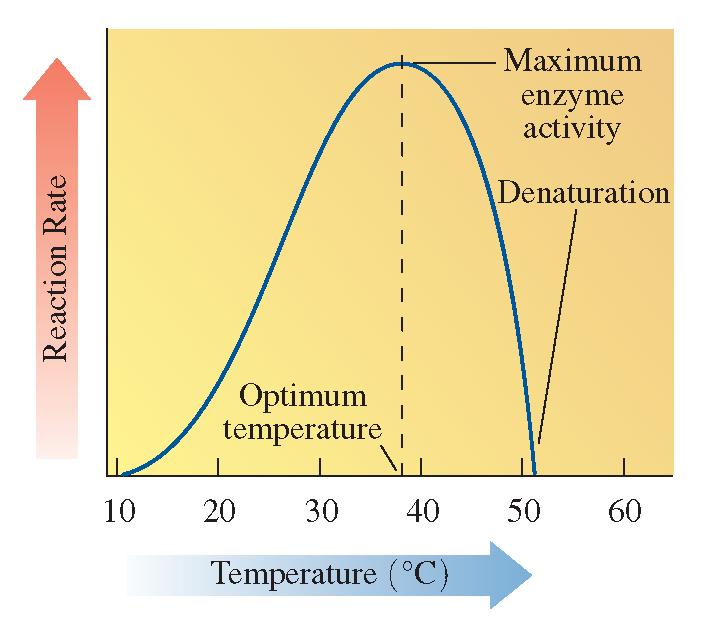
Factors Affecting Enzyme Activity

**Learning Objective: Describe the effect of temperature, pH, and inhibitors on enzyme activity.**

The **activity** of an enzyme describes how fast an enzyme catalyzes the reaction that converts a substrate to product. This activity is strongly affected by reaction conditions, which include **temperature, pH,** and **the presence of inhibitors.**

**1. Temperature**

Enzymes are very sensitive to temperature. At low temperatures, most enzymes show little activity because there is not a sufficient amount of energy for the catalyzed reaction to take place. At higher temperatures, enzyme activity increases as reacting molecules move faster to cause more collisions with enzymes. Enzymes are most active at **optimum temperature**, which is **37 °C**, or body temperature, for most enzymes (see Figure 7.1). At temperatures **above 50 °C**, the tertiary structure, and thus the shape of most proteins, is destroyed, which causes a loss in enzyme activity. For this reason, equipment in hospitals and laboratories is sterilized in autoclaves where the high temperatures denature the enzymes in harmful bacteria. Certain organisms, known as **thermophiles,** live in environments where temperatures range **from 50 °C to 120 °C.**

In order to survive in these extreme conditions, thermophiles must have enzymes with tertiary structures that are not destroyed by such high temperatures.

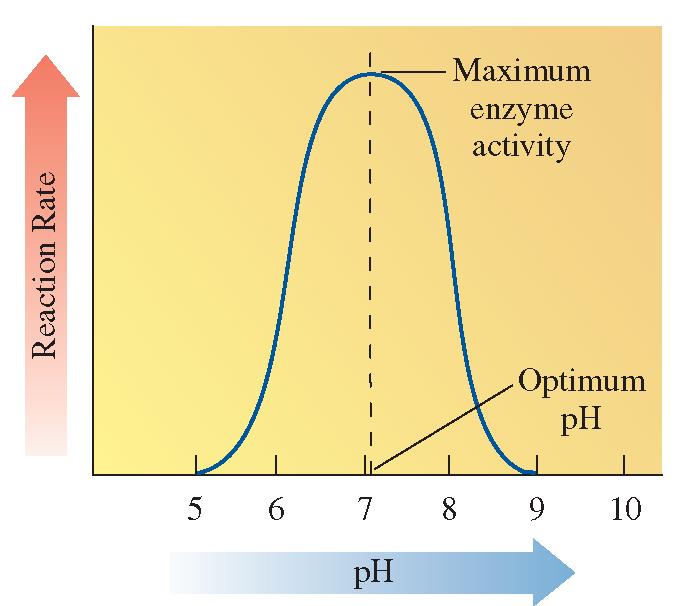
Some research shows that their enzymes are very similar to ordinary enzymes except ***they contain more hydrogen bonds and salt bridges that stabilize the tertiary structures at high temperatures and resist unfolding and the loss of enzymatic activity.***

**Figure 7.1: An enzyme attains maximum activity at its optimum temperature, usually 37 °C. Lower temperatures slow the rate of reaction, and temperatures above 50 °C denature most enzymes with a loss of catalytic activity.**

**Question:** **Why is 37 °C the optimum temperature for many enzymes?**

**2. pH**

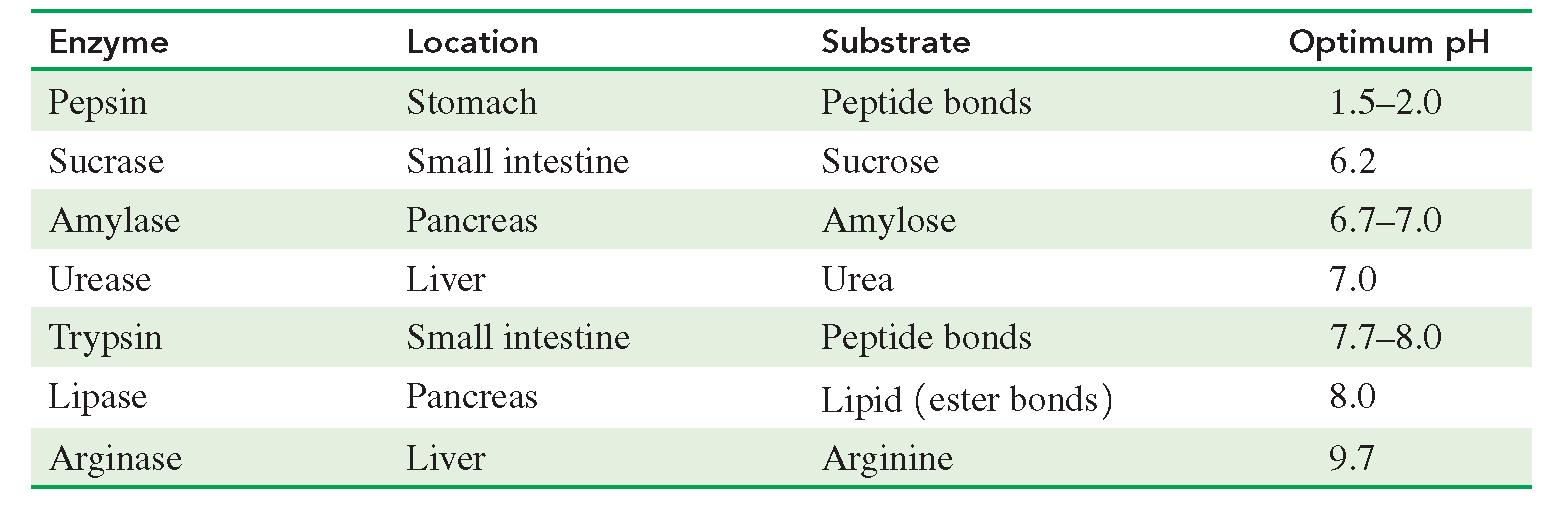
Enzymes are most active at their **optimum pH**, the pH that maintains the proper tertiary structure of the protein **(see Figure 7.2).** If a pH value is **above or below the optimum pH,** the R group interactions are disrupted, which destroys the tertiary structure and the active site. As a result, the enzyme no longer binds substrate, and no catalysis occurs. Small changes in pH are reversible, which allows an enzyme to regain its structure and activity. However, large variations from optimum pH permanently destroy the structure of the enzyme.

Enzymes in most cells have optimum pH values at physiological pH around 7.4. However, enzymes in the stomach have a low optimum pH because they hydrolyze proteins at the acidic pH in the stomach**. For example**, pepsin, a digestive enzyme in the stomach, has an optimum pH of **1.5 to 2.0.** Between meals, the pH in the stomach **is 4 or 5** and pepsin shows little or no digestive activity. When food enters the stomach, the secretion of HCl lowers the pH to about 2, which activates pepsin. **Table 7.1** lists the optimum pH values for selected enzymes.

**Figure 7.2 : Enzymes are most active at their optimum pH. At a higher or lower pH, denaturation of the enzyme causes a loss of catalytic activity.**

**Question: Why does the digestive enzyme pepsin have an**

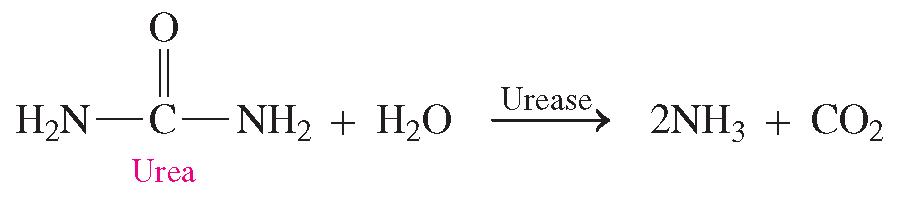
**optimum pH of 2?**



**TABLE 7.1 Optimum pH for Selected Enzymes**

**Example :** **Describe the effect that lowering the temperature to 10 °C would have on the rate of the**

**reaction catalyzed by urease**.

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SOLUTION

Because 10 °C is lower than the optimum temperature of 37 °C, there is a decrease in the rate of the reaction.

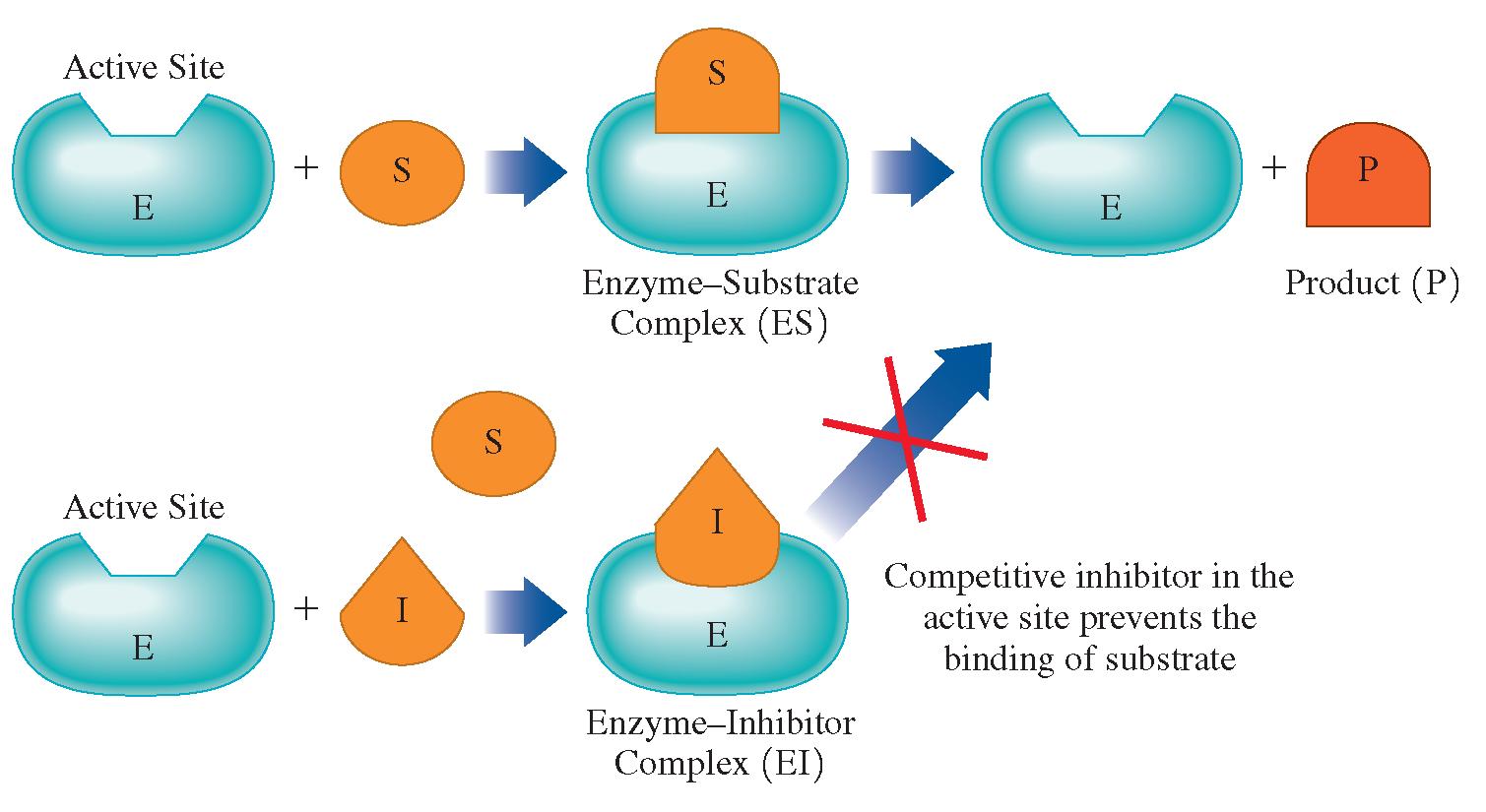
**STUDY CHECK**:

**If urease has an optimum pH of 7.0, what is the effect of lowering the pH to 3?**

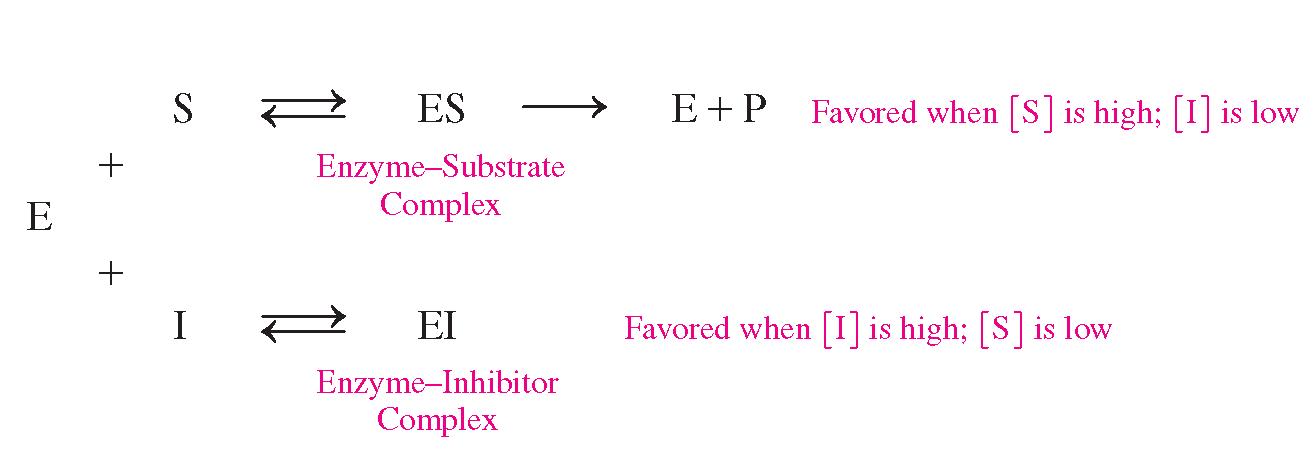
**3. Enzyme Inhibition:**

Many kinds of molecules called **inhibitors** cause enzymes **to lose catalytic activity**. Although inhibitors act differently, they all prevent the active site from binding with a substrate. An enzyme with **a *reversible inhibitor***can regain enzymatic activity, but an enzyme attached to **an *irreversible inhibitor*****loses** **enzymatic activity permanently.**

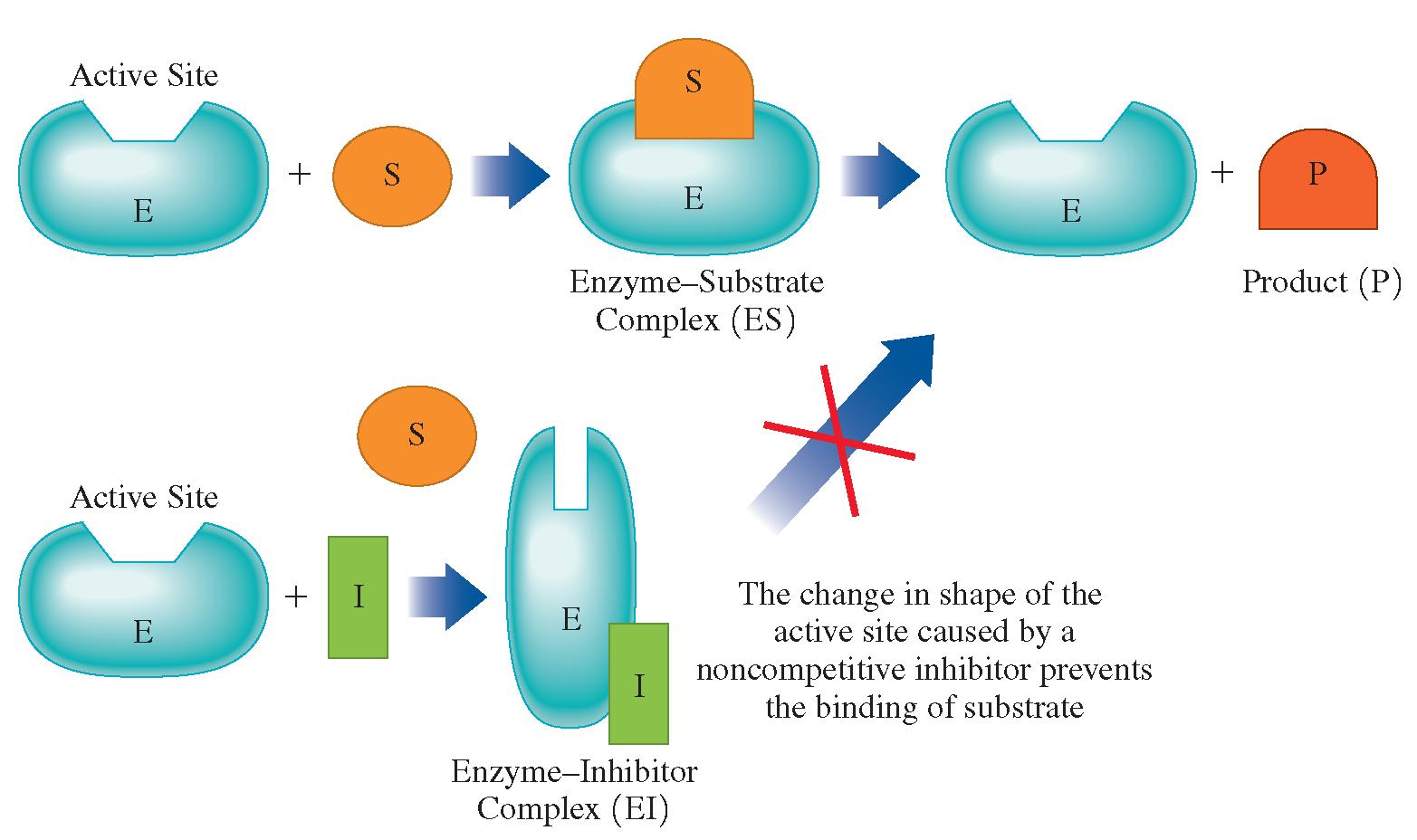
1. **A competitive inhibitor** has a chemical structure and polarity that is similar to that of the substrate. Thus, a competitive inhibitor competes with the substrate for the active site on the enzyme. When the inhibitor occupies the active site, the substrate cannot bind to the enzyme and no reaction can occur **(see Figure 7.3)**



**Figure (7.3) :With a structure similar to the substrate for an enzyme, a competitive inhibitor also fits the active site and competes with the substrate when both are present**.

As long as the concentration of the inhibitor is substantial, there is a loss of enzyme activity. However, adding more substrate displaces the competitive inhibitor. As more enzyme molecules bind to substrate (ES), enzyme activity is regained.

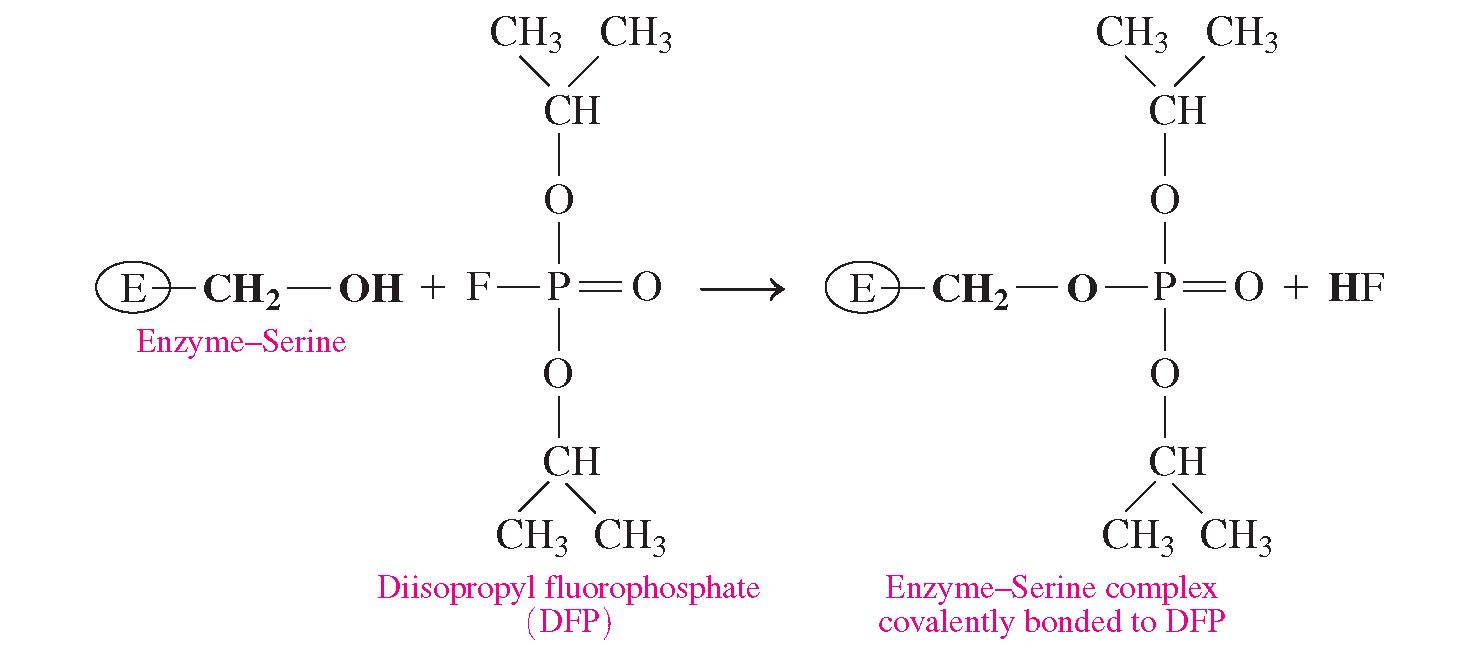
The structure of a **noncompetitive inhibitor** does not resemble the substrate and does not compete for the active site. Instead, a noncompetitive inhibitor binds to a site on the enzyme that is not the active site. When the noncompetitive inhibitor is bonded to the enzyme, the shape of the enzyme is distorted. Inhibition occurs because the substrate cannot fit in the active site or it does not fit properly. Without the proper alignment of substrate with the amino acid side groups, no catalysis can take place **(see Figure 7.4)** .

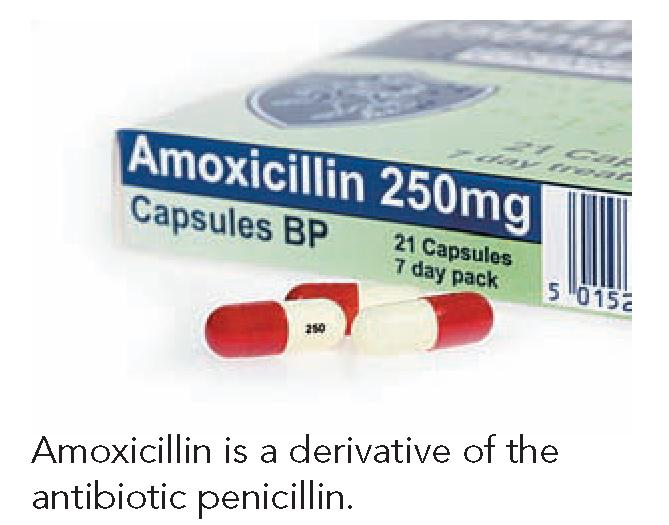
Because a noncompetitive inhibitor is not competing for the active site, the addition of more substrate does not reverse this type of inhibition. Examples of noncompetitive inhibitors are the heavy metal ions Pb2+, Ag+, and Hg2+ that bond with amino acid side groups such as ¬COO- or ¬OH. Catalytic activity is restored when chemical reagents remove the inhibitors.

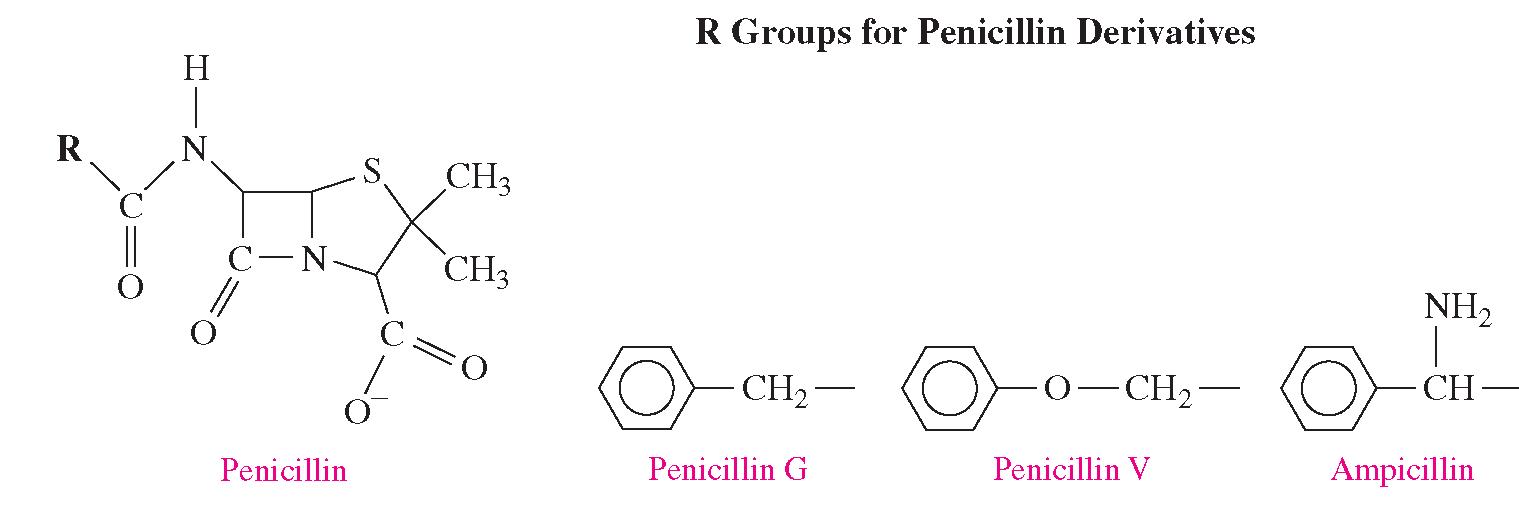
**Figure (7.4) A noncompetitive inhibitor binds to an enzyme at a site other than the active site, which distorts the enzyme and prevents the proper binding and catalysis of the substrate at the active site.**

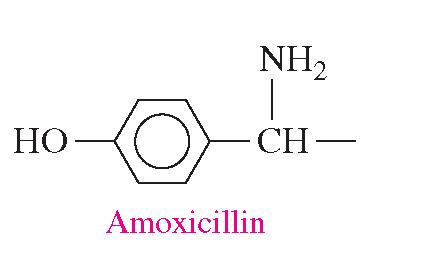
* **Irreversible Inhibition**

In irreversible inhibition, a molecule causes an enzyme to lose all enzymatic activity. Most irreversible inhibitors are toxic substances that destroy enzymes. Usually an irreversible inhibitor forms a covalent bond with an amino acid side group within the active site, which prevents the substrate from binding to the active site or prevents catalytic activity. Insecticides and nerve gases act as irreversible inhibitors of acetylcholinesterase, an enzyme needed for nerve conduction. The compound DFP (diisopropyl fluorophosphates), an organophosphate insecticide, forms a covalent bond with the side chain ¬CH2OH of serine in the active site. When acetylcholinesterase is inhibited, the transmission of nerve impulses is blocked, and paralysis occurs.

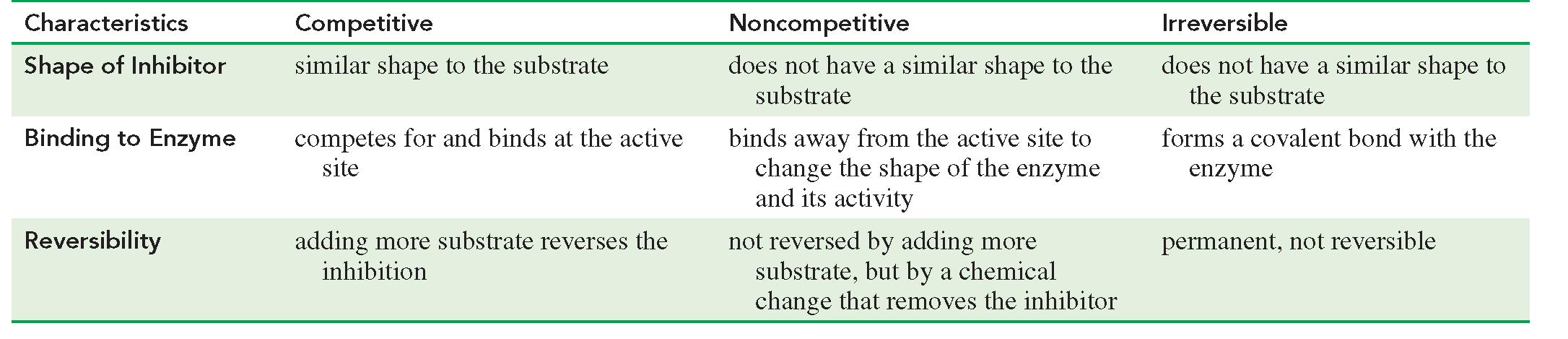


Antibiotics produced by bacteria, mold, or yeast are irreversible inhibitors used to stop bacterial growth. For example, penicillin inhibits an enzyme needed for the formation of cell walls in bacteria, but not human cell membranes. With an incomplete cell wall, bacteria cannot survive and the infection is stopped. However, some bacteria are resistant to penicillin because they produce penicillinase, an enzyme that breaks down penicillin. Over the years, derivatives of penicillin to which bacteria have not yet become resistant have been produced.





**Table 7.2: Summary of Competitive, Noncompetitive, and Irreversible Inhibitors**



SAMPLE PROBLEM :Enzyme Inhibition

State the type of inhibition in the following:

**a.** The inhibitor has a structure that is similar to the substrate.

**b.** This inhibitor binds to the surface of the enzyme, changing its shape in such a way that it cannot bind to substrate.

**SOLUTION**

1. When an inhibitor has a structure similar to that of the substrate, it competes with the substrate for the active site. This type of inhibition is competitive inhibition, which is reversed by increasing the concentration of the substrate **(see Table 7.2).**
2. When an inhibitor binds to the surface of the enzyme, it changes the shape of the enzyme and the active site. This type of inhibition is noncompetitive inhibition because the inhibitor does not have a similar shape to the substrate and does not compete with the substrate for the active site **(see Table 7.2)**

**H.W : What type of inhibition occurs when Sarin, a nerve gas, forms a covalent bond with the R group of serine in the active site of acetylcholinesterase?**

Because Sarin forms a covalent bond with an R group in the active site of the enzyme, the inhibition by Sarin is irreversible