Liquid-liquid extraction is a useful method to separate components (compounds) of a mixture.

Let's see an example.

Suppose that you have a mixture of sugar in vegetable oil (it tastes sweet!) and you want to separate the sugar from the oil. You observe that the sugar particles are too tiny to filter and you suspect that the sugar is partially dissolved in the vegetable oil.
How about shaking the mixture with water
Will it separate the sugar from the oil? Sugar is much more soluble in water than in vegetable oil, and, as you know, water is \textit{immiscible} (=not soluble) with oil.

Did you see the result? The \textit{water phase} is the bottom layer and the \textit{oil phase} is the top layer, because water is \textit{denser} than oil.
*You have not shaken the mixture yet, so sugar is still in the oil phase.

By shaking the layers (phases) well, you increase the contact area between the two phases. The sugar will move to the phase in which it is most soluble: the \textit{water layer}.

Now the water phase tastes sweet, because the sugar is moved to the water phase upon shaking.**You extracted sugar from the oil with water.** In this example, water was the extraction solvent; the original oil-sugar mixture was the solution to be extracted; and sugar was the compound extracted from one phase to another. Separating the two layers accomplishes the separation of the sugar from the vegetable oil.

Did you get it? .....the concept of liquid-liquid extraction?

Liquid-liquid extraction is based on the transfer of a solute substance from one liquid phase into another liquid phase according to the solubility. Extraction becomes a very useful tool if you choose a suitable extraction solvent. You can use extraction to separate a substance selectively from a mixture, or to remove unwanted impurities from a solution. In the practical use, usually one phase is a water or water-based (aqueous) solution and the other an organic solvent which is immiscible with water.

The success of this method depends upon the difference in solubility of a compound in various solvents. For a given compound, solubility differences between solvents is quantified as the "\textit{distribution coefficient}"
Partition Coefficient $K_p$ (Distribution Coefficient $K_d$)

When a compound is shaken in a separatory funnel with two immiscible solvents, the compound will distribute itself between the two solvents.

Normally one solvent is water and the other solvent is a water-immiscible organic solvent.

Most organic compounds are more soluble in organic solvents, while some organic compounds are more soluble in water.

Here is the universal rule:

At a certain temperature, the ratio of concentrations of a solute in each solvent is always constant. And this ratio is called the distribution coefficient, $K$.

\[
K = \frac{\text{concentration in solvent}_2}{\text{concentration in solvent}_1}
\]

For example, suppose the compound has a distribution coefficient $K = 2$ between solvent$_1$ and solvent$_2$.

By convention the organic solvent is (1) and water is (2).

(1) If there are 30 particles of compound, these are distributed between equal volumes of solvent$_1$ and solvent$_2$.

(2) If there are 300 particles of compound, the same distribution ratio is observed in solvents 1 and 2.

(3) When you double the volume of solvent$_2$ (i.e., 200 mL of solvent$_2$ and 100 mL of solvent$_1$), the 300 particles of compound distribute as shown.

If you use a larger amount of extraction solvent, more solute is extracted.
What happens if you extract twice with 100 mL of solvent_2?
In this case, the amount of extraction solvent is the same volume as was used in Figure 3, but the total volume is divided into two portions and you extract with each.

As seen previously, with 200 mL of solvent_2 you extracted 240 particles of compound. One extraction with 200 mL gave a TOTAL of 240 particles.

You still have 100 mL of solvent_1, containing 100 particles. Now you add a second 100 mL volume of fresh solvent_2. According to the distribution coefficient K=2, you can extract 67 more particles from the remaining solution.

An additional 67 particles are extracted with the second portion of extraction solvent (solvent_2). The total number of particles extracted from the first (200 particles) and second (67 particles) volumes of extraction solvent is 267. This is a greater number of particles than the single extraction (240 particles) using one 200 mL portion of solvent_2.

It is more efficient to carry out two extractions with 1/2 volume of extraction solvent than one large volume.

If you extract twice with 1/2 the volume, the extraction is more efficient than if you extract once with a full volume. Likewise, extraction three times with 1/3 the volume is even more efficient.... four times with 1/4 the volume is more efficient.... five times with 1/5 the volume is more efficient... ad infinitum

The greater the number of small extractions, the greater the quantity of solute removed. However for maximum efficiency the rule of thumb is to extract three times with 1/3 volume.
Chemically active (acid-base) extraction

Can you change the solubility property of a compound? How?

Most organic compounds are more soluble in organic solvents than in water, usually by the distribution coefficient $K > 4$

However, specific classes of organic compounds can be reversibly altered chemically to become more water-soluble.

This is a powerful technique and allows you to separate organic compounds from a mixture -- if they belong to different solubility classes.

What type of organic compounds can be made water-soluble? Compounds belonging to the following solubility classes can be converted to their water-soluble salt form.

(1) **Organic acids** include carboxylic acids (strong organic acids) and phenols (weak organic acids).

Examples of **Carboxylic acids**

- Benzonic acid
- Butyric acid

Examples of **Phenols**

- Phenol
- Vanillin

(2) **Organic bases** include amines.

Examples of **Amines**

- $\alpha$-Chloroaniline
- $\left(\text{CH}_2\text{CH}_2\text{CH}_2\right)_2\text{NH}$ (Tributylamine)
How can organic acids or bases be converted to a water-soluble form?

1. Organic Acids can be converted to their salt form when treated with an aqueous solution of inorganic base (e.g., NaOH (sodium hydroxide) and NaHCO₃ (sodium bicarbonate)). Salts are ionic, and in general, ions are soluble in water but not soluble in water-immiscible organic solvents. Remember: water is a very polar solvent thus salts (i.e., ionic species) are well dissolved in it.

A. Carboxylic Acids are converted to the salt form with 5% NaOH aqueous solution. NaOH is a strong inorganic base.

Carboxylic acids are strong organic acids (pKa = 3 to 4), so they can also be ionized with weak inorganic bases (e.g., NaHCO₃ (sodium bicarbonate)) aqueous solution.

Let's try a sample problem.
Here is a mixture of naphthalene and benzoic acid, dissolved in dichloromethane.

You want to separate these two compounds. What will you do?

You may use an aqueous solution of either 5% NaOH or sat. NaHCO₃, to extract benzoic acid as a salt form.
B. Phenols are considered to be weak organic acids. Phenol, the parent compound, is partially water-soluble (1 g will dissolve in 15 mL of water), whereas substituted phenols are not. Sodium bicarbonate (NaHCO₃) aqueous solution, a weak inorganic base, will not deprotonate phenols to make it ionic, because it is not strong enough. However, treatment with NaOH, a strong inorganic base, can change phenol to its ionic (salt) form.

Let's try a another sample problem.

Here is a mixture of benzoic acid and p-methoxyphenol, dissolved in dichloromethane.

You want to separate these two compounds. What will you do?

You cannot use 5% NaOH to separate these two compounds. NaOH will react with both benzoic acid and p-methoxyphenol, thus both compounds will be extracted into the aqueous layer.

Let's try this problem again.

Here is another mixture of benzoic acid and p-methoxyphenol, dissolved in dichloromethane.

NaOH was too strong a base, thus it does not differentiate the strong and weak organic acids. Use of weak inorganic base such as NaHCO₃ will differentiate between the compounds.

Strong organic acids such as benzoic acid would be deprotonated and ionized, while weak organic acids such as phenols would NOT be deprotonated.
2. Organic Bases (amines) can be converted to their salt form when treated with an aqueous solution of an inorganic acid such as HCl (hydrochloric acid).

Recall that salts are ionic and generally soluble in water but not soluble in water-immiscible organic solvents.

Let's try a third sample problem.
Here is a mixture of benzoic acid and p-chloroaniline, dissolved in dichloromethane.

You want to separate these two compounds. What will you do?

You may use an aqueous solution of either 5% HCl, to extract the amine as a salt form and benzoic acid has remained in the organic layer.

You can separate four different classes of compounds from a mixture based on differing solubility properties. The four classes are: 1. Amines (organic base) 2. Carboxylic acids (strong acid) 3. Phenols (weak acid) 4. Neutral compounds.
After the separation of the mixture of four components, we will have four solutions: each solution contains one component. The first three compounds are chemically altered, existing in their salt form dissolved in aqueous solution. The fourth compound is not chemically altered, but it is dissolved in an organic solvent. We now want to recover each compound in its original state (i.e., in the non-ionic form) to complete the experiment. We call this step isolation or recovery.

Let’s see, one by one, how to recover each compound obtained from the separation process.

Isolation (Recovery) of amines

An amine is a basic compound. It is protonated in the presence of excess HCl forming a salt that is soluble in aqueous solution. This is how you separated the amine from the original mixture containing it.

An amine is soluble in acidic aqueous solution because it forms a salt, an ionic form.

However, if you change the pH of the solution to basic the amine can no longer stay dissolved because it is no longer ionic! This process is called basification.

Basification is done by carefully adding concentrated NaOH solution to the solution containing the amine salt until it becomes basic.

* In the basification step, you use concentrated NaOH solution to minimize the volume of the final solution. Recall that a dilute solution of HCl was used to extract the amine as its water-soluble salt (see the picture on the right side).

* Basification must be done carefully, portion by portion, with swirling each time because the acid-base neutralization reaction is exothermic.

* Check the pH of the solution to ensure that it is basic. (~pH 10)
There are two different groups of organic acids: **carboxylic acids** (strong acids) and **phenols** (weak acids). In the separation procedure, acids were extracted using (weak or strong) basic aqueous solutions. Both acids can be returned to the original form in the same manner! Organic acids are currently dissolved in a basic aqueous solution, because the acid forms a salt, an ionic form. When you make the aqueous solution acidic, the organic acids no longer remain dissolved because they are no longer ionic and usually precipitate out of solution. This process is called **acidification**.

Acidification is done by carefully adding concentrated HCl solution until the mixture becomes acidic.

When the weak base, NaHCO₃, was the extracting solution, CO₂ gas will evolve during acidification.

* The recovery of organic acids requires acidification with **concentrated** HCl solution. Recall that in the extraction step for the separation of an organic acid either dilute NaHCO₃ or NaOH was used. Concentrated HCl will now help minimize the volume of the final aqueous solution.

* Acidification must be done carefully, portion by portion, with swirling each time because the acid-base neutralization reaction is exothermic.

* Check the pH of the solution to ensure that it is acidic. (~pH 3)
Separatory Funnel Extraction Procedure

Separatory funnels are designed to facilitate the mixing of immiscible liquids.

1. Support the separatory funnel in a ring on a ringstand. Make sure stopcock is closed.
2. Pour in liquid to be extracted.
3. Add extraction solvent.
4. Add ground glass Stopper (well greased).

Pick up the separatory funnel with the stopper in place and the stopcock closed, and rock it once gently.

Then, point the stem up and slowly open the stopcock to release excess pressure. Close the stopcock. Repeat this procedure until only a small amount of pressure is released when it is vented.
Separatory Funnel Extraction Procedure

Shake the separatory funnel vigorously.

Now, shake the funnel vigorously for a few seconds. Release the pressure, then again shake vigorously. About 30 sec total vigorous shaking is usually sufficient to allow solutes to come to equilibrium between the two solvents.

Vent frequently to prevent pressure buildup, which can cause the stopcock and perhaps hazardous chemicals from blowing out. Take special care when washing acidic solutions with bicarbonate or carbonate since this produces a large volume of CO₂ gas.

Separatory Funnel Extraction Procedure

Separate the layers.

Let the funnel rest undisturbed until the layers are clearly separated.

While waiting, remove the stopper and place a beaker or flask under the sep funnel.

Carefully open the stopcock and allow the lower layer to drain into the flask. Drain just to the point that the upper liquid barely reaches the stopcock.