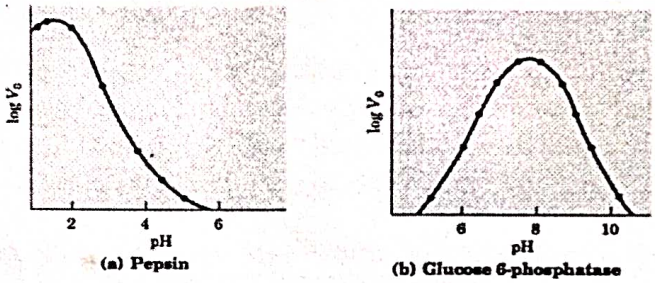
All notes have been taken & modified from:
Nelson and Cox, Lehninger Principles of Biochemistry (2004).
Stryer (5th Edition)

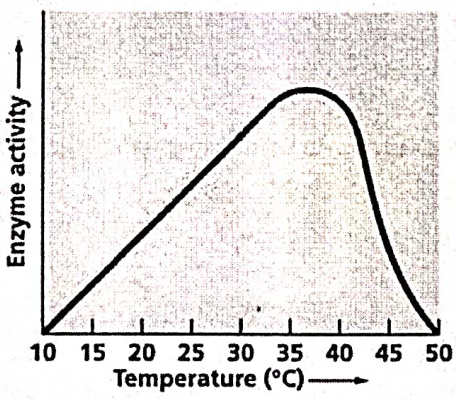
Effect of pH on enzymatic reactions

Enzymes have an optimum pH (or pH range) at which their activity is maximal. At higher or lower pH, the activity decreases. The main reason for this is that the amino acid side chains in the enzyme's active site may act as weak acids and bases with critical functions that depend on their maintaining a certain state of ionization and these ionized side chains may play an essential role in the interactions that maintain protein structure. Thus, change in pH may cause disturbances in the side chains thereby affecting the conformation of the enzyme. The range is different for different enzymes, as shown below in an example for pepsin and glucose-6-phosphatase



Effect of temperature on enzymatic reactions

Like pH, the structure and activity of an enzyme is also sensitive to changes in temperature. The range of temperature wherein the enzyme shows maximum activity is known as optimum temperature. This range is again different from different enzymes.



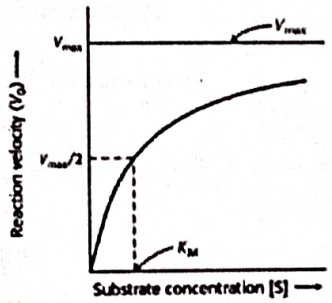
Effect of substrate concentration on enzymatic reactions

Although raising the substrate concentration increases the rate of an enzymatic reaction, after a certain concentration, the enzyme becomes completely saturated with the substrate

and attains the highest rate of reaction that is possible under the given set of conditions. This highest rate is known as the maximum velocity (Vmax).

According the Michelis Mentin kinetics, the substrate concentration at which an enzyme can attain half of Vmax is denoted by Km.

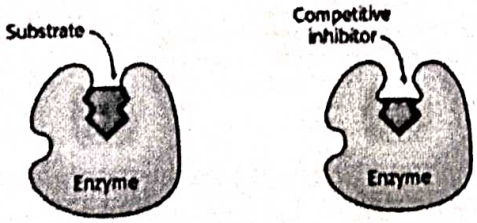
Thus, the Michelis Mentin equation states that: Km = Vmax/2.



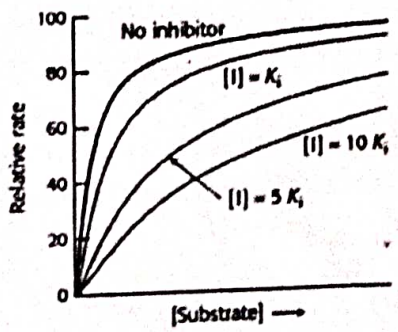
Apart from temperature, pH and the substrate itself, the activity of many enzymes can be regulated by the binding of specific molecules or ions. These molecules can either be inhibitors (inhibiting the enzyme activity) or activators (enhancing the enzyme activity). The regulation of enzyme activity serves as a major control mechanism in biological systems.

Reversible enzyme inhibition: A reversible inhibitor is able to rapidly dissociate from its target enzyme and thereby displays its effects only transiently. There are several types of reversible inhibitions:

a. **Competitive inhibition**

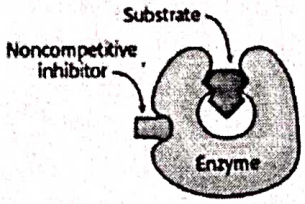


In case of competitive inhibition, the inhibitor competes with the substrate to bind to the active site. Thus, the enzyme can either bind to the substrate, to form an ES complex or to the inhibitor, forming an EI complex, but never both.

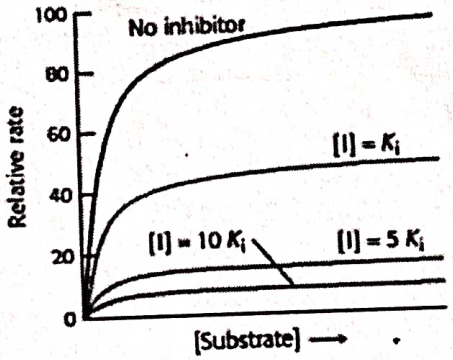


In a competitive inhibition, as the concentration of inhibitor [I] goes on increasing, higher substrate concentrations are required to attain a particular velocity (compare graphs with [I]=Ki and [I]=10Ki. To attain the same reaction velocity 60, a much higher substrate concentration is required for [I] = 10Ki. At lower concentration of [I], attaining the Vmax is still possible- compare graph with "no inhibitor" and graph with [I]=Ki.

b. Non-competitive inhibition



In case of a non-competitive inhibition, the inhibitor binds to a site distinct from the active site of the enzyme, which is known as the "allosteric site". Thus, the enzyme is able to bind to the substrate as well as inhibitor at the same time, forming an ESI complex, apart from ES and EI complexes. The ESI complex cannot be converted into a product.



In a non-competitive inhibition, as the possibility of ES complex alone is extremely low, there is a very low turnover of the product. Thus, even at lower concentration of [I], attaining the Vmax is not possible- compare graph with "no inhibitor" and graph with [I]=Ki.

c. Uncompetitive inhibition

This is a modification of the non-competitive inhibition, wherein, the inhibitor can bind only to the ES complex, thus there is never a formation of just an EI complex.

Irreversible enzyme inhibition: An irreversible inhibitor usually binds covalently to the enzyme or destroys a functional group on an enzyme that is required for the enzyme activity.