Enzymes

Presented By

Dr. Salwa Abo El-khair
Catalytic Proteins 7: Enzymes
Isoenzymes
- **Isoenzymes (isozymes)** are multiple forms of the enzyme that have the same catalytic activity.

- Although they have the same catalytic activity, they are physically distinct and differ in electrophoretic mobility and liability to inhibitors.

- *Iso* means the same and *isoenzyme* means the same enzyme.
Example of isoenzymes

Many enzymes are present in isoenzyme form:

1. Lactate dehydrogenase
2. Creatine kinase
3. Acid phosphatase
4. Alkaline phosphatase
Lactate dehydrogenase (LDH)

It is an enzyme that catalyzes the removal of 2 hydrogen atoms from lactic acid forming pyruvic acid.
Its level in plasma increases in:

1. Myocardial infarction (heart diseases).
2. Viral hepatitis (liver disease).
3. Leukaemia (blood disease).
- **LDH** enzyme is a tetramer formed of 4 protein subunits; each subunit is called protomer.

- The protomers of LDH are of 2 types, H (after heart) and M (after muscle).

- **LDH isoenzymes** are clinically important to differentiate between heart, liver and blood diseases.
LDH has 5 isoenzymes:

- LDH$_1$ is formed of **HHHH**. It increases in **myocardial infarction**.
- LDH$_2$ is formed of **HHHM**. It increases in **myocardial infarction**.
- LDH$_3$ is formed of **HHMM**. It increases in **leukaemia**.
- LDH$_4$ is formed of **HMMM**. It increases in **viral hepatitis**.
- LDH$_5$ is formed of **MMMM**. It increases in **viral hepatitis**.
Creatine kinase (CK)

It is an enzyme that catalyzes phosphorylation of creatine.

Creatine Kinase

Creatine → Creatine phosphate

ATP  ADP
Its level in plasma increases in

1. Brain tumors.

2. Myocardial infarction (heart disease).


CK isoenzymes are clinically important to differentiate between brain, heart and skeletal muscle diseases.
CK enzyme is a dimmer formed of 2 protein subunits (protomers), B (after brain) and M (after muscle).

CK has 3 isoenzymes:

- CK BB which increases in brain tumors.
- CK MB which increases in heart diseases.
- CK MM which increases in skeletal muscle diseases.
Source of isoenzymes

- Isoenzymes may be produced by the same gene but the subunits undergo different post-translation modifications in different organs.

- Isoenzymes may be produced by more than one gene; each gene produces one subunit.
Medical importance of isoenzymes

- Isoenzymes are not only important for diagnosis but also indicate the diseased organ.
- Lactate dehydrogenase enzyme (LDH) increases in myocardial infarction (heart disease), viral hepatitis (liver disease) and leukaemia (blood disease).
LDH isoenzymes indicate the diseased organ:

- LDH\textsubscript{1} and LDH\textsubscript{2} isoenzymes increase only in myocardial infarction,
- LDH\textsubscript{3} increases in leukaemia
- LDH\textsubscript{4} and LDH\textsubscript{5} increase in viral hepatitis.
Antienzymes
These are **substances** secreted by **living cells** or organisms that **inhibit enzyme activity** e.g.:

- *Ascaris worms* living in the intestine secrete antienzymes (*anti-trypsin* and *anti-pepsin*) so; they are **not digested by proteolytic enzymes** present in the digestive juices.
Mucin lining the stomach contains antienzyme (anti-pepsin) that prevents digestion of stomach wall by pepsin.

Blood plasma contains natural antienzyme (anti-thrombin) that inactivates thrombin after blood coagulation to prevent its intra-vascular spreading.
Riboenzymes
Ribozymes are enzymes but they are **not protein** in nature, they are **nucleic acid** in nature formed of RNA.

- Ribozymes **catalyze cleavage of RNA by hydrolysis of phosphate diester bonds** e.g. cleavage of **pre-mRNA to form mRNA**.
Got any Questions?!
1- The enzyme Creatine kinase levels are increased in the blood of patients with

A) Prostate cancer.
B) Hepatitis
C) Heart attack
D) Osteoporosis

2- The isoenzymes of LDH

(A) Differ only in a single amino acid
(B) Differ in catalytic activity
(C) Exist in 5 forms depending on M and H monomer contents
(D) Occur as monomers
Activity

- Discuss antienzymes (def, examples, biomedical importance).

- Discuss iso-enzymes (def, 2 examples & clinical importance).

- Creatine kinase & Lactate dehydrogenase can be used for diagnosis and follow up of some diseases (explain)
Plasma Enzymes
Blood plasma contains many enzymes.

**Plasma enzymes are classified into:**

1- **Functional** plasma enzymes

2- **Non-functional** plasma enzymes.
<table>
<thead>
<tr>
<th></th>
<th><strong>Functional plasma enzymes</strong></th>
<th><strong>Non-functional plasma enzymes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Concentration in plasma</strong></td>
<td>Present in plasma in higher concentrations in comparison to tissues</td>
<td>Normally, present in plasma in very low concentrations in comparison to tissues</td>
</tr>
<tr>
<td><strong>Function</strong></td>
<td>Have known functions</td>
<td>No known functions</td>
</tr>
<tr>
<td><strong>The substrates</strong></td>
<td>Their substrates are always present in the blood</td>
<td>Their substrates are absent from the blood</td>
</tr>
<tr>
<td><strong>Site of synthesis</strong></td>
<td>Liver</td>
<td>Different organs e.g. liver, heart, brain and skeletal muscles</td>
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<td><strong>Effect of diseases</strong></td>
<td>Decrease in liver diseases</td>
<td>Different enzymes increase in different organ diseases</td>
</tr>
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<td><strong>Examples</strong></td>
<td>Clotting factors e.g. prothrombin, Lipoprotein lipase and pseudo-choline esterase</td>
<td>ALT, AST, CK, LDH, alkaline phosphatase, acid phosphatase and amylase</td>
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</table>
Sources of non-functional plasma enzymes

1. Increase in the rate of enzyme synthesis e.g.
   bilirubin increases the rate of synthesis of alkaline phosphatase in obstructive liver diseases.

2. Obstruction of normal pathway e.g.
   obstruction of bile ducts increases alkaline phosphatase.
3. **Increased permeability** of cell membrane as in tissue hypoxia.

4. **Cell damage** with the release of its content of enzymes into the blood e.g. myocardial infarction and viral hepatitis.
Medical importance of non-functional plasma enzymes

Measurement of non-functional plasma enzymes for:

1. **Diagnosis of diseases**: diseases of different organs cause elevation of different plasma enzymes.

2. **Prognosis of the disease**: follow up the effect of treatment by measuring plasma enzymes before and after treatment.
Examples of medically important non-functional plasma enzymes

1. Amylase and lipase enzymes increase in diseases of the pancreas as acute pancreatitis.

2. Creatine kinase (CK) enzyme increases in heart, brain and skeletal muscle diseases.

3. Lactate dehydrogenase (LDH) enzyme increases in heart, liver and blood diseases.
4. **Alanine transaminase (ALT)** enzyme, it is also called serum glutamic pyruvic transaminase (SGPT). It increases in liver and heart diseases.

5. **Aspartate transaminase (AST)** enzyme, it is also called serum glutamic oxalacetic transaminase (SGOT). It increases in liver and heart diseases.
6. **Acid phosphatase** enzyme increases in cancer prostate.

7. **Alkaline phosphatase** enzyme increases in obstructive liver diseases, bone diseases and hyperparathyroidism.
Got any Questions?!
Activity

- Discuss non-functional plasma enzymes (def, sources, biomedical importance & 3 examples)
- Compare between functional and nonfunctional plasma enzymes.
Thank you