8.1 Metabolism

Enzymes

Explain how enzymes catalyse chemical reactions

Enzymes speed up the rate of a chemical reaction by lowering the activation energy threshold

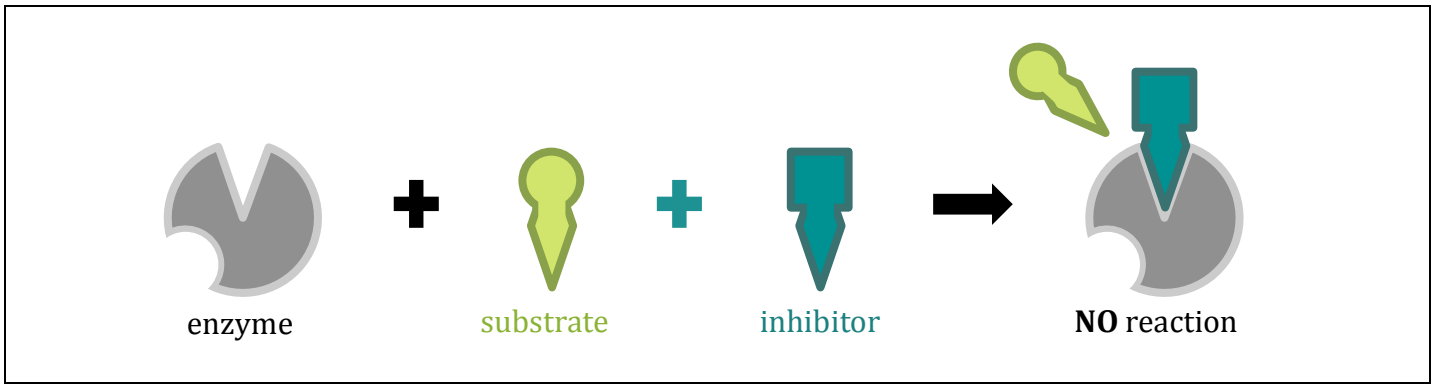
Distinguish between exergonic and endergonic reactions

Exergonic reactions release energy (i.e. reactants have more stored energy than products)

Endergonic reactions absorb energy (i.e. reactants have less stored energy compared to products)

Inhibitors

Outline, with the aid of a diagram, how a competitive inhibitor affects enzyme activity



A competitive inhibitor is similar in structure and chemical properties to the substrate

It can bind to the active site and block substrate binding

Increasing substrate concentrations will reduce the effect of a competitive inhibitor

Give a specific example of a competitive inhibitor

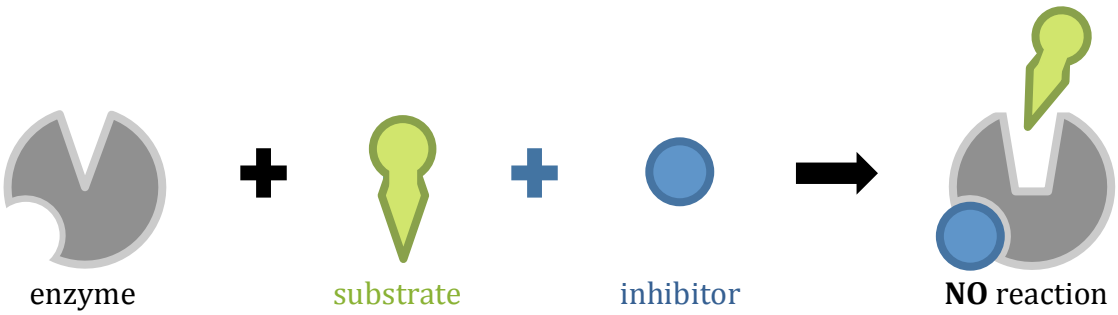
Relenza is a drug designed to treat infection with the influenza virus

Influenza virions tether to infected cells via haemagglutinin and are released by the enzyme neuraminidase

Relenza competitively inhibits the neuraminidase active site, preventing cleavage from haemagglutinin

Thus virions cannot be released and the spread of infection is diminished

Outline, with the aid of a diagram, how a non-competitive inhibitor affects enzyme activity



Non-competitive inhibitors bind to a site other than the active site (called an allosteric site)

These inhibitors cause a conformational change in the enzyme, which alters the shape of the active site

Thus the substrate can no longer bind (increasing substrate concentration will have no effect on inhibition)

Give a specific example of a non-competitive inhibitor

Cyanide binds to a carrier protein in the electron transport chain and causes a conformational change

The carrier can no longer shuttle electrons, so oxidative phosphorylation (aerobic respiration) is shut down

Without energy (ATP) the cells die, making cyanide a very potent poison

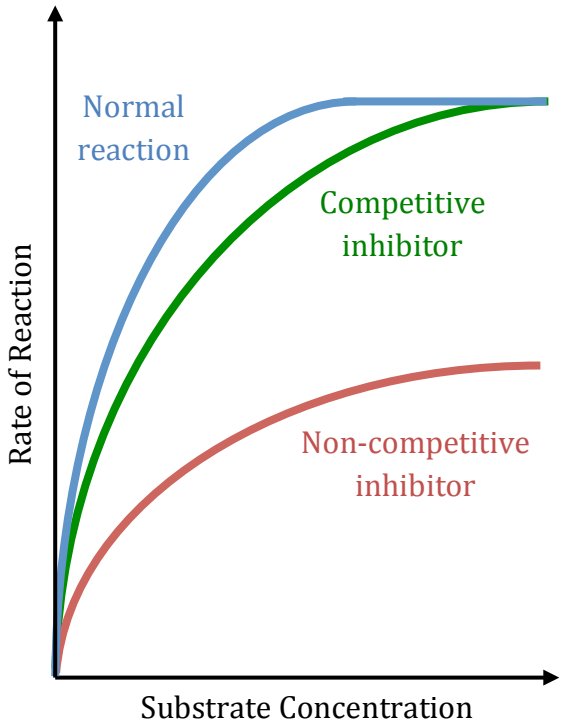
On the graph below, show the impact of a competitive and non-competitive inhibitor on reaction rate

Competitive inhibitor:

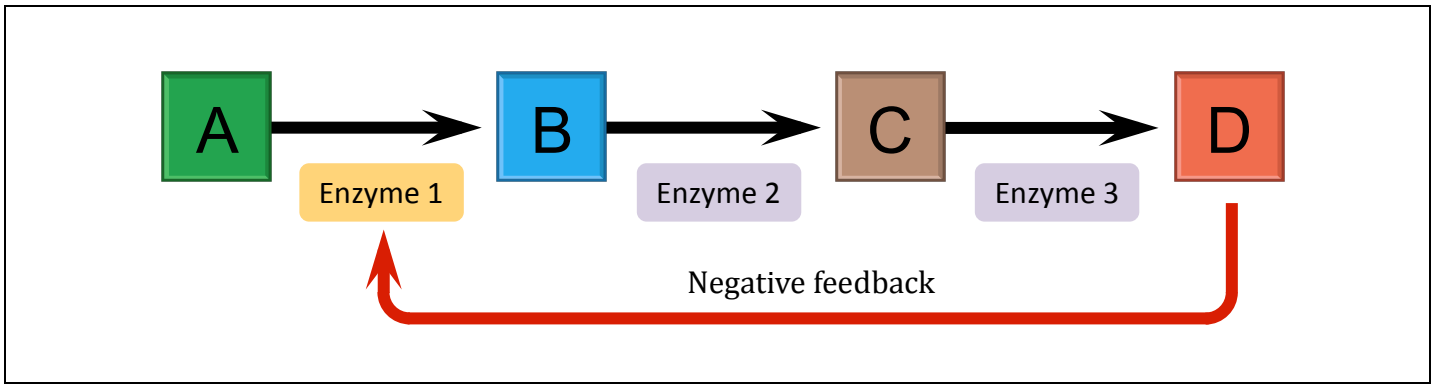
- Rate of reaction is slowed (graph shifts right)
- Maximal rate of reaction is still achievable (but requires higher substrate concentrations)

Non-Competitive inhibitor:

- Rate of reaction is slowed (graph shifts right)
- Maximal rate of reaction is less (graph shifts down)
- Increasing substrate concentration will not increase maximum reaction rate



Outline, with the aid of a diagram, how metabolic pathways are controlled by end-product inhibition



End-product inhibition (or feedback inhibition) is when a product of a metabolic pathway inhibits one of the enzymes involved in its production

This allows reaction rates to be tightly regulated

Give a specific example of end-product inhibition

In plants and bacteria, isoleucine can be synthesised from threonine

This multi-step reaction involves the enzyme threonine deaminase

Isoleucine can bind to an allosteric site on threonine deaminase and non-competitively inhibit it

Thus when isoleucine levels are high its production is reduced, but when levels are low, production proceeds

Outline, with an example, how bioinformatic databases are used to identify potential new drugs

Malaria is caused by the protozoan Plasmodia (whose metabolism is controlled by specific enzymes)

Bioinformatic databases can be searched to identify molecules that structurally resemble specific substrates

Combinatorial chemistry can then be used to modify these molecules to form effective inhibitors

This modelling of desired chemicals is called rational drug design

Identify an example of a metabolic pathway that forms a chain

Glycolysis

Identify an example of a metabolic pathway that forms a cycle

Krebs cycle (citric acid cycle) or Calvin cycle