Separation Technologies

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Chapter 4: Advanced Solvent Extraction Techniques and Processes

4.1. Introduction

Conventional solvent extraction is a proven technology for the isolation of solutes from comparatively concentrated feeds found in the industrially produced chemicals and metals by hydrometallurgy. Dilute streams, instead, are quite challenging. A very large value of distribution ratio is required to treat these streams using the conventional liquid-liquid extraction method; otherwise, the organic phase volume would become excessively high from environmental and safety concerns (Hennion, 1999; Gilbert-Lypez et al., 2009).

In the last decades, the established innovative solvent extraction technologies tried to address these challenges. The potential of these technologies to enhance the outcome of conventional solvent extraction is explored in this chapter consistent with modern trends in the principles and solvent development (Figure 4.1) (Aulakh et al., 2005; Sónchez-Rojas et al., 2009).
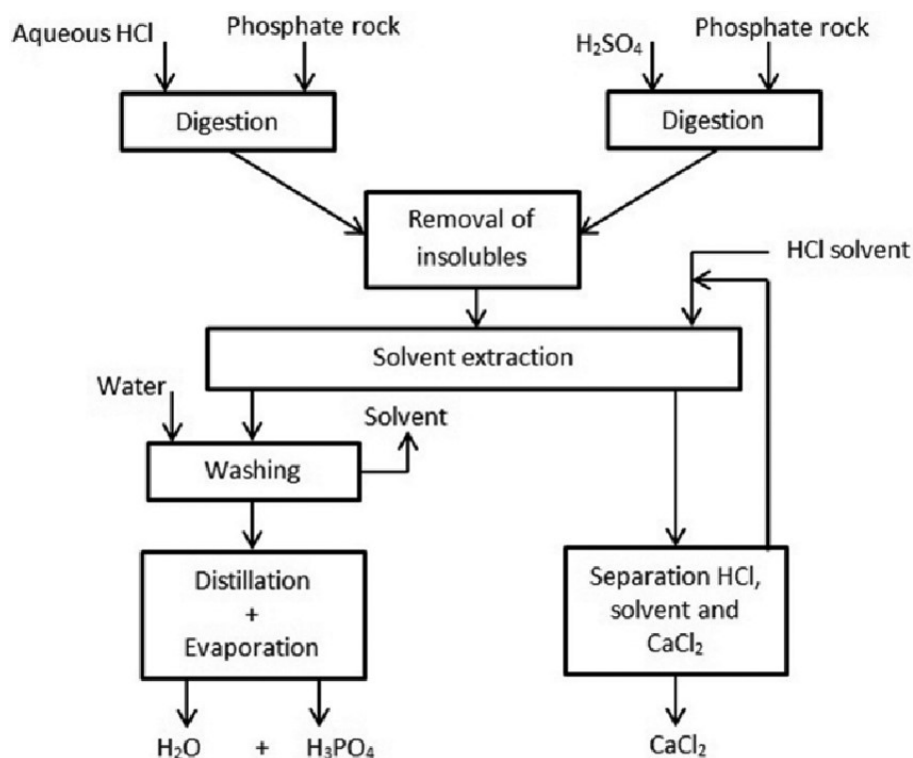
Figure 4.1. *Diagram of the solvent extraction process.*
Source: https://www.researchgate.net/figure/Diagram-of-solvent-extraction-process_fig3_318397493.

The preparation of treated solutions endures a key role in the development of safer, faster, and more environmentally friendly techniques for extraction, leaching, and extract cleaning as observed in the

last two decades. The primary driving force for developing these techniques is the process of reduction of organic solvent consumption. Some approaches include miniaturization (e.g., headspace solid-phase microextraction (SPME), stir bar sorptive extraction, SBSE, HS-SPME), adsorption of solutes on solids (e.g., matrix solid-phase dispersion, solid-phase extraction, MSPD, SPE), and enhanced solvent-extraction (e.g., pressurized liquid extraction, microwave-assisted extraction, MAE, PLE, etc.), which at present perform a vital role in the handling of a sample in analytical labs. Deep considerations have also been paid for using alternate solvents, primarily supercritical fluids, and more lately, ionic liquids (ILs). Majority of these state-of-the-art techniques are established initially by analytical chemists for preparation of samples and determination necessities, but modern and future propensities in extraction-based technologies use and develop them (Du et al., 2010; Rodriguez et al., 2010).

Some innovative technologies developed in the last decades will be deliberated in the following sections.

4.2. Equipment Design and Scale-Up Considerations

Lab-scale solvent extraction studies are generally carried out using test tubes, a procedure that is inexpensive but more arduous, time-consuming, and typically produces more dispersed data than using Lewis-type cells or semi-continuously stirred baffled beakers. Highly precise distribution data can be acquired resourcefully through mechanical means by continuous-flow centrifugal separators, or physically by utilizing distinctive phase separating filter devices—few of these techniques are described. Even though these techniques are intended for improvement, new, and more progressive methods are expected to appear shortly (Hauthal, 2001; Buszewski and Studzinska, 2008).

Particular reagents with exotic structures are expensive to create, which needs the experimentalist to utilize slight amounts to prepare these reagents. It indicates a desire of shifting from "milli-experiments" (e.g., mixing 10 mL of each phase) to micro experiments (mixing 50 µL of each phase), which is now transpiring, to even smaller sizes (volumes and amounts)—the nano experiments. Development in this field entails a high degree of creativity (Anklam et al., 1998).

Though single-stage laboratory techniques deliver the first step toward multistage industrial procedures, such process development typically obliges small-scale multistage and pilot-plant scale equipment. Numerous exceptional designs exist, and we consider additional fundamental developments (Del Valle and Aguilera, 1999).

The industrial application of solvent extraction is an established technique, and it is now possible to transfer from laboratory experiments to a new extraction system for complete industrial exercise with slight technological risk. A sufficient variety of large-scale types of equipment is available to manage most of the problems that come across in this application, even though much of the equipment remains relatively massive. Efforts to miniaturize, such as, by employing centrifugal forces to mix and isolate different phases, yet need further developments (Ravento et al., 2002).

Various industrial processes start with a leaching stage, yielding a slurry that must be clarified earlier than solvent extraction. The solid-liquid separation is an expensive step. The solvent extraction of unclarified liquids (solvent-in-pulp) has been suggested to eliminate solid-liquid separation. Large revenue and abridged energy cost have made this process attractive, but many complications remain unresolved: equipment design optimization, loss of solutes and extractants to the solid phase, effluent removal, etc., (Hildebrand and Scott, 1958).

Regeneration of the extractant is a critical step in the industrial solvent extraction technique. This can be accomplished through numerous ways, e.g., by evaporation, distillation, or stripping (back-extraction). Even though distillation and evaporation do not differentiate between solutes (the diluent is merely removed by heating), stripping, by a cautious choice of strip solution and conditions, can be made extremely selective. Otherwise, all the solutes can be stripped and then exposed to a selective extraction by varying the extractant. There are many opportunities, and it may be valuable to explore new pathways (Valcárcel and Tena, 1997).

Membrane extraction is comparatively a new technique for solvent extraction, in which a solute is transported from one aqueous phase to another through a membrane holding an extractant dissolved in a diluent. This resourceful scheme has only been explored to some extent, though it proposes great potential forthcoming, e.g., for cleaning of wastewater (Bungert et al., 1998).

The step from laboratory experiments through pilot plants to industrial-scale necessitates serious deliberations of all the points here; practical exposure is priceless to avoid inaccuracies and excess expenditures (Erkey, 2000).

4.3. Supercritical Fluid Extraction (SFE)

Solvent extraction processes commonly require ambient temperature and pressure to run. Higher pressures and elevated extraction temperatures are required when equilibrium or mass transfer conditions are more advantageous at higher temperatures and pressure. In the case of distillation, the difference in vapor pressures of the constituents to be separated is considered, whereas in solvent extraction, differences in intermolecular interactions in the liquid phase are used (Teja and Eckert, 2000). The combination of both distillation and solvent extraction to some extent gives rise to another separation technique known as supercritical fluid extraction (SFE).

Because of having various physicochemical characteristics, SFE delivers numerous operational benefits over conventional extraction methods. Since, because of having low viscosity and high diffusivity, supercritical fluids possess improved transport properties than other liquids, which make them diffuse easily through solid materials, thereby providing faster extraction yields. One of the foremost features of a supercritical fluid is the prospect of altering the density of the fluid by varying its temperature and/or its pressure. As density is interrelated to solubility, solvent strength of the fluid can be adjusted by changing the extraction pressure (Tonthubthimthong et al., 2004). Similarly, supercritical fluid possesses other advantages as compared to other extraction methods, such as

consumption of solvents usually acknowledged as safe, higher efficiency of the extraction process (increased yields with lower extraction times), and the prospect of direct coupling with analytical chromatographic methods like gas chromatography (GC) or supercritical fluid chromatography (SFC) (Figure 4.2).
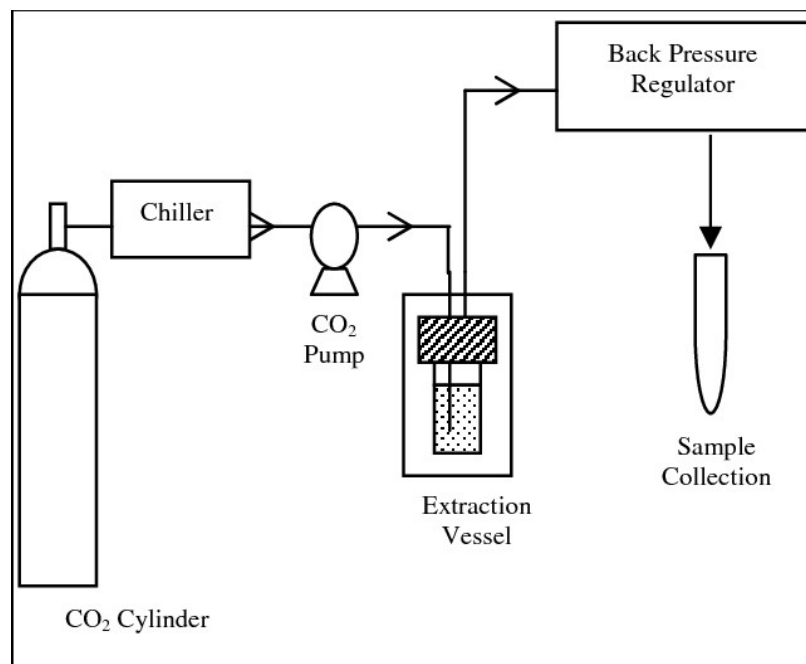

Figure 4.2. *Flow diagram of supercritical fluid extraction system.*
Source: https://www.researchgate.net/figure/Flow-diagram-of-supercritical-fluid-extraction-system_fig1_26439786.

By increasing temperature at constant pressure, solvent density decreases, resulting in lowering solubility. Conversely, an increase in temperature leads to an upsurge in vapor pressure. At elevated pressures, the reliance of density on temperature is lesser compared to that on vapor pressure, resulting in improved solubility. At low pressure, the density effects are more dominating at increased temperatures, triggering a reduction in solubility (Figure 4.3) (Fernández-Ronco et al., 2010).

Figure 4.1 shows the characteristic curve for various mixtures depicting limited mutual solubility of the components. From the figure, it is pertinent to derive abridged, general principles from the figure in the supercritical area for extraction processes, demonstrated schematically in Figure 4.2 (Perakis et al., 2010).
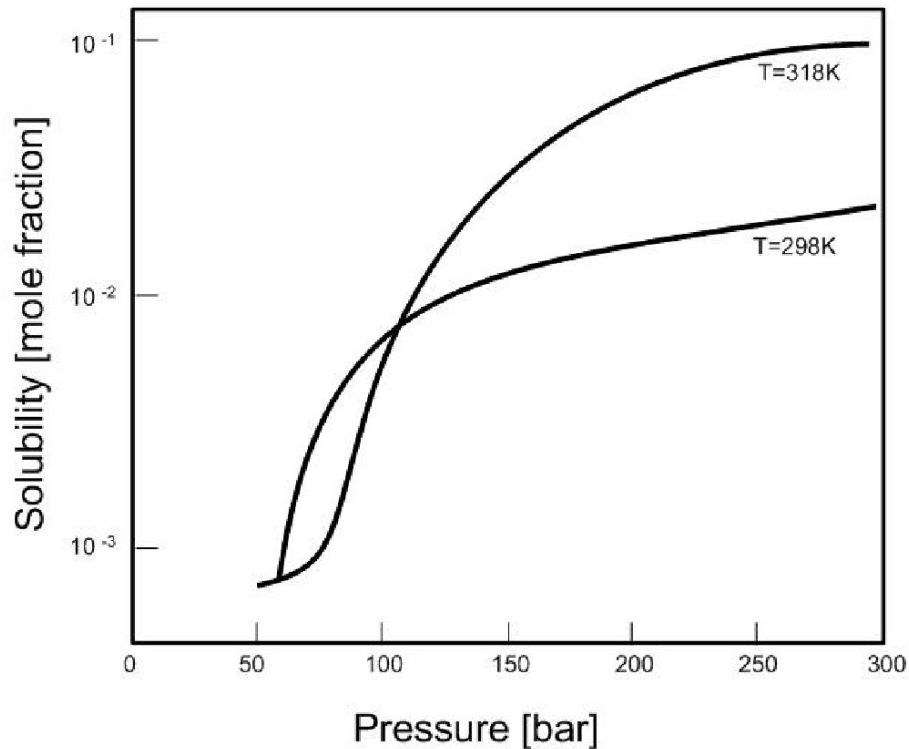
Figure 4.3. *Solubility of naphthalene in dense ethylene as a function of pressure at two different temperatures: The solubility enhancement in the vicinity of the critical point, as well as the crossover effect, is evident.*
Source: https://www.semanticscholar.org/paper/Solubility-of-Solids-and-Liquids-in-Supercritical-Aim-Fermeglia/1d8ded2348b676fc74f821f2bbab32406b5781a4/figure/0.

Figure 4.2 demonstrates the principle for extraction and solvent retrieval by changing pressure. The point E1 shown in Figure 4.1 denotes the state in the extractor (30 MPa). The extract phase is passed via an expansion valve at a reduced pressure of 8 MPa (point S1 in Figure 4.1). Resultantly, naphthalene starts to precipitate in the separator. Later, the solvent is recompressed and reverted to the extractor (Klesper et al., 1962).

In Figure 4.2, naphthalene is extracted at a pressure of 6 MPa and temperature 285 K (point E2 shown in Figure 4.1). The extract phase is passed through a heat exchanger at an increased temperature of 315 K (point S2 shown in Figure 4.1). Additionally, naphthalene also precipitates in the separator. The solvent is passed through one more heat exchanger to reduce the temperature and is then reverted to the extractor (Griffiths, 1988).

As shown in Figure 4.2, the extracted substances can also be retrieved through adsorption (e.g., on activated carbon). Varying the density of the solvent avoiding passing through any phase borders makes the supercritical area more exciting because of separation. It can be achieved by gradually decreasing the pressure, e.g., to fractionate a mixture of substances (Figure 4.4) (Harris, 2002).
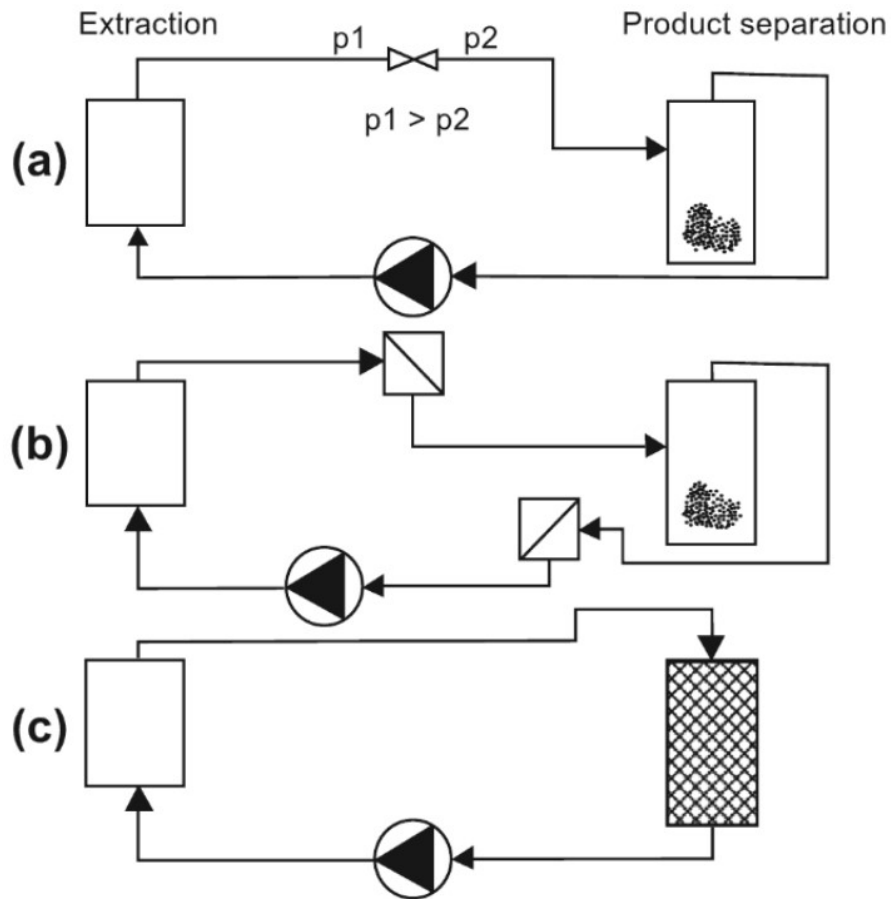
Figure 4.4. *Extraction and separation through reducing the pressure; (b) extraction and separation through a temperature change; and (c) extraction and separation through adsorption. Source: https://www.sciencedirect.com/book/9780444537782/solvent-extraction.*

A range of compounds can be consumed as supercritical fluids (Table 4.1). The main focus has been given to supercritical carbon dioxide solvent because of having traits like low cost, nontoxicity, environmentally friendly, low critical temperature (31.3°C) as well as moderate critical pressure (72.9 atm). Carbon dioxide is a nonpolar solvent and dissolves primarily nonpolar solutes (Taylor, 2009). The solubility and selectivity can be modified by the addition of small amounts of polar solvents, called entrainers (e.g., water or ethanol).

Carbon dioxide exists in the gas phase at room temperature, therefore when the extraction is finalized, and the system decompressed, a significant amount of CO_2 eliminated without residues, producing a solvent-free extract. When carbon dioxide usage is high as in industry, the operation can be organized to recycle it. Nevertheless, because of the low polarity of supercritical CO_2, where solubility parameter, *d*, that provides a capacity of the solvent polarity, has minimal effect on extracting considerable polar compounds from natural matrices. To overwhelmed this problem, modifiers (also

known as entrainers or cosolvents) are usually used. These modifiers are highly polar, and by adding small amounts, they can yield significant changes in the solvent properties of neat supercritical CO_2 (Welch et al., 2005; Taylor, 2009).

4.3.1. Applications of SFE

Several vegetable matrices as a natural source have been utilized for compressed fluid extraction. Natural antioxidant compounds have been obtained by processing aromatic plants, legumes, spices, and fruit beverages, like natural orange juice, etc. Till now, more than 60 SFE extraction plants have been explored which are operating around the world. In SFE much more interest has been given to carbon dioxide to utilize it to extract various natural products from solid and liquid materials. Examples of bulk use of carbon dioxide are processes in the pharmaceutical industry, food, decaffeinating coffee beans, cosmetics, and oil and hop extraction. For extraction of solutes from aqueous solutions, several processes have been vetted in feasibility tests that use carbon dioxide as a solvent. SFE carbon dioxide extraction of metal ions from aqueous solutions has been studied enormously. A partial list contains acetic acid, dioxane, ethanol, acetone, and ethylene glycol which are used as a solute. The reason behind these efforts is to achieve potentially low energy costs as compared to distillation and the environmental benefits of using carbon dioxide (Bolanos et al., 2004; Toribio et al., 2006).

The design of an SFE system is designed simple or highly complex depending upon the particular requirements. It is conceivable to discriminate between analytical systems and pilot- or industrial-scale systems. An analytical system is used for sample preparation preceding, e.g., a chromatographic analysis. Several configurations exist depending upon the degree of automation (Figure 4.5) (Pinkston et al., 2006; Ramirez et al., 2007).
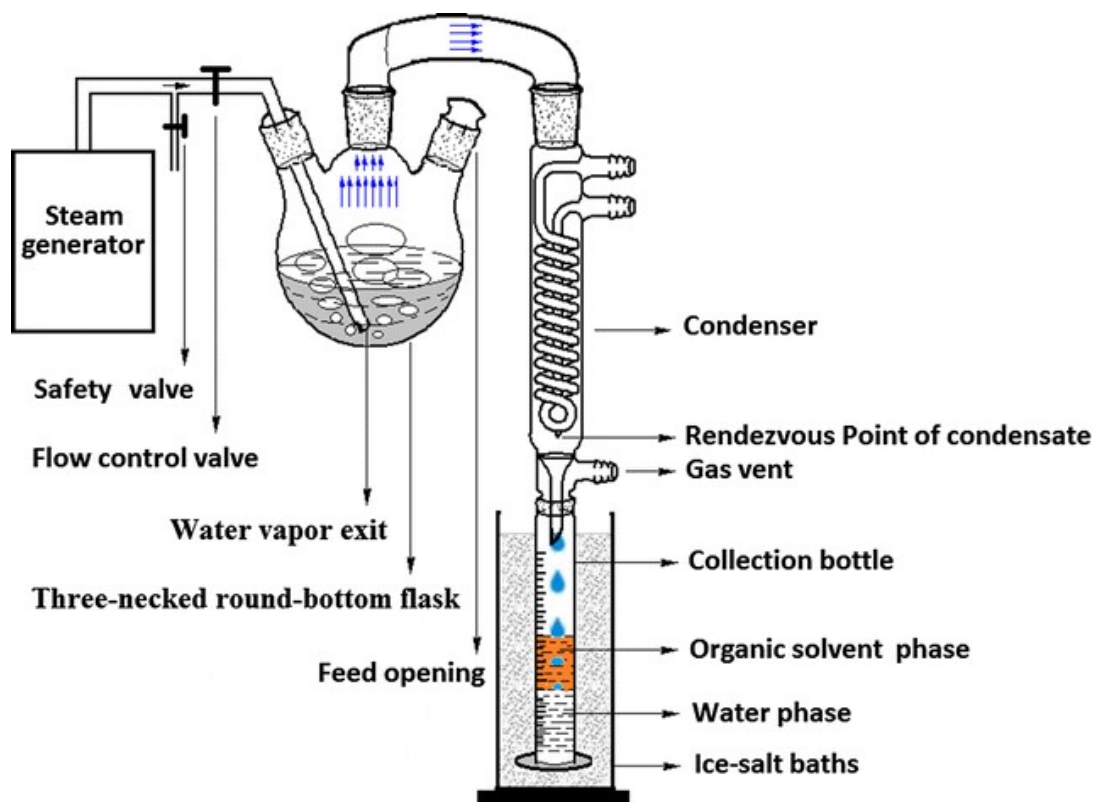
Figure 4.5. *The diagram of steam distillation/drop-by-drop extraction device.*
*Source: https://bmcchem.biomedcentral.com/articles/10.1186/s13065-017-0329-6.*

For extraction in grams, pilot systems are utilized, whereas, industrial-scale is used for extracting in kilograms. Generally, the system on a pilot-scale plant (Figure 4.3) comprises a solvent pump, which distributes the fluid all over the system, a modifier pump if necessary, an extraction cell or extraction column, depending on the system configuration (i.e., for solids or liquids), and one or more separators (also known as fractionation cells) for collection of the extract and the solvent is depressurized. Similarly, the extraction cell or column and the separators are generally fitted with independent control of temperature and pressure to carry out fractionations of the extracted compounds by stepwise depressurization. As a result, different compounds can be acquired within each separator, based on their differential solubility in the supercritical fluid. Moreover, a specially designed refrigerated system can also be installed to trap highly volatile compounds, as well as a reprocessing system to recycle the fluid employed (Luque et al., 1999; Miller and Hawthorne, 2000).

As mentioned earlier, the major difference between pilot plants to process a solid or a liquid sample lies in the use of an extraction cell or an extraction column. Solid processing is carried out in batch in a discontinuous or semicontinuous mode, whereas liquid processing is done under countercurrent conditions in a continuous process. In process of liquid-sample extractions, the supercritical fluid (CO_2) moves upwards, whereas the sample feed, whether introduced from top or bottom in the system, moves in a downward direction with the help of gravity (Li et al., 2000).

Other systems that are inspected include the separation of biocides from edible oils and isolation of different components in vegetable oils. The utilization of SFE in different applications are studied in detail in different literature references (Luque de Castro and Jiménez, 1998).

4.3.2. Supercritical Fluid Chromatography (SFC)

While using supercritical fluids in mobile phases in chromatography should act as constituent carriers similar to the mobile phases in GC and should dissolve these constituents as mobile phases do in LC. This chromatographic technique, called supercritical fluid chromatography (SFC), was explored by Klesper et al. (1962) and proved as a bridge between GC and LC. However, the technique became prevalent by introducing capillary columns. Key elements of those open tubular columns SFC instruments comprise the capillary columns, pump, restrictor, GC-like oven, and flame ionization detector (Jiménez et al., 1997). Open tubular SFC was principally applied in the petrochemical industry because of the lipophilic character of supercritical CO_2. Nevertheless, the technique possessed severe limitations owing to its poor reproducibility and limited application range (Figure 4.6) (Hawthorne et al., 1994; Yang et al., 1995).
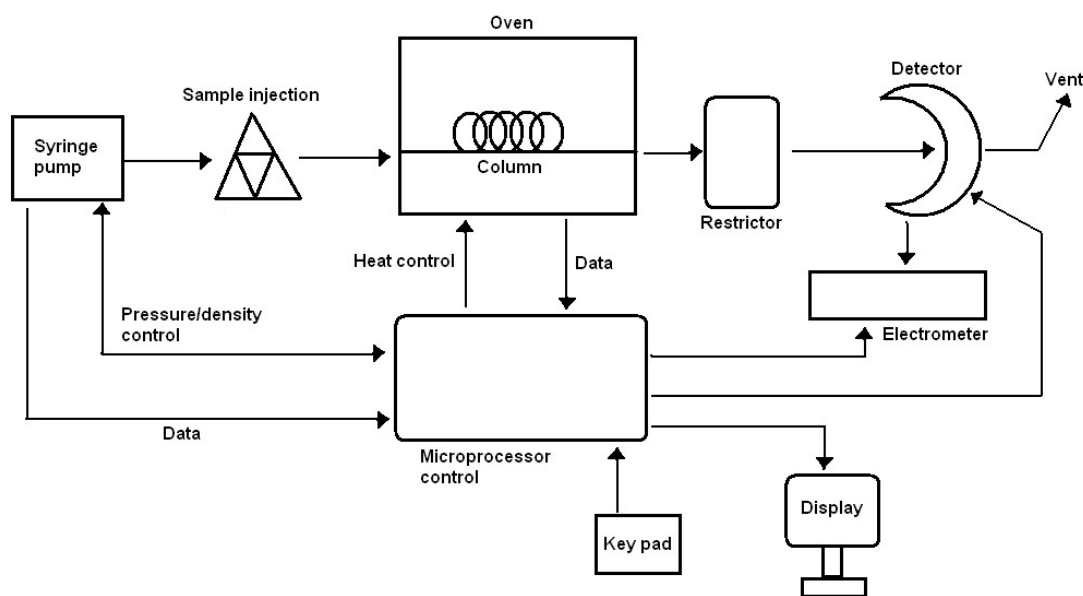
Figure 4.6. *Scheme of a supercritical fluid chromatography instrument.*
Source:
https://chem.libretexts.org/Bookshelves/Analytical_Chemistry/Book%3A_Physical_Methods_in_Che mistry_and_Nano_Science_(Barron)/03%3A_Principles_of_Gas_Chromatography/3.03%3A_Basic_ Principles_of_Supercritical_Fluid_Chromatography_and_Supercrtical_Fluid_Extraction.

On the other hand, the packed column SFC technique has widespread applications in major sectors because of having components similar to those of LC instruments comprising packed columns,

injectors, digital back pressure controllers, UV detectors, and organic modifiers for increasing the solvating tendency and decreasing the retention time of polar solutes (Basile et al., 1998). The main reasons behind the last revitalization of the technique are: steady flow rates, automatically controlled modifier addition, the elimination of back-pressure regulation problems, automation, and new stationary phase incorporation, the increased claim for environment-friendly methods that exterminate or significantly decrease the use of organic solvents, sample injection, and the hyphenation of packed column SFC to MS. Currently, it is extensively acknowledged that SFC is a sort of normal-phase LC, deprived of many of the problems related to normal-phase LC (Kipp et al., 1998).

The use of packed columns in SFC is emphasized currently, although numerous studies appear every year which use open tubular columns. Packed column SFC applications comprise chiral separations, 26 mass spectrometric detections of pharmaceutical compounds, 27 and natural product applications with preparative separations (Fernández et al., 2000).

In brief, SFC constitutes a green alternative, i.e., CO_2 as a mobile phase and occasionally altered amounts of green organic modifiers, like ethanol or methanol, to lessen the organic solvent usage in analytical chemistry (Gámiz-Gracia et al., 1999).

4.3.3. Advantages and Disadvantages of Supercritical Extraction

The foremost disadvantage of SFE is to use of expensive process equipment to generate the elevated pressure. The critical pressure requirements are lower than the pressures used in many high-pressure processes in the petrochemical industry these days. Table 4.1 gives information regarding critical data for commonly used solvents in high-pressure extraction. It demonstrates the satisfactory mass transport properties that can be attained in the supercritical area in consequence of low viscosity and high diffusivity, compared with the liquid phase. The separation properties in SFE are determined by the selection of solvents and solutes (Jiménez et al., 1999).

Table 4.1. Critical Properties of Several Solvents Used in Supercritical Fluid Extraction (SFE)

Solvent	Critical property			
	Temperature (°C)	Pressure (atm)	Density (g/mL)	Solubility parameter δ_{SFC} (cal$^{-1/2}$ cm$^{-3/2}$)
Ethene	10.1	50.5	0.2	5.8
Water	101.1	217.6	0.322	13.5
Methanol	-34.4	79.9	0.272	8.9
Carbon dioxide	31.2	72.9	0.47	7.5
Ethane	32.4	48.2	0.2	5.8
Nitrous oxide	36.7	71.7	0.46	7.2

Sulfur hexafluoride	45.8	37.7	0.73	5.5
n-Butane	-139.9	36	0.221	5.2
n-Pentane	-76.5	33.3	0.237	

4.4. Subcritical Water Extraction (SWE)

In subcritical water extraction (SWE), hot water under pressure (critical point of water, 22.4 MPa, and 374°C) is used for extraction. This useful tool is recently emerged to substitute the traditional extraction methods. SWE is an environment-friendly technique that delivers higher extraction yields from solid samples. SWE is employed using hot water (from 100 to 374°C,) under high pressure (from 10 to 60 bar) to sustain the liquid phase of water (Figure 4.7) (Jiménez and Luque de Castro, 1999).
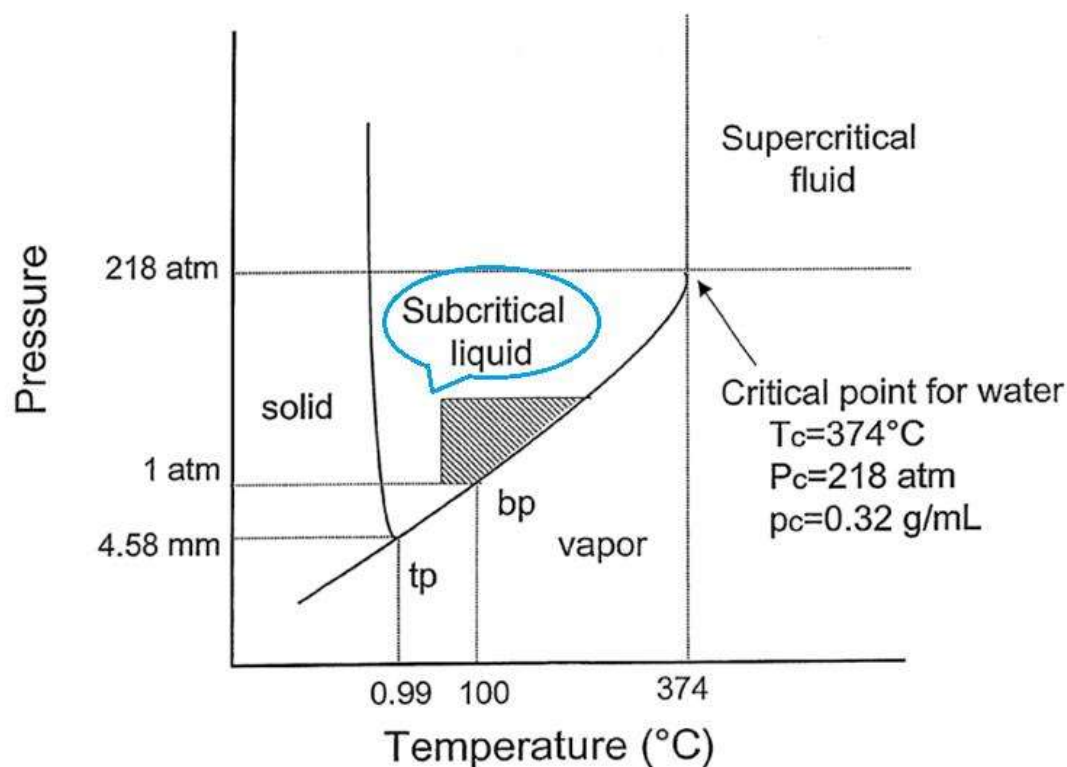
Figure 4.7. *Phase diagram of water as a function of temperature and pressure.*
Source: https://www.intechopen.com/books/mass-transfer-advances-in-sustainable-energy-and-environment-oriented-numerical-modeling/subcritical-water-extraction.

4.4.1. Extraction Technique

Imperative factor to deliberate in this sort of extraction procedure is the changeability of the dielectric constant with temperature. Water is a polar solvent having a dielectric constant close to 80 at room temperature. But, the value of the dielectric constant significantly drops to 27 while increasing

temperature up to 250°C and keeping water at its liquid state under appropriate pressure. This dielectric constant value is comparable to that of ethanol, i.e., 30 (Chalchat et al., 1991).

At elevated temperatures (beyond the boiling point of water: 100–374°C), pressurized steam is required proficient transfer through the material. A user-friendly experimental device is required for SWE. Essentially, the arrangement comprises a water reservoir attached to a high-pressure pump to transfer solvent into the system, a heating oven, where the extraction cell is sited, and extraction occurs, and a restrictor or valve to sustain the pressure. Extracts are accumulated in a container located at the end of the extraction system. Additionally, for rapid cooling of the resulting extract, a coolant device can also be attached to the system (De-Pooter et al., 1995; Soto et al., 2001).

Even though this technique has been employed mainly as a batch process, studies also reported some continuous techniques as well as online coupling of an SWE system to an HPLC equipment through a solid phase trapping (Verma et al., 1990).

4.4.2. Extraction From Plants Using SWE

The SWE is evolving as a prevailing substitute for the extraction of solid substances. It has been utilized for the extraction of pollutants comprising a wide range of polarities from environmental samples as well as for the extraction of pesticides and polycyclic aromatic hydrocarbons from soils (Kubatova et al., 2001). Basile et al. (1998) suggested utilizing SWE as a very prevalent alternate system as compared to conventional and supercritical CO_2 extraction methods for the separation of necessary oils. Studies revealed that the suggested SWE method is rapid, economical, and more operative than hydrodistillation (Ibañez et al., 2003). In the meantime, this method has shown its widespread utilization in the field of essences compared to other conventional techniques such as steam distillation and solvent extraction, which possess some renowned disadvantages: extended extraction time, low extraction proficiency, and large amounts of toxic solvent waste. It also has the benefit of being selective (Kubatova et al., 2001).

SWE has been employed extensively for the extraction of various compounds from numerous vegetable matrices. Similarly, rosemary (*Rosmarinus officinalis* L.) is one of the materials studied in detail using SWE. De-Pooter et al. (1995) carried out a study on the extraction of antioxidant compounds of rosemary using SWE at various temperatures. Different temperatures, ranging from 25°C to 200°C, were tested to explore the extraction selectivity toward antioxidant compounds. The effect of water temperature was evident by the extraction yield, which was further improved at higher extraction temperatures. Researchers proved that the "rosmanol" was the main and most polar compound extracted at low temperatures (25°C). However, it was observed that the extraction performed at 200°C, decreased the ability of water to dissolve the most polar compounds, instead, a high concentration of other compounds, like carnosic acid, was obtained. Antioxidant extraction by SWE could be acquired similar to those achieved by using supercritical carbon dioxide (Ozel et al., 2003; Moreda-Piñeiro et al., 2006).

Generally, the use of SWE delivers numerous advantages over conventional extraction techniques (i.e., organic solvents, hydrodistillation, and solid-liquid extraction). These provide rapid extraction at low operational temperatures, consequently evading losses and degradation of volatile and thermolabile compounds. It is beneficial of being selective because, through kinetic experiments, manipulation of the extract composition is conceivable in certain working conditions. Additional advantages of the technique are the optimum quality of the extracts (for essential oils), reduced costs of the extracting agent, and environmental compatibility (Lou et al., 1997).

The extraction of essential oil from *Thymbra spicata* was explored. The impacts of several factors, for instance, pressure (20, 60, and 90 bar), temperature (100, 125, 150, and 175°C), and flow rate (1, 2, and 3 mL/min) were studied in detail. It was revealed that the optimal extraction yields (3.7%) were achieved at 150°C and 60 bar, with a flow rate of 2 mL/min for 30 min. The essential oils of *T. spicata* were found to prevent the mycelial development of several fungi species (Guillemin et al., 1981; Alonso-Rodríguez et al., 2006).

4.4.3. Pressurized Liquid Extraction (Also Known as Accelerated Liquid Extraction (ALE))

PLE technique is more or less similar to SWE—the difference lies only in the use of solvents. PLE is utilizing organic solvents or diluted organic acids including acetic and formic acids, at elevated temperature and pressure without attaining the critical point. For instance, the PLE system testing intended for pretreatment of biological material for extraction and trace element leaching is explained below (Smith et al., 1999; Su et al., 2005).

This system comprises a stainless-steel extraction cell for the placement of samples and where electronically controlled heaters and pumps are used to regulate the programed parameters like temperature, static extraction time, pressure, and extraction steps. When the sample is loaded in the extraction cell, the solvent is added, and the required temperature and pressure parameters are selected to heat and pressurized the extraction cell. Subsequently, a static extraction period follows when the sample releases solutes to the solvent. After completion of the static step, the valve is untied and the solvent is moved to the collection container. Residues of the solvent are expelled from the sample to the collection vial using a suitable gas. By increasing the pressure on the sample cell (from 4 to 20 MPa), the solvent can be kept in a liquid phase even at comparatively high extraction temperatures (up to 200°C). This increases productivity over classic extractions by reducing extraction times and decreasing solvent volumes (Coym and Dorsey, 2004; Smith, 2006).

PLE procedures are deliberated to be comparatively straightforward because of having limited parameters to be optimized, thus decreasing the time dedicated to the development of the extraction procedure (Ingelse et al., 1998). The use of PLE to support trace metals acid leaching could preferably provide several advantages while compared to mechanical shaking, ultrasound (water bath or probe), or microwave-assisted acid leaching techniques (Pawlowski and Poole, 1999).

The following are the advantages of the technique (Teutenberg et al., 2001; Kondo and Yang, 2003):

- Weak organic acids can be used in place of strong concentrated mineral acids, usually needed for leaching. Besides, small volumes of such acids are used, which infers low toxic wastes.
- Short leaching or extraction times are adequate to conclude the extraction, which further escalates the sample output.
- PLE offers a high degree of automation and therefore no supplementary filtration step is required after acid leaching assisted PLE.
- Ever since diluted organic acids could be utilized to leach the metals, chemical species integrity is assured, which makes PLE to be useful for studying organometallic speciation (Hatti-Kaul, 2000).

To extract or leach entire elements PLE may be completely exploited in ores leaching and extraction evading concentrated mineral acids use. While applying PLE conditions, diluted weak carboxylic acids can react with the matrix, and can proficiently leach major trace elements. Variables that affect the carboxylic acid can be found by testing the PLE process using multivariate approaches compromising acid leaching and extraction conditions (Sanagi and See, 2005).

4.4.4. Superheated Water Chromatography (SHWC)

In reversed-phase liquid chromatography (RPLC), water is utilized to decrease the elution strength of the organic modifiers, like acetonitrile, methanol, and tetrahydrofuran. Though, the same enhanced solvation strength defined in the preceding section also empowers superheated water to be used as a mobile phase in LC. This approach of separation has been termed superheated water chromatography (SHWC), pressurized water chromatography, or subcritical water chromatography (Wilkes and Zaworotko, 1992).

The detailed study of separation about the use of hot water as the mobile phase offers an introduction to the technique and designates the huge potential of the technique governing greening analytical chemistry (Rogers and Seddon, 2002). The equipment required is similar to that used in conventional LC, with the addition of a high-temperature oven and a method of regulating the backpressure of the column (Figure 4.7). An additional advantage of SHWC includes the use of water with wide-ranging detectors. It is well-suited with refractive index, UV, and fluorescence, electrochemical, evaporative light scattering, and mass spectroscopy (MS) detection. Furthermore, it also possesses compatibility with flame ionization detection, being convenient for revealing analytes lacking chromophores, like amino acids, aliphatic alcohols, and carbohydrates (Rogers et al., 1999, 2000).

Nevertheless, the limited accessibility of commercial systems appears to be the foremost cause for the shortage of widespread implementation of the method. The selectivity variations on heating

water are not much effective compared to adding an organic modifier, like methanol, acetonitrile, or 2-propanol. Though, high-temperature water could deliver a complementary selectivity which makes it most suitable for polar analytes. A 3.5°C increase in water temperature relates to a 1% increase in methanol and a 5–8°C rise in temperature corresponds to a 1% increase in acetonitrile, by employing a series of aromatic analytes (Nakashima et al., 2003; Cornmell et al., 2008).

SHWC has been effectively applied in the pharmaceutical industry, where the polarity of analytes is mostly compatible with an aqueous eluent. For example, separation of anticancer drugs is accomplished by using polystyrene-divinylbenzene column with buffered superheated water as the mobile phase. The temperature range was maintained between ambient temperature up to 160°C, and the pH value of water was adjusted to 11.5 and 3.5 using phosphate buffer. The aggregate elution time was below 13 min. Another study successfully executed the separation of alkyl aryl ketones and barbiturates by using water-rich and superheated water at elevated temperature (100−200°C) as the eluent (Visser et al., 2001a, b). SHWC may be explored to provide benefits in the environmental and food industries.

4.5. Aqueous Two-Phase Systems

Under certain circumstances, polymer unsuitability in aqueous solutions can result in the creation of two phases with high water content. With such kind of system, it is likely to separate delicate biological molecules, such as proteins, without denaturation, which could be faced by using an ordinary aqueous-organic solvent system (Visser et al., 2002; Liu et al., 2005).

Biotechnological processes, on the whole, work at small concentrations of reactants and products. One cause of this is the high sensitivity of biocatalysts to product inhibition. The reaction may probably stop after the conversion of a small fraction of the substrate into the product. In such conditions, continuous extractive processes are highly desirable in which the product is uninterruptedly removed (Fadeev and Meagher, 2001). The combination of bioconversion and extraction is termed extractive bioconversion. The unfolding of enzymes may occur when exposed to the interface between the two solvents having considerable differences in surface tension and dielectric constants such as water and common organic solvents. This issue can be resolved through extractive bioconversions in aqueous two-phase systems. A series of innovative methods envisioned to deliver practical strategies for the area of separations in two-phase systems have been studied (Vidal et al., 2007).

4.6. Extraction Processes with Ionic Liquids (ILs)

Ionic liquids (ILs) are a new class of extractants of pronounced interest deliberated as potential "green solvents." Essentially, zero vapor pressure and thermal stability of ILs mark them attractive solvents for numerous applications. ILs are achieving high significance as novel solvents in chemistry, though they are not new, e.g., $[EtNH_3]^+ NO_3^-$, was discovered in 1914. They are also recognized as nonaqueous

ILs, molten salts, room-temperature (RT) ILs (not all ILs are RTILs), liquid organic salts, or fused salts. Ethyl methylimidazolium tetrafluoroborate as one of the new IL, is getting much consideration being used as a novel medium for homogeneous catalysis, as reported in 1992. The use of ILs to separate analytes in analytical chemistry, is valuable because of having some exceptional properties like high thermal stability, negligible vapor pressure, tunable viscosity, and miscibility with water and organic solvents, along with good extractability for several organic compounds and metal ions (Cull et al., 2000). Being nonvolatile and nonflammable, make them environment-friendly solvents for "clean processes" and "green chemistry," and good substitutes for traditional volatile and flammable organic solvents. However, high viscosity at ambient temperature could be their less favorable property (Huddleston et al., 1998; Banerjee et al., 2008).

4.6.1. ILs in Separation Techniques

The use of ILs as extractants for the extraction of metal ions, such as lanthanides, and actinides, are of particular industrial attention. Furthermore, the extraction of Cd^{2+}, Co^{2+}, Ni^{2+}, Fe^{3+}, Na^+, Cs^+, Sr^{2+}, $Hg^{2+,}$ and Cd^{2+} from wastewater by using task-specific ILs has been effectively achieved with high yield (Marták and Schlosser, 2003). Likewise, ILs have also been used for the extraction of multiple organic compounds including carbohydrates, biofuels, substituted benzene derivatives, and erythromycin from aqueous solutions.

Experiments comprising the use of ILs for solvent extraction of organic acids revealed promising results in the extraction of organic acids, particularly lactic acid. In the extraction of lactic acid, butyric acid, and phenol, fairly higher distribution coefficients were observed for solvents with tested developmental ionic liquid IL-A compared to the solvents comprising tertiary amines. The value of the distribution coefficient of lactic acid obtained is up to 30 at reduced acid concentrations. IL-A extractant creates undissociated lactic acid/IL-A complexes with ratios of 1:1 and 2:1 (lactate anions are not extracted).

In the pertraction of LA through the supported liquid membrane (SLM), the entire mass-transfer coefficient rises with decreasing concentration of lactic acid in the aqueous phase, which directly relates to the increasing value of its distribution coefficient. Amplified concentration of the carrier IL-A showed no effect on the value of the mass-transfer coefficient in pertraction of lactic acid differing from the improved value of the distribution coefficient. This may specify that either the slower kinetics of the interfacial reaction in the decomposition of the complex plays a vital role or the increased viscosity of the membrane is responsible for this (Marták and Schlosser, 2004a, b).

Separation of taurine (2-aminoethanesulfonic acid) and sodium sulfate is accomplished by leaching a solid mixture by ILs as observed elsewhere. Dialkylimidazolium chloride IL was developed as a leaching agent and organic solvent including ethanol as a precipitating agent, showed promising results. Selective separation of taurine from a solid mixture comprising a large amount of sodium sulfate could yield 67–98.5% within a single separation step (Gu et al., 2004).

Transport of amines and neutral organic substances through liquid membranes having IL has also been investigated in references. Similarly, pertraction of organic acids through liquid membranes aided by enzymatic reactions on L-L interfaces by using ILs as a liquid membrane was also explored. Modifications in ILs for attaining better partitioning of particular solutes and adequate viscosity of IL may bring about remarkable results (Branco et al., 2002; Fortunato et al., 2002).

Extraction of formaldehyde from mushrooms by LPME using ILs has also been explored. Furthermore, the approach has also been implemented to the screening of chlorobenzenes, phenols, dichlorodiphenyltrichloroethane, and its metabolites, and chlorophenols in water samples. But, this SDME procedure is irreconcilable with GC due to the nonvolatile and nonflammable nature of the IL (Miyako et al., 2003a, b).

4.6.2. Ionic Liquids (ILs) in Analytical Separations

Scientists are paying more attention to exploring applications of ILs in separation and analysis. Numerous reports comprise the use of ILs as running electrolytes in capillary electrophoresis (CE). Furthermore, ILs possess many promising characteristics, such as nonvolatility, nonflammability, high viscosity, high solubility for numerous compounds, and polarity, making them distinctive stationary phases in GC, however, both the topics are beyond the scope of this chapter and are not addressed in detail. Alternatively, ILs cannot be used as a mobile phase because of high viscosity, instead, these can only be used as beneficial additives in mobile phases. For detailed information work of Marsza and Kaliszan (2007) on the use of ILs in LC is referred (Wood and Stephens, 2010).

4.7. Liquid Membrane and Nondispersive, Membrane-Based Solvent Extraction Techniques

Membrane separation is a comparatively new and emerging field of supramolecular chemistry. The liquid membrane process is a three-phase system comprising two phases of identical nature with varying compositions (aqueous-aqueous, gas-gas, organic-organic) separated by the third phase of different nature as well as insoluble with the other two phases. This central phase is designated as the liquid membrane (Bekou et al., 2003).

Liquid membrane separation techniques comprise three major configurations which are extensively explored due to their potential industrial use (Liu et al., 2005, b):

- Emulsion liquid membrane (ELM), or surfactant liquid membrane;
- Supported liquid membrane (SLM); and
- Bulk liquid membrane (BLM).

In the ELM configuration, the liquid membrane is made by dispersing emulsion of the stripping phase in an organic phase containing an emulsifying agent. In the SLM process, the liquid membrane phase infuses into the solid support containing pores of micron size and located between the two bulk phases.

The liquid membrane becomes stable by capillary forces or through bonding. Two types of support configurations, i.e., hollow fiber or flat sheet membrane modules, are usually used.

BLM involves three bulk phases—two phases of an identical nature with varying composition and the third immiscible phase is located between them. Separation of phases is done by using hollow fiber or flat sheet membrane supports or may have no support. Numerous different BLM techniques are published, based on membrane-based nondispersive selective solvent extraction attached to permselective diffusion of solute-extractant complexes and selective stripping of the solute in one continuous dynamic process (Peng et al., 2005).

Nondispersive solvent extraction belongs to one of the configurations of the BLM. In "non-dispersive solvent extraction," phases are intacted through porous membrane instead of generating a drop dispersion of one phase in the other phase (Ye et al., 2006, 2007).

Two dissimilar arrangements exist for this process. One comprises two modules—one for extraction and the other for stripping—having close similarity with conventional solvent extraction. The other configuration utilizes one three-liquid phase module in which all the three phases flow through. In the hollow fiber module, the liquid membrane phase lies in the shell, and the feed and the stripping phase get passed through the lumen of various fibers in the module. The solution to be extracted is provided to the lumen side of a microporous hollow fiber membrane module, with extracting organic solvent being fed to the shell side. The selected membrane is especially wetted by one of the phases (organic phase), and the pressure is controlled in such a way as to avoid capillary penetration of the aqueous phase into the membrane. As follows, the solvent-water interface is stabilized at the boundary of membrane-aqueous solution, and extraction of the particular component into the organic phase occurs through transmembrane diffusion and convection. The solute-enriched organic phase is then transported to a second membrane unit where the solute is shifted into an aqueous solution in which it has eminent solubility—the solute-depleted organic is then recycled to the first unit (Liu et al., 2005c).

This technique partakes significant advantages over conventional solvent extraction—it considerably eradicates emulsification, and requirement of phase separation equipment such as centrifugal separators; it delivers a stable, large interfacial area for interphase mass transfer; and it avoids contamination of the organic phase and extracted substance from solid impurities in the feed. Certainly, if hollow fiber membranes of large lumen diameter are utilized, processing of whole fermentation broths holding high concentrations of suspended biomass is possible, which may result in "continuous extractive fermentation," in which the product-bearing whole broth is transferred to the extraction unit, and the product-depleted broth (containing viable cells) is reverted to the fermenter (Jiang et al., 2003).

4.8. Supramolecular-Based Extraction Techniques

During the last few decades, numerous innovative separation techniques were established based on supramolecular extractants. Some examples of these techniques are shown below, which retain many perspectives in the future developments of separation technologies (Breitbach and Armstrong, 2008).

4.8.1. Nano- and Microtechnological Extraction

Nanometer-sized amphiphilic aggregates, made utilizing a self-assembly process, remain growing by the addition of surfactant, and this is the second self-assembly process in supramolecular solvent development. This process cannot occur without the previous one being in place. Aggregate growth will continue till a separate, amphiphilic-rich, liquid phase is created. The phenomenon of liquid-liquid phase separation, usually taking place in colloidal solutions, is called coacervation. These are micrometer-sized aggregates or reversed micelles (Marszałł MP and Kaliszan, 2007).

Ordered structures of molecules in supramolecular solvents comprise a hydrophilic and a hydrophobic part. Resultantly, these structures contain different polarity regions that deliver different interactions for solutes. The type of interaction may be adjusted varying the hydrophobic part of the polar group of the amphiphile and, in theory, one may design the most suitable aggregate for a specific application because of the ubiquitous nature and synthetic chemistry of amphiphiles.

The type of polar compounds which can be extracted by supramolecular extractants depends upon the nature of polar groups located in the ordered structures governing these polar compounds. Until now, frequently used polar groups in analytical applications include carboxylic acids, sulfates, polyethylene oxides, carboxylates, sulfonates, and ammonium and pyridinium ions. Binding interactions intricated during the extraction of polar compounds mostly contain ionic, hydrogen bonding, π-cation, and π-π. Hydrogen bonding is an exceedingly effective preservation mechanism for polar compounds. Instead, when the surfactant comprises a benzene ring, electrophilic interactions are delivered through delocalized electrons in π-orbitals. These delocalized electrons interact with conjugated groups such as aromatic rings or double/triple bonds. The foremost property of supramolecular compounds is their ability to extract amphiphilic compounds (e.g., surfactants, drugs, pesticides, etc.), through the development of mixed aggregates with the amphiphiles resulting in the ordered aggregates. Both hydrophobic and polar interactions manage the development of mixed aggregates. These nanometer- and micrometer-sized aggregates or micelles are innovative extractants for several separation techniques (Michaels, 1990).

While using liquid-phase microextraction (LPME), the solvent is employed in a hollow fiber. Analytes are moved from the donor phase (aqueous) to a receptor phase via an organic phase immobilized in pores of the hollow fiber. In a two-phase mode, the solvent in the pores of the fiber is similar to that in the fiber. In a three-phase mode, the solvent located in the pores of fiber varies from that present in the fiber. Extraction of polar analytes is carried out using a three-phase model, while the two-phase model is used for extracting nonpolar and/ or semi-polar analytes. The amount of solvent in

the fiber is about 10–25 L. The advantage of LPME over SDME is the existence of the fiber supporting organic solvent by decelerating the evaporation and dissolution of solvent.

4.8.2. Surfactant-Based Extraction

Alternate extraction methods, based on the usage of surfactant solutions, are suggested to lessen the environmental influence of analytical approaches. Aqueous solutions of some surfactants have also been used in micellar extraction (ME) as well as in cloud point extraction (CPE). ME is based on the fact that the Micellar aggregates, which are capable to solubilize various compounds and have a size that inhibits them from crossing ultrafiltration (UF) membranes, form the basis of the ME technique. The CPE technique is based on the cloud point effect revealed by the aqueous micellar solution of some surfactants while heating or cooling below or above a certain temperature (Figure 4.8) (Chou and Bell, 2007).
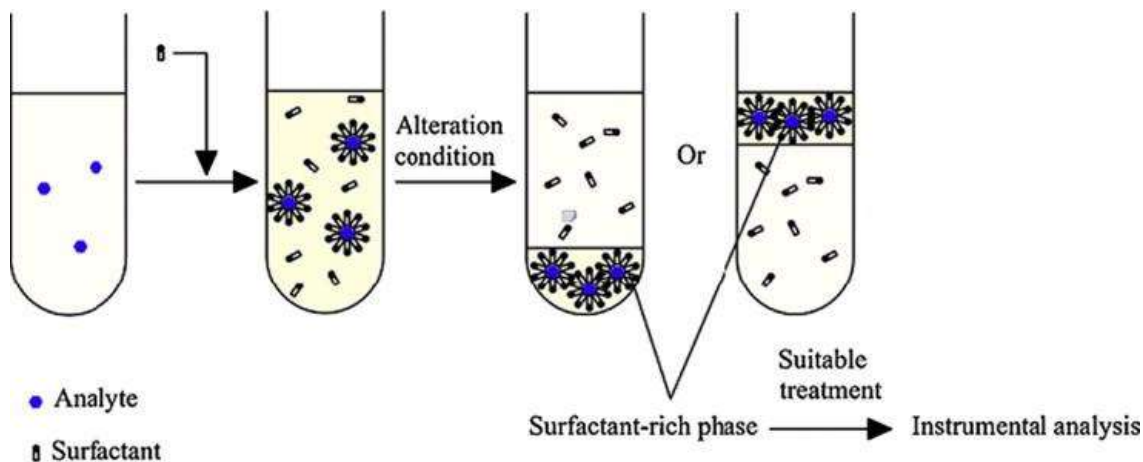
Figure 4.8. *Surfactant based extraction process.*
Source: https://www.sciencedirect.com/science/article/abs/pii/S0165993611000951.

CPE is also recognized as a micelle-mediated extraction technique, extensively used for the extraction and preconcentration of organic acids, trace metal analysis, and hydrophobic proteins. Though, in recent times, CPE has been employed for the extraction of organic molecules excluding biomolecules. CPE has been effectively exploited for the extraction and preconcentration of PAHs as a primary step to determine them by liquid chromatography (LC) using nonionic surfactants and anionic surfactants, like SDS, sodium dodecylbenzene sulfonic acid (SDBSA), and sodium dodecanesulfonic acid (SDSA). Similarly, various nonionic surfactants have been utilized in the preconcentration of PCBs and dibenzofurans (PCDFs) from seawater. The existence of organophosphorus pesticides, such as paraoxon, methyl, and ethyl parathion, and fenitrothion, has been determined in river water samples by using CPE with the nonionic surfactant Triton X-114 before their separation by LC. The use of the nonionic surfactant poly(oxyethylene glycol) monooctyl ether headed for better extraction yield even

for polar species, such as chlorinated phenols and anilines, with recoveries of 88–99% (Seike and Oishi, 2003).

4.8.3. Solvent Extraction with Microemulsions

Some examples of microemulsion application in solvent extraction of metal ions and biological compounds are given below for reference. The effect of extraction parameters is deliberated shortly.

4.8.3.1. Metal Ion Extraction with Microemulsion

Relative to conventional extraction, the organic phase is replaced by a W/O microemulsion containing the reactant in metal ion extraction. Two possible ways are given for the formation of a W/O microemulsion in the solvent phase (Li Guan-Shan, 2008):

- The extractant creates reverse micelles in the organic phase resulting in the development of a microemulsion when this phase is contacted with the aqueous one; and

- The extractant does not make reverse micelles under the conditions of the process, in such case, a surfactant, and occasionally a cosurfactant too must be added to the organic phase to create a reverse micellar phase. In this situation, the reverse micelles are ordinarily mixed, i.e., contain reactant and the additives in the micellar shell.

Only case (2) shows a comparison between conventional and ME. The few comparisons reported in the literature on the metal extraction efficiency of microemulsions comprising an extractant with that of the extractant on its own are, at first sight, inconsistent. In certain circumstances, microemulsions yield both synergism and extraction rate improvement about the single surfactant, whereas in others they significantly decrease the metal distribution coefficient and the extraction rate, or leave them unaffected. Extraction with di(2-Ethylhexyl)phosphoric acid (DEHPA) is a relevant, interesting example. DEHPA does not produce microemulsions in aliphatic solvents at pH 4 or below; however, it forms microemulsions by adding a surfactant and a cosurfactant, e.g., sodium dodecylbenzene sulfonate and *n*-butanol. Enhancements in the extraction of trivalent and tetravalent metals of the conventional system with a DEHPA microemulsion were reported. At extraction of Al(III) using similar microemulsion enhancements were also obtain but not at the extraction of Zn(II), which was considerably reduced concerning the conventional DEHPA system. The researchers tried to elucidate this phenomenon of the microemulsion by the different interfacial behavior of their complexes—the aluminum complex being more hydrophilic have greater desorption energy as compared to the zinc complex, making the interface its desired place, whereas the zinc complex has a high solubility in the organic phase (Drioli et al., 2002). This proposal remains to be confirmed. The same trend of microemulsion in the extraction of Bi(III) and Zn(II) was observed increased yield in the extraction of Bi(III) only, but not of Zn(II).