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Review

Fluorous media for extraction and transport

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ABSTRACT

Selective partitioning can be useful for sample cleanup or the isolation and purification of desired compounds. Fluorocarbon solvents and polymers, and solvents or polymers with similar properties that are not composed solely of carbon and fluorine (so-called 'fluorous' solvents or polymers) have a low ability to dissolve or sorb solutes or penetrants. This lack of solvating ability can lead to selective extractions. Fluorous phases will solvate, and therefore extract or transport, fluorous solutes, or non-fluorous solutes that are stabilized in the fluorous phase by non-covalent interactions with a 'host' or 'receptor' molecule that is in the fluorous phase. In this review, there is a brief discussion of molecular recognition as applied to selective extraction. Fluorous solvents are introduced, and there is a description of some recent applications, chiefly in synthetic organic chemistry. In particular, it is important to understand solute partitioning behavior and methods to predict it when one of the solvents is fluorous. Fluorous polymers Teflon AF1600 and AF2400 have been used in separations. Their rather complex and still not completely understood properties in separations and transport are described. There is a discussion of molecular recognition in fluorous phases as well as a brief discussion of efficient methods of carrying out extractions for analytical or physicochemical purposes.

Contents

1. Introduction

Despite the rapid development of analytical instrumentation, most analytical methods still incorporate some kind of pretreatment step or sample preparation. Sample preparation methods typically involve a separation step in which analytes and other species are removed from the sample and concentrated with the overall goal of increasing the signal-to-noise ratio of the measurement. Despite the significant impact that sample preparation methods have on the success of the overall analytical process, they have traditionally been laborious, time consuming, waste generating, and practically neglected by the research community [1]. Today, because of developments in high-throughput measurements, sample preparation is often the rate determining step in the analytical process, thus driving the need for improvement. In addition, increasing awareness of our impact on the environment has placed a greater emphasis on analytical methods that produce less waste.

Extraction and adsorption/elution are the most widely used sample preparation techniques. The goal of any such operation is the selective removal of a target analyte from the sample matrix. Liquid–liquid extraction (LLE) is a method to separate compounds based on their distribution between two immiscible liquid phases. LLE is an equilibrium process, thermodynamically driven by a difference in chemical potential of the solute in each phase. Concentration is achieved when the analyte, *x*, has a high distribution

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coefficient (D_c) between phase *a* and *b*. D_c, given by Eq. (1), is the ratio of the sums of the concentrations (C_x) of all forms of the analyte in each phase.

$$D_c = \frac{C_{x,b}}{C_{x,a}} \quad (1)$$

D_c is distinguished from a partition coefficient (K_c) in that D_c includes all forms of the sample component (i.e. free, complexed, ionized, dimerized, etc.) while K_c only considers one particular form.

Solid phase extraction (SPE) is one of the most common sampling techniques in environmental, pharmaceutical, clinical, and food chemistry [2]. In SPE, analytes are exhaustively removed from a flowing sample matrix by transfer and sorption to a solid phase. Solid phase microextraction (SPME) is another widely accepted technique that was later developed by the Pawliszyn group [3,4]. SPME most often involves the non-equilibrium removal of chemical constituents from a sample matrix by retention on a sorbent or in a film with subsequent desorption of target analytes. SPME differs from SPE in that the sorbent material is coated on a fine rod which makes the approach particularly suitable for analysis by gas chromatography. Selection of the sorbent material can be crucial to the success of the separation. It must be able to sorb sample constituents rapidly and reproducibly [5] yet components must be easily eluted from the sorbent [6], meaning that the sorption process must be reversible. Many materials are used as the solid phase in SPE and SPME, however there is no universal sorbent for all applications [7] and retention behavior can vary dramatically among sorbent materials. Therefore, it is necessary to continue to explore new materials for SPE and SPME applications and design sorbents for specific analyte/matrix systems.

2. The selectivity of an extraction

The selectivity of an extraction is defined as the ratio of the relative concentrations of the analyte and interfering species in the two phases. Approaches to altering or improving the selectivity of an extraction include the choice of the extraction solvent, manipulation of the properties of the extracting solvent (i.e. temperature and pressure if the extracting medium is compressible, e.g. CO_2) or adsorbent (e.g. an adsorbent's activity), and by the application of restricted access media (RAM) and molecularly imprinted polymers (MIPs) [8]. It has also been shown that extraction selectivity is enhanced through incorporating an artificial molecular receptor into the receiving phase [9,10].

Artificial receptors work based on molecular recognition, a chemical phenomenon involving non-covalent interactions between a receptor and substrate. It is one of the most fundamental phenomena in chemistry. Selectivity is attained by arranging non-covalent forces (e.g. electrostatic and van der Waals interactions) between substrate and receptor to occur in a sterically and geometrically defined way. Selective molecular recognition plays an essential role in many life processes, including DNA base pairing, tRNA binding to amino acids, enzyme-substrate binding, neurotransmitter and neuropeptide binding at receptors, cell organelle self-assembly, and pheromone-mediated chemical communication [11]. Many novel approaches to analytical chemistry are based on molecular recognition, or host–guest chemistry such as chiral separations, immunoassays, aptamer-based systems, ionophores, and sensors.

Our group has been interested in combining molecular recognition processes with separation and sample preparation methods. It is interesting to contrast *molecular* recognition with *metal ion* recognition that has been used for selective extraction and analysis for decades. Metal ion recognition typically involves multidentate ligands that are of one type—Lewis base. Although the geometry

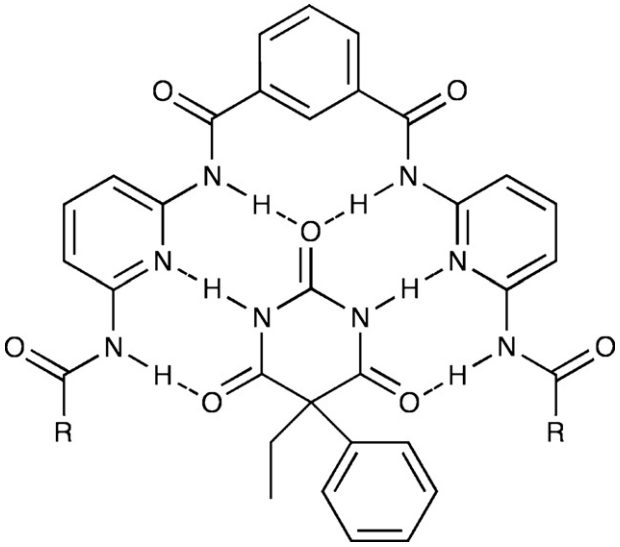

Fig. 1. Artificial molecular receptor (R = 1-propyl) binding with phenobarbital.

may vary, they are always capable of being arranged convergently, pointing to a central metal ion. The Lewis base/Lewis acid interactions are often very strong. When applied in extractions, it is almost always the case that the partitioning of the metal ion to the organic phase in the absence of a chelator is negligible. Thus, the selectivity of the extraction is completely defined by the selectivity of the chelating agent and the partition coefficients of the complexes. In *molecular* recognition, the receptor or host may have a variety of functional groups—acidic, basic, hydrophobic, aromatic. The interaction energies are not necessarily large. When applied in extractions, the natural tendency of solutes (both desired solutes, i.e. analytes and undesired solutes, i.e. interferences) to partition in part controls the selectivity of the molecular-recognition-assisted extraction. Valenta et al. [12] observed a 40-fold increase in extraction yield when they incorporated an artificial molecular receptor (Fig. 1) into a chloroform receiving phase in the extraction of phenobarbital from human control serum compared with receptor-free chloroform. This work was pivotal in demonstrating the effectiveness of artificial receptors in analytical applications.

With suitable modification of the receptor (R = 2-ethylhexyl) it can be made soluble in plasticized poly(vinyl chloride) (PVC). Li et al. [10] developed a plasticized PVC extraction medium coated on a fine rod for SPME with capillary electrophoresis (CE) detection of barbiturates (Fig. 2) [10].

In a series of investigations on the influence of the plasticizer, which acts as a solvent [9,13–15], it became clear that the solvent plays a strong role in the selectivity of the receptor-based extraction. Among the plasticizers used for PVC in extractions with the receptor (Fig. 1), chloroparaffin had the lowest polarity (as determined by its values for Kamlet-Taft solvatochromic parameters). It showed the highest selectivity for a series of barbiturates. Here, selectivity is defined as the ratio of the distribution coefficient of the drug in the presence of receptor to the same quantity in the absence of the receptor. This demonstrates the general premise that in molecular recognition-based extractions, selectivity for a target is high if non-covalent intermolecular interactions between receptor and target dominate the standard-state free energy change for the extraction process. The most selective extractions are those in which the receptor is completely responsible for the partitioning or distribution of the analyte into the extracting phase. Thus a matrix that is a poor solvent will provide a more selective environment for molecular recognition interactions [10,16]. It makes sense, then, to consider the worst possible solvents as matrices for selective