

SEPARATION

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Summary

There are several unit operations concerned with modifying the composition of solutions and mixtures that do not involve chemical reactions. Their main objective is to separate a substance into components. Among these processes are 1) distillation, where a liquid-gas relationship is used to separate mixtures, 2) leaching, where a liquid phase is used to remove a solute or solutes from a solid, 3) crystallization, where a solute is purified and removed from a solution in the form of a crystal, 4) liquid-liquid extraction, where a liquid phase is used to remove a solute or solutes from another liquid phase (non-miscible phase), and 5) membrane processing, where a physical barrier is used to retain certain types of molecules while allowing others to pass across the barrier. This review will cover liquid-liquid extraction, solid-liquid extraction, mechanical separation, membranes, chromatography, and distillation.

1. Liquid-Liquid Extraction

1.1. Introduction

Liquid-liquid extraction consists of removal of a solute from a solution by using a second solvent that is insoluble or with limited solubility in the solution being extracted. The solute(s) must have high affinity for the extraction solvent. The extraction process is described and summarized in the following diagram (Figure 1):

The extraction solvent is intended to recover the solute/solutes contained in the solution-feed. The contactor/mixer is where the extraction solvent and the solution feed are mixed. The extraction process takes place in the separator where both phases are separated into two independent streams. The extract stream is the liquid phase containing mainly the solvent and the solute(s) extracted from the solution feed. The raffinate is the phase that contains most of the liquid phase after the extraction process.

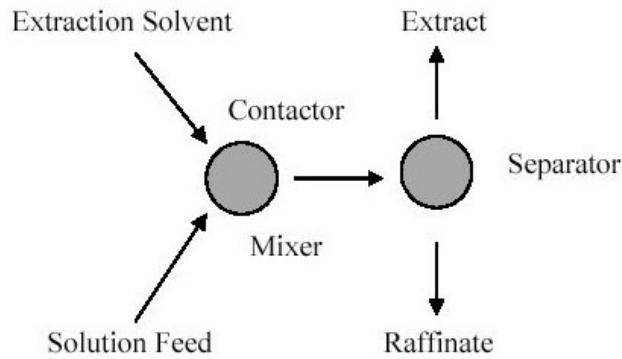


Figure 1. General principle for liquid-liquid extraction.

The transfer of solute(s) from one liquid phase to another is an equilibrium relationship that needs to be discussed for a better understanding of the extraction phenomena.

1.2. Theoretical Aspects

1.2.1. Triangular Coordinates and Equilibrium Data

Equilateral triangular coordinates are used to represent the equilibrium data of a three-component system. Each corner in the triangle represents a pure component **A**, **B**, or **C**. The following (Figure 2) is an example of a triangular diagram representing the equilibrium data for a ternary system:

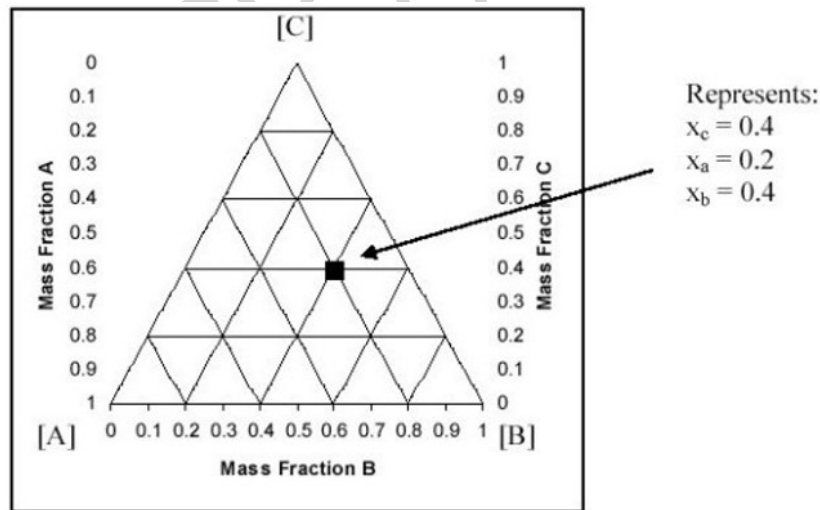


Figure 2. Triangular diagram representing the equilibrium data for a ternary system.

The perpendicular distance from a particular point to any of the bases (AB, AC, or BC) represents the concentration of the third component. This type of diagram is very useful when evaluating the effect of combining mixtures at different concentrations. If R kg of a mixture at composition R is added to E kg of a mixture at composition E, the resulting M kg mixture will have a composition M on the straight line RE:

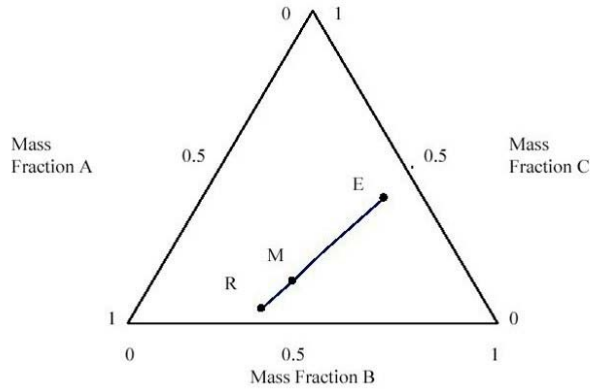


Figure 3. The mixture rule.

A mass balance for component C can be used to demonstrate the previous example:

$$R + E = M \tag{1}$$

$$R x_R + E x_E = M x_M \tag{2}$$

By replacing M:

$$E (x_E - x_M) = R (x_M - x_R) \tag{3}$$

Or

$$R / E = (x_E - x_M) / (x_M - x_R) \tag{4}$$

where R is the mass of solution at composition R, E is the mass of solution at composition E, M is the mass of solution at composition M, and x is the mass fraction of component C in each case (R, M, and E).

In cases where the extraction solvent and the solution feed are partially miscible, the diagram will have a curved envelope containing a region with two phases, and therefore separation occurs (Figure 4). This type of diagram is called Type I.

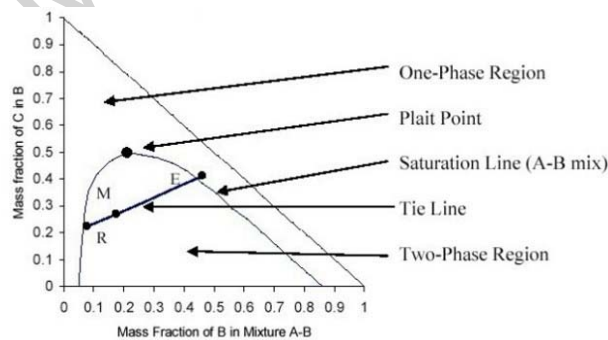


Figure 4. Liquid-Liquid diagram with components A and B partially miscible.

Any binary mixture of the two partially miscible liquids will form two phases if the composition falls between the limits defined by the saturation line according to the

relationship previously discussed for R and E. Meanwhile, the saturation line indicates the change in solubility for the A and B phases upon addition of solute C. Any mixture M with a composition underneath the saturation line will form two saturated and insoluble liquid phases with an equilibrium composition indicated by R and E. The line RE passing through M is known as a Tie Line. There are infinite numbers of Tie Lines in the two-phase region and they are rarely parallel, changing their slope slowly in one direction. The Plait Point represents the last tie line and is the point where the solubility of A and B merge; the two phases are identical and have the same concentration as the solute, $x_C = y_C$.

A plot of the mass fractions for each of the phases using the tie lines is used to predict the distribution coefficient. Figure 5 shows a distribution diagram for a system with two partially miscible liquids.

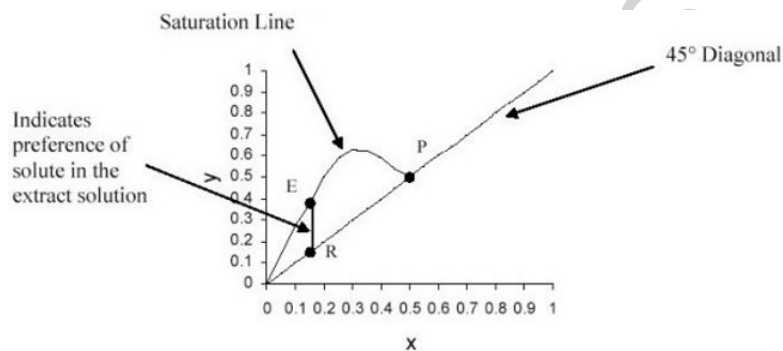


Figure 5. Example of distribution diagram for a system containing two partially miscible liquids.

The line ER and all the data points for the distribution diagram lie above the diagonal, $x = y$, which indicates a preference of the solute used in the phase intended as extract solution. Opposite behavior can be observed when the solution feed has a better affinity for the solute than the extract solution. Expressing the data in terms of solvent free coordinates (Y_A vs. X_A) results in the Maloney-Schubert diagram.

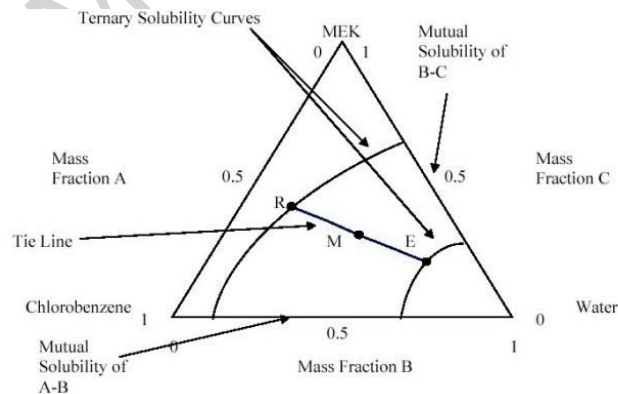


Figure 6. Example of system with two pairs of immiscible liquids.

Type II ternary diagrams are used when the system consists of two pairs of immiscible

liquids (i.e., chlorobenzene (A), water (B), methyl ethyl ketone (C), where A-C is miscible but A-B and B-C are immiscible). The phase diagram shows no Plait Point and two ternary solubility curves for each of the systems in equilibrium. Solutions outside the band between the curves form homogeneous single-phase liquid solutions. Figure 6 shows a system with three liquids with two pairs of immiscible liquids.

Similar to the Type I ternary diagram, an equilibrium distribution curve can be drawn to identify the preference of the solute with respect to the two liquid phases in the system.

1.3. Selection of Solvent

A key step in liquid-liquid extraction is the proper selection of the extract solution. There is a wide range of liquids available for use as solvents in this type of unit operation. Nevertheless, a perfect match cannot be found every time, since the desirable properties for extraction are not necessarily present and some limitations are unavoidable. The following parameters should be considered in designing an extraction process:

Selectivity

The separation factor is the ratio of two additional ratios: 1) weight fraction of C in the extract over the weight fraction of A in the extract and 2) weight fraction of C in the raffinate over weight fraction of A in the raffinate. The relationship can be expressed as:

$$\frac{y_E^*}{x_R} \quad (5)$$

where y_E^* is the mass fraction of C in the extract at equilibrium and x_R the mass fraction of C in the raffinate. A useful extraction will have a selectivity ratio greater than unity. No separation is possible if the selectivity is equal to one.

Distribution Coefficients

This parameter is defined as the ratio of y^*/x at equilibrium. There is no requirement that this coefficient be greater than one, but from an operational point of view, the amount of solvent needed to carry out the extraction process decreases as the value of the coefficient increases.

Insolubility of solvent

It is necessary to evaluate the solubility of the solution feed and the proposed extract solvent. The main target of the extraction process is to remove a solute contained in the solution feed. Therefore, the extract solution will only remove the solute, with little (if any) solution feed carried away in the raffinate. Increased amounts of extract solvent will be required, as the solubility of the solvent increases in the solution feed or in removing part of the solution feed.

Density

A difference in density is required for the saturated liquid phases. The larger the difference, the better. In the case of Type I extractions (Figure 4), the difference reaches

zero at the Plait Point. Any equipment intended as a continuous-contact extractor cannot operate at concentrations in which the density difference is zero.

Interfacial Tension

The interfacial tension between equilibrium phases will reach zero at the plait point for partially miscible systems. High interfacial tension is important since coalescence of emulsions is of great relevance in the extraction process (see *Surface Phenomena*).

Chemical Reactivity

The solvent should be chemically stable and inert toward all materials it is in contact with during the extraction process.

Viscosity, vapor pressure, and freezing point

These characteristics should be as low as possible for ease of handling and storage.

Safety Issues

The solvent should be non-toxic, non-flammable, and low cost.

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Biographical Sketch

Dr Humberto Vega-Mercado is originally from Puerto Rico. He is Senior Process Engineer at Bio Sterile Validation, Merck & Co., West Point, Pennsylvania. Merck & Co., Inc., which is a leading research-driven pharmaceutical products and services company. Merck discovers, develops, manufactures, and markets a broad range of innovative products to improve human and animal health, directly and through joint ventures. Dr. Vega-Mercado was previously Manufacturing Head (1998-2000) of Animal Health – Drug Products after having served in positions of increasing responsibility within the Animal Health organization at Merck Sharp & Dohme Química de Puerto Rico.

Dr. Vega-Mercado received a Ph.D. degree in Engineering Science from Washington State University in 1996, M.S. in Chemical Engineering (1989) from University of Puerto Rico, Mayaguez, Puerto Rico, as well as a B.S. in Chemical Engineering (1987). Prior to joining Merck, Dr. Vega-Mercado was Researcher, in the Food Technology Laboratory at the University of Puerto Rico, Rio Piedras, Puerto Rico (1988-1990). Dr. Vega-Mercado has completed over 40 publications and 30 presentations in food and pharmaceutical related subjects. Dr. Vega-Mercado is member of the Institute of Food Technologists, American Institute of Chemical Engineers, Sigma XI The Scientific Society, and the Puerto Rico Board of Engineers (CIAPR).