Topic 8 Metabolism

Topic 8.1 Metabolism

Essential idea: Metabolic reactions are regulated in response to the cell's needs.

Understandings:

- 8.1.U1 Metabolic pathways consist of chains and cycles of enzyme-catalysed reactions.
- 8.1.U2 Enzymes lower the activation energy of the chemical reactions that they catalyse.
- 8.1.U3 Enzyme inhibitors can be competitive or non-competitive.
- 8.1.U4 Metabolic pathways can be controlled by end-product inhibition.

Applications:

- 8.1.A1 End-product inhibition of the pathway that converts threonine to isoleucine.
- 8.1.A2 Use of databases to identify potential new anti-malarial drugs.

Skills

- 8.1.S1 Calculating and plotting rates of reaction from raw experimental results.
- 8.1.S2 Distinguishing different types of inhibition from graphs at specified substrate concentration.

I. Metabolic Pathways

A. Metabolic pathways consist of chains and cycles of enzyme-catalyzed reactions

Challenge:
By changing just one letter at a time, get from 'TREAD' to 'BLINK'. All intermediates must be real English words.

TREAD _____ _____ _____ _____ _____ **BLINK**

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I. Metabolic Pathways

1. Metabolism: the sum total of all chemical reactions that occur within an organism.
2. Metabolic (biochemical) pathways: cycles or chains of enzyme catalyzed reactions. *The chemical change from one molecule to another often does not happen not in one large jump, but in a sequence of small steps. The small steps together form what is called a metabolic pathway.*

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I. Metabolic Pathways

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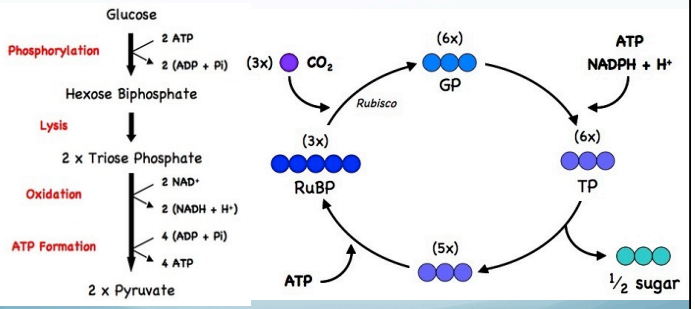
I. Metabolic Pathways

Glycolysis, a part of respiration, is an example of a metabolic chain

The Calvin cycle, a part of photosynthesis, is an example of a metabolic cycle



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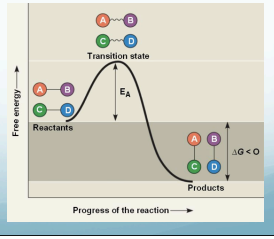
II. Enzymes and Activation Energy

A. Enzymes lower the activation energy of the chemical reactions that they catalyze.
   1. The reactants must absorb energy from the environment in order to reach an unstable transition state, where the bonds between them can break and reform as products.
   2. The energy needed is called activation energy (E_A).

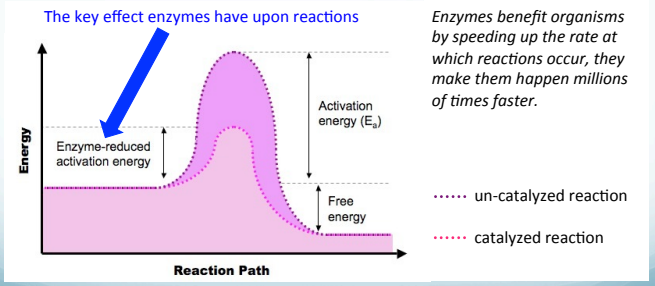
In an exergonic reaction the reactants will lose energy overall resulting in products with less energy that are more chemically stable. Many of exergonic reactions can also be exothermic.



metabolismcook.wikispaces.com

II. Enzymes and Activation Energy

3. Enzymes lower activation energy, the initial input of energy that is required to trigger a chemical reaction.



Enzymes benefit organisms by speeding up the rate at which reactions occur, they make them happen millions of times faster.

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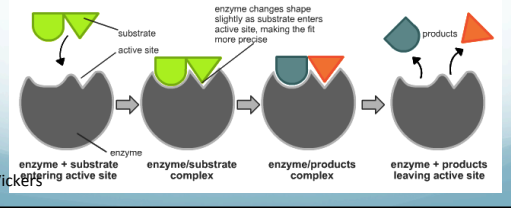
II. Enzymes and Activation Energy

B. How do enzymes lower the activation energy of a reaction?

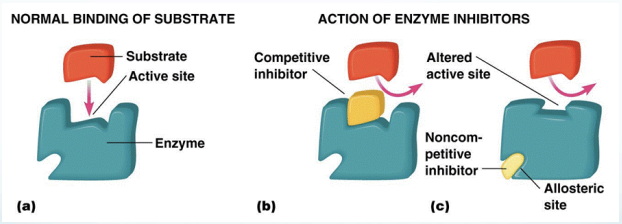
- *The substrate binds to the enzymes' active site and the shape of the active site is altered.*
- *The **bonds** in the substrate molecules are **stressed/become less stable** due to change in shape of the active site.*
- *The energy level of the transition state is reduced also decreasing the activation energy of the reaction.*
- *The bonds between the substrates reform to make products.*
- *The products to be released from the active site because of the lack of chemical attraction.*
- *The net amount of energy released by the reaction is unchanged.*



TimVickers

III. Types of Enzyme Inhibitors

A. Enzyme inhibitors can be competitive or noncompetitive-
   1. Inhibitors are molecules that bind to an enzyme and slow down or stop the enzyme's function.



Enzymes do not need to convert substrates to products all the time. Inhibitors can slow or stop a reaction so products do not build up or energy is not wasted making unneeded products.

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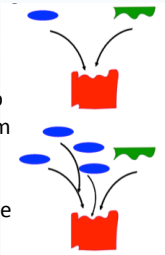
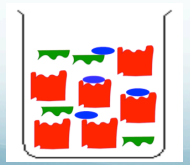
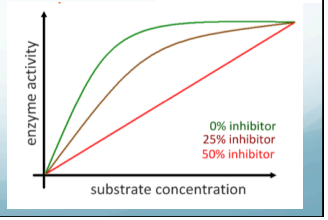
III. Types of Enzyme Inhibitors

B. Enzymes can be inhibited in several ways:
   1. Competitive inhibition:
      a. The competitive inhibitor binds directly to the active site, blocking the substrate from entering the active site.
      b. The higher the concentration of inhibitor, the slower the rate of reaction. This can be overcome by increase the amount of substrates.







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Overcoming alcoholism: an example of competitive inhibition

Normal metabolism of ethanol (alcohol):

ethanol —oxidation→ acetaldehyde —aldehyde oxidase→ acetic acid

Antabuse (competitive inhibitor)

Antabuse (disulfiram) competes with the aldehyde oxidase and prevents the acetaldehyde from being converted to acetic acid.

A build up of acetaldehyde follows, resulting in a strong feeling of nausea and other strong hangover symptoms - a good deterrent from drinking.

Antabuse is administered as a daily pill, so its efficacy relies on the patient's own motivation - if they stop taking it, they can drink again.

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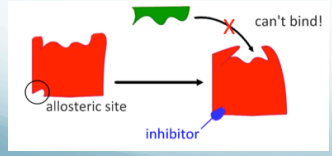
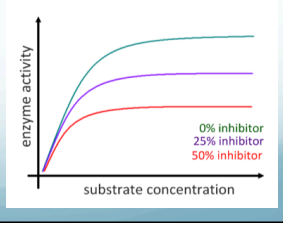
III. Types of Enzyme Inhibitors

2. Noncompetitive inhibition:
   a. Non-competitive inhibitors bind to an allosteric (other) site on the enzyme.
   b. The active site is altered such that the substrate cannot attach and react.
   c. Increasing the concentration of inhibitor decreases the rate of reaction. The maximum rate is also reduced, even if the substrate concentration is increased.





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ACE Inhibitors: Helping Control Blood Pressure

The RAA system causes *vasoconstriction* (tightening of blood vessels) when blood pressure drops (such as after heavy bleeding).

In people with hypertension or heart failure, the action of angiotensin II can make their problem worse.

Vasoconstriction:

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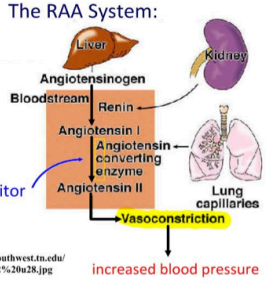
The RAA System:

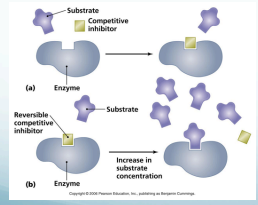


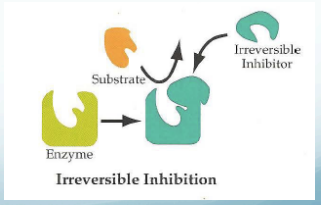
ACE Inhibitors are medications that inhibit Angiotensin Converting Enzymes - they prevent increased blood pressure.

They are non-competitive and reversible.

III. Types of Enzyme Inhibitors

3. Reversible inhibitors are hydrogen (weakly) bonded to the enzyme and can be released, allowing the enzyme to function again.
4. Irreversible inhibitors are covalently (permanently) bonded to the enzyme and cannot continue to catalyze reactions.





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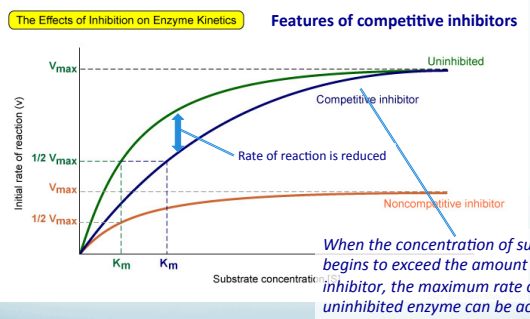
III. Types of Enzyme Inhibitors

4. Distinguishing between competitive and non-competitive inhibition



When the concentration of substrate begins to exceed the amount of inhibitor, the maximum rate of the uninhibited enzyme can be achieved. However, it takes a much higher concentration of substrate to achieve this maximum rate.

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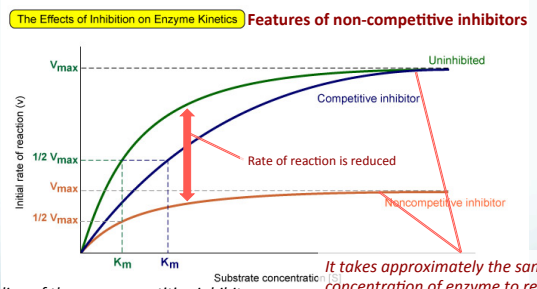
III. Types of Enzyme Inhibitors

4. Distinguishing between competitive and non-competitive inhibition



The binding of the non-competitive inhibitor prevents some of the enzymes from being able to react regardless of substrate concentration.

It takes approximately the same concentration of enzyme to reach the maximum rate, but the maximum rate is lower than the uninhibited enzyme.

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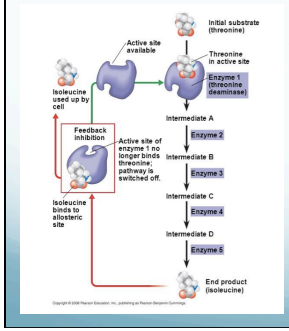
IV. End-Product Inhibition

A. Metabolic pathways can be controlled by end-product inhibition-
   1. Many enzymes are regulated by the products they produce, by binding to an allosteric site on the enzyme.

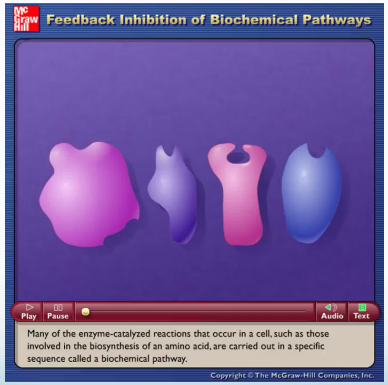


Isoleucine is an essential amino acid (must be obtained from food):

- *Bacteria synthesize isoleucine from threonine in a series of five enzyme-catalysed steps.*
- *As the concentration of isoleucine increases, some of it binds to the allosteric site of threonine deaminase.*
- *Isoleucine acts as a non-competitive inhibitor to threonine deaminase.*
- *The pathway is then turned off, regulating isoleucine production.*
- *If the concentration of isoleucine later falls (as a result of its use) then the allosteric sites of threonine deaminase are emptied and the enzymes recommences the conversion of threonine to isoleucine takes place.*
- *This is negative feedback inhibition.*

Pearson Education

IV. End-Product Inhibition



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