



GREEN ANALYTICAL CHEMISTRY: SUSTAINABLE APPROACHES FOR SAMPLE PREPARATION AND METHOD DEVELOPMENT

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Abstract

Background: Green analytical chemistry is concerned with cutting or minimizing the quantities of hazardous materials used and produced in analytical work via advancements in chemical procedures, methods, or techniques

Aim: This research aims to quantify efficiency to determine which analytical tool is the most efficient in solvent use, time, recovery rate, and environmental friendliness among the above-listed tools.

Methods: The efficiency was measured for several factors including solvent use, time, recovery percentage, and effects on the environment for three sample preparation techniques. MAE used 5 mL solvent; SFE and SPME no solvent was used. Comparisons were made in terms of performance with the assessment of recovery rate. For chromatography, solvent volume, analysis time, resolution, and sustainability performance of UHPLC and HPLC were evaluated. In using UHPLC, 1 mL of solvent and 5 minutes per analysis were applied, while HPLC used 10 mL of solvent and took 20 minutes.

Results: According to the findings of the study, SPME exhibited the highest recovery rate of 92%, less time (15 minutes), and low environmental impact. Compared with the HPLC, the UHPLC had lower solvent demands, shorter analysis time (5 vs 20 min), better resolution (1.5 vs 1.2), and less impact on the environment.

Conclusion: Solid phase microextraction (SPME) was the most effective and energy-saving sample preparation method, and ultra-high-performance liquid chromatography (UHPLC) was the best chromatographic method as it was faster, more efficient, and environmentally friendly.

Keywords: Green chemistry, Supercritical Fluid Extraction, Solid-Phase Microextraction, Ultra-High-Performance Liquid Chromatography, Resolution

Introduction:

The ongoing metamorphosis in scientific fields to become environmentally sustainable has prompted changes in the approach to sample preparation analysis and other laboratory practices used in analytical chemistry. Green analytical chemistry is concerned with cutting or minimizing the quantities of hazardous materials used and produced in analytical work via advancements in chemical

procedures, methods, or techniques. This paper presents a brief literature evaluation of the current trends in the aspects of green sample preparation and green analytical method development. Sample preparation may be described as a section of analytical chemistry that involves the separation and identification of analytes from the sample matrix.[1,2]

Sample preparation methods include liquid-liquid extraction and Soxhlet extraction which use large volumes of dangerous solvents including chlorinated organics which are dangerous to the environment and human health. According to green chemistry principles, the sample preparation processes should be designed in such a way that the chemicals used are less hazardous, wastes generated are minimized, energy used is conserved and hazardous solvents are eliminated or reduced. Other green extraction techniques are ultrasound/microwave-assisted extraction, solid-phase microextraction, molecularly imprinted solid-phase extraction, and supercritical/sub-critical fluid extraction using CO² and water.[3]

These techniques reduce the use of organic solvents, capture energy by physical forces, and/or use extraction solvents that are not hazardous. Even further, dilute solutions of bio-derived solvents can also have green benefits of their own.[4] Further, progressing the objectives of sustainability is the ability to miniaturize the volumes of the analyzed samples. Concerning the method development of analytical methods, conventional high-performance liquid chromatography methods that use high volumes of toxic organic mobile phase are under reconsideration based on the priority of green chemistry.[5]

UHPLC-derived alternatives enhance analysis through the application of a smaller particle size column, which requires diminished volumes of solvents for usage while expressing improved resolution. HILIC which stands for Hydrophilic Interaction Liquid Chromatography employs high organic solvents which are very suitable for the separation of highly polar materials. Supercritical fluid chromatography excises organic solvent completely from the picture by replacing it with supercritical CO² modulated by organic solvent. SFC technology can improve the work scope speed and reduce the time needed for the analysis.[6]

Thin-layer chromatography (TLC) employs very small volumes of solvents for the preliminary sample separation, identity confirmation, and approximate concentration estimation at a relatively low cost of equipment. Used with mass spectrometry, direct analysis in real-time DART ion sources provides real-time analysis of samples in the open air at ambient conditions and does not require any sample preparation or chromatography though quantitative measurements pose a challenge. One of the critical goals in sustainability benchmarks to be achieved by analytical laboratories is the mindful minimization of solvent consumption and disposal. This goal can be attained by making underlying alterations in the method development and optimization stage based on proposed green analytical principles. Primary scouting experiments employ fast TLC that requires microliter samples instead of milliliters found in HPLC until the number of potential modes is reduced to a couple of the best chromatographic conditions. Instead of automatically switching to isocratic systems with highly organic mobile phases, attempts are made with gradient elutions, starting with lower organic DP's in the mobile phase.[7,8]

Transfer of a method from HPLC to UHPLC or from normal phase to HILIC sometimes means practical savings in solvent consumption. Labs can also dump used organic mobile phases to be concentrated in roto-evaporation units and then redistilled onsite thus recapturing solvents. Other advancements in analytical instrumentation engineering may create even better impacts for enhancing the environmental benchmarks for green laboratories.[9] Another new technology adopting the strategy of miniaturization of the whole system by reducing the inner diameters of columns and tubes to ≤ 2 mm minimizes solvent and sample requirements. There are various detection modes developed for micro flow rates such as LED-induced fluorescence, mass spectrometer, and many other detectors. As much as nano-flow liquid chromatography-mass spectrometry (nLC-MS) and capillary-flow chromatography-mass spectrometry (cLC-MS) setups claim higher sensitivities, there are drawbacks like blockage.[9,10]

Another innovative technology carries out chromatographic separations within the body of mass spectrometer vacuum-containing structures. Called in-vacuum chromatography-mass spectrometry

(IVC-MS), such a method employs a small-scale column nested within the inlet capillary of the mass spectrometer and removes solvents and gases inside the vacuum chamber. Microwave-assisted reactions, microscale calorimetry, infrared heating, and flow systems are the other green laboratory instruments and techniques relevant to one or the other steps in the analytical workflow. Microwaves use electromagnetic radiation to heat the substance and make it transfer reactions carried out by conductive or convective heat. Since microwaves interact with reactive species as well as their surrounding medium and not the vessel wall then there is faster as well as uniform heating achieved using a lesser amount of energy.[11]

Microscale calorimetry in turn reduces the necessary amount of sample for thermochemical determinations to milligrams in an anhydrous environment. Renewable-produced infrared heating can replace electrical heating mantle equipment. Finally, flow techniques execute reactions steadily, without interruption. Integration of telemetrics to monitor and operate analytical instrumentation from a distance in the future would also contribute to the establishment of optimal environmental burdens regarding transportation and commuting. The principles of green chemistry are applied in any relevant process or action of experimental analytical chemistry, guiding innovative, more sustainable concepts. In terms of green extraction techniques, sample preparation does not involve reducing, or minimizing the use of hazardous solvents through the advancement of techniques like different modes of stirring, the invention of a new extraction phase, and the introduction of nontoxic fluids like supercritical carbon dioxide or water in subcritical state.[12,13]

Green points involve the need for the use of low sample and solvent amounts through improved detection capabilities, optimized separations, or the combination of preparative and analytical stages in single systems. While there may be increased expenditure bearing the cost of instrumentation, there are benefits to the environment and a favorable economy in the long run. The evolution of best practices as the field moves beyond searching for analytes will be determined by method development in line with green analytical principles. Jointly, the growth of waste reduction will increase for analytical laboratories when operating under these principles which will advance the triple bottom line of economy, environment, and health for the public. In totality, there is no linear pathway to perfect green analysis, there is instead an approach where improvement and innovation can be attained in making the sample preparation and the quantization of chemical determination causing minimal harm to the environment. [14]

It is at the method development and optimization phases that many conscious decisions are required to minimize the solvent intensities, replace them with less toxic solvents, or employ simpler or more efficient analytical technologies without compromising the analytical performance and at the same time improve sustainability. A growing number of chemists understand green analytical chemistry as a scientific and social responsibility; newcomers miss the potential adverse environmental or financial implications if the status quo prevails. By converting common working processes into mental visions with visionary and responsible practices, the analytical chemistry field can alter the current norms for procedures and encourage novel developments of environment-friendly solutions.[15,16]

Material and Methods

Material

Sample Preparation Techniques

Microwave-Assisted Extraction (MAE)

Microwave-assisted extraction (MAE) is a type of sample preparation that employs microwave energy to improve the solvent extraction process. This work shows that the use of microwave energy has lowered the extraction time as well as the volume of solvent needed in comparison with the traditional methods of extraction. This technique was developed on the premise of elevating the kinetic rate by using microwave energy to warm up the solvents in contact with fixed sample bodies. From the setup above, several attributes of the extraction solvent, time and the microwave radiation power applied, and characteristics of the sample matrix were varied to optimize the process. Various solvents had varying abilities to absorb microwave radiation that affected the rate at which the preparations were heated. Faster extraction times of between a few seconds to a few minutes were achieved. The power

of the microwave was directly proportional to the temperature that was realized during the process. Sample matrix factors such as moisture content also affected the microwave heating behavior. In general, MAE was more efficient and environmentally friendly for sample preparation compared with conventional extraction techniques because of the redistributive nature of microwave energy in the extraction medium.

Supercritical Fluid Extraction (SFE)

Supercritical fluid extraction analytes use supercritical carbon dioxide as a solvent for extracting analytes and reducing organic solvent consumption. This technique functioned under situations whereby carbon dioxide was made to exceed its critical temperature of 311K and critical pressure of 730Kpa and was therefore considered as a supercritical fluid possessing both the properties of a gas and a liquid. Scholars used this supercritical CO² as a green solvent that had solvating capacities like hexane, and methanol, but it had diffusion rates and viscosity more like a gas. By adjusting the temperature and pressure of the SFE system, the solvent strength of the supercritical CO² thus extraction was fine-tuned for the analytes of interest within a specific matrix. Extraction periods ranged between 30 to 120 minutes where the investigators flowed the supercritical fluid through the solid sample and collected the solvent that contained the analyte in a separator downstream where the release of pressure from the CO² caused the analyte to precipitate. Compared to conventional extraction methods like the use of organic solvents in liquid form, SFE was faster and had the potential of not using hazardous organic solvents if the data was interpreted correctly.

Solid-Phase Microextraction (SPME)

SPME was a non-destructive extraction method of volatiles/ semi-volatiles without the use of any solvent. It was initially designed in the 1990s as an easy-to-perform and high-throughput technique for the extraction of analytes of interest from combinatorial biological matrices. The technique used a fused silica fiber where the extracting phase was a polymer or a sorbent material. For the extraction, the SPME fiber was plunged into the sample matrix in a liquid or gaseous state or withdrawn in the headspace above the sample matrix. The analytes oriented themselves into the coating on the fiber until the sample matrix and extracting phase were in equilibrium. The compounds of interest were concentrated on the small SPME fiber and can be desorbed and directly introduced into an analytical instrument such as GC for separation and identification. Sample characteristics such as fiber type, extraction time, and conditions of the sample were optimized based on the analyte of interest, matrix, and analysis goal. SPME offered a gentle and extraction-friendly approach to capturing volatile and semi-volatile compounds from samples.

Method Development

Green Chromatography Techniques

Ultra-High Performance Liquid Chromatography (UHPLC)

UHPLC refers to green chromatography that uses low volumes of solvent and which offers high levels of analysis in the shortest amount of time. The method was meant to yield better-performing and greener chromatographic separation. Several aspects of UHPLC include mobile phase constitution, flow rate, and the sort of column utilized which were tweaked to lower the volume of the solvent used per analysis. This technique used columns filled with small proportions, (sub-2 μ m) that allowed increased flow rates, and thus higher separation speed. Besides, chemistries of stationary phases including C18, C8, phenyl columns, and HILIC were investigated for methods development, as well as the mobile phases including various pH and the organic modifier of acetonitrile or methanol. This was because gradient elution methods were used conventionally to enable faster elutions for the analytes on the column. Mentioned flow rates were ranged from 0.2 to 1 mL/min. Apart from that, UHPLC was considered as the method allowing to minimization of the analysis times and solvent consumption compared to HPLC methods thus conforming to GC principles. This fast and sensitive method was used widely for pharmaceutical, biomedical, and other research applications.

Electrochemical Methods

Electrochemical techniques were adopted for field analysis, thereby minimizing sample shipment and generation of dangerous wastes. These methods included working electrodes, reference electrodes, and counter electrodes in an electrochemical cell sample solution. For the choice of working electrodes, Glassy carbon, Gold, Platinum, and Copper electrodes were used depending on the analyte being analyzed. An appropriate applied potential was then chosen and regulated through the potentiostat and electrochemical reactions such as oxidation or reduction on the electrodes took place. The current that was obtained was recorded and plotted to the concentration of the analyte. Many parameters such as several applied potentials and sample concentration were well controlled in the system. These electrochemical techniques offered rapid and portable analysis and also consisted of the chemical species. In general, electroanalytical methods offered certain benefits over conventional wet chemical techniques which entailed sample transport to different facilities and the generation of chemical byproducts – challenges that were eliminated when moving from off-site wet chemistry to on-site electrochemical analysis.

Results:

Comparison of Sample Preparation Techniques

Table 1 compares three sample preparation techniques: Some of the modern extractive techniques include microwave-assisted extraction (MAE), supercritical fluid extraction (SFE), solid phase microextraction (SPME), and the like. MAE employed 5 mL of solvent and optimization was done in 10 minutes with a recovery rate of 90%. It was to have a relatively small bearing on the environment. SFE did not require any solvent and took twenty minutes with an 85% recovery rate. It was characterized by a very low environmental footprint. Like SPME, no solvent was used in the extraction process and the method only took 15 minutes, thus having the highest extraction recovery at 92%. Same as in SFE, it had a very low level of environmental footprint. Taking into account the utilization of solvent's usage, SFE and SPME were the most versatile since they did not include any use of solvent at all. SPME took the shortest time of 15 minutes to prepare the samples. It also gave the overall highest recovery rate of 92% for the extract compared to 90% of MAE and 85% of SFE. Using these parameters, it was found that SPME was the best all-around method with the highest recovery rate, short extraction time, and nearly negligible environmental effect. SFE followed closely behind. MAE needed solvent and was therefore more of an environmental burden but the recovery percentage was good.

Table 1: Comparison of Sample Preparation Techniques

Method	Solvent Usage (mL)	Time (min)	Recovery (%)	Environmental Impact
Microwave-Assisted Extraction (MAE)	5	10	90	Low
Supercritical Fluid Extraction (SFE)	0	20	85	Very Low
Solid-Phase Microextraction (SPME)	0	15	92	Very Low

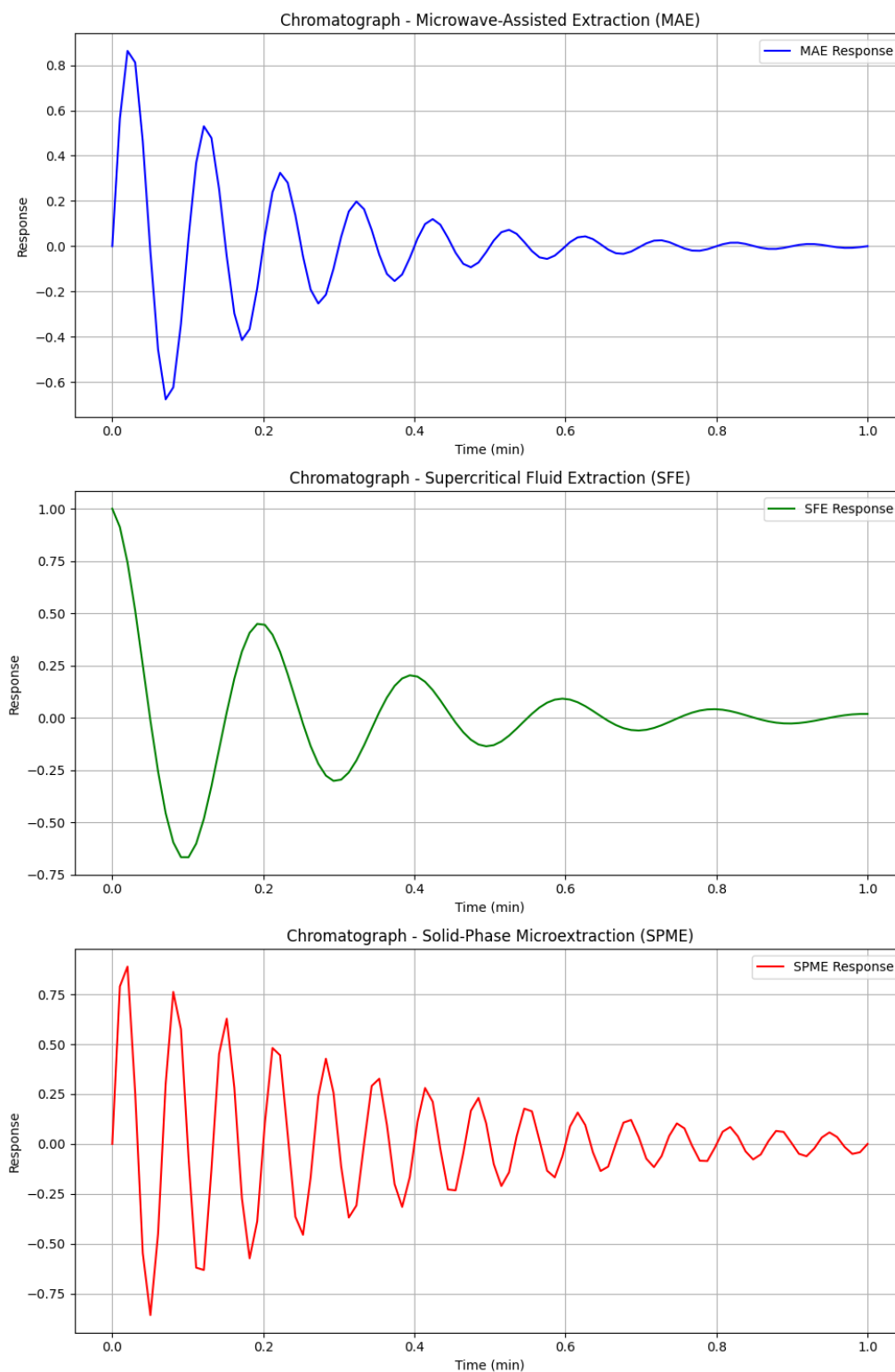


FIGURE 1: Comparison of Sample Preparation Techniques

Figure 1 provides the comparison of three sample preparation techniques used in analytical chemistry; Microwave-Assisted Extraction (MAE), Supercritical Fluid Extraction (SFE,) and Solid-Phase Microextraction (SPME). A comparison was made based on three criteria – amount of solvent used, time duration, and percentage yield of the compound. The solvent consumer trend, indicated by blue bars, found that MAE utilized the least amount of solvent followed by SFE and relatively low solvent usage by SPME. The time taken associated with the red bars illustrated that MAE grabbed the least amount of time, SFE needed more time than all the other methods, and SPME required a decent amount of time. The percent of recovery represented by the yellow bar showed that all three methods

had a high percent of recovery in the region of 90-100%. Comparing the two methods, SFE and SPME had the highest recovery, and since they are almost the same, MAE had a slightly lower recovery rate than both SFE and SPME. Overall recovery was always high for all methods while MAE which used minimal solvent took the shortest time while SFE took the longest period but gave the highest results similar to SPME.

Performance of Green Chromatography Techniques

Table 2 displayed data comparing two chromatography techniques: and two types of chromatographic types of equipment named ultra-high-performance liquid chromatography (UHPLC) and conventional high-performance liquid chromatography (HPLC). Several criteria were used for assessing the techniques. By using UHPLC, the store volume per analysis was found to be 1 ml and that of conventional HPLC was found to be 10 ml. The analysis time done using the UHPLC was shorter at 5 minutes while using the conventional HPLC took 20 minutes to complete one analysis. The resolution of the samples was higher with UHPLC at 1.5 while conventional HPLC had only a resolution of 1.2. The comparison between UHPLC and conventional HPLC brought out the fact that the former had relatively small solvent volumes and shorter analysis times, hence a relatively low environmental impact as compared with conventional HPLC which had relatively large solvent demands and longer analysis time.

Table 2: Performance of Green Chromatography Techniques

Chromatography Technique	Solvent Volume (mL)	Analysis Time (min)	Resolution	Environmental Impact
UHPLC	1	5	1.5	Low
Conventional HPLC	10	20	1.2	High

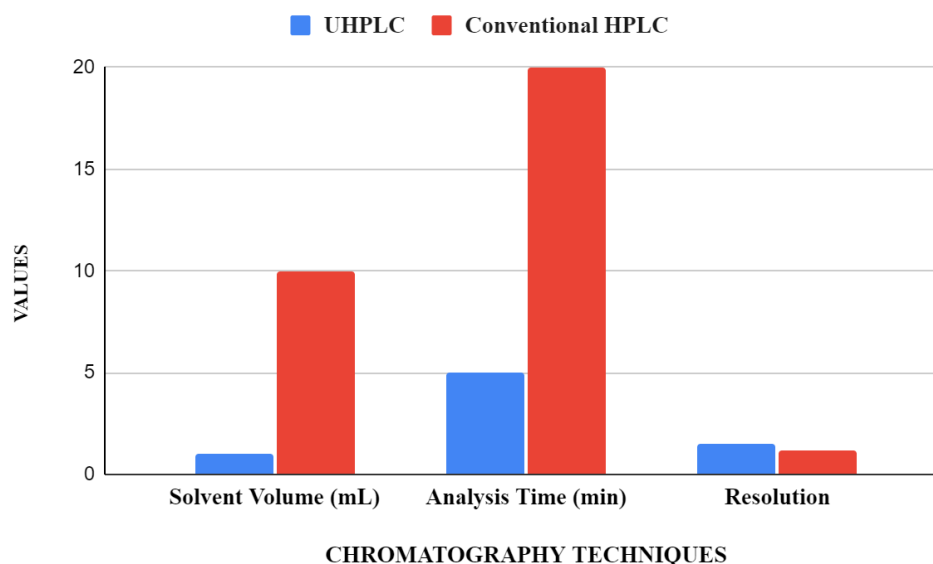


Figure 2: Performance of Green Chromatography Techniques

Figure 2 compares Ultra High-Performance Liquid Chromatography (UHPLC) to Conventional High-Performance Liquid Chromatography (HPLC) across three parameters: concerns with solvent volume and analysis time, as well as the resolution of the method. Solvent volume was notably less in UHPLC than in Conventional HPLC the blue bar representing this parameter is much shorter for UHPLC. Furthermore, the gap between the duration of analysis of the two methods was significantly different with the bar for UHPLC short and the bar for Conventional HPLC long. Finally, with a low

compaction factor, UHPLC resolved the samples slightly better than Conventional HPLC; the blue bar for UHPLC resolution was a little higher than the red bar for Conventional HPLC. Finally, based on the results obtained in the study, UHPLC offered a shorter analysis time together with lesser solvent consumption yet offered similar or improved peak separation to that offered by Conventional HPLC. Compared to conventional HPLC, the separation achieved in this experiment was less time-consuming and required a lesser amount of solvent for the analysis. The most significant finding of the study was that solvent usage, time of analysis, and resolution stood to benefit from the transition from Conventional HPLC to UHPLC.

Discussion

Green and sustainability considerations have emerged remarkably as critical and critical issues in modern analytical chemistry. Saving as much solvent as possible, shortening the analysis time, and decreasing detrimental effects on the environment, while preserving the performance of the analysis are the general objectives.[17] For example, the sample preparation techniques depicted in Table 1 and Figure 1 show some of the development heading to green extraction methods. On the other hand, the chromatographic methods discussed in Table 2 and Fig 2 show how enhanced methods that employ ultrahigh pressure liquid chromatography (UHPLC) can enhance sustainability compared to conventional liquid chromatography methods such as HPLC. Comparing the sample preparation techniques namely MAE, SFE, and SPME with LLE, the former methods proved to offer lower solvent consumption and be more ecologically friendly than the last one.[18] Some differences are revealed while considering solvent use, time, and recovery percentage, which prove the advantage of SPME in this aspect. Using no solvent, having a 15-minute extraction time, and a 92 % analyte recovery, SPME fits well with the strategy of green chemistry. In a similar league, but a distant second to SM is SFE which does not employ the use of solvent, produces a negligible environmental effect, and has a recovery of 85%. There is an equivalent disadvantage that is associated with the longer procedure which takes 20 minutes. MAE employs a 5 mL solvent volume but extraction takes 10 minutes and has 90% recovery efficiency. Compared with the green chemistry point of view, the requirement of solvent leads to the relative inferiority of MAE compared to SPME and SFE. It is used as an argument that shows that new technologies can lead to an enhancement of analytical sustainability.[19] What makes SFE and SPME favorable techniques is that they do away with one of the sources of waste and pollution – organic solvents. Lesser extraction time also saves energy and material. Recovery levels do not seem to be irrelevant in the process as well. As such, they have to be very efficient with excellent analyte recoveries to introduce the quality of analyses required in places like pharmaceutical analysis or environmental analysis, where the chance of detection is minor. Therefore, the 92% recovery from SPME in a solvent-free, 15-minute extraction is as green as can be expected. Similarly to other principles in synthetic chemistry, such as the atom economy, analytical chemists should strive for more efficient, ‘shorter’, and solvent-based methods, which at the same time would not compromise the accuracy of the determination and quality of the results. Switching to chromatography, Table 2 and Figure 2 also elucidate that a later instrumental technique such as The UHPLC has over conventional HPLC for sustainability. Compared to three parameters; usage of solvent, time for analysis, and resolution, UHPLC performed better. Comparing 1 mL solvent per analysis to 10 mL for HPLC is a clear indication of the achievable conservation as a result of the method presented. Organic mobile phases being one of the major materials of concern due to their resource intensity in chromatography, a 90% reduction in the volumes is indeed in harmony with green aims. Solvent-minimized methods also attempt to preserve or maintain separation capacities since the capacity is directly proportional to the means of quantification.[20] Thus, once more since UHPLC achieved not less than 1.2 in resolution as HPLC did, the principles of green analysis that focused on the minimum usage of resources are achieved. Equally, the 75% faster sample analysis (5 mins/20 mins) has positive sustainability consideration to other resources such as electricity, gases, and man-hours in the laboratory. Higher throughput means that more samples can be run through the same instrumentation and consumables and in this way, efficiency is achieved. While the costs of instrumentation are likely to be higher upfront, additional productivity from UHPLC offsets this

investment expense in the long run.[21,22] Together with tunable UHP conditions, and perfecting column design to enhance resolution, UHPLC therefore provides an efficient and sustainable chromatographic system. Comparing UHPLC and HPLC also shows how advanced equipment and techniques can increase the efficiency of analytical tools many times. Similarly to process intensification activities in chemical engineering, the newly emerged physical systems, like for example UHPLC, intensify throughput and productivity to decrease the environmental load per analysis. However, the applicability of instrumentation for sustainability must be complemented with prudent method development.[23,24] The ideal mobile phase, gradient and flow conditions that help in the reduction of organic solvent are critical. It is also necessary to choose small OD column sizes to reduce wastage. Combining instrumental approaches and attention to detail is therefore crucial on the way to further progress in green chromatography. All in all, the idea of sustainable approaches to analytical chemistry is to protect already available resources and to avoid the generation of waste compromising analytical performance. Accordingly, the recent innovations in sample preparations as well as chromatography, such as SPME, SFE, and UHPLC, correlate with these objectives.[23] When green criteria such as solvent consumption, time, recovery, and resolution are deemed critical, technique selection for profitable green processes becomes easy. Further, the looks for integrated methods using ideal instruments and parameters help facilitate green analysis. By these collective means, analytical chemists can lead the way to sustainability across the discipline. Such trends are evident from increasing reports on potential extraction media, mobile phases of biological renewables, and environmentally sensitive detection. Green analytical science benefits due to the advancement of green analytical principles will spearhead the change needed in chemistries within industry and academic establishments.[24]

Conclusion

By comparing all four techniques in terms of extraction efficiency and environmental considerations it was determined that SPME was the best all-around technique with an extraction time of 15 minutes, a recovery rate of 92% and no solvent was used. SFE was recovering Cu ions with 85% efficiency along with stirring, and its impact on the environment was almost negligible. Although MAE employed solvents in contrast to SFE and SPME, the recovery rate was relatively satisfactory, standing at 90%, and the method had low environmental effects compared with other solvent-based methods. Therefore, both SPME and SFE are suggested for the application of green chemistry principles when solvents are needed, though MAE can be used as a good second choice. In the same manner, UHPLC dominated conventionally traditional HPLC in essential performance indicators such as solvent consumption, analysis time, resolution, and destructiveness to the environment. Compared to legacy UHPLC, UHPLC used 10 times less solvent per analysis, the analysis time of 20 mins was reduced to 5 mins, the resolution of 1.2 to 1.5 was achieved and lower environmental impact was recorded. Hence, we strongly recommend such chromatography analysis to shift from the conventional HPLC to a more sustainable form, UHPLC. UHPLC offers higher speed analysis coupled with high resolving power, which reduces the usage of solvent and adverse impact on the environment to a very low level. It does this while perfectly meeting green chemistry objectives without compromising on analysis capabilities. New trends in sample preparation such as SPME and SFE together with new chromatographic trends such as UHPLC make it possible to perform analysis in analytical chemistry with high performance while, at the same time, implementing the principles of green chemistry in a sustainable manner as possible. That allows their high recovery, efficiency, resolution, and environmental compatibility should make them suitable for substitution of more conventional and less green procedures such as solvent extractions or HPLC in many instances.

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