claimed by Gałuszka et. al.[8]. i. Waste prevention (principle # 1); ii. Non hazardous solvents and safer auxiliaries (principle # 5); iii. Energy efficiency designs (principle # 6); iv. Eliminate or reduce derivatization (principle # 8).

Considering the broader application and importance of analytical chemistry, the 12 principles for GAC have been framed, and these are: i. To eliminate sample pre-treatment steps like dissolution, extraction, filtration, evaporation etc., introduce direct analytical techniques wherever possible. ii. Target small sample size with the least number of samples. iii. Wherever possible, run in-situ measurements. iv. To reduce the reagent consumption and save the energy, integrate the analytical processes and operations, v. Develop miniaturized methods and execute automation, vi. Avoid the use of derivatizing agents, vii. Set up process for proper management of analytical waste and avoid generation of excess analytical waste, viii. Develop the methods to analyze multi-analytes or many parameters, instead of one analyte or parameter at a time. ix. Minimize energy consumption. x. Preference should be for the reagents obtained from renewable sources. xi. Avoid or replace toxic reagents. xii. Increase the safety of the operator with better processes or methods.

The analysis starts with sample treatment and its preparation for further separation into components. These separated components are then detected and quantified for their identification. In a broader sense, analysis can be considered to get involved in following steps (Figure-4).

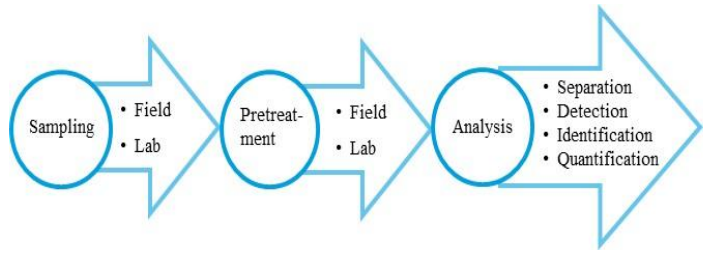

Figure-4: Main steps involved in chemical analysis.

Each must be executed correctly for the analytical results to be accurate**.** Although, the modern analytical instrumentation has many advancements, but all these steps are required to agree on green analytical chemistry principles. The principles have to be met while greening the analytical methods, in terms of elimination of hazardous chemical substances, energy-friendly, and management towards the prevention of waste[10,13]. The analytical techniques in which reagents and solvents are limited (calculated per one analytical cycle) and can be considered as environmental friendly are[12] i. Solid-phase extraction, ii. Accelerated solvent extraction, iii. Solid-phase microextraction, iv. Liquid-liquid micro-extraction, v. Micro-extractions, vi. Sono extraction, vii. Extraction using supercritical fluids, viii. Soxhlet extraction, ix. Distillation under vacuum, x. Membrane extraction.

Development of analytical instrumentation, miniaturization of analytical devices, reducing the analysis time etc. are important aspects of GAC. In many cases, it is necessary to carry out many operations, which requires a large quantity of solvents for extraction, and reagents to make the sample amenable to the instrument, resulting in a lot of waste generation and loss of analyte. Hence, application of alternative solvents and solvent-less extraction techniques are considered as the primary approaches to be in line with GAC principles. Analysis via green; instrumentation, sample preparation, extraction, sampling, micro and nanotechnology, chromatography, control methods, sub and supercritical fluid technology, catalysts, reagents, are the few approaches[14,15].

Organic solvents used in many syntheses are a great threat. They pollute the environment via leakage and volatilization i.e., volatile organic compounds (VOCs). Supercritical fluids (SCFs) usage in chemical process is increasing due to its better properties with varied temperatures and pressures.

There are SCFs, used for dissolving many compounds and are in great use for insoluble matrices/reactions. However, carbon dioxide (sc-CO_2) and water (sc-H_2O) are fulfilling the green chemistry needs from all aspects. A supercritical fluid (SCF) will dissolve many types of materials[16,17]. Hence, use of carbon dioxide or water in the form of SCF provides a substitute for an organic solvent. SCF-based processes have helped to eliminate the use of harmful organic solvents such as hexane and methylene chloride. The use of SCFs is increasing because of strict rules on VOCs and regulatory aspects on solvent residues in pharmaceuticals, and medical products. The fluid shows properties of both liquid (density) and gas (viscosity), hence these fluids provide exciting opportunities in various processing needs. They can be applied in several fields such as drug delivery, chromatography, synthesis, purification, and extraction. SCF processes are being commercialized in industries. Green solvents are environmentally friendly solvents or bio-solvents and are established as an alternative to toxic /hazardous solvents. Green solvents will enable to reduce the volatile organic contents, which directly impact the environment. The most popular green solvent is water, sc-CO_2, and room temperature ionic liquids. Commonly used SCF is carbon dioxide (CO_2) and referred as green solvant, since it is inert, low cost, non-toxic, non-flammable and available all the time with in high purity. It will be used in the temperature range of 40-60°C and it will not generate any toxic residues. Similarly the water, in the subcritical phase, can solubilise compounds that are tending to repel or fail to mix with water. Hence, hot compressed water can be used for the efficient extraction, processing, and in oxidation reactions. For specific applications, other compounds like ethane, propane, methanol, ethanol are also used in their supercritical phase.

In early 1980s, in the solvent category, new class of compound investigated, were named as ionic liquids[18-22]. An ionic liquid (IL) is a salt and will be in liquid form below 100°C, or even at room temperature. They are called "designer solvents", since they can be used at room temperature like an organic solvent. An important feature of ILs is immeasurably low vapor pressure and contains cation and anions. They are nonvolatile, thermally stable, and non-flammable. The chemical structures of RTILs can cause changes in properties such as water miscibility, viscosity, melting point, and density[23]. Alternative to common organic volatile solvents (VOCs), the ionic liquids are emerging as promising green solvent[24-26]. They can be reused and they have ability to dissolve a variety of organic and organometallic compounds. Due to their specific properties and environment-friendly behavior, RTILs are finding lots of applications in many of the analytical methods/ processes for separation, extraction etc.[27-31].

The other aspect in terms of hyphenation of instrumentation techniques/methodologies being employed for various analyses, can further make green analytical chemistry more purpose solving. The hyphenation of two or more techniques is done in such a way that the product of one can be used directly as input for others. This process will reduce solvent consumption and also waste generation. Thus problems or challenges being faced by an analytical chemist in the context of green chemistry can be solved by hyphenated techniques[32-34]. In the hyphenated instruments, the separation method is coupled with diverse selective and sensitive detection methods. Some of the popular hyphenated techniques based on chromatography are listed in Table-3.

Table-3: Some popular hyphenated techniques.

Separation	Hyphenation mode
Fast gas chromatography	Fast Gas chromatography- Mass spectrometry (F-GC-MS)
	Gas chromatography-Fourier transform infrared (GC-FTIR)
	Pyrolysis-Gas chromatography mass spectroscopy (Py-GC-MS)
	Gas chromatography -Inductively coupled plasma mass spectrometry (GC-ICP-MS)
Ultrafast liquid chromatography (UFLC)	Ultrafast Liquid chromatography-Mass spectrometry (UFLC-MS)
	Liquid chromatography- Fourier transform infrared (LC-FTIR)
	Liquid chromatography-nuclear magnetic resonance (LC-NMR)
Ion chromatography (IC)	IC-MS, IC-ICP-MS
Size exclusion chromatography (SEC)	SEC – ICP- MS
Thin layer chromatography	Thin layer chromatography- Mass spectrometry (TLC-MS)
	Thin layer chromatography-surface-enhanced Raman spectroscopy (TLC-SERS)

Based on the individuals requirement to analyse any particular analyte or the complex, the hyphenation technique will be designed. In the hyphenation technique, we can hook more than one detectors and accessories for separation for identification or composition analysis in single run. The hyphenation concept because of vast application and numerous advantages is continually developing and gaining more and more importance. The application areas include chemical, petrochemical, environmental, drugs and forensics, pharmaceutical, foods, flavour, fragrances, and polymer industries.

Pyrolysis-Gas Chromatography-Mass spectroscopy (Py-GCMS) is a useful hyphenation technique for the identification and characterization of any polymeric/complex solid materials[35,36]. Py-GCMS is advantageous for the direct determination without sample preparation, speed, no usage of solvent, small amount of sample, flexibility on temperature selection (100-1000°C) for identification and structural elucidation of a wide variety of components.

The elements such as arsenic, antimony, and thallium are toxic and thus have a substantial impact on the environment. Therefore, the determination and speciation of such elements have received attention, as these are at a very low level in the complex metrics. It is vital to know the level of toxicity for quality control of chemical compounds, medicines, and food products. The use of various hyphenated techniques (HPLC-ICP-MS, HPLC-ESI-MS, IC-ICP-MS etc.) have been discussed recently for speciation analysis of arsenic, antimony, and thallium, in different clinical, environmental and food matrices by R. Michalski et al.[37]. There will be many advantages like; low detection and quantification, minimum or no interference, accuracy, and reproducibility of the measurements. The approaches of implementation of the green chemistry principles into gas chromatography have been explained by Wardencki and Namiesnik[38]. High-Speed Gas Chromatography involves reduction of overall analysis time by using capillary columns of small inner diameter, fast temperature programming, and shorter columns. This can be attractive when results are needed in short time and routine samples are many. Korany et al[39], explained the importance of green chemistry criteria, evolution of GAC and advantages of hyphenation techniques. They also outlined the green chromatography, with some of its applications.

The hyphenated techniques offer several advantages like; fast composition / fingerprint / customer issue resolution / identification analysis with automation and minimum amount of samples in mg level, less sample preparation, enhanced reproducibility, less interference etc. Further, since separation and quantification achieved at the same time, this helps in the reduction of solvent consumption. Being a closed system produces less contamination and no or very low waste generation and ensure safety to the worker. With all these merits, hyphenated techniques can solve the challenges of GAC and have the potentials for greening the analytical methods. Since these are expensive, their potential for GAC is yet to be explored. However, new advent and instrument developments can hopefully become economical soon to be exploited for GAC methods.

Single-drop micro-extraction (SDME), is an emerging technique, for quantitative determination of many analytes. In SDME, a drop of solvent is used for the determination of VOC. Besides the advantage of high selectivity, useful quantitation, and low detection limits, it leaves no/less carryover (waste) and involves minimal sample preparation. SDME with these features could be explored for green aspects[40-43].

Tools of green analytical chemistry (GAC)

The analytical processes followed in different industries are different. Mostly processes depend on the type of the work, products, scale and environment. However, the goal is same for all the industries or any other sectors, while inventing, designing, developing and establishing the technologies, products and processes. Everywhere the goal is to reduce or eliminate the use and generation of toxic substances, and wherever possible utilize renewable resources. Although the analytical laboratories will generate less amount of waste, but the variety of chemical substances used are on higher side. The reagents for derivatization, solvents used for dissolution, isolation of impurities using solvent extractions, all these steps creates more challenges and issues to keep everything in control. But there is a way to reduce the waste generation, although unable to eliminate completely. To overcome these issues and to address health, safety and environmental concerns, the pharmaceutical industries have established the solvent selection guide[44-46]. These guides act as quick harmonised reference dictionary type of tool to proceed with better human and environment friendly solvents or for replacement of toxic solvents in the existing process /methods. After understanding all the points from the green chemistry view, few points are important in the industries from all the aspects; i. Safety of the scientist from the health aspects (carcinogens, mutagens etc.), ii. Safety of the process from hazardous and environment aspects (volatiles, odour etc.), iii. Regulatory aspects (ground water contamination, ozone depletion, laws, compliance etc.).

In addition, the analytical methodologies /process are aiming for new techniques with direct analysis (no solvent), solid-phase analysis, water usage etc. Further aim is to use renewable feedstock, biodegradable chemicals/solvents/reagents, low VOC chemical substances, easy to recycle and moderate toxic materials in analytical process. Similar to solvent guide, reagent guides will enable and encourage the scientists to select the user-friendly reagents for new methods or to replace with the existing toxic reagents[47]. The reagents used in the laboratory can pollute the environment so before using any reagents in the process/methods, their environmental impact has to be discussed and defined properly. There are different tools and techniques available to evaluate the impact on environmental and “greenness” of analytical methodologies.

Among many, the life cycle assessment (LCA) is one of the well-established tool. The objective of this tool is to assess the environmental impacts in all the stages during life-cycle of a commercial product, process, or service. The aim is to evaluate the greenness of solvents, chemicals, reagents used in the process[48,49]. Many of the guidelines or the tools are established, developed and implemented by United States along with environmental protection agency, industries, government, other sectors and other countries. The one important guide or the tool is Toxics Release Inventory list; it will include chemical substances that cause carcinogenic, chronic and toxic on both living organisms and environment. Till 2019, the list of toxic chemical substances added to this list are 767 (individual toxic chemicals) and 33 the toxic categories of different chemicals. Every year the list will be changed, since the new chemicals or the categories of chemicals will be added accordingly. Other one is National Environmental Methods Index (NEMI), it is kind of data base which includes; methods, protocols, statistical understanding and procedures. At each stage to look in to the contaminants, toxic waste, pollutants etc., the scientists can refer this database and find out the suitable data to proceed further with better and proper decisions.

The concept of Eco-scale is another procedure to evaluate the analytical process/methods. If the method or the process is deviating from the green concepts/parameters, then to evaluate and catch those easily with some fine, this tool is very useful. Another tool recently proposed is, Green Analytical Procedure Index (GAPI), it is depending on the previously mentioned guides/tools, both NEMI and Eco-Scale. This tool is used to verify the entire process in the analytical methods, starting to end.In GAPI, a specific symbol will be used to evaluate and quantify the environmental impact involved in each step of an analytical methodology. The green color indicates low impact on environment, yellow indicates medium impact and red represents high impact. Based on these indications, scientists can rethink, redesign and work towards right direction while developing the analytical methodologies. Few other similar tools to evaluate the procedures for their environmental impact are; Technique for Order of Preference by Similarity to Ideal Solution (TOPSIS), Preference Ranking Organization Method for Enrichment Evaluations (PROMETHEE), Environmental Assessment Tool (EAT), analytical method volume intensity (AMVI) to evaluate safety, health, and environmental factors[50-55].

Examples of green analytical chemistry

Some of the illustrative examples mentioned in Table-4, explain how the analytical methodologies and techniques used the concept of green chemistry and applied in many fields[8]. There is no harmful or toxic substance released in these techniques and very limited amount of chemicals are used, hence waste generation also reduced. These types of environment friendly methods are in need in the scientific community with great extent[56-58].

Table-4: Some examples of green alternative methods in analytical chemistry.

Determination	Conventional method	Green method
Mercury (Hg) in soils	Spectrometry based method Advantage : Simple and fast Disadvantage: Consumes reagents, produces wastes	Solid sampling GF-AAS (Graphite furnace -Atomic absorption spectrometry) Advantage: Direct, cost-effective, fast, useful for screening, Disadvantage: Analyte loss can happen due to volatilization
Lead in water	GF-AAS Advantage: Sensitive and accurate Disadvantage: Consumes reagents, produces wastes, time consuming and costly	Stripping voltammetry Advantage: Sensitive with low detection limits, fast, inexpensive, reliable Disadvantage: Interference with other metals
Nitrate in tap water	HPLC (High performance liquid chromatography) Advantage: low cost and fast, require small quantity of sample, sensitivity, accuracy & selectivity are good Disadvantage: Repeatability issues and reagents consumption is high	Microchip electrophoresis Advantage: Sample volume is low, significant reduction in reagent & energy, analysis is fully automated and fast Disadvantage: There are challenges in reproducibility and sensitivity
Bisphenol-A in waste water	GC-MS (Gas chromatography-mass spectrometry) Advantage: Both selectivity and sensitivity are excellent, detection limit and accuracy is also good Disadvantage: Sample treatment is very tedious and involves multistep with toxic reagents, end up with large amount of wastes	Electrochemical sensor Advantage: The sensitivity, accuracy, selectivity are excellent, very fast, energy consumption is low and cost effective Disadvantage: Reproducibility issues
Total petroleum hydrocarbons in soils	GC-FID (Flame ionization detector) Advantage: Detection limit and sensitivity is excellent for broad range of hydrocarbons, also cost is low Disadvantage: Resolution is not good, technique is	Hand-held FTIR (Fourier transform infrared spectrometry) Advantage: In-situ method, fast and nondestructive without any sample treatment, no reagents consumed,

	destructive, involves toxic reagents, end up with toxic waste generation and consuming lot of time	cost-effective, Disadvantage: Saturation and useful for only screening purposes
Folic acid in pharmaceuticals	Spectrophotometry Advantage: Simple, fast, low cost Disadvantage: High detection limit, consumes reagents, produces wastes, colored product formed with instability.	Electrochemical biosensor Advantage: Very cost effective, needs small quantity of sample Disadvantage: Sensitivity is not good, needs lot of time for the preparation of immuno-reagents
Blood glucose	Spectrophotometer Advantage: Fast, user friendly and cost effective Disadvantage: Involves hazardous reagents and generating toxic waste, fast detector saturation	Biosensor Advantage: With the small sample can carry out in-situ analysis, economic Disadvantage: Lots of interferences, accuracy is not good

Several useful applications of GAC have been reported in diverse fields of research[59-63]. For instance, Carasek et. al. in his recent review has covered various aspects of supramolecular solvents (SUPRAS), deep eutectic solvents (DES), and switchable hydrophilicity solvents (SHS) and reported their uses for the extraction of different analytes from various matrices (food, biological and environmental)[59]. A green approach has been followed using ionic liquid in determination of trace metallic constituents in U matrix by ICP-OES which has resulted drastic reduction in organic waste burden and time of analysis as reported by S K. Jayabun[60]. Nuclear magnetic resonance (NMR) method has been demonstrated as green analytical method in metabolomics and proteomics analysis as it uses deuterated water (D_2O) as basic solvent (recognized green solvent by GSK)[61]. Sudha et. al. recently developed a method to capture and analyze aldehydes in diverse matrices using reagent activated cotton fiber which complies with green analytical chemistry principles like solvent reduction, waste generation, sample size, use of biodegradable substrate and cost-effective[62].

Metal-organic frameworks (MOFs) are being used in analytical chemistry for diverse applications like as sensors, as stationary or pseudo-stationary phases in chromatography techniques and as sorbents used for microextraction or extraction processes. Considering these potential applications, Rocío-Bautista et.al. presented a review on uses of MOFs within the framework of green analytical chemistry requirements[63]. Here the authors gave special emphasis on most critical issues like toxicity of neat MOFs and green approaches in their preparation. Molecularly imprinted polymers (MIPs) are also becoming very popular as these have extensive analytical applications in sensing, chromatographic separation, extraction and SPME. MIPs are also useful in quantification of inorganic and organic analytes from waste water, blood and urine. The properties of MIPs like mechanical/ chemical stability and re-usability meet the green chemistry concepts. Further to control waste generation and toxicity Madikizela et. al. have discussed the applications of computational tools and miniaturized techniques which fit well as green analytical chemistry requirement. In this review they have emphasized on green aspects in molecular imprinting technology inclusive from design to environmental applications[64]. With further developments on greener initiators and cross-linking monomers MIPs will attract more and more applications in chemical, biological/medical or food sectors.

Conclusion

The practice of green chemistry can decrease the amount of chemical waste released to the air, water, and land. This field is promised to be the future of all chemistry. With the main focus of this article, i.e., green analytical chemistry, it is realized that to make analytical methods as green, we need specific improvements through making use of green solvents, reagents, replacing or removing toxic reagents and extra energy. In the entire analytical process, like starting from sampling to treatment of analytical waste, all the necessary modifications are must in order to comply with green analytical chemistry principles. Further, different strategies could be useful in this direction like; use of the chemometric approach for reducing sample number, integrated systems, hyphenated techniques for analytical efficiency, and miniaturization of methods to reduce the hazard and waste. The principles of green analytical chemistry will provide required guidelines to make analytical laboratories greener.

In summary, to implement the GAC concept in the analytical laboratory in the true sense, the environmental impact and greenness of analytical methods and procedures are to be measured at every stage. Hence, the proper utilisation of green chemistry metrics/tools is necessary in all the stages. In addition, we need to develop new software and tools to evaluate greenness of different parameters and processes.

Acknowledgements

The authors would like to thank the leadership team of SABIC Research & Technology Center-Bengaluru, India, for their support to publish this work.

References

1. Anastas, P. T., & Warner, J. C. (1998). Principles of green chemistry. *Green chemistry: Theory and practice*, 29, 14821-42.

2. Williamson, T. C., & Anastas, P. T. (Eds.). (1998). Green chemistry: Frontiers in benign chemical syntheses and processes. Oxford University Press.

3. Mut Günzler, I. I., & Williams, A. (2001). Handbook of analytical techniques. *Evolution*, 1, 1-2.

4. Song J. & Han B. (2015). Green chemistry: a tool for the sustainable development of the chemical industry. *National Science Review*, 2(3), 255-256. https://doi.org/10.1093/nsr/nwu076

5. KARAGÖLGE, Z., & Bahri, G. Ü. R. (2016). Sustainable chemistry: green chemistry. *Journal of the Institute of Science and Technology*, 6(2), 89-96. https://doi.org/10.21597/jist.2016218851

6. Manahan, S. E. (2006). Green Chemistry and the Ten Commandments of Sustainability 2nd Ed, Chem. Char Research, Inc. Publishers Columbia, Missouri U.S.A. p-347-363. ISBN: 0-9749522-4-9

7. Wardencki, W., Curylo, J. and Namieœnik, J. (2005). Green Chemistry - Current and Future Issues. *Polish J. of Environ. Studies*, 14(4), 389-395.

8. Gałuszka, A., Migaszewski, Z., & Namiesnik, J. (2013). The 12 principles of green analytical chemistry and the Significance mnemonic of green analytical practices. *Trends in Anal. Chem.*, 50, 78–84. https://doi.org/10.1016/j.trac.2013.04.010

9. Ivankovic, A., Dronjic, A., Bevanda, A. M., & Talic, S. (2017). Review of 12 Principles of Green Chemistry in Practice. *International J. of Sustainable and Green Energy*, 6(3), 39-48.

10. Keith, L.H., Gron, L.U. and Young, J. L. (2007). Green Analytical Methodologies. *Chem. Rev*., 107(6), 2695−2708

11. Tobiszewski, M., Mechlińska, A., & Namieśnik, J. (2010). Green analytical chemistry—theory and practice. *Chemical Society Reviews*, 39(8), 2869-2878.

12. Curyło, J., Wardencki, W., & Namieśnik, J. (2007). Green Aspects of Sample Preparation--a Need for Solvent Reduction. *Polish Journal of Environmental Studies*, 16(1).

13. Koel, M. & Kaljurand, M. (2006). Application of the principles of green chemistry in analytical chemistry. *Pure Appl. Chem*., 78, 1993–2002. https://doi.org/10.1351/pac200678111993

14. Guardia, M.D. and Garrigues, S. (2020). Past, Present and Future of Green Analytical Chemistry. Green Chemistry Series No. 66 in Challenges in Green Analytical Chemistry: 2nd Edition Edited by Salvador Garrigues and Miguel de la Guardia The Royal Society of Chemistry.pp-1-18.

15. Kaya, S.I., Cetinkaya, A., & Ozkan, S.A. (2022). Green analytical chemistry approaches on environmental analysis. *Trends in Environ. Anal. Chem.* 33, e00157. https://doi.org/10.1016/ j.teac.2022.e00157

16. Sankula, K., Kota, S. and Nissankarrao, S. (2014). Supercritical Fluid Technology: Green Chemistry for the 21st Century. *The Pharma Innovation Journal*, 3(5), 19-24.

17. Caputo, G., Fernandez, I.G., Saldana, M.D.A., & Galia, A. (2013). Advances and Perspectives of Supercritical Fluid Technology. *J. of Chem.*, 13, 1-3. http://dx.doi.org/10.1155/2013/243653

18. Hayes, R., Warr, G.G., & Atkin, R. (2015). Structure and Nanostructure in Ionic Liquids. *Chem. Rev*., 115, 6357–6426. https://doi.org/10.1021/cr500411q

19. Jarosova, R., Wang, Y., Swain, G. M. and Blanchard, G. J. (2018). Ionic Liquids. A Unique and Useful Class of Materials. *Chem. Educator*, 23, 265–272.

20. Wilkes, J.S. (2002). A short history of ionic liquids--from molten salts to neoteric solvents. *Green Chem*., 4, 73-80. https://doi.org/10.1039/B110838G

21. Pham, T. P. T., Cho, C. W., & Yun, Y. S. (2010). Environmental Fate and Toxicity of Ionic Liquids: A Review. *Water Res*., 44, 352−372. https://doi.org/10.1016/j.watres.2009.09.030

22. Ho, T. D., Zhang, C., Hanto, L.W., & Anderson, J. L. (2014). Ionic Liquids in Analytical Chemistry: Fundamentals, Advances, and Perspectives. *Anal. Chem*., 86, 262−285.

23. Pandey, S. (2006). Analytical applications of room-temperature ionic liquids: A review of recent efforts. *Analytica Chimica Acta*, 556(1), 38-45. https://doi.org/10.1016/j.aca.2005.06.038

24. Kharissova, O.V., Kharisov, B.I., Oliva González, C.M., Méndez, Y.P. & López, I. (2019). Greener synthesis of chemical compounds and materials. *R. Soc. Open Sci.* 6, 191378. http://dx.doi.org/10.1098/rsos.191378

25. Tobiszewski, M., Mechlinska, A., Zygmunt, B., & Namiesnik, J. (2009). Green analytical chemistryin sample preparation for determination of trace organic pollutants. *Trends in Anal. Chem.*, 28(8), 943.

26. Polyakova, Y. and Row, K.H. (2007). Analysis of linear regressions applied to water-methanol eluents modified with ionic liquid. *J. Liq. Chromatogr. Related Technol.*, 30, 2557-2573.

27. Liu, J. F., Jonsson, J. A. and Jiang, G. (2005). Application of ionic liquids in analytical chemistry. *TrAC, Trends Anal. Chem*., 24, 20-27.

28. Antonio, V. H., Javier, H., & Miguel, A. R. (2008). Ionic liquids as mobile phase additives for the high performance liquid chromatographic analysis of fluoroquinolone antibiotics in water samples. *Anal. Bioanal. Chem*, 392, 1439-1446. https://doi.org/10.1007/s00216-008-2442-9

29. Mandal, S., Swagata, M., Ghosh, S. K., Pintu Sar, Ghosh, A., Saha, R., & Saha, B. (2016). A review on the advancement of ether synthesis from organic solvent to water. *RSC Adv.,* 6, 69605–69614.

30. Marsh, K. N., Boxall, J. A. & Lichtenthaler, R. (2004). Room temperature ionic liquids and their mixtures, a review. *Fluid Phase Equilibr*., 219(1), 93-98. https://doi.org/10.1016/j.fluid.2004.02.003

31. Villa, R., Alvarez, E., Porcar, R. Eduardo, G.V., Luis, S.V. & Lozano, P. (2019). Ionic liquids as an enabling tool to integrate reaction and separation processes. *Green Chem*., 21, 6527.

32. Phalke, P. and Kavade, S. (2013). Review on Hyphenated Techniques. *Internat. J. of Chem. Stud.*, 1(3), 157-165.

33. Devi, T., Rani, T., & Pravalika, P. (2016). A Review on Hyphenated Separation Techniques Used in Pharmaceutical Analysis. *IOSR J. of Pharmacy and Biological Sci.*, 11, 65-74. DOI: 10.9790/3008-1106026574

34. Patel, K. N., Patel, J. K., Patel, M. P., Rajput, G. C., & Patel, H. A. (2010). Introduction to hyphenated techniques and their applications in pharmacy. *Pharmaceutical methods*, 1(1), 2-13.

35. Kusch, P. (2012). Pyrolysis-gas chromatography/mass spectrometry of polymeric materials. Advanced Gas Chromatography-Progress in Agricultural, Biomedical and Industrial Applications, Germany.

36. Yuzawa, T., Watanabe, C., Nemoto, N., & Ohtani, H. (2013). Rapid evaluation of photo, thermal and oxidative degradation of high impact polystyrene by a xenon lamp-based online ultraviolet irradiation-pyrolysis-GC/MS system. *Polym. Degrad. and Stab.*, 98(2), 671–676. http://id.nii.ac.jp/1476/00005780/

37. Michalski, R., Szopa, S., Jablonska, M. & Lyko, A. (2012). Application of Hyphenated Techniques in Speciation Analysis of Arsenic, Antimony, and Thallium. *The Scientific World J*., Article ID 902464, 1-17.

38. Wardencki, W. and Namiesnik, J. (2002). Some Remarks on Gas Chromatographic Challenges in the Context of Green Analytical Chemistry. *Polish J. of Environ. Studies*, 11, 185-187.

39. Korany, M.A., Mahgoub, H., Haggag, R.S., Ragab, M.A.A. & Elmallah, O. A. (2017). Green chemistry: Analytical and chromatography. *J. of Liq. Chromat. & Related Technol*., 40(16), 839-852.

40. Jain, A., Pillai, A.K.K.V., Sharma, N., & Verma, K. K. (2010). Headspace single-drop microextraction and cuvetteless microspectrophotometry for the selective determination of free and total cyanide involving reaction with ninhydrin. *Talanta*, 82, 758-765.

41. Sharma, N., Jain, A., Singh, V.K. & Verma, K. K. (2011). Solid-phase extraction combined with headspace single-drop microextraction of chlorophenols as their methyl ethers and analysis by high-performance liquid chromatography-diode array detection. *Talanta*, 83, 994–999. https://doi.org/10.1016/j.talanta.2010.11.003

42. Hakkarainen, M. (2010). Multiple headspace single-drop micro-extraction for quantitative determination of lactide in thermally-oxidized polylactide. *Polym. degrad. and stab.*, 95, 270-273.

43. Sharma, N., Pillai, A.K.K.V., Pathak, N., Jain, A. & Verma, K.K. (2009). Liquid-phase microextraction and fibre-optics-based cuvetteless CCD-array micro-spectrophotometry for trace analysis. *Anal. Chim. Acta* 648, 183–193. https://doi.org/10.1016/j.aca.2009.07.006

44. Prat, D., Haylera, J. and Wells, A. (2014). A Survey of Solvent Selection Guides. *Green Chem*., 16, 4546-4551.

45. Alfonsi, K., Colberg, J., Dunn, P. J., Fevig, T., Jennings, S., Johnson, T. A., Kleine, H. P., Knight, C., Nagy, M.A., Perry, D.A., & Stefaniak, M. (2008). Green chemistry tools to influence a medicinal chemistry and research chemistry based organisation. Green Chem. 10, 31-36. https://doi.org/10.1039/B711717E

46. Alder, C.M., Hayler, J.D., Henderson, R.K., Redman, A.M., Shukla, L., Shuster, L.E. & Sneddon, H.F. (2016). Updating and further expanding GSK's solvent sustainability guide. *Green Chem*., 18, 3879

47. Adams, J. P., Alder, C. M., Andrews, I., Bullion, A. M., Campbell-Crawford, M., Darcy, M. G., ... & Walker, M. D. (2013). Development of GSK's reagent guides–embedding sustainability into reagent selection. *Green chemistry*, 15(6), 1542-1549.

48. Armenta, S., Garrigues, S., Guardia, M. D. & Turrillas, F.A.E. (2018). Green Analytical Chemistry. *Encyclopedia of Analytical Science*, 3rd Edition, 1-3. https://doi.org/10.1016/B978-0-12-409547-2.13980-0

49. Armenta, S., Garrigues, S., Turrillas, F.A.E, & Guardia, M.D. (2019). Green extraction techniques in green analytical chemistry. *Trends in Anal. Chem.*, 116, 248-253. https://doi.org/10.1016/j.trac.2019.03.016

50. Tobiszewski, M. (2016). Metrics for green analytical chemistry. *Analytical methods*, 8(15), 2993-2999.

51. Tobiszewski, M., Marć, M., Gałuszka, A., & Namieśnik, J. (2015). Green chemistry metrics with special reference to green analytical chemistry. *Molecules*, 20(6), 10928-10946.

52. Saroj, S, Shah, P., Jairaj, V. & Rathod, R.. (2018). Green Analytical Chemistry and Quality by Design: A Combined approach towards Robust and Sustainable Modern

Analysis. *Current Anal. Chem.*, 14, 367 – 381. http://dx.doi.org/10.2174/1573411013666170615140836

53. Martínez, J., Cortés, J.F., & Miranda, R. (2022). Green Chemistry Metrics, A Review. *Processes* 10, 1274. https://doi.org/10.3390/pr10071274

54. Derbenev, I. N., Dowden, J., Twycross, J., & Hirst, J. D. (2022). Software tools for green and sustainable chemistry. *Current Opinion in Green and Sustainable Chemistry*, 100623.

55. Sajid, M., & Płotka-Wasylka, J. (2022). Green analytical chemistry metrics: A review. *Talanta*, 238, 123046. https://doi.org/10.1016/j.talanta.2021.123046

56. Bryan, M. C., Dunn, P. J., Entwistle, D., Gallou, F., Koenig, S.G., Hayler, J.D., Hickey, M.R., Hughes, S., Kopach, M. E., Moine, G., Richardson, P., Roschangar, F., Steven, A., & Weiberth, F.J. (2018). Key Green Chemistry research areas from a pharmaceutical manufacturers' perspective revisited. *Green Chemistry*, 20(22), 5082-5103.

57. Pena-Pereira, F., Lavilla, I. & Bendicho, C. (2021). Greening sample preparation: An overview of cutting edge contributions. *Curr. Opin. Green Sustain. Chem.*, 30, 100481. https://doi.org/10.1016/j.cogsc.2021.100481

58. Billiard, K.M., Dershem, A.R., & Gionfriddo, E. (2020). Implementing Green Analytical Methodologies Using Solid-Phase Microextraction: A Review. *Molecules*, 25(22), 5297. https://doi.org/10.3390/molecules25225297

59. Carasek, E., Bernardi, G., Morelli, D., & Merib, J., (2021). Sustainable green solvents for microextraction techniques: Recent developments and applications. *J. Chromatography A* 1640.

60. Jayabun, S., Pathak, S., & Sengupta, A. (2021). Analytical application of ionic liquid in determination of trace metallic constituents in U matrix by ICP-OES: A'green' approach for drastic reduction in organic waste burden and time of analysis. *Journal of Molecular Liquids*, 343, 117584. https://doi.org/10.1016/j.molliq.2021.117584

61. Mielko, K. A., Pudełko-Malik, N., Tarczewska, A., & Młynarz, P. (2021). NMR spectroscopy as a "green analytical method" in metabolomics and proteomics studies. *Sustainable Chemistry and Pharmacy*, 22, 100474.

62. Tantry, S., Tharpa, K., Kumar, A., Kumar, A., & Thimmappa, B. H. S. (2021). Reagent Activated Cotton Fiber for Rapid Determination of Aldehydes in Diverse Matrices. *Nature Environment & Pollution Technology*, 20(3).

63. Rocío-Bautista, P., Taima-Mancera, I., Pasán, J., & Pino, V. (2019). Metal-organic frameworks in green analytical chemistry. *Separations*, 6(3), 33.

64. Madikizela, L. M., Tavengwa, N. T., Tutu, H., & Chimuka, L. (2018). Green aspects in molecular imprinting technology: From design to environmental applications. *Trends in Environmental Analytical Chemistry*, 17, 14-22.