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Solid phase analytical derivatization as a sample preparation method

Sanka N. Atapattu*, Jack M. Rosenfeld

Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON L8S 4K1, Canada

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ABSTRACT

Analytical derivatization (AD) is an important procedure in analysis as it improves the sensitivity, selectivity and chromatographic separation. Solid phase analytical derivatization (SPAD) combines extraction and derivatization into a single step fulfilling many aspects of a good sample preparation technique, which includes low organic solvent consumption, economical, ease of automation with any chromatographic system and applicability in a wide range of complicated matrices. In this review we have focused on wide applications of SPAD when used in combination with different sample preparation methods, such as solid phase extraction, ion exchange resins, solid phase microextraction, in-tube, microfluidic devices, and hollow fiber extraction methods.

1. Introduction

1.1. Overview of sample preparation

Sample preparation (SPrep) is a critical step in analytical chemistry. It is certainly required in most standard analytical equipment and even the methods based on the advanced instruments benefit by the separation of analyte from matrix components [1,2]. The techniques for this separation generally involve fractionation between an aqueous phase and a water immiscible extracting phase. The extracting phase could be a volatile organic solvent or a pseudophase sorbed on a solid phase. Once partition is complete, the extracting phase is removed and analytes are isolated/concentrated by a number of techniques. A considerable body of research was and remains focused on simplifying and automating sample preparation.

1.2. Liquid–liquid extraction (LLE)

LLE is the classical SPrep for biological and environmental samples [2,3]. Developed in the 1950s and used into the mid-70s this technique led to the first analytical methods for measuring drugs and their metabolites in biofluids. While leading to the classical bioanalytical and environmental chemistry LLE, is nevertheless time consuming, labor intensive and requires large amounts of organic solvents. It is also relatively difficult to automate [4,5].

Investigators addressed these problems of this classical with a variety of innovative techniques that are discussed below. Throughout these studies the focus was on high throughput techniques, simplification, automation and miniaturization.

1.3. Solid phase extraction (SPE)

Development of SPE overcame some of these disadvantages and reduced solvent consumption, labor requirements and advanced automation [3,5]. In SPE, the analyte is partitioned between the biological or environmental aqueous liquid phase and a reverse phase column typically C_{18} linked to a silica support or an organic polymer [5]. The solid phase retains the analyte during removal of the aqueous phase and subsequent washing to remove various components. Analyte can then be desorbed by solvent or thermal desorption.

Although an improvement over LLE, use of SPE presented other problems [3]. It required careful control of the flow rate through the column both for sorbing analyte from the aqueous phase and eluting the analyte with organic solvent. Although SPE requires less eluting solvent, than the corresponding LLE technique the solvent burden is still large. This would be particularly true for laboratories with high throughput.

Matrix solid-phase dispersion extraction (MSDE), “quick, easy, cheap, effective, rugged and safe” (QuEChERS), purge-and-trap extraction and static headspace extraction are some of the recently reported alternatives for SPE.

1.4. Solid phase micro-extraction (SPME)

Elimination of the eluting solvent became possible with the creation of SPME [6–8]. This is a completely solvent-less technique for separating analytes from their matrix and is fully automated

* Corresponding author at: 3N26-1280 Main Street West, McMaster University, Hamilton, ON L8S 4K1, Canada. Tel.: +1 905 818 4008; fax: +1 313 577 2099.
E-mail address: sanka@wayne.edu (S.N. Atapattu).

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[8]. SPME is thoroughly investigated for determination of analytes from numerous matrices and is one of the most cited techniques in the analytical chemistry literature. SPME involves the use of a fiber coated with the extracting phase which extracts analytes. After extraction analytes are thermally desorbed from the SPME fiber by transferring into an injection port of a chromatographic instrument. Although widely used, SPME cost of equipment and the fibers themselves can be an issue.

A variant of SPME is stir bar sorptive micro extraction (SBSME) in which typically a 0.5–1 mm thick polydimethylsiloxane coating of stir bars is the extraction phase. Stir bars are contacted in aqueous medium to extract analytes [9,10]. After extraction, either thermal desorption or liquid desorption can be used before analysis.

1.5. Single drop microextraction (SDME)

This LLE technique was developed as an inexpensive alternative to SPME. Jeannot and Cantwell reported the first SDME method for chromatographic analysis [11]. In their first report few microliters of octane was immersed in aqueous sample aid of a Teflon rod. The sample solution was stirred to accelerate extraction. After extraction the rod was removed and a portion of the octane solvent was injected to a GC/FID for analysis. It found a variety of applications but exhibited some deficits such as a small interfacial area, droplet instability when the aqueous phase was stirred at high speed to provide efficient extraction.

1.6. Hollow fiber liquid–liquid–liquid extraction (HFLLLE)

The HFLLLE addressed the issue of droplet instability by using a porous hollow fiber with the impregnated organic solvent acts as an interface between the acceptor and donor phases. Pedersen-Bjergaard and Rasmussen reported the first LLLME method based on the use of porous hollow fibers made out of polypropylene [12]. In HFLLLE methods the analytes of interest are extracted from the aqueous donor phase to the thin layer organic solvent impregnated in the pores of the hollow fiber and then to the acceptor phase inside the lumen of the hollow fiber [12,13]. In the two phase mode the acceptor solution is an organic solvent and therefore more compatible with GC analysis. The acceptor solution is aqueous in the three phase mode which is more compatible with LC analysis. The major advantage of the HFLLLE method is very clean extracts resulting from the small pore size of the hollow fiber which prevents interfering substance particles present in the donor phase entering the acceptor phase and due to the low solubility of organic phase present in the pores. HFLLLE methods have been successfully applied to analyze biological and environmental sample with complex matrices.

1.7. Dispersive liquid–iquid microextraction (DLLME)

This is a three solvent component system consisting an aqueous phase, extracting solvent (nonpolar water immiscible solvent), and disperser solvent (polar water miscible solvent) [14,15]. A mixture of disperser and extracting solvents are injected to the aqueous phase to form a cloudy solution. The cloudiness consists of micro-droplets of water immiscible solvent and the high surface area speeds the extraction process. Extracting solvent containing the target analytes are then separated from the aqueous phase by centrifugation.

1.8. Ionic liquids (ILs)

These ionic solvents possess low melting points, low vapor pressures, high thermal stability, nonflammability, and good solubility for inorganic and organic compounds [16]. Many physical properties of ILs can be varied by varying the structure according to analyte extraction selectivity, efficiency, and sensitivity needs. These features make ILs an excellent extraction media for many liquid phase microextraction techniques such as DLLME, HFLLLME, and SDME.

2. Analytical derivatization

Current requirements of analytical methods are high sensitivity, high throughput, ease of use, precision, accuracy and automation. Although instrumentation meets some of these requirements, sample preparation that takes place prior to instrumental analysis is still under active research and development. Despite extra steps reagents, analytical derivatization (AD) of the analyte during SPrep can substantially improve sensitivity of detection, chromatographic separation, and selectivity [2]. Even in the case of mass spectrometry (MS), which is the most sophisticated detector, AD increases sensitivity by one to three orders of magnitude [17]. The use of this technique is limited because it includes an extra step in sample preparation which can be time consuming and cumbersome to execute. Despite these drawbacks advantages of AD generated efforts to simplify, reduce the solvent burden and automate the process [1,2,17,18].

2.1. Applications with extractive alkylation/phase transfer catalysis

Classical AD methods involve extraction of the analyte into an organic phase, isolation of the analyte by evaporation of the extracting phase followed by derivatization in a homogenous phase [17]. It is time consuming and labor intensive. The first effort to circumvent these problems was the development of extractive alkylation (EA) or phase transfer catalysis (PTC) which combines extraction and derivatization in a single step [19,20]. In the presence of counter-ions the ionized analytes form a lipophilic ion-pair which is extracted from an aqueous phase to an organic phase containing reagent. Analyte is usually derivatized in the organic phase. Although EA combined the extraction and derivatization step, it is a LLE method and required large amounts of organic solvents. Clearly there was a need to improve the efficiency of this and other early derivatization technique. Table 1 is a compilation of some of the EA/PTC examples.

2.2. Applications with SDME

SDME is a very simple, low cost and easy to operate liquid–liquid extraction sample preparation method. Typically 1–5 μL of organic extractive solvent suspended with the aid of a need syringe tip. After the analyte of interest is extracted the solvent is retracted into the needle and injected for analysis [30]. Analytes of interest can be derivatized in four ways, derivatizing in the donor aqueous phase, in the extractive solvent droplet, GC injector port in the syringe needle barrel [30,31]. Few examples of AD using SDME as the sample preparation method are listed in Table 2.

2.3. Applications with solid phase extraction

Many AD applications have been reported combining SPE and derivatization in literature. There are four modes of AD with SPE: (i) impregnating the solid phase with the derivatizing reagent and then passing the sample solution through the solid phase, (ii) passing the sample solution in order to adsorb on the solid phase and then percolate the derivatizing reagent, (iii) derivatize the analyte before the SPE step, and (iv) derivatize the analyte after the SPE step