Nutrients and Solubility

Solubility Product Experiment

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Key Concepts

- The Body's Need for Vitamins and Minerals in the Diet
- Molecular Basis for Water Solubility and Fat Solubility (e.g., of Vitamins)
  - Polarity of Solvent and Solute
  - Thermodynamics of Dissolution
- Structures and Functions of Key Vitamins
- Effect of Olestra (Artificial Fat) on Vitamin Solubility
- Quantitative Measures of Mineral Solubility
  - Solubility Product ($K_{sp}$)
  - Solubility (S)
- Calcium in the Body
  - Role of Calcium in the Body
  - Solubility and Absorption of Calcium
  - Control of Calcium Levels in the Body

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- Drug Strategies to Target HIV: Enzyme Kinetics and Enzyme Inhibitors
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Vitamins and Minerals as Essential Dietary Components

The majority of the food that we consume provides us with water, which accounts for approximately 50% to 70% of our body weight, and energy-yielding nutrients such as carbohydrates (sugars and starches), lipids (fats), and proteins (Figure 1). In addition to these major nutrients, our bodies require a variety of other molecules and ions to maintain its proper function. These nutrients, which are required in much smaller amounts, are known collectively as vitamins and minerals.
Carbohydrates, proteins, fats, and water account for most of our nutritional requirements. Vitamins and minerals are required in much smaller amounts, yet their contributions to the body's functioning are essential.

Fourteen vitamins have been shown to be essential for normal growth and health in humans. **Vitamins** are organic molecules (i.e., molecules containing the elements C, H, N, or O) that are needed in trace amounts to help catalyze many of the biochemical reactions in the body. In general, vitamins do not themselves provide chemical energy or act as biochemical building blocks for the body. Many vitamins (e.g., the B vitamins) assist enzymes (act as coenzymes) in activities ranging from vision to growth ability. Other vitamins, such as vitamin C and vitamin E, help to maintain structures within cells. Despite their important roles, the essential vitamins do not have any particular structure in common. They can, however, be classified as fat-soluble (nonpolar) or water-soluble (polar) molecules. Plants and bacteria have the necessary enzymes to synthesize their own vitamins; animals do not have this ability and must consume vitamins in the diet. One exception is Vitamin D, which we can synthesize from cholesterol if we get enough sunlight.

**Minerals** are elements (excluding C, H, N, or O) used in the body to help promote certain reactions or form structures in the body. Minerals are typically consumed in the form of an inorganic salt containing the mineral element. For example, the calcium in Tums is in the form of calcium carbonate (CaCO₃). Minerals, like vitamins, perform a wide variety of functions in the body. Some, such as Mg²⁺ and Zn²⁺, assist enzymatic reactions. Others, such as Na⁺, K⁺, Ca²⁺, and Cl⁻, help maintain electrical and water balance in the body, transmit nerve impulses, and stimulate muscle contraction. Still others, such as calcium and phosphorus, form the compound hydroxyapatite that is responsible for bone growth and structure.

**Solubility of Nutrients and Vitamins**

In order to use the nutrients that we take in when we eat, we must first break the food down into its components. The body then either absorbs these components through the lining of the intestinal tract into the blood, or they pass the intestinal tract and exit the body in the feces. The blood carries the absorbed nutrients to different sites, where they will be reassembled and used by the body. If the nutrients are not used immediately, they will either be stored for later use or they will be excreted in the urine. All three fates of nutrients (immediate use, storage, or excretion) require that the components be soluble, or be solubilized by some other particles (e.g., proteins) that are carried in the blood. To be transported from the stomach to other parts of the body or to be excreted, the nutrients must be soluble.
in water, which is the main component of blood plasma and urine. Alternatively, stored nutrients are held in fat cells, and thus need to be fat soluble.

**Molecular Basis for Water Solubility and Fat Solubility**

The solubility of organic molecules is often summarized by the phrase, "*like dissolves like.*" This means that molecules with many polar groups are more soluble in polar solvents, and molecules with few or no polar groups (i.e., nonpolar molecules) are more soluble in nonpolar solvents. Hence, vitamins are either water-soluble or fat-soluble depending on their molecular structures.

What makes polar vitamins soluble in polar solvents and nonpolar vitamins soluble in nonpolar solvents? The answer to this question lies in the types of interactions that occur between the molecules in a solution. A solution is a homogeneous mixture of solutes and solvent. The dissolution of a substance (solute) can be separated into three steps:

1. The *solute* particles must separate from one another.
2. The *solvent* particles must separate enough to make space for the solute molecules to come between them.
3. The *solute and solvent* particles must interact to form the solution.

Solubility depends on the change in free energy (ΔG) of the process. For a process (in this case, a vitamin dissolving in a solvent) to be spontaneous, the change in free energy must be negative (i.e., ΔG<0). The free energy (G) depends on both the energetics (H) and the randomness (S) of a process (ΔG=ΔH-TΔS, where T is the absolute temperature). The enthalpy and entropy changes that occur in the dissolution process are shown in Figures 2A and 2B.

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**Figure 2A**
The figure on the left schematically shows the enthalpy changes accompanying the three processes that must occur in order for a solution to form: (1) separation of solute molecules, (2) separation of solvent molecules, and (3) interaction of solute and solvent molecules. The overall enthalpy change, ΔH_{soln}, is the sum of the enthalpy changes for each step. In the example shown, ΔH_{soln} is slightly positive, although it can be either positive or negative in other cases.

**Figure 2B**
The figure on the right schematically shows a large, positive entropy change, ΔS_{soln}, that occurs when solute molecules and solvent molecules mix to form a solution. Note that in certain situations involving dissolution of strong ions, ΔS_{soln} could be negative.
In the dissolution process, steps 1 and 2 require energy because interactions between the particles (solute or solvent) are being broken. Step 3 usually releases energy because solute-solvent interactions are being formed. Therefore, the change in enthalpy ($\Delta H$) for the dissolution process (steps 1 through 3) can be either positive or negative, depending on the amount of energy released in step 3 ($\Delta H_3$) relative to the amount of energy required in steps 1 and 2 ($\Delta H_1 + \Delta H_2$). Most dissolution processes increase the randomness of the particles, thus the change in entropy ($\Delta S$) is usually positive. In fact, for a large number of dissolution reactions, the entropic effect (the change in randomness) is more important than the enthalpic effect (the change in energy) in determining the spontaneity of the process. In general, if the solute and solvent interactions are of similar strength (i.e., both polar or both nonpolar), then the energetics of steps 1 and 2 are similar to the energetics of step 3. Therefore, the entropic effect ($\Delta S_{\text{soln}}$) overcomes the enthalpic effect ($\Delta H_{\text{soln}}$) and the process is spontaneous. However, if the solute and solvent interactions are of differing strength (i.e., polar with nonpolar), then the energy required for steps 1 and 2 would be much greater than the energy released from step 3. Hence, the increase in entropy that can occur is not enough to overcome the large increase in enthalpy; thus, the dissolution process is nonspontaneous. To illustrate the importance of $\Delta H$ and $\Delta S$ in determining the spontaneity of dissolution, let us consider three possible cases:

a. The dissolution of a polar solute in a polar solvent.

The polar solute molecules are held together by strong dipole-dipole interactions and hydrogen bonds between the polar groups. Hence, the enthalpy change to break these interactions (step 1) is large and positive ($\Delta H_1 > 0$). The polar solvent molecules are also held together by strong dipole-dipole interactions and hydrogen bonds, so the enthalpy change for step 2 is also large and positive ($\Delta H_2 > 0$). The polar groups of the solute molecules can interact favorably with the polar solvent molecules, resulting in a large, negative enthalpy change for step 3 ($\Delta H_3 < 0$). This negative enthalpy change is approximately as large as the sum of the positive enthalpy changes for steps 1 and 2; therefore, the overall enthalpy change ($\Delta H_{\text{soln}}$) is small. The small enthalpy change ($\Delta H_{\text{soln}}$), together with the positive entropy change for the process ($\Delta S_{\text{soln}}$), result in a negative free energy change ($\Delta G_{\text{soln}} = \Delta H_{\text{soln}} - T\Delta S_{\text{soln}}$) for the process; hence, the dissolution occurs spontaneously.

b. The dissolution of a nonpolar solute in a polar solvent.

The nonpolar solute molecules are held together only by weak van der Waals interactions. Hence, the enthalpy change to break these interactions (step 1) is small. The polar solvent molecules are held together by strong dipole-dipole interactions and hydrogen bonds as in example (a), so the enthalpy change for step 2 is large and positive ($\Delta H_2 > 0$). The nonpolar solute molecules do not form strong interactions with the polar solvent molecules; therefore, the negative enthalpy change for step 3 is small and cannot compensate for the large, positive enthalpy change of step 2. Hence, the overall enthalpy change is large and positive ($\Delta H_{\text{soln}} = \Delta H_1 + \Delta H_2 + \Delta H_3 > 0$). The entropy change for the process ($\Delta S_{\text{soln}}$) is not large enough to overcome the enthalpic effect, and so the overall free energy change ($\Delta G_{\text{soln}} = \Delta H_{\text{soln}} - T\Delta S_{\text{soln}}$) is positive. Therefore, the dissolution does not occur spontaneously.

c. The dissolution of a nonpolar solute in a nonpolar solvent.
The **nonpolar** solute molecules are held together *only* by weak van der Waals interactions. Hence, the enthalpy change to break these interactions (step 1) is small. The **nonpolar** solvent molecules are also held together *only* by weak van der Waals interactions, so the enthalpy change for step 2 is also small. Even though the solute and solvent particles will also not form strong interactions with each other (only van der Waals interactions, so \( \Delta H_3 \) is also small), there is very little energy required for steps 1 and 2 that must be overcome in step 3. Hence, the overall enthalpy change (\( \Delta H_1 + \Delta H_2 + \Delta H_3 \)) is small. The small enthalpy change (\( \Delta H_{\text{soln}} \)), together with the positive entropy change for the process (\( \Delta S_{\text{soln}} \)), result in a negative free energy change (\( \Delta G_{\text{soln}} = \Delta H_{\text{soln}} - T \Delta S_{\text{soln}} \)) for the process; hence, the dissolution occurs spontaneously.

The principles above illustrate why polar vitamins dissolve in water (a polar solvent) and nonpolar vitamins are only soluble in lipids (a nonpolar solvent). Note that there are exceptions to the principle "like dissolves like," e.g., when the entropy decreases when a solution is formed; however, these exceptions will not be discussed in this tutorial.

In general, it is possible to predict whether a vitamin is fat-soluble or water-soluble by examining its structure and determining whether polar groups or nonpolar groups predominate. In the structure of calciferol (Vitamin D\(_2\)), shown in Figure 3 below, there is an -OH group attached to a bulky arrangement of hydrocarbon rings and chains. This one polar group is not enough to compensate for the much larger nonpolar region. Therefore, calciferol is classified as a fat-soluble vitamin.

![Figure 3](https://example.com/fig3.png)

*Figure 3*

This is a 2D ChemDraw representation of the structure of calciferol, Vitamin D\(_2\).

**Structures and Functions of Vitamins**

Table 1 shows the structures and functions of several fat- and water-soluble vitamins. To view a larger representation of the 2D and 3D structures, click on the name of the vitamin. To view and rotate the molecules interactively using [Chime](https://example.com/chime), click on the three-dimensional structures for the coordinate (pdb) file. Can you predict the solubility properties of each vitamin by examining its structure?

<table>
<thead>
<tr>
<th>2D-Representation(^1)</th>
<th>3D-Representation(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="https://example.com/ascorbic.png" alt="Ascorbic Acid" /></td>
<td><img src="https://example.com/ascorbic3d.png" alt="Ascorbic Acid" /></td>
</tr>
</tbody>
</table>

**Ascorbic Acid** (Vitamin C): Coenzyme for collagen (connective tissue protein) formation; antioxidant; antibody production; hormone synthesis; cholesterol formation and excretion

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**Calciferol (Vitamin D₂):** Calcium and phosphorus absorption and regulation (needed for bone, teeth, and proper nerve function); some role in insulin secretion

**Pantothenic Acid (Part of the Vitamin B Complex):** Release of energy from food; manufacture of coenzyme A (needed for breakdown of fats and carbohydrates); production of neurotransmitters; hemoglobin production

**Pyridoxine (Vitamin B₆):** Release of energy from food; synthesis and breakdown of amino acids; prostaglandin manufacture (needed for blood pressure regulation and heart function); skin and hair maintenance; hormone production

**Retinol (Vitamin A):** Vision; growth and repair of epithelial cells; embryonic development; production of myelin (nerve coating) and other membranes; immune system enhancement.

**Riboflavin (Vitamin B₂):** Tissue respiration; metabolism of carbohydrates, amino acids, and fats; growth and repair of body tissues; blood cell development and iron metabolism
**α-Tocopherol (Vitamin E):** Antioxidant (protects cells from toxic compounds, heavy metals, radiation, and free radicals); retinal development; protects vitamin A in eyes

### Olestra and Vitamin Solubility

The solubility properties of vitamins determine how well they will be absorbed by the body. Water-soluble vitamins can easily enter the bloodstream by diffusion since the stomach contents, extracellular fluid, and blood plasma are all aqueous solutions. Fat-soluble vitamins must be consumed with dietary fat to be absorbed. The vitamins are first dissolved in the dietary fat. Then, bile released from the gall bladder solubilizes dietary fat (with vitamins) in micelles that are absorbed into the blood stream. Some newly-developed food products, however, have been found to disrupt the pathway for absorbing fat-soluble vitamins in the body.

In recent years, many types of "fat-free" foods have come into the marketplace. Some of these products contain non-digestible artificial fats that act as substitutes for natural fats and oils. The main artificial fat used commercially is **Olestra**, which is marketed as Olean by Proctor and Gamble, Inc. How does it work? Natural fat comes from digestion of triglyceride, which consists of three nonpolar hydrocarbon chains (derived from fatty acids) attached to glycerol via ester linkages (Figure 4). An intestinal enzyme, lipase, can break down the ester linkage. Then, the loose fatty acids are emulsified (by forming micelles with the bile juice) and absorbed by the body. Olestra consists of seven to eight fatty acid chains attached to a sucrose molecule and behaves like a fat (Figure 5). However, the crowded fatty acid chains block lipase from reaching the sucrose backbone to break down the ester linkages. The Olestra molecule is too large to form absorbable micelles with the bile, so it passes through the intestinal tract, undigested and unabsorbed by the body (and thus adds no calories or fat to the diet). Despite the fact that Olestra may cause uncomfortable gastrointestinal symptoms for some, it was approved by the FDA for use in savory snacks, such as potato chips, in 1996.

**Figure 4  Fatty Acid and Triglyceride**

On the left is a 2D ChemDraw representation of a fatty acid molecule, where \( n \) is commonly 14 – 16. Some fatty acids may contain \( \text{C} = \text{C} \) double bonds.

On the left is a 2D ChemDraw representation of a triglyceride molecule. The glycerol backbone is in blue. The ester linkage is in red. When the ester bonds are broken, the triglyceride molecule reacts with \( \text{H}_2\text{O} \) and turns into 3 fatty acids and a glycerol molecule.
Unfortunately, Olestra may not be as healthy as it seems. Olestra interferes with the absorption of fat-soluble vitamins from food when it is present in the small intestine at the same time as other foods. Because it is nonpolar, Olestra competes with micelles in the intestine for absorption of fat-soluble vitamins and carotenoids. Any vitamins that Olestra absorbs are carried out of the body, and are thus not available for the body to use. Despite the harm Olestra may cause, it could be useful in treating victims of dioxin poisoning. Researchers discovered that Olestra facilitates the removal of dioxins from the body, as it apparently dissolves dioxins similarly to the way it solubilizes fat-soluble vitamins and carotenoids.

Mineral Solubility

Most minerals in the diet are in the form of water-soluble salts. When these salts dissolve, they dissociate into aqueous cations and anions. It is customary to describe the solubility of these salts (i.e., the solubility of minerals) quantitatively, as described below.

Quantitative Measures of Mineral Solubility (\(K_{sp}\) and \(S\))

To quantify the solubility of the ionic salts containing dietary minerals, two distinct quantities are used: the solubility product (\(K_{sp}\)) and the solubility (\(S\)). The solubility product is the equilibrium constant of the dissociation reaction of the mineral-containing salt in water. The solubility of a mineral salt is the amount of the salt that is dissolved per unit volume. This quantity may vary, depending on the conditions. For instance, phytic acid from grain can bind to Zn\(^{2+}\) ions, making these ions unavailable to the body. Suppose that you take a zinc supplement in the form of ZnSO\(_4\). For your body to absorb the zinc, this compound must dissociate into Zn\(^{2+}\) and SO\(_4^{2-}\), as shown in Equation 1.

\[
\text{ZnSO}_4 (s) \rightleftharpoons \text{Zn}^{2+} (aq) + \text{SO}_4^{2-} (aq)
\]  

(1)
The equilibrium constant for this dissociation is a constant given by the Law of Mass Action: \( K_{sp} = [\text{Zn}^{2+}][\text{SO}_4^{2-}] \). If you also consume a large amount of phytic acid with the supplement, the phytic acid will, in effect, remove free \( \text{Zn}^{2+} \) ions from solution. How does this affect the solubility of \( \text{ZnSO}_4 \)? According to Le Chatelier's Principle this will shift the equilibrium in Equation 1 toward the right, and so the solubility of \( \text{ZnSO}_4 \) would increase (in order to keep the solubility product, \( K_{sp} \), constant).

Although the solubility of \( \text{ZnSO}_4 \) increases, we must be careful not to equate solubility of the salt with absorption of that mineral by the body. In the example above, the absorption of zinc decreases with phytic acid because the zinc is not present as the free ion in solution; rather it is bound to phytic acid and is therefore unavailable for absorption. One way to overcome the problem of poor zinc absorption due to phytic acid is to eat leavened, rather than unleavened bread. When yeast is used to make bread rise, it destroys the phytic acid, and so the \( \text{Zn}^{2+} \) ions remain free in solution to be absorbed by the body.

**Calcium in the Body**

Our bodies contain a staggering 1200 g of calcium. Only 1% of this calcium is in the body fluids (the extracellular fluid, the blood, and the cellular fluid). The calcium in the blood is important for a number of functions, including blood clotting, transmission of nerve impulses, muscle contraction, stability of cell membranes, and cell metabolism. The remaining 99% of the calcium in the body is contained in the bones in the compound **hydroxyapatite**, \( \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \). This mineral provides the structural integrity of the skeleton.

The calcium in the body fluids can exist in three forms: (1) as the free cation \( \text{Ca}^{2+} \) (about 50% of the calcium in the fluids), (2) bound to proteins (about 40% of the calcium in the fluids), and (3) complexed with other ions (about 10% of the calcium in the fluids). Of these three forms, the free cation is the most important for the physiological functions described in the paragraph above, and its concentration must be carefully maintained. For instance, muscle contraction is initiated by a sudden increase in calcium concentration in the muscle cells. The \( \text{Ca}^{2+} \) concentration in the extracellular fluid is kept at approximately \( 10^{-3} \) M, and the \( \text{Ca}^{2+} \) concentration inside the cells is kept at approximately \( 10^{-6} \) M. The body has several mechanisms to maintain these ion concentrations. Cells have channels and pumps that regulate the flow of calcium ions between the cells and the extracellular fluids via the cell membrane. In addition, the calcium ions can be removed from or bound to the calcium-binding proteins in order to increase or decrease the free-ion concentration.

The two mechanisms for \( \text{Ca}^{2+} \)-concentration maintenance described above involve only exchange between the different forms of calcium storage in the fluids. What happens if the overall amount of calcium in the fluids gets too low? In this case, calcium can be supplied from two sources: (1) calcium can be consumed in the diet; (2) calcium can be removed from the bones. Calcium removal occurs if too little calcium is supplied in the diet. If this depletion of calcium in bones continues over time, bone mass will decrease; resulting in the condition known as **osteoporosis**.

Despite the importance of consuming calcium in the diet, we absorb only 30% of calcium taken in via diet. Several factors influence absorption: (1) calcium must be dissolved in the intestine, and (2) it must pass through the intestinal walls into the body fluids. Some of the details of how these two factors are regulated are listed below.

- **Factors controlling the solubility of calcium in the intestine**
- The form of the dietary calcium affects calcium solubility. Different calcium salts have different solubilities in the intestinal environment. Calcium citrate, for instance, is more soluble than calcium carbonate.
- The pH of the intestinal tract affects calcium absorption. Most of the calcium absorbed in the body is absorbed in the upper intestine, where the pH is low due to stomach acid entering the intestine. Calcium requires a pH of less than 6 in order to enter solution as Ca\(^{2+}\).

- **Factors controlling the absorption of dissolved calcium**
  - Parathyroid hormone (PTH) promotes calcium absorption directly, by increasing Ca\(^{2+}\) reabsorption in the kidneys.
  - Vitamin D, which is activated as a result of increased PTH levels, also stimulates intestinal calcium absorption.

**Summary**

The nutrients required by our bodies must be dissolved, and then they must be absorbed by the body if they are to be used. The solubility of nutrients is determined by the molecular properties (e.g., polarity) of the nutrients. Although dissolution is a necessary step for nutrients to be absorbed, absorbance depends on more than the solubility of the nutrients. Certain substances in the digestive tract, such as Olestra and phytic acid, can interfere with the absorbance of some nutrients even if the nutrients are dissolved; other substances, such as vitamin D, can enhance nutrient absorption. All of these processes are governed by fundamental chemical properties and principles, such as polarity, molecular structure, intermolecular interactions, thermodynamics, and equilibrium.

**Footnote:** ¹ The 2D representations shown in Table 1 and Figure 5 were drawn using CS ChemDraw Pro, and the 3D coordinates were obtained by MM2 minimization using CS ChemDraw Pro.

**Additional Links:**

The [Olean](#) promotional homepage provides access to a large body of research documenting the effects of Olestra consumption and how Olestra works. This informative site also contains a search engine to locate information of particular interest.

The [Center for Science in the Public Interest](#) maintains a web site warning about the health risks associated with Olestra consumption.

The [Modeling Biological Molecules](#) shows 3D-molecular models of molecules such as sucrose, amylase, glycerol, selected fatty acids, triglyceride, and phospholipids membrane, etc.

**References**


Schlagheck, T. *et al.* "Olestra's effect on vitamins D and E in humans can be offset by increasing dietary levels of these vitamins," (1997) *Journal of Nutrition*, 127, 1666S-1685S.


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