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"Green" nature of the process of derivatization in analytical sample preparation

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Abstract

Nowadays, Green Analytical Chemistry idea is of high importance what impact on the rapid growth in the sample preparation area with special emphasis on sample preparation simplification, miniaturization and automation. Because the derivatization process is often an essential element of the analytical procedure, it should be important to focus on this issue and conduct a series of experiments in order to develop the most favourable conditions. Application of microextraction techniques coupled with the derivatization perfectly meets the specified requirements. Other approaches to perform derivatization process in "green" way include application of eco-friendly solvents/reagents, enhanced parameters such as microwaves or ultrasound and application of in-port, on-column/in-capillary derivatization modes. This review describes factors that allow making derivatization process more green, different modes and ways of derivatization procedures involving less toxic, hazardous reagents/solvents and more efficient forms of energy. Moreover, microextraction techniques that are often coupled to derivatization are described with examples.

Keywords

Green analytical chemistry; derivatization; ionic liquids; supercritical fluids; ultrasounds; microwaves; microextraction techniques

1. Introduction

The low amounts of analytes present in different kinds of samples, the sample characterized by complex matrix composition, and the need for several isolation steps makes accurate quantification difficult. Thus, it is necessary to select an appropriate method of sample preparation for analysis including choice of extraction type, and a final determination technique. In addition, the fact that many compounds do not possess structural properties which enable determination by means of gas (GC) or liquid chromatography (LC). Therefore, derivatization process (chemical conversion of analytes) is often performed because it allows for a significant increase in the possibilities and scope of application of both techniques. For example, application of derivatization impact on decreasing of polarity and reactivity and increase volatility of the target compounds which is desirable in the case of GC analysis. Furthermore,

this contributes to an increase in the sensitivity and selectivity and, thus, a lowering of the detection limit [1].

The analytical derivatizations are so flexible that they can be switched between different matrices and applications. The same derivatization will work adequately for the aldehydes and ketones present in breath or atmospheric air. Similarly, the isolation of amino acids from different type of samples ranging from foods to complex biological matrices will be accomplished by the similar derivatization process [2, 3].

Derivatization is performed using pre-, on-, and post-column methods. Generally, pre- and on-column modes are used with GC systems. These modes improve thermal stability, volatility, and/or detection of target analytes. There are some examples where pre-column extraction is used with LC-MS/MS, the major objective is to improve the retention, and ionization efficiency of the analytes. Pre-column mode is performed before the injection of the sample into the instrument. For the GC, pre-column mode is suitable for thermally labile and polar or ionic analytes as it converts them into volatile and less-polar derivatives. Post-column derivatization is a common approach for liquid chromatography after separation of the analytes from the column. Basically, separated analytes are converted into forms which are detectable UV or fluorescence detector [3].

Despite the fact that derivatization process is an undesirable process by the analytical chemist, because it constitutes a further step of preparing the sample for analysis, which may affect the loss of the analytes and the introduction of additional impurities, and also extends the entire length of the proceedings, it is often a process necessary to carry out the analysis. Another challenge is the need for derivatization process in accordance with the green chemistry and green analytical chemistry (GAC) [4], which arise directly from the principles of sustainable development. In fact, the 6th principle of GAC says that derivatization should be avoided. Because the process of converting chemical analytes is often an essential element of the whole analytical procedure, it should be important to focus on this issue and conduct a series of experiments in order to develop the most favourable conditions for the chemical conversion process of analytes. In the literature, it can be found that miniaturization and automation are key elements that should be taken into account during optimization of "green" analytical procedure, in which there is a step derivatization of analytes [5]. The result of this approach is to reduce the waste of reagents and thus reduce the amount of waste generated. Application of microextraction techniques in conjunction with the derivatization perfectly meets the specified requirements. Other approaches to perform derivatization process in “green” way include application of environmentally friendly solvents and reagents; application of enhanced parameters such as microwaves, UV radiation or ultrasound; application of in-port (in GC), on-column/in-capillary (LC and CE, respectively) derivatization modes.

In this article, factors that allow to make derivatization process improved green, different modes and ways of derivatization procedures involving less toxic and hazardous reagents/solvents and enhanced efficient forms of energy are discussed. Moreover, microextraction techniques that are often coupled to derivatization process are described with examples. This review is based on literature data from the last two decades and refers to different type of samples characterized by complex matrix composition. Databases like Web of Science, Mendeley and Scopus were used to select literature commented in the body. Instead of covering all the articles, selective publications highlighting the major trends were included.

The keywords such as green analytical chemistry, green derivatization, enhanced parameters, microextraction techniques, green solvents, automation and connected to them were applied during literature searching.

2. Ways to make derivatization process more green

Several ways to make derivatization process more green exist (Figure 1). In past, the most often techniques used for introducing derivatives into the chromatographic system when the reaction takes place directly in the aqueous medium have been solid phase extraction (SPE) [6, 7] and liquid-liquid extraction (LLE) [8, 9]. However, these techniques present some drawbacks including high level of organic solvent consumption (especially LLE) and considerable manipulation of the sample (SPE, LLE). Moreover, the automation of either technique has been scarcely addressed. In the era when it is recommended to apply the principles of green chemistry in analytical laboratories, it is difficult to justify extraction methods, which use large quantities of toxic, organic solvents in the sample preparation stage [8]. Therefore, sample preparation techniques where solvent consumption is reduced are preferred, for example dispersive liquid-liquid microextraction (DLLME) or single drop microextraction (SDME). These techniques resolve many aspects of green chemistry while keeping advantages of using the well understood long used liquid-liquid extraction. Also, solventless sample preparation techniques based on the extraction of analytes in sorption processes have become effective and environmentally friendly alternatives compared with traditional solvent extraction techniques. These techniques include solid phase microextraction (SPME) and stir bar sorptive extraction (SBSE). Both techniques are successfully applied to the in-situ derivatization of target compounds.

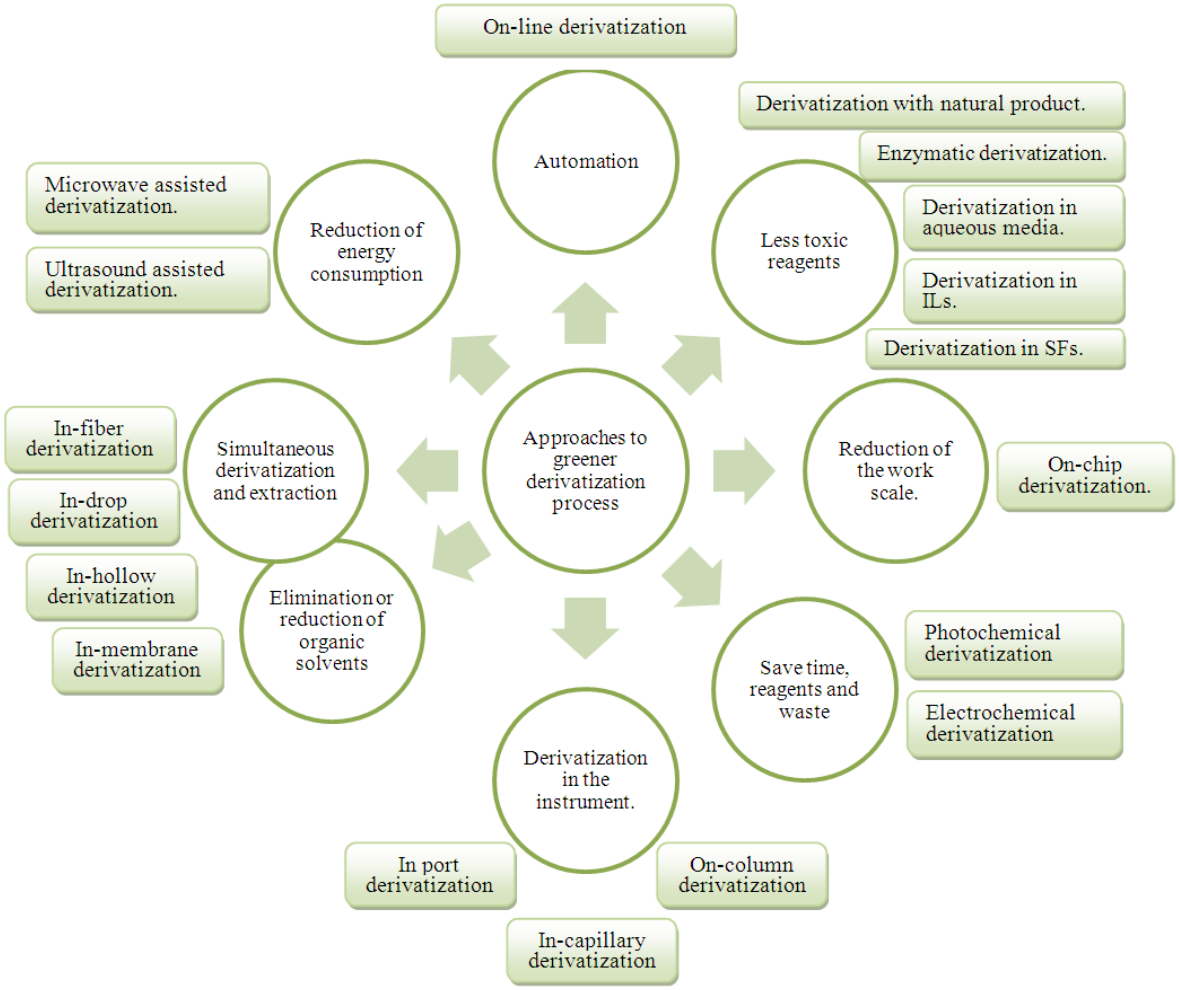

Figure 1. Schematic representation of approaches to greener derivatization process.

Another approach for greening the derivatization procedure include some instrumental configurations. Here, on-column or in-capillary derivatization with LC and capillary electrophoresis (CE), respectively [10] are of high importance. In these cases, derivatization process takes place during the separation stage, thus, they are advantageous over the most conventional pre-column, post-column or capillary modes of derivatization because consumption of sample and derivatizating agents is low and full automation occurs without additional equipment [10]. In addition, in-port derivatization (introduction of sample and derivatization agent in the injection port) performed mainly in case of GC, allow for simplification of sample preparation and reduction of solvent consumption as well as allow to avoid the application of hazardous conditions and waste generation.

The application of such enhanced factors as microwaves, ultrasound (US) and UV radiation, which provide to perform derivatization process at soften derivatization conditions as well as often accelerate the chemical conversion of analytes is also in accordance with GAC principles. Moreover, application of reagents and solvents that are less toxic in order to reduce their impact on the environment and laboratory staff has received increasing attention [10].

3. Greener reagents and solvents in derivatization process

Due to the fact that reagents and solvents used in derivatization process are often toxic, corrosive and irritant, thus, their replacement by more suitable, eco-friendly agents could bring positive features of whole analytical method. Moreover, less toxic and corrosive chemicals used in derivatization, more eco-friendly wastes are produced.

One of the most comprehensive and easy ways to evaluation the greenness of analytical procedures used for environmental purposes is the National Environmental Methods Index (NEMI), which can be found at the website http://www.nemi.gov. Four criteria that refer to the properties of reagents as well as wastes applied in the procedure are taken into consideration to rate the existing methods [5, 11]. These are: i) persistent, bioaccumulative, toxic; ii) hazardous; iii) corrosive (pH <2 or >12); and, iv) volume (mass) of waste is >50 mL(g). Another example of an Internet database which is oriented towards chemicals and processes that can be changed to reduce the hazardous and volume of wastes produced is the Green Chemical Alternatives Wizard (http://ehs.mit.edu/greenchem/) developed by Massachusetts Institute of Technology.

Persistent, bioaccumulative and toxic substances (PBT) as well as hazardous chemicals which are listed in the Toxic Release Inventory (published on The Environmental Protection Agency website [12]), are not only toxic, but also pose special risks because they remain in the environment for long periods of time and can be accumulated in biological tissues. Therefore, without a doubt it is important to look for alternatives which will be eco-friendlier.

Although, the application of solvent free derivatization process is the most welcome in the context of Green Analytical Chemistry, most derivatization processes use traditional organic solvents. Therefore, replacement of these solvents by other greener classical solvents is the simplest strategy, despite being rarely used [10]. However, this solution may be difficult to accomplish due to the fact that solvents have a substantial effect on reactions such asthe reaction rate, the stereoselectivity and the outcome.

Very good example of application of green solvents in the determination of organic acids and phosphates as trimethylsilyl derivatives in plant extracts instead of the most popular chemicals (pyridine or dimethylformamide) was presented by Englmaier [13]. The research was focused on the preparation, kinetics of silylation and effect of a different solvent on the quantitative reaction and stability of the derivatives; and the acetone was proposed as more green option. However, nowadays, the better option seems to be the application of greener alternatives.

Considering these greener alternatives to popular traditional organic solvents applied in derivatization, should be mentioned: i) water; ii) bio-derived solvents; iii) natural deep eutectic solvents; iv) ionic liquid (ILs) and v) supercritical fluids (SFs). Among these chemicals, the most desirable solvent that could be used in the derivatization reaction is water, however, this possibility is limited by the low solubility of organic substances in aqueous media [10].

Due to such properties as non-flammability, low volatility and thermal stability, room temperature ionic liquids have attracted increased attention as an alternative to traditional volatile organic solvents. ILs are used in different stages of analytical chemistry, starting from the sample preparation (extraction procedures), by separating the analytes using various analytical techniques (GC, LC, CE) and ending at the final determination stage (matrix-assisted laser desorption/ionization mass spectrometry). Also, derivatization process coupled with microextraction in ILs is often performed. In this combination, mainly dispersive liquid liquid

microextraction (DLLME) [2, 14] is applied. From the other side, several disadvantages of ILs from the GAC point of view are known, including:

i) Due to their slow degradation, they have high persistence in the environment;
ii) Due to their significant solubility in water, they may be released into the aquatic environment;
iii) Some of the ILs are toxic, however, their toxicity varies for different organisms as well as depends on composition of ILs.

Other green solvents, which are sometimes, applied in derivatization process are SFs, in particular carbon dioxide [15]. This is mainly due to their advantages such as chemical inertness, low toxicity and easy disposal. From the other side, high cost of production (high consumption of energy) and low polarity make them relatively rarely used.

Among the application of SFs in derivatization process, Supercritical Fluid Extraction with in situ derivatization is the most popular technique used. This brings such positive features as simplification of sample handling and sample preparation step, minimizing number of stages of whole analytical procedure and shortening of analysis time. In addition, it is not necessary to remove the excess of solvent from the extracts obtained, thus, they can be directly transferred to the chromatograph for on-line analysis [10]. In the case when derivatizing agents will be used as modifiers of supercritical fluid, it is required to select its carefully to ensure their compatibility with extraction conditions (pressure and temperature).

Not only solvents, but also other chemicals should be investigated when derivatization process is considered from the sustainable environment point of view. However, despite the fact that the search for less toxic as well as natural compounds for derivatization should be a goal in new analytical developments, achievements in this area are very scarce. However, some examples of such solution can be found in the literature. For instance, with the objective of utilizing the nontoxic chemicals, novel oxidative coupling reactions resulted using Cisapride (CPE) as green analytical spectrophotometric reagent were performed [16]. Furthermore, this reagent was investigated in the research focused on the determination of bromate in drinking water, bread and flour additives. The proposed methods have distinct advantages of sensitivity and selectivity. Besides, the methods do not require heating or distillation and they exhibit reliability due to their reproducibility. Such proceeding is worth to be followed. In another work, a sequential injection method was developed for the spectrophotometric determination of chlorine in tap-water and surface water samples based on the reaction between tetramethylbenzidine (TMB) and free chlorine [17]. The application of the TMB/chlorine reaction in a sequential injection system was successful and adds other advantages as it enhances the degree of automation, minimisation of reagent consumption and low effluent production. Moreover, TMB proved to be a highly selective reagent, yielding a very sensitive methodology resulting in fairly low quantification limit.

Different examples of the use of unrefined natural reagents derived from plant and animal tissues or microbial cell for derivatization have been published [18]. Crude plant extracts may contain chemical compounds that enable their use as chromogenic or fluorogenic agents. The application of natural reagents in conjunction with a flow injection system can confer a number of advantages. First of all, the enhanced kinetic control that flow analysis offers may assist in avoiding undesirable side reactions that would otherwise occur using impurified reagents [18].

The natural reagents lifetime may be prolonged when applied in a flow analysis system because their exposure to light or air can be monitored.

4. Microextraction coupled with derivatization

Over the last few decades, numerous microextraction techniques have been developed and broadly used to different type of samples. They are featured by minimum or no use of organic solvents, shorter extraction times, opportunities for automation, and miniaturized dimensions. Among number of miniaturized extraction techniques, solid phase microextraction (SPME) and liquid phase microextraction (LPME) are pertinent to mention here.

SPME is a green alternative to conventional solid phase extraction (SPE). It requires very little amount of the sorbent coated on a silica fiber or metallic support. Moreover, it allows thermal desorption of analytes when coupled with gas chromatography and very little volumes of solvents are required when coupled with liquid chromatography. As analytes are extracted into very small amount of sorbent, SPME provides very high enrichment factors and thus the sensitivity. The selectivity can be fine-tuned by selecting suitable sorbent phase.

LPME is a miniaturized format of liquid phase extraction (LLE). LLE is famous for its simplicity, effective cleanup ability, and high selectivity through the selection of suitable solvents. Despite all the advantages, it does not represent a green extraction due to excessive use of toxic solvents (hundreds of mL). Furthermore, it is time consuming and cannot be automated due to emulsion formations. However, compared to LLE, LPME utilizes very little volume of the organic solvent (in μL) which renders it as a green approach. Some famous versions of LPME technique include single drop microextraction (SDME), hollow-fiber liquid phase microextraction (HF-LPME), and dispersive liquid-liquid microextraction (DLLME) [19].

There are different aspects through which environmental impact of derivatization can be minimized. Apart from several universal approaches that include use of greener derivatizing reagents, decrease in their volumes, less-generation of waste, etc miniaturization and automation of the analytical extraction process may help to implement green practices. Several emerging trends indicate faster and simpler derivatization procedures based on their coupling with microextraction techniques. The derivatization process can get greenness from the nature of the microextraction itself. If derivatization is combined with SPE or LLE, it will require large volumes of derivatizing reagents relating to the sample volume requirement for these extractions. However, the similar derivatization will require much-reduced amounts of derivatizing reagents in case of SPME, LPME or other microextration techniques.

4.1. Combination of derivatization and microextractions: A way forward to green process

Apart from the green nature of the process, the need for the combination of derivatization with microextration arises from the facts that derivatization alone, in some cases, may introduce impurities, excess reagents, side-reaction products, and incomplete reactions that may interfere with target analytes.

In general, pre-column derivatization can be combined with microextraction in the following ways:

i) Pre-extraction derivatization: it is performed in sample solution or donor-phase before microextraction. This approach may provide higher partition coefficients and improve separation of the analytes.

ii) Post-extraction derivatization: This approach is adopted when pre-extraction is not required or derivatization can make extraction process impossible or can induce adverse effects on the extraction itself by complicating the matrix. In this way, the purpose of post extraction is to convert the analytes into the form, which is analyzable by the instrument.

iii) In-situ derivatization: it involves one step extraction and derivatization. It seems to be more focused recently. It has advantages of being simple, rapid, relatively greener.

iv) Injection port derivatizations: Most of the derivatization procedures include off-line coupling with microextractions. Such protocols are performed prior to the analysis. However, in some cases, offline derivatizations lead to experimental errors due to loss of analyte through evaporation, transfer, and re-suspension steps, contamination of samples during work-up. Moreover, interference of moisture in the reaction system can cause some major issues as some of the derivatizing reagents and the resulting derivatives are very sensitive to water. On-line derivatization techniques are emerging to solve such issues.

Online derivatizations are time-effective, require less amount of reagents, and result in better efficiency of the analysis. Inlet-based or in-port derivatization allow direct injection of the sample and derivatization reagent into the hot GC inlet, where the derivatization reaction takes place in the gaseous phase. The sample and the derivatization reagent can be injected separately or by a single injection. In later case, the syringe is filled with both the sample and the derivatization reagent, but with an air gap between them.

Derivatization can be combined both with solid and liquid phase microextractions. In the coming sections, we will discuss the green aspects of coupling microextractions and derivatization. The description of derivatization reactions and their types have already been emphasized in many reviews and is beyond the scope of this article.

4.2. Sorbent microextraction and derivatization

4.2.1. Solid phase microextraction

Solid phase microextraction (SPME) was introduced almost 27 years ago and it laid the foundations of research in area of microextractions [20]. SPME has different formats and configurations. In fiber SPME, analytes are directly extracted into a solid extracting phase and then desorbed into the instruments. SPME fulfils the requirements of green analytical chemistry (GAC) being solventless (or minimal use of solvent), less waste production etc. This technique has been widely used in environmental, food, and biological analysis and it has many advantages over conventional extraction techniques that have been described in detail in scientific literature.

Although SPME is in good agreement with the principles of GAC but still the search for green materials as well as derivatizing reagents continues. Thus, it has been used for extraction and

derivatization of analytes from the samples of varying composition and matrix complexity. Due to solventless nature of the technique, there are various options for its combination with derivatization.

The coupling of SPME with derivatization was first reported by Pan and Pawliszyn in 1997. This coupling was performed in three ways; in the sample matrix, in the fiber coating, and in the GC injection port [21]. Again, in the SPME, derivatization is performed with the objectives of conversion of polar analytes into less polar equivalents, therefore enhancing their coating/water or coating/gas partition coefficients and improving SPME efficiency and method sensitivity. Derivatization using SPME has several advantages over conventional methods such as low solvent use, relatively low cost, easy to perform, and all desired features of GAC.

In the following section, some latest examples of each category of derivatization are described.

4.2.1.1.In-situ SPME-derivatization

It involves conversion of the analytes into their derivatives within the sample (in situ) plus extraction employing SPME technique. Recently, silk fiber was used as an adsorbent in in-tube SPME for extraction of in-situ chemically derivatized aldehydes. Silk fibers are green, biocompatible, porous, and cost-efficient materials, which are enriched with hydroxyl, amino, carboxyl, and other hydrophilic groups, making them good adsorbents [22].

4.2.1.2.Pre- or post-SPME-derivatization

As an example of pre-SPME-derivatization, multiclass organic UV filters were first derivatized within the sample vial and then extracted by direct immersion SPME. Low cost derivatization reagents, short extraction times, and low sensitivities were major advantages of this work [23].

The second way is to perform derivatization on the fiber. This is possible either before or after extraction. A derivatizing agent can be adsorbed onto the fiber before extraction and then analytes can be extracted using DI or HS mode. The analytes can be extracted first onto the fiber and then can be derivatized chemically by immersion, vapor exposure, or spraying the fiber with derivatizing agent.

Recently, a rapid and environment friendly SPME method involving on-fiber derivatization coupled with GC-MS was developed for quantitation of four non-volatile biogenic amines (putrescine, cadaverine, histamine, and tyramine) in fish samples. SPME fiber was first dipped into a solution containing isobutyl chloroformate as derivatization reagent and isooctane as extraction solvent. This resulted in formation of a thin organic liquid membrane coating. The modified fiber was then directly immersed into sample solution for extraction of biogenic amines. The analytes were then thermally desorbed into the GC-injection port. Only few microliters of the reagents were employed that were not harmful to the environment and the analyst [24].

A fully automated post-HS-SPME-derivatization method was developed by modifying the programming of SPME autosampler and coupled online with GC-MS for determination of clenbuterol in meat. This type of automation provides better reproducibility as well as reduced exposure of workers to the toxic analytes [25].

4.2.1.3.SPME-Injection port-derivatization

In this type of derivatization, SPME is performed first for extraction and concentration of certain analytes in different matrices. SPME fiber is then injected to GC injection port and analytes are thermally desorbed for a fixed period with split closed. After that derivatization reagent is injected with the same closed split and a reaction is allowed to occur. This mode of derivatization was used for determination of chlorinated bisphenol-A in human plasma samples [26]. The amount of derivatizing reagent is much reduced compared to in matrix derivatization. Additionally, all the reaction takes place within a controlled environment with decreased chances of analyte loss and contamination.

4.2.2. Stir-bar sorptive extraction

Stir bar sorptive extraction (SBSE) was developed in 1999 to overcome some limitations of existing techniques including SPME. In SBSE, a sorbent generally PDMs, is coated on a stir bar and it is used for extraction of hydrophobic/non-polar molecules from different media. The PDMS extracts based on van der Waals forces as well as the hydrogen bonds which form with its oxygen atoms depending on the molecular structure of the analytes.
In case of thermal desorption, apolar polymer coating in SBSE may be useful only for semi-volatile and thermally stable compounds. However, its coupling with derivatization can extend its application to polar and thermally labile compounds. SBSE can be coupled with derivatization process in the following ways: pre-SBSE derivatization, in-situ SBSE-derivatization, and on-stir bar microextraction.

4.2.2.1.Pre-SBSE-derivatization

In this mode of derivatization, analytes are first derivatized in the sample solution using suitable derivatizing reagent under optimum conditions. In the second step, they are extracted using SBSE and then desorbed thermally or in suitable solvent.
Carbonyls were determined in the rain water using this approach. For the 100 mL of the rainwater sample, 1 mL of the derivatizing reagent (PFBHA 1 mg/mL) was employed. After adjusting the pH, the mixture was left overnight to complete the derivatization reaction. SBSE was performed under optimum conditions and finally the analytes were desorbed into 2 mL of acetonitrile with the aid of ultrasonication. This led to high enrichment factors due to concentration of derivatized analytes from large volume sample to very small volume of desorption solvent. The extract was injected to GC-MS for analysis and very low LODs (10 – 30 ng/L) were obtained [27].

4.2.2.2.In-situ SBSE-derivatization

This is the simplest way to change the analytes into the derivatives in the respective sample media before or simultaneously with SBSE. The SBSE can be performed both in DI or HS modes. After extraction of derivatized analytes, stir bar is placed with a desorption chamber coupled to GC, or analytes can be desorbed with suitable solvent for LC.
Chlorophenols were determined in water and body fluids by SBSE with in situ derivatization. To the sample solution, derivatizing reagent and stir bar were subsequently added, all affecting parameters were suitably optimized. After extraction, stir bar was transferred to thermal desorption tube which was further connected to GC-MS. Up to 100 µL of acetic anhydride was

used as derivatizing reagent [28]. This type of derivatization procedure has potential of being green and amenable to automation.

4.2.2.3.On stir bar derivatization

This mode works in two ways: first includes preloading or adsorption of derivatizing reagent on polymer coating. This mode performs simultaneous derivatization and extraction. Secondly, extraction is performed on SBSE device, followed by the derivatization on the stir bar (through vapour spraying). Another approach is used with thermal desorption. In this approach, a small capillary containing derivatizing reagent is placed with stir bar in desorption chamber. This is a good approach for silyalting agents. In case of liquid desorption, derivatizing reagent is added to desorption solvent after stir bar desorption.

4.2.2.4.Hollow fiber stir bar sorptive extraction

In order to fulfil ever-growing demands for ultra-trace analysis, recently, some efforts have been made to combine extraction procedures together. These combinations can synergistically derive benefits from individual microextractions. Such fusion may help to get better matrix clean–up, higher sensitivity and selectivity. Here, we describe some representative examples of combined microextraction techniques combined with derivatization. With this aim, hollow fiber based SPME was combined with SBSE to design a new technique HF–SBSE. Porous HF acts as filter and carrier for stir-bar, and dispersed sorbent. HF-SBSE device can be used for direct extraction in complex biological matrices as HF protects its contents against the interferences. This technique can also be coupled with microwave or ultrasonic assisted derivatization [29].

HF-SBSE was coupled with microwave assisted derivatization for determination of amino acids in biological matrices. After the extraction of analytes onto the HF-SBSE device, the derivatization and desorption was performed simultaneously using derivatizing reagent and solvent. Trimethylsilylation was the reaction of choice (Figure 2). This method has several benefits in terms of the green process:

i) desorption solvent also served as reaction media for derivatization,

ii) microwave assisted derivatization was time and energy efficient; derivatization requires only 2 min microwave assistance while 30 – 60 min are needed in case of conventional heating.

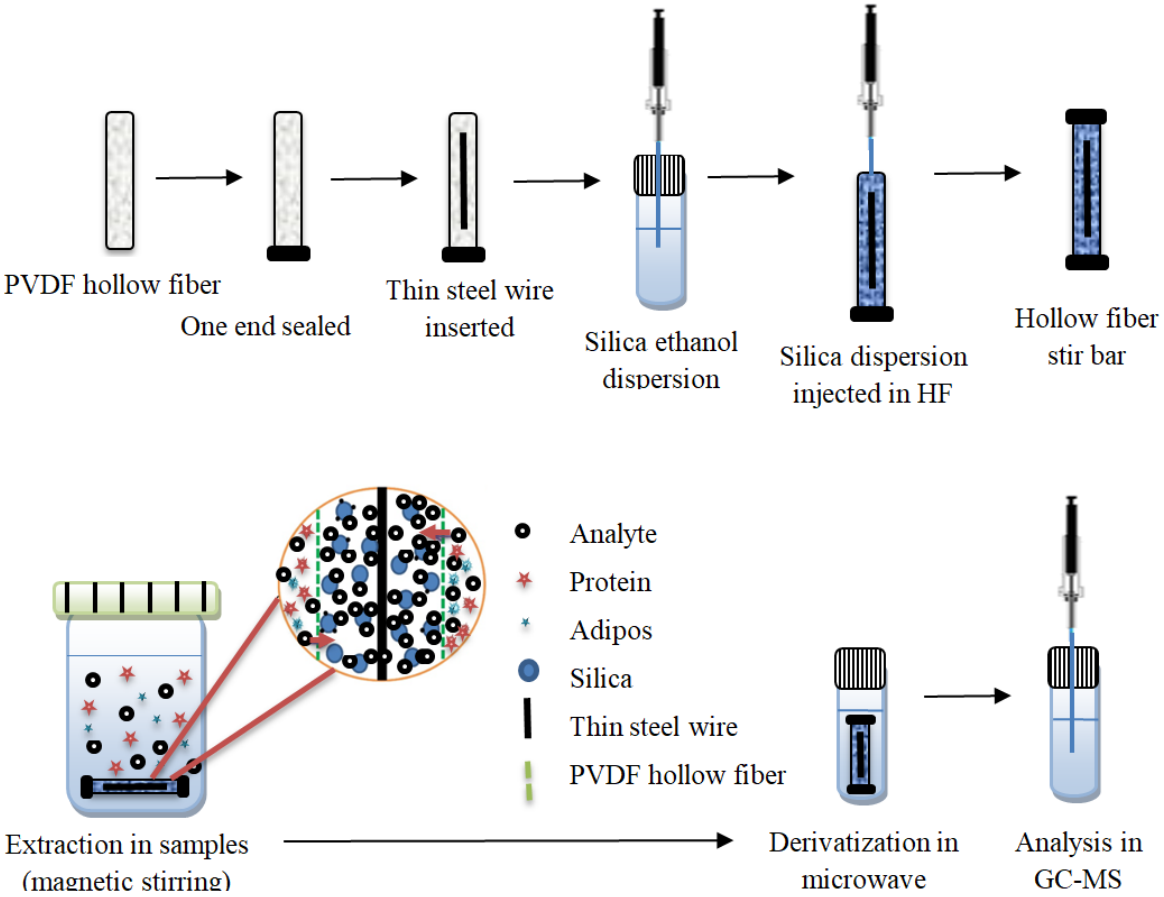

Figure 2. Schematic figure of preparation, extraction and derivatization of the hollow fiber stir bar for amino acids [29]

4.2.3. Microextraction by packed sorbent

Microextraction by packed sorbent (MEPS) is based on the same principles as SPE. MEPS is more than just a miniaturized version of SPE as it allows packing of the sorbent (1 – 4 mg) inside the cartridge or special container within the injection syringe. This sorbent containing cartridge is positioned between barrel and needle (Barrel insert and needle BIN). The sorbent can be reused for several times. MEPS integrates sample preparation with analytical instrumentation. It can be coupled with GC, LC, and CE.

There are some examples where MEPS was used in combination with derivatization. The most famous mode, however, is the pre-extraction derivatization, where derivatization is completed first and then MEPS is performed. Some authors termed it “in-situ derivatization” because derivatization is followed by MEPS using a sequence of steps controlled by an automated system.

Haloacetic acids were in situ derivatized in aqueous samples, extracted by MEPS, and determined by GC-MS. The whole process from addition of derivatizing reagents into the sample to extraction to analysis was automated. Derivatization was performed in a sample vial of the auto sampler. The derivatization process was completed within 10 min at room temperature in the aqueous media. From the perspectives of automation, time and energy-efficiency, and medium for reaction; the derivatization process was greener [30].

The beauty of the MEPS lies in its automated procedure and online coupling with analytical instruments. The derivatization is also amenable to be the part of the same automated procedure which gives it an additional green perspective. In addition, derivatizations which require little volume of derivatizing reagent, work in green medium such as water, and complete in shorter times add more value on green aspects. One example of this kind is determination of polyamines and related compounds in urine using in situ aqueous derivatization followed by automated MEPS. The derivatization was performed using ethyl chloroformate in aqueous medium and reaction completed within 1 min [31].
MEPS has also been combined with large volume injection in-port-derivatization GC-MS for selective determination estrogenic compounds in water [32].

4.2.4. Dispersive/magnetic solid phase extraction

Dispersive solid phase extraction (DSPE) is based on the dispersion/addition of the few milligrams of the sorbent into the sample solution. The sorbent is dispersed within the solution by shaking or assistance of the vortex. After the extraction, sorbent is separated from the sample solution by centrifugation. Analytes are then back extracted from sorbent into suitable solvent. DSPE offers fast extraction due to increased interfacial area for the interaction of the sorbent and the analytes. The other potential problems associated with SPE such as packing inside the cartridge, blockage of the column, and requirement of large amounts of sorbents, sample volumes, and organic solvents can be avoided. Magnetic SPE is another form of DSPE in which magnetic sorbent is employed. It provides some additional advantages of fast phase separation using an external magnet.

There are several opportunities by which derivatization can be combined with DSPE/MSPE:

i) it can be performed in the sample solution prior to extraction;
ii) the sorbent can be coated/loaded with derivatizing reagent (in situ); and
iii) it can be performed after extraction.

The example of derivatization in the sample solution prior to addition of magnetic sorbent include the extraction of methylmercury in seawater. $NaBPh_4$ was used derivatizing reagent in this work, the derivatized analytes were extracted using Fe_3O_4/PANI composite based MSPE [33]. Here derivatization step was performed just before extraction steps and it was named as in situ derivatization.
In another example, MSPE-in situ derivatization, was used for extraction and derivatization of aldehydes in human urine samples. Instead of adding derivatizing reagent 2,4-Dinitrophenylhydrazine (DNPH) into sample solution, it was first adsorbed/loaded on the magnetic sorbent [Fe3O4/SiO2/P(MAA-co-EGDMA)] which was then used for extraction of hexanal and heptanal in human urine samples. Different steps involved in this procedure are shown in Figure 3.The whole process was completed within 9 min [34].Table 1 lists sorbent phase microextraction methods combined with derivatization.

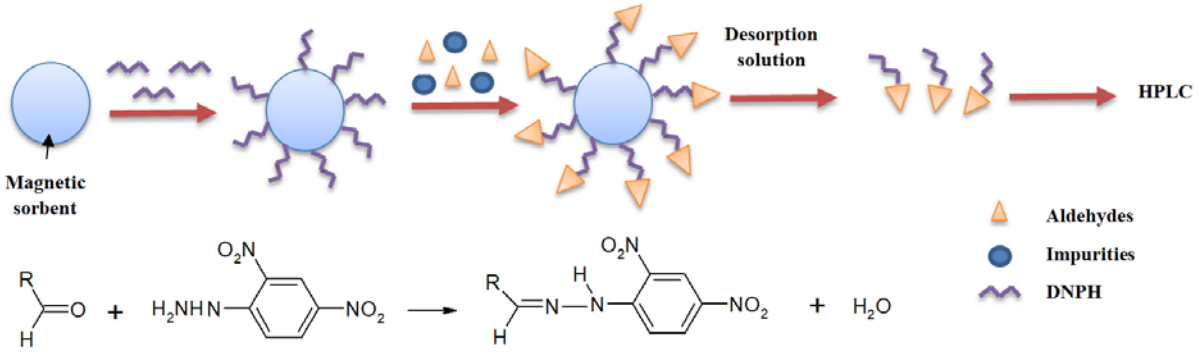

Figure 3. The scheme of magnetic solid phase extraction-in situ derivatization procedure [34]

4.3. Liquid phase microextraction and derivatization

LMPE is a miniaturized version of LLE. It eliminates some major drawbacks of LLE such as huge consumption of toxic solvents, long extraction times, and tedious process. LPME performs extraction with very small volumes of extractant typically in several microliters. Moreover, it performs extraction and preconcentration in a single step leading to very high enrichment factors. LPME is performed in different formats such as SDME, HF-LPME, DLLME etc. Due to low volumes of extraction solvents, these techniques require extremely low volumes of derivatizing reagents.

4.3.1. Hollow fiber liquid phase microextraction (HF-LPME)

HF-LPME implies porous hollow fibers for extraction. These fibers are impregnated with an organic solvent prior to use. Extraction solvent is filled inside the lumen of the fiber. The fiber is then placed in sample solution for a defined period, after which extraction solvent is taken out of the fiber and injected into the instrument. For every extraction, a fresh piece of hollow fiber is used, which removes the chances of contamination or carryovers. The beauty of HF-LPME lies on the use of extremely low volumes of extraction solvents, thus contributing toward greenness of the extraction process. HF-LPME has also been combined with derivatization where direct analysis of target compounds is not possible using analytical instrument.

4.3.1.1.HF-LPME coupled with injection port derivatization

Basheer and Lee reported coupling of HF-LPME with injection port derivatization for extraction, derivatization, and determination of endocrine disrupting alkylphenols, chlorophenols, and bisphenol-A in aqueous samples [35]. These analytes are polar and semi-volatile in nature, and therefore require derivatization before analysis by GC. The analytes were extracted from sample solution using direct immersion HF-LPME containing 5 µl of water immiscible organic solvent inside the hollow fiber. The sample was stirred during 30 min extraction time. After extraction, an aliquot (2 µl) of the extract and 2 µl of BSTFA were consecutively injected into the GC injection port. This method provided very high enrichment factors and better results than HS-SPME and LLE.

Since in HF-LPME very little volume (5 µl) of extract is accessible for derivatization. Instead of further dilution that can decrease sensitivity of the analysis, injection port derivatization is

preferred. Besides, it reduces volume of the derivatization reagent, derivatization time, and degradation of analytes due to moisture exposure [35].

4.3.1.2.Pre-HF-LPME derivatization

Derivatization can be performed before HF-LPME to convert the analytes into extractable and analyzable product. For example, formaldehyde was derivatized using acetyl acetone in presence of ammonium acetate buffer to convert into 5-diacetyl 1,4-dihydrolutidine which was extracted using HF-LPME and analyzed by spectrophotometer. The derivatization reaction was supported by ultrasonic energy for 30 min at 70°C. This work utilized only 25 μL of octanol as extraction solvent [36]. The same mode of derivatization was used to determine cocaine and its derivatives in hair samples which were subjected to methanolic extraction followed by derivatization. The derivatization process was completed in 6 minutes with the aid of ultrasonic bath. LPME was used for cleanup [37].

Electromembrane extraction (EME) is modified form of HF-LPME where extraction of ionizable analytes is performed by the provision of electric field. Pulsed EME was used for extraction of derivatized amino acids prior to their analysis by HPLC-UV. The purpose of derivatization was to enhance the UV absorbance and hydrophobicity of selected amino acids [38].

4.3.1.3.Post-HF-LPME derivatization

Sample preparation such as conjugate metabolite hydrolysis is required for determination of BPA and phthalate metabolites in urine samples. This is performed by using specific enzymes that work under defined temperature and pH environment. Then analytes can be extracted using some extraction technique. Such processes can be simplified using derivatization. BPA and other phthalates were determined in urine using HF-LPME followed by derivatization [39]. The derivatization completes within few minutes under ambient conditions. In this way, this is another time and energy efficient approach.

4.3.1.4.HF-LPME coupled with SPME

HF-LPME is performed either in two-phase or three-phase modes. Two-phase mode (HF-LPME) is suitable for extraction of hydrophobic analytes into an organic solvent from sample solution. Three-phase mode (HF-LLLPME) is used for extraction of ionizable compounds (basic or acidic) from aqueous samples into an organic solvent that is impregnated in the pores of HF, and finally into an aqueous acceptor phase filled inside the lumen of the HF. pH gradient drives this extraction. The final extract is aqueous and cannot be injected directly into GC. Secondly, the polar or ionic analytes should be derivatized to convert them more volatile and less-polar analytes before injection to GC. To make the aqueous extract analyzable by GC, HF-LLLPME was combined with SPME with simultaneous on fiber derivatization for analysis of chlorophenols [40]. This combination provided very low LODs 0.0004 – 1.2 μg/L and enrichment factors in the range of 432 – 785. The schematic of this combination involves some steps indicated in below Figure 4.

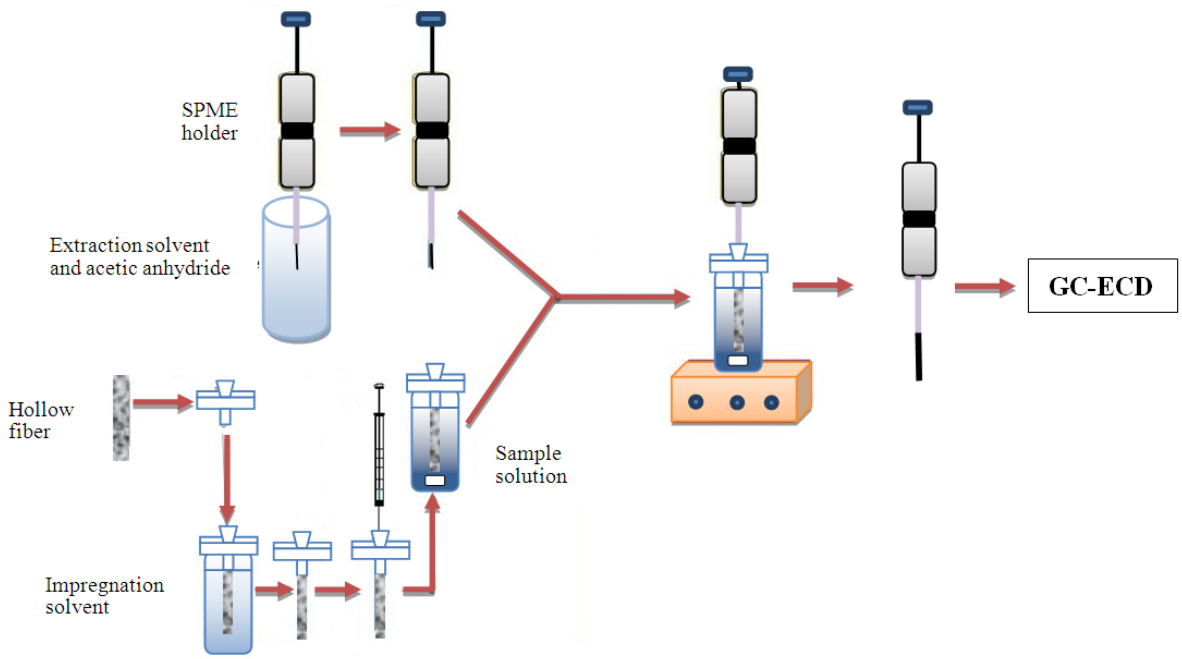

Figure 4. The schematic diagram of the extraction device and extraction procedure [40]

4.3.2. Dispersive liquid liquid microextraction

Dispersive liquid–liquid microextraction (DLLME) was introduced about a decade ago by Assadi and coworkers[41]. DLLME relies on ternary component solvent system, the proper mixture of extraction and disperser solvent is injected into the aqueous sample, leading to a cloudy solution. After centrifugation, the organic layer is separated for analysis. This technique provides high enrichment factors. In addition, it is fast and consumes low volumes of organic solvents due to which it is relatively a green approach. Additionally, due to the use of organic solvents, it compatible with direct injection to GC. However, in case of polar or non-volatile compounds, DLLME can be combined with derivatization to convert the analytes in less polar and volatile derivatives suitable for GC analysis. DLLME has been widely coupled with derivatization. There are opportunities to make this coupling greener through:

i) reduction of the sample size,
ii) using or developing less toxic derivatizing agents,
iii) reduction in the volumes of extraction and dispersive solvents,
iv) in many cases, the solvent used for derivatizing agent, also acts as dispersive solvent for DLLME and it attributes a green aspect in terms of solvent consumption,
v) dispersive solvent may be avoided by performing dispersion using air or some other sources,
vi) green dispersive solids can be used instead of dispersive solvents,
vii) automation and online coupling of DLLME with analytical instrument.

4.3.2.1.In-situ derivatization-DLLME

It is most widely used mode of DLLME coupled derivatizations. In situ derivatization-DLLME performs simultaneous derivatization and extraction. It reduces the number of extraction steps, sample size, and consumption of the solvents. In this way, in situ approach is greener than performing derivatization and DLLME separately.

Melamine is used as food adulterant to enhance the apparent protein content in the milk. Dabsyl chloride was used for chemical derivatization of melamine in the milk and powdered infant formula prior to its extraction by DLLME and subsequent determination by HPLC. In this work, 100 μL of 4 mg mL^{-1} of dabsyl chloride was used. Dabsylation is fast, and resulting derivatives are very stable. They absorb in the range of 436–460 nm and the interferences from UV-absorbing biological species in the food matrix can be prevented [42].

Simultaneous monitoring of several neurotransmitters has special importance in Parkinson's disease pathology, pharmacology and drug screening. A simple method that combines in situ derivatization and UADLLME (in situ DUADLLME) was used for determination of catecholamines and their biosynthesis precursors and metabolites in rat brain microdialysates. Other than simplicity and speediness, this method utilized relatively green extraction solvent (bromobenzene, 50 μL) and required very small volume of sample (30 μL) [43].

4′-carbonyl chloride rosamine (CCR) was used as derivatizing agent for in situ ultrasound-assisted derivatization DLLME of amino acid and monoamine neurotransmitters and their metabolites in rat urine of Alzheimer's disease. CCR works at mild derivatization conditions, easy to handle and provides better sensitivity [44]. Being mass-spectrometry sensitive, CCR was also used a derivatizing agent for simultaneous determination of biogenic amines and amino acids in food samples using in situ DUADDLLME coupled with UHPLC-MS/MS [45].

DLLME was also used for simultaneous extraction and derivatization of 13 biogenic amines in homemade wine samples. This method required very little quantities of extraction solvents and derivatization reagents. Secondly, it was rapid and did not require aid of external energy for derivatization [2].

Numerous modified DLLME methods have been described in the literature for in-situ derivatization and extraction where dispersive solvent was replaced by some other procedures such as assistance of air, vortex, up and down shaking, temperature, etc. These methods introduce greenness in the process by avoiding the use of dispersive solvent.

A modified version of DLLME known as fast syringe-assisted liquid–liquid microextraction was used for simultaneous extraction and derivatization of parabens in aqueous and cosmetic samples using GC-FID. In this method, derivatizing agent, catalyst, and disperser solvent were rapidly injected to salt-added and pH adjusted sample solution. Then, extraction solvent was added to the solution which was withdrawn to a glass syringe for several times and evacuated in a conical tube. This resulted in a turbid solution and analytes extracted into extraction solvent. The solution was again withdrawn into syringe, and needle was replaced with a filter through which organic and aqueous phase were separated. This whole process was completed in 1.5 min and derivatization was not supported by any external energy source and was accomplished in aqueous media. Moreover, very minute volumes of solvents were used [46].

In another modified version of DLLME known as air-assisted LLME, where dispersive solvent was replaced by performing the dispersion step with a syringe through aspirating and dispensing the solution (sample, extraction solvent, and derivatizing reagent) for several times in a glass test tube. After completion, extraction solvent was separated through centrifugation. This

method was employed for determination of non-steroidal anti-inflammatory drugs in biological fluids using GC-FID [47].

Similarly, in another method, emulsification was attained using up-and-down shaker-assisted dispersive liquid-liquid microextraction (UDSA-DLLME). This method was used for simultaneous extraction and derivatization of chlorophenols in water samples. The whole process was completed within a minute under normal temperature conditions. The relatively less toxic solvent 1-heptanol (12 µL) was used as extraction solvent [48]. The schematic representation of this procesis shown in Figure 5.

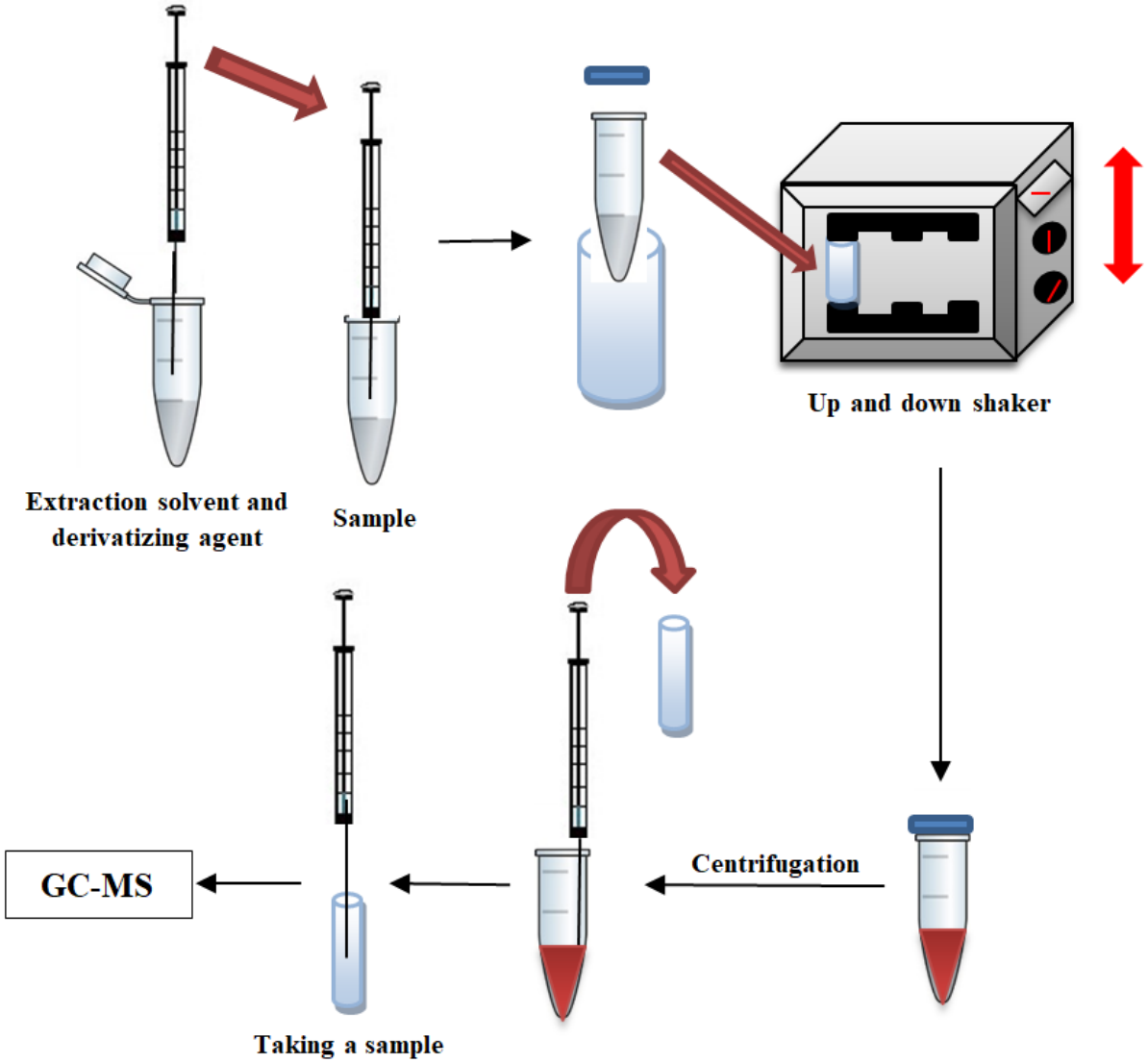

Figure 5. Diagrammatic sketch of the up-and-down shaker-assisted dispersive liquid-liquid microextraction. The conical glass tubes were secured by in-house designed plastic holders and then equipped to the up-and-down shaker [48].

Temperature-assisted DLLME was used for simultaneous extraction and derivatization of three anti-depressants in the urine which was further determined by GC-FID. In this method, a mixture of extraction solvent, dispersive solvent, and derivatization reagent was rapidly injected into a heated sample which was then cooled to room temperature to obtain a cloudy solution. The analytes were simultaneously derivatized and extracted into extraction solvent. The

temperature of the sample was initially kept high as it accelerates solubility of extraction solvent, rate of derivatization, and mass transfer of the analytes. The decrease in temperature will reduce the solubility of extraction solvent in aqueous media leading to enhanced turbidity due to formation of larger droplets that can be centrifuged [49].

Another green approach that can be realized from the existing literature suggests the use of solid disperser instead of dispersive solvent. In this regard, sugar cube loaded with extraction solvent and derivatizing reagent was dissolved in sample solution containing the analytes and a catalyst. Dissolution of the sugar cube slowly release extraction solvent and derivatizing reagent into sample solution changing it cloudy and simultaneous extraction and derivatization takes place. After centrifugation, sedimented phase is separated and injected to the analytical instrument. This method was used for determination of some pharamaceutical drugs in urine and plasma samples by GC-FID [50].

The automation and coupling of in-situ derivatization-DLLME with analytical instrumentation can introduce an additional advantage of eliminating personnel effort and thus reducing the chances of error. Moreover, better control on overall process can be achieved with lesser exposure of chemicals to the workers. A fully automated in syringe magnetic stirring assisted DLLME (with extraction and derivatization simultaneously) was coupled online with GC-MS for determination of UV filters in the environmental water samples [51]. DLLME can be automated in a lab-in-syringe system. As in-syringe-DLLME can precisely handle small volumes, its reproducibility and precision will be better than the manual mode. In addition, it can be supported with automated magnetic stirring system for proper mixing and dispersion. The automation will simplify the whole process as well as the intervention of the analyst.

4.3.2.2.Pre-DLLME derivatization

In some cases, derivatization is performed prior to DLLME. For example, isotope-labelling derivatization was combined with ultrasound-assisted dispersive liquid–liquid microextraction (UA-DLLME) to deal with low concentrations of NTs in brain microdialysates and matrix effect [52]. Stepwise procedure is shown in Figure 6.

Similarly, 2-(11H-benzo[a]carbazol-11-yl) ethyl carbonochloridate (BCEC-Cl) labelled steroidal and phenolic EDCs were extracted by DLLME. Here derivatization was used to enhance the detection sensitivity toward fluorescence detector, selectivity and hydrophobicity of the analytes. However, due to complex nature of the real food samples and ultra-trace levels of EDCs, derivatization was followed by DLLME [53].

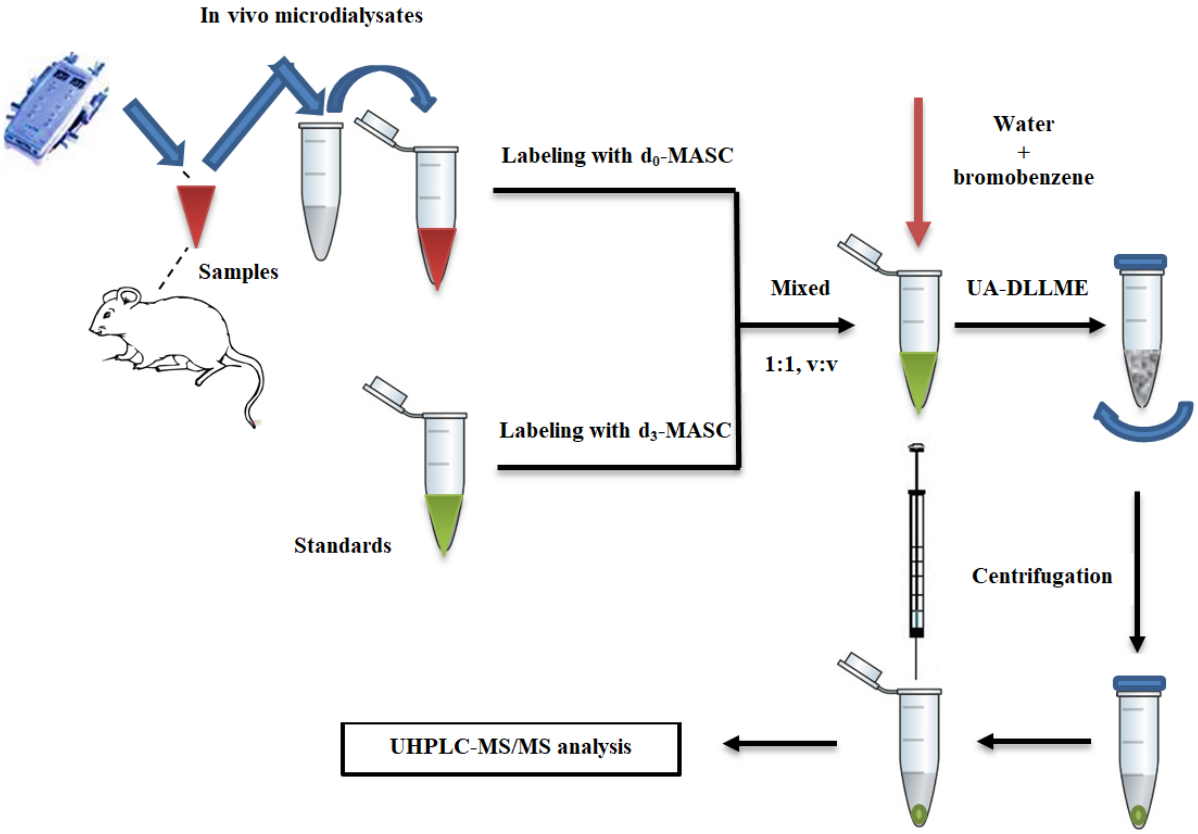

Figure 6. Isotope labelling derivatization followed by ultrasound-assisted dispersive liquid–liquid microextraction for the determination of neurotransmitters in rat brain microdialysates by UHPLC-MS/MS [52].

4.3.2.3.Post-DLLME derivatization or in between two microextractions

Addition of derivatizing reagents may further complicate the matrix for extraction, particularly when they are reactive toward matrix components other than compounds of interest. In such cases, extraction can be performed first.

An automated in syringe magnetic stirring assisted DLLME used for simultaneous extraction and preconcentration of estrogens in wastewater. DLLME was performed inside a syringe using an automated system. Mixing and dispersion was achieved through magnetic stirring. After DLLME, a certain amount of extract was taken in an amber vial where derivatizing reagents, internal standards, and other chemicals were added manually [54]. Recently, a dual ultrasound-assisted DLLME (dual-UADLLME) procedure, coupled with microwave-assisted derivatization (MAD) between two DLLMEs, has been reported for extraction of phytosterols in functional foods and medicinal herbs [55].

4.3.2.4.DLLME-Injection port derivatization

The recent example of this mode is determination of lipophilic compounds in fruit juices. DLLME was performed offline and then extract from DLLME and derivatizing reagent were injected into GC-injection port. For derivatization, the temperature of injection port, purge off time, sample: derivatization reagent ratio (v/v) were optimized. The green aspect of this

derivatization is demonstrated by the requirement of low volumes of extract and derivatizing reagent which was 1 µL each in this case [56].

4.3.2.5.DLLME-Post-column derivatization

In this approach, a post-column reactor is used after the chromatographic column to convert the analytes into some detectable derivatives. DLLME extracted aflatoxins in yogurt were determined by post-column derivatization HPLC Photo-Induced Fluorescence Detection [57]. Although DLLME is not directly coupled with derivatization in such instances, but it affects overall green nature of the process. It makes complex matrix suitable for injection to analytical instrument. The analytes after extraction are confined to a small volume of the solvent, which will ultimately require reduced amounts of derivatizing reagents. Table 2 lists DLLME based derivatization methods along with their analytical figures of merit.

4.3.3. Single drop microextraction

As apparent from the name, single drop microextraction (SDME) utilizes very little volume of the solvents compared to traditional liquid–liquid extraction. In this procedure, a syringe is employed to append a microliter drop of an extracting solvent in either direct immersion or headspace mode. After the extraction, microliter drop is directly injected into the analytical instrument. The technique represents “a highly green process” which utilizes about a single drop of the solvent with the advantages of completing extraction as well as pre-concentration in a single step. Moreover, it has other advantages such as low-cost, simple to operate, selective, and very sensitive. Some disadvantages of SPME concerning to carry over and fiber degradation can be avoided. It is suitable for the cleanup of the samples that represent matrix complexity. The most prominent advantage is its provision of automation with analytical instruments [1].

SDME is combined with derivatization in different ways

i) SDME followed by in-syringe derivatization
ii) Derivatization of the analytes in the sample solution followed by SDME.
iii) Simultaneous derivatization and extraction of the analytes within the suspended drop that is a mixture of extraction solvent and derivatizing reagent.

SDME was employed for the extraction of phenols from water samples using SDME. The analytes were extracted within a drop (2.5 µL hexylacetate) that was suspended from the syringe tip 1 cm below the surface of the sample solution (3.0 mL). After the extraction, the drop was retracted back into the syringe. Then 0.5 µL of derivatizing reagent (BSA) was withdrawn into the syringe and mixed with extract by success movement of the plunger through the syringe barrel. Then, the microsyringe was sealed by putting a GC septum over the syringe needle tip and heated at 50°C for 5 min in an oven. Since, in-syringe derivatization utilizes very small volume of the derivatizing reagent, the issues related to excess derivatizing reagent, interfering by products, and additional cleanups are not encountered. Secondly, the possibility of analyte loss due to transferring of extract is also eliminated because derivatization reaction takes place within the syringe [59].

Prior to HS-SDME, short chain fatty acids were derivatized within the sample solution. This work utilized very small volumes of derivatizing reagent (60 µL) and extraction solvent (1µL).

In addition to the green nature of overall process that arises from less use of chemicals, this method provided LODs much lower than reported by previous methods [60].
Recently, fully automated SDME that performs extraction and derivatization in a single step was used for extraction of hydroxylated PAHs from seawater. A mixture of the extracting solvent and derivatizing agent with total volume of 1.0 μL was suspended as single droplet at the tip of the syringe that was connected to an autosampler [61]. Greenness comes both from automation and reduced use of chemicals. Automation saves human efforts while reduced use of chemicals make overall process green. Table 3 provides list of some solvent based microextraction combined with derivatization.

5. Energy saving in derivatization processes

Without a doubt, the amount of energy consumed in chemical reactions is always necessary from the standpoint of Green Chemistry due to the fact that energy generation as well as consumption are considered crucial for the environment. Taking into account the fourth and ninth principles of Green Analytical Chemistry, operations that saves energy should be performed to reduce the energy consumption. Thus, it is recommended to conduct synthesis at ambient temperature and pressure. The application of high temperatures in the sample-preparation step is key in the energy consumption of any laboratory [10]. Such proceedings pushes up the analysis costs and the environmental impact. Moreover, the sample preparation and measurements steps should be carried with saving energy, thus, microextraction techniques or microextraction techniques coupled with derivatization are recommended because it not only allow to minimize the energy consumption but also shortens of the whole analysis time what also impact on energy saves.
Despite the fact that the aim is to conduct the derivatization process at room temperature, most of these processes need energy inputs (e.g. heating the reaction mixture for long time). Therefore, it is recommended to use the alternative energy sources in order to minimize energy consumption in derivatization processes. Several forms of energy could be proposed, such as microwaves, vortex, ultrasound, photochemical or electrochemical. These are considered not only more sustainable but also more effective than conventional heating sources in the laboratory [10, 64].
Application of microwaves are an alternative form of energy reduces significantly the reaction time, even though that depends strongly on the substances involved [10]. For example, in the case of application of such energy type in derivatization process occurred in reaction mixture of polar nature, the heating time is reduced from several hours to less than 5 min [65]. In addition, strict control over the temperature and the time of irradiation allows focus on a small volume of sample, resulting in increased precision [10].
Moreover, microwaves heating can be applied in digestion as well as extraction what also enhanced these processes. It is common to perform the microwave derivatization coupled to extraction what allow to carry out these processes simultaneously. Such proceeding was applied in a procedure for the determination of chlorophenolic compounds in ash samples obtained from the incineration of waste materials [66]. Analytes were simultaneously derivatized with acetic anhydride in presence of triethylamine and extracted from the sample in a mixture of *n*-

hexane acetone using a microwave system equipped with closed extraction vessels. The recoveries as well as quantification limits of the proposed procedure were very satisfied.

Nowadays, also two enhanced factors are applied in the derivatization and extraction processes. For example, multi polar groups containing biothiols were derivatized using microwave energy [63]. Due to difference of polarity, all the groups are difficult to derivatize in aqueous medium. Thus, researchers used a tandem derivatization approach which includes first derivatization in aqueous medium and then salt-assisted extraction of intermediate derivatives and excess derivatizing reagent into small volume of organic phase where remaining groups were derivatized through the aid of microwave energy. This approach is relatively greener as it allows the recovery and reuse of excess derivatizing reagents. The extraction solvent also works as aprotic derivatization medium in the second step [63]. The other example is extraction of biogenic amines in fruit juices and alcoholic beverages after derivatization with 1-naphthylisothiocyanate. This reagent overcomes disadvantages associated with other derivatizing reagents such as temperature dependent stability [67].

Nowadays, simultaneous microwave derivatization is often performed with microextraction techniques such as SPME, DLLME [68, 69]. In addition, microwave-assisted derivatization can be performed on-line what brings additional advantages (provides high sensitivity, reduces the amounts of reagents and the analysis time). Such derivatization mode can be carried out for certain reactions (for instance an on-line microwave system [70] or by application of flow injection system [71]. However, a large number of derivatization reactions do not easily adapt to flow injection systems due to the requirement for long heating times. Unfortunately, the application of microwaves for derivatization purposes is still rare in analytical laboratories. Therefore, researches are still performed in order to know better such processes.

Another factor enhanced the derivatization and extraction process of analytes reducing consumption of energy are vortex and stirring. The main advantage of mixing is the possibility to obtain high analyte enrichment without the need to use factors such as pressure, temperature, or ultrasound radiation, which may cause a degradation of analytes. In addition, a great advantage of this solution is also a much lower cost of analysis compared to solutions where ultrasonic bath or ultrasonic probes are used. This has led to the introduction to the laboratory practice of many new methodological solutions, such as vortex-assisted liquid-liquid microextraction (VALLME), vortex-assisted surfactant-enhanced emulsification microextraction (VASEME), stirring solidified floating microextraction (SC- SF-SLDME). Malondialdehyde (MDA) in human plasma was derivatized to highly fluorescent compound MDA-TBA using thiobarbituric acid (TBA) prior to its extraction VALLME. This method employed only 90 μL of n-heptanol as an extraction solvent and extraction time was about 1 min. The whole process of derivatization, extraction, and analysis was completed in 10 min. [62].

Ultrasonic assistance has become a popular enhancing factor in many chemistry fields including derivatization process because of the presence of cavitation phenomena. Generally, ultrasounds (US) causes important acceleration of reactions using softer conditions. Moreover, cavitation in a solution involves high temperatures and pressures that promote the formation of reactive radicals [10]. Mainly conventional baths are applied, however more powerful systems including probe or cup horn can also be used to increase cavitation and, in turn, sono-chemical effects on

reactions [10]. Application of US in derivatization process impact on a significant reduction in reaction time.

As was previously mentioned, simultaneous US-assisted extraction and derivatization has also been reported and both solid-liquid and liquid-liquid extraction approaches have been exploited. For example, ultrasonic assisted extraction-derivatization-DLLME was used for extraction of acrylamide from potato chips. UAE was used for extraction of acrylamide into water. This extraction was followed by derivatization using xanthydrol. The green aspect of this derivatization include use of very small volume of derivatizing agent and perfor5ming dervatization under ambient conditions within 40 min. Derivatization was followed by DLLME [58]. Such solution can bring many advantages including: shortening of extraction/derivatization time, reduction of reagent consumption, and reduction of temperature required during process. In addition, solvents used in the microextraction can be replaced by ILs enhancing the green character of the procedure. Continuous systems are appreciated in the application of US-assisted derivatization because this approach allows automation and coupling with other steps of the analytical. From the other side, ultrasounds can cause degradation and compositional changes of the analyte.

6. Conclusions and future trends

Although, the main objective of derivatization is to enhance the sensitivity, selectivity, and detectability of the analysis but greener derivatizations are getting substantial consideration in Analytical Chemistry [72]. The reason behind that is the corrosive, persistent and toxic nature of most commonly used derivatizing reagents. Moreover, the conventional derivatizations utilize extremely large volumes of derivatizing reagents, solvents, and are time-consuming. Nevertheless, the selected references indicate that many objections to the incorporation of these reactions are being circumvented. In a broader sense, there are two strategies which are of prime importance in accomplishing the goals of greener derivatizations: search and use of environment-friendly derivatizing reagents, solvents, reaction conditions, and energy sources; and miniaturization and automation of the analytical procedure [73]. Development of automated and/or miniaturized techniques demonstrated that the concerns regarding extra steps and time requirements are not necessarily at issue. Moreover, exploitation of these techniques allows to reduce the amounts of derivatizing reagents as well as generate less amount of waste. It also need to be noted that and novel separation techniques have reduced the potential of interferences arising from excess reagents. It is evident that appropriate application of analytical derivatizations brings benefits in getting higher sensitivity and more informative mass spectral data. However, some drawbacks and limitations of analytical procedures connected with derivatization still exist. And due to the fact that green analytical chemistry is an important idea nowadays, it challenges analytical chemists to devise techniques and instrumentation – particularly those that are highly automated – that take advantage of the increases in sensitivity and specificity but also reduce or eliminate the disadvantages of derivatizations.

Nowadays, to help analytical chemists to follow principles of GAC, it is common to develop a solvent selection guides, enabling the selection of greener alternatives to harmful solvents typically used in scientific and technological processes. In 2017, a guide which provides an

assessment, in terms of greenness, of almost three hundred of LC, GC and chiral derivatisation reagents typically used in analytical chemistry and related fields was published [74]. The preference rankings were performed for each group of derivatisation agents by means of multicriteria decision analysis (MCDA) which consists of a set of tools for solving complex decision problems. In the future, such tools as MCDA will be applied before the starting of analytical procedure development. Such proceeding will allow to choose the best option for an analytical problem, for example, the best analytical methodologies reagents, chemicals, derivatizing agents, etc. used for specific purposes.

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References

[1] J. M. Płotka-Wasylka, C. Morrison, M. Biziuk, J. Namieśnik, Chemical Derivatization Processes Applied to Amine Determination in Samples of Different Matrix Composition, Chem. Rev. 115 (2015) 4693−4718.

[2] J. Płotka-Wasylka, V. Simeonov, J. Namieśnik, An in situ derivatization – dispersive liquid–liquid microextraction combined with gas-chromatography – mass spectrometry for determining biogenic amines in home-made fermented alcoholic drinks, J. Chromatogr. A, 1453 (2016) 10–18.

[3] J. Rosenfeld, Enhancement of analysis by analytical derivatization, J. Chromatogr. B. 879 (2011) 1157–1158.

[4] A. Gałuszka, Z. Migaszewiski, J. Namieśnik, The 12 principles of green analytical chemistry and the significance mnemonic of green analytical practices, Trends Anal. Chem. 50 (2013) 78-84.

[5] L. H. Keith, L.U. Gron, J.L. Young, Green Analytical Methodologies, Chem. Rev. 107 (2007) 2695-2708.

[6] A.R. Fischer, N.T.P. Lan, C. Wiedemann, P. Heide, P. Werner, A.W. Schmidt, G. Theumer, H. Knoelker, Determination of 4-Nonylphenol in Water Samples Using 4-(2,6-Dimethylhept-3-yl)phenol as New Internal Standard, J. Chromatogr. A, 1217 (2010) 2950-2955.

[7] C.-E. Baños, M. Silva, In situ continuous derivatization/pre-concentration of carbonyl compounds with 2,4-dinitrophenylhydrazine in aqueous samples by solid-phase extraction Application to liquid chromatography determination of aldehydes, Talanta, 77 (2009) 1597-1602.

[8] G.G. Noche, M.E. FernándezLaespada, J.L.P. Pavón, B.M. Cordero, S.M. Lorenzo, In situ aqueous derivatization and determination of non-steroidal anti-inflammatory drugs by salting-out-assisted liquid-liquid extraction and gas chromatography-mass spectrometry, J. Chromatogr A, 1218 (2011) 6240-6247.

[9] M. A. Farajzadeh, N. Nouri, P. Khorram, Derivatization and microextraction methods for determination of organic compounds by gas chromatography, Trends Anal. Chem., 55 (2014) 14-23.

[10] I. Lavilla, V. Romero, I. Costas, C. Bendicho, Greener derivatization in analytical chemistry, Trends Anal. Chem., 61 (2014) 1–10.

[11] A. Gałuszka, P. Konieczka, Z. M. Migaszewski, J. Namieśnik, Analytical Eco-Scale for assessing the greenness of analytical procedures, Trends Anal. Chem. 37 (2012) 61-72.

[12] https://www.epa.gov/toxics-release-inventory-tri-program [Available on: 1.12.2017]

[13] P. Englmaier, Trimethylsilyl esters of plant acids and their application in gas chromatography. Preparation, kinetics of silylation and effect of a different solvent on the quantitative reaction and stability of the derivatives, J. Chromatogr. A 194 (1980) 33–42.

[14] X. Xu, R. Su, X. Zhao, Z. Liu, D. Li, X. Li, H. Zhang, Z. Wang, Determination of formaldehyde in beverages using microwave-assisted derivatization and ionic liquid-based dispersive liquid–liquid microextraction followed by high-performance liquid chromatography, Talanta 85 (2011) 2632-2638.

[15] J.W. King, Z. Zhang, Derivatization reactions of carbamate pesticides in supercritical carbon dioxide, Anal. Bioanal. Chem. 374 (2002) 88–92.

[16] R.A. Al-Okab, Cisapride a green analytical reagent for rapid and sensitive determination of bromate in drinking water, bread and flour, Spectrochim. Acta A. 103 (2013) 333–337.

[17] R.B.R. Mesquita, M.L.F.O.B. Noronha, A.I.L. Pereira, A.C.F. Santos, A.F. Torres, V. Cerdá, A.O.S.S. Rangel, Use of tetramethylbenzidine for the spectrophotometric sequential injection determination of free chlorine in waters, Talanta 72 (2007) 1186–1191.

[18] K. Grudpan, S.K. Hartwell, S. Lapanantnoppakhun, I. McKelvie, The case for the use of unrefined natural reagents in analytical chemistry. A green chemical perspective, Anal. Methods 2 (2010) 1651–1661.

[19] H. Lin, J. Wang, L. Zeng, G. Li, Y. Sha, D. Wu, B. Liu, Development of solvent micro-extraction combined with derivatization, J. Chromatogr. A 1296 (2013) 235–242.

[20] C.L. Arthur, J. Pawliszyn, Solid phase microextraction with thermal desorption using fused silica optical fibers, Anal. Chem. 62 (1990) 2145–2148.

[21] L. Pan, J. Pawliszyn, Derivatization/Solid-Phase Microextraction: New Approach to Polar Analytes, Anal. Chem. 69 (1997) 196–205.

[22] X. Wang, L. Pan, J. Feng, Y. Tian, C. Luo, M. Sun, Silk fiber for in-tube solid-phase microextraction to detect aldehydes by chemical derivatization, J. Chromatogr. A. 1522 (2017) 16–22.

[23] M. Vila, M. Celeiro, J.P. Lamas, C. Garcia-Jares, T. Dagnac, M. Llompart, Simultaneous in-vial acetylation solid-phase microextraction followed by gas chromatography tandem mass spectrometry for the analysis of multiclass organic UV filters in water, J. Hazard. Mater. 323 (2017) 45–55.

[24] J. Huang, N. Gan, F. Lv, Y. Cao, C. Ou, H. Tang, Environmentally friendly solid-phase microextraction coupled with gas chromatography and mass spectrometry for the determination of biogenic amines in fish samples, J. Sep. Sci. 39 (2016) 4384–4390.

[25] Y. Jiang, Y. Ni, Automated headspace solid-phase microextraction and on-fiber derivatization for the determination of clenbuterol in meat products by gas chromatography coupled to mass spectrometry, J. Sep. Sci. 38 (2015) 418–425.

[26] M. del Olmo, A. Zafra, B. Suárez, A. Gonzalez-Casado, J. Taoufiki, J.L. Vílchez, Use of solid-phase microextraction followed by on-column silylation for determining chlorinated bisphenol A in human plasma by gas chromatography–mass spectrometry, J. Chromatogr. B. 817 (2005) 167–172.

[27] X. Pang, A.C. Lewis, M.D. Shaw, Analysis of biogenic carbonyl compounds in rainwater by stir bar sorptive extraction technique with chemical derivatization and gas chromatography-mass spectrometry, J. Sep. Sci. 40 (2017) 753–766.

[28] M. Kawaguchi, Y. Ishii, N. Sakui, N. Okanouchi, R. Ito, K. Saito, H. Nakazawa, Stir bar sorptive extraction with in situ derivatization and thermal desorption–gas chromatography–mass spectrometry for determination of chlorophenols in water and body fluid samples, Anal. Chim. Acta. 533 (2005) 57–65.

[29] J. Li, H.-Y. Qi, Y.-B. Wang, Q. Su, S. Wu, L. Wu, Hollow fiber–stir bar sorptive extraction and microwave assisted derivatization of amino acids in biological matrices, J. Chromatogr. A. 1474 (2016) 32–39.

[30] A.M. Casas Ferreira, M.E. Fernández Laespada, J.L. Pérez Pavón, B. Moreno Cordero, In situ derivatization coupled to microextraction by packed sorbent and gas chromatography for the automated determination of haloacetic acids in chlorinated water, J. Chromatogr. A. 1318 (2013) 35–42.

[31] A.M. Casas Ferreira, B. Moreno Cordero, Á.P. Crisolino Pozas, J.L. Pérez Pavón, Use of microextraction by packed sorbents and gas chromatography-mass spectrometry for the determination of polyamines and related compounds in urine, J. Chromatogr. A. 1444 (2016) 32–41.

[32] A. Prieto, A. Vallejo, O. Zuloaga, A. Paschke, B. Sellergen, E. Schillinger, S. Schrader, M. Möder, Selective determination of estrogenic compounds in water by microextraction by

packed sorbents and a molecularly imprinted polymer coupled with large volume injection-in-port-derivatization gas chromatography–mass spectrometry, Anal. Chim. Acta. 703 (2011) 41–51.

[33] A. Mehdinia, F. Roohi, A. Jabbari, Rapid magnetic solid phase extraction with in situ derivatization of methylmercury in seawater by Fe_3O_4/polyaniline nanoparticle, J. Chromatogr. A. 1218 (2011) 4269–4274.

[34] J.-F. Liu, B.-F. Yuan, Y.-Q. Feng, Determination of hexanal and heptanal in human urine using magnetic solid phase extraction coupled with in-situ derivatization by high performance liquid chromatography, Talanta, 136 (2015) 54–59.

[35] C. Basheer, H.K. Lee, Analysis of endocrine disrupting alkylphenols, chlorophenols and bisphenol-A using hollow fiber-protected liquid-phase microextraction coupled with injection port-derivatization gas chromatography-mass spectrometry, J. Chromatogr. A. 1057 (2004) 163–9.

[36] M. Ganjikhah, S. Shariati, E. Bozorgzadeh, Preconcentration and spectrophotometric determination of trace amount of formaldehyde using hollow fiber liquid-phase microextraction based on derivatization by Hantzsch reaction, J. Iran. Chem. Soc. 14 (2017) 763–769.

[37] A.M.F. Pego, F.L. Roveri, R.Y. Kuninari, V. Leyton, I.D. Miziara, M. Yonamine, Determination of cocaine and its derivatives in hair samples by liquid phase microextraction (LPME) and gas chromatography–mass spectrometry (GC–MS), Forensic Sci. Int. 274 (2017) 83–90.

[38] M. Rezazadeh, Y. Yamini, S. Seidi, A. Aghaei, Pulsed electromembrane extraction for analysis of derivatized amino acids: A powerful technique for determination of animal source of gelatin samples, Talanta, 136 (2015) 190–197.

[39] M.A.M. Fernandez, L.C. André, Z. de L. Cardeal, Hollow fiber liquid-phase microextraction-gas chromatography-mass spectrometry method to analyze bisphenol A and other plasticizer metabolites, J. Chromatogr. A. 1481 (2017) 31–36.

[40] M. Saraji, M. Ghani, Hollow fiber liquid–liquid–liquid microextraction followed by solid-phase microextraction and in situ derivatization for the determination of chlorophenols by gas chromatography-electron capture detection, J. Chromatogr. A, 1418 (2015) 45–53.

[41] M. Rezaee, Y. Assadi, M.-R. Milani Hosseini, E. Aghaee, F. Ahmadi, S. Berijani, Determination of organic compounds in water using dispersive liquid-liquid microextraction, J. Chromatogr. A, 1116 (2006) 1–9.

[42] M. Faraji, M. Adeli, Sensitive determination of melamine in milk and powdered infant formula samples by high-performance liquid chromatography using dabsyl chloride derivatization followed by dispersive liquid–liquid microextraction, Food Chem., 221 (2017) 139–146.

[43] Y. He, X.-E. Zhao, S. Zhu, N. Wei, J. Sun, Y. Zhou, S. Liu, Z. Liu, G. Chen, Y. Suo, J. You, In situ derivatization-ultrasound-assisted dispersive liquid–liquid microextraction for the determination of neurotransmitters in Parkinson's rat brain microdialysates by ultra high

performance liquid chromatography-tandem mass spectrometry, J. Chromatogr. A, 1458 (2016) 70–81.

[44] X.-E. Zhao, Y. He, M. Li, G. Chen, N. Wei, X. Wang, J. Sun, S. Zhu, J. You, Analysis of amino acid and monoamine neurotransmitters and their metabolites in rat urine of Alzheimer's disease using in situ ultrasound-assisted derivatization dispersive liquid-liquid microextraction with UHPLC–MS/MS, J. Pharm. Biomed. Anal. 135 (2017) 186–198.

[45] Y. He, X.-E. Zhao, R. Wang, N. Wei, J. Sun, J. Dang, G. Chen, Z. Liu, S. Zhu, J. You, Simultaneous Determination of Food-Related Biogenic Amines and Precursor Amino Acids Using in Situ Derivatization Ultrasound-Assisted Dispersive Liquid–Liquid Microextraction by Ultra-High-Performance Liquid Chromatography Tandem Mass Spectrometry, J. Agric. Food Chem. 64 (2016) 8225–8234.

[46] M. Rajabi, A. Sarhadi, M. Bazregar, A. Asghari, E. Mirparizi, Rapid derivatization and extraction of paraben preservatives by fast syringe-assisted liquid–liquid microextraction and their determination in cosmetic and aqueous sample solutions by gas chromatography, Anal. Methods. 9 (2017) 5963–5969.

[47] M.A. Farajzadeh, H. Nasrollahpour, M.R.A. Mogaddam, L. Khoshmaram, Determination of widely used non-steroidal anti-inflammatory drugs in biological fluids using simultaneous derivatization and air-assisted liquid–liquid microextraction followed by gas chromatography–flame ionization detection, J. Iran. Chem. Soc. 13 (2016) 289–298.

[48] K.-D. Wang, P.-S. Chen, S.-D. Huang, Simultaneous derivatization and extraction of chlorophenols in water samples with up-and-down shaker-assisted dispersive liquid–liquid microextraction coupled with gas chromatography/mass spectrometric detection, Anal. Bioanal. Chem. 406 (2014) 2123–2131.

[49] A.A. Alizadeh Nabil, N. Nouri, M.A. Farajzadeh, Determination of three antidepressants in urine using simultaneous derivatization and temperature-assisted dispersive liquid-liquid microextraction followed by gas chromatography-flame ionization detection, Biomed. Chromatogr. 29 (2015) 1094–1102.

[50] M.A. Farajzadeh, P. Khorram, H. Ghorbanpour, Simultaneous derivatization and solid-based disperser liquid–liquid microextraction for extraction and preconcentration of some antidepressants and an antiarrhythmic agent in urine and plasma samples followed by GC-FID, J. Chromatogr. B. 983–984 (2015) 55–61.

[51] S. Clavijo, J. Avivar, R. Suárez, V. Cerdà, In-syringe magnetic stirring-assisted dispersive liquid–liquid microextraction and silylation prior gas chromatography–mass spectrometry for ultraviolet filters determination in environmental water samples, J. Chromatogr. A. 1443 (2016) 26–34.

[52] L. Zheng, X.-E. Zhao, S. Zhu, Y. Tao, W. Ji, Y. Geng, X. Wang, G. Chen, J. You, A new combined method of stable isotope-labeling derivatization-ultrasound-assisted dispersive liquid–liquid microextraction for the determination of neurotransmitters in rat brain microdialysates by ultra high performance liquid chromatography tandem mas spectrometry, J. Chromatogr. B. 1054 (2017) 64–72.

[53] H. Wu, G. Li, S. Liu, N. Hu, D. Geng, G. Chen, Z. Sun, X. Zhao, L. Xia, J. You, Monitoring the contents of six steroidal and phenolic endocrine disrupting chemicals in chicken, fish and aquaculture pond water samples using pre-column derivatization and dispersive liquid–liquid microextraction with the aid of experimental design methodology, Food Chem. 192 (2016) 98–106.

[54] A. González, J. Avivar, V. Cerdà, Estrogens determination in wastewater samples by automatic in-syringe dispersive liquid–liquid microextraction prior silylation and gas chromatography, J. Chromatogr. A. 1413 (2015) 1–8.

[55] J. Sun, X.-E. Zhao, J. Dang, X. Sun, L. Zheng, J. You, X. Wang, Rapid and sensitive determination of phytosterols in functional foods and medicinal herbs by using UHPLC-MS/MS with microwave-assisted derivatization combined with dual ultrasound-assisted dispersive liquid-liquid microextraction, J. Sep. Sci. 40 (2017) 725–732.

[56] A. Marsol-Vall, M. Balcells, J. Eras, R. Canela-Garayoa, Dispersive liquid–liquid microextraction and injection-port derivatization for the determination of free lipophilic compounds in fruit juices by gas chromatography-mass spectrometry, J. Chromatogr. A. 1495 (2017) 12–21.

[57] A.M. Hamed, D. Moreno-González, A.M. García-Campaña, L. Gámiz-Gracia, Determination of Aflatoxins in Yogurt by Dispersive Liquid–Liquid Microextraction and HPLC with Photo-Induced Fluorescence Detection, Food Anal. Methods. 10 (2017) 516–521.

[58] M. Zokaei, A.-S. Abedi, M. Kamankesh, S. Shojaee-Aliababadi, A. Mohammadi, Ultrasonic-assisted extraction and dispersive liquid-liquid microextraction combined with gas chromatography-mass spectrometry as an efficient and sensitive method for determining of acrylamide in potato chips samples, Food Chem. 234 (2017) 55–61.

[59] M. Saraji, M. Bakhshi, Determination of phenols in water samples by single-drop microextraction followed by in-syringe derivatization and gas chromatography–mass spectrometric detection, J. Chromatogr. A. 1098 (2005) 30–36.

[60] Y. Chen, Y. Li, Y. Xiong, C. Fang, X. Wang, An effective pre-treatment method for the determination of short-chain fatty acids in a complex matrix by derivatization coupled with headspace single-drop microextraction, J. Chromatogr. A. 1325 (2014) 49–55.

[61] X. Wang, Y. Li, F. Cai, Q. Qing, K. Yuan, B. Chen, T. Luan, Fully automatic single-drop microextraction with one-setp extraction and derivatization and its application for rapid analysis of hydroxylated polycyclic aromatic hydrocarbons in seawaters, Talanta, 164 (2017) 727–734.

[62] H. Yahyavi, M. Kaykhaii, M. Hashemi, A rapid spectrofluorimetric method for the determination of malondialdehyde in human plasma after its derivatization with thiobarbituric acid and vortex assisted liquid–liquid microextraction, RSC Adv. 6 (2016) 2361–2367.

[63] C.-J. Tsai, F.-Y. Liao, J.-R. Weng, C.-H. Feng, Tandem derivatization combined with salting-out assisted liquid–liquid microextraction for determination of biothiols in urine by gas chromatography–mass spectrometry, J. Chromatogr. A. 1524 (2017) 29-36.

[64] A. Stankiewicz, Alternative sources and forms of energy for intensification of chemical and biochemical processes, Chem. Eng. Res. Des. 84 (2006) 511–521.

[65] A. Dasgupta, P. Banerjee, Microwave-induced rapid preparation of acetyl, trifluoroacetyl and tert-butyl dimethylsilyl derivatives of fatty alcohols and diacylglycerols for gas chromatography-mass spectrometric analysis, Chem. Phys. Lipids 65 (1993) 217–224.

[66] M. Ramil Criado, S. Pombo da Torre, I. Rodriguez Pereiro, R. Cela Torrijos, Optimization of a microwave-assisted derivatization-extraction procedure for the determination of chlorophenols in ash samples, J. Chromatogr. A 1024 (2004) 155–163.

[67] A. Jain, M. Gupta, K.K. Verma, Salting-out assisted liquid–liquid extraction for the determination of biogenic amines in fruit juices and alcoholic beverages after derivatization with 1-naphthylisothiocyanate and high performance liquid chromatography, J. Chromatogr. A. 1422 (2015) 60–72.

[68] J.T. Hsu, C.W. Whang, Microwave-assisted SPME/on-fiber derivatization of chromium (III) in water followed by GC-MS analysis, Chromatographia 71 (2010) 957–961.

[69] X. Xu, Z. Liu, X. Zhao, R. Su, Y. Zhang, J. Shi, Y. Zhao, L. Wu, Q. Ma, X. Zhou, H. Zhang, Z. Wang, Ionic liquid-based microwaveassisted surfactant-improved dispersive liquid-liquid microextraction and derivatization of aminoglycosides in milk samples, J. Sep. Sci. 36 (2013) 585–592.

[70] G. Chávez, B. Bravo, N. Piña, M. Arias, E. Vivas, F. Ysambertt, N. Márquez, A. Cáceres, Determination of aliphatic alcohols after on-line microwave-assisted derivatization by liquid chromatography-photodiode array detection, Talanta 64 (2004) 1323–1328.

[71] X.Q. Zhao, Z.Q. Zhang, Microwave-assisted on-line derivatization for sensitive flow injection fluorometric determination of formaldehyde in some foods, Talanta 80 (2009) 242–245.

[72] D. R. Knapp, Handbook of analytical derivatization reactions, Wiley, New York, USA, 1979.

[73] C.F. Poole, Microreactions in separation science: Reagents and techniques, J. Chromatogr. A 1296 (2013) 1.

[74] M. Tobiszewski, J. Namieśnik, F. Pena-Pereira, A derivatisation agent selection guide, Green Chem. 19 (2017) 5911–5922.