Enzyme inhibition

This article has been translated from WikiSkripta; ready for the **editor's review**.

There are many substances capable of influencing the function of enzyme in the sense of increasing (**activators**') or decreasing (**inhibitors**) its activity. The inhibition of enzyme activity is one of the most important regulatory mechanisms in living systems. The action of many drugs is also based on the inhibition of specific enzymes of metabolic pathways. Therefore, it is important to know the inhibitory mechanism of their action, which affects, for example, the possibilities of neutralizing their effect. Based on the *reversibility of the effect* there are two main forms of inhibition:

1. Reversible inhibition,
2. Irreversible inhibition.

Reversible inhibition

Reversible inhibition can be suppressed. The inhibitor binds **non-covalently** (weak chemical bonds) either to or outside the active site of the enzyme. The effect of the inhibitor can be removed, for example, by an increased supply of substrate or dialysis.

Competitive inhibition

A competitive inhibitor **competes** with a substrate molecule for the enzyme's active site. These are often substances structurally similar to the substrate molecule, but incapable of undergoing an enzyme-catalyzed reaction – the inhibitor just binds to the enzyme. By increasing the concentration of the substrate, the inhibition can be suppressed by displacing the inhibitor from the active site.

A competitive inhibitor **does not affect v_{max}**, it only delays its achievement (the inhibitor must be displaced by an increased concentration of the substrate). K_M therefore increases (apparently the affinity of the enzyme to the substrate is reduced).

Graph of dependence of vmax on substrate concentration

Noncompetitive inhibition

In non-competitive inhibition, the inhibitor binds '*outside* of the substrate binding site. This location is sometimes referred to as the modulation location. By binding, it changes the conformation of the enzyme in such a way that it also affects the conformation of the active site. This makes the binding of the substrate impossible. Inhibition cannot be suppressed by increasing the concentration of the substrate, because the substrate has no tendency to bind to the modulatory site (so there is no fight - competition for the binding site). This inhibition can only be reversed by removing the inhibitor (e.g. dialysis).

Since none of the enzyme-inhibitor complexes (or even enzyme-inhibitor-substrate) is catalytically active, the total amount of enzyme available for the substrate is reduced. This will **reduce v_{max}** of the reaction. **K_M** is **not changed** in this case.

Acompetitive inhibition

This is an inhibition in which the inhibitor binds only to the **enzyme-substrate complex'**. This creates a ternary enzyme-inhibitor-substrate complex.

There is a **decrease in$_{max}$** (occupied complexes are enzymatically ineffective) **and K_M**, but their mutual ratio does not change. The inhibitor is very ineffective at low substrate concentration because it does not have enough ES complexes to bind to.

Irreversible inhibition

In the course of this inhibition, also referred to as ``irreversible*, a ``covalent modification* of the enzyme molecule occurs. The inhibitor binds covalently into or outside the active site of the enzyme, and therefore the inhibition cannot be removed (for example, by dialysis or by increasing the concentration of the substrate).

> *An example is heavy metals (Ag^+, Hg^{2+},...) or organophosphates and their derived nervous gases like sarin and tabun.*

Another described phenomenon is **inhibition by an excess of substrate**. When the concentration of the substrate is too high, there is a fight for the binding site between its molecules. This is reflected in the graph by a slight decrease in v_{max} in the region of higher substrate concentration.