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# The ten principles of green sample preparation

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ABSTRACT

The ten principles of GSP are presented with the aim of establishing a road map toward the development of overall greener analytical methodologies. Paramount aspects for greening sample preparation and their interconnections are identified and discussed. These include the use of safe solvents/reagents and materials that are renewable, recycled and reusable, minimizing waste generation and energy demand, and enabling high sample throughput, miniaturization, procedure simplification/automation, and operator's safety. Further, the importance of applying green metrics for assessing the greenness of sample preparation methods is highlighted, next to the contribution of GSP in achieving the broader goal of sustainability. Green sample preparation is sample preparation. It is not a new subdiscipline of sample preparation but a guiding principle that promotes sustainable development through the adoption of environmentally benign sample preparation procedures.


## 1. Introduction

Green Chemistry has emerged in the 1990s as a way that the skills, knowledge, and talents of chemists can be used to avoid threats to human health and the environment in all types of chemical processes [1]. A year after its introduction, Paul Anastas recognized the crucial role of analytical method development and assigned Green Analytical Chemistry (GAC) as an emerging area in Green Chemistry, relevant to the research arena and the commercial sector [2]. Analytical Chemistry has two distinct and contradictory roles in Green Chemistry: it contributes to protect the environment by evaluating the impact of chemical activities, and, at the same time, may contribute to further environmental problems mainly due to the quantities of hazardous substances used/generated throughout an analytical procedure and the high energy demand. GAC aimed to redefine and reevaluate analytical methods by addressing safety of solvents/reagents, toxic laboratory waste generation, workers' safety, and energy efficiency.

A chemical measurement procedure comprises several steps, summarized as sampling, sample preparation, analytical measurement, and data evaluation. During the sample preparation step, samples are frequently converted to a form compatible with the instrument used for analysis, or cleaned up from interfering matrix components. In other cases, sample preparation involves analyte enrichment to meet the sensitivity needs of the analytical method [3]. Early sample preparation methodologies were tedious, time-consuming, and, more importantly, expended large quantities of resources that resulted in the generation of hazardous laboratory waste. Back then, sample preparation represented a major source of the total negative impact of analytical

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methodologies on the environment and was therefore considered central to achieve the Green Chemistry goals. To exemplify this, in the first report by Paul Anastas [2] describing the role of analytical methodology development in Green Chemistry, three illustrative examples were given, two of which focused on the negative impact of traditional sample preparation techniques on the greenness of the overall analytical method. However, the same report further discussed improvements achieved when replacing these methods with contemporary ones. The importance of sample preparation in settling greener analytical methods continued to be the focus of subsequent studies [4–6] up until 2013 when Gałuszka et al. [7] proposed 12 principles as general guidelines for greening analytical methods. In this approach, the first principle suggested applying direct analytical techniques to avoid sample preparation. Furthermore, the same report concluded that any "green" action taken during the sample preparation step (e.g., minimal use of energy, safety for operator, use of non-toxic reagents or reagents from renewable source) was impacting negatively accuracy, precision, selectivity, sensitivity, and detectability of the analytical process [7]. This was a not well-reflected assumption, especially when considering the analytical performance of mature sample preparation technologies available at that time. For example, solid-phase microextraction (SPME), a solventless and reagentless sample preparation method, performed substantially better than direct analytical techniques and could also be used for sampling complex samples [8].

The first principle of GAC is commonly misinterpreted and creates the false impression that omitting the sample preparation step is a green approach, fully neglecting the "green" technological advances in the field. It also does not take into account cases where direct analysis is not an option and conversion into a form suitable for analysis is needed (e.g., solid and other complex samples such as food or biological samples). Moreover, the "dilute-and-shoot" approach, where samples are diluted by factors typically ranging from 1:1 to 1:100 [9,10] and then directly submitted to analysis, leads to a detriment in the sensitivity of the method. Current technological advances in analytical instrumentation can partly overcome sensitivity and matrix-related problems associated with direct analysis (e.g., direct analysis of human fluids and tissues using desorption electrospray ionization mass spectrometry [11]). However, this approach typically requires the use of expensive instrumentation that is not readily available in many routine laboratories. Thus, the first principle of GAC cannot be fulfilled in many applications since sample preparation is essential for (i) the selective extraction of the target analyte(s) from complex matrices; (ii) preconcentrating the analyte(s) to achieve the required sensitivity in methods, (iii) transforming the sample into a form that is suitable for the measurement technique, and (iv) cleaning-up the sample.

The "exclusion" of sample preparation from GAC created a gap; instead of neglecting this step, efforts should have been devoted to fully defining it within the context of Green Chemistry and the GAC approach. After all, Green Chemistry was never about what to stop doing, but was always about invention and the things one can do better. Today, analytical scientists and practitioners face increasingly complex and interrelated problems both on-site and at the laboratory and, thus, a sample preparation step is commonly needed. At the same time, the current global environmental challenges that humanity faces impose transitioning in green practices. In this direction, (re) defining sample preparation within the context of Green Chemistry and GAC to address sustainability issues and promote the practice of green sample preparation (GSP) is more relevant than ever.

## 2. The ten principles of green sample preparation

The GSP approach provides clear and effective guidelines for the comprehensive and systematic improvement of the greenness of sample preparation methods and, ultimately, analytical methodologies. The fundamental difference between the GSP and GAC concepts is that the GSP approach builds around sample preparation, whereas GAC assigns a negative connotation to sample preparation and focuses on the measurement step (Fig. 1).

The ten principles of GSP are presented in Fig. 2. They are all directly related to sample preparation and describe the breadth of GSP, which is not the case in the GAC approach. They embed the required design to achieve greenness in sample preparation and minimize the impact on the environment and human health by setting guidelines on aspects dealing with solvents/reagents, materials, waste, energy demand, speed, miniaturization, procedure simplification/automation and operator's safety. At the same time, the GSP approach considers sample preparation as a step in the overall analytical chemical procedure and connects it to the sampling and measurement steps.

GSP sets goals, which are common to GAC but also have several distinctive features. Compared to the GAC approach, GSP introduces for the first time, the principle of sample throughput, which is related to the number of samples prepared per unit time (principle 6) i.e., the speed at which samples are processed. The GSP approach also considers that sample preparation often involves the use of solid materials (e.g., sorbents in (micro) extraction processes) and sets a principle (principle 3) that relates the greenness of the method to these materials being sustainable, from renewable sources but also having the ability to be used more than once (i.e., reusability). On the contrary, the GAC approach only considers the greenness of reagents (such as solvents, derivatization agents, pH and redox indicators), which in GSP is described in principle 2. GSP's principle 1, describing *in situ* sample preparation is also different from the one defined in the GAC approach. In GAC *in situ* measurement is connected to sampling and measurement and excepts sample preparation. On the other hand, GSP considers *in situ* sample preparation and connects it to *in situ* sampling and measurement. Furthermore, GSP focuses on sample preparation and at the same time views sample preparation as a step in the overall analytical chemical procedure. In this context, next to *in situ* practices, GSP also considers the greenness of the post-sample preparation configuration for analysis (principle 9). The remaining principles cover similar aspects to those found in the GAC approach (principles 2, 4, 5, 7, 8 and 10), but it should be emphasized that in the GSP approach these features are clearly adapted to the needs and requirements of sample preparation.

For convenience, the ten principles are presented in numerical order in the text. Nonetheless, readers should be aware that the principles do not need to be considered in a sequential way, as can be inferred from the different interconnections between the principles. It is equally important to note that the ten principles of GSP are not isolated but, similarly to GAC and Green Chemistry, are an integrated system of design (Fig. 3). Thus, the improvements in terms of GSP achieved by considering the recommendations for the fulfillment of a given principle can synergistically help to reduce the deficiencies associated with other interconnected principles. The key elements of GSP are summarized and exemplified below, emphasizing on the features and design that are necessary for greening sample preparation. The interconnections between principles (Fig. 3) can be clearly deduced from the information provided. For the sake of simplicity and to avoid redundancies, the interconnections are

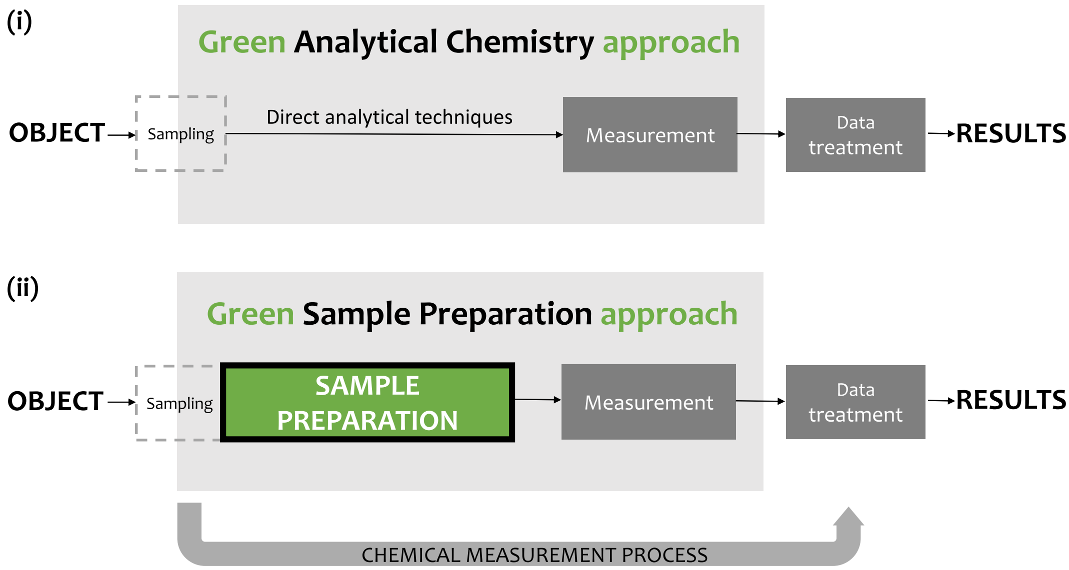


**Fig. 1.** Conceptual elements of the (i) GAC and (ii) GSP approaches.

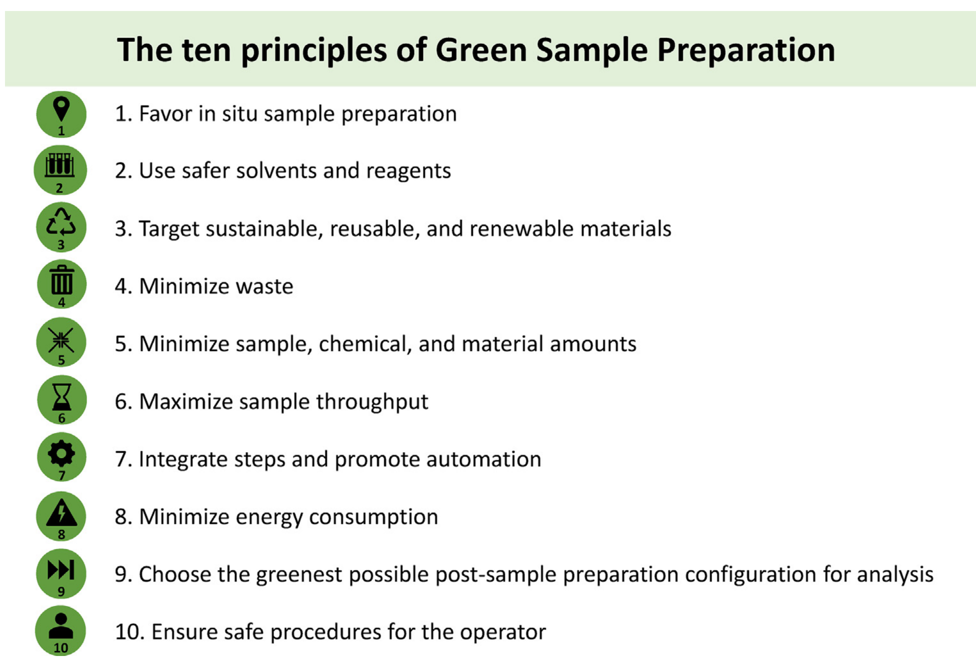


**Fig. 2.** The ten principles of Green Sample Preparation.

identified in parentheses by the number of the principle related to the one discussed.

**Principle 1. Favor *in situ* sample preparation**

This first principle of GSP favors *in situ* sample preparation and is related to the "portability" of the method, also connected to miniaturization (principle 5). The use of devices/materials for performing part or all sample preparation steps *in situ* saves time and energy (principles 6 and 8) as well as minimizes the amount of sample/materials to be transported to the laboratory for analysis and, as such, the amount of waste generated (principle 4). For example, solid-phase extraction (SPE) procedures for water analysis may require 1 L sample volumes to be transported back the laboratory for extraction and analysis. Because sampling sites are very often located far from the laboratory, samples may degrade during transport if not properly stored, and *in situ* sample preparation also minimizes the possibilities of this type of decomposition [12].

One option to perform *in situ* sample preparation is to have the device installed permanently on the investigated object with the overall operation being typically fully automated [13,14]. In other cases, *in situ* sample preparation integrates sampling and sample preparation with extracts being brought to the laboratory for analysis [12]. They may also involve the low- or even non-invasive *in vivo* sample preparation that is non-lethal and eliminates the need to remove living organisms from their habitat [15–17]. Examples of *in vivo* sample preparation include sorptive tape

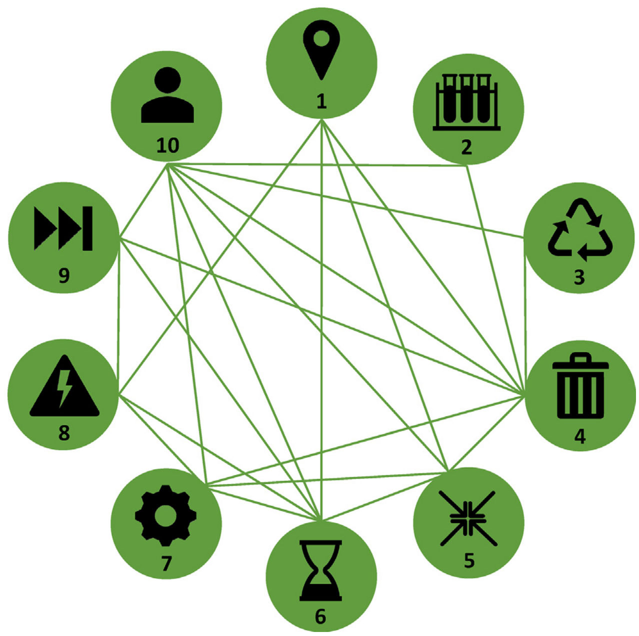


**Fig. 3.** The integrated system of GSP showing the interconnections between the ten principles.

extraction used to analyze the human skin surface [18], and SPME devices that allow plant [19], organs [20] or breath [21] analysis, as well as short-lived metabolites to be extracted from marine organisms on site and in a non-exhaustive way [22,23]. It should be noted that living organisms (plants or animals) can be used as (bio) samplers for the *in situ* determination of inorganic and organic contamination [12,24].

**Principle 2. Use safer solvents and reagents**

The nature of solvents and reagents used in sample preparation is a key aspect and a common limiting factor for the greenness of sample preparation methodologies. The second principle of GSP prevents the use of solvents and reagents that are hazardous to the environment and human health. This is an important trend in GSP that is also related to the reduction of waste generation and the protection of operators (principles 4 and 10). Instead, the use of solvent-free or virtually solvent-free approaches is promoted, along with the development and use of alternative greener solvents, i.e., supercritical fluids, deep eutectic solvents, liquefied gases, and some ionic liquid or bio-based solvents [25–27]. Surfactants and micellar solvents are also convenient alternatives owing to their negligible toxicity, volatility and inflammability, as well as low price, which render them suitable to replace dangerous organic solvents [28]. In addition, the use of water as an extractant [29] is very interesting from the point of view of GSP (i.e., in subcritical water extraction technique (SWE)). Notwithstanding, solvents should be assessed individually since differences in terms of greenness within a given family of solvents may occur. For example, certain ionic liquids [30] and bio-based solvents (e.g., terpenes) do not necessarily possess better properties than several conventional solvents in terms of Green Chemistry [31].

Further, some of the traditional transformations or derivatization processes carried out to adapt the sample to the measurement conditions use hazardous reagents leading e.g., to highly reactive intermediates or exothermic reactions, and should therefore be avoided. In this context, greening the derivatization step and wet digestion procedures should be promoted [32]. For example, the use of mineral acids in acid digestion can be reduced by applying microwave irradiation in closed vessels at a higher pressure. Moreover, the application of ultrasound energy may allow the use of less concentrated reagents. Several additional strategies that enable a significant reduction of the amount of acids used in digestion methods, such as wet digestion in flow systems, microwave-assisted UV digestion, and microwave-induced combustion, can have sustainability advantages [33].

**Principle 3. Target sustainable, reusable and renewable materials**

GSP targets the use of sustainable, renewable and reusable materials in sample preparation, which is related to waste minimization and protecting the operator (principles 4 and 10). A particularly relevant field of research in the sample preparation arena is focused on the synthesis and application of materials with advantageous properties for (micro)extraction processes. Selected representative examples include graphene and graphene oxide, nanoparticles (NPs) of different nature, metal-organic frameworks, molecularly imprinted polymers, or the materials used in fabric phase sorptive extraction [34–41]. Improved sorption capacity and selectivity, enhanced mechanical and/or thermal stability and reusability are some of the benefits offered by these materials. In particular, the third principle of GSP promotes reusable materials over those of disposable nature, since regenerating materials and using them more than once reduces the waste and generally results in low-cost methods. Representative examples include the solid sorbents used in microextraction that can be reused after thermal or liquid analyte desorption.

The use of materials whose fabrication involves reagents and solvents showing significant environmental, health, and safety issues should be prevented. Instead, efforts should be focused on replacing, whenever possible, petrol-derived chemicals (such as petroleum-derived polymeric materials) with bio-based alternatives in order to minimize the dependence on fossil reserves, next to increase their potential for biodegradability (e.g., aliphatic polyesters and polycarbonates) [42]. In this context, chemicals derived from bio-based resources have demonstrated their potential and applicability in sample preparation [43–46], and many of them can be repeatedly used in a miniaturized format whilst exhibiting similar or superior performance to other conventional materials [47]. Principle 3 also promotes the use of renewable materials. Examples include nature-based materials such paper [48] and lignocellulosic materials (e.g., cotton [49,50] or wooden tips [51]). It is noted that the use of solid waste as a sorbent in sample preparation is also promoted having the additional benefit of increasing its life-cycle [52–54].

**Principle 4. Minimize waste**

GSP ultimately seeks to eliminate waste generation and considers all related actions as key elements inextricably linked to environmentally benign methods. This zero-waste objective is ambitious and has not been reached so far in most sample preparation procedures. According to the AGREE metric approach used for evaluating the greenness of an analytical procedure, the maximum possible score (i.e., the top level of greenness) in the criterion related waste generation is achieved when the amount of waste is equal to or lower than 0.1 g (mL). In comparison, 100 g (mL) of waste would yield 10% of the maximum score for this criterion [55]. The AGREE evaluation tool considers as waste all the liquid or solid reagents, the solvents, acids or bases used, also taking into account all consumables and non-reusable devices next to the mass/volume of the sample if this may be or become hazardous. It is important to highlight the environmental impact of disposable plastics being used in sample preparation, with some of these methods substantially relying on such materials/devices. GSP promotes reducing their use and, whenever possible, switching to greener alternatives (e.g., using glass containers and tools) or reusing them.

Solvents and other chemicals (such as acids and bases and derivatization agents) employed in e.g., extraction, digestion, and/or derivatization steps are the main sources of chemical waste generation in sample preparation (principle 2). The elimination or reduction of solvent consumption is possible by e.g., using safe materials (principle 3) instead of solvents for extracting analytes or adopting microextraction-based methods (principle 5). For example, SPME when coupled to thermal desorption can be considered as a solventless technique [56]. In addition, automated or portable sample preparation procedures (principles 1 and 7) reduce the use of solvents and, as such, the generation of waste, further minimizing operator's exposure to chemicals (principle 10).

An alternative strategy to reduce waste is to make good use of resources by carefully designing the experiments so as to significantly reduce the number of experiments needed. For example, the use of chemometric tools (such as Plackett-Burman, central composite, Box-Behnken, or Doehlert designs, among others) during method development are valuable in terms of enabling method optimization based on a reduced number of experiments [57–60].

It is important to highlight that in addition to the goal of reducing the waste, proper treatment and disposal of the generated waste must always be considered. Suitable classification and management of waste next to proper recycling of the materials and substances is a must. It is noted that automated sample preparation systems may allow online waste treatment and recycling, expanding the lifetime of the solvents and reagents. On-line decontamination of analytical wastes via e.g., solvent recycling, degradation of toxic compounds and trace-element passivation should be considered instead of external waste treatment [6]. Finally, as will be discussed in principle 9, the choice of post-sample configuration for analysis may impact the amount of waste generated by the overall analytical procedure.

**Principle 5. Minimize sample, chemical and material amounts**

The greenness of sample preparation methods is also linked to the sample size/volume and the required amounts of chemicals as they generally have an impact on the amount of waste generated (principle 4). In this direction, substantial developments have been achieved toward the miniaturization of the different steps of the analytical process, and these efforts have been particularly profuse in the case of sample preparation [61,62]. Compared to their traditional counterparts, downscaled sample preparation methods have a greater potential to become portable or automated (principles 1 and 7) and generally result in faster procedures (principle 6) that minimize exposure risks for operators (principle 10). In some applications, the use of small sample sizes is mandatory (e.g., blood samples), but there are cases where samples are not expensive or scarce. It should be kept in mind that an excessive reduction of the sample size might deteriorate the analytical features of the overall analytical method without substantially improving the greenness of the method. It is also important to note that sample representativeness must always be ensured, and this condition can be challenged when the sample amount is substantially reduced [63,64].

As mentioned, the use of none or reduced amounts of chemicals and materials in sample preparation favors greener analytical methods. This is generally fulfilled when miniaturized approaches and/or reagent-less sample preparation techniques are used. Nonetheless, greatly reducing the amounts of chemicals used does not necessarily entail a green sample preparation method, especially when the chemicals considered are toxic. For instance, the use of hazardous solvents such as carbon tetrachloride, banned by the Montreal Protocol of substances that deplete the ozone layer [65], was common in certain liquid-phase microextraction approaches. It is generally appreciated that the sequence of actions 'remove – replace – reduce' should be applied with regard to the type and amount of chemicals used when greening sample preparation methods.

**Principle 6. Maximize sample throughput**

The treatment of a high number of samples per unit of time, translates into lower energy consumption (principle 8), exposure risks (principle 10), and analysis costs. There are two ways to maximize sample throughput: (i) accelerating the sample preparation step and many times adjusting it to the time needed for instrumental analysis (related to principle 9), and (ii) treating several samples in parallel. The latter is illustrated in the 96-well format used in parallel electromembrane extraction [66] or SPME [67]. In this format, long sample preparation times can be used, since the parallel treatment of several samples overall improves the sample turnaround time and generally lowers energy consumption.

There are different strategies to accelerate mass transfer in sample preparation [68] and these include: (i) applying an assisting field, (ii) using additives to enable phase transfer based on adsorption or partition, size-based classification with membranes, and/or chemical conversion, (iii) reducing the sample size (principle 5), and (iv) integrating steps and using automated procedures (principle 7). It should be reminded here that *in situ* sample preparation also reduces the overall sample treatment time (principle 1).

Regarding the use of an assisting field for accelerating the sample preparation step, different approaches have been reported, all of which have the additional advantage of being low-energy demanding. The assisting fields to use include ultrasound [69] or microwave [70] for accelerating extractions and microextraction processes and improving the efficiency of the procedure. Other alternatives include the use of an electric field in electromembrane extraction [71,72], vortex mixing [73], and combining various assisting fields [74].

**Principle 7. Integrate steps and promote automation**

Sample preparation methods commonly consist of multi-step procedures that can be time consuming and may result in material loss and increased expenditure of energy and chemicals. At the same time, multistep sample preparation methods can adversely affect the precision and accuracy of a method, especially when handling complex samples. The task of integrating steps in sample preparation procedures aims to achieve operational simplicity, increased sample throughput, and the additional benefits related to the reduced consumption of chemicals, materials and energy, generation of waste (principles 4, 5, 6 and 8) and risk of contamination [75]. Several examples of analytical methods that involve integrated steps (e.g., extraction, derivatization, and clean-up or extraction and injection) can be found elsewhere [76–78].

Automation of sample preparation (e.g., flow-based systems enabling online sample preparation [79–82]) is particularly advantageous in terms of Green Chemistry, GAC, and functionality. Several benefits can be identified in automated systems, including increased sample throughput, lower consumption of reagents and solvents, and, consequently, reduced generation of waste (principles 4, 5, 6 and 8). In addition, human intervention is significantly minimized and, therefore, handling mistakes are avoided, and operator's exposure to chemicals and risk of accidents are also reduced (principle 10).

**Principle 8. Minimize energy consumption**

GSP contributes toward sustainability goals and aims at reducing the energy consumption of sample preparation procedures. This principle is related to principles 1, 6, 7 and 9 as discussed in their description. A representative example of minimizing energy demand concerns the frequent use of convective heating systems comprising of temperature gradients for accelerating and/or enhancing analyte transfer (e.g., Soxhlet extraction of organics from soils). Such systems require heating the sample for extended times at elevated temperatures and in the presence of solvents. This type of sample preparation should be replaced by contemporary solventless extraction methods where heating is applied for much shorter times or can even be replaced by other means such as microwave heating [70], sonication [83] or vacuum sampling in cases where headspace (micro)extraction sampling is performed [84]. It should be mentioned here that, whenever possible, laboratories should pursue the use of renewable sources of energy, which have lower carbon footprints.

In some sample preparation procedures, part of the energy needed is used for separation processes, encompassing isolation of the extracting phase from the sample matrix (e.g., emulsion breakup), purification, and some type of cleaning. Systems designed to facilitate "self-separation" can decrease energy consumption and material usage when appropriately developed [85]. For example, solid or liquid sorbents with magnetic properties can be easily separated by applying a magnetic field after extraction is completed [86,87].

**Principle 9. Choose the greenest possible post-sample preparation configuration for analysis**

Sample preparation is part of a suite of steps in the overall analytical procedure. In many cases, multi-analyte instrumental methods of analysis are needed (e.g., in environmental and food analysis applications). In other cases, it is possible to use "green" analytical instrumentation, such as spectrophotometers, with a low-energy demand and low-waste generation (principles 4 and 8); although this type of analyses is potentially obstructed by problems of poor reproducibility, sensitivity, selectivity and matrix effects. At the same time, sample preparation methods are versatile in terms that a number of analytical and instrumental methods can be typically used to analyze the final prepared extract. For example, in stir bar sorptive extraction (SBSE), analytes can be desorbed either by thermal or liquid desorption [88]. In the former case, a thermo-desorption unit coupled to a gas chromatograph – mass spectrometer (GC-MS) will result in an energy-demanding analytical method [55]. In the latter case, desorption of analytes proceeds by ultrasound-assisted extraction (which is part of the sample preparation procedure) followed by high-performance liquid chromatographic (HPLC) separation of analytes with UV detection. In this case, HPLC is a less energy-demanding analytical technique, yet solvent use and waste generation are unavoidable (principle 4).

The greenness of a sample preparation method is inextricably linked to reducing the use of unsafe solvents and harmful chemicals for a particular chemical measurement procedure. It also includes proper selection of post-sample preparation configuration for analysis that suits the purpose in a given application and saves materials and energy (principle 8) while also reducing health and safety hazards for both the analyst and the environment (principle 10). The selection of the instrument to use for subsequent analysis typically depends on the needs of the user (e.g., detection limits and accuracy available for a given analyte) or is simply based on availability. In any case, the choice of the instrumental technique to be used is critical for the overall greenness assessment of the analytical method, and analysts should carefully select the greenest option. An example of employing different methods to solve similar problems is using capillary electrophoresis (CE) instead of HPLC [89], with CE offering flexibility, high-efficiency separations, low consumption of solvents, and shorter analysis times, and, depending on the application, CE can even be more effective than HPLC.

**Principle 10. Ensure safe procedures for the operator**

GSP seeks to reduce the environmental impact of sample preparation methods and, at the same time, protect operators from potential harm. To achieve the latter, sample preparation methods should be revised to minimize or eliminate chemical hazards and exposure risks as discussed earlier. To fulfill this requirement a multiapproach can be adopted that may include: (i) ensuring the use of less toxic or harmless natural chemicals in the procedure to decrease the exposure risks for the operator (related to principles 2, 3 and 4), and (ii) targeting the use of fast, automated or miniaturized sample preparation methods having integrated steps that minimize handling and operator exposure (principles 5, 6, 7 and 9). In general, the risk can be expressed as the product of exposure and hazard and, in this sense, reducing each of these two aspects (or both) would be of paramount importance toward safer procedures for the operator.

Operational hazards are not limited to chemical hazards and also include electrical, physical and biological hazards that need to be avoided. Electrical hazards tend to have more health and safety risks in laboratories than in other workplaces. These include but are not limited to electrical units positioned close to liquids or units directly used with sample preparation devices [90]. Physical hazards are another major concern for laboratory managers, with team members susceptible to physical injury if not following safe handling requirements. Representative examples include amongst others thermal hazards, exposure to radiation, handling of compressed gases and pressurized equipment. Finally, performing sample preparation on biological samples can involve biological hazards as these samples can carry diseases or hazardous allergens which could put the operators at risk. Proper storage and protection are key to prevent such biological emergencies during sample preparation procedures.

## 3. Green metrics and sustainable sample preparation

GSP promotes sustainable development in the laboratories by providing guiding principles for making sample preparation procedures more environmentally benign. Although the ten principles presented herein are clearly defined, they do not measure the environmental performance of sample preparation methods nor enable an objective comparison of two different procedures [91–93]. In GAC, green metrics were introduced to address the problem of "self-assigned" green analytical methods that exclusively focused on improving one particular principle of GAC and ignored other aspects [94]. Indeed, green metrics provide data on the true environmental impact of analytical methods and help claiming the sustainability of a method, harmonizing existing methods to new ones, or, even, identifying improvable aspects of an analytical method under development [93]. Hitherto, different metric tools of varying complexity and comprehensiveness have been reported [95]; the most popular being the analytical Eco-Scale [96], Green Analytical Procedure Index (GAPI and the recently reported ComplexGAPI) [97,98], RGB model [99,100], Analytical GREEnness Metric Approach (AGREE) [55] and hexagon-CALIFICAMET [101]. These tools are based on the incorporation of different criteria from the GAC point of view and generally provide easy-to-read pictograms that map the degree of compliance with evaluated criteria.

The motivation for using metrics is the expectation that quantifying technical and environmental improvements can render the benefits of new technologies more tangible, perceptible, or understandable. Despite being essential, green metrics were rarely used in Analytical Chemistry [93], and, only recently, they attracted the attention they deserve. Clearly, it is often under-appreciated that in order for a method to be claimed green, an assessment of greenness is necessary and should be provided. Whether optimizing or applying an analytical procedure, the use of green metrics is critical and should precede any analytical practice including that of sample preparation.

Green metric tools are dominated by the environmental impact of methods. However, for a development to be truly sustainable, several other aspects need to be considered. There are many different ways one can interpret the concept of sustainable development, but the core is an approach to development that balances different, and often competing, needs against an awareness of the environmental, social and economic limitations our society faces. Sustainable Chemistry should use resources, including energy, at a rate at which they can be replaced naturally, and the generation of waste cannot be faster than the rate of their remediation [42]. In essence, Chemistry is defined as sustainable if it contributes in a sustainable manner to sustainability [91]. The GSP approach is interrelated to the broader view of the fundamental role of Chemistry toward a sustainable society [91]. The environmental aspects of sample preparation have been extensively discussed so far, and for sample preparation to be sustainable the economic and societal aspects need to be considered. To this end, sample preparation methods should be cost-efficient, which is often related to high-throughput, fully automated systems or portable devices. In reality, the advances in sample preparation over the past decades have encompassed efforts in simplifying steps, miniaturization and automation, as well as the development of low-cost tools, which in turn, have reduced the costs of the methods and enabled economically sustainable progress in the field. In addition, a variety of low-cost and widely available and renewable materials and sorbents have been reported or being explored [48,49,51]. The use of such materials not only reduce the environmental and financial costs of sample preparation but also favor circular economy and contribute to a sustainable future [102,103]. At the same time, safer solvents and reagents are used and constantly introduced with the aim to reduce waste generation and, as such, the costs for their remediation. In practice, sample preparation is often considered a low-cost analytical practice, and this acted as a driver for intensive related research in universities and institutions based in developed as well as developing countries. Compared to other analytical subdisciplines, sample preparation does not require the use of expensive analytical instrumentation and as such, is not necessarily the practice of wealthy and powerful analytical laboratories; instead it is linked to some sort of “academic” equity [104].

It is generally accepted that the increasing awareness of the importance of sample preparation in an analytical procedure creates opportunities for new jobs and businesses, making it more relevant to society. In reality, the societal aspects of sustainable sample preparation are far more diverse and align with those of sustainable analytical chemistry. Meeting society needs requires its development in areas where there is a significant societal importance. This could imply anything from determining environmental effects of novel materials (e.g., nanoparticles in marine environments) or *in situ* assessment of reactions in engineering systems [93]. Indeed, sample preparation overcomes challenges associated with analysis (e.g., in analyzing trace amounts of chemicals in complex matrices), that are directly linked to critical issues such as food security and soil/air/water quality. It should be noted that most of such relevant research questions require multi-disciplinary efforts, which is considered in many cases as a challenge [105].

GSP complies with sustainable development, and greening the sample preparation protocols will contribute directly or indirectly in achieving the sustainable development goals (SDGs) established by the 2030 Agenda of the United Nations. The technological overlaps between the SDGs and green-sustainable sample preparation are “easy” to identify as sample preparation is relevant to a wide range of topics. Accordingly, GSP may contribute to good health and well-being (SDG 3), as the amount of hazardous chemicals released to the environment is reduced, and safer procedures for the operators are pursued, which is also related to improving the quality of work (SDG 8). The elimination of solvents and toxic reagents will have a positive impact on the quality of water (SDG 6), protect life below water (SDG 14), and life on land (SDG 15). Practicing sustainable sample preparation, i.e., reducing the generation of waste, using renewable and natural sorbents for extraction purposes, and recycling and reusing of materials, is related to responsible consumption and production (SDG 12). In addition, the use of materials from renewable sources and the low energy consumption are related to affordable and clean energy (SDG 7). The efficient use of energy, size economy, and reduction or elimination of waste will contribute toward sustainable cities and communities (SDG 11). Finally, adopting the GSP principles is also in line with SDG 13 aiming to combat climate change. Indeed, shifting laboratories towards carbon neutrality can help reducing greenhouse emissions and assist in the implementation of national climate plans. In this direction, the minimization of energy and emissions are also in line with the “Fit for 55” package presented by the European Commission on July 14, 2021, which refers to the at least 55% emission reduction target the EU has set for 2030, and aims to bring the EU's climate and energy legislation in line with the 2030 goal.

## 4. Concluding remarks

The first principle of GAC suggests eliminating sample preparation. Notwithstanding, removing this step is practically impossible for complex samples and when high sensitivity is needed. Thus, instead of omitting or neglecting this step, efforts must be placed in adopting a framework for green sample preparation. This work presents the 10 principles of GSP in a straightforward and clear fashion with the aim of providing a road map that can be helpful for the systematic development of greener sample preparation methods. Different important aspects are considered with the aim to minimize the environmental impact of sample preparation methods including promoting *in situ* over *ex situ* sample preparation, eliminating, replacing or minimizing harmful solvents and reagents, promoting the use of sustainable and renewable materials that can be reused and protecting the operator. GSP also aims at increasing sample throughput, minimizing energy consumption and waste generation, and promotes the use of the lowest possible amounts of resources to achieve timely analytical information. Next to miniaturization, the GSP approach also promotes portability, automation and integration of steps as enabling strategies.

At all times, analysts need to be aware of the hazardous and/or non-sustainable resources, products, processes, and systems they use and try to minimize them. Understanding the characteristics and physicochemical properties of chemicals, materials, analytes, and matrix is also essential for tuning experimental conditions in a sustainable manner. For example, in microextraction-based methods, analytes having a high affinity for the extracting phase will be efficiently extracted without wasting resources (e.g., extended sampling times or heating the sample). It should be stressed that the selection of experimental conditions will depend on the specific analytical problem faced and, therefore, optimal conditions are not necessarily, in every case, those that yield the highest analytical response. In this sense, compromise solutions can be determined to ensure the required sensitivity and selectivity, whilst using the minimum amount of resources. For instance, heating the sample can increase the sensitivity of a method, but if this level of sensitivity is not needed then the method wastes resources.

Based on the advances in sample preparation, a wide number of methodologies offer opportunities for the development of greener sample preparation methods while ensuring high analytical performance. Accordingly, the implementation of GSP principles can also improve the analytical characteristics of the overall analytical method. This is in contrast to GAC that faces the challenge to find a compromise between reducing the environmental impact of the methodologies without negatively impacting the analytical efficiency of the method, i.e., sensitivity, selectivity, accuracy, precision, robustness, and, in turn, the quality of the analytical information obtained.

In sample preparation, several meaningful and practical developments have been introduced, and analytical chemists have in hand a large variety of sample preparation methods to choose. Selecting the "right tool for the right job" is a very basic practice in sample preparation and analytical methods in general. Currently, decisions about methods are based on method performance and price. They should be complemented by a sustainability factor, which is a measure of how green the method is. In this context, analysts must always choose sample preparation technologies suited to the task at hand and provide metrics-based evidence that the selected procedure is the greenest option with a minimal impact on the environment and human health.

Hitherto, the greenness of sample preparation methods is assessed using metric tools anchored in the 12 principles of GAC. However, it is acknowledged that the philosophy of the GAC approach renders these metric tools inadequate for providing sufficient levels of accuracy and specificity and as such, gauging progress toward greening sample preparation. The wide range of parameters that influence the greenness of sample preparation creates the need to develop a metric system specific for sample preparation, which is the focus of ongoing investigations of the authors.

Current global challenges and stressors highlight the urgency in which sustainability issues must be addressed. The application of environmentally benign sample preparation methods is one of the social responsibilities of analysts as it aligns with pollution abatement and the principles of sustainable development. For this reason, reducing the environmental impact of sample preparation practices should be a priority for all researchers, practitioners, and routine analysts for the benefit of the environment, human health and society. Green sample preparation is sample preparation. It is not a new subdiscipline of sample preparation but a guiding principle toward sustainability.

Creating a list of the technological overlaps between the SDGs and green-sustainable sample preparation was indeed a straightforward task. The less obvious problem is the non-technical aspects of sustainability as discussed for Sustainable Chemistry in a recent report by Anastas and Zimmermann [104]. If sample preparation wants to contribute in achieving the power and potential of using Analytical Chemistry for achieving SDGs, then a number of challenges needs to be addressed in the future across all aspects of economics, society, policy, interdisciplinary engagement, equity, education, regulation, metrics, and awareness [104]. GSP alone, no matter how broad in reach and impact, is only an element for achieving sustainable development. Nonetheless, enabling and empowering the conduct and impact of GSP contributes toward a sustainable future for all.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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