University of Al-Ameed
College of Pharmacy

2nd stage , 1st Semester

Practical Physical Pharmacy I

Partition coefficient/ lab7

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Introduction

Partition coefficient or Distribution coefficient

- The partition coefficient, often denoted as (**Kpc**) or (**PC**), is a fundamental parameter used in chemistry, pharmacology, and environmental science to describe the distribution of a solute between two immiscible phases, typically a hydrophobic phase (such as an organic solvent) and a hydrophilic phase (such as water).
- So the Partition coefficient is defined as the ratio of the concentration of this substance in the first solvent to the concentration of this substance in the second solvent and it is constant at constant temperature and it is independent on the total amount of the substance added.

Mathematically, the partition coefficient is defined as the ratio of concentrations of a solute in the two phases at equilibrium:

$$\mathbf{Kpc} = \frac{[\textit{Solute}]\ \textit{in organic solvent}}{[\textit{Solute}]\ \textit{in aqueous sovent}}$$

Where:

- “[Solute] in organic solvent” is the concentration of the solute in the organic phase (e.g., solvent).
- “[Solute] in aqueous solvent” is the concentration of the solute in the aqueous phase (e.g., water).

Factors Affecting Partition Coefficient:

The partition coefficient depends on several factors including the **nature of the solute** and the **solvent, temperature, pressure, and pH of the aqueous phase**. Generally, non-polar solutes have higher partition coefficients in non-polar solvents compared to polar solvents.

Applications:

- Partition coefficients are crucial in drug design and pharmacology. They help predict drug distribution within the body, absorption rates, and the ability of a drug to cross biological membranes.
- Partition coefficients are used in extraction techniques like liquid-liquid extraction and solid-phase extraction for sample preparation and purification.

Measurement of partition coefficients

Partition coefficients can be experimentally determined using various techniques such as **shake-flask method**, **chromatography**, and **spectroscopy**. These methods involve equilibrating the solute between the two phases and quantifying its concentrations.

Shake-Flask Method for determining partition coefficients:

The success of the Shake-Flask Method relies on achieving equilibrium between the solute and the two phases. Equilibrium is typically achieved through vigorous shaking or stirring of the mixture for a sufficient amount of time.

Factors such as temperature, pH, and the presence of other solutes can influence the equilibration process and should be carefully controlled.

Choice of Solvents:

- The selection of solvents is crucial as they should be immiscible and have different polarities to create distinct phases.
- Common solvent pairs used include water and organic solvents like octanol, hexane, or chloroform.
- Care must be taken to ensure that the solvents chosen are appropriate for the solute being studied and do not interact significantly with it.

Calculation of Partition Coefficient:

Once the concentrations of the solute in each phase are determined, the partition coefficient (Kpc) can be calculated using the following formula:

$$\text{Kp.c} = \frac{\textit{Concentration of solute in Organic layer}}{\textit{Concentration of solute in Aqueous layer}},$$

If Kp.c < 1 so this means that the substance has more solubility in aq. Phase than in org. phase.

If Kp.c > 1 so this means that the substance has more solubility in org. phase than in aq. Phase.

If Kp.c = 1 so this means that the substance has the same solubility in aq. phase and in org. Phase (semi polar).

Example: What is the Partition Coefficient of Boric acid which is distributed between water and amyl alcohol at 25º C if its concentration in water is 0.051 M and its concentration in amyl alcohol is 0.0155 M ?

Answer:

$$\text{Kp.c} = \frac{\boldsymbol{Concentration\ of\ Boric\ acid\ in\ Amyl\ alcohol}}{\boldsymbol{Concentration\ of\ Boric\ acid\ in\ Water}}$$

$$\text{Kp.c} = \frac{0.0155}{0.051} = 0.304 \text{ at } 25\ °\text{C}$$

Kp.c < 1 so this means that the Boric acid has more solubility in water than in amyl alcohol.

Experiment

- **Title:** Partition coefficient
- **Aim:** To calculate the Kp.c of Iodine and then determine whether Iodine is hydrophilic or lipophilic.
- **Materials and equipment**

1. Iodine, Chloroform, distilled water, $Na_2S_2O_3$.
2. Conical flask, burette, pipette, measuring cylinder, separator funnel and balance.

Procedure

1. Pipette 25 mL of iodine solution (1% iodine in organic solvent) into the separating funnel.
2. Add 25 mL of the aqueous solvent to the same separating funnel.
3. Stopper the funnel securely and shake it gently for 10–15 minutes, intermittently releasing pressure by opening the stopcock.
4. Allow the separating funnel to stand undisturbed until the aqueous and organic layers separate completely.
5. Identify the two layers (aqueous layer is the upper layer; organic layer is the lower layer).

7. Carefully drain the organic layer into a clean, dry conical flask and label it properly.
8. Collect the aqueous layer in another clean, dry conical flask.
9. Pipette a known volume (e.g., 10 mL) of the aqueous layer into a separate conical flask.
10. Titrate the aqueous sample with 0.01 N sodium thiosulfate until the solution the color just disappears.
11. Record the burette reading (Endpoint 1).

12. Pipette 5 mL of the organic layer into another conical flask.
13. Add 5 mL of 10% potassium iodide solution to the organic sample.
14. Titrate with 0.1 N sodium thiosulfate using the same endpoint as above and record the burette reading (Endpoint 2).
15. Calculate the concentration of iodine in both phases and determine the partition coefficient (Kp,c).

25 ml. of 1% iodine in chloroform and then add 25 ml. of D.W.

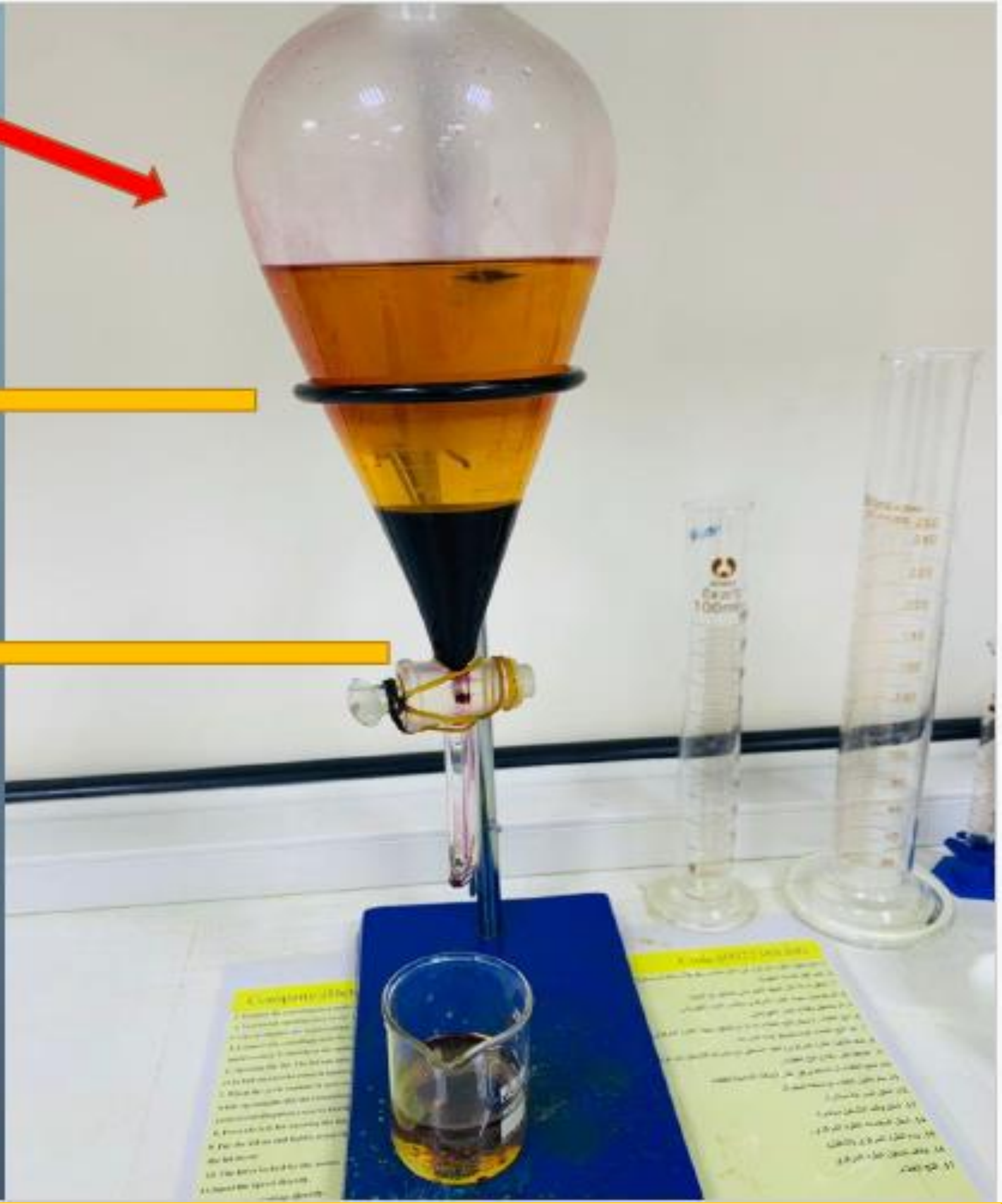
Titrate against
0.02 N $Na_2S_2O_3$ solution

Withdraw 10 ml

Withdraw 5 ml sample

Add 5 ml of 10% KI solution

Titrate against 0.1 N $Na_2S_2O_3$ solution



Calculation

$$C_{\text{iodine}} V_{\text{iodine}} = C_{Na_2S_2O_3} V_{Na_2S_2O_3}$$

1. In aqueous: $C_{\text{iodine}} \times 10 = 0.02 \times \text{Endpoint1}$

2. In organic : $C_{\text{iodine}} \times 5 = 0.1 \times \text{Endpoint2}$

$$\textbf{K p.c iodine} = \frac{\textbf{\textit{Conc . of} iodine \textit{in Organic layer}}}{\textbf{\textit{Conc . of} iodine in \textit{Aqueous layer}}}$$

Results

Flask no.	$Na_2S_2O_3$ (N)	E.P	[Iodine] In aqueous	[Iodine] In organic	Kpc
1					
2					

Note:

1. We added KI for the organic layer only because iodine solubility in chloroform is much more than that in water, so we convert iodine to a an ionized soluble complex (KI_3) to be more soluble in water and then it can react easily with $Na_2S_2O_3$ solution (which is aqueous solution) i.e., KI will extract iodine from the organic layer by converting it into water soluble complex (KI_3)
2. We use the concentration 0.02 N $Na_2S_2O_3$ solution with aqueous layer but 0.1 N Na2S2O3 solution with organic layer, Why ?. With organic layer because in the aqueous layer there is a low conc. of iodine dissolved in water so it required a low concentration of $Na_2S_2O_3$ solution. While in organic layer there is a high conc. of iodine dissolved in chloroform so it required a high concentration of $Na_2S_2O_3$ solution. And for the same reason we withdraw 10 ml from the upper layer but 5 ml from the lower layer, as a result the E.P will be reasonable and accepted.

Thank You