ASSET BULLETIN

ASSOCIATION OF SEPRATION SCIENTISTS AND TECHNOLOGIESTS

asset.org.in

March 2020

SEPARATIONS IN LIQUID PHASE

ASSET BULLETIN ON SEPARATION SCIENCE

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EDITORIAL

Over the past four decades, theory and application of separation science have substantially advanced and touched almost every sector – from environment to electronics. The growth of modern separation techniques is momentous. Considerable progress has been made in understanding the mechanisms that control entire classes of separation processes. However, separations are often overlooked and underappreciated. This necessitates making the subject accessible to the students and academicians who do not work in this field by presenting it in an understandable form.

Solvent extraction and Ion exchange, the conventional separation methods, have realised notable advancements through innovations. Traditionally, Solvent extraction involves contacting of an aqueous and organic phase in order to extract solutes such as metal ions from mixtures or to concentrate them. The approach in Ion exchange is to immobilize the chelating or ion exchange ligands to a polymeric solid support. High Performance Liquid Chromatography (HPLC) and High Performance Ion Chromatography (HPIC) are the versatile analytical chromatographic techniques in separation science. They are the most widely applied separation techniques because of their superior performance and reliability, especially in pharmaceutical, environmental, forensic, clinical, food and flavour sciences. Membrane separation is based on the selective permeation of one or more components. Membranes have gained an important place in industrial separations. Electrochemical separations are quite interesting for separating the

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EDITORIAL (Contd.)

ionic components from a medium of high ionic strength. Although ASSET has published many bulletins on various themes in the past, the present one is different from the previous bulletins as it covers the fundamental aspects of some five major separation techniques namely Solvent extraction, Ion exchange, Liquid chromatography, Membrane separation and Electrochemical separation. I wish to thank all the contributing authors for their efforts and cooperation in making timely submission. My special thanks to Dr. P.G. Jaison, Mr. Vijay Telmore and Mr. Mrinal K. Das for their kind support and help in editing the articles.

President's Message

Dr. P. K. Pujari
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Advancements in Separation Science and Technology have been expanding exponentially in all fields of science and engineering. Chemical separations are imperative to almost every aspect of our lives. Separation science and technology play pivotal roles in producing energy, synthesising medicines, manufacturing high purity materials and so on. An impressive example is the development and commercialization of reverse-osmosis membranes for water desalination. Thanks to step-change advances in separation technology, hundreds of millions of people now have ready access to potable water.

Conventional extraction techniques have seen improvements viz. miniaturization and hybrid techniques especially in solvent extraction with nano and microtechnological extraction, subcritical water extraction, supercritical fluid extraction, superheated water chromatography, supercritical fluid chromatography etc. In addition, pressurized liquid extraction, accelerated liquid extraction, solvent extraction with microemulsions are some of the techniques undergoing rapid change in separation science. Tremendous progress has been achieved in the field of Ion exchange separations after the introduction of high capacity pellicular and totally porous ion exchangers that can withstand the rigors of fast flow and high pressure. HPLC and HPIC applications have expanded globally leading to a large number of separations relevant to pharmacology and biology; exceptionally in the case of liquid chromatography hyphenated to mass spectrometry.

Membrane separations find many applications dominantly in the field of desalination, food processing, waste water treatment etc., because they offer advantages like easy operation, cost effectiveness, high selectivity and a high pre-concentration factor. Ion-imprinted membranes are capable of selectively separating and detecting ions and have great potential for industrial separations. Research is making rapid expansion in this field due to advanced membrane technologies and synthetic strategies. Electrochemical separations are the emerging methods and have wide applications in diverse fields. The use of electrochemistry and electrical behaviour as control and manipulation factor in the extraction of analytes led to a new area known as electromodulated extractions, wherein the electromodulation strategy offers great opportunities for selectivity. The role of electrochemical separations is noteworthy while developing biosensors for many biologically active molecules. Electrochemistry provides the ability to manipulate solid-phase extractions by controlling the solid-phase applied potential and it helps in manipulating the liquid-liquid extractions by controlling the interfacial potential difference. The thematic bulletin being brought out by our Association is a long-standing demand from the academicians and students who wish to understand the fundamentals of separation methods. I am sure they will find this bulletin very useful.

Separations in Liquid Phase

Fundamental Aspects and Applications of Solvent Extraction

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1. Introduction

Liquid-liquid extraction commonly known as "Solvent Extraction" which involves the distribution of a solute between two immiscible liquid phases in contact with each other is a versatile separation technique. It is extensively utilized in both industrial applications and in the laboratory and has numerous applications in chemical industries to produce pure chemical compounds ranging from pharmaceuticals and bio-medicals to heavy organics and metals [1]. Its use in the petroleum industry as well as in organic chemical industry has been known since the early twentieth century. Solvent extraction has applications in food industry for the extraction of lipids, flavours, aroma etc. Applications of solvent extraction in hydrometallurgy include recovery of various metals such as copper, nickel, cobalt, cadmium, zinc, tungsten, molybdenum etc[2, 3]. It is also being used in analytical chemistry for the separation and estimation of metal ions [1].

Though solvent extraction has a long history, many details are not reported in the literature. During the development of chemistry in the nineteenth century, it was found that many metal salts such as chlorides of iron, mercury and gold dissolved in alcohols and ethers. Bertholot and Jungfleisch investigated the distribution of a large number of organic and inorganic compounds between ether/carbon disulphide and water for the practical use of solvent extraction for the separation and purification of different substances. In 1872, they introduced a term to describe how a solute is distributed between the organic and aqueous phases.

Although E. Peligot reported about the extraction of uranyl nitrate by ether from its solution in nitric acid in 1842, the first large-scale industrial solvent extraction plant for production of high purity uranium by the selective extraction of uranyl nitrate using ether from aqueous solutions was built in 1942 by Mallinckrodt chemical company in St. Louis, USA almost after a century. This initiated a surge in the interest in solvent extraction in 1940s and 1950s. Till 1950, ether based extraction was the only process for the production of nuclear grade uranium. Diethyl ether was also used for the laboratory scale separation of zirconium and hafnium from aqueous thiocynate medium by solvent extraction technique. Thus, historically diethyl ether is considered as the most important extractant. However, major limitations of ether based extraction processes such as use of high concentration of salting out agent, fire hazard issues terminated its use in solvent extraction and subsequently ether was replaced by dibutylmethanol and methylisobutyl ketone. In 1940's, a wide variety of efficient metal extractants such as tri-*n*-butyl phosphate (TBP), trioctyl amine etc were introduced. This resulted in the use of solvent extraction as a separation and purification process in numerous chemical and metallurgical industries in the 1950s and early 1960s [1].

2. Principles of solvent extraction

When a solute particle is introduced into a solvent, it interacts with the solvent molecules in its vicinity. Based on the fact that "opposite charges attract each other", solute particles can interact with solvent by ion-dipole, dipole-dipole, dipole-induced dipole and induced dipole-induced dipole interactions. Among these interactions ion-dipole is the strongest and induced dipole-induced dipole is the weakest. The force of attraction depends upon the nature of the solvent and solute. The resultant effect of these interactions is called the "solvation" which is responsible for the dissolution of a solute in a particular solvent. Generally, non-polar solutes dissolve in non-polar solvents and polar solutes dissolve in polar solvents.

Due to the variations in the strength of the interactions between the solute and solvent molecules, solutes can show different solubilities in different solvents. Thus, in a system of two immiscible liquids, different solutes get unevenly distributed between the two liquid phases. A partial separation occurs when solutes have different relative affinities in the two solvents. This forms the basis for the solvent extraction based separations. Solvent extraction commonly takes place with an aqueous solution as one of the liquid phases and an organic solvent as the other phase. In the simplest case, if one solute (X) is present in a feed solution, which is mixed with an immiscible liquid by agitating the two liquids, the solute distributes between the two phases. When the distribution reaches equilibrium, the ratio of the concentration of solute in the organic and aqueous phases is called distribution ratio (D) with respect to that solvent and feed.

$$D = \frac{[X]_{org}}{[X]_{aq}} \quad (1)$$

where, $[X]_{org}$ and $[X]_{aq}$ are the total analytical concentrations of the solute in the organic and aqueous phases, respectively. The solute can be present in various complexed forms in the aqueous phase as well as in different forms in the organic phase. Distribution ratio D involves sum of various species in each phase and it is not a constant and it varies with the concentration of the solute. It is different from the distribution constant or distribution coefficient, $K_{D,}$ which involves the distribution of the same species between the two phases. If the solute has the same molecular weight in the organic phase as in the aqueous phase, then K_D is independent of the concentration of the solute. Depending on the system and their extraction mechanism, it has been found that the distribution ratio depends on various parameters such as temperature, pH of the phases, type of extractant, the concentration of chemical species in the system etc. The value of distribution ratio is one of the main parameters used to establish the minimum solvent–feed ratio that can be used in the extraction processes.

In order to have a detailed understanding of the distribution law, it is essential to probe into the thermodynamic aspects of extraction. A system at a constant temperature and pressure is said to attain equilibrium state when the chemical potentials (ϕ) or partial molal free energies of the solute molecules in each of the phases are equal as given in equation (2).

$$\phi_{org} = \phi_{aq} \quad (2)$$

Substituting suitable expressions for ϕ, we get the following relation

$$\phi_{org}{}^{0} + RT \ln m_{org} + RT \ln \gamma_{org} = \phi_{aq}{}^{0} + RT \ln m_{aq} + RT \ln \gamma_{aq} \quad (3)$$

where, ϕ^0_{org} and ϕ^0_{aq} represent the standard chemical potentials of the solute in the organic and

aqueous phases, m_{org} and m_{aq} are their respective solute concentrations (expressed in molality) and γ_{org} and γ_{aq} represent the activity coefficients in the organic and aqueous phases, respectively. From this we obtain an expression for the molal distribution coefficient, K_D as given below

$$K_D = \frac{m_{org}}{m_{aq}} = \frac{\gamma_{aq}}{\gamma_{org}} e^{-(\phi_{org}{}^0 - \phi_{aq}{}^0)/RT} \quad (4)$$

As for most of the systems of concern, the presence of solute does not significantly alter the mutual solubilities of the two phases, ϕ^0 remains constant and hence the equation can be re-written as

$$K_D = \frac{\gamma_{aq}}{\gamma_{org}} K' \quad (5)$$

When the solute concentration is low, the activity coefficients γ_{org} and γ_{aq} approach unity and the molal distribution coefficient K_D becomes constant.

The percentage extraction (% E) of the solute of interest which provides a useful picture of extraction can be calculated from the distribution ratio (D) and the volumes of the organic (V_o) and aqueous phases (V_a) using the following equation

$$\%E = \frac{100D}{D + (V_a / V_o)} \quad (6)$$

If the feed stream contains two components 'A' and 'B' with distribution ratios 'D_A' and 'D_B', respectively, then the concept of selectivity can be given as equation (7).

$$\beta_{A/B} = \frac{D_A}{D_B} \quad (7)$$

where,"$\beta_{A/B}$" is the selectivity of that solvent with respect to the components. It is also called "separation factor". For the separation of a solute between two phases by the use of a particular solvent to occur, the selectivity must be greater than 1 and higher the selectivity, separation will be more effective. In the analytical laboratory, depending on the degree of separation, solvent extraction step can be carried out either as a batch method for extractants with high D value or as a continuous operation when the D values of the solvent extraction systems are relatively low. However, for industrial purposes involving the processing of large quantity of materials with the consumption of a huge volume of solvent, continuous process is preferred over batch process in economic point of view.

3. Batch extraction

The batch solvent extraction can be carried out using laboratory glassware, preferably in a separating funnel by contacting a given volume of a feed solution with a given volume of the solvent followed by the separation of the two liquid layers after the attainment of the equilibrium. This is considered to be the simplest extraction procedure possible and is the most preferred method for analytical separations. Solvent extraction has to be performed in this manner to yield fundamental distribution data for the investigation of unknown solvent systems before the final choice of the extraction process.

Since the distribution ratio is a concentration ratio, the actual fraction of the total solute extracted varies with the ratio of volume of organic and aqueous phases. Let v_1 ml of the aqueous solution (phase 1) containing w g of the solute be contacted with v_2 ml of the solvent (phase 2) which is immiscible with the phase 1. If w_1 g of the solute is remaining in the phase 1 after the attainment of equilibrium, then the concentration of the solute in phase 1 is w_1/v_1 g per ml and that in phase 2 is $(w-w_1)/v_2$ g per ml. Hence,

$$D = \frac{C_2}{C_1} \equiv \frac{(w - w_1)/v_2}{w_1 / v_1} \quad (8)$$

and

$$w_1 = w\left(\frac{v_1}{Dv_2 + v_1}\right) \qquad (9)$$

After the first extraction, if the aqueous phase is subjected to second extraction with another portion of v_2 ml of the solvent, w_2 g of the solute is remaining in phase 1. After the second extraction

$$w_2 = w_1\left(\frac{v_1}{Dv_2 + v_1}\right) \qquad (10)$$

$$w_2 = w\left(\frac{v_1}{Dv_2 + v_1}\right)^2 \qquad (11)$$

If the same volume of the solvent (v_2) is used in each successive extraction and if w_n represents the weight of the solute remaining in the feed after n number of extractions, then

$$w_n = w\left(\frac{v_1}{Dv_2 + v_1}\right)^n \qquad (12)$$

It is clear from the above equation that for the complete extraction, n should be as high as possible and v_2 should be as low as possible for a given amount of the solvent. This implies that batch extraction is more effective by carrying out a large number of extractions with small amounts of the solvent. Batch extraction may be suitable for solvent systems with larger distribution ratio and in such cases a few extractions will effect quantitative separation. However, in general batch extraction is considered to be inefficient, because it implies batch rather than continuous operation. Industry prefers continuous operation because it can be controlled automatically and it makes better use of labor and hence more economical. Continuous operation demands the use of liquid-liquid contactors as the solvent extraction equipment.

4. Liquid-liquid contactors

Liquid-liquid contactors can be classified in different ways: (i) stage-wise or differential (ii) gravity or centrifugal (iii) un-agitated and (iv) agitated extractors. Stage-wise extractors consist of discrete units wherein equilibrium is achieved in each of these stages. Differential contactors provide continuous contact and mass transfer along the length of the contactor and equilibrium is never established at any point along the length of the column and phases are separated only at the ends of the equipment. Among the un-agitated contactors, spray column is the simplest and has very low mass transfer efficiency due to poor phase contacting and excessive back mixing. The packing in packed column improves the mass transfer efficiency due to better phase contacting.

In general, an extractor has three major functions (1) bringing the two liquid phases into contact (2) creating droplets of dispersed phase to provide interfacial area for mass transfer, and (3) separation of the liquid phases after the completion of the extraction. Various types of contactors are available for solvent extraction applications. In these contactors, two immiscible liquids are brought into intimate contact to transfer the solute of interest from one phase to the other. For better efficiency and mass transfer, they are always operated in counter-current mode. Contact within the extractor can be differential or in a multiple of stages. The rate of interface mass transfer depends on the interfacial area through which transfer occurs, the mass-transfer coefficient, which is a measure of the specific rate of transport of mass across the interface and the concentration difference which is the “driving force” for the transfer. Dispersing one of the phases into small droplets of desired size in the other continuous phase by giving sufficient energy to overcome the interfacial tension

(IFT) of the liquid pair can increase the interfacial area [4].

Mixer-settlers, liquid pulsed perforated-plate columns and centrifugal extractors are the main extractors used in nuclear industry [5, 6]. Though each one has its own merits and demerits, mixer-settlers dominate over the other contactors. In mixer-settlers, which belong to discrete stage-wise category, two phases are mixed in the mixer and then separated in the settler of the same stage before passing to the next stage for equilibration. Mixers also provide a pumping action to avoid the need for separate pumps for interstage liquid transport. Complete disengagement of the mixed phase takes place in a settler before the transfer to the adjacent mixers. Air pulsed mixer-settlers of different designs have been developed for fuel reprocessing applications [7]. A novel mixer-settler based on ejector as the mixing device has also been designed and developed [8].

Phase dispersion and coalescence phenomena are important in liquid-liquid extraction with either stage-wise or differential contact [9]. During mixing, dispersed droplets of small size have high tendency to coalesce. Hence, equilibrium is established between the continuous breakup and coalescence processes. The mean equilibrium drop size depends on the mode of operation of the contactor and the type and the extent of agitation. Systems with high IFT require mechanical agitation to be applied in order to achieve adequate dispersion. However, for systems with low IFT, non-agitated gravity columns are preferred. For systems with an emulsification tendency and low density difference between phases, phase separation is difficult and this can be achieved by using centrifugal extractors, which provide the force required for phase separation.

5. Classification of continuous processes

Continuous extraction processes can be carried out by different ways. The simplest process is "single-stage extraction", in which the feed and the solvent flow with controlled flow rates into a mixing chamber from which the mixed phase flows to a separator which separates extract and raffinate which are withdrawn continuously. This corresponds to the use of a single stage mixer-settler.

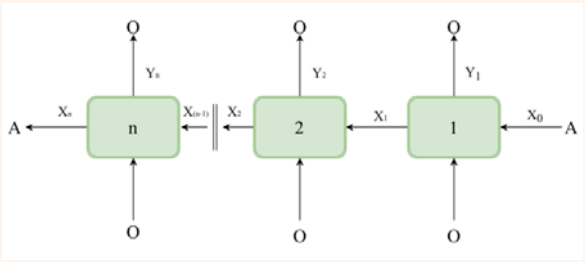

Figure 1: Cross-current extraction

In the "multistage cross-current extraction" as shown in Figure 1, the feed is passed successively through a number of stages arranged in series with a separate feed of fresh solvent to each stage. Complete extraction can be achieved by increasing the number of stages without any solute loss into the raffinate stream. However, the solvent consumption is high and the solute concentration in the mixed extract is correspondingly low. In Figure 1 "*O*" denotes the organic flow rate and "*A*" corresponds to aqueous flow rate and the concentrations of the extractable species are "*x*" and "*y*" in the aqueous and organic phases, respectively. The mass balance for *n* stages is given in equation (13).

$$A\times(x_0-x_n)=O\times\sum_{i=1}^{i=n}y_i \qquad (13)$$

"Co-current extraction" is performed by introducing feed and solvent in the same direction as shown in Figure 2. As ideally no additional extraction takes place after the first stage in the co-

current flow because the two streams leaving are already at equilibrium when they are re-contacted in subsequent stages. The arrangement is considered to have a mass transfer limit determined by the phase equilibrium. Thus, co-current extraction has low extraction efficiency, enrichment factor and has no merit except for systems which have slow extraction kinetics where it is not possible to achieve equilibrium in one stage.

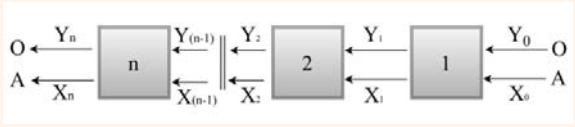

Figure 2: **Co-current extraction**

"Continuous counter-current extraction" can be carried out in equipment by introducing feed and solvent at opposite ends, where the extract and raffinate, respectively, are withdrawn as shown in the Figure 3. This can be achieved by using either a mixer-settler cascade or a counter-current column. In this case the outgoing extract is brought into contact with the entering feed containing the highest concentration of solute, ensuring a low solvent consumption which results in high extract composition. In counter-current extraction scheme, which is extensively used in commercial processes, the solvent enters the stage or the end of the extractor farthest from the feed and the two phases flow counter-current to each other. If the contactor is an actual stage device such as mixer-settler, the phases separate before leaving each stage. For a counter-current process consisting of n stages, mass balance is given in equation (14).

$$A \times x_0 + O \times y_{(n+1)} = A \times x_n + O \times y_1 \qquad (14)$$

$$y_1 = \frac{A}{O} \times (x_0 - x_n) + y_{(n+1)} \qquad (15)$$

Equation (14) can be rearranged to equation (15), which represents a straight line of slope A/O. The values, x_0 and $y_{(n+1)}$, composition of feed and fresh solvent, respectively, are constants. Here, the composition of the organic phase leaving the first stage (y_1) is a linear function of the composition of the aqueous phase leaving the n^{th} stage (x_n). Therefore, concentration of the solute in the extract (y_1) increases with decrease in the concentration of the solute in the raffinate (x_n). If *A/O* ratio is maintained as 1, for a counter-current extraction process which performs with a fresh solvent ($y_{(n+1)}$ = 0), without any loss of solute into the raffinate stream (x_n = 0), then the concentration of extract (y_1) is equal to that of feed (x_0).

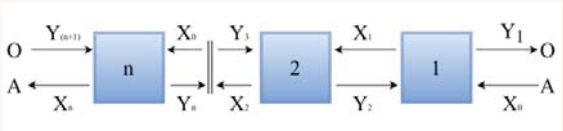

Figure 3: **Counter-current extraction**

In general, a single-stage extraction requires more solvent than a cross-current extraction, which in turn needs more than a counter-current extraction. Single-contact and multistage cross-current extraction are used only for relatively small operations. On the other hand, counter-current extraction uses the solvent much more efficiently and is widely used in both organic and inorganic separations in industries.

6. Basic steps in a solvent extraction process

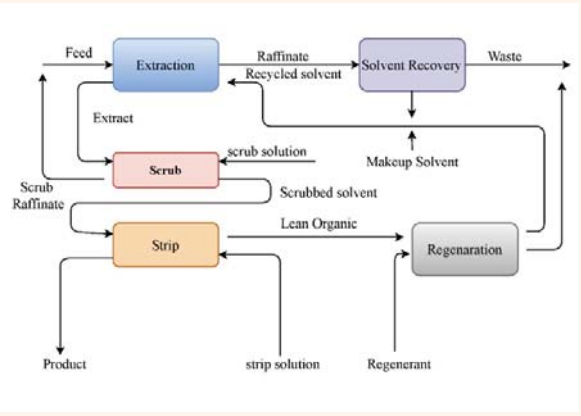

Figure 4: Various steps in a solvent extraction process

In a process as shown in Figure 4, the fresh solvent and the feed (the phase containing the desired and the undesired components) enter into the "extraction stage" where extraction takes place. The aqueous solution leaves the extraction stage after the extraction and is called "raffinate" which can be allowed to pass through a "solvent recovery stage" where any dissolved or entrained solvent is recovered and recycled. The loaded solvent comes out of the extraction stage is called "extract" which is allowed to pass through a "scrub stage" to wash out some of the undesired components with a scrub solution and the scrub raffinate is recycled to the feed. Stripping takes place in the "strip stage" where the strip solution back extracts the desired component from the extract or the scrubbed extract. The product solution is then sent to "product recovery stage" in which the desired component is finally recovered. The stripped solvent (lean solvent) can either be recycled directly to the extraction stage or can be sent to a "regeneration stage" where it is contacted with a regenerant to restore its purity which is desired for efficient extraction. Figure 4 is only a general system and processes can be carried out with a few variations.

7. Solvent Selection

Solvent selection, operating conditions, mode of operation, extractor type and design criteria with respect to mixing, settling, selection of continuous and dispersed phase etc., are the important parameters which have to be optimized for the design and operation of a solvent extraction process. Among these, solvent selection is the most important one and the success of a liquid-liquid extraction process is dependent on the selection of the most appropriate solvent [10]. It can often have a more significant impact on the process economics. Several factors influence the choice of a solvent for the extraction of metal ions. A final choice involves a compromise between various factors as shown below.

- Ease of regeneration – This is as important as selectivity and in any extraction process, the solvent must be regenerated and recycled to the extractor.
- Significant difference in density between feed and solvent – In solvent extraction, the driving force for settling is the difference in density between the organic and aqueous phases. Preferably this difference should be around 5% or more.
- Moderate interfacial tension – Interfacial tension has significant impact on mixing. Lower the IFT, lesser the energy required to create a droplet dispersion. However, a very low value (<1 $mN.m^{-1}$), may trigger emulsions that are either impossible to settle or take impractically long time. For systems with high IFT (around 50 $mN.cm^{-1}$), higher mechanical energy has to be imparted in the system to create droplets.
- Low viscosity – It is desirable to run extraction systems with viscosities less than 10 cp, to enhance mass transfer rate.
- High metal loading capacity.

But none of the solvent extraction reagents which are also called 'extractants' satisfy all the characteristic properties. In most of the solvent extraction processes, the solvent extraction reagent is dissolved in another organic compound (diluent). The mixing of the extractant with a diluent with which it is miscible modifies the physical properties of the resultant binary solution (solvent). Addition of diluent confers appropriate hydrodynamic properties of the solvent. Diluent also reduces the extracting power, and hence improves the selectivity. Several advantages such as improved

mass transfer, improved phase separation, decreased entrainment of aqueous phase in the organic phase etc., are obtained as a result of the decreased density and viscosity. However, the use of diluent which is non-polar in nature at times leads to the splitting of the organic phase (third phase formation) during the extraction. Other components such as phase modifiers and synergists are also added to alter physicochemical characteristics and to increase extraction.

Extractants are molecules which possess both hydrophilic and hydrophobic properties. Polar hydrophilic groups take part in the complexation with metal ions present in the aqueous phase. The hydrophobic character provided by the organic part of the reagent molecule is required to maximize the solubility of metal-complex in the organic phase and also to reduce the aqueous solubility of the reagent itself, thus minimizing the reagent losses to the raffinate stream. For an extractant to be used for commercial solvent extraction processes, it has to satisfy the following properties (i) it should have low solubility in aqueous phase and high solubility in aliphatic diluents, (ii) its density and viscosity should be low, (iii) it should be nonvolatile, nonflammable and nontoxic, (iv) it should have good kinetics of extraction as well as stripping and (v) it should have good selectivity for desired metal ions and stripping of loaded metal should be easy. In addition, it should have good stability (thermal, chemical as well as radiation) and it should be relatively inexpensive and commercially available.

8. Classification of Extractants

To transfer a metal ion from an aqueous solution in which it exists as a hydrated ion, to an organic phase, it has to be converted to an extractable species. Such a conversion requires the charge neutralization of the metal species and replacement of some or all of its water of hydration by extractants (solvent extraction reagents). Hence, chemical reactions between the metal species present in the aqueous phase and the extractant molecules present in the organic phase are involved in the solvent extraction of metals. Therefore, complexation of a metal ion can be viewed as a conversion of a hydrophilic species into a hydrophobic species. Since it involves the replacement of hydrated water molecules by extractants or ligands, all complexing reactions are substitution reactions.

Based on the complexing reactions which involve compound formation, ion association and solvation of a metal ion, extractants can be broadly classified into four groups as acidic, basic, neutral and chelating extractants [10]. Acidic extractants extract cations by compound formation, basic extractants extract anionic species by ion-pair formation, neutral extractants extract neutral salts by solvation and chelating extractants extract metal ions by chelation with the formation of ring structures involving the extractant molecule and metal ion.

8.1. Acidic Extractants

Acidic extractants extract metal ions by cation-exchange mechanism, in which hydrogen atom of the extractant molecule is exchanged with metal ion as shown below

$$M^{n+}{}_{(aq)} + n\,HA_{(org)} \Leftrightarrow M(A)_{n(org)} + n\,H^{+}{}_{(aq)} \quad (16)$$

Since the extraction takes place with the release of hydrogen ions, usually the extraction of metal ions by acidic extractants takes place at lower acidity. Extracted metal can be stripped at higher acidity. Molecules of these extractants have functional groups such as -COOH, -P(O)OH and -SO_3H. For example, organic derivatives of phosphorous acids and monocarboxylic acids belong to this category [11].

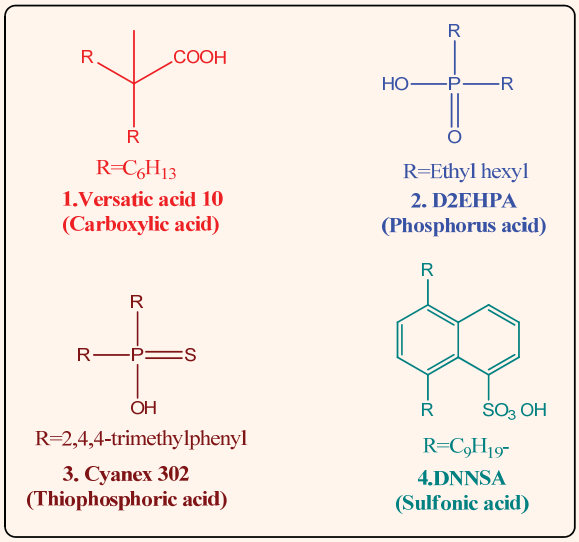

Figure 5: Some commercial acidic extractants for hydrometallurgy: *(i) 2-hexyl-2-methyloctanoic acid (Versatic acid 10)(ii) di-2-ethyl hexyl phosphoric acid (D2EHPA) (iii) Di-2,4,4-trimethylpentyl thiophosphinic acid (Cyanex 302) (iv) 5,8-dinonyl naphthyl sulfonic acid (DNNSA)*

Alkyl or aryl groups present in the extractant can influence its acidic nature and the distribution ratio for the extraction increases with increase in the acid strength of the extractant. Among the esters of phosphoric, phosphonic and phosphinic acids and similar compounds containing polyfunctional groups, alkylphosphoric acids are the most promising, especially di(2-ethylhexyl) phosphoric acid (D2EHPA). It has been used for the extraction of many metals such as uranium, cobalt, nickel, rare earths and vanadium on commercial scale. Di(2-ethylhexyl) phosphonic acid (PC-88A) is another important acidic extractant and has been employed for several applications.

It can be seen from equation (16) that the equilibrium is pH dependent. The term $pH_{1/2}$ which is the pH value at 50% extraction of the metal ion into the organic phase (%E=50) is generally used to understand the strength of various acidic extractants. Stronger extractants for metal cations have low $pH_{1/2}$ values, indicating that they are capable of recovering metals from more acidic feed solutions. Conversely, a weak extractant for metal cations is only capable of recovering metals at high pH. The pH-dependence of the equilibrium shown in equation (16) makes it possible to control the loading and stripping of the metal in the organic phase by varying the pH of the aqueous phase with which it is in contact. Moreover, the difference in $pH_{1/2}$ values for two metals having the same oxidation number can be used as a measure of the degree of separation of these metals.

8.2. Basic Extractants

Basic extractants extract metal ions by ion association resulting from the physical attractive forces between oppositely charged species. Hence, ion association enhances with decrease in the distance between the centers of oppositely charged ions which are in contact. It also increases with decrease in the dielectric constant (ε) of the medium. Hence, water with high ε tends to inhibit ion association, whereas organic solvents with low ε enhance ion association. The extraction of anionic metal species (MY^-) such as $CoCl_4^{2-}$, $FeCl_4^{2-}$, $MoCl_3^{2-}$, $UO_2(SO_4)_2^{2-}$, $ZnCl_4^{2-}$etc by long chain primary (RNH_2), secondary (R_2NH), tertiary (R_3N) amines and quaternary ammonium salts $(R_4N)^+X^-$ belong to this category [11]. The nature of the alkyl chain as well as the number of carbon atoms in the alkyl chain can influence the metal extraction by amines. Aliphatic amines are preferred as compared to amines with aromatic substituents. High degree of branching of the alkyl chain leads to a decrease in extractive properties, probably due to the steric effects. In general, the ease of extraction of the anionic species by amines from Cl^- media follows the order: quaternary>tertiary>secondary>primary. The anionic metal species present in the aqueous

phase is exchanged with the anion of the amine salt which is formed by the amine and an acid (HX) and these reactions are shown below

$$R_3N_{(org)} + HX_{(aq)} \Leftrightarrow R_3NH^+X^-{}_{(org)} \quad (17)$$

$$R_3NH^+X^-{}_{(org)} + MY^-{}_{(aq)} \Leftrightarrow R_3NH^+MY^-{}_{(org)} + X^-{}_{(aq)} \quad (18)$$

Tri-*n*-octyl amine (Alamine 336) and tri-octyl methyl ammonium chloride (Aliquat 336) are two important basic extractants used for several applications.

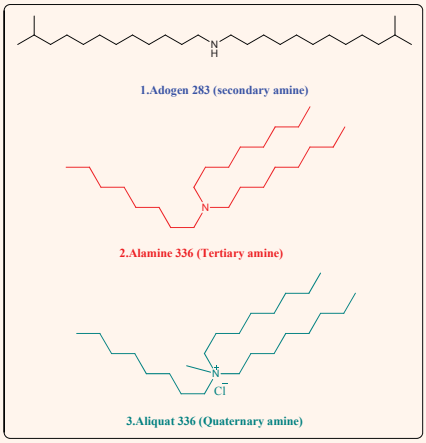

Figure 6: Some commercial basic extractants for hydrometallurgy: *(i) Diisotridecylamine (Adogen 283) (ii) tri-octyl amine (Alamine 336) (iii) tri-octyl methyl ammonium chloride (Aliquat 336)*

8.3. Neutral Extractants

Neutral extractants are reagents containing donor atoms with lone pair of electrons for the solvation of neutral inorganic species. Extraction involves the formation of an addition complex comprising undissociated electrically neutral salt and the extractant. The addition complex thus formed is more soluble in the organic phase than in the aqueous solution. Two main groups of extractants in this category are organic reagents containing oxygen bonded to carbon such as ethers, esters, ketones and amides and those containing oxygen or sulphur bonded to phosphorus, as in alkyl phosphates or alkyl thio phosphates [11]. Organic reagents such as triesters of phosphoric, phosphonic and phosphinic acids, organic sulphoxides, organic sulfides etc., belong to the family of neutral extractants. The solvating power depends strongly on the basicity of the reagent. Thus, the extraction ability of the organophosphorusextractant depends on the basicity of the phosphoryl oxygen and the nature of the substituents attached to phosphorus atom. The basicity of phosphoryl group can be enhanced by replacing the C-O-P group in the extractant by a C-P group. The basicity on the phosphoryl oxygen in the neutral organophosphorusextractant series increases in the order phosphates <phosphonates<phosphinates< phosphine oxides. The extraction of any metal salt by a neutral solvating type extractant such as tri-*n*-butyl phosphate (TBP), can be expressed as follows

$$M^{n+}{}_{(aq)} + n\,A^-{}_{(aq)} + x\,S_{org} \Leftrightarrow M(A)_n \cdot xS_{(org)} \quad (19)$$

Where *A* is assumed for the sake of simplicity to be a univalent anion, *S* is the extractant, *(aq)* is the species present in aqueous phase and *(org)* is the species present in organic phase. From the above-mentioned expression, the equilibrium constant *K* can be derived as shown in equation (20),

$$K = \frac{[M(A)_n \cdot xS]_{org}}{[M^{n+}]_{org} \times [A^-]^n{}_{aq} \times [S]^x{}_{org}} \quad (20)$$

where the terms in the square bracket indicate the activities of the various species. For the sake of simplicity, activity coefficients for the various species are assumed to be unity, and hence the terms represent the concentration. The ratio $[M(A)_n \bullet xS]_{(org)}/[M]_{(aq)}$ is nothing but *D* and hence the above equation (20) can be written as,

$$D = K \times [A^-]^n{}_{aq} \times [S]^x{}_{org} \quad (21)$$

Equation (21) indicates that *D* values for the extraction of nitric acid and metal nitrates by TBP increase with increase in the concentration of nitrate ion in aqueous phase as well as increase in the extractant concentration in the organic phase. When the nitrates of thorium, uranium and plutonium are extracted by TBP, from varying concentrations of nitric acid solutions, *D* values initially increase with aqueous nitric acid concentration, due to the increase in the nitrate concentration which enhances the formation of un-dissociated neutral species that are readily extracted by TBP. But at higher acidities, H^+ from HNO_3itself competes with metal ions and therefore there is a decrease in the *D* values. Hence, generally metal salts can be extracted from feed solution having acidity of 2-4 M HNO_3 and can be stripped from the organic extract with very dilute HNO_3 such as 0.01 M HNO_3. The extraction reactions of H^+, Th^{4+}, UO_2^{2+} and Pu^{4+} by TBP from nitrate media are as follows

$$H^+{}_{(aq)} + NO_3^-{}_{(aq)} + TBP_{org} \Leftrightarrow HNO_3 \cdot TBP_{(org)} \quad (22)$$

$$Th^{4+}{}_{(aq)} + 4NO_3^-{}_{(aq)} + 3TBP_{org} \Leftrightarrow Th(NO_3)_4 \cdot 3TBP_{(org)} \quad (23)$$

$$UO_2^{2+}{}_{(aq)} + 2NO_3^-{}_{(aq)} + 2TBP_{org} \Leftrightarrow UO_2(NO_3)_2 \cdot 2TBP_{(org)} \quad (24)$$

$$Pu^{4+}{}_{(aq)} + 4NO_3^-{}_{(aq)} + 2TBP_{org} \Leftrightarrow Pu(NO_3)_4 \cdot 2TBP_{(org)} \quad (25)$$

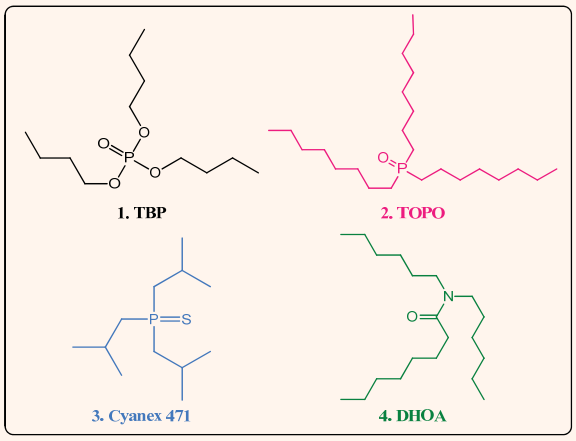

Figure 7: Some commercial neutral extractants for hydrometallurgy. *(i) tri-n-butyl phosphate (TBP) (ii) tri-n-octyl phosphine oxide (TOPO) (iii) tri-iso-butyl phosphine sulphide (Cyanex 471) (iv) Di-N,N-hexyl octanamide (DHOA)*

8.4. Chelating Extractants

The essential feature of chelating extractants is that they show chelation behaviour, the formation of ring structures involving the extractant molecule as a ligand to the metal ion.

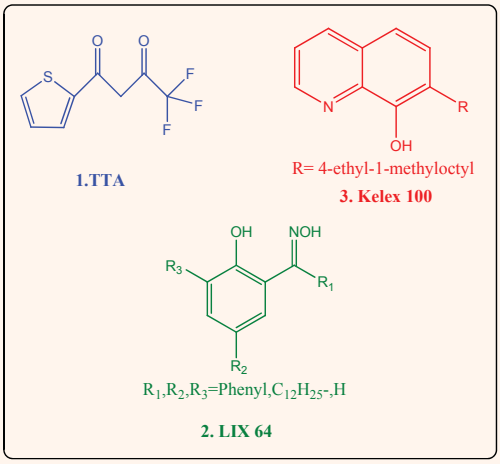

Figure 8: Some commercial chelating extractants for hydrometallurgy. *(i) thenoyltrifluoro acetone (TTA) (ii) 7-(5-ethylnonan-2-yl)quinolin-8-ol (Kelex 100) (iii) (5-dodecyl-2-hydroxyphenyl) (phenyl)methanoneoxime (LIX 64)*

Reagents such as hydroxyoximes and diketones belong to this category. 5,8-diethyl-7-

hydroxy-6-dodecanone oxime (LIX 63), 2-hydroxy-5-dodecylbenzophenone oxime (LIX 64), thenoyltrifluoro acetone (TTA) etc., belong to this family of extractants [11].

9. Third Phase Formation

"Third phase formation" refers to the phenomenon observed in solvent extraction when, at high metal and/or mineral acid loading of the organic phase under suitable experimental conditions, the organic phase splits into two phases [12, 13]. The light phase contains most of the diluent and little extractant and metal-solvate, and the heavy phase contains a high concentration of extractant and metal-solvate and little diluent. The heavy phase is known as "third Phase", with density intermediate between light organic and aqueous phases and hence usually accumulates in the interface [14-18]. Generally, it is believed that third phase is formed due to the incompatibility of polar metal-solvate and acid-solvate with non-polar hydrocarbon diluent. Several parameters such as temperature, nature of diluent, equilibrium aqueous phase acidity, extractant structure, extractant concentration etc., can influence third phase formation.

It creates density and viscosity effects, which usually complicate aqueous-organic mixing in solvent extraction processes. Hydrodynamic problems like flooding in which organic streams following aqueous and vice versa may also arise during the operation of liquid-liquid extraction equipment. In the case of plutonium, the phenomenon has great significance with respect to the danger of criticality. If third phase is formed, it is likely to get collected in some parts of the contactor, its accumulation is criticality hazard. Tetravalent metal ions have higher tendency towards third phase formation in the extraction by TBP and this has profound influence on the applications of solvent extraction in nuclear industry. In order to avoid third phase formation, higher loading in the organic phase has to be restricted, which means that this phenomenon limits the metal loading, which can be theoretically achieved in the organic phase and hence reduces the throughput of the processes. Also, if the metal loading is well below the theoretical capacity of the solvent, unwanted metal ions get extracted and hence the purity of the product decreases. A knowledge of the limiting organic concentration (LOC), which is the concentration of metal ion in the organic phase above that the organic phase splits into two phases and critical aqueous concentration (CAC) which is the corresponding equilibrium concentration of metal ion in the aqueous phase is needed to design the flow sheets for extraction processes. Studies carried out in the last few decades have shown that the aggregation of the species in the organic phase into reverse micelle like structure at a molecular level is responsible for third phase formation [19].

10. Applications of Solvent Extraction

Solvent extraction is widely employed in a variety of industries for both the upgrading and purification of a range of elements and chemicals. Solvent extraction techniques have a broad field of applications in ore processing, pharmaceuticals, agriculture, biochemical industries, petrochemicals, food industry, refining of precious metals and waste water treatment. In addition, solvent extraction is a good technique for studying fundamental understanding of equilibrium and kinetics of complex formation processes. In metal recovery processes, solvent extraction is one of the favoured separation techniques because of its simplicity, speed and wide scope. By utilizing relatively simple equipment and requiring less time to perform, extraction procedures offer much to chemists and chemical engineers [20].

10.1. Non-nuclear Applications of Solvent Extraction

10.1.1. Extraction in Hydrometallurgy

Solvent extraction techniques were developed and used to extract a wide range of metals from different feeds including low-grade ore, scrap, waste leachates, and dilute aqueous solutions. Development of selective chelating extractants for the mutual separation of metals has made this method as the preferred one over classical separation techniques. Separation of copper from its acidic solution is being carried out with LIX 64 N (a mixture of LIX 63 and LIX 64) as the extractant on industrial scale for many years. Separation of nickel from cobalt is extremely challenging due to similar chemical behaviour of their ions. However, the formation of different chlorocomplexes such as $CoCl_4^{2-}$ and $Ni(H_2O)_6.Cl_2$ from its acidic solution led to the separation of Ni from Co through solvent extraction method. *Bul□n* □operation was established to separate Ni from a solution of cobalt, zinc, manganese and nickel with CYANEX 272 as the extractant along with TBP as the modifier. The nickel from the raffinateis further extracted with a carboxylic acid, Versatic 10 as the extractant. . Subsequently, □*a*□□*e* and *Murrin□Murrin* process was also developed for Ni-Co separation from its solution. Precious group metals separation can also be achieved by solvent extraction method. All precious group metals readily form chloride complexes with various concentrations of chloride ions. The chloro – species of the metal ions differ in their rates of substitution in their co-ordination sphere. The order of the substitution reaction are as follows: Au(I) ~ Ag(I) >>Pd(II) > Au(III) >Pt(II) >Ru(III) >> Rh(III) >Ir(III) >Os(III) >>Ir(IV) ~ Pt(IV). Au(I) can be effectively separated from a solution containing the above metal ions using CYANEX 471X as the extractant and can be stripped with sodium thiosulpahte as the strippant. The Pd(II) and Pt(II) can be co-extracted with di-*n*-octylsulfide or hydroxyoxime as extractants.

10.1.2. Solvent Extraction in Analytical Chemistry

Solvent extraction technique also finds applications in the quantitative estimation of metal ions from trace level to macro level. Thus, the role of solvent extraction method is very crucial to purify the analyte in the analysis of samples derived from diverse fields such as hydrometallurgy, radiochemistry, biochemistry, medicine, ecology, engineering, etc. Besides, it also plays a major role in sample pre- or post-treatment to improve the analysis.

10.1.3. Solvent Extraction in Biotechnological Separations

Solvent extraction process has been recognized as a potential method in the primary recovery of fermentation cell culture products, such as carboxylic acids, proteins, and amino acids. For example, citric acid formed in the fermentation broth is extracted using TBP as the extractant and stripped using water. It should be noted here that since proteins are not suitable for conventional solvent extraction process because of their incompatibility with organic solvents, it should first be converted into their corresponding cation prior to the extraction process. Similarly, amino acids which are sparingly soluble in an organic solvent are converted into their ionic form and then extracted by acidic extractants such as DEHPA or DNNSA.

10.1.4. Pharmaceutical Separations

Liquid-liquid extraction is extensively used in the pharmaceutical industry for the production of drugs and isolation of natural products. The best example for the use of solvent extraction process in

pharmaceutical industry is the purification of the antibiotic, penicillin. Penicillin from fermentation broth is first filtered to remove mycelium and the pH is adjusted to 2–2.5 in order to convert penicillin to penicillinic acid. The resulting acid is extracted into an organic phase using butyl acetate as the extractant. This is followed by the addition of 2% potassium phosphate solution to precipitate penicillin in the form of its corresponding salt. As butyl acetate has low boiling point, it was chosen as the extractant for the above process in which the extractant can be regenerated easily by simple vacuum distillation method.

10.1.5. Effluent Treatment

Waste stream generated from various industrial activities such as plating, pickling, etching etc can be treated by solvent extraction to reduce the environmental pollution. During the extraction, certain metal ions can be removed from the industrial effluents so that the waste solution can be discharged into the environment. For example, Zn(II) from the waste water can be extracted by DEHPA and stripped with sulphuric acid.

10.2. Solvent Extraction in Nuclear Industry

A variety of separation processes such as floatation, controlled precipitation, ion-exchange, solvent extraction etc., are being employed at the various stages of nuclear fuel cycle. However, the high degree of purity of materials needed for nuclear applications, together with the high cost of these materials, favoured solvent extraction as the separation method of choice as compared to other methods. Solvent extraction plays a key role in all the stages of nuclear fuel cycle, starting from the recovery of valuables from ores to the back end of the fuel cycle, i.e., reprocessing and waste management. Important applications of solvent extraction in nuclear industry include separation of rare earths, thorium and uranium from monazite ore, extraction of uranium from ore, purification of uranium, Zr/Hf separation, Nb/Ta separation, recovery of uranium and plutonium from irradiated nuclear fuel as well as the recovery of ^{233}U from irradiated thorium [21].

Several organic reagents have been tested and employed as extractants in various solvent extraction processes for the development of nuclear technology in 1940s [22]. In 1942, ether was used to produce large quantity of high purity uranium required for the Manhattan project. Ether extraction was the only process for the production of nuclear grade uranium till 1950. Ether has also been used as the extractant for the laboratory scale Zr/Hf separation from thiocyanate medium. However, limitations of ether based extractions such as the use of high quantity of salting agent and fire hazard have terminated its use in solvent extraction. Based on the known use of diethyl ether for the purification of uranium, processes based on ethers and ketones were investigated for nuclear fuel reprocessing. BUTEX process based on the selective extraction of U(VI) and Pu(IV) by dibutyl ether of diethylene glycol (Butex, C_4H_9-O-C_2H_4-O-C_2H_4-O-C_4H_9) as solvent from 3 M nitric acid solution was used in the Windscale plant, UK for the processing of spent nuclear reactor fuel, from 1952 to 1964. Fuel reprocessing has also been carried out, from 1952 to 1966 byhexone process (REDOX process) based on the selective extraction of U(VI) and Pu(VI) from 0.3 M nitric acid solution with 1.3 M Aluminium nitrate as the salting out agent and methyl isobutylketone (Hexone, CH_3-CO-CH_2-$CH(CH_3)_2$) as the solvent at Hanford, USA. Trigly, Cl-C_2H_4-O-C_2H_4-O-C_2H_4-Cl as solvent has also been used in a small plant at Chalk River in Canada during 1948 to 1954.

However, limitations of these reagents prompted researchers to identify better extractants

for nuclear fuel reprocessing. Important limitations of REDOX process are low flash point and high toxicity of solvent and generation of large waste volume due to the addition of aluminium nitrate. For BUTEX process, high viscosity and high density of the solvent, chemical reaction of the solvent with nitric acid are the major limitations. The Trigly plant recovered only plutonium leaving uranium with fission products. Moreover, chlorine released from trigly molecules by radiolysis caused problems related to corrosion. Following Warf's discovery on separation of Ce(IV) from trivalent rare earths, the above-mentioned processes have been replaced by a process based on the extraction by TBP diluted with a hydrocarbon or a mixture of hydrocarbons [23].

At present, TBP is the most important and widely used extractant for the separation of metals in nuclear technology [21, 24]. It is being used in refining of "Yellow Cake" to produce nuclear grade uranium. It is also being used for the separation of rare earths, thorium and uranium from monazite ore, Zr/Hf separation and Nb/Ta separation. However, TBP finds its most important applications for nuclear fuel reprocessing in PUREX (Plutonium Uranium Recovery by Extraction) process for the separation of plutonium and uranium from each other and from fission products and THOREX process, to separate thorium and uranium from each other and from fission products.

10.2.1. Uranium Ore Processing

The uranium ore is concentrated by removing sand particles followed by leaching. Nitric acid, sulphuric acid and sodium carbonate are generally used as leachants to separate uranium from its ore. The leaching agent, acidity, extractant and its concentration, extraction and stripping conditions are chosen based on the chemical nature of the uranium ore. Bis(2-ethylhexyl)phosphoric acid (HDEHP)-TOPO mixture, trialkyl amine and TBP are commonly used as extractants to recover uranium from leach solution. High-grade pitchblende ores are leached with nitric acid solution followed by the extraction of uranium with TBP. Subsequently, the refining of crude uranium is performed with TBP in nitric acid medium.

10.2.2. Monazite Ore Processing

Monazite ore is the principal ore for thorium and rare earth elements as well as secondary ore for uranium. The monazite ore, which exists in phosphate form, is subjected to sulfuric acid leaching or sodium hydroxide leaching methods depending on the chemical nature. Generally, sodium hydroxide leaching is preferred over sulfuric acid leaching method as the by-product sodium phosphate can be recovered and used as fertilizer. The hydroxide residue is then dissolved in acid solution and the metal ions are separated by solvent extraction. Amine extraction (Amex) process has been adopted for the recovery of uranium and thorium from rare earths solutions in sulphuric media. In this process, initially thorium is extracted from the monazite leach solution using a primary amine and later uranium can be extracted using a secondary amine. However, amines have low metal loading capacity, high crud formation tendency and there are also problems with respect to the entrainment of amine in the aqueous phase. Some of the process plants utilize di-2-ethyl hexyl phosphonic acid (PC88A) for the extraction of Th(IV) from monazite leach solution. TBP is utilized in several process plants for monazite ore processing. Thorium, uranium, cerium and cerium-free rare earth elements are recovered from monazite feed solution in 8 M HNO_3 by solvent extraction with TBP. Solutions of TBP in a diluent are being used for the separation of uranium and thorium from rare earths in the processing of monazite ore. Separation and purification of

individual lanthanides from monazite feed solutions can also be performed by solvent extraction.

10.2.3. Zr-Hf Separation

The demand for the high purity Zr, which is free from Hf has created a need for the application of solvent extraction for the separation of Zr and Hf. Zr in nature invariably contains 2-3 % of Hf and both are chemically similar (both having +4 oxidation state in aqueous solutions and almost identical ionic size). For reactor applications, concentration of Hf in Zr should not exceed 100 ppm as the former has thermal neutron capture cross-section about 600 times more than that of Zr. The most common process routes for solvent extraction are the methyl isobutyl ketone (MIBK) – thiocyanate (SCN) system developed at Oak Ridge National Laboratory (ORNL), USA and the TBP-HNO_3 process developed at U.S AEC Ames laboratory [25]. The hexone – thiocyanate process is based on the preferential extraction of Hf(IV) as a neutral thiocyanate complex by hexone.

TBP - HNO_3 method is followed in India for the production of reactor grade zirconium. The zircon is treated with molten sodium hydroxide to convert silica into water soluble sodium silicate and zirconium into insoluble zirconium hydroxide. Removal of silica from the ore is the crucial step as the unreacted silica forms gelatinous mass during the preparation of feed solution for solvent extraction. Subsequent to complete removal of silica the precipitate is dissolved in nitric acid and diluted to prepare the feed solution suitable for the solvent extraction of zirconium. Zirconium is extracted from the feed solution using 60% TBP in a diluent leaving behind hafnium and other impurities in the aqueous phase which is further treated for the recovery of hafnium. In general, a nitric acid concentration of 4-5 M is chosen as the feed solution acidity for Zr(IV)/Hf(IV) separation due to higher separation factor of Zr(IV) from Hf(IV) ($\beta_{Zr(IV)/Hf(IV)}$) in this range of nitric acid concentration. The zirconium loaded organic phase is scrubbed with nitric acid to achieve the desired decontamination factor from hafnium and stripped with dilute nitric acid. However, this process has also been modified with 33% TBP/*n*-DD and is being employed in zirconium sponge production plants in India.

10.2.4. Nb/Ta Separation

Tantalum (Ta) is selectively extracted by 50% TBP/kerosene from 0.5 M HF – 2 N H_2SO_4. After complete removal of Ta, the raffinate is adjusted to 5 N HF – 9 N H_2SO_4 and niobium (Nb) is extracted with 50% TBP **[21]**. Extracted Nb is then stripped with demineralized water.

10.2.5. Spent Nuclear Fuel Reprocessing - PUREX Process

Spent fuels have to be processed for the separation and purification of uranium and plutonium from each other and from fission products. The group, working at ORNL developed TBP based solvent extraction process for recovery of uranium and plutonium from the dissolver solution of spent fuel and is known as “PUREX” Process. The first plant using the PUREX process for the processing of nuclear fuels started operating in 1954, at Savannah River. Subsequently the Hanford plant also changed from hexone process to this process in 1956. After an explosion in Windscale plant, dibutylcarbitol was completely replaced by TBP.

PUREX process uses TBP diluted with n-dodecane or a mixture of hydrocarbons (HNP) as solvent [26]. TBP has several advantages over ethers and ketones, with respect to its stability towards nitric acid. Salting out agents such as aluminium nitrate used in previous extraction processes are no longer required in TBP extraction

process. TBP is highly selective for most of the tetravalent and hexavalent actinide ions. Diluting it with an inert diluent like kerosene compensates its unfavorable properties such as its high density (0.976 g/cm^3) and high viscosity (33.2 cp at 25^{o}C). A concentration of 30% (V/V) of TBP in a suitable diluent (1.1 M TBP) has been used in PUREX process.

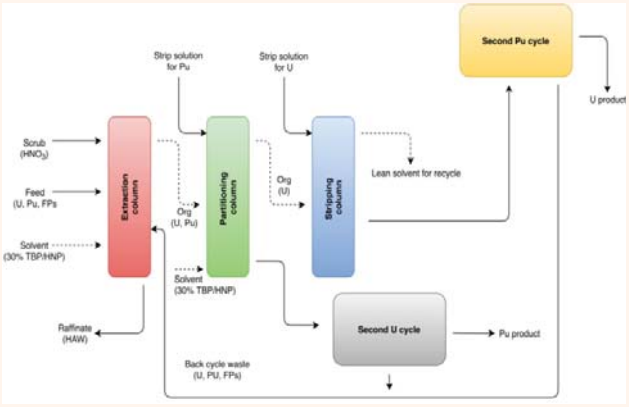

Figure 9: Flow scheme of PUREX Process

PUREX process involves the chemical or mechanical decladding of the fuel followed by dissolution in nitric acid. After adjusting the acidity of the dissolver solution to 3-4 M and maintaining the tetravalency of plutonium, the feed solution is subjected to solvent extraction. In the co-extraction step, the conditioned feed is fed to the center of the contactor, solvent stream is fed at the bottom of the contactor and 2-3 M HNO_3 enters the contactor from the top. The organic stream loaded with uranium and plutonium is scrubbed with 2-3 M HNO_3 to remove the FPs and leaves the extractor from the top. The aqueous waste containing the fission products (raffinate) leaves the contactor from the bottom. Subsequently the scrubbed loaded organic containing uranium and plutonium is subjected for their partitioning. This is achieved by back extracting plutonium from TBP phase by reducing it to inextractable trivalent state with an aqueous solution containing a suitable reducing agent. After partitioning both uranium and plutonium, streams are treated separately for their final purification as shown in Figure 9.

10.2.6. THOREX Process

The thorium uranium extraction (THOREX) process uses a solution of TBP in n-dodecane or HNP as the solvent to separate thorium and uranium from each other and from fission products [27, 28]. Even though the THOREX and PUREX processes have the same general features in solvent extraction cycles, there are some important differences in the process chemistry and flow conditions of the two processes. In PUREX process, separation of plutonium from uranium is achieved by reducing tetravalent plutonium to the relatively inextractable trivalent state. However, such a separation scheme is not possible in the case of U/Th system due to the high stability of the tetravalent oxidation state of thorium. In addition to this, higher organic-to-aqueous phase ratios (O/A) are required in the THOREX process because of the limited solubility of $Th(NO_3)_4$ – TBP complex in the organic medium.

This process was originally developed in the early 1950's to recover ^{233}U from irradiated thorium targets. The process which was first developed at ORNL and at the Knolls Atomic Power Laboratory, utilized a high concentration of $Al(NO_3)_3$ as the salting out agent in the feed solution. The high concentration of aluminium had the disadvantage of increasing the bulk of the high-level waste. The acid-THOREX process was developed at ORNL in the late 1950s to eliminate most of the $Al(NO_3)_3$ by replacing it with nitric acid. The acid THOREX process is the preferred method because of the advantages related to waste management. Process like Interim-23 has also been developed for the recovery of ^{233}U with TBP concentration as low as 1.5%. However, this process uses aluminium nitrate as the salting out agent.

10.2.7. Radioactive Waste management Applications

Solvent extraction also finds applications for the separation of radionuclides from high level waste (HLW). The high level waste solution generated from spent nuclear fuel reprocessing composed of fission products, activation products and minor actinides (Am, Np and Cm). Minor actinides (long-lived α-emitters) are the major contributors to the long-term radiotoxic hazards associated with the HLW. Presently, HLW is vitrified into glass matrices as immobilized forms and deposited in deep geological repositories. However, continuous long-term surveillance of these repositories for thousands of years is needed and hence it is an expensive option. Alternatively, removal of radionuclides especially minor actinides from HLW followed by their transmutation into short-lived isotopes (Partitioning & Transmutation) can be a better option with respect to waste management.

Solvent extraction technologies have been developed for the separation of the transuranic elements (TRUs), ^{137}Cs, and ^{90}Sr from actual acidic waste solution. Transuranic Extraction (TRUEX) process was established for the removal of TRUs from acidic radioactive wastes by using octyl(phenyl)-N,N-di-isobutyl carbamoyl methyl phosphine oxide (CMPO) as the extractant and tri-n-butyl phosphate (TBP) as a phase modifier in hydrocarbon diluent. Several other reagents have been synthesized and investigated for the extraction of trivalent lanthanides and actinides from waste solutions. After the removal of actinides from the waste solution, ^{90}Sr can be separated by Strontium Extraction process (SREX) with 4,4(5),di(t-butyl cyclohexano)-18-crown-6 as the extractant. In addition, the Universal Extraction (UNEX) process has been developed to remove Sr and Cs with chlorinated cobalt dicarbollide (ChCoDiC) and TRUs elements with CMPO based extractant [20].

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An overview of Ion Exchange: Classical to the Current Status

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1.1 Introduction

Ion exchange is defined as reversible interchange of ions between a solid and a liquid in contact with it. During this process solid does not undergo any permanent change in its structure. The solid is called as ion-exchange material or ion exchanger. The ions are held on the exchanger by means of electrostatic forces of attraction. Hence, ion exchange is an adsorption phenomenon where the mechanism of adsorption is electrostatic. Some of the elegant properties of ion exchanger are insoluble matrix, stochiometric exchange, selectivity, feasibility for column operation and regeneration. It is due to these properties, ion-exchange offers several advantages as a separation technique:

a) As the ion exchange material is an insoluble matrix, it can be easily separated from the liquid and reused.

b) The process of exchange is stoichiometric as shown eg. a divalent ion will replace two monvalent ions from the ion exchanger. It is the basis for the different separations

$$R{-}2Na^{+} + Ca^{2+} \rightleftharpoons R{-}Ca^{2+} + 2Na^{+}$$

c) The ion exchange material has different selectivities for different ions hence it can be used for selective separation of ionic species

a) The operation can be carried out in the form of column

e) Feasibility to regenerate using acids or bases and reuse

1.2 Historical Developments

The first ion exchange was reported in 1850, by H. S. Thompson and J. T. Way, soil scientists from England [1-2]. They showed that when various clays were treated with ammonium sulfate/ammonium carbonate solution, the ammonium ions were extracted and calcium and Mg were released in the solution. In 1905 a German scientist, R. Gans, developed a process for water softening using sodium aluminosilicate which he called zeolites. In 1935 work of two English chemists, B.A. Adams and E.l. Holmes led to synthesis of organic ion exchange resins [3]. During World War II new synthetic resins were developed to separate and concentrate the radioactive elements needed in Manhattan Project. This gave birth to modern version of ion exchange chromatography (IEC). In the early 1970, Hamish Small and co-workers William Bauman and Tim Stevens at Dow Chemical Company made the breakthrough in ion exchange chromatography, as they developed a novel method usable in automated analysis [4]. The ion chromatograph developed used weaker ionic resins for its stationary phase and an additional neutralizing stripper, or suppressor column to remove background eluent ions followed by detection using conductivity detector. The modern ion chromatograph is a high performance technique for separation and quantification of anions and cations at trace concentrations. New ion exchange resins were developed for specific purification of biological molecules and inorganic ions.

1.3 Applications of Ion Exchange Separations

1.3.1 Water Treatment

Ion exchangers find extensive application in water treatment. Ion exchangers are employed in softening the water, deionization, and in desalination plants.Softening of water is removal of calcium and magnesium ions from the hard water using ion exchange method. Deionisation (DI) requires removal of all cations and anions from water using cation and anion exchange columns operating in series. Treatment of water for drinking, its use for commercial, industrial, and residential purposes, wastewater treatment is all carried out by means of ion exchangers.

In nuclear reactors, ion exchange plays an important role in the treatment of coolant in primary and secondary circuits, water used in cooling towers and waste water generated for the removal of cations, anions and silica. Due to stringent requirement in reactors, the removal of cations and anions from coolant water is carried out using nuclear grade resins. The resin should be in highly purified form and withstand high radiation and temperature. The quality of the ions encountered varies from one circuit to another, from one nuclear power station to another, from one moment to the next, since it is dependent on the activity of the primary circuit. The ions most frequently found are the isotopes of Cs, I, Co, Sr, Mo, Cu, Te, Sb, Mn, Cr and Na. In practice, however the water requiring treatment often contains relatively large amount of conditioning ions such as ethanolamine, Li^+ or Na^+ for which the resin have a strong affinity and a very small quantity of active ions requiring a maximum efficiency of removal for which the resin have no obvious affinity. In such cases, the plant is planned with two columns in series. The first a cation exchanger has the function of removing the maximum quantity of cations while the second a mixed bed is designed to remove the active cations.

1.3.2 Ion Exchange Chromatography

Ion exchange chromatographyis one of the widely used chromatography system which employs the principle of ion exchange for separation of ionic species. The separation of different species is carried out using ion exchange column containing ion-exchange resins. Anions are separated using anion-exchange resin while cations are separated using cation exchange resin. The ions are held on the resin by electrostatic force of attraction. The separation of anions / cations is based on the difference in their affinities towards the ion exchange resin. The affinity of the ion is governed by two factors (i) charge on the ion and (ii) size of the ion (hydrated).

The separation of anions (F^-, Cl^-, NO_3^-, PO_4^{-3}, SO_4^{-2}), separation of cations (Li^+, Na^+, K^+, Ca^{+2}, Mg^{+2}), separation of transition metal ions and rare earths in aqueous solutions is all accomplished by ion exchange chromatography [5-6].Isotope separation is another important application of ion exchange chromatography. In nuclear industry ion exchange reaction is applied for the separation of isotopes of boron and isotopes of lithium [7].

1.3.3 Pre-concentration

Trace analysis (concentrations in few ppb range) of environmental samples (air, water, waste water), biological extracts, employ a preconcentration step. Preconcentration can be referred to as the enrichment process which involves separating the minor component (analyte) from complex matrix or extraction of particular analyte selectively from one phase to the other. Ion exchange is extensively used as preconcentration step in chemical analysis. Preconcentration offers several advantages such as improved analytical detection limits, increased sensitivity by several orders of magnitude which in turn facilitate enhanced accuracy of results of the

method used. eg. determination of U in natural waters, sea water etc., determination of transition metals in environmental samples.

Chromium occurs in aqueous systems in the trivalent and hexavalent forms. Out of the two forms, hexavalent chromium is more hazardous to living organisms than the chromium (III). Rapid oxidation of chromium (III) to chromium (VI) state in aquatic and solid wastes situations accounts for mobility of chromium. Hence determination in natural water is very important. This is accomplished by pre-concentration of Cr on anion exchange column followed by its determination using HPLC/AAS/plasma emission spectroscopy techniques.

1.3.4 Removal of Interferents

Ion exchange separation is employed extensively for the removal of interfering ions in the quantitative analysis eg. in the determination of NO_3^-, SO_4^{-2} in seawater there is severe interference from the matrix Cl^-, this difficulty is overcome by removal of Cl^- selectively using cation exchange resin in Ag^+ form by the following reaction

$$R\text{-}Ag^+ + NaCl \rightleftharpoons R\text{-}Na^+ + AgCl_{\downarrow}$$

1.3.5 Purification

For carrying out trace and ultratrace analysis high purity reagents are needed. The removal of different cationic, anionic impurities from reagents is achieved by means of ion-exchange e.g. HCl is treated with strong base anion exchanger to remove trace concentration of transition metal chlorides.

The fractionation of proteins is another important application of ion-exchange separation. It exploits the differences in the charge of different proteins. The charge of a protein depends upon the number and type of ionizable amino acid side chain groups eg. lysine residues, have a positively charged side chain group when ionized, whereas glutamic acid residues are negatively charged when ionized.

The commonly used ion exchangers for protein separation are carboxymethyl- cellulose (CM-cellulose) and diethylaminoethyl-cellulose (DEAE-cellulose). The functional groups for the two ion-exchange stationary phases are shown below:

Name	Functional Groups	Type
Diethyl aminoethyl (DEAE)	$(CH_2)_2$-$NH(CH_2CH_3)_2$	Anion exchanger
Carboxymethyl (CM)	CH_2-COO^-H^+	Cation exchanger

1.3.6 Drug Formulations

Ion exchange resins are being used in pharmaceutical and clinical industries for solving various formulations related problems.Ion-exchange resinates (Drug-Resin complex) of drugs is suitable for drug delivery, including controlled release, topical, transdermal, nasal and as well as taste masking. The stability of vitamin B12 can be prolonged by completing it with a weak acid cation exchange resin (INDION 264). Another example is nicotine; it discolours quickly on exposure to air and light, but the resinates used in nicotine chewing gums and lozenges, is much more stable. Ion exchange resins are also used as carrier for immobilized enzymes to provide extended activity at localized sites [8].

1.4 Classification of Ion Exchangers

Ion exchange materials are categorized into two broad types:

1. Inorganic: These are typically naturally occurring zeolite and other alumino-silicate minerals

with a well-defined crystal lattice structure. They find extensive application in water purifiers and softners.

2. Organic: These are carbon-based polymeric materials, often known as "resins".

1.4.1 Inorganic Ion Exchangers

They can be further categorized into two types:

A. Cation exchangers: Zeolites, clay minerals, zirconium phosphates, belong to this class of inorganic exchangers.
B. Anion exchangers: Hydrotalcite, hydrous oxides of metals like Cr, Fe, Ni act as anion exchangers

The inorganic ion exchangers offer several advantages over organic ion exchangers. They are generally stable to relatively high temperatures and ionizing radiation [9]. Hence they are used in radioisotope separations and nuclear waste problems. Also they exhibit very high selectivities for specific ions like Cs^{137}. The selectivity is so high that the reaction is irreversible. It is due to these properties, inorganic exchangers find several applications in nuclear technology. Clay materials are often employed as backfill or buffer materials for radioactive waste disposal sites because of their ion exchange properties, low permeability, and easy workability. They are used for Cs fixation in radioactive waste management. Good results have been reported for the removal of caesium by clays [10]. In case of three mile nuclear reactor accident, zeolites were used to remove large quantity of Cs^{137} and other contaminants from sea water.

1.4.2 Inorganic Cation exchangers

Zeolites and clay minerals are naturally occurring cation exchangers. Zeolites are crystalline hydrate aluminosilicates of group I and group II metal ions (i.e. alkali and alkaline earth metal ions). They are formed by cross-linking tetrahedral network of SiO_4 and AlO_4. Due to this they are porous in nature and have cavities and channels. The backbone of this structure is negatively charged because some of the tetravalent Si atoms are replaced by trivalent Al atoms. In order to neutralize the negative charge alkali and alkaline earth metal ions are trapped in the matrix. These ions have sufficient mobility in the structure; hence the material behaves as cation exchanger. Clay mineral has the same basic constituents as that of zeolite, the difference being that clay mineral has a layered structure.

There are several synthetic inorganic cation exchangers. An example of commonly used synthetic cation exchanger is ammonium phosphomolybdate (AMP) $(NH_4)_3PO_412MoO_3$. It finds extensive application in nuclear industry for the removal of ^{137}Cs isotope. Antimony silicates (SbSi), tin substituted antimony oxides and antimony substituted tin oxides are other examples of cation exchangers. Antimony silicate is specific for Rb^+ ion while antimony substituted tin oxide is specific for ^{63}Ni (again a long lived isotope- half life of 100 yrs).

There are several cation exchangers, having the general formula $M(IV)(HXO_4)_2 \times nH_2O$, where M(IV) = Zr, Ti, Sn, Ce, Th, etc. and X = P, W, As, Mo, Sb etc. These materials possess structural hydroxyl groups, the H of the –OH being the exchangeable sites. They possess an appreciable ion exchange capacity as well as high selectivity for certain metal ions.

1.4.3 Inorganic Anion Exchangers

Clays like hydrotalcite are naturally occurring clays which exhibit anion exchange properties. Hydrotalcite is magnesium–aluminum hydroxycarbonate, having chemical composition $Mg_6Al_2(OH)_{16}CO_3.4H_2O$. It has a layered double hydroxides structure. The layer structure arises from the catenation of $M(OH)_6$ octahedra where M is the doubly charged magnesium ion, when such cations

are partially replaced by triply charged Al cations, the layer acquires a positive charge, for each such substitution carbonate anions and water molecules are inserted into the interlayer region to preserve electroneutrality. Hence, such clays behave as anion exchangers.

There are synthetic inorganic anion exchangers as well. The hydrous oxides of different metals belong to this class of this ion exchangerseg. $SnO_2.H_2O$, $ZrO_2.H_2O$ etc. The surface is largely covered with hydroxyl groups and both coordinated and hydrogen bonded water molecules. Ion uptake is a function of pH i.e. the higher the pH, the greater is the uptake of cations and conversely anion uptake increases with increase in acidity of the solution. Thus, these hydrates are both cation and anion exchangers. The inorganic ion exchangers both natural and synthetic have certain limitations. Their properties vary with mode and condition of preparation so reproducibility of ion exchange process is poor. Other disadvantages are:

i. They cannot be regenerated as they undergo reaction with strong acid and strong base
ii. Exchange process is slow
iii. Poor mechanical stability

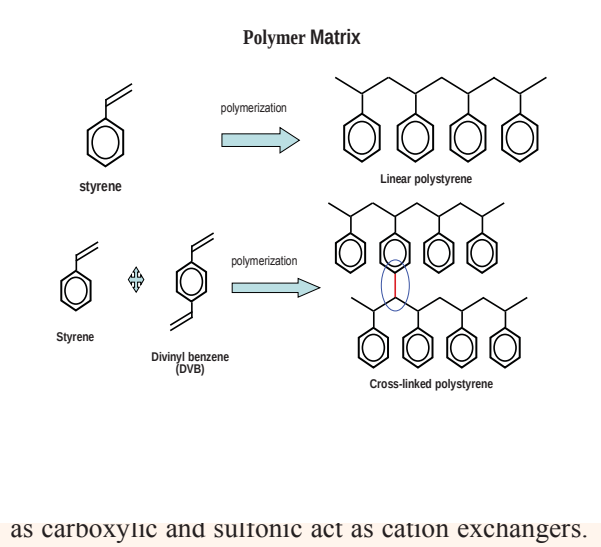
In order to overcome these disadvantages organic ion exchangers were synthesized. They are found to fulfill all the requirements of ion exchange material.

1.4.4 Organic Ion Exchangers

Organic ion exchangers also referred to as ion exchange resins have organic polymer backbone with functional groups like $–SO_3H^+$, $-NR_3^+OH^-$ attached to the network. In most cases, the copolymer of styrene with divnylbenzene (DVB) forms the backbone of the resin. It is because of the following properties of the copolymer

1) It has 3-D network with high porosity to enable the water molecules to go inside the core of resin bead for the ion exchange to take place.
2) It is highly insoluble in water and other solvents. This is achieved by the cross-linking agent - divnylbenzene.
3) It also has high mechanical stability again due to divnylbenzene.
4) Its density is higher than water even after swelling.
5) Styrene is inexpensive and available easily.
6) It is not easily subjected to degradation by oxidation or hydrolysis at elevated temperature.

The aromatic rings in the polymer can be reacted with reagents to produce ion-exchange resins. eg. the copolymer is treated with H_2SO_4 to introduce SO_3H groups which makes it a strong cation exchanger resin. The copolymer is subjected to chloromethylation followed by ammination reaction to yield ammine groups, which in turn imparts it anion exchange property. In this way a host of different resins are synthesized. The overall scheme of synthesis of different resins is summarized in the figures below:



as carboxylic and sulfonic act as cation exchangers. Cation resins are further classified into strong and

weak resins on the basis of functional group. Cation resins with sulfonic group are classified as strong acid cation exchange (SAC) and resin with carboxylic group are classified as weak cation exchanger. Strong cation exchangers can be used in the entire pH range 0-14 while weak cation exchangers can function as cation exchanger only in the alkaline pH >8.

1.4.6 Organic Anion Resins

Resins that contain basic groups, such as primary, secondary, tertiary ammine and quaternary ammonium group act as anion exchangers. Anion resins with quaternary ammonium group as the functional group are classified as strong base anion exchanger (SBA) and it can be used in the entire pH range of 0-14. Strong base anion exchanger is further classified as Type I and Type II based on the alkyl group R. If all the R groups are methyl then it is called SBA (Type I). If one of the methyl group is replaced by ethanol group then this SBA exchanger is called as (TypeII). The anion resins having primary, secondary and tertiary amine groups are classified as weak base anion exchangers (WBA) because they behave as anion exchangers only in the acidic pH range < 6. The classification of different resins is summarized in the figures.

1.5 Properties of Ion Exchange Resins

The efficacy of ion exchanger resins mainly depends upon their properties such as the degree of cross linking, mesh size, stability, purity, capacity, acid-base strength and porosity. Important properties of ion exchange resins are discussed here.

1.5.1 Degree of Cross-linking

Percentage of DVB plays an important role in the nature and properties of ion-exchangers. As it cross links the polymer chains it affects the physical properties like

i. Porosity - Resins with high % of cross linkage agent have lower porosity.
ii. Solubility - Resins with high % of cross linkage agent have low solubility.
iii. Hardness - Resins with high % of cross linkage agent have more hardness.
iv. Swelling – Resins with low % of cross linkage agent swell remarkably upon hydration.
v. Mechanical strength- Resins with high % of cross linkage agent have higher mechanical strength.

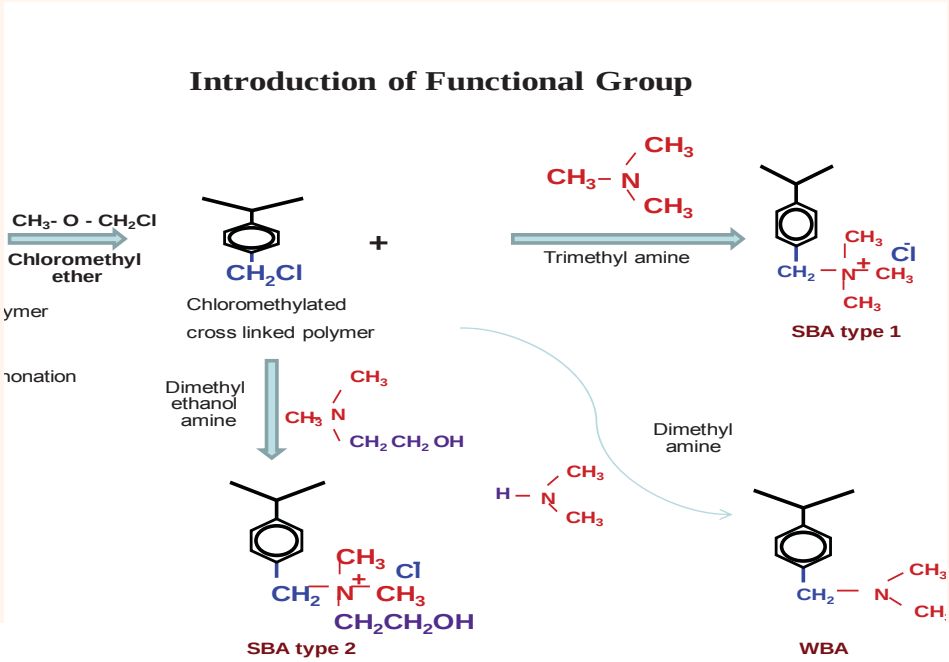
Percentage DVB varies from 4%, 8%, 12% and 16% and this is indicated in the name of the resin. e.g. Commercially available Dowex resins use following criteria to identify different resins: eg. Dowex 1 X 8 and Dowex 50 X 8:

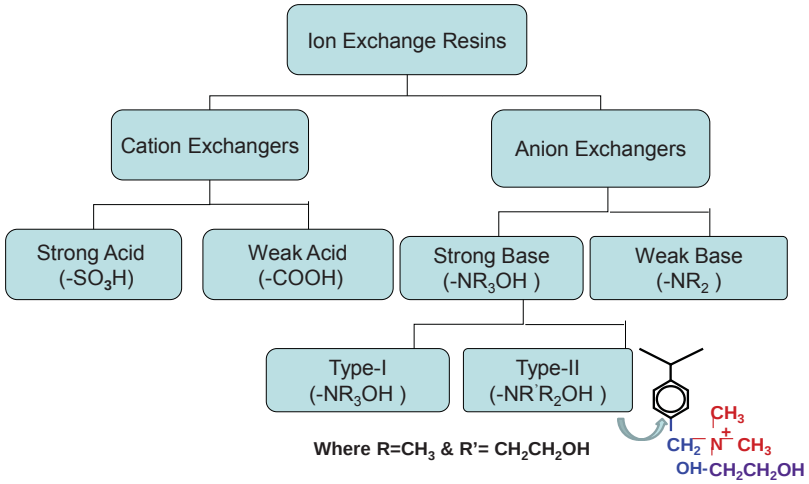
- Dowex - Manufacturer's name
- 1 - strong anion; 50 - strong cation
- X 8 - 8 % crosslinking agent DVB

For analytical applications 8% DVB resins is preferred because of their optimum properties of hardness and swelling.

1.5.2 Mesh Size

The mesh size of resins is expressed as 100-200 mesh, 200-400 mesh and so on. The standard size of resins for analytical applications is 100-200 mesh. This is because as the mesh size increases, size of the particle becomes smaller. Particle size is inversely related to mesh size ie. 200-400 mesh resin has smaller size than 100-200. Higher the mesh size, smaller the bead and lower is the flow rate. 200-400 mesh resin has greater surface area





leading to better separation efficiency and hence is used for the separation of actinides.

1.5.3 pH Range

Different resins have different working pH range as shown in the Table.

	Working range
Strong cation exchanger	0-14
Weak cation exchanger	> 7
Strong anion exchanger	0-14
Weak anion exchanger	< 7

In other words in case of strong anion and cation exchanger the exchange capacity is independent of pH while in case of weak ion exchanger it is dependent on pH.

1.5.4 Capacity

Ion exchange capacity is a major characteristic of ion exchange materials. Exchangeable ions carried by ion exchangers are also referred to as counterions. Ion exchanging capacity is the number of groups capable of entering into ion exchange reactions. This measurement, expressed as milliequivalents of exchangeable ion per dry gram of polymer (meq g^{-1}) is called capacity. From a practical point of view, an ion exchanger can be considered as a "reservoir" containing exchangeable counter ions. The counter ion content in a given amount of material is defined essentially by the number of fixed charges which must be compensated by the counter ions and thus is essentially constant. This is a consequence of the electroneutrality requirement. Various methods for its determination have been dealt with by Helfferich [11]. The number of groups capable of exchanging cations is conveniently determined by converting the resin groups to the hydrogen form with an excess of acid, rinsing to remove this excess acid, and equilibrating the resin with a known excess of standard sodium hydroxide. The exchange capacity is determined readily by titration after the exchange reaction is complete.

The capacity is important property because we need to know the amount of resin that is needed for carrying out a separation. The relevance of capacity is illustrated in the example given below:

10ml of 0.1N $NaClO_4$ needs to be treated using cation exchanger having capacity of 4 meq/g. What amount of resin needs to be taken

0.1 N $NaClO_4$ =0.1 eq/lit

=0.1 meq/ml

10 ml 0.1N $NaClO_4$ = 1 meq Na^+

Amount of resin = $\frac{1x\ 20\ meq}{4}$ = 5g since, resin should have a capacity of 10-20 times higher than the total concentration of the ion to be treated. Thus, 5g of resin must be taken in this case.

Break through capacity: when the ion comes out of the column without being exchanged, it is called the break through capacity of the column.

1.5.5 Selectivity Coefficient

Another important parameter is the selectivity coefficient for the exchange of two ions A and B.

Selectivity coefficient (K) : It indicates the affinity of an ion for a charged site on the resin eg. if the resin contains ion A and ion B is present in the solution,

$$R - A^+ + B^+_{sol} \rightleftharpoons R - B^+ + A^+_{sol}$$

Applying mass law action relationship, it is defined as

$$K_A^B = \frac{[A]}{[B]} \cdot \frac{[\bar{B}]}{[\bar{A}]}$$

K_A^B is the equilibrium constant, specific for the pair of ions and type of resin, where the bar indicates the resin phase.

When $K_A^B > 1$, resin has more preference for B

$K_A^B < 1$, resin has more preference for A

This gives an idea about which ions can be separated. Factors that affect the selectivity coefficient are the charge and the hydrated radius of the ion.

Charge on the ion: higher the charge, higher is the selectivity for the resin e.g. the selectivity of different anions and cations follows the order shown below

$Cl^- < SO_4^{-2} < PO_4^{-3}$

$Na^+ < Ca^{+2} < La^{+3}$

Thus, selectivity increases in the order : monovalent ion < divalent ion < trivalent ion < multi-charged ion

Hydrated radius of the ion: For the ions having same charge, selectivity for the resin decreases as the hydrated radius increases. This is because the effective charge felt by the resin decreases as the hydrated radius of the ion increases. Smaller the ionic size higher is the hydrated radius. Hence the selectivity of different anions and cations follows the order shown below:

$F^- < Cl^- < Br^- < I^-$

$Li^+ < Na^+ < K^+ < Rb^+ < Cs^+$

$La^{+3} < Gd^{+3} < Lu^{+3}$

Selectivity decreases as hydrated radius increases, due to lanthanide contraction Lu has got smallest size.

Based on these two factors the order of affinity for sulphonic acid resin of some common cations is:

$Hg^{2+} < Li^+ < H^+ < Na^+ < K^+ \approx NH_4^+ < Cd^{2+} < Cs^+ < Ag^+ < Mn^{2+} < Mg^{2+} < Zn^{2+} < Cu^{2+} < Ni^{2+} < Co^{2+} < Ca^{2+} < Sr^{2+} < Pb^{2+} < Al^{3+} < Fe^{3+}$

A corresponding list for amine based anion exchanger is:

$OH^- \approx F^- < HCO_3^- < Cl^- < Br^- < NO_3^- < HSO_4^- < PO_4^{3-} < CrO_4^{2-} < SO_4^{2-}$

1.5.6 Distribution Ratio

Similar to solvent extraction, there is a closely related parameter defined in ion exchange separation called as distribution ratio or partition coefficient (D). It is defined as

$$D = \frac{\text{amount of metal ion per g of dry resin}}{\text{amount of metal ion per cm3 of solution}}$$

For a very dilute solution of an ion A, the distribution coefficient for any ion exchange can be given by the expression

$D = [A]_r / [A]_{aq}$

where, $[A]_r$ is the concentration of ion A in the resin phase and $[A]_{aq}$ is the concentration of ion A in the aqueous phase. The distribution coefficient can be evaluated by determining the metal ion concentration in an equilibrated solution by simple analytical methods. Both static and dynamic methods with or without the presence of radioisotopes have been used for the determination of distribution coefficients of ion-exchange resins.Similarly, there is a parameter called separation factor β. It is defined as

$$\beta = D_1 / D_2$$

where, D_1 and D_2 are the distribution ratio of the two ions to be separated.

1.6 Different Types of Ion-Exchanger Resin Beads

1.6.1 Microporous Resin

The porosity of this type of resin beads is extremely small and when the resin is dry there is no porosity. But when the resin is brought in contact with a liquid, it swells and then it shows porosity. The structure becomes like a gel when it swells up. So, it is also called gel or gellular type of resin. This was the first type of ion-exchanger that was synthesized, it had a disadvantage. This type of resin would get poisoned easily. As we know water contains different metal ions and also large organic molecules like humic acid etc. These organic molecules are trapped in the small pores. So this type of resin would get poisoned very easily and frequently it had to be replaced. To overcome this limitation the method of preparation was improved and macroporous ion-exchanger resin was developed.

1.6.2 MacroporousResin

They have measurable porosity even in dry condition. Organic molecules are not trapped so it would not get poisoned soon. But here the difficulty is that it takes a very long time to elute out the ions because the ions exchange throughout the bead. This gives rise to broad peaks. Hence, there was a need to modify the resin in such a way that the elution time is reduced. This led to the development of pellicular type of resin.

1.6.3 Pellicular Resin

The name pellicular is derived from pellicle meaning a thin skin or film, such as on a photographic emulsion – here in case of ion exchange resins, the ion exchange groups are present only on the surface over an inert core of the resin bead. So the resin has very few exchangeable groups hence the capacity is very low. As the ion-exchange process is restricted to the surface, it is extremely fast and time required is very less. The chromatography peak obtained is much sharper as compared to macroporous resins. This type of resin bead was synthesized by controlling the time of reaction during the sulphonation or ammination process. But, there was a difficulty and it was to get reproducible layer of negatively or positively charged group on the resin bead. This difficulty was further overcome by the synthesis of latex coated resin beads.

1.6.4 Latex Coated Resin Beads

These are the latest type of resin beads. Synthesis of this type of resin involved surface agglomeration technique eg. Preparation anion exchange resin was carried out in the following way.Styrene – DVB beads were sulphonated so that the surface of the bead has a fixed negative charge RSO_3^-. These beads are held in a column and the latex of $R_4\text{-}N^+OH^-$ is passed through the column. This group binds to the RSO_3H^+gp so we get $[RSO_3\text{-}R_4N^+]\ OH^-$. This is how surface agglomerated resin beads are synthesised.

So the capacity of Macroporous>Pellicular> Latex coated resins. As the capacity of latex coated resin beads is very low (*u*eq/g), it can be used for dilute solutions. It plays an important role in trace and ultra trace analysis.

1.7 Chelating Ion Exchangers

Separation of lanthanides using cation exchanger is not effective as the selectivity coefficients are very close. The need for such complex separations led to the development of chelating ion-exchange resins. In the case of chelating ion-exchange resin, chelating group is incorporated in the polymeric matrix. The chelation is governed by ionic radius, smaller the ionic radius greater is the chelation. So Lu^{+3} forms a stronger chelate than La^{+3} hence it will be held by the ion exchange for longer time. Thus, by introducing a chelating agent we are able to change the K. Due to high selectivity of chelating resin they are highly useful for preconcentration of trace elements. An important class of chelating ion exchanger contains iminodiacetic acid in the styrene – DVB matrix. This iminodiacetic acid group is selective for transition metal ions. It is used for the preconcentration of transition metal ions on the resin from different environmental samples (eg. sea water, ground water etc.). The alkali metal ions are not held on the resin. The commercial name of this chelating ion exchanger resin is Chelex – 100. Binding energy of chelex – 100 for transition metal ions is 60-103 KJ in comparison to the conventional ion exchanger 8-13 KJ.

Some examples of chelating ion exchange resins for different metals are given in the Table.

Chelating Group	Selective for Cation

Aminophosphonic Acid	U
SH or Dithicarbanates	Hg
Crown Ethers	Alkali / Alkaline Earth Metals

1.8 Comparison of Ion-Exchange And Solvent Extraction

Ion exchange offers several advantages over solvent extraction as separation technique. They are

i. It is a cost effective method of separation, because one could regenerate the resin and use it again and again. Hence, the process becomes highly economical.
ii. Ion-exchange can be applied for the separation even if D value is low as it can be turned into a multistage operation by employing a column for the separation. The efficiency of ion exchange separation could be easily improved by increasing column height or in other words increasing the number of theoretical plates (HETP).

At the same time ion-exchange process of separation has few drawbacks like it is very slow and time consuming. This drawback was overcome by means of liquid ion-exchangers.

1.9 Liquid Ion-Exchangers

Liquid ion-exchangers combine the process of solvent extraction and ion exchange. They are very selective, cost effective, fast and bring about efficient separation. It is due to these reasons that most of industrial processes for recovery of metals from minerals prefer the use of liquid cation exchanger like LIX 64 N or liquid anion exchangers like Alanine 336 or Amberlite LA-1.Review articles by Khopkar et al. have brought out examples of the extraction of metal ions with high molecular weight amines [12].

1.9.1 Cation Liquid Ion-Exchanger

All high molecular weight dialkyl or monoalkyl acidic phosphoric acids or alkyl sulphonic acids are examples of liquid cation exchangers. This is because the extraction proceeds in same manner as that in solid cation exchange reaction in column. If 'o'–refers to organic phase, R = ligand and M is metal:

$$[H_2R]_o + M^{2+} \quad \leftrightarrow \quad (M_2\,R)_o + 2H^+$$

In this example we note that the proton was replaced by metal ion in cation exchange reaction in the organic phase. In view of the fact that the exchange proceeds with reference to cation and since extractants were mostly used in liquid form, these processes are designated as "liquid cation exchange reaction". The metal ion is stabilized by solvation and chelation process.

1.9.2 Anion Ion-Exchanger

All high molecular weight aliphatic amines (HMWA) were termed as liquid anion exchangers. These amines might be primary, secondary, tertiary or quaternary and depending upon the kind of extraction one, two, three or four hydrogen atoms are replaced by anionic species to form the complex e.g. if R_3NH^+ was tertiary amine and underwent reaction with anion in the following manner to form an uncharged complex.

$$(R_3\,N)_o + \ HCl \leftrightarrow (R_3\,NH^+Cl^-)_o$$

Now this salt of amine when contacted with anionic chloro complex e.g. $FeCl_4^-$

$$(R_3\,NH^+Cl^-)_o + H^+FeCl_4^- \leftrightarrow (R_3\,NH^+FeCl_4^-)_o + HCl$$

Thus organic layer now acts as anion exchanger. The Cl^- will exchange for $FeCl_4^-$. So we have an ion pair with cation as (R_3NH^+) with anion as $FeCl_4^-$ forming a paired complex. Such extraction

is common in purex process for recovery of uranium e.g. the sulphate complex$UO_2(SO_4)_3^{-4}$ extraction with HMWA. Since we use amine in liquid form and since the reaction proceeds with the exchange of anion, it was called 'liquid anion exchangers'. There are many amines such as Tri-n-octylamine (TOA), Tri-iso-octylamine (TIOA), Trilaurylamine(TLA), Methyloctylamine (MDOA) that behave as liquid anion exchangers. Further we have synthetic amines like Amberlite LA-2 (tertiary) or Aliquat 336 (quaternary) amine which are also examples of liquid anion exchangers.

1.9.3 Merits and Demerits of Liquid Ion Exchangers

Unlike resin beads liquid ion-exchanger have high radiation stability hence they are used in nuclear fuel reprocessing for separation of U, separation of Zr from Hf, separation of fission products (FPs). Most of the liquid ion exchangers are commercially available in pure form, so further purification is not necessary. The extraction equilibrium is attained in a few seconds. The stripping of the metals is possible with dilute mineral acids or water. The only disadvantage was the formation of third phase during extraction. To mitigate this problem one had to use modifiers. Such modifiers consisted of decanol, or similar polyhydroxy alcohol. Third phase formation was specially a serious problem in industrial separations, which delayed separation and reduced efficiency. The phases were easily separated in the presence of the modifiers. It was possible to regenerate this liquid ion-exchanger by treating with a fresh acid.

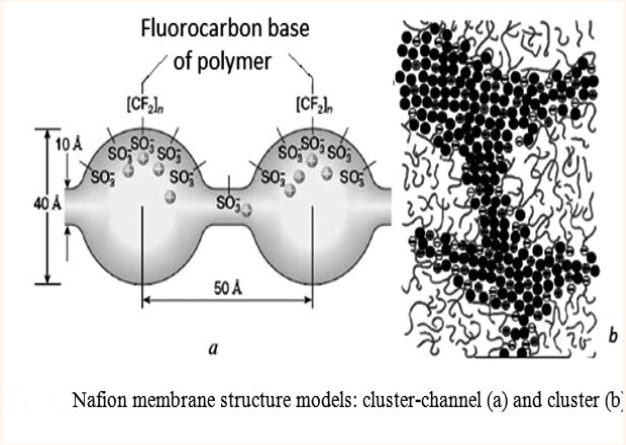
2. Ion-Exchange Membrane (IEM)

IEMs are an important class of dense polymeric membranes that bear fixed charges in the polymer matrix. Due to the existence of fixed carriers (ion-exchange groups) these membranes can selectively allow the passage of oppositely charged ions (counter-ions), while obstructing similarly charged ions (co-ions). IEM permselectivity for counter-ions was first elucidated by Donnan [13]; thus, the mechanism is referred to as the Donnan effect or Donnan exclusion (towards co-ions). Due to this ion permselectivity, several industrial processes based on IEMs, including electrodialysis (ED), diffusion dialysis (DD), and electrolysis, has been established.

Ion exchange membranes are being studied and developed for applications in new energy conversion and storage systems as well as efficient desalination and wastewater treatment processes. Thus ion-exchange membrane has characteristics:

i. Ion conductivity: ions can permeate through the membrane
ii. Hydrophilicity: along with the ions water molecules can permeate through the membrane

One of the most studied and industrially used cation-exchange membrane is Nafion [14]. Nafion is a perfluorocarbon membrane with sulphonic acid groups. Its structure has been studied using TEM (transmission electron microscopy), wide and small angle x-ray diffraction, differential scanning calorimetry, IR and NMR spectroscopy. The studies revealed that Nafion membranes are quite heterogeneous on a microscale with distinct crystalline areas formed by the fluorocarbon polymer and separated by amorphous, highly hydrophilic domains formed by the side chains with the ionic group. The amorphous region containing a cluster of fixed charges counterions and is extremely hydrophilic and swells in water or aqueous solution while the crystalline region acts as cross-linkage and restricts the swelling of the membrane. The clusters are special regions with a dia 40-60A^0 connected by bottlenecks between crystalline region. The transport of the counterions from one cluster to the next is of 50 A^0.



Nafion membrane structure models: cluster-channel (a) and cluster (b)

2.1 Ion exchange membrane applications

It finds several applications; few of these are listed below:

i. Chlor – alkali process: i.e. electrolysis of NaCl solution to produce chlorine gas, hydrogen gas and caustic soda use IEM.

ii. Battery and fuel cells as solid polymer electrolytes and proton conductive membrane

iii. In gas sensors and modified electrodes as permselective membranes

iv. Desalination of saline water

v. Biosensors for the removal of anionic interferents

3. Conclusion

Ion exchange is a most versatile separation technique on account of its properties such as stochiometric exchange, selectivity, feasibility for column operation, regeneration and wide variety of ion exchange materials. Ion exchange materials are natural and synthetic, organic and inorganic, cationic and anionic exchangers. They can be in the form of solid, liquid or membrane. They find wide applications in industries ranging from power, nuclear, food, drugs, etc. for the treatment of water, purification, separation and several other processes.

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Column Liquid Chromatography

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1. Introduction

Chromatography is a physical method of separation in which the components to be separated are distributed between two phases, one of which is stationary (stationary phase) while the other (mobile phase) moves in a definite direction. Chromatography is broadly classified as gas chromatography, liquid chromatography and super-critical fluid chromatography based on the physical state of the mobile phase used. Liquid chromatography (LC) is one of the most commonly used analytical separation techniques in research and industry due to the easy amiability of samples with a wide choice of mobile phases. This technique is extensively used for the qualitative as well as quantitative determination of various components present in a mixture. LC has become an indispensible tool for the separation of a wide range of inorganic, organic, bio-molecular and ionic species pertinent to pharmaceutical industry, environmental science, life sciences, food analysis, organic chemistry, geochemistry, nuclear technology etc. The technique also finds use in the isolation of sample components at higher concentration scales, known as preparative as well as semi-preparative chromatography. Column liquid chromatography involves the separation of components based on their difference in physicochemical interactions between a stationary phase packed in a column and a liquid mobile phase. The interactions which form the basis of separation can be charge, hydrophobicity, specific steric interactions, and size of the analyte species.

1.1. Historical Background

Russian botanist Mikhail Tswett is credited for the invention of chromatography and he discovered this technique in early 20th century while working on the separation of plant extracts using a glass column filled with a stationary phase made of calcium carbonate. Since the separated fractions of plant pigments were seen as bands of different colours, he named the technique as 'chromatography" which is a combination of Greek words 'chroma' and 'graphein' and the name literally translates to "color writing". Incidentally, in Russian language the meaning of ‘Tswett’ is colour which further accentuates the selection of name for this separation technique. The technique gradually grew in the diversity of approach as well as technologically. In 1931 E. Lederer and R. Kuhn achieved the separation of carotenoids by normal phase chromatography using small glass tubes packed with pellicular adsorbent beads and gravity-fed mobile phase. The concept of thin layer chromatography (TLC) and ion exchange were introduced in 1938. In the late 1930s, A. J. P. Martin and R. L. M. Synge introduced a form of chromatography using silica gel as the stationary phase for the separation of aminoacids. The duo is also credited to bring out a major breakthrough in

chromatography concepts (height equivalent theoretical plate, namely, HETP) when they proposed the use of small particles and high pressures in LC to improve the separation efficiency which later led to the development of high performance liquid chromatography (HPLC). They also suggested the replacement of the liquid mobile phase with a suitable gas for improving the mass transfer between the two phases resulting efficient separations and this concept culminated in the development of gas chromatography. The early 1950s saw the development of reversed-phase liquid chromatography which later went on to become the most preferred separation methodology for organic molecules, especially in the pharmaceutical industry. This era also witnessed the introduction of a very simple and easily adoptable form of liquid chromatography known as paper chromatography. Two important forms of liquid chromatography, viz. affinity chromatography and size exclusion chromatography took birth in 1953 and 1955, respectively. While size exclusion chromatography helped to separate the components based on their molecular size, affinity chromatography is used for separating complex samples such as biomolecules based on their specific reversible reaction with the stationary phase. The first commercial liquid chromatographic system with UV detection was launched in 1967 by Waters Corporation and eight years later Dionex Corporation presented the first commercially available ion chromatograph. The commercial liquid chromatographic system was named as 'high performance chromatography' (HPLC) during 1970 Pittsburgh Conference by Csaba Horvath who also coined famous terminologies associated with separation such as 'pellicular packing', 'multimodal separations' etc. Mid to late 1970s saw HPLC systems maturing from 30 bar to 400 bar pressure and incorporation of injectors and different detection systems. Columns with smaller particles (<2 micron] and holistically developed instrumentation with pressure capabilities ≥ 1,000 bar was introduced in 2004 with the name Ultra-high performance liquid chromatography (UHPLC or UPLC). Advancements in interfacing liquid chromatography to mass spectrometry (LC-MS) catapulted this technique to become one of the most widely used chemical analysis techniques as it combines the separation capabilities of LC with the high selectivity and sensitivity of mass spectrometry. Research is being carried out by leading instrument manufacturers to pack columns containing sub-micron size particles and to develop instrumentation capable of performing at pressures > 6800 bar.

1.2. Types of Liquid Chromatography

Depending on the geometry by which the mobile phase and solid phase are brought to contact, liquid chromatography is broadly categorized into planar chromatography and column liquid chromatography. In planar chromatography, the stationary phase is supported by a flat surface and the mobile phase moves through the stationary phase by capillary action. Thin layer chromatography (TLC) and paper chromatography are examples of this mode of chromatography. In column liquid chromatography, the stationary phase is retained in a narrow tube through which mobile phase is passed either by gravity or by application of pressure. As this chapter focuses on column liquid chromatography, the classifications relevant to this mode of chromatography alone shall be discussed. Based on the instrumentation used, advanced column liquid chromatographic systems are classified as High Performance Liquid Chromatography (HPLC) and High Performance Ion Chromatography (HPIC or IC). IC technique has evolved from HPLC to overcome the limitations of the latter technique, especiallyin the separation and detection of metal ions and anions.

1.2.1. High Performance Liquid Chromatography (HPLC)

1.2.1.1. Normal Phase Chromatography

Normal phase refers to the original version of chromatography. When chromatography used for the very first time, Mikhail Tswett separated the plant pigments on a calcium carbonate filled column using petroleum ether as the mobile phase. Thus normal phase chromatography refers to the combination where the stationary phase is more polar than the mobile phase. In this mode of chromatography, silica gel and alumina are the commonly used stationary phases while non-polar solvents such as n-hexane, dichloromethane, diethyl ether etc are used as the mobile phase. Separation was achieved on the basis of polar interaction of analytes or the mobile phase with the stationary phase. Normal phase chromatography was used for the separation of polar analytes e.g. polyaromatic hydrocarbons, vitamins, chlorophylls, etc. However, owing to the existence of multiple interaction mechanisms between analytes and stationary phase as well as the over-sensitivity of retention of analytes to the presence of water, this mode of chromatography became less popular.

1.2.1.2 Reversed-Phase Chromatography

In contrast to normal phase, this mode employs a stationary phase which is significantly less polar than the mobile phase. Here the separation takes place based on the hydrophobic interaction of the analytes between the mobile phase and stationary phase. As the principle employed here is opposite to that of the classical chromatography, it is termed as reversed-phase chromatography. Typically alkyl or aromatic hydrocarbons covalently bonded to silica support forms the stationary phase while aqueous solutions containing methanol, acetonitrile and/or buffers are used as mobile phase. Because of their ruggedness, reproducibility and versatility, reversed-phase chromatography has become a preferred choice especially in the separation of pharmaceuticals and metabolites, and this mode constitutes to more than 75% of analytical chromatographic separations.

1.2.1.3. Hydrophilic Interaction Chromatography

Hydrophilic interaction chromatography (HILIC) is considered as a variant of normal phase chromatography, even though the mechanism of separation is more complex. Similar to normal phase, HILIC uses a polar stationary phase like silica or modified silica, but the mobile phase used is acetonitrile or methanol similar to reversed-phase. The mechanism of adsorption of the analyte can be (i) adsorption of the analyte onto surface of the adsorbent (ii) partition of an analyte with aqueous rich layer sorbed on to the stationary phase, (iii) ion-exchange with bonded phase or ionized surface silanol groups or (iv) combination of the above mechanisms. HILIC offers several advantages over the normal phase such as better solubility of the polar analytes, enhanced mass transfer as a result of low viscosity, and relatively more environmentally friendly solvents as the mobile phase. Thus in the recent past, HILIC has become an established technique for the separation of polar compounds.

1.2.1.4. Ion Interaction Chromatography

This mode of chromatography enabled HPLC to achieve the separations of ionic analyte without modifying the existing hardware. Similar to reversed-phase chromatography, this mode employs hydrophobic stationary phase. An ion interaction reagent(IIR) or ion pairing reagent is added to the mobile phase. This regent has a large hydrophobic part and carries a charge which is opposite to that of the analytes of interest. The ionic analytes after pairing up with the ion interaction reagent behaves as a neutral entity and hence can be separated on a

reversed phase stationary phase. In certain occasions, the hydrophobic ion of the IIR would be retained on to the hydrophobic stationary phase, providing ion exchangeable sites which later on facilitate the retention of the ionic analytes. Because of the excellent resolution, this method is one of the most successful methods for the separation of metal ions e.g. transition metals and lanthanides.

1.2.1.5. Affinity chromatography

In affinity chromatography or more specifically biospecific interaction chromatography, the unique biological specificity of the analyte and ligand interaction is utilized for the separation. The stationary phase must contain specific group or molecules which can absorb the analyte species only if certain steric and charge conditions are satisfied. The affinity ligand can be an enzyme, antigen, or a protein immobilized in a column. Due to the high selectivity, this technique is extensively used for the isolation of specific target molecules even they are present in complex matrices such as biological samples.

1.2.1.6. Size Exclusion Chromatography

Size exclusion chromatography (SEC) separates molecules by differences in size as they pass through a resin packed in a column. In SEC, contrary to other modes of chromatography, molecules do not bind to the stationary phase. Small sized molecules penetrate deep into the pores and hence migrate slowly through the column. On the other hand large sized molecules do not enter the pores and hence quickly move out of the column. Consequently, in this mode, the separation is based on the degree of inclusion or exclusion of an analyte from the pores within the stationary phase and this implies that mobile phase composition is not very critical in deciding the separation. This translates to a greater flexibility of the mobile phase conditions to suit the type of sample or the requirements for further analysis. The role of mobile phase is to mainly dissolve the analytes and this is the only technique where mobile phase does not play any other role. Two important subsets of SEC are gel filtration chromatography (GFC) and gel permeation chromatography (GPC), the former uses aqueous solution while the latter uses an organic solvent to transport the sample through the column. SEC is often used for obtaining molecular weight distribution of a polymer and for the separation of protein molecules.

1.2.1.7. Extraction Chromatography

Extraction chromatography involves the application of conventional solvent extraction chemistry in a chromatographic mode. The hydrophobic extractant immobilized on a solid support is used as a stationary phase while inorganic acids are used as eluting phases. This mode of chromatography combines the advantages of good selectiveness of extractants with multistages of chromatography. Application of extraction chromatography has resulted in significant improvements in the preconcentration and separation of rare earth elements and actinides.

1.2.2. Ion chromatography (IC) or High Performance Ion Chromatography (HPIC)

High Performance Ion Chromatography (HPIC) is popularly known as “Ion chromatography (IC)”. IUPAC defines this method as a separation method where the “separation is based mainly on the ion exchange affinities of the sample components”. IC is broadly classified as (i) ion exchange chromatography (ii) ion exclusion chromatography and (iii) ion pair chromatography.

1.2.2.1. Ion Exchange Chromatography (IC)

In this method the separation is based on an ion-exchange process between the mobile phase and ion-exchange groups bonded to the support material.

The ion-exchange occurs due to ionic (or electrostatic) interactions between ionic and polar analytes, ions present in the eluent and ionic functional groups fixed to the chromatographic support. Separations are carried out on small particle filled high efficiency columns and the separated fractions of ions are detected with electrochemical detectors (mostly conductivity) or spectroscopic detectors. Anions are separated on an anion exchange column whereas cations are separated on a cation exchange column. Ion exchange chromatography is used for separating both organic and inorganic ions. In the case of ions with high polarizibility, additional non-ionic adsorption processes contribute to the separation mechanism.

1.2.2.2. Ion Exclusion Chromatography (IEC)

The separation mechanism prevailing in IEC is different from the ion exchange mechanism. Here the separation is realised based on three processes viz. donnan exclusion, steric exclusion and sorption. In fact, ions of the strong electrolytes get repelled on the ion exchanger surface whereas the ions of the weak electrolytes get interacted and thus retained on the stationary phase. IEC is very useful in the separation of weak inorganic and organic acids from other acids that would dissociate completely at the eluent pH. As strong cation exchanger column (sulfonate group) is generally employed in IEC. By employing suitable detection techniques, IEC can be used for separating alcohols, aldehydes and amino acids.

1.2.2.3. Ion Pair Chromatography (IPC)

The separation mechanism in IPC is mostly on ionic interaction based sorption. Neutral surface such as silica based ODS, polymeric reversed phase columns are employed in IPC. In this method an ion pairing agent is added in the mobile phase. Depending upon the ions to be separated, an anionic or a cationic ion pairing agent would be added in the eluent. For instance, to separate anions tetrabutyl ammonium hydroxide (TBA-OH), an anionic ion pairing agent may be used. This IP reagent provides TBA+ ions in the mobile phase, which forms an ion pair with the anions (analytes). Therefore, the selectivity of the column is solely controlled by the mobile phase.

1.2.2.4. Merits of Ion chromatography

Ion chromatography offers the following advantages:

(i) Speed: due to the incorporation of innovative technology in the column chemistry and increased sophistications in the instrumentation made tremendous reduction in the analysis time. This improvement in the speed of analysis brought out the separations of many common ions within ten minutes.

(ii) Sensitivity: modern stationary phases in conjunction with microprocessor technology in the detection system, ensures achieving higher sensitivity. The introduction of on-line pre-concentration columns and other separation cartridges enabled IC system to detect analytes at ppt levels.

(iii) Selectivity: IC offers good analyte selectivity (ions of organic, inorganic, polarisable etc.) by selecting suitable stationary phase. In addition to the stationary phases, the detection mode also has paramount importance. For example, conductivity detector is never employed to detect trace amounts of nitrite in presence of high amounts of chloride and for this purpose an UV detector is employed. Recent developments in the field of post column reagent (PCR) addition show that certain group elements like transition, heavy metals etc, are selectively detected and quantified by adding a chromogenic reagent after the separator column.

(iv) Multi-elemental: IC has multi-elemental capability as it sequentially separates the analytes and offers their simultaneous detection.

1.2.3. Instrumentation

Though the concept for enhancing separation efficiency was established in the late 1940s, the wide acceptance of liquid chromatography had been waiting for the development of instrumentation suitable for transforming the concepts in to practicality. The schematic diagram showing the major parts of the modern column liquid chromatographic system are shown in Fig. 1. The important components are pump, sample injector, column, detector and data acquisition cum processing system.

1.2.3.1. Pump

The pump or solvent delivery system must be able to deliver mobile phase at precise flow rates against a high pressure drop and with minimum pulse in the flow profile. Typically HPLC pump consists of 1 to 4 solvent reservoirs. The two modes of operation of the pump are isocratic and gradient. In isocratic mode, the composition of mobile phase remains the same throughout the chromatographic run whereas in the gradient mode, it is continuously altered or a in stepwise mode. In isocratic elution, no equilibration time is needed between the successive injections. Gradient elutions are useful for obtaining rapid and efficient separation of mixtures containing a number of components with widely varying affinity for the stationary phase. There are two basic types of configurations employed for achieving the solvent delivery in the gradient mode. In the first,

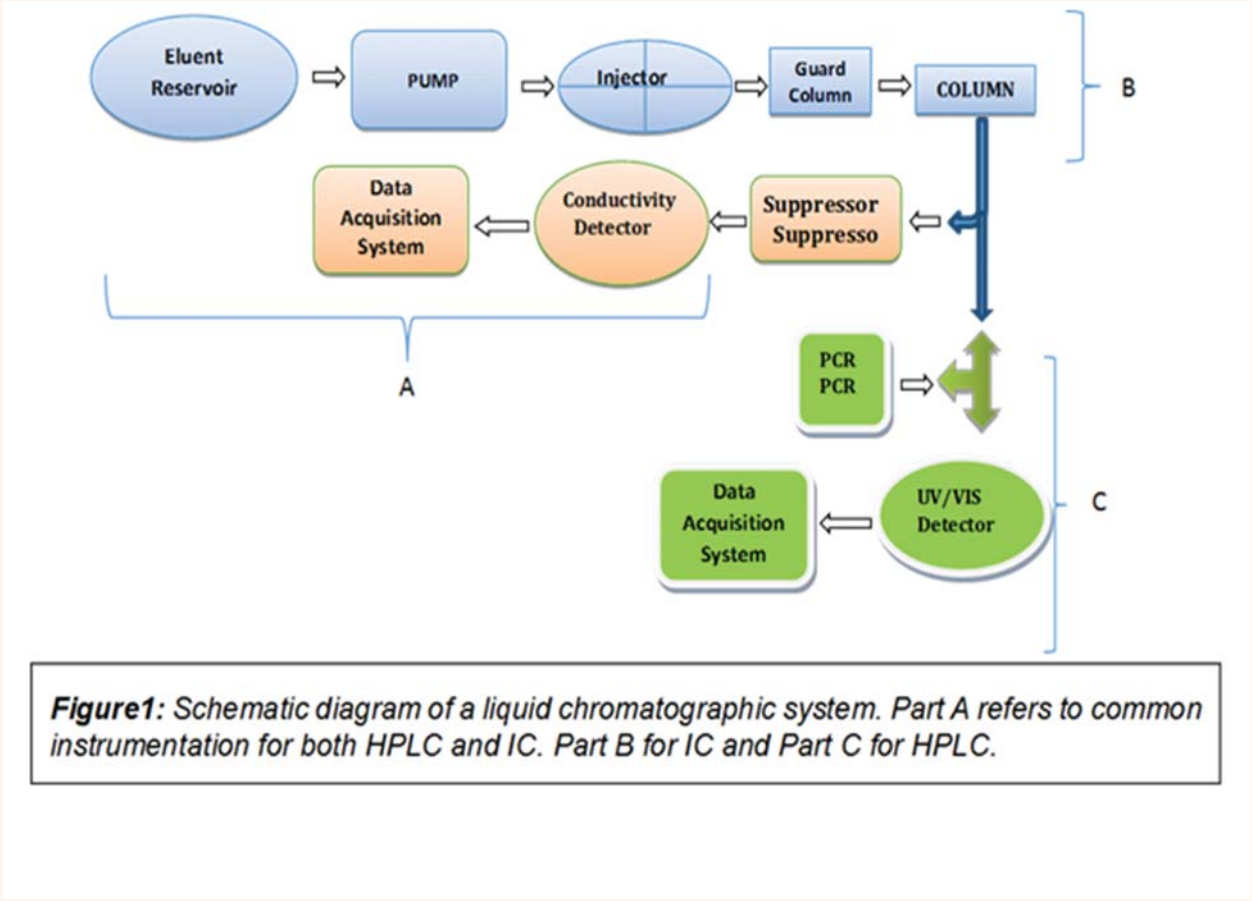


Figure1: *Schematic diagram of a liquid chromatographic system. Part A refers to common instrumentation for both HPLC and IC. Part B for IC and Part C for HPLC.*

individual pumps are used for each solvent and solvent mixing occurs at high pressure and hence called high pressure gradient system. In the second approach, the individual solvents are pre-mixed at low pressure and a single pump is employed for the delivery of the mixture and it is known as low pressure gradient system.

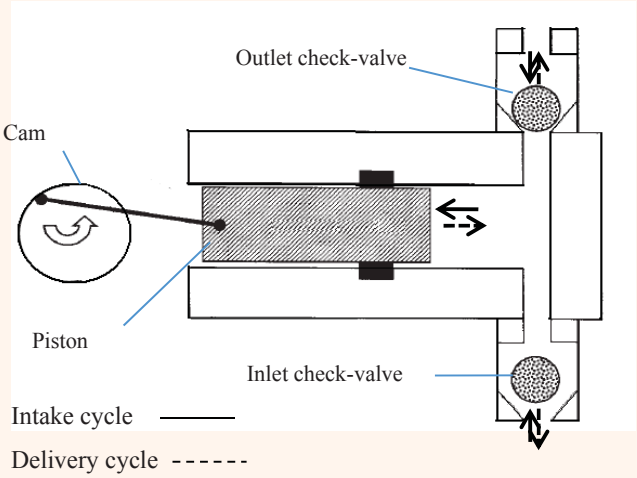


Figure 2: Schematic diagram of a reciprocating pump

Some of the different types of pumps used in liquid chromatography are direct gas pressure systems, syringe pump, pneumatic intensifier pump, and reciprocating pump. Pneumatic pumps can provide extremely high pressures and have high flow capacity and are mostly used for column packing. Syringe pumps are typically used where small volumes of mobile phase are required to be delivered with extremely low pulsation. Reciprocating piston pumps are the most commonly employed analytical pumps by virtue of their low hold-up volume, accuracy, precision and trouble-free operation. The working of a typical single piston reciprocating pump is shown in Fig.2

1.2.3.2. Injector

The sample has to be introduced as a narrow band in order to minimize the band broadening inside the column. Direct introduction of the sample into the column is not possible due to the flow of the mobile phase at very high pressure. Six port sample injection valves with fixed volume loops are, therefore, used to seamlessly inject the precise amount of the sample. The hold-up volume of injector system must be as low as possible to minimize the possibility of band broadening. Figures 3 (a) and (b) show the commonly used sample injector in load mode and in inject mode, respectively. When a large number of samples are to be analyzed, an auto-sampler is employed to carry out the precise and accurate sample injection in unattended manner.

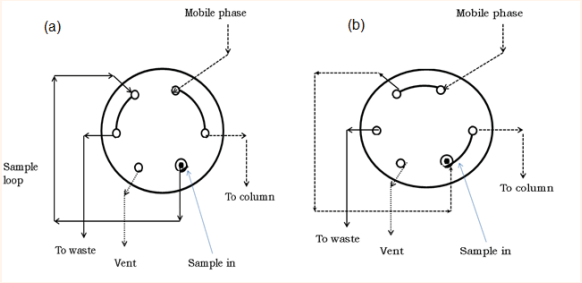


Figure 3: Schematic diagram of injectors in (a) load position and (b) inject position

1.2.3.3. Detectors

A detector is required to determine the presence of a solute as it flows out of a column. The selection of a detector for a given liquid chromatographic application is decided based on the nature of an analyte, detection limit, affordability etc. LC detectors can be categorized based on their selective nature of response to solute presence in the mobile phase. A non-selective detector would respond to the change in the bulk property of mobile phase e.g. refractive index. A detector which responds to a property specific to a solute is known as selective detector e.g. UV-Vis detector. UV-Vis detector is one of the most widely used and robust LC detector and is preferred if the analyte absorb light in the wavelength range of 200 to 800 nm.

Fluorescence detectors offer highly selective and sensitive detection (10-100 times more as compared to UV-Vis) for fluorescence active compounds. Electrochemical detector is useful for identifying compounds that can be easily electrochemically reduced or oxidized, such as phenols and aromatic amines. . Refractive index detectors are used when the analyte components do not have any specific property suiting selective detectors and have poor sensitivity is very low (100 – 1000 times lower than that of UV-Vis detector) and are not suitable for gradient elution chromatography. Evaporative light scattering detector is also a bulk property detector but as the detection is after the complete evaporation of solvents, this detector is adoptable to gradient elution method. In view of high specificity and sensitivity, mass spectrometric detectors have gained huge popularity in spite of being expensive. Tandem mass spectrometers offer the advantage of being a universal detector in MS mode and a highly selective detector in MS/MS mode. They complement liquid chromatography as an indispensible tool for identification and characterization of unknown species in complex samples.The detection modes employed in ion chromatography can be broadly classified into two categories viz. (i) electrochemical detection and (ii) spectroscopic detection. The electrochemical detection mode includes (i) conductometric (ii) amperometric and (iii) voltametric detections whereas the spectroscopic mode of detection includes (i) ultraviolet-visible absorption (ii) fluorescence and (iii) refractive index detections. The most common detection modes applied to ion chromatography are conductometry and UV-Vis.

***UV-VIS detection*:** An online spectrophotometer with a flow cell is used for the UV-VIS detection of analyte molecules that are separated from the separator column. Detection is based on the Beer-Lambert's law. The mathematical expression of this law is given as:

$$A = log\frac{I_o}{I_t} = \varepsilon cl$$

where, A is absorbance, I_0 is intensity of incident light, I_t is intensity of transmitted light,ε is absorption coefficient, c is the concentration of absorbing species and l is the path length in cm.

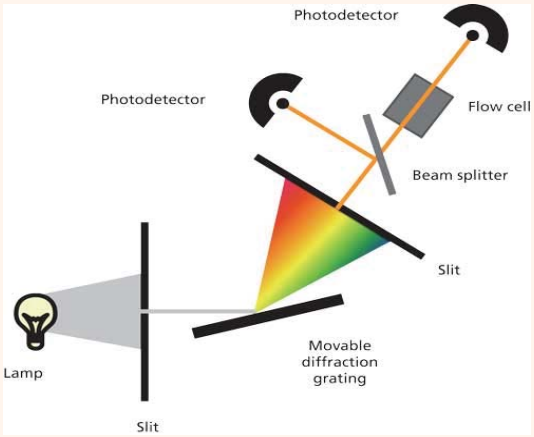


Figure 4: Schematic diagram of a UV-Vis Detector

The detection wave length is selected in such a way that the mobile phase components will have bare minimum absorption at the wavelength of detection. In the cases where sequential detection of many analytes having different absorption wave lengths, effective monitoring of eluted species is achieved by a technique called Post-Column Reagent Addition (PCR) where a chromophoric reagent is added to effluent from a column, prior to the detector. Figure 4 shows the schematic diagram of a UV-Vis Detector.

***Conductivity detection*:** In a conductivity detector, eluate from a column or suppressor passes through a conductivity cell (flow cell). This cell consisted of two electrodes, between which an AC potential is applied. The ionic concentration of mobile phase increases when the sample enters into a conductivity

cell and thus, conductivity increases. This increase is proportional to the concentration of the analyte.

The distance between the electrodes is usually represented by d and the electrode area by A. The ratio d/A is termed as *cell constant,* K of the detector and has the unit cm^{-1}. The conductance G between the electrodes is continuously measured and is dependent on $|z_i|$ i.e. the ion charge magnitude, the ion concentration c_i, and the electric mobility u_i of the ions in the cell. The conductivity is specific for every ion and linearly dependent on the concentration in "solutions of infinite dilution". The conductivity K is an intrinsic property of solution and can be calculated from conductanceand cell constant. Thus, when a sample ion passes through the detector, the conductivity increases and a peak is obtained on the chromatogram.

$$\text{Conductance (S or } \Omega^{-1}\text{):} \quad G = \frac{1}{R} \tag{1}$$

where, R is the resistance in ohm.

Electrolylic conductivity ($S.cm^{-1}$), k can be written as:

$$k = K.G = \left(\frac{d}{A}\right) G \tag{2}$$

The conductivity of a dilute solution is the sum of the individual contributions to the conductivity of all the ions in solution multiplied by their concentrations. This is known as Kohlraush's law of independent migration and is stated as an equation:

$$K = \sum \mathrm{I}\, \lambda_i^0\, c_i/1000 \tag{3}$$

where, K is the measured conductivity in S/cm, c_i is the concentration of the ions in equivalents/L, λ_i^0 is the ionic limiting equivalent conductivity,which is specificfor each ion and expressed in $S.cm^2$/equivalent. λ is the molar ionic equivalent conductivity of the positive and the negative ions in a salt, respectively, expressed in S. cm^2.

The conductivity depends on the temperature and the molar ion conductivity. Molar ion conductivity at a given temperature T can be related to tabled values at 25ºC, using the formula:

$$\lambda_T = \lambda_{25} e^{k(25-\mathrm{T})} \tag{4}$$

where, the temperature coefficient 'k' is a constant for a given ion in a given solvent, usually about 2% per ºC for an anion in water at 25°C.

Due to the temperature sensitivity, it is clear that the background conductivity will be more stable if the temperature of detector cell is controlled. Detectors are usually constructed to measure the conductivity and the temperature simultaneously in the detector cell. Usually the output signal will be the conductivity that the detector response would correspond to at a standard temperature, typically 25°C. A detector with this feature is termed as temperature compensated detector.

1.2.3.4 Stationary Phase

Stationary phase is responsible for the retention of analytes, which are being carried through the system by the mobile phase. Stationary phase is considered to be the 'heart' of the liquid chromatographic system. Porous particles, pellicular particles, perfusion particles and monolithic based stationary phases are employed for column packing depending upon the application.

Most of the stationary phases are prepared by filling the column with particles with a size of 3 µm to 5 µm for analytical HPLC whereas UHPLC (UPLC) typically uses stationary phase with particle size less than 2 µm. As an alternative to wholly porous sub-2-µm particles, some UHPLC applications employ 1.7 µm fused-core particles surrounded by a 0.5-µm porous silica layer to reduce operating pressure without compromising on the separation efficiency. Such type of particle is called pellicular packing. Another innovation in the LC

stationary phase is the development of monolith stationary phases. The porous rod-like structure of monolith stationary phase is highly permeable and provides large surface area for separation in comparison with particle-based stationary phases. Since monolith stationary phase offer shorter diffusion distances, they can be operated at higher mobile phase flow rates without any significant lose in the separation efficiency.

2. Theory of Chromatography

2.1 Band Broadening in Chromatography

When a mixture of components is introduced into a chromatographic system, the difference in interaction of components between the stationary phase and mobile phase leads to differential migration of components. This result in the formation of different bands corresponding to individual components and leads to separation. However, differences in the migration of different molecules of the same component would lead to spreading or broadening of individual bands and this can hamper the effective separation of different bands. Different processes contributing to broadening of bands in a chromatographic process are Eddy diffusion, longitudinal diffusion and mass transfer effects.

Eddy diffusion: It arises due to the different microscopic flow paths that the mobile phase takes while flowing between different stationary phase particles inside a column. Due to Eddy diffusion, different molecules of the same solute may travel unequal distance and thus reach the detector at different time intervals, leading to broadening of a peak. Fig. 5 demonstrates the different flow streams taken by three different molecules of the same solute, contributing to the band broadening.

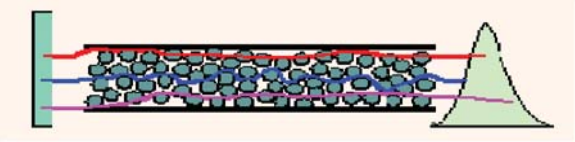


Figure 5: Eddy diffusion

Longitudinal Diffusion: When the analyte is introduced in to the mobile phase, due to the concentration gradient, analyte molecules would diffuse out randomly in all the directions in the mobile phase and this phenomenon also contributes to the broadening of solute band. This effect is more prominent at low flow velocities as the solute spends more time in the mobile phase. Longitudinal diffusion of the analyte in the column ($t_0 < t_1 < t_2$) are presented in Fig. 6.

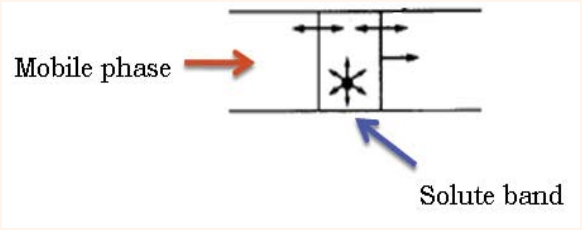


Figure 6: Illustration of longitudinal diffusion of an analyte band.

Mass Transfer Effects: The three components of mass transfer effects contributing to band broadening are (i) flow distribution, (ii) mass transfer in the stagnant mobile phase and (iii) mass transfer in the stationary phase. Flow distribution refers to differing flow rates of a single flow stream at different points between surrounding particles. Due to friction, mobile phase layer adjacent to the particles moves slowly, whereas the one at the centre between two particles moves faster. The intermediate layers would have a gradation of flow rates due to viscosity. Thus the analyte molecules moving along the different layers are expected to exit the column at different times as illustrated in Fig. 7 and this leads to broadening of band.

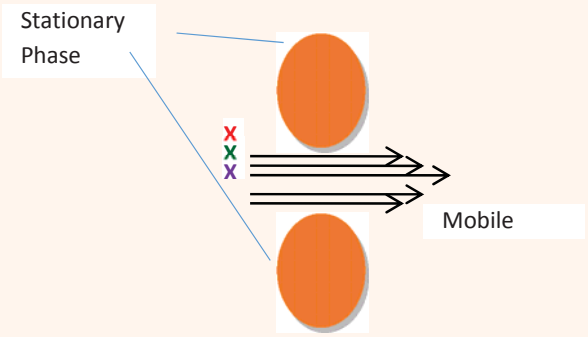


Figure 7: Band broadening due to flow distribution.

Irrespective of the flow rates or pressure applied externally, the mobile phase is stagnant in the pores of the stationary phase. Analyte molecules move in and out of these pores by diffusion. Thus if an analyte molecule has diffused only to a small distance into the pore and then move out into the mobile phase, would travel faster compared to another molecule of the same analyte diffused to a longer distance into the pore, as demonstrated in Fig. 8.

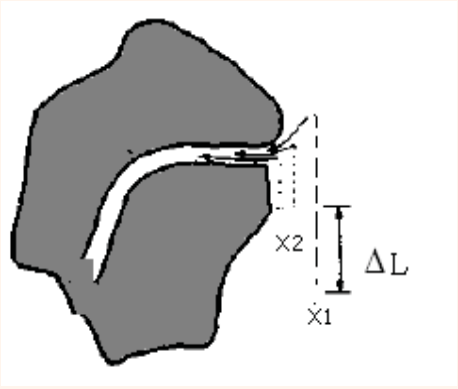


Figure 8: Mass transfer in the stagnant mobile phase.

During diffusion into the stationary phase, a given analyte molecule can attach to the periphery of the particle or penetrate deep inside the stationary phase. In the former situation, the molecule would spend lesser time in the stationary phase and hence travel faster in the column as compared to the analyte molecule in the latter situation. Figure 9 shows the relative movement of molecules X1 and X2 of the same analyte as a result of mass transfer in the stationary phase.

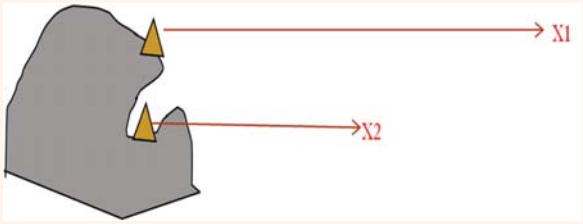


Figure 9: Mass transfer in the stationary phase.

An examination of all these band broadening mechanisms reveal that the effects would become less significant as the particle size of the packing material used in the stationary phase decreases. Thus smaller particle size has become integral to high performance separations. Though the efficiency improves, pressure required to force the mobile phase through a stationary phase increases at a rate inversely proportional to the square of the particle size. Hence, HPLC is also called as high pressure liquid chromatography. The efficiency of a given chromatographic separation can be represented by factor known as height equivalent to a theoretical plate (HETP). The plot depicting the change in HETP as a function of average linear velocity is known as van Deemter plot.

van Deemter Plot: A popular way of quantifying the efficiency of separation is based on 'theoretical plates'. Theoretical plate is a conceptual quantity which corresponds to that portion of a column where the solute is in equilibrium with the mobile phase and stationary phase. H is the height (or length) of one such plate and it is used as a measure of the efficiency of a given column. The solute moves down the column by transfer of equilibrated mobile phase from one plate to another. The chromatographic column contains a large number of such 'plates' as indicated in Fig.10.

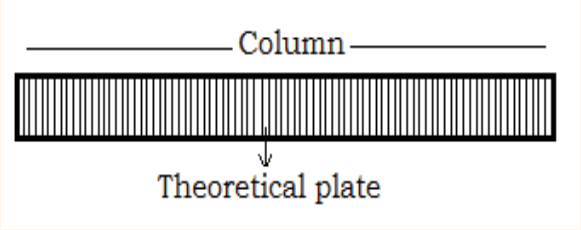


Figure 10: Illustration of theoretical plates in a chromatographic column.

The contributions of important band broadening mechanisms are combined as a function of mobile phase velocity for evaluating the efficiency of a given separation condition. HETP can be written as:

$$H = A + \frac{B}{u} + Cu \qquad (5)$$

Where, terms A, B and C represent Eddy Diffusion, Longitudinal diffusion and mass transfereffects, respectively.

Lesser the height (thickness) of an individual plate, more number of plates can be accommodated in a given column and more number of equilibrations would be taking place of the solute between the stationary and the mobile phases. Thus a small value of H of a given column is indicative of high efficiency of separation conditions. N, the number of theoretical plates in the column is related to the plate height, H as N = L/H where, L is the length of the column. Van Deemter plot helps to calculate HETP in terms of the average linear velocity of mobile phase, is shown in Fig. 11.

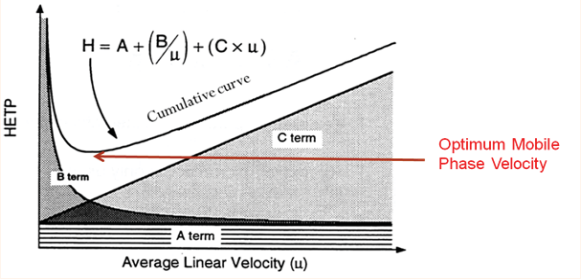


Figure 11: van Deemter plot.

A central goal in LC practice is the attainment of small H values for achieving maximum N for enhancing the separation efficiencies. Thus separations must be carried out at the optimum flow rates of the mobile phase to achieve the best efficiency possible.

From the different factors contributing to band broadening, it is clear that the value of H is small when small particle sized columns (dP) are employed. Thus overall efficiency of separation or performance increases on columns packed with small particles. High performance liquid chromatography (HPLC) refers to separations carried out using columns containing ≤10 µm particles. Figure 12 shows the Van Deemter curves obtained with columns packed with three differentparticle sizes viz. 1.8 µm, 3 µmand 5 µm. It is seen that the lowest value of H and hence the highest column efficiency is possible for column packed with the smallest size particles. Some of the benefits of using columns packed with small particles are narrow and taller peaks, better sensitivity and more peak capacity. The plot highlights the basis for the achievement of superior separation efficiencies by UPLC compared to classical HPLC.

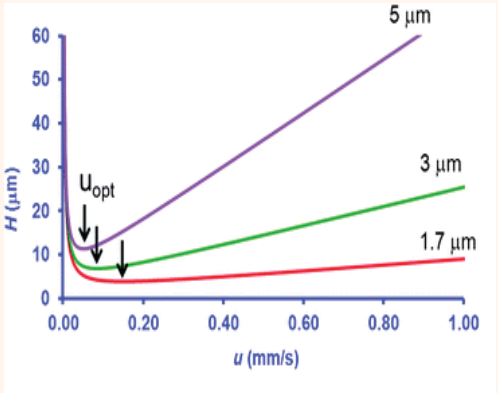


Figure 12: Comparison of van Deemter curves of LC columns packed with particles of different sizes.

2.2. Terminologies in Chromatography

Various terminologies commonly used in chromatography are presented in Fig. 13.

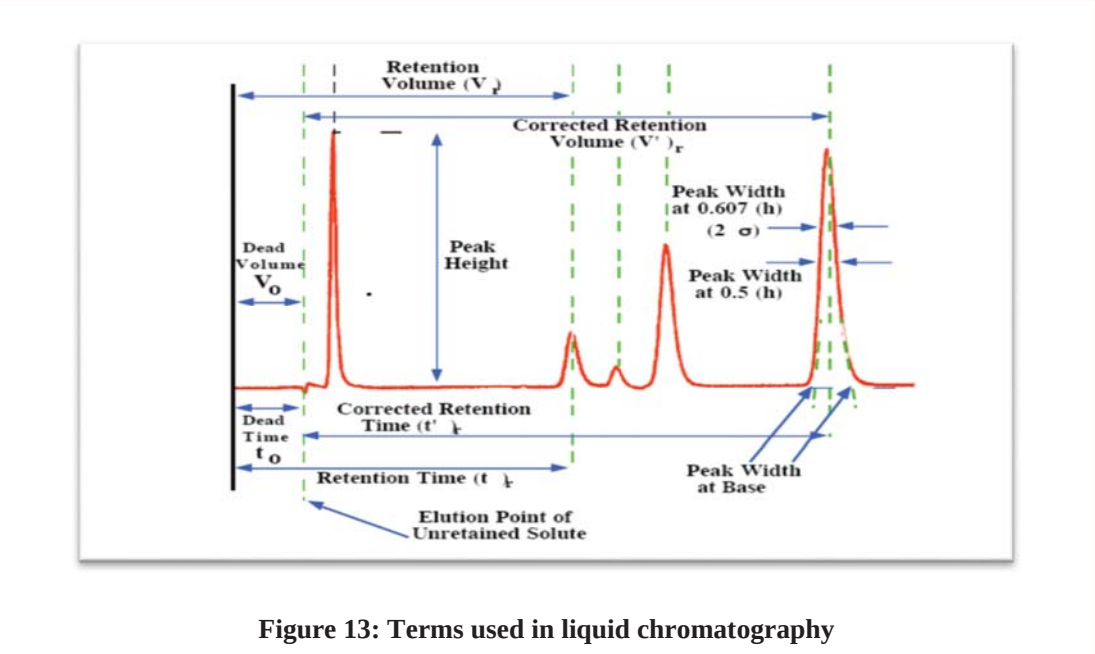


Figure 13: Terms used in liquid chromatography

Base line: It is any part of the chromatogram where only the mobile phase is emerging from the column.

Column dead time (t_0): it is the time necessary for a non-retained solute component to pass through the column. And the volume of mobile phase corresponding to the dead time is known as dead volume (V_0).

Retention time (t_R):The time in which the components do take to emerge out from a column. This includes the dead time of the column.

Resolution (R):The resolution R of two neighbouring peaks is defined as the quotient of the difference in the absolute retention times and the arithmetic mean of their peak widths w at the respective peak base.

$$R = \frac{(t_{R2} - t_{R1})}{\frac{(w_1 + w_2)}{2}} \qquad (6)$$

where t_{R2} and t_{R1} are the retention times for components 1 and 2 respectively, w_1 and w_2 are their corresponding peak widths.

Selectivity (α):the selectivity is defined as the ratio of the solute retention times of two different components.

$$(t_{R2} - t_0)/(t_{R1} - t_o) \qquad (7)$$

Selectivity is a thermodynamic quantity and at constant temperature and is determined by the properties of the stationary phase. Selectivity of the column is due to several factors, e.g., in IC, the support material and the chemical structure of the ion exchange group. In addition to the characteristics of the stationary phase material and the groups that are attached therewith, the following factors are also significantly influencing the separation selectivity:

(i) The charge of the analyte ions (monovalent or multivalent)

(ii) The hydrated radii of the sample ions and the degree of cross linking of the support material

(iii) The ability of the analyte ions to either contribute to, or disrupt the hydrogen bonding structure of the surrounding water.

The selectivity factor (α) of two analyte ions A and B eluting close to each other is the measure of how well these ions are separated, and is calculated according to the equation given below:

$$\alpha = {}^{k'_B}/_{k'_A} \quad (8)$$

where, k'_A and k'_B are the retention factors (capacity factors) for the first and the last eluted ion, respectively.

Retention factor (k'): it is also known as Capacity factor. It is the product of the phase ratio Φ between stationary and mobile phase in the separator column and the Nernst distribution coefficient, K.

$$k' = K\left({}^{V_s}/_{V_m}\right) \quad (9)$$

$$K = {}^{C_s}/_{C_m} \quad (10)$$

Where, K is Nernst distribution coefficient, V_s *is volume of the stationary phase,* V_m *is volume of mobile phase, C_s and C_m are solute concentrations in the stationary and mobile phase respectively.*

Practically k' for any peak of a component is measured as

$$k' = {}^{(t_R - t_0)}/_{t_0} \quad (11)$$

Column Efficiency: An efficient chromatographic system will generally produce high and narrow chromatographic peaks, and thus provide good sensitivity. The efficiency is controlled by the column choice and careful selection of other components of the flow system. As discussed earlier, one of the issues in chromatography is the broadening of the sample component zone during its passage through the separation system. Peak broadening can be measured as plate number, N, or the plate height, H, which is independent of the column length, L.

$$H = {}^{L}/_{N} \quad (12)$$

The theoretical plate height, H, is defined as the ratio of the peak variance and column length L. Mathematically the same is expressed as follows:

$$= \left({}^{1}/_{8\ln 2}\right) * \left({}^{b_{0.5}}/_{L}\right)^2 \quad (13)$$

where, $b_{0.5}$ is peak width at half the peak height .

The dependency of resolution with column efficiency (N), selectivity or separation factor (∞) and retention factor **(k')** can be expressed in a single equation as :

$$R = \frac{1}{4}\sqrt{N}.\left(\frac{\alpha-1}{\alpha}\right)\left(\frac{k'}{k'+1}\right) \quad (14)$$

a b c

In the above equation, term 'a' stands for column efficiency; term 'b' stands for column selectivity and term 'c' stands for capacity factor.

3. Types of Stationary Phases

3.1 Stationary Phases for HPLC

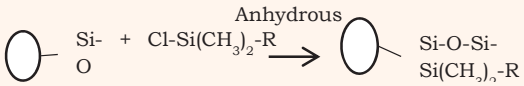
Different types of HPLC conditions may be required to achieve a specific separation and this often necessitates selection of the most appropriate stationary phase depending on the properties of the analytes and the sample matrix.

Normal Phase: In this mode, the dominant interactions between the analytes and stationary phase that cause retention and selectivity are polar in nature. Silica was initially used extensively as stationary phase material due its high surface area, porosity, polar nature and good mechanical strength. However, free silanols groups on silica stationary phases are weakly acidic and hence strongly interact with solutes with basic nature leading to the tailing of these analytes. Silanols near the metal cations are strongly acidic. Water can be hydrogen bonded to

the hydroxyl groups and multi-layers of water adsorbed on the top of the silica surface. Thus unmodified silica offers a host of interaction mechanisms based on hydrogen bonding, dipole-dipole and ion exchange, and thus adsorption process is difficult to understand, reproduce and is less efficient. Silanol groups on the surface of the silica particles can be chemically modified to give stationary phase with specific properties and these are called modified silica stationary phase. Cyano, diol and amino bonded phases are also used for this mode of separations. Bonded stationary phases have the advantage that they equilibrate more rapidly than silica columns and hence are amenable for gradient elution. As previously mentioned, in this mode, the mobile phase has to be less polar than stationary phase and typically organic solvents such as hexane, ethyl acetate are used as the mobile phase. The analytes having higher degree of polarity shall retain strongly and hence elute after the elution of less polar analytes.

Bare silica, diol and amide phases are also suitable stationary phase for hydrophilic interaction liquid chromatography (HILIC) used for separating hydrophilic and polar ionic compounds. Zwitterionic groups (contains both cationic and anionic functional groups) containing stationary phase capable of providing additional electrostatic interactions are also used increasingly in HILIC mode. Compared with traditional normal phase liquid chromatography methods, HILIC permits the use of relatively green and water-soluble mobile phase composition which enhances the solubility of hydrophilic and polar analytes.

Reversed-Phase As mentioned earlier, in this mode, the stationary phase has to be lesser polar than the mobile phase. Hence the reversed-phase stationary phases are hydrophobic in nature and are mostly prepared by the chemical bonding of long chain hydrocarbon tio silica support particle.



When R = $-(CH_2)_{17}-CH_3$, the product is known as octadecylsilane (ODS) which is the most widely used modified stationary phase and is also called as C_{18}. As it is extremely non-polar, this stationary phase is an ideal candidate for reversed-phase chromatography. Chemical modification may not convert the entire silanol groups into ODS. The unreacted silanol groups are subsequently reacted with trimethylchlorosilane to minimize the silanol activity and this treatment is known as 'end-caping'. Instead of $-CH_3$, bulkier side chains can be incorporated in the ODS to protect the analytes from exposing to the residual silanol groups. Modified silica has a narrow pH range for safe operation as use of lower pH conditions leads to the cleavage of siloxane bond, Si-O-Si-R and higher pH causes dissolution of silica.

The cross-linked polymer obtained by the co-polymerization of styrene and divenyl benzene is a resourceful stationary phase for LC. The degree of cross-linking and the porosity can be controlled by the proportion of divinylbenzene in the reaction mixture. These polymers are stable over a wide range of pH conditions and can be used in reversed phase separations. However, polymeric stationary phases do not have the same mechanical strength as silica and they are susceptible to dimensional changes under extreme conditions of pressure.

In reversed-phase mode, the mobile phase consists of water and an organic modifier such as acetonitrile or methanol which is used to vary the polarity of the mobile phase. Organic solvents can be selected based on their position in the "Eluotropic Series" where the common solvents are arranged in the order of relative strengths.When ionisable analytes are present, buffers are added to the mobile phase to control the ionization of the analytes and

thus their retention, e.g. addition of low pH buffers during the separation of weak acids. Similarly ion pairing agents (ion interaction reagents) are added in the mobile phase to facilitate the retention of ionic analytes on to the hydrophobic stationary phases. While selecting the additives, their compatibility with the column as well as detection system has to be kept in mind.

Size Exclusion:The separation process in size exclusion chromatography is based on the hydrodynamic size of the molecules. Cross-linked dextran, agarose, polyacrylamide, and polystyrenes obtained with controlled porosity can also be used as the stationary phase for size exclusion chromatography. Porous silica is also used as packing material in size exclusion chromatography. The mode of separation occurs when the analyte moves into the pores by differing degrees based on their hydrodynamic size.

Stationary phases made of alumina, hydroxylalkylmethacrylate gel, porous graphitic carbon,titania, zirconia etc. are found in special applications and are less commonly used.

Some physical parameters of stationary phases such as particle size, its distribution, porosity, pore size, surface area, pH range etc. should be given due consideration while developing the separation methods as they contribute to the efficiency of the separation process.

3.2 Stationary Phases for IC

The stationary phases or columns that are used in ion chromatography are ion exchange columns, which essentially have two parts. One of which is a bulk group (polymeric resin) modified with opposite charge of the counter ion and is called support material and the second one is exchangeable ion that comes from the mobile phase. The first part of the stationary phase usually made from inert organic matrix chemically derivative with ionizable functional groups (fixed ions) which carry displaceable oppositely charged ion.

Support materials:The support materials that are used in the ion exchange columns are:

i. Coated silica gels (pH 2-8)

ii. Polymethacrylate, polyhydroxy alkyl methacrylate (pH 2-11)

iii. Polystyrene / divinyl benzene copolymers (pH 0-14)

Silica and methacrylate-based columns have restriction with regard to the working pH range whereas the polystyrene/DVB columns have no pH limitations. Depending upon the nature of the analyte ions, besides ion exchange mechanism, interactions of the analytes with support material also occur and this is more prominent for organic ions than for the inorganic ions. Therefore, depending on the column chemistry, the separation profile may vary. Hence, selection of an appropriate column is one of the important aspects.

Besides the classification based on the support materials of columns, the stationary phases have been classified on the basis of functional group present in the support materials. Details have been provided in one of the articles in the same bulletin viz. ion exchange separation.

Ion exchange capacity: pore size and ion-exchange capacities of the columns are also very important in determining the retention of the analytes. The ion-exchange capacity of a resin is defined as the number of ion-exchange sites per weight equivalent of the column packing. It is normally expressed in terms of milli equivalent or micro equivalent per gram of resin. The retention times of ions increase with increasing ion-exchange capacity. However, the desired elution of ions can be partially controlled by varying the ionic strength of the mobile phase.

Styrene / DVB copolymer columns: Styrene polymerises into a long chain and DVB is added as a copolymer. The percentage of DVB in the resin is termed as "percent crosslinking". The rigidity of the resin increases with increasing percent cross linking. The degree of crosslinking, or DC, relates to the number of groups that interconnect two materials and it is expressed in mole percent. The DC determines the porosity of the resin, which is an important characteristic of the resin. Based on the porosity, the resins can be classified as "Microporous" and "Macroporous" resins. Microporous resins are also known as Gel type resins and they have a natural porosity limited to intermolecular distances. It is a microporous type structure. Macroporous type resins have an additional artificial porosity which is obtained by adding a substance designed for this purpose. Macroporous resins show high mechanical strength and less prone to swelling and shrinkages due to change in mobile phases.

Ion-Exchange separation mechanism: For example, we consider a typical anion exchanger where the fixed ions are quaternary ammonium ions ($R_4N^+$where 'R' represents the polymeric resin part) and the displaceable ion attached with R_4N^+ is Cl^-. When a mobile phase, e.g. Na_2CO_3, the CO_3^{2-}ions (eluent ion) will replace equivalent numbers of Cl^-. While introducing a sample containing different anions (F^-, Cl^-, NO_2^-, NO_3^-, Br^-, SO_4^{2-} etc.) into the mobile phase the exchange of those anions would takes place against the CO_3^{2-} on the column surface. The exchanged analyte ions on the surface will be replaced again with CO_3^{2-} ions present in the mobile phase which termed as elution. The adsorption of the analyte to the stationary phase and desorption by the eluent ions is repeated during their journey in the column, resulting in the separation due to ion-exchange.

The anion-exchange processes can be depicted as:

$$\underset{\text{Resin}}{R\text{-}NR_3} + \underset{\text{counter ion}}{HCO_3^-} + \underset{\text{sample anion}}{A^-} = R\text{-}NR_3^+A^- + HCO_3^-$$

Similarly cation-exchange processes can be depicted as:

$$\underset{\text{Resin}}{R\text{-}SO_3^-H^+} + \underset{\text{counter ion}}{B^+} = R\text{-}SO_3^-B^+ + \underset{\text{sample cation}}{H^+}$$

The corresponding counter ions of the resins get exchanged with the similar charged ions of the sample. For every ion, the exchange ion is characterised by a corresponding ion-exchange equilibrium, which determines the distribution between the mobile and stationary phase. For instance, we shall see the equilibrium of cation exchange process.

$$K = \frac{[B^+]_{SP}}{[B^+]_{MP}} . \frac{[H^+]_{MP}}{[H^+]_{SP}}$$

where, K is the Equilibrium Constant

Therefore, the different ionic components of sample can be separated on the basis of their different affinities for the stationary phase of the ion exchanger. This shows that every ion will have different K values and thus the separation is realised. The different ions present in a sample exhibit different charges, size (size of the hydrated ion) and thereby different charge density. The charge density variation determines the degree of interaction on the oppositely charged ions of the column (fixed ions) and their displacing capability with the exchange ion. This decides the elution order of the ions. In general, retention times of the ions increase with increasing charge on the ions. However, between the ions of the same charges the elution order follows as per their charge density. For instance, between fluoride and chloride, fluoride elutes earlier, followed by chloride although both are bearing single negative charge. This is because the size of the hydrated fluoride is more than that of chloride and

hence, fluoride exhibits least interaction resulting in an early elution.

It is important to note that the net charge of molecules is highly pH dependent. For example, we consider H_3PO_4 and it has three pKa values which is pH dependent. When carbonate buffer is used as a mobile phase (pH <10), H_3PO_4 dissociates as $H_2PO_4^-$ and it is getting eluted prior to SO_4^{2-}. But the same appears after sulphate when hydroxide eluent is used. This is due to the hydroxide eluent, which has pH in the region of 12 -13 and hence, the H_3PO_4 dissociates to HPO_4^{2-}. Obviously, the net surface charge of all molecules with ionizable groups is highly pH dependent. Therefore, pH of the mobile phase should be selected according to the net charge.

Choice of mobile phase or eluent: Eluent is the mobile phase which transports the ions or analytes in a column and facilitates sequential interaction of ions between the stationary and mobile phase. The most common type of elution is isocratic, i.e., where the eluent has a constant concentration and composition during the entire run. Another mode of elution is a gradient. In gradient elution mode, the eluent concentration is changed with respect to time of run (it is called concentration gradient)

Table 1: Influence by different eluent parameters on the retention of ions in ion chromatography

Parameter	Effect on retention in anion IC
Ion strength	The eluting ability increases with eluent ionic strength. The selectivity among ions of equal charge is only marginal, whereas the selectivity between ions of different charge (mono or polyvalent) is far more sensitive to changes in ion strength.
pH	The retention times for anions of weak acids increase when pH of the eluent increases in the vicinity of pK_a of a acid. Whereas in the cation exchange for separation cations (alkali and alkaline), dilute acids like HNO_3, H_2SO_4 are used.
Temperature	The ion exchange rate increases with increasing temperature. Separation efficiency and column selectivity improves as the viscosity of the eluent and the column back-pressure decrease.
Flow rate	The ions are eluted faster with higher eluent flow rates, but faster elution will decrease the separation efficiency. The flow rate is also limited by the pressure durability of the separation column.

or the pH of the mobile is changed during a run (pH gradient). The purpose of using gradient elution is to get the peaks of weakly retained as well as strongly retained peaks within reasonable time so as to have all peaks with acceptable retention factors. Several considerations govern the choice of eluent. The first factor is the kind of sample ions that will be separated and the second factor is the type of separation column to be employed. In ion chromatography, for separating anions, the two most common eluents used are based on hydroxide or carbonate as eluting anion. The parameters that can influence ion exchange separation are described in Table 1.

In the case of separating the transition and inner transition metal ions with ion chromatography, simple cation exchange chromatography is not employed as these metal cations exhibit very close charge density and therefore, almost similar selectivity. Hence, the separation is achieved based on the techniques like ion interaction chromatography (IIC), chelation ion chromatography (CIC) etc. In these cases the mobile

phase will essentially have a chelation agent which forms different complex species with the metal ions of interest and introduces a secondary equilibrium in the separation process.

4. Separations by Liquid Chromatography

4.1 Separations by HPLC

4.1.1. Normal Phase Liquid Chromatography

In normal phase LC, the major interaction is polar in nature i.e. between the analyte and stationary phase. In case of dipole-dipole interactions, the charge centres on analyte molecules, get attracted by complementary charge centres on the stationary phase. The dipole can be permanent or induced by another molecule which is having a permanent dipole. In some case, the interaction between the stationary phase and the analyte can be through hydrogen bonding. Silica is one of the most commonly employed stationary phase in this mode of chromatography in combination with n-hexane or other non-polar solvent or solvent mixtures as the mobile phase. Less polar analytes would have lower interaction with the stationary phase and hence move faster through the column while polar analytes move slowly due to the stronger interaction with the stationary phase. Silica stationary phase due to its multiple interactions often offers the possibility to separate very similar components.

Figure 14 shows the chromatogram obtained for the separation of a mixture of fat soluble vitamins by a silica column. Tocopherol is a class of vitamin E compounds naturally found in oils, nuts, and vegetables. Menadione also known as Vitamin K3 and is fund in liver. Cholecalciferol is also known as vitamin D3 which is made by the skin when exposed to sunlight. Though the availability of multiple modes of interactions in silica stationary phase can be beneficial in some instances, it can also make the

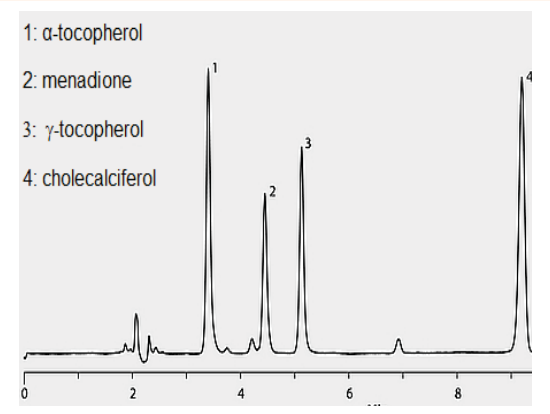


Figure 14: Normal phase liquid chromatographic separation of fat soluble vitamins.*Column: Ascentis Si, 15 cm x 4.6 mm. Mobile phase consisting of hexane and ethyl acetate with composition of ethyl acetate changed from 10% to 30% (v/v) in 12 min. Courtesy to Merck column application note.*

retention process less reproducible or difficult to understand the mechanism of retention. Silanol groups on the surface of the silica particles are therefore chemically modified with cyano, diol or amino groups. Bonded silica stationary phases offer the additional advantage of rapid equilibration with the mobile phase. The separation of a mixture of aromatic compounds using silica stationary phase modified with aminopropyl groups has been reported to demonstrate the utility of this type of stationary phase (Ref: *Anal.Methods*, 2018,10,1538–1546).

4.1.2. HILIC

The term hydrophilic interaction chromatography is used to describe normal-phase chromatography with mobile phases dominated by acetonitrile or methanol in combination with a small proportion of water. It is proposed that a thin layer of water is sorbed on to the polar stationary phase and the partitioning of the analytes occurs between the mobile phase and the layer of water. HILIC offer several advantages over the normal phase such as improved solubility of the polar solutes, enhanced mass transfer as a result of low viscosity and

relatively more environmentally friendly solvents as mobile phase. Another advantage of HILIC solvents is the improved sensitivity when coupled to ESI-MS due to its ease of desolvation. Mass spectrometry based methods can provide the selectivity and sensitivity needed for the detection and identification of unknown compounds or co-eluting species.

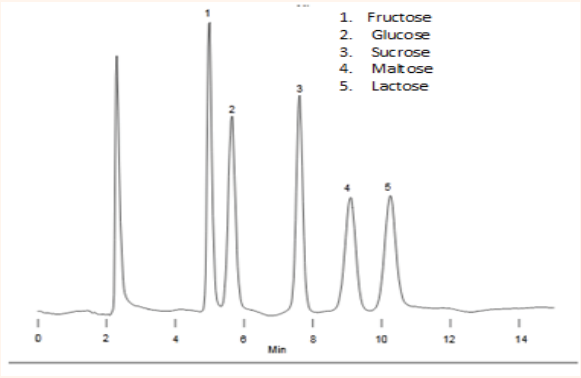


Figure 15: Separation of a mixture of carbohydrates in fruit juice by under HILIC chromatography. *Stationary phase: aminopropyl-modified silica. Mobile phase: acetonitrile : water in 75:25 proportion. Courtesy: Supleco Application Bulletin*

Since carbohydrates exhibit very close similarities in their physical properties and chemical reactions, they are difficult to separate. Due to the absence of any chromogenic groups in these class of compounds refractiveindex (RI) detection is most commonly used in analyses of carbohydrates. Figure 15 shows the normal phase separation of a mixture of carbohydrates on a silica-based, aminopropyl-modified stationary phase. A mobile phase containing acetonitrile:water in 75:25 proportions was found to give adequate separation among different carbohydrates found in fruit juices and soft drinks.

4.1.3 Reversed-Phase Liquid Chromatography

As it was discussed, reversed phase liquid chromatography (RPLC) employs a nonpolar stationary phase and an aqueous based mobile phase containing a water-miscible organic solvent, known as modifier. RPLC is a very versatile separation mode having applications encompassing a wide variety of fields such as environmental, clinical, pharmaceutical, food and industrial analyses etc. The popularity of RPLC is attributed to the development of chemically stable, microparticulate bonded phases that provide rapid mass transfer and a high degree of flexibility of the mobile phase to adopt to the samples. Separation mechanism in RPLC is based on the partitioning of analyte molecules between the mobile phase and the hydrophobic ligand immobilised on to the stationary phase. The

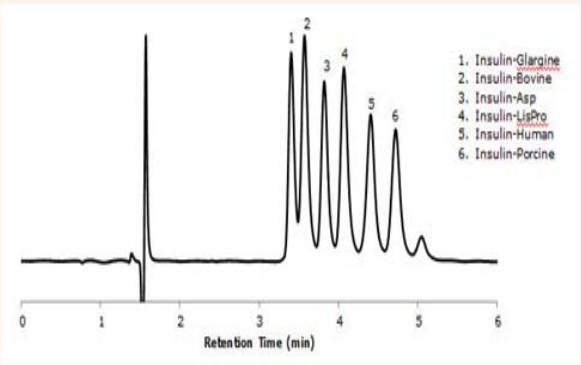


Figure 16: Separation of different forms of insulin. *Stationary phase: C_{18} column (15 cm x 2.1 mm ID, 2.7 µm). Mobile phase: water, 0.1% TFA and acetonitrile gradient (Courtesy: Merck application note).*

components having greater degree of hydrophobicity would be retained strongly by the stationary phase and thus exhibit longer retention compared to components, which are polar in nature. Thus the elution pattern in RPLC is in opposite to what is expected in the case of normal phase LC. Figure 16 shows the RPLC separation of different forms of insulin which is a hormone used to regulate the glucose level in blood. It is important in the quality control procedure followed in the pharmaceutical labs to know whether a given sample contains different formulations of the hormone.

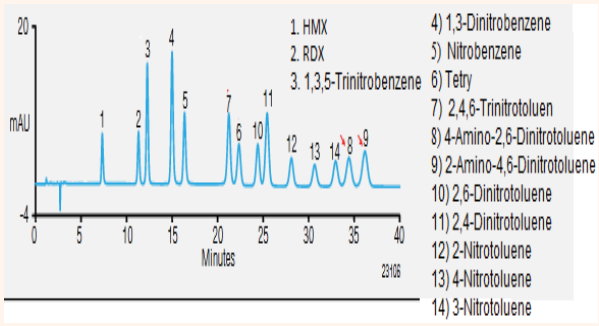


Figure 17: Separation of 14 explosives on reversed phase column. *Stationary phase: Acclaim HPLC column; mobile phase: 47:53 MeOH:H_2O. Courtesy: Thermo Fisher Acclaim Applications note.*

Reversed phase separation of 14 explosive substances obtained with a water-methanol eluent is shown in Fig. 17. It is seen that base line separation is obtained for many compounds of close chemical structures, demonstrating the efficiency of the separation procedure.

4.1.4 Ion Interaction Chromatography

In this technique, a suitable ion-pairing reagent (camphor sulfonic acid) is added to mobile phase along with a complexing agent (citrate / lactate / hydroxyl-isobutyrate); the mobile phase pH would be adjusted and the eluent would be passed through a C18 column. Mixture of metal ions e.g. lanthanides will be injected after about 30 min of equilibration of mobile phase with stationary phase. Metal ions are sorbed based on their interaction with IPR and elution is decided by ability of a metal ion to form a complex with complexing agent, e.g. hydroxyl-isobutyrate. Figure 18 shows chromatographic separation of lanthanides on a reversed phase column dynamically modified as cation exchanger using camphor -10- sulphonic acid (CSA). High resolution separation of lanthanides is important in nuclear technology for the burn-up determination of irradiated fuels and for the characterization of nuclear fuels with respect to trace constituents. A

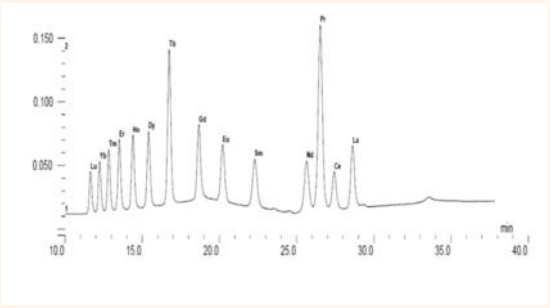


Figure 18: Separation of lanthanides by Ion Interaction Chromatography. *Column: ODS-2, HYPERSIL RP (4.6 x 250 mm) dynamically modified with CSA. Eluent: α-HIBA FR: 1ml/min.*

comparison study of different ion interaction reagents showed that reversed-phase columns modified with n-octadecane sulphonate yields good resolution for the separation of lanthanides in addition to long term retention which obviates the need to introduce the ion interaction reagent during the chromatographic separation. Separation of lanthanides on an RP column modified with n-octadecane sulphonate is shown in Fig. 19.

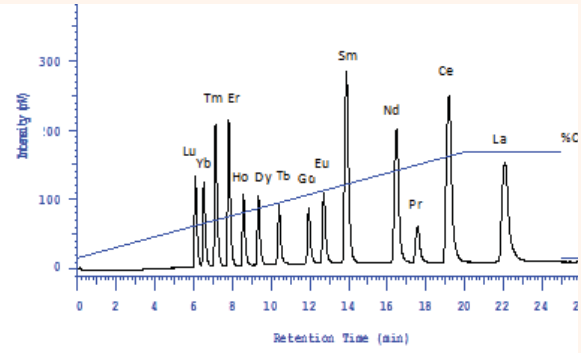


Figure 19: Separation of 14 lanthanides on a C18 column coated with n-octadecane sulphonate.*Stationary phase: Chromolith (10 cm x4.6 mm). Mobile phase: a-HIBA of pH 6.0 [C] changed from 0.03 to 0.35 M in 20 min.*

4.1.5. Size Exclusion Chromatography

Size exclusion chromatography (SEC) is separates molecules according to their hydrodynamic radius. The stationary phase consists of spherical, porous

particles with a carefully controlled pore size. Commonly used stationary phase consists of cross-linked polystyrene and porous-silica particles. The analyte molecules diffuse into the stationary phase pores depending on their size which results in thier separation. SEC can also be used to estimate the molecular weight of an unknown analyte by creating a calibration curve using known molecular weight standards. Figure 20 shows the separation of different protein molecules on a size exclusion LC stationary phase. It is seen that the analyte with larger molecular weights are eluting first while the one with the lowest molecular weight elutes the last.

4.2. Separations by Ion Chromatography

Theory of ion-exchange:

The mechanism of the separation has not completely

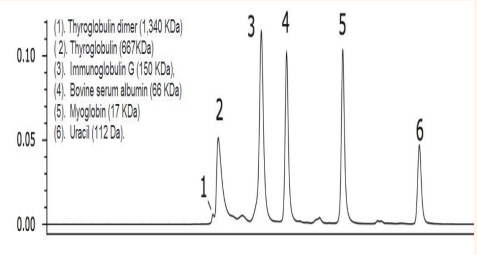


Figure 20: Separation of six proteins by Size exclusion chromatography. *Stationary phase: ACQUITY UPLC BEH450 SEC column. mobile phase: 25 mM sodium phosphate, 250 mm sodium chloride, pH 6.8 at 0.35 mL/min. Courtesy: Waters Application Note 2013.*

been elucidated this method does not provide direct information on events occurring at the surface of the stationary phase. Ion exchange is similar to sorption; however, ion exchange differs from sorption due to its stoichiometric nature. For the sake of simplicity, we consider anion exchange process. Let's say a sample anion; X^- is getting exchanged with an element ion HCO_3^-

The selective coefficient K is written as

$$K = \frac{[X^-]_{SP}}{[X^-]_{MP}} . \frac{[HCO_3^-]_{MP}}{[HCO_3^-]_{SP}} \quad \textbf{(15)}$$

where, the subscript s and m stands for stationary and mobile phases, respectively.

The efficiency of an ion as element for IC can be known as the basis of the K value. The ions that have high Selectivity Coefficient will have high elution power and they are used preferentially as eluent.

The affinity of a solute ion towards the stationary phase of the ion-exchange resin may be measured through another parameter called "weight distribution coefficient, Dg.

$$Dg = \frac{[X^-]_{SP}}{[X^-]_{MP}} \quad (16)$$

In IC, instead of Dg, we use Capacity factor or Retention factor, k'. It has a relation with K as follows:

$$k' = K . \frac{V_c}{V_m} \quad (17)$$

$$k' = \frac{[X^-]_{SP}}{[X^-]_{MP}} . \frac{V_c}{V_m} \quad (18)$$

$k'$is defined in terms of time as

$$k' = \frac{t_R - t_0}{t_0} \quad (19)$$

Where, t_R and t_0 are the retention times of the solute and void volume peaks, respectively.

Based on the above equation, we can write k' as

$$k' = \frac{V_{sp}}{V_d} . K^{1/x} . Q^{y/x} . [E]^{-y/x} \quad (20)$$

where, Q = ion exchange capacity of the resin. [E] = Eluent ion concentration.x = charge number of the eluent ion. y = charge number of the solute ion.

Considering all the constant factors, the equation can be rewritten as

$$k' = Constant.\ [E]^{-y/x} \quad (21)$$

Taking logarithm

$$log\ k' = -\frac{y}{x}.log[E] + C \quad (22)$$

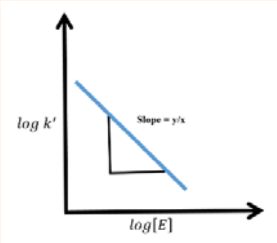


Figure 21: plot of retention factor as function of concentration of the eluent ion [E]

Slope of the strait line is proportional to the quotient of charge number of both eluent ion and sample ion. The following figures of chromatogram and its plot of log [E] Vs log k/ help in understanding the theory discussed here.

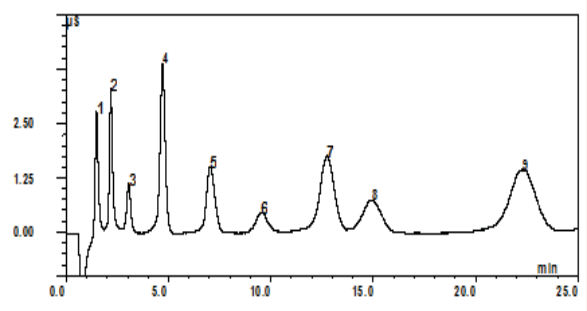


Figure 22: Separation of anions. *Col: Waters IC Pak A, Eluent: 0.8M mannitol in 6.5mM $NaHCO_3$, FR: 1mL/min. Detection: suppressed conductivity. Peaks: (1) borate (2) F^- (3) AcO^- (4) Cl^- (5) NO_2^- (6) Br^- (7) NO_3^- (8) HPO_4^{2-} and (9) SO_4^{2-} .*

Separation of anions: The separation of inorganic anions and organic anions are being separated by ion exchange chromatography employing anion exchange columns. Weak organic acid anions and very weak inorganic acid anions (borate) are separated by ion exclusion method. Majority of the

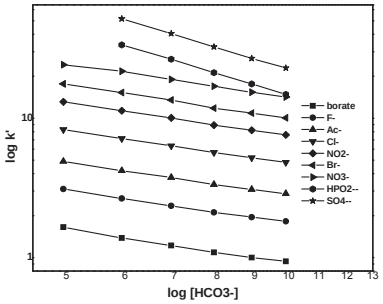


Figure 23: plot of log [HCO_3^-] Vs log k`

anion separation methods use either strong anion resin (with quaternary ammonium group) or weak anion (primary, secondary and tertiary amine group). Presently, the most common mobile phases used are hydroxide, bicarbonate, carbonate and carbonate/bicarbonate buffer solutions. These mobile phases are amenable to conductivity suppression of mobile phase and therefore, capable of achieving very low detection limit for the anions. In addition, hydroxide mobile phases can be used for concentration gradient elution, which provides high selectivity coefficient for those ions that are least retained during isocratic separation.

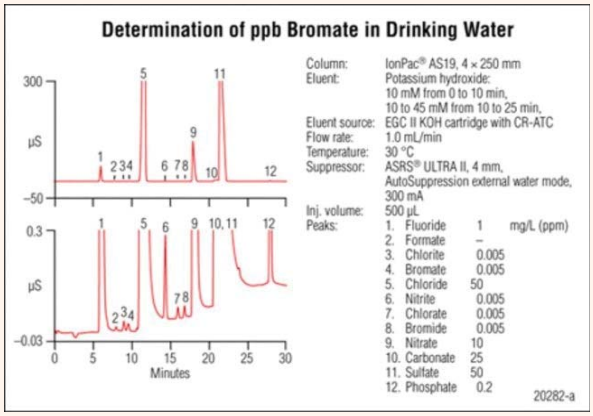


Figure 24: Separation of anions in drinking water. *Courtesy: Thermo Fisher manual.*

Separation of Cations:

Alkali and alkaline metals

Separation of metal ions by ion chromatography (IC) can be classified broadly into two categories and are (i) simple ion exchange and (ii) separation using complexing agents. In simple ion exchange separation, the metal ions to be separated are getting exchanged with the counter ions of the stationary phase. This mode of separation is widely used with conductivity detection for separating alkali and alkaline earth metal ions. Mobile phases of mineral acids and organic sulphonic acids are used for separating the alkali, alkaline earth metals.

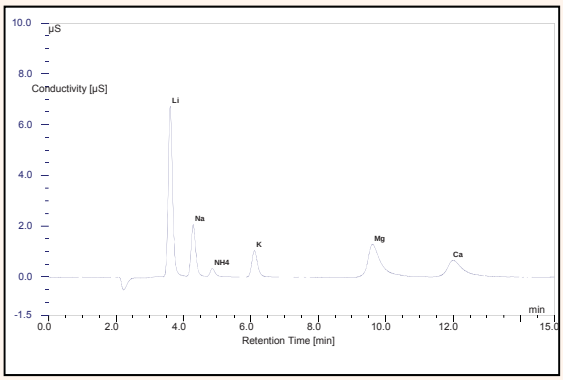


Figure 25: Separation of alkali and alkaline metals. *Column: Ion Pac CS12 Eluent: Methane sulphonic acid; Detection: Suppressed Conductivity*

Transition and inner transition metals: However, this mode of separation alone is inadequate in separating the transition and inner transition metal ions due to the similar ion exchange behaviour. Moreover, the selectivity coefficients for transition metals of the same charge do not differ significantly to enable good separation. In order to obtain a good separation among the transition metal ions, their selectivity need to be changed and such a change can be brought by adding a suitable complexing agent. In addition to the primary equilibrium between the ion exchanger and metal ions, a secondary equilibrium is established in the system due to the addition of the complexing agent and which is responsible for bringing out the desired change in the selectivity coefficients. Therefore, the use of complexing agents to the mobile phase is a known method of regulating separation. The added complexing agent decreases the effective charge of the separated cations proportionally to the corresponding conditional stability constants. While adding weak complexing agents like α-hydroxyisobutryic acid (HIBA), tartaric acid, citric acid etc., can form complex with the metal ions andbrings about considerable speed in the elution as well as change in the selectivity.

Separation of metal cations in IC can be carried out on different stationary phases including (i) using cation exchange columns with non-complexing or complexing eluents, where separation is based on electrostatic sorbate-sorbent interactions, (ii) using anion exchange columns with complexing eluents, where on-column formation of negatively charged complexes of the metal ions are formed and separation is achieved due to relative differences in their stability constants and (iii) using the chelating ion-exchange substrates as stationary phase to form kinetically labile surface complexes and retain metal ions according to the stability of corresponding complexes. The later method is known as chelation ion chromatography.

To separate lanthanides and actinides on cation exchange column, a relatively weak metal-complexing agent, usually an organic acid is used. The cation exchange column what we mention here about is high efficiency ion exchange substrates with sulphonate functional group. A similar kind of separations is provided in the HPLC separation of inner transition metals, where a column with neutral surface is dynamically modified ascation exchanger by adding a suitable ion interaction reagent in the mobile phase.

Complex formation and theory of separation: As it has been discussed in the preceding section that

complexing additives in the eluent control the retention times of metal ions and they enhance the resolution by differences in their stability constants. While separating metal ions as their complexes the retention time is decided by the interactions between (i) metal and ligand (ii) metal and ion exchanger and (iii) competing cation and ion exchanger. In conventional ion exchange chromatography, the extent of separation is measured in terms of distribution coefficient D_m, which is defined as the ratio of analyte concentration in the stationary phase and in the mobile phase at equilibrium. In ion chromatography D_m is measured in terms of retention factor.

Distribution coefficient, Dm, in a cation exchange separation with noncomplexing agent as eluent is expressed as

$$logD_m = logK_{MA} + n.log\ C - n.log[A^+] \quad (23)$$

Where, K_{MA} is the equilibrium constant (selectivity coefficient), C is ion exchange capacity of the resin, n is the absolute number of the charge of the metal ion and $[A^+]$ is the concentration of eluent cation. The equation shows that the D_m depends linearly on the eluent cation concentration $[A^+]$. This equation will not hold good in the case of transition metal ions particularly with the metal ions having same charge numbers as they have very close selectivity coefficient values. When adding complexing agents in the eluent, the metal ion forms complexes of different metal to ligand ratios. Therefore, the competing equilibrium of the complex formation needs to be considered in the equation of distribution coefficient or retention factor, which is accomplished by introducing 'complex formation coefficient, $a_{M(L)}$ and the same is expressed as

$$a_{M(L)} = 1 + [L]\beta_{ML} + [L]^2\beta_{ML2} + \cdots \quad (24)$$

where, $a_{M(L)}$ is the complex formation constant, [L]: concentration of ligand, L^{x-} , β_{ML} : formation constant for equilibrium $M^{n+} + L^{x-} \Leftrightarrow ML^{n-x}$ and βML_2: formation constant for equilibrium $M^{n+} + 2L^{x-} \Leftrightarrow ML_2^{n-2x}$

By considering this factor, the distribution coefficient of a metal ion in the presence of complexing agents is expressed as

$$logD_m = logK_{MA} - loga_{M(L)} + n.log\ C - n.log[A^+] \quad (25)$$

Metal ions can be separated on the anion exchangers also where the separation is based on the ability of these metal ions to form anionic complexes. The difference in the stability of the metal complexes and the affinity of the anionic complexes with anion exchange sites of the stationary phase decides the separation. Separation using anion exchangers is not discussed here as this presentation is restricted to the separation of metal ions on the cation exchangers.

Choice of complexing agents: To separate the transition metal ions on a cation exchanger using complexing agent, appropriate selection of the complexing agent is must. Weak organic acids are often preferred for this purpose as they form complexes with the metal ions at very low concentration level. For a set of metal ions, different complexing agents will provide different selectivity as they will have different stability constant values. The important excerpts from the literature with regard to the guidelines for separating of metal ions with complexing agents using cation exchange columns are: (i) metal ion and ligand must form anionic or neutral complexes; and (ii) the transition metal complex formed should be thermodynamically stable and kinetically labile. Fig.26 shows a typical application of a commercial cation exchanger column (sulphonic acid functional group) used for the rapid separation of uranium and thorium using 2,6-pyridine dicarboxylic acid (PDCA) and nitric acid as eluent whereas Fig. 27 shows chromatographic separation of transition metals on a reversed phase column dynamically modified

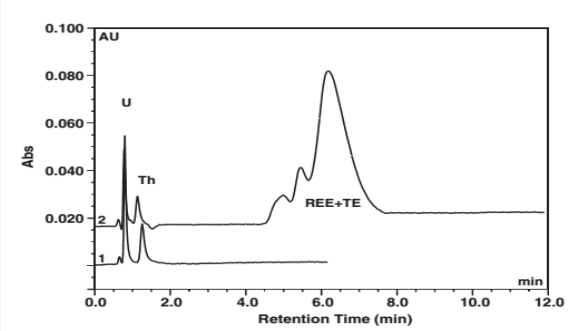


Figure 26: Chromatograms obtained for (1). Standard solution of U and Th (2).an effluent water sample. *Column: ICPakCation, Eluent: PDCA and HNO3. Detection: as Arsenazo III complex at 665 nm.*

as cation exchanger using camphor -10- sulphonic acid (CSA). Ion exclusion chromatography is a useful technique for the separation of weak inorganic and organic acids, alcohols, aldehydes, amino acids and carbohydrates. The separation is effected by three phenomena and they are (i) Donnan exclusion (ii) Steric exclusion and (3) Adsorption. The columns used in this case is a fully sulphonated high cation exchange resins.

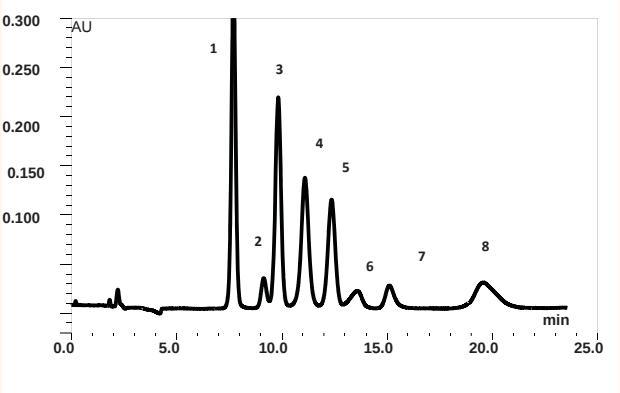
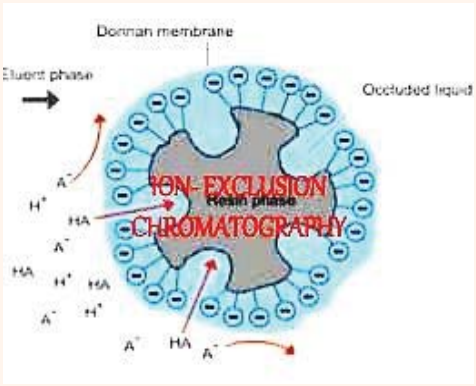


Figure 27: Separation of transition metal ions using tartaric acid and mandelic acid. *Peaks (1) Mn^{+2}; (2) Cd^{+2}; (3) Co^{+2}; (4) Ni^{+2}; (5) Zn^{+2}; (6) Fe^{+3}; (7) Pb^{+2}; (8) Cu^{+2} (conc. 2 ppm each). Column: C-18 ODS Hypersil mL/min.; Detection: 10^{-4} M PAR as PCR and detected at 520 nm.Source: S. Jeyakumar et al. (unpublished work).*

4.2.1 Ion exclusion chromatography According to the reported retention model, in the vicinity of -SO_3^- H^+ group a layer of water gets formed and this layer is called as hydration shell. This makes some of the water molecules are there in the higher state of order compared with the water molecules in the mobile phase. A negatively charged layer nalogous to Donnan membrane forms an



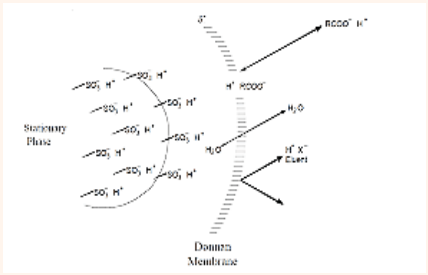


Figure 28: Ion exclusion retention model based on Donnan exclusion theory

interface between the hydration shell and the bulk mobile phase. This interface only permits the undissociated compounds to enter into the pores of the resin. Due to this the non-ionic interactions between solute and the stationary phase occur which results into separation. The Donnan exclusion mechanism causes stronger acid anions to elute before weaker acid anions according to increasing pKa; for example, acetate (pKa=4.56) elutes before propionate (pKa=4.67).

4.2.2 Ion-Pair Chromatography (IPC)

Neutral and low polarity columns cannot be used for separating ionic or polar compounds. However, IPC makes it possible to separate both the anions and cations on a neutral stationary phase like reversed phase columns by adding an appropriate ion-paring agent in the mobile phase. The main separation mechanism in Ion-Pair Chromatography is adsorption. The stationary phase consists of neutral porous divinylbenzene resin of low polarity and high specific surface area. The chemically bonded silica phases of the octyl or octadecyltype (ODS) with an even lower polarity columns can also be used. The selectivity of the separator column is determined solely by the mobile phase. Besides an organic modifier, an ion-pair reagent is added to the eluent depending on the chemical nature of the analytes. IPC method is particularly suited for the separation of surface-active anions and cations as well as transition metal complexes.

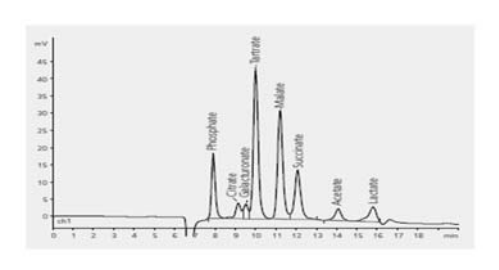


Figure 29: Separation of organic acids by ion exclusion method. *Column: Ion exclusion HPLC column (H^+ form), 25 cm x 8 mm; Mobile Phase: 1.9 mM H_2SO_4 + 2% acetonitrile in ultra-pure water, Col. Temp.: 75°C; Flow Rate: 0.6 mL/min; Det.: Conductivity. Courtesy: Merck.*

Ion-pairing chromatography (IPC) can be used for both positively and negatively charged analytes. Typically an ion-pair reagent has both negative and positive ionic parts. One of the ions will have a long alkyl chain or aromatic moiety so that it can interact with the neutral surface of the column and projecting the ionic part at the top or upward direction. For instance, sodium salt of octane sulphonic acid has an ionic base of octane sulphonate (negative charge). So this reagent is called negatively charged ion-pairing agent and is used for separating positively charged analytes. Whereas quaternary ammonium (NR_4^+) salts have positively charged ionic base and they are used for separating negatively charged analytes.

$A^- + R^+ \Leftrightarrow A^-R^+$ Eg. Alkylsulfonates (R-SO_3^-)

where, A^- is the negatively charged part of the analyte molecule, R^+ is the positively charged part of the IPR molecule and A^-R^+ is the ionpair during the separation.

$B^+ + R^- \Leftrightarrow B^+R^-$ Eg. Quaternary ammonium (R_4N^+)

where, B^+ is the positively charged part of the analyte molecule, R^- is the negatively charged part of the IPR molecule and B^+R^- is the ionpair during the separation.

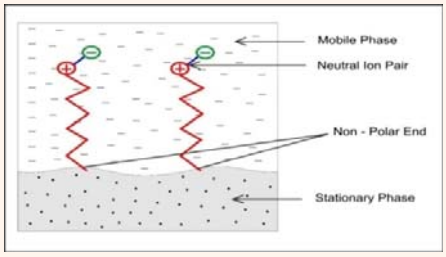


Figure 30: Interaction of Ion-pair reagent with column

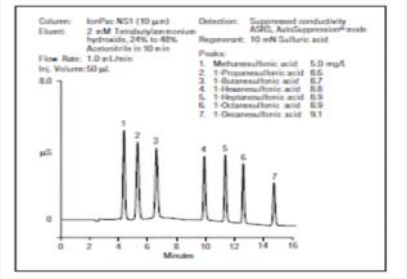


Figure 31: separation of organic acids using IPR

Separation of organic acids on a polymeric neutral column (IonPac NS1) with TBA-OH ion-pairing agent is a typical example (Fig.31).

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Fundamentals of Liquid Membrane Separation

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1. Introduction

Separation in chemical industry is not a new word, and sometimes, it may not need an introduction. The terminologies explaining the separation phenomenon may vary depending on the type of readers and the context of the article. For chemists and chemical engineers, a separation process is a method that segregates a solid mixture or a solution mixture having different substances into its individual constituents or a mixture of desired product from the rest of the constituents. In few cases, a separation process may fully divide the mixture into pure constituents. Any separation process exploits the differences in the chemical or the physical properties (such as size, shape, mass, density, chemical affinity, etc.) between the constituents of a mixture. Separation processes are often classified according to the type of methodologies used for separation. In several cases, if no single methodology accomplishes the desired separation, multiple operations are often combined to achieve the same. The traditional chemistry or chemical engineering methods of separation and purification include distillation, crystallization, adsorption, ion-exchange, solvent extraction, and membrane processes. Detail discussions on all these processes are out of scope of this article, and therefore, are not included. However, a brief about the fundamentals of solvent extraction is given here which is desired for understanding the liquid membrane separation processes.

2. Liquid-Liquid Extraction

Liquid-liquid extraction, very often known as solvent extraction, is a separation technique that works on the principle of distribution of a species or a compound or a solute between the two immiscible liquid phases. The solvent extraction systems can be thermodynamically explained with the help of phase rule, which is usually stated as:

$$P + V = C + 2 \qquad (1)$$

where P, V and C denote the number of phases, variances and components, respectively. In general a binary liquid-liquid distribution system has two phases, one is the organic phase and other is the aqueous phase (P =2), and contains three or more components (two solvents and one or more solutes). When a system contains only one solute, the components become 3 (C = 3), and according to the phase rule the variance is three. It means by keeping any two variables constant the system can be defined by the third variable. In other words, at fixed temperature and pressure, if the concentration of solute in the aqueous phase is known, the concentration of solute in the organic phase will remain fixed (or constant). In other words, at a given temperature and pressure, the concentration of solute in the organic phase and in the aqueous phase will be constant, and this is well known as the "*distribution law*". Let us assume the distribution of a metal ion between the aqueous phase and the organic phase. In such case, following the equilibrium reaction can be given.

$$M_{(aq.)} \leftrightarrows M_{(org.)} \qquad (2)$$

where, the subscripts (aq.) and (org.) represent aqueous and organic phases, respectively.

According to the distribution law, the distribution coefficient (K_d) is represented as,

$$K_d = [M]_{(org.)} / [M]_{(aq.)} \quad (3)$$

The above distribution coefficient equation is valid for the ratio of a given species in the organic phase to the same species in the aqueous phase. Since in the case of metal ions, which are charged species, they appear in different species in the aqueous phase, therefore, above equation may not be valid. To avoid this, a simple term "*distribution ratio (D)*" is very often used for metal ion distribution measurement, which is defined as the total concentration of the metal ions in all forms in the organic phase to the total metal ion concentration in all forms in the aqueous phase.

$$D = [M]_{(org., total)} / [M]_{(aq., total)} \quad (4)$$

The distribution of neutral species, for example molecular iodine, between the aqueous phase and organic phase (carbon tetra chloride) is well known experiment we perform in the laboratory. This system is simple and can be explained based on the difference in solubility of iodine in CCl_4 and water. Since we get the *D* values of iodine in CCl_4 as 80, we can confidently say that iodine is 80 times more soluble in CCl_4 than in water. However, this may not be the case for metal ions as they are charged species. The solubility of the charged metal ions in the organic solvents is very less as they tend to remain in the aqueous phase due to ion-dipole interaction (metal ions are hydrophilic). For the extraction of metal ions in the organic phase, therefore, the charge on the metal ions must be neutralized so as to enhance its solubility in the non-polar organic solvents. Therefore, a suitable ligand is generally added in the organic phase which upon complexation with metal ions forms neutral hydrophobic species which is then extracted in the organic phase. In such cases, the extraction of metal ions may follow one of the following extraction mechanisms.

(i) Solvation: The extraction of metal ions by neutral ligands is followed by solvation mechanism. We know that when a metal ion in present in the aqueous phase, its primary coordination sphere is occupied by the water molecules, which makes the metal ions hydrophilic and will not allow it to go into the organic phase. In such cases, a neutral ligand makes complex with the metal ion by replacing the water molecules from its co-ordination sphere, therefore, making the complex hydrophobic which is then transferred into the organic phase. Since the complexation occurs via donor atoms of the ligands such as '*O*' or '*N*', which solvates the coordination sphere of the metal ion, the method is known as solvation. Here the charge on the metal ions is not neutralized by the ligands but by the counter-anions which may be present in the inner sphere or outer sphere of the overall complex. The well known example is the extraction of U(VI) by tri-*n*-butyl phosphate (TBP) from nitric acid medium as described by the following equilibrium reaction.

$$UO_2^{2+}{}_{(aq.)} + 2NO_3^-{}_{(aq.)} + 2\ TBP_{(org.)} \leftrightarrows [UO_2(NO_3)_2 \cdot (TBP)_2]_{(org.)} \quad (5)$$

In above equilibriumreaction, the overall six available coordination sites of UO_2^{2+} cations are occupied by the two TBP molecules and two nitrate ions.

(ii) Chelation: In this method, a chelating ligand is utilized as the extractant, which forms a chelate complex with the metal ion, thereby making the metal complex hydrophobic which is then transferred into the organic solvent. The separation of nickel from aqueous solution by dimethylglyoxime (DMG) ligand comes under this category. Here DMG forms a nickel bis(dimethylglyoximate) chelate complex (bright

pink colour) which is then extracted into the organic solvent.

$$Ni^{2+}_{(aq.)} + 2\ DMG_{(org.)} \leftrightarrows [Ni(DMG)_2]_{(org.)} + 2\ H^+_{(aq.)} \quad (6)$$

In aboveequilibriumreaction, the overallcomplexisneutral as 2 units of charge on Ni^{2+} cation isneutralized by the –OH group of DMG moleculeafterliberating protons.

(iii) Ion-pair extraction: This type of extraction mechanism is seen in the liquid ion exchangers, such as quaternary ammonium salts. Here the ionic species of the metal ions form ion pair with the bulky anionic part of the ligand, which then becomes soluble into the organic phase. For example, the separation of uranium with aliquot 336 (tri(octyl)methyl ammonium chloride) which is immiscible with water but miscible with polar organic solvent such as chloroform.

$$[UO_2Cl_2]^{2-}_{(aq.)} + 2\{[R_4N]^+\cdot[Cl]^-\}_{(org.)} \leftrightarrows \{2[R_4N]^+\cdot[UO_2Cl_2]^{2-}\}_{(org.)} + 2Cl^-_{(aq.)} \quad (7)$$

Here uranium at 6 M HCl forms anionic $UO_2Cl_4^{2-}$ species, which forms ion-pair with the two aliquot 336 molecules by replacing Cl^-ions. The resultant ion-pair complex is then extracted into the chloroform phase. Since there is an exchange of ions in this method, this mechanism is also referred to as ion-exchange mechanism.

The scientific principles that govern the separation of metal ions in the solvent extraction are: (i) the chemical reaction between the metal ions and the ligand at the aqueous and organic phase interface, (ii) the kinetics of the chemical reaction at organic-aqueous interface, and (iii) the fluid mechanics and mass transfer of the metal/ligand complex (or any species to be separated) from the aqueous phase to the organic phase. The principles that govern the separation of metal ions in solvent extraction are essentially same to that observed in liquid membrane. Apart from solvent extraction principles, the other important principle that governs the permeation of species in the liquid membrane is the diffusion of the species inside the liquid membrane, and the path length that the species travels with in the membrane. Since a brief of solvent extraction mechanism has been explained in this section, details about the liquid membrane separation process is described in the following section.

3. Membrane Separation Processes

In any membrane separation process, two bulk phases, one is the feed phase and other is the receiver phase, are physically separated by a membrane. In this case, one or more of the species from the feed mixture are selectively allowed to pass through the membrane. In a broad sense, the separation of any species through a membrane is fundamentally described by one of the following mechanism:

(i) Size exclusion,

(ii) Donan exclusion, and

(iii) Diffusion.

A brief note about the above membrane separation mechanism is given in the following section. During membrane separation process by any of the above mechanism, the driving force to the permeating species from one side to other side of the membrane is provided by: (i) the trans-membrane hydrostatic pressure, (ii) osmotic pressure, and (iii) the concentration gradient across the membrane. For example, in size exclusion separation process (or simply filtration), the trans-membrane hydrostatic pressure is the main factor that governs the efficiency of the process. Similarly, the permeation taking place in the biological membranes is due to osmotic pressure. On the other hand, the permeation in liquid membrane is governed by the concentration gradient of the species at two sides of the membrane.

(i) Separation based on size exclusion principle: As

the name indicates, these membrane separation works on the principle of size exclusion, where bigger size molecules are retained but the smaller size molecules are allowed to pass through the membrane filters. Such membrane processes are, therefore, simply known as filtration process. Depending upon the pore size of the membrane filters the processes are classified as microfiltration, ultrafiltration or nanofiltration. A brief about the different types of filtration membranes, their pore size and their applications are depicted in **Figure 1**.

(ii) Separation based on Donan exclusion principle: The Donan effect (also known as Donan law, Donan equilibrium, or Gibbs–Donan equilibrium) is a name for the diffusion of charged particles through a semi-permeable membrane. This type of process is seen in the solution which contains a large size charged species (positive or negative) that is unable to pass through the membrane but its small counter ion passes through it, thus creates an uneven electrical charge across the membrane surface. The electric potential arising between two phases, separated by the semi-permeable membrane, is called the Donan potential. For example, the large anionic proteins in blood plasma are not permeable to blood capillary walls, but other small cations like K^+ and Na^+ permeates through the wall. The other example is the separation of sodium ion from the water soluble dyes. It should be noted that dyes are generally sodium salts of large anionic molecules. When an aqueous solution of such dyes is separated by a semi-permeable membrane and an electrical potential is applied across the membrane, the sodium ion penetrates through the membrane, where as the large dye anion is retained. However, it is not possible fora large number of sodium ions to be separated from dye anion as this would result in an excess positive ion at one side of the membrane and an excess negative ion on the other side. This would be against the rule of electrochemistry. To retain the electrical neutrality, water molecule is split, the OH^- ion will migrate with Na^+ ion and equivalent number of H^+ ions will associate with the

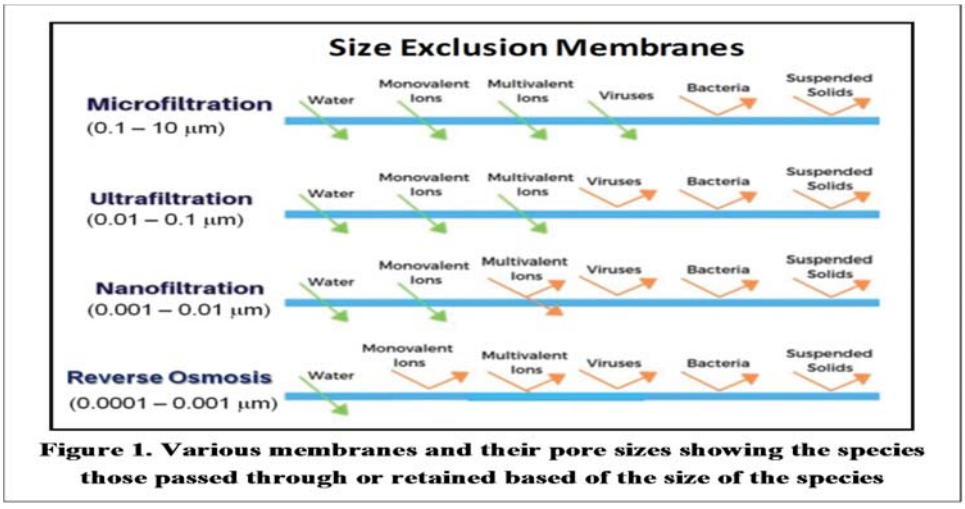


Figure 1. Various membranes and their pore sizes showing the species those passed through or retained based of the size of the species

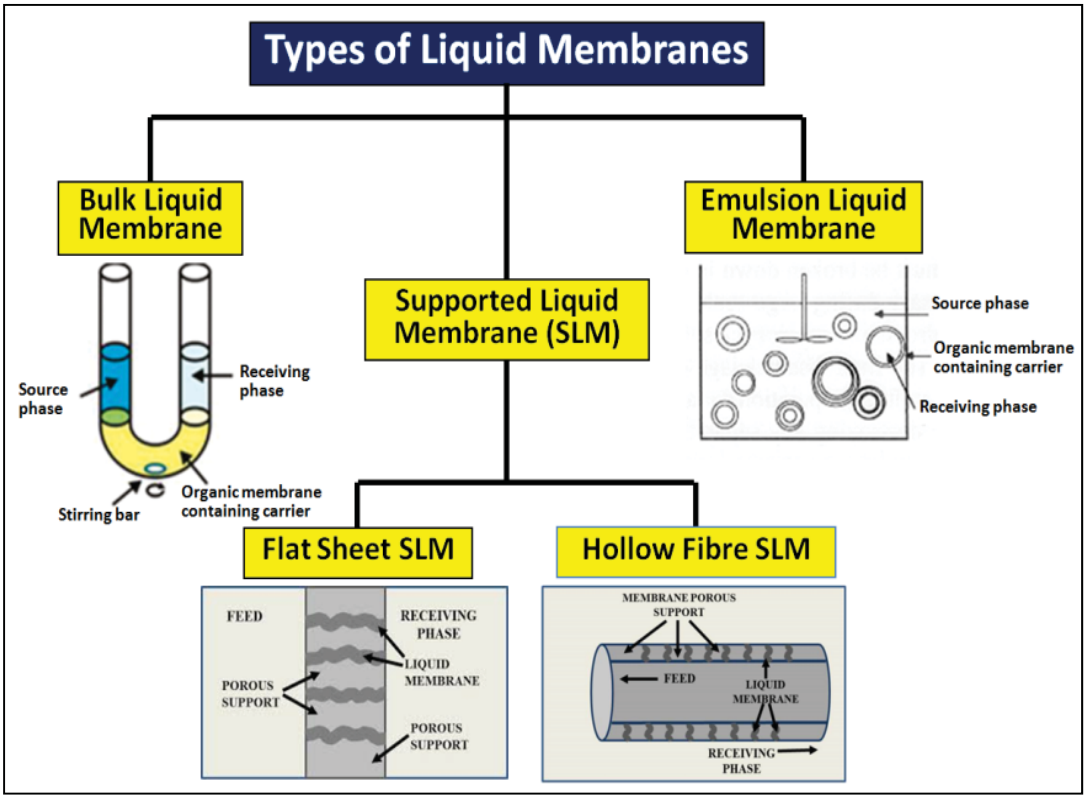


Figure 2. Representation of different types of liquid membranes

dye anion. The result is high concentration dye acid in one compartment and that of sodium hydro-oxide in the other.

(iv) ***Separation based on diffusion principle:*** In case of membrane operating on diffusion mechanism, the molecules or the species are first absorbed or complexed on one side of the membrane surface. This results in concentration of the species on one side of the membrane surface as compared to the other side. This will cause diffusion of the species fromone side to the other side surface of the membrane, thus the species gets permeated from one side to the other side of the membrane. The best example of diffusion controlled process is seen in the liquid membrane separations, which is the interest of this article.

4. Liquid Membrane Based Separation

Pressure driven membrane systems such as reverse osmosis, ultrafiltration and microfiltration are the industrial workhorse for treatment of industrial liquid waste, particularly, aqueous waste. These membrane systems differentiate between various species by the principle of size exclusion which renders their poor selectivity, particularly for the separation of metal ions. A liquid membrane, on the other hand, gives very high selectivity as it employs ligands which are selective for a given metal ion. Here a ligand solution immiscible with water phase (known as carrier) acts as a liquid membrane, which selectively complex the target metal ion on one side of the membrane. Subsequently, the metal-ligand complex travels

across the membrane due to diffusion, and reaches to the other side of the membrane. Such transport processes are, therefore, referred to as "*carrier mediated transport*" or "*carrier facilitated transport*" processes.

A liquid membrane is basically consists of a water immiscible organic layer (usually a solution of a suitable ligand) which acts as a barrier in between the two aqueous solutions, one is the source (or feed) phase containing a mixture of metal ions, while the other is the receiver (or strip) phase where the metal ion of interest gets concentrated preferentially. The liquid membrane may be a stirred organic phase separating the aqueous feed and the receiver phases (know as Bulk Liquid Membrane), a dispersion of water (receiver phase) containing oil droplets in aqueous feed phase (known as Emulsion Liquid Membrane), or a water immiscible organic phase immobilized in the pores of a microporous polymeric film (which acts as an inert support) separating the feed and the receiver phases (supported liquid membrane (SLM)). When a flat sheet membrane support is used the method is known as flat sheet SLM. Similarly, if hollow fibre membrane is used as support the method is described as hollow fiber SLM. The classification various types of liquid membrane are shown in Figure 2. The emulsion liquid membranes have very high surface area per unit volume and extremely small membrane thickness. Consequently, fast separation and accumulation of the separated species inside the emulsion ventricles takes place. However, the emulsion globules have to be prepared before the separation process and their stability need to be good enough to avoid the leakage of strip solution from inside the emulsion globules. Since the separated metal ions are collected after breaking these emulsion globules, they should not have large stability so that they could be destroyed after the separation. As a result, the process has to use several unit operations and becomes technologically not very attractive. In SLMs, the organic liquid is usually filled in small pores of a polymer support, used to partition the feed and the receiver phases, held by capillary forces. If the organic liquid is immiscible with the aqueous feed and receiver phases, the SLM can be used for the selective transport of the solute from one aqueous (feed) phase to the other (receiver). Relatively small volume of the organic components in the membrane offers the advantage of possible usage of expensive ligands as the carrier in SLM. At the same time, extremely low solvent inventory in SLM makes the technique eco-friendly.

5. Carrier Facilitated Transport in Liquid Membrane

The basic mass transport mechanism in liquid membranes has been described as '*carrier mediated transport*' of the solute in which a carrier ligand transports the metal ion from one side to other side of the membrane through a complexation, diffusion, de-complexation, and diffusion cycle. A schematic representation showing the transport process of metal ion by a neutral ligand is shown in Figure 3. In the facilitated transport process, the transport of a species (for example metal ion) from feed to receiver side takes place in four steps. *Step I:* The metal ion from the bulk feed comes to the aqueous diffusion layer near the membrane and finally reaches to the surface of the membrane, and gets complexed with carrier ligand present in the membrane, forming a metal-ligand complex (ML). *Step II:* The ML complex then diffuse from feed side to the receiver (or strip) side with in the membrane. This diffusion of the ML complex is purely due to the concentration gradient between the two sides of the membrane as per the Fick's law described later. *Step III:* Subsequently, the ML complex gets dissociated at the membrane- receiver phase interface when the metal ion is released into the strip solution, and the free ligand being insoluble in

aqueous phase remains in the membrane phase. *Step VI:* Finally, the free ligand diffuses back from received side of the membrane to the feed side of the membrane. This diffusion also takes place due to negative concentration gradient of the ligand at the two side of the membrane.

Consider the equilibrium reaction given in Figure 3 is taking place at the membrane –aqueous phase interface. Here the condition in the feed solution is maintained such that the equilibrium reaction is favoured and ML complex is formed instantaneously on the fee-membrane interface. This mean, all the ligands at this interface will be complexed with the metal ions forming ML, and the free ligand concentration will be very low. On the other hand, the conditions in the strip side solution are maintained such that the equilibrium reaction undergoes back reaction, resulting in dissociation of the ML complex. Due to this effect, the concentration of ML complex will be very low and free ligand concentration will be very large on the strip side of the membrane. This will result into positive concentration gradient of the ML complex at the feed side, which will diffuse to the strip side. Similarly, the concentration gradient for the free ligand will be positive at the strip side, which will diffuse to feed side to complete the cycle. It is important to note that the diffusion of the ML complex from feed side to the strip side is always slower than the diffusion of the free ligands from strip side to the feed side. This can be well understood by the Wilke–Chang empirical equation that describes the diffusion coefficient (D_o) of the species in the liquid membrane as:

$$D_o = 7.4x10^{-8}\left(\frac{\chi^{0.5}M^{0.5}T}{\eta V_m^{r0.6}}\right) \qquad (8)$$

where, M, χ and η are the molecular weight, solvent association parameter and the viscosity of the solvent, respectively, V_m is the molar volume of the carrier and T is the temperature. Since molar volume of the ML complex will be always larger than the free ligand, the back diffusion of the free ligand from strip side to the feed side will be faster, and therefore, the ligand at the feed side will always be available for complexing a fresh metal ions.

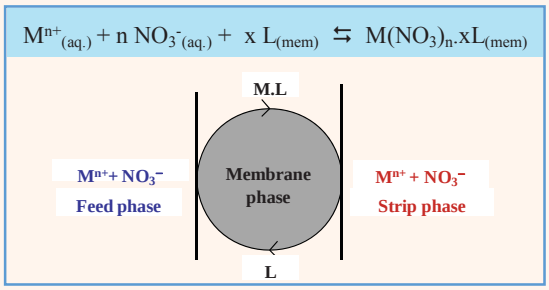


Figure 3. Schematic representation showing the transport process of metal ion by a neutral ligand where co-transport of counter anion takes place.

6. Transport Equations in Liquid Membrane

Transport equations in liquid membrane are obtained by soling the equilibrium concentrations of the permeating species at two sides of the membranes, *viz.* Feed side and strip side. As described in Figures 3, the quantitative description of the carrier mediated transport requires a detailed knowledge of the following steps:

(i) Diffusion of the metal ion in the aqueous boundary layer near the membrane surface on the feed side,

(ii) Reversible chemical reaction taking place at the aqueous feed-membrane interface,

(iii) Diffusion of the metal-carrier complex in the membrane phase, and

(iv) Dissociation reaction of the metal-carrier complex at the membrane-aqueous strip interface.

The basic mathematical relationships for the permeation of metal ion in the facilitated membrane transport have been derived by few simple

assumptions. Usually, it is assumed that the chemical reaction between the metal ions and the ligand occurs very fast (relative to the diffusion processes) at the aqueous-membrane interfaces (both feed-membrane as well as membrane-receiver). It implies that the local chemical equilibrium always occurs at the aqueous-membrane interface, and the metal ion transport rate is determined by the diffusion of the metal/ligand complex in the liquid membrane phase. Therefore, the fundamental equation that governs the transport of metal ion in liquid membrane is governed by the diffusion law.

According to the Fick's first Law of diffusion, the flux (J) of the permeating species in the membrane phase is given as:

$$J = -\frac{\partial C}{\partial t} \cdot \frac{V}{A} \qquad (\text{mg/cm}^2\text{/s}) \qquad (9)$$

where, V is the volume of the feed solution, C is the concentration of the metal ion and A is the surface area of the membrane. Since the term flux depends on the concentration of species present in the feed solution, a concentration independent term permeability coefficient (P, cm/s) is very often used to describe the efficiency of the membrane processes. This term is obtained by dividing the flux with the concentration. Therefore, flux can also be written as:

$$J = P \cdot C \qquad (10)$$

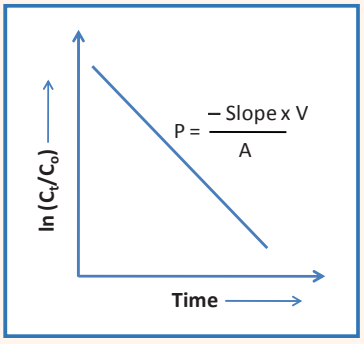
Therefore, equation (1 and (2) can be equated as:

$$P \cdot C = -\frac{\partial C}{\partial t} \cdot \frac{V}{A} \qquad (11)$$

$$\int \frac{\partial C}{C} = -P\left(\frac{A}{V}\right) \int \partial t \qquad (12)$$

$$\ln\left(\frac{C_t}{C_o}\right) = -P\left(\frac{A}{V}\right) t \qquad (13)$$

in the feed solution at time t (C_t) to its initial concentration (C_o) is plotted with time t, and the value of P is obtained from the slope of linear fit of the plot, since the experimental parameters such as feed volume (V) and surface area of the membrane



As mentioned above, the diffusion of the metal/ligand complex inside the membrane phase is the rate determining step. According to Fick's Law, the flux of any diffusing species is given as:

$$J = -D_o \frac{\partial C}{\partial x} \qquad (14)$$

where, D_o is the diffusion constant of the permeating species, C is the concentration and x is the path length (or thickness in the case of membrane). In case of metal ion transport in liquid membrane, the above equation can be modified as:

$$J = -D_o \cdot \frac{[ML]_{f,i} - [ML]_{r,i}}{d_o} \qquad (15)$$

where, the term $[ML]_{f,i}$ and $[ML]_{r,i}$ is the concentration of the metal/ligand complex at membrane feed interface and receiver interface, and d_o is the thickness of the membrane. In liquid membrane, an extractant dissolved in suitable solvent is filled in the membrane support pores, which acts as liquid membrane. Depending on the properties of the ligands for a given metal ion, the condition in feed solution is kept such that equilibrium reaction (**Figure 3**) is favoured, and metal/ligand complex formation occurs instantaneously at the feed-membrane interface. Just opposite condition is maintained in the receiver phase of the membrane where the metal/ligand complex breaks instantaneously. As a results, the component $[ML]_{f,i}$will always remain higher than the component $[ML]_{f,i}$in equation (15). Due to this reason, the term ΔC will always remain positive and

transport will occur till all the metal ions in the feed is transported to the receiver phase. This is termed as *uphill*" transport as the metal ions is transported through the membrane against their own concentration. The driving force in such processes is provided by the concentration gradient of the metal/ligand complex at the two sides of the membrane surface not the concentration of metal ions in the bulk.

Since it is clear from the diffusion law that the permeation of the species through the membrane will depend on the diffusion coefficient of the species in the membrane phase (D_o), it is important to understand the factors that affect the D_o. According to the Einstein-Stoke equation,

$$D_o = \frac{k \cdot T}{6 \pi \eta r} \qquad (16)$$

where, k is the Boltzmann constant, T is the absolute temperature, η is the viscosity o the medium and r is the size (radius) of the diffusing molecules. It is clear from the above equation that for a given diffusing species, the D_o value can be enhanced by reducing the viscosity of the solvent. It is for this reason, it is advised to use low viscous solvent for liquid membrane, and therefore, most of the ligands are diluted (or dissolved) in organic solvent of lower viscosity such as dodecane, kerosene, etc. The other important parameter in the diffusion equation is the thickness of the membrane. For highest transport, the membrane thickness should be less. In supported liquid membrane, the thickness of the membrane is basically the thickness of the membrane support where ligands solutions are impregnated into the pores of the membrane. Therefore, the thickness of the membrane can be controlled by choosing the membrane support having optimum thickness and physical stability.

It is now clear from the above discussions that for an optimum transport of metal ion in liquid membrane, one should focus on the following parameters. (i) The carrier ligand or the extractant should be selected such that it forms a reversible complex with the target metal ion, and over all ligand solution (that is membrane phase) should have minimum viscosity, (ii) The carrier ligand should be selective for the given metal ion, it should have large distribution ratio for the target metal ion at a given aqueous feed condition, and should have very low distribution ratio at a given receiver phase condition, and (iii) Membrane surface area should be large, and membrane thickness should be low. By optimizing above parameters, efficient transport of the metal ions in liquid membranes can be achieved.

7. Experimental Procedure for SLM studies

As shown in **Figure 4**, the experimental setup for SLM studies is simple. Experiment is generally performed with a two compartment cell having flanges where the membrane support can be fixed dividing the two compartments. The capacity of each compartment, one for feed and other for receiver phase, may be of 10 – 50 mL capacity. The membrane support is an inert polymeric membrane having pore size in the range of 0.05 – 0.5 μm having sufficient porosity. Use of circular membrane filters made up of PTFE, PP and PSF are very commonly used as membrane support. Thickness of the membrane is other important parameter, as discussed above, and it should have an optimum membrane thickness so as to avoid physical breaking during the experiment. The membrane support must by hydrophobic to avoid the direct contact of aqueous phase and to avoid the channel formation which otherwise may cause mixing of the aqueous solutions in the two compartments. At the same time, the hydrophobic membranes will help in holding the ligand solution, which is generally water immiscible organic solvent.

For SLM studies, the membrane supports are soaked by dipping in the ligand solution of required

concentration. The excess carrier solution from the surface of the membrane is then removed by wiping carefully with a tissue paper. Sometimes, the soaked membrane are washed with water current to remove the excess of ligand solution present on the surface. The membrane support filled with the carrier ligand is mounted between the two compartment of the transport cell which separated the feed and strip phases. The feed solution containing metal ions (or species need separation), and the strip solution (receiver solution) are filled in the respective compartments of the cell. The solutions in the two compartments are stirred suitably. The transport of the metal ion is then estimated by taking out suitable volume of samples from both the compartments at regular intervals. The cumulative percent transport (%*T*) of the metal ions at any given time *t* is calculated as:

$$\%T = \left(\frac{C_{f,o} - C_{f,t}}{C_{f,o}}\right) \cdot 100 \qquad (17)$$

where, $C_{f,o}$ and $C_{f,t}$ are the concentrations of metal ion in the feed at $t = 0$, and at time t. The permeability coefficient of the membrane is also obtained experimentally by plotting the equation (13) described in the earlier section.

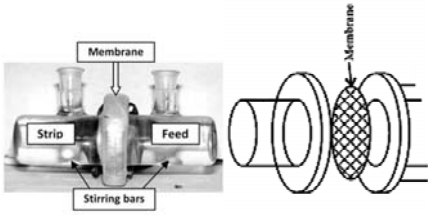
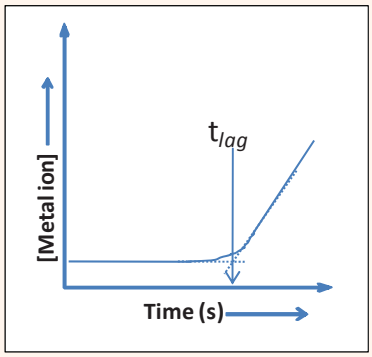


Figure 4. Experimental setup for SLM studies

One of the important parameter that is obtained experimentally is the diffusion coefficient (D_o) of the diffusing species (or metal/ligand complex) in the liquid membrane phase. As described in the previous section, this value can be calculated theoretically by using Wilke–Chang empirical equation (8). However, several parameters in Wilke–Chang equation is not known or sometimes it becomes difficult to calculate them. Therefore, a simple experimental method is used to obtain the D_o value using time-lag method. In time-lag method, the transport of metal ion (or any other species) is monitored as a function of time, and the time at which the metal ion is detected into the receiver solution is noted. From this time, the Do values are calculated using the formula:

$$D_o = \frac{d_o^2 \cdot \epsilon}{6\, t_{lag}} \qquad (18)$$

where, d_o, ε and t_{lag} are the membrane support thickness, membrane porosity and time obtained from the graph. Thus,the diffusion coefficient of the permeating species can be obtained experimentally.



8. Stability of Supported Liquid Membrane

We know by this time that the supported liquid membranes are basically impregnated ligand solutions which are held inside the membrane pores by capillary action. Despite the several advantages of SLM based separation, these membranes are not used at industrial scale. The major reason for this is the membrane stability or the lifetime, which is in generally very low for a good commercial application. Instability of SLMsis due to the loss of carrier and / or membrane solvent from the membrane phase.Depending on the amounts of carrier and solvent lost from the support pores, the solute flux decreases, and when all liquid

membranephase is lost, the membrane breaks down and a direct transport between the two phases adjacent to the liquid membrane may takes place with a complete loss of selectivity. The reason for the loss of carrier and or membrane solvent from the support can be due to:

(i) Pressure difference over the membrane,

(ii) Solubility of carrier and membrane solvent in adjacent feed and strip solutions,

(iii) Wetting of support pores by the aqueous phases,

(iv) Blockage of support pores by precipitation of the carrier or by water,

(v) Emulsion formation of the LMphase in water induced by lateral shear forces, and

(vi) Nature of the organic solvent used for dissolving the ligand.

The above mentioned reasons for SLM stability are self explanatory. Sometimes any one of the above described reasons or a combination of more than two reasons may be responsible for the SLM instability. For example, if pressure difference across the membrane exceeds certain limit, it will drag out the carrier filled in the pores by capillary force. Similarly, if the carrier ligand is water soluble, it will be slowly dissolved in the feed and strip phase resulting in loss of the membrane. Stability will also depend on the wettabilty of the membrane support which may cause water pass through it by making water channels. Wetting phenomenon is defined in terms of contact angles of aqueous drops lying on membrane surface, and higher the contact angle higher will be hydrophobicity of the surface. At the same time, membrane should be able to wet (or soak) the hydrophobic ligand solution to make a stable SLM. The stability of the SLM will also be affected by the formation of coagulated species on the surface which will block the pores. This effect is seen for the ligands which forms third-phase at the given feed condition. Sometimes if the string speed in feed or strip side are very high, this will create a shear force at the membrane surface; as a result, the ligand solution will come out of the pore by forming emulsion. Studies have shown that the stability of the SLM is greatly influenced by the viscosity and miscibility of the membrane phase diluent. While chloroform is volatile, diluents such as nitrobenzene react with nitric acid leading to its elimination from the membrane pores. Keeping above discussions in mind, one can easily deal with the stability issue in the case of SLM.

9. Advantages and Disadvantages of SLM

The SLM technique is generally compared with that of solvent extraction as both the techniques use the principle of solvent extraction with the use of selective ligands. Few advantages of SLM technique are:

(i) Extraction and stripping processes in single unit. Unlike conventional solvent extraction where one needs to extract and then strip the extracted species back, in SLM pure product is directly obtained in the strip phase.

(ii) Low ligand inventory. The ligand invitatory in SLM are extremely low. Therefore, use of expensive and exotic ligands in SLM will be a judicious choice.

(iii) Low secondary waste generation. Generation of secondary waste in terms of organic solvent is extremely low in SLM as compared to conventional solvent extraction technique.

(iv) Easy to scale up with low cost of operation. Process scaling up in SLM is easy and less expensive as compared to solvent extraction in terms of equipment cost and operating cost. Large membrane surface area in SLM can be increased by using hollow fibre membrane modules. Commercial hollow fiber membrane modules having surface area

in the rage of few square meters are available.

In spite of several advantages of SLM technique, it has not seen its application on commercial scale. The long term stability of the SLM is a major issue for its application on large scale. Few limitations for its commercial application are also encountered due to its scaling up issues. On the other hand, the organic ligands which are volatile in nature or soluble only in high polar diluent may not be useful for their use in SLM due to membrane instability. The other important factor for SLM that limits its use in industries is the lack of application oriented research as focus are more towards well established hydrometallurgical processes such as solvent extraction and chromatography.

10. Conclusions and Perspectives

Supported liquid membrane is a promising and potential emerging technology that may leads to its numerous applications especially in hydrometallurgical separation process. Owing to its several advantages, such as low ligand inventory, low energy consumption, ease of operation, and low cost operation, may be the driving force for implementation of this technique. However, extensive research is essential to look at several important parameters for their actual application. One may look into designing the ligands which are extremely selective for the given metal ions, and the same ligand may be used in SLM studies. Scope is also open to use the known ligands in SLM studies and compare their separation performances in membrane *vis-a-vis* other conventional technique such as solvent extraction and extraction chromatography. The SLM technique will be highly suitable for researchers with limited lab facilities and material inventory as the experiment can be performed in a very simple transport cell with extremely low ligand inventory. Though mathematical modelling in SLM has been explored, scope is always open to develop new models so as to predict the transport and separation behaviour of the species very accurately. Even transport modelling can be extended to large scale operation in hollow fibre membrane processes.

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Electrochemical Separation: Fundamentals, Challenges and Opportunities

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1. Introduction

1.1. Basic Principle of Separation Chemistry

Separation is defined as a methodology by which a mixture is resolved into its components and is achieved by using two methods viz. analytical and preparative. In analytical method, one aims at the isolation of the required component in a high degree of purity for quantitative measurements. Separation step is used only in situations where the component to be quantitatively measured is subject to interference from the goal, one aims at the measurement step.

In the preparative goal, one aims at the separation of the component with the degree of purity required for a specific use of the separated component [1]. In

the analysis of air for pollutants, for example,some of the compounds may be present in too low concentration to be analyzed straightaway. In such case, it becomes necessary to raise concentration of those compounds to the level where the required analysis becomes practical. Other example include analysis of river water for metals that are present in trace concentrations, wherein

Table 1: Different Separation processes with examples

Process Types	*Description*	*Examples*
Phase Creation or Addition	*Chemical species in a single-phase feed mixture (gas, liquid, or solid) can be separated by developing or introducing a second immiscible phase. The second immiscible phase is created by supplying additional energy or solvent that selectively dissolves certain chemical species.*	*Distillation, Stripping, Liquid/liquid–extraction, Crystallization*
Barrier	*Porous or non-porous membranes act as barriers that regulate or restrict transfer of certain species present in feed mixture. Porous membranes separate species via pore size, while nonporous membranes work via diffusivity and solubility of the species in the membrane material.*	*Reverse osmosis, Microfiltration* *Ultrafiltration, Pervaporation*
Solid Agent	*Solid material can act as an inert support for absorbents or active material for chemical reactions with specific chemical species to achieve separation.*	*Adsorption, Chromatography Ion exchange*
External Field	*Chemical species and components can be separated by applying an external force and/or gradient such as pressure, electrical field, magnetic field, or temperature gradient.*	*Centrifugation, Thermal diffusion Electrodialysis*

erroneous results are obtained because of the interference by organic compound and thus it becomes imperative to remove them before analysis. In modern era separation has become an integral tools in the clinical and forensic laboratories [2]. The basis of most of the techniques which achieve separation and purifications is that they bring about distribution of component of the starting material between two phases. This partitioning is based on difference in properties like volatility, solubility, adsorption, molecular size etc. on a suitable solid material. In the process of separation, one of the two phases gets considerably enriched in respect of one component(c1), and the other phase in respect of the second component(c 2) of starting mixture. The c1 and c2 are subsequently recovered from the two phases by using appropriate procedures. In some separation method chemical reaction are required to convert or modify a component of mixture to form a new phase or enable the substance to be distributed to second phase [2]. Few of the separation processes are listed in Table 1.

1.2. Electrochemical Separation

Separation processes are used to recycle valuable resources, remove impurities and toxic reagents, and selectively isolate specific ions. As listed in table 1, separation can be achieved by phase addition or creation, barriers, solid agents, and external field. It can be achieved on either the large or small scale with the afore mentioned concepts which are driven by addition of energy or mass to alter the physical and chemical properties of the mixture, enabling separation. Electrochemical separation is categorized as a novel process that utilizes an external field, solid agent and often barrier, since many of the electrochemical separation processes requires electrical energy, electrodes to interact with ions, and membranes to regulate ion transportation. Note that often barriers such as ion exchange membranes are also included to construct various types of system architectures. When electrochemical energy is applied to the system, anions and cations present in the feed mixture are separated as they are electrochemically captured by the positive and negative electrodes, respectively. The captured ions can then be released back to the electrolyte regenerating the electrodes. In this process, the effluent produced can be separated into two phases: deionized and concentrated streams, as shown in Fig. 1. Through cycles of consecutive capture and release, electrochemical separation can be operated to achieve bulk or specific ion separation. Nevertheless, owing to its simplicity, rapid operation, low energy requirements, and low material cost, the process is actively being studied as a promising next-generation ion separation technology.

1.3. Types of Electrochemical Based Separation

Electrochemical processes since its inception in the 1960s as electrochemical “demineralization” using porous carbon electrodes [3] have drawn attention as novel separation technology for their simple, environmentally-friendly, energy-efficient, and cost-effective characteristics., It indeed has made significant progress the field of ion separation with incorporation of non-Faradic (NFR) (electrical double layer (EDL) formation [4, 5]) and Faradaic reactions (FR) (pseudocapacitive/intercalation reactions [6–8]). Conventionally, NFR employ capacitive electrodes (e.g. activated carbon) which are advantageous for low-cost, facile synthesizability and rapid ion transportation with non-selective ion capturing behavior. FR on the other hand often utilize pseudocapacitive or intercalation electrodes which have been used in batteries or pseudocapacitors. These electrodes are considered as prominent candidates for ion separation technology as well, because of their large ion storage capacity and selective ion capturing property. In general both NFR and FR based

electrochemical separations are exploited in various aspects of water treatment such as desalination, hard-water, heavy metal and nutritive salts removal.

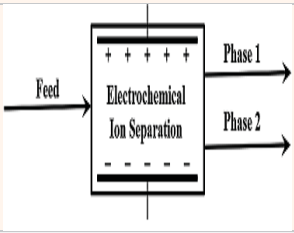

Figure 1: Representative schematic diagram of the electrochemical ion separation process. After the feed water passed through the separation system, the effluent can be separated into two phases: deionized aqueous solution (Phase 1) and concentrated solution of the released ions (Phase 2).

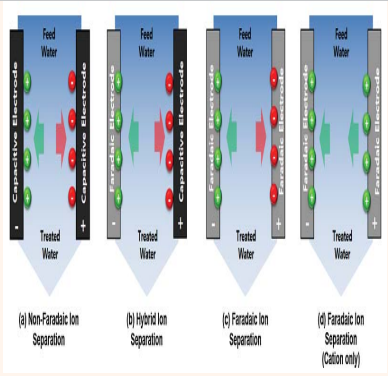

Figure 2: Four different types of electrochemical ion separation processes based on non-Faradaic and Faradaic mechanisms: (a) Non-Faradaic ion separation, (b) hybrid ion separation, (c) Faradaic ion separation and (d) Faradaic ion separation (cation only).

In these applications, electrochemical methods are toned to specifically separate portion of ions in water by selective and non-selective ion removal mechanisms.

Although various electrochemical processes have been designed for different target ions and industrial purposes, they all have in common that ions are captured and released by electrodes sharing similar fundamental separation principles. The operation mechanism and selectivity of ion separation depends on the electrode materials used in the electrochemical separation system. Since many electrochemical separation processes are inspired from the energy storage systems (ESS) including super-capacitors and batteries [9], electrochemical separation can be divided into two major types: NFR ion separation based on a capacitive mechanism [3,10] and FR ion separation based on a pseudo capacitive or intercalation mechanism [6,11,12]. As shown in Figure 2, different types of system designs can be formulated based on electrodes operating with NFR and FR.

1.3.1. Non-Faradaic Separation

The most representative technology of NFR type is capacitive deionization (CDI), which uses two separate capacitive electrodes. Conventionally, CDI electrochemically adsorbs/desorbs ions through an electrochemical double layer (EDL) developed on the electrode surface as an electric bias is imposed on the system. Ideally, in NFR ion separation, electron transfer through redox pairs does not occur [13]. The ion adsorption mechanism through the EDL can be expressed using the Helmholtz [14, 15] and Gouy –Chapman –Stern (GCS) models [16-18]. According to the Helmholtz model, the surface charge of the electrode changes according to the potential applied, and ions are adsorbed on the positively and negatively polarized electrodes to compensate for the developed surface charge. In the GCS model, this concept is expanded to include the diffusion layer, where the charge compensation at

the surface of the electrode is not completed by the single layer but occurs over a certain thickness of diffusion layer formed at the electrode surface. The schematic image of the GCS model is shown in Figure 3a. For example, at the negative electrode surface, inner Helmholtz plane (IHP) forms, this comprises of specifically adsorbed de-solvated anions and solvent molecules. On the other hand, hydrated cations are present at the outer Helmholtz plane (OHP).

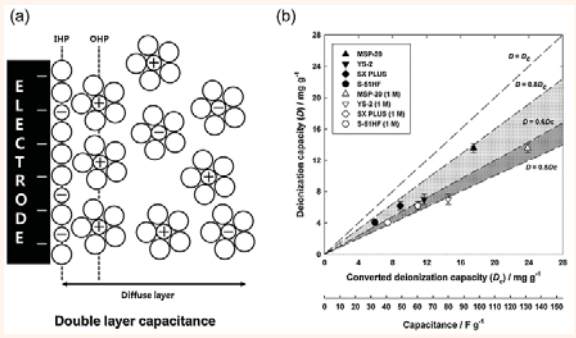

Figure 3: (a) Schematic diagram of an electric double layer (EDL) formed on the surface of the capacitive electrode based on Gouy-Chapman-Stern model. (b) Relationship between double layer capacitance and salt adsorption capacity evaluated with various activated carbon materials.

Lastly, hydrated cations and anions are distributed in the diffuse layer, where the ion concentrations decrease with distance from the electrode surface. The thickness of the diffusion layer and concentration of ions captured in the layer depends on the electrolyte concentration and applied voltage, and these characteristics are expressed as capacitance. Capacitance is the total quantity of charge adsorbed on an electrode per applied unit of electric potential. Generally, capacitance is considered to be the maximum amount of ions that can be adsorbed through EDL formation on the electrode. In the CDI system using activated carbon electrodes, the fraction of the charge capacity evaluated from the capacitance value was utilized for deionization, which is represented as the salt adsorption capacity (Figure 3b). According to the reported work, approximately 60–80% of the charge capacities were utilized when deionizing 10 mMNaCl solution [19]. Since CDI store charges at the electrode surface, the adsorptive performance of the system heavily depends on the physicochemical properties of the electrodes [20]. Apparently, in order for the electrodes to demonstrate high capacity and rapid ion transport, the electrodes should have high specific surface area, suitable pore size distribution, low electrical resistance, and good wettability towards electrolyte. Carbon is an excellent candidate for such NFR are majorly conducted in four ways as shown in Figure 4.. Carbon electrode materials in usage are activated carbons (ACs) [21,22], activated carbon fibers (ACFs) [23], template nanoporous carbons[24], carbon aerogels [9,25], carbon nanotubes(CNTs) [26], carbon nanofibers (CNFs) [27], graphene[28,29].

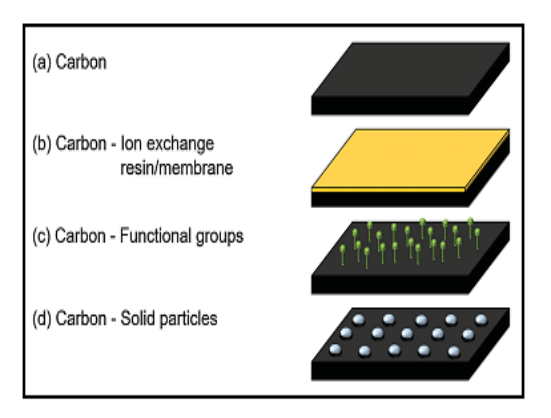

Figure 4: Classification of carbon electrode: (a) carbon, (b) carbon with ion exchange resin or membranes, (c) carbon with functional groups,(d) carbon with solid particles

Among the various carbonaceous materials, ACs are identified to be economically feasible option since

they are easy to fabricate and cheap with outstanding adsorptive performance. For example, several commercially available ACs synthesized from coconut shell, wood, charcoal or polymer precursors provided large specific surface area with high salt adsorption capacity [19, 30].

The performance of bare carbon electrodes in electrochemical separation was further improved through the addition of ion-exchange resins or membranes, functional groups, and solid particles. Ion-exchange resins or membranes act as a barrier to selectively penetrate counter-ions, thus significantly increasing the charge efficiency of the CDI system (Figure. 4(b)). The ion-exchange resins or membranes can further be altered to provide selectivity towards specific ions such as separation of monovalent and divalent ions, and removal of oxyanions (e.g. SO_4^{2-}, NO_3^-). Another strategy to increase wettability, selectivity towards counter-ions, and adsorptive performance of the electrodes were conducted by surface modification through the introduction of functional groups and metal oxide particles. Various works were performed to obtain hetero atom-doped carbon materials (e.g. N, P, S etc) which showed a significant improvement in the hydrophilicity and charge efficiency [31–35]. Similarly, the coating of metal oxides including TiO_2[36-38], MnO_2[12, 39], and SiO_2 [40,41] to carbon surface resulted in improvement in specific capacitance because of increased ion adsorption sites and enhanced surface wettability. Due to the active studies in the developing capacitive materials, the salt adsorption capacity of CDI systems increased rapidly. Over the past years, exponential progress has been made in non-Faradaic ion separation technology and it has shown potential in various applications such as desalination, water softening, and nutritive salt removal.

1.3.2. Faradaic Separation

FR is another ion capturing process based on the charge transfer reaction. Compared to the NFR ion sorption process, FR ion separation has several advantages including larger storage capacity and selective ion separation characteristics. In case of the FR, ions are captured through intercalation or conversion reaction, which occurs over bulk of the electrode materials. Therefore, Faradaic electrodes exhibit much larger capacitance compared to

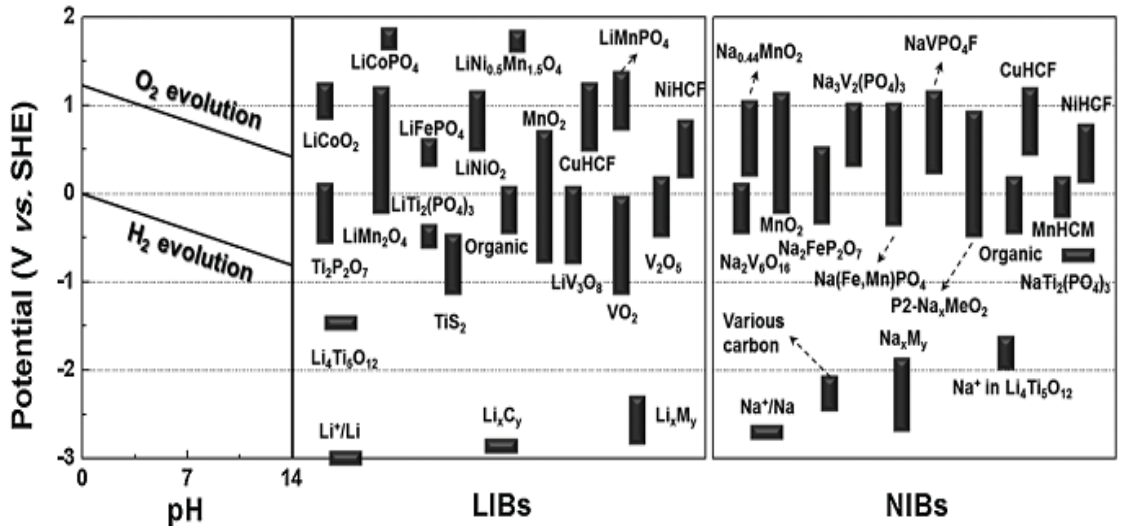

Figure 5: *Potential diagram of stable potential window of water and the working redox potential of various insertion materials of lithium and sodium ion batteries*

capacitive carbon electrodes which only utilize their surface to capture ions [42]. For intercalation materials, the insertion of ions into the crystal structure enables redox reactions in the bulk electrode. Generally, battery cathode materials have been used for FR ion separation which can separate ions based on the intercalation mechanism. Various kinds of intercalation materials have been excavated for aqueous battery application, and the examples of candidate materials that undergo specific redox reactions with lithium and sodium within the potential window in aqueous solution are shown in Figure.5.

Among them, manganese oxide [6, 43, 44], iron-based phosphate [45,46], and hexacyanoferrate materials[8,47,48] for lithium, sodium and potassium ions intercalation have been suggested for cation separation. Specifically, introducing the cathode materials used in sodium ion battery to electrochemical separation has brought a huge advance in desalination performance. Sodium manganese oxide and Prussian blue are representative examples of sodium intercalation material, which showed high performance for Na^+ uptake from aqueous solution. Intercalation electrodes with high ionic diffusion coefficients are actively being researched to improve the rate of ion removal using Faradaic systems.

In addition, selective intercalation is a useful characteristic of intercalation materials, which can be applied for selective separation of specific ions. Since the intercalation-based electrode takes ions into their anionic framework, diffusion rate of ions inside the crystal structure is very important. In particular, the size and oxidation state of captured ions have a major parameter which affect to the diffusion rate inside the lattice. In

general, separation of small size substances is advantageous, because ions with small size diffuse faster than other ions inside the framework. It is also known that monovalent cations are more easily intercalated because of their rapid diffusion rate inside the anionic framework. Therefore, selective separation of ions using intercalation electrode has been mainly studied for monovalent ions, especially for Li^+ and Na^+ with small dehydrated ionic radii and Cs^+ and NH_4^+ with small hydrated radii. On the other hand, based on conversion reaction, silver (Ag) and bismuth (Bi) could capture Cl from aqueous solution. These two materials react with Cl and are converted to silver chloride (AgCl) and bismuth oxychloride (BiOCl) [6,49, 50].Hence, various combinations of cation and anion capturing electrodes could be made to formulate ion separation as shown in *Fig. 2 (c)*.

To achieve high capacity with a fast ion removal rate, hybrid ion separation consisting of both Faradaic and non-Faradaic electrodes has been proposed (*Fig. 2(b)*). The Faradaic electrode provides a large capacity and low self-discharges, whereas the non-Faradaic electrodes exhibit fast removal rates. In addition, typically non-Faradaic materials such as AC can easily be mass-produced from cheap precursors, and hence, provide merit in terms of costs. The hybrid system takes advantage of both Faradaic electrodes and non-Faradaic electrodes, bridging the performance gap between battery and capacitor-based separation systems [51].

2. Applications of Electrochemical Separation Process

2.1. Desalination

Desalination technologies have gained attention for its significant industrial value as demand for fresh water is increasing rapidly due to the global industrialization and population growth. Although current distillation and membrane-based processes are well established, desalination using electrochemical separation processes has been

actively researched with the aim to develop highly energy efficient, simple, and eco-friendly technologies. Among various electrochemical processes, CDI is one of the most commonly used desalination technologies. CDI removes charged particles, molecules, and ionic species via the electrosorption mechanism [9,20,52-61]. The theoretical and technological background were covered with detail outlining trends in electrode materials, system designs, operating modes, economic evaluation for commercialization, and issues of long-term stability to provide direction for the further development of CDI. In addition, electrodes ranging from carbon-based composites to redox-active materials were suggested for the development of novel systems. Owing to the explosive development in the field of electrochemical desalination, the urgent need for standardized matrices, analysis methods, and classification of related technologies were raised. Biesheuvel*et al.* proposed to broaden the terminology of CDI, which refers to electrochemical desalination with carbon electrodes operating based on an EDL mechanism, to also include systems with other mechanisms such as pseudo-capacitive and intercalation reactions. Thus, the term CDI was proposed to incorporate all electrochemical desalination systems that operate in charging/discharging steps to separate ions, regardless of specific mechanisms or materials [62].Unlike conventional membrane-processes such as reverse osmosis (RO), CDI is advantageous for low-cost infrastructure since the system do not have to withstand extreme pressure, high water recovery ratio and high energy-efficiency when treating brackish water [63,64]. Note that it is indubitable that RO is effective tool to treat high concentrated solution (e.g. seawater), but it was reported that at concentration below 2000 mg L^{-1} TDS, CDI can consume less than 0.5–2.5 kWh m^{-3} [63,65] that is the energy consumption range of RO. Also CDI provides rapid desalination performance and its operation is simple without requiring occasional separation with the draw solute and water when compared with forward osmosis [66].As a basic configuration, porous carbon materials are used as the positive and negative electrodes. When a potential difference is applied to the system, the ionic species are captured on the electrode surfaces (Fig. 8(a)) [5,20]. Typically, CDI operates in cell voltage within 1.2 V to prevent unwanted water-splitting reaction (hydrogen and oxygen gas evolution) at the carbon surface [67]. CDI operation can be separated into two consecutive steps: charging and discharging steps. In the charging step, ions are stored in the EDL at the surface of the electrode removing ions from the electrolyte. Subsequently, in the discharging step, the stored ions are released into the electrolyte and the ion concentration of the solution increases. This releasing step accompanies an energy output that can be transferred to charge neighboring cell or separate supercapacitor using converters to recover partial amount of energy supplied [68,69]. In CDI the electrochemical energy can be applied in two different ways: applying constant voltage (CV) [36,70] or constant current (CC)[22,63,71]. Recent studies indicated that CC mode consumes significantly less amount of energy compared to CV mode because CC mode allows lower dissipation of energy from initial ionic resistance and have relatively shorter time for the cell to operate in voltage range that results in parasitic reactions [72-75]. Also, approximately, 40% of energy consumed in charging process could be recovered when operated in CC mode while only 5.7% can be recovered in CV mode [75].In the CDI system, loss of charge is inevitable due to the co-ion expulsion effect at the surface of the electrode. For a positively charged electrode, some charge will be allocated to attract anions whereas some will be used to repel cations. The same phenomenon occurs for a negatively charged electrode. Hence, inefficient

allocation of charge is a major drawback in CDI. To overcome this limitation, ion-exchange membranes (IEM) have been introduced in front of the electrodes and this novel system has been referred as membrane-assisted CDI (MCDI), as shown in *Fig. 6(b)*.

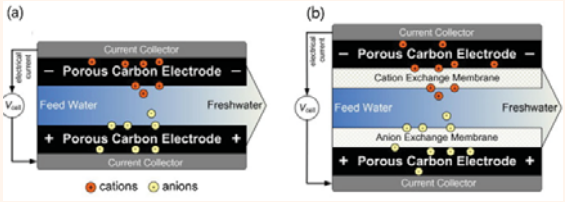

Figure 6:Representative schematic diagram of (a) capacitive deionization (CDI) and (b) membrane capacitive deionization (MCDI)

2.2. Impurity Removal

The production of highly purified chemical compounds is a main goal of the separation process. Impurities present in chemical reagents may form as by-products, which decreases the overall quality of the final products. Therefore, many studies have been conducted to develop efficient methods to separate impurities from final materials, which can significantly enhance their economic value. Conventionally, crystallization has been used for purification, but this method is time-consuming and energy-intensive due to the inevitable concentration step such as distillation process [76-78]. Electrochemical separation can be an alternative to conventional purification methods, since it can separate ionic species at low concentrations with high energy efficiency and low environmental impacts. For example, potential of electrochemical separation of ions was demonstrated in purifying insulin. MCDI system was adopted to remove $ZnCl_2$ which is one of the impurities present in the purifying process of insulin. By utilizing MCDI system, 75% of $ZnCl_2$ was removed from the mixture of insulin and $ZnCl_2$ and approximately 99% of insulin was recovered [79]. In addition, a sodium manganese oxide and silver (NMO/Ag) Faradaic ion separation system was

developed for the purification of industrial KCl (the precursor of KOH) by removing the small amount of NaCl impurities [44]. Owing to the smaller ionic radius of Na^+ compared to K^+, Na^+could be selectively inserted into the lattice structure of NMO. In case of NMO, Na^+ is intercalated with dehydrated form, which maximizes the difference of ionic radii of Na^+ and K^+. In addition, it was observed that divalent ions ($Mg^{2+}$and Ca^{2+}) were also excluded in NMO lattice structure, which might be ascribable to the low diffusion rate and high dehydration energy.

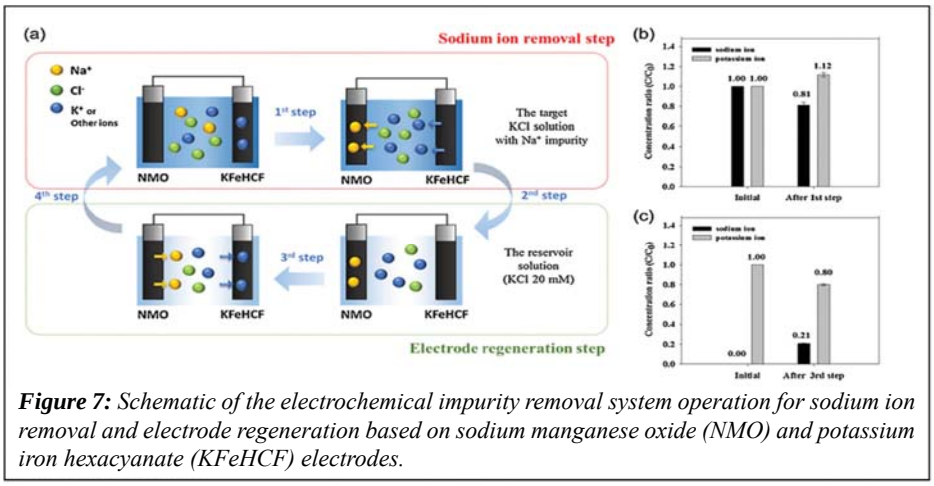

Figure 7: *Schematic of the electrochemical impurity removal system operation for sodium ion removal and electrode regeneration based on sodium manganese oxide (NMO) and potassium iron hexacyanate (KFeHCF) electrodes.*

The high selectivity for Na^+ over other cations in the NMO/Ag system enabled the successful purification of the raw material (KCl) for subsequent production of high-purity KOH. However, the expensive silver counter electrode hindered the further practical application of the NMO/Ag system. Hence, as an alternative, potassium iron hexacyanate (KFeHCF), which is a Prussian blue analogue, was investigated as a counter electrode. The NMO/KFeHCF system operates based on the rocking chair principle, separating Na^+ and K^+ as shown in *Figure. 7*.KFeHCF has a higher affinity towards capturing K^+ compared to Na^+ or other divalent cations. In addition, the raw material is cheap and easy to fabricate, making the NMO/KFeHCF system more suitable for industrial purposes. The NMO/KFeHCF system can further concentrate potassium which is released from KFeHCF, while the sodium ions are captured by NMO. As a result, the purity of the industrial KCl solution was increased to over 99.8% through several cycles of operation [48].

Compared to conventional crystallization method that can effectively function in a KOH solution contains NaCl impurities of more than 200 mg kg^{-1}[80], electrochemical separation can be a more efficient alternative pretreatment technology. From the example of purifying the KCl reagent, the feasibility of electrochemical separation as an impurity removal method has been demonstrated and it can be applied in various industries as long as appropriate electrode materials with specific ion exchange behavior are selected [44,79].

2.3. Water Softening

Calcium, magnesium, ferric, and ferrous ions dissolved in water are representative hardness ions, whose presence results in problems such as membrane fouling, clogging of pipes, and scaling. To prevent the afore mentioned problems, various technologies for water softening have been developed [81,82], including chemical precipitation method[83,84], ion-exchange process based on resins [85] and nano filtration, and reverse osmosis membrane technologies[86,87].However, these conventional technologies require a high energy input which increases operating costs and hazardous chemicals which pose environmental problems. As a representative non-Faradaic ion separation process, CDI has been proposed as a promising alternative to address issues of water hardness.CDI technology is expected to be appropriate for removal of hardness ions because of the Columbic interaction and substitution phenomenon. First, Columbic interaction occurs via electrostatic attraction between two charges and its magnitude is proportional to the size of the charge and inversely proportion to the distance between the charges. Capacitive electrodes show stronger affinity towards hardness ions because they are generally multivalent and experience stronger Columbic attraction compared to monovalent cations[88].Cations with higher charge and small hydrated radius were strongly attracted to the carbon surface following the order of Ca^{2+}> K^+> Na^+[88, 89]. Ion substitution is an important phenomenon underlying the superior performance of CDI in removing hardness ions. Here, substitution phenomenon refers to the replacement of adsorbed ions on the carbon electrode with ions dissolved in the bulk solution.

The evidence of this substitution is presented from the results of several research groups in *Fig. 8*. The substitution reaction is schematically shown in *Fig. 8(d)*, where captured Na^+ on the capacitive electrodes is replaced by Ca^{2+},indicating the divalent Ca^{2+} experiences stronger attraction to the electrode surface (Fig. 8(a–c)) [88-90].

2.4. Nutritive Salt Removal

Disposal of nutritive salts to water sources is an increasing concern due to the excessive use of

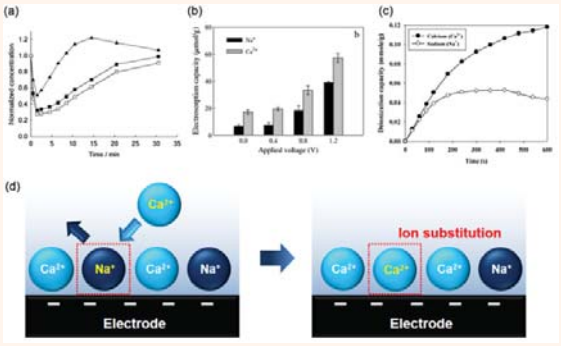

Figure 8:Deionization performance of capacitive deionization (CDI) for hardness control (a) in solution containing monovalent (e.g. Na^+) and divalent (e.g. Mg^{2+},Ca^{2+}) cations, (b) at various applied voltage, and (c) in system with calcium-alginate coated carbon electrode. (d) Schematic diagram of the substitution effect on the carbon electrode.

fertilizers and leakage of municipal and industrial wastewater. Eutrophication is a serious ecological problem which results in the massive production of floating plants and the rapid growth of algae accompanied with dissolved oxygen depletion, severely damaging or even destroying the aquatic ecosystem. To prevent eutrophication, various methods have been investigated to reduce the amount of nitrogen and phosphorus in water which are the main nutrients for plant growth. Most conventional technologies for removing nutritive salts involve chemical precipitation, activated sludge, and adsorption processes. These processes offer high removal efficiency but generate additional wastes and require a large amount of chemicals increasing the overall operational costs [91-93]. As an alternative, electrochemical separation have been studied to selectively capture and release nutritive salts dissolved in water. Nitrogen sources, such as nitrate or ammonium, are key nutrients that contribute towards the eutrophication problem. Various parameter studies of non-Faradaic and Faradaic ion separation technologies have been conducted to remove nitrate or ammonium present in aqueoussolutions [94-97]. The capacitive system demonstrated a significant removal ratio of nitrates or ammonium even in the presence of other ions. The affinity of CDI towards the nitrate ion can be enhanced by coating nitrate-selective ion exchange resins on the capacitive electrodes [98, 99]. The ion exchange coating resin was fabricated by mixing a commercial anion exchange resin which contains amine functional group with an anion exchange polymer (*Fig. 9(a)*). As a result, the selectivity towards nitrate was significantly improved compared to chloride, as shown in *Fig. 9(b)*. In addition, novel coating resins materials were applied to carbon electrodes without anion exchange polymers, and also showed higher selectivity for nitrate over chloride and sulfate ions [99]. In addition, the effects of the hydration ratio (the ratio of hydrated radius to ion radius) and valence of the ions present in solution were studied. Although CDI showed strong affinity towards ions with high valence, this experiment demonstrated that among monovalent anions (NO_3^-,Cl^-, F^-, and Br^-) and cations (Na^+, K^+, and NH_4^+), $NO_3^-$and NH_4^+were captured by the carbon electrodes with the highest efficiency. The normalized concentrations of monovalent anions are shown in Fig. 9(c). The small hydration ratio of NO_3^- and NH_4^+ resulted in the observed behavior [100,101]. In addition, flowable carbon electrodes were used as part of the capacitive stripping method to recover ammonia from diluted wastewater. By applying potential bias, ammonium ions migrated across the cation exchange membrane and were converted to dissolved ammonia. Subsequently, the ammonia was recovered in an acidic solution containing $(NH_4)_2SO_2$**.**

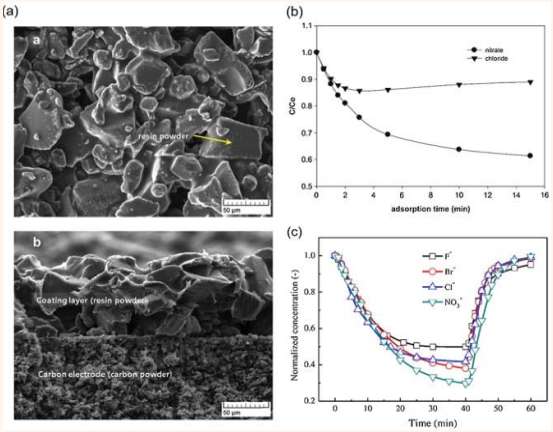

Figure 9:(a) Scanning electron microscopy (SEM) images of the top and cross-sectional view of the anion exchange resin coated activated carbon electrode,(b) deionization performance of the anion exchange resin coated CDI which shows high selectivity towards nitrate over chloride ions, and (c) deionization performance of conventional CDI showing affinity towards nitrate over the other monovalent anions (fluoride, bromide, and chloride ions).

2.5. Nuclear Industry

2.5.1. Spent Fuel Reprocessing

The electrochemical separation process basically exploits the differences in the standard reduction potential of metal ions to separate the metal ion of interest under the influence of an applied potential. A mixture of metal ions having adequate difference in their formal potentials values in an electrolytic medium can be mutually separated by selective electrodeposition of one metal on an electrode surface under the application of the applied potential. With regard to the application of an electrochemical separation process for nuclear industry in separation of lanthanides and actinides in reprocessing of spent nuclear fuel and preparation of radionuclide generator, it requires careful control of the applied potential to achieve selective electrodeposition of a particular lanthanide/actinide/ daughter radionuclide on a metallic electrode. In this respect various modified electrodes can be used.

Electrochemical separation of U from interfering lanthanides ions in 0.1 M KCl on poly(3,4-ethylenedioxythiophene) poly(styrenesulfonate) modified platinum electrode was reported. Uranium separation was achieved in a two step process: (i) UO_2^{2+}reduction to insoluble urania (UO_2) which gets deposited on modified electrode in the presence of lanthanides (La^{3+},Ce^{3+}, and Sm^{3+}) ions and (ii) oxidation of electrodeposited UO_2 to UO_2^{2+} in fresh 0.1 M KCl (pH = 2) solution. 94% recovery of UO_2^{2+} was achieved from mixed solution of uranium and lanthanides at the modified electrode **[102].** A schematic of electrochemical separation of uranium from lanthanides is given in *Figure 10*.

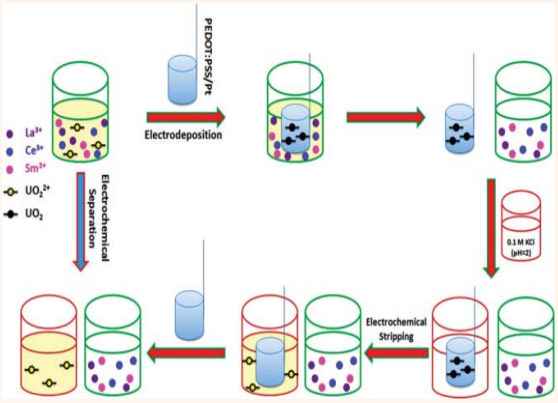

Figure 10:A schematic of electrochemical separation of uranium from lanthanides

2.5.2. Nuclear Medicine

For the application of electrochemical separation for the preparation of nuclear medicine, the potential of the working electrode is maintained constant (or within a narrow range) by regulation of the voltage applied to the cell in such a way to permit the quantitative deposition (by reduction) of the daughter radionuclide on an electrode surface, from a suitable electrolyte solution containing parent−daughter mixture. The parent radionuclide is

generally more difficult to reduce in that electrolytic medium. The electrodeposited daughter radionuclide then can be conveniently recovered in a small volume of solution of interest, and the electrode can be reused for subsequent deposition of the daughter radionuclide. The key to success in the electrochemical technique is to select an appropriate electrobath and to identify how this approach can be successfully applied to separate the daughter radionuclide from a solution containing parent−daughter radionuclides within a reasonable period of time (1−2 h). **[103]**

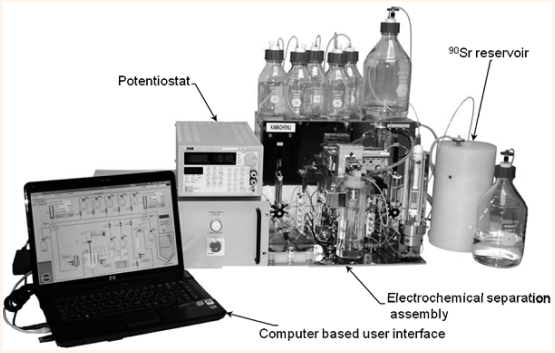

Figure 11: Fully automated ^{90}Sr/^{90}Y generator (Kamadhenu) commercially available from Isotope Technologies Dresden (Germany)

For example, there is a great deal of interest in the use of ^{90}Y for targeted radionuclide therapy owing to its favorable characteristics such as emission of high-energy β^- radiations, suitable half-life, and its decay to a stable daughter product, ^{90}Zr.In view of the necessity to achieve a satisfactory degree of separation of ^{90}Y from ^{90}Sr, resorting to two-step electrolysis was found to be effective. The two-step electrolysis enabled extraordinarily high decontamination factors to be achieved. Platinum seemed to be the best choice for the electrode and was hence adopted here. The first electrolysis was performed for 90 min in $^{90}Sr(NO_3)_2$ feed solution maintained at pH 2−3, applying a potential of −2.5 V (100−200 mA current) with respect to saturated calomel electrode. After the first electrolysis, the cathode was removed without switching off the voltage, washed with acetone, and transferred to a new electrolysis cell containing fresh electrolyte solution (0.003M HNO_3) and a new platinum electrode. The polarity of the electrodes was reversed, and the electrolysis process was repeated for another 45 min. The $^{90}Sr(NO_3)_2$ solution after the first electrolysis is stored for growth of ^{90}Y and future recovery. The two-step electrolysis provides the scope for obtaining ^{90}Ywith acceptable radionuclide purity. The ^{90}Y deposited on the circular cathode after the second electrolysis was dissolved in acetate buffer to obtain ^{90}Y acetate, suitable for radiolabeling. The noteworthy feature on the use of the electrochemical separation technique was to achieve a high overall yield (>90%) of ^{90}Y. A picture of fully automated ^{90}Sr/^{90}Y generator (Kamadhenu) commercially available from Isotope Technologies Dresden (Germany) is given for reference in *Figure 11*.

3. Conclusions

In this article, general concept covering fundamentals and principles of electrochemical separation processes used for different sectors were discussed. Various representative electrochemical processes were shown based on different applications such as desalination, resource recovery, impurity removal, control of hardness, nutritive ions, separation of actinides and lanthanides, nuclear medicine etc. were elaborated.

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