Non-competitive inhibitors bind to the enzyme at a location other than the active site – allosteric site. The binding of the inhibitor causes the tertiary structure to change so the active site changes shape. This results in the active site no longer having a complementary shape to the substrate so it is unable to bind to the enzyme. The enzyme is inhibited. The inhibitor doesn't compete with the substrate for the active site.

Many non-competitive inhibitors bind permanently to enzyme molecules (irreversible), and any enzyme molecules bound by inhibitor molecules are effectively denatured.

Increasing the enzyme/substrate concentration will not overcome the effect of a non-competitive inhibitor. Increasing the inhibitor concentration will decrease the rate of reaction further as more active sits become unavailable.

Organophosphates used as insecticides and herbicides irreversibly inhibit the enzyme acetyl cholinesterase, an enzyme necessary for nerve impulse transmission. This can lead to muscle cramps, paralysis, and even death if accidently ingested.

Protein pump inhibitors (PPIs) are used to treat long-term indigestion. They irreversible block an enzyme system responsible for secreting hydrogen ions into the stomach. They reduce the production of excess acid which, if left untreated, can lead to the formation of stomach ulcers.

End-product inhibition is an example of reversible non-competitive inhibition. It is enzyme inhibition that occurs when the product of a reaction acts as an inhibitor to the enzyme that produces it. This serves as a negative-feedback control mechanism for the reaction. Excess products aren't made or wasted.

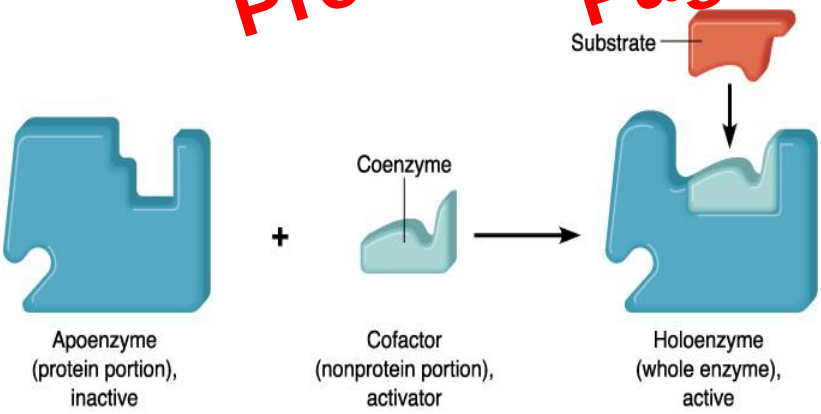
Respiration is an example of end-product inhibition which results in the production of ATP. Two phosphate groups are added to the glucose molecule. The addition of the second phosphate group, which results in the initial breakdown of the glucose molecule, is catalysed by the enzyme phosphofructokinase (PFK). This enzyme is competitively inhibited by ATP. ATP therefore regulates its own production.

Metabolic poisons may be enzyme inhibitors as they inhibit the action of enzymes involved in metabolic processes, which disturbs an organism. For example, potassium cyanide is an irreversible Inhibitor of the enzyme cytochrome c oxidase, which takes part in respiration reactions in cells. If this enzyme is inhibited, ATP cannot be made since oxygen use is decreased. This means that cells can only respire anaerobically, leading to a build-up of lactic acid in the blood. This is potentially fatal.

Some medicinal drugs work by inhibiting the activity of enzymes which in turn treats conditions. Infection by viruses can be treated by Inhibitors to the viral enzyme protease, often competitive inhibitors. This means that viruses cannot build new protein coats and therefore cannot replicate. Penicillin works by inhibiting a bacterial enzyme that is responsible for forming cross-links in bacteria cell walls. This therefore halts reproduction.

The same enzyme may act as both a poison and a drug, depending on the amount of inhibitor and its location.






Many enzymes are produced in an inactive form, known as inactive precursor enzymes, particularly enzymes that can cause damage within the cells producing them or to tissues where they are released, or enzymes whose action needs to be controlled and only activated under certain conditions.

Precursor enzymes often need to undergo a change in their tertiary structure, particularly to the active site, to be activated. This can be achieved by the addition of a cofactor. Before the cofactor is added, the precursor protein is called an apoenzyme. When the cofactor is added and the enzyme is activated, it is called a holoenzyme.

Sometimes the change in tertiary structure is brought about by the action of another enzyme, such as protease, which cleaves certain bonds in the molecule. In some cases a change in conditions results in a change in tertiary structure and activates a precursor enzyme. These types of precursor enzymes are called zymogens or proenzymes.