Phase equilibrium (part 4)

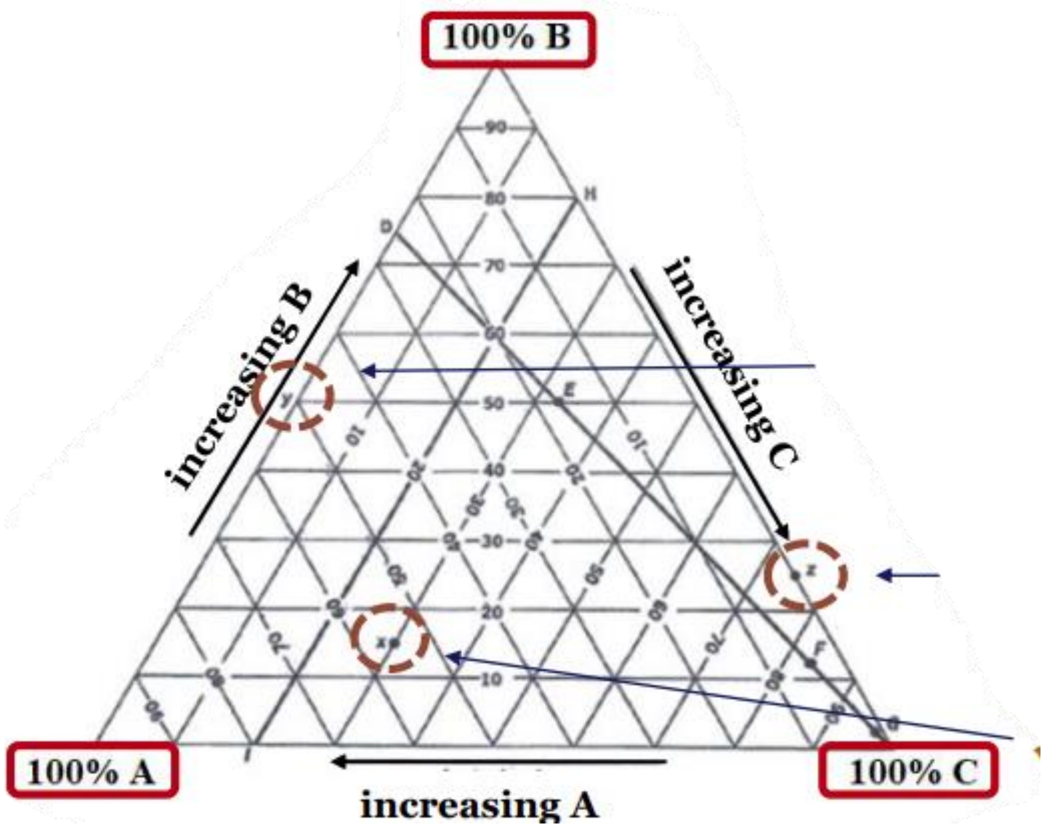
THREE-COMPONENT SYSTEMS

A three-component diagram delimits the homogeneous and heterogeneous regions in a three-component system at constant temperature and pressure (usually atmospheric). When we want to observe changes in equilibrium composition at different temperatures, we have to use three-dimensional diagrams.

THREE-COMPONENT SYSTEMS

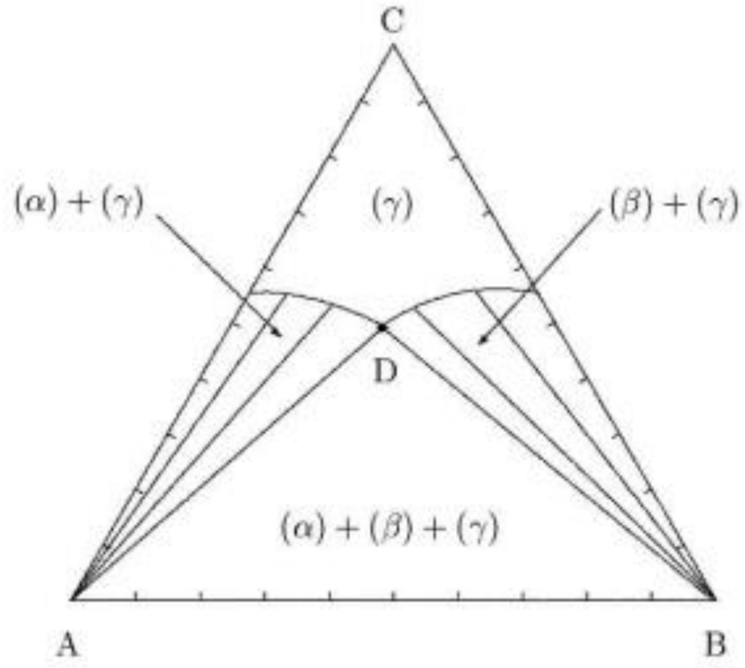
- In a non-condensed system containing three components but only one phase, F=3-1+2=4 (temperature, pressure, and the concentrations of two of the three components)
- Only two concentration terms are required because the sum of these subtracted from the total will give the concentration of the third component.
- If we regard the system as condensed and hold the temperature constant, F=2, thus we can use a planar diagram (generally triangular graphs are used) to illustrate the phase equilibria.
- Several areas of pharmaceutical processing such as Crystallization, Salt form selection, and Chromatographic analyses rely on the use of ternary systems for optimization

RULES RELATING TO TRIANGULAR DIAGRAMS



- The concentration in ternary systems are accordingly expressed on a weight basis. 100 % B 0 % A, 0 % C increasing A
- The lines AB, BC, and AC are used for two-component mixtures and can be divided into 100 equal units. Examples:
- Point y, on the line AB, represents a system containing 50% B and 50%A □Point z, along BC, signifies a system containing 75%C.
- Point x, 15% of B 85% of A + C

ISOBARIC-ISOTHERMAL DIAGRAM OF A THREE-COMPONENT SYSTEM



The region (α) + (β) + (γ) is also heterogeneous. Here the system is formed by three phases: pure substance A, pure substance B, and a mixture of the composition given by point D

Three-component system containing two liquid phases

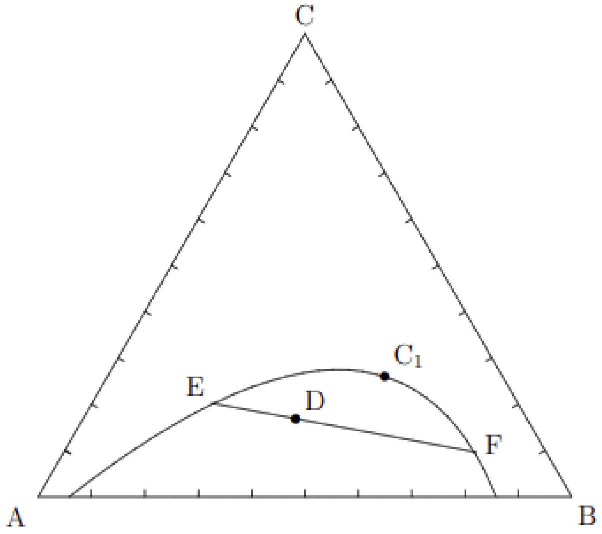


Figure shows a binodal line EC_1F and a tie line EDF. The system of a global composition given by point D split into two liquid phases whose composition is given by points E and F on the binodal line. The amount of substance ratio of both liquid phases is given by the lever rule. The compositions of both coexisting phases merge at point C_1 (the critical point).

The distribution coefficient is defined as the ratio of the molar fractions or concentrations of the i^{th} component in one and the other liquid phase

$$K_{x,i} = \frac{x_i^{(\ell_2)}}{x_i^{(\ell_1)}} \qquad \text{or} \qquad K_{c,i} = \frac{c_i^{(\ell_2)}}{c_i^{(\ell_1)}}\,, \qquad i = 1, 2, 3\,.$$

The distribution coefficient generally depends on temperature, pressure and composition.

EXTRACTION

- In laboratory conditions, extraction is usually carried out with the help of a separating funnel. A water solution containing the solute to be extracted and an organic solvent not miscible with water, which extracts the extracted substance from the water solution, is placed in this funnel. The funnel is vigorously shaken (usually 2-5 minutes). In this case, both liquid phases are dispersed in each other, forming droplets of different sizes. The extracted substance passes through the interface of the aqueous and organic phases hum the aqueous phase to the organic phase until an interface equilibrium is established in the system, at which equilibrium concentrations of the extracted substance in the aqueous and organic phases are achieved. By reaching an interface equilibrium the rate of solute transfer from aqueous to organic phase becomes equal to the transfer speed of the same substance from the organic phase into the water phase, i.e., the state of dynamic equilibrium. After the shaking is stopped, both liquid phases separate, and it happens the faster, the greater is the difference in the density of water (aqueous solution) and the used organic solvent, the density of which can be higher or lower than the density of water.

ORGANIC SOLVENTS

- The used organic solvents must be able to efficiently and, if possible, selectively extract the extracted substance from the water solution, to have low solubility in water in water (and water must have low solubility in them), not undergo hydrolysis, to have low saturated steam pressure at normal temperatures — to be non-volatile and sufficiently high-boiling (the boiling point at atmospheric pressure must be above 50 °C).
- Their density should be as different as possible from the density of water.
- Organic solvents should also be non-flammable, non-toxic and cheap.

SELECTED KEY TERMS OF LIQUID EXTRACTION

- **The extractant** is an organic solvent in an individual state or containing any reagents, that extract the substance from the aqueous phase.
- **Extracting agent** is a component of the extractant, that interacts with expectable substance with the formation of extraction compound. In the example above, in the extraction of aluminum ion by chloroform solution of o-hydroxyquinoline the role of extraction reagent is played by 8-hydroxvquinoline. J
- **Extract** is a separated liquid organic phase, containing a substance extracted from the aqueous phase. In the examples above, the “extract” is the chloroform solution containing extracted molecular iodine or aluminum oxyquinolinates.

SELECTED KEY TERMS OF LIQUID EXTRACTION

- **Re-extraction** is the process of reverse extraction of a substance from an extract into the aqueous phase.
- **A re-extractant** is a reagent solution (usually aqueous) used to retrieve a substance from an extract.
- **A re-extract** is a separated aqueous phase containing a substance retrieved from an extract.
- **A diluent** is a relatively inert organic solvent added to an extractant to improve its physical or extraction properties.
- **Cleansing** is the process of partial or complete removal of impurities from the extract or re-extract.

SELECTED KEY TERMS OF LIQUID EXTRACTION

- **Cleansing solution** is an aqueous or organic solution used for cleansing. Periodic extraction is the extraction of a substance from the same phase, carried out in separate portions of the extractant.
- **Continuous extraction** is extraction carried out with the continuous movement of one liquid phase (the other liquid phase remains stationary).
- **Countercurrent extraction** is the extraction carried out with a countinuous movement of both phases.
- **An extractor** is an apparatus for carrying out the extraction.

EXTRACTION EQUILIBRIUM.
NERNST'S DISTRIBUTION LAW.

- Let us consider the distribution of a substance A between the contacting immiscible liquid organic and aqueous phases at a constant temperature (T= const).

A(organic) = A(aqu.)

Equilibrium constant P, equal to

$$P = \frac{a(\text{organic})}{a(\text{aqu.})},$$

where ***a* (organic)** and ***a* (aqu.)** — are equilibrium activities of substance A in organic and aqueous phase respectively. The value P, in this case, is called the distribution constant (true thermodynamic), it is constant at a constant temperature for a given system.

THE DISTRIBUTION CONSTANT (P)

$$a(\text{organic}) = f_{\text{organic}}[\text{A}]_{\text{organic}} \text{ and } a(\text{aqu.}) = f_{\text{aqu.}}[\text{A}]_{\text{aqu.}},$$

$$P = \frac{f_{\text{organic}}[\text{A}]_{\text{organic}}}{f_{\text{aqu.}}[\text{A}]_{\text{aqu.}}}. \qquad P = \frac{[\text{A}]_{\text{organic}}}{[\text{A}]_{\text{aqu.}}}.$$

This form of distribution law is most commonly used in analytical chemistry. The distribution constant P, described by the ratio, depends on the nature of the distributed substance and liquid phases as well as temperature.

The ratios and reflect the **Nernst's distribution law.**

DISTRIBUTION COEFFICIENT D

- The distributed substance is often in present in the immiscible contacting liquid organic and aqueous phases in different chemical forms. For example, organic acids RCOOH, where R is an organic radical, in an aqueous solution undergo electrolytic dissociation:

$$RCOOH + H_2O = RCOO^- + H_3O^+$$

$$2RCOOH = (RCOOH)_2$$

$$D = \frac{\sum c_{\text{organic}}}{\sum c_{\text{aqu.}}},$$

where ∑C(ganic) - is the sum of the equilibrium concentrations in the organic phase of all forms of the distributed substance; ∑C(aqu.) - is the sum of the equilibrium concentrations in the aqueous phase of all forms of the distributed substance.

EXTRACTION DEGREE (R)

- **The extraction degree** is a percentage of the total mass (total quantity) of the extracted substance in the organic phase to its total mass (total quantity) in both phases.

$$R = \frac{\dfrac{c_{\text{organic}} V_{\text{organic}}}{c_{\text{aqu.}} V_{\text{organic}}} \cdot 100\%}{\dfrac{c_{\text{organic}} V_{\text{organic}}}{c_{\text{aqu.}} V_{\text{organic}}} + \dfrac{c_{\text{aqu.}} V_{\text{aqu.}}}{c_{\text{aqu.}} V_{\text{organic}}}} = \frac{D}{D + \dfrac{V_{\text{aqu.}}}{V_{\text{organic}}}} \cdot 100\%.$$

EXTRACTION CONSTANT K_{EX}.

- Extraction constant Kex — is a constant of heterogeneous chemical equilibrium established during extraction. Thus, for example, during the extraction of a metal cation Mn+ from an aqueous solution using an extraction reagent— HA acid, a heterogeneous reaction occurs at the phase - boundary

$$K_{ex} = \frac{a(\mathrm{MA}_n(\mathrm{organic}))a(\mathrm{H}^+(\mathrm{aqu.}))^n}{a(\mathrm{M}^{n+}(\mathrm{aqu.}))a(\mathrm{HA}(\mathrm{organic}))^n}.$$

CLASSIFICATION OF EXTRACTION SYSTEMS

Non-ionized compounds.

- ***1. Covalently bonded*** molecular substances (Cl_2, Br_2, I_2, OsO_4). Almost all non-ionic organic compounds are also included in this group. The distribution law is most strictly followed for substances of this group. These substances are characterized by selective extraction.
- ***2. Intracomplex compounds*** are the most common class of extractable substances. The following compounds are used as chelating extraction agents: 8-hydroxyquinoline, dithizone, cupferon, 3-diketones, sodium diethyl dithiocarbaminate.
- ***3 Coordination solvated*** complexes are coordination compounds of metals With a mixed internal sphere, which includes inorganic ligand and neutral extraction reagent.

CLASSIFICATION OF EXTRACTION SYSTEMS

Ionic associates.

Ionic associates include compounds consisting of large cations and usually large anions with a small charge. These compounds decompose into ions in aqueous solutions and exist in the non-ionized form in the organic phase.

- ***4.Mineral acids*** (HC1, HBr, HI, HNO_3 , $HClO_4$) are extracted from aqueous solutions best with solvents having base properties, such as tributyl phosphate, high molecular weight amines, as well as ketones, alcohols,
- ***5.Complex metal acids and their salts*** ($HFeCl_4$, $HSbCl_6$, H_2CoCl_4, $HInBr_4$) are extracted with such organic solvents (ketones, alcohols, ethers and esters, amines), that are capable to protonate with the formation of sufficiently large cations. Such acids are formed by gold, gallium, indium, antimony, niobium, and iron. ,
- ***6.Coordination - unsolvated ionic associates*** are salts of tetraphenylarsomum and tetraphenylphosphonium cations, which are large hydrophobic canons, or large hydrophobic anions, for example, tetraphenylborate anion $[B(C_6H_5)_4 1$. In this case, heavy alkali metals (cesium Cs^+, rubidium Rb^+ cations) are extracted.
- **7.Heteropoly compounds** extracted by oxygen-containing solvents. These systems are used for the extraction of arsenic, molybdenum, phosphorus silicon, tungsten, vanadium.
- ***8.Other ionic associates*** not included in groups 4-7 of extraction systems.

USE OF EXTRACTION

- Extraction is one of the most effective methods of substances separation. Extraction methods are used for obtaining various components from herbal and mineral raw materials, for releasing gases from metals and alloys at high temperatures, for separation of solution components from each other, etc. Cases of extraction by molten salts or metals are described.

Use of extraction processes in pharmaceutical analysis

- In the quantitative pharmaceutical analysis, extraction is often combined with some physicochemical method. Extraction-photometric, extraction- chromatographic and other combined methods of quantitative analysis have been developed. Extraction-photometric methods are used, for example, in identifying some vitamins.
- Extraction methods are especially widely used in the analysis of herbal medicinal raw materials, and also for obtaining infusions, decoctions, tinctures, extracts of medicinal substances. In this case, the extract refers to the drug dosage form, obtained by the extraction method in accordance with fi vermin requirements.
- In the preparation of infusions and decoctions, the extraction of medicinal substances from crushed medicinal raw materials is carried out with water, in the preparation of extracts — with water, ethanol and other extractants.