

VIVEKANANDA COLLEGE  
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NAAC ACCREDITED 'A' GRADE



Topic : Enzymes in Medicine and Industry  
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Name of the Department : Biochemistry

## 59 Enzymes in clinical medicine

The principles of enzymology outlined previously are **applied** clinically in 3 ways:

- 1) **Diagnosis and prognosis of diseases.**
- 2) **Some enzymes are used as therapeutic agents**
- 3) **Enzymes as diagnostic reagents.**

## Uses of Enzymes in Medicine

- Diagnostic – enzyme levels altered with disease
  - Heart attack:
    - Lactate dehydrogenase
    - Creatine phosphate
    - Serum glutamate-oxaloacetate transaminase (SGOT)
  - Pancreatitis:
    - Amylase
    - Lipase
- Analytical reagents – enzyme used to measure another substance
  - Urea converted to  $\text{NH}_3$  via urease
  - Blood urea nitrogen (BUN) measured
- Replacement therapy
  - Administer genetically engineered  $\beta$ -glucocerebrosidase for Gaucher's disease

## Enzymes as diagnostic reagents

Enzyme	Used for testing
Urease	Urea
Uricase	Uric acid
Glucose oxidase	Glucose
Cholesterol oxidase	Cholesterol
Lipase	Triglycerides
Alkaline phosphatase	ELISA
Horse radish Peroxidase	ELISA
Restriction endonuclease	Recombinant DNA technology
Reverse transcriptase	Polymerase chain reaction

## Enzymes as Analytical Agents

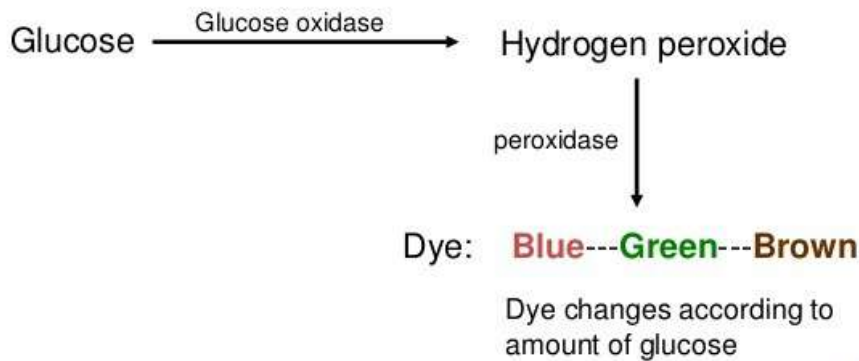
**The sensitivity and specificity of enzymes makes them useful tools in medicine for the detection and measurement of chemicals in fluids such as blood and urine**

**Because of their specificity, enzymes will bind to only one substrate – they can therefore be used for the identification of a specific substance in a biological sample**

**Because of their sensitivity, enzymes are able to detect the presence of specific molecules even when they are present at very low concentrations**

**The enzyme glucose oxidase is used in an immobilised form for the detection of glucose in biological fluids**

## Enzymes in Medicine



Enzyme-linked immunosorbent assays (ELISAs) detect antibodies to infections.



### A. Plasma Enzymes as diagnostic tools

- Diseases that cause tissue damage result in increased release of intracellular enzymes into the plasma.
- Determination of the level of these enzymes is used for diagnosis of heart, liver, skeletal muscle, etc.
- The level of these enzymes in plasma correlates with the extent of tissue damage.

### Enzymes of diagnostic importance

Enzyme	Diagnostic use
<i>Amylase and lipase</i>	Pancreatitis
<i>Acid phosphatase</i>	Prostate cancer
<i>Alk.phosphatase</i>	Bone , liver diseases and hyperparathyroidism
<i>Creatine kinase</i>	Recent myocardial infarction
<i>Lactate DH.</i>	myocardial infarction liver diseases, Leukemia
<i>Transaminases</i>	myocardial infarction(SGOT) liver diseases(SGPT)

### Serum Enzymes used for diagnostics

Serum Enzyme	Major Diagnostic Use
Aminotransferases Aspartate aminotransferase (AST, or SGOT) Alanine aminotransferase (ALT, or SGPT)	Myocardial infarction Viral hepatitis
Amylase	Acute pancreatitis
Ceruloplasmin	Hepatolenticular degeneration (Wilson's disease)
Creatine kinase	Muscle disorders and myocardial infarction
$\gamma$ -Glutamyl transpeptidase	Various liver diseases
Lactate dehydrogenase (isozymes)	Myocardial infarction
Lipase	Acute pancreatitis
Phosphatase, acid	Metastatic carcinoma of the prostate
Phosphatase, alkaline (isozymes)	Various bone disorders, obstructive liver diseases

Serum enzymes are used as markers to detect the cellular damage which in turn helps in the diagnosis of diseases.

Table 4.4 Serum enzymes

Serum enzyme	Disease
Amylase	Acute pancreatitis
GPT or ALT	Liver diseases (hepatitis), jaundice, cirrhosis of liver
GOT or AST	Heart attack
Alkaline phosphatase	Rickets, obstructive jaundice, bone cancer, hyperparathyroidism.
Acid phosphatase	Cancer of prostate gland

Serum enzyme	Disease
Lactate dehydrogenase (LDH)	Heart attack, liver diseases, leukemia, pernicious anemia
Creatine Kinase (CK)	Myocardial infarction (early marker), hypothyroidism, alcoholism.
Aldolase	Muscular dystrophy, liver diseases
5'-Nucleotidase	Hepatitis, obstructive jaundice, tumour
$\gamma$ -Glutamyltranspeptidase ( $\gamma$ -GT)	Alcoholism, infective hepatitis, obstructive jaundice.

### Enzymes used in Therapy

- Digestive enzymes
  - chymotrypsin
  - bromilain
  - rennin
  - papain
  - cellulase
- DNase I
- Alginate lyase
- Adenosine deaminase
- Dihydrofolate reductase
- Lipase
- Streptokinase

## Therapeutic Enzymes

- Therapeutic enzymes have a broad variety of specific uses
  - Oncolytics
  - Anticoagulants
  - Thrombolytics
  - Replacements for metabolic deficiencies
    - Digestive aids
    - Metabolic storage disorders, etc
  - Miscellaneous enzymes of diverse function

## Enzymes as therapeutic agents

Enzyme	Therapeutic Application
Streptokinase/Urokinase	Acute MI, Pulmonary embolism, DVT(Deep vein thrombosis)
Trypsin, lipase and amylase	Pancreatic insufficiency
Asparaginase/Glutaminase	Acute lymphoblastic leukemias
Hyaluronidase	Enhanced local anesthesia and for easy diffusion of fluids
Papain	Anti inflammatory
Chymotrypsin	Pain killer and Anti inflammatory
Alpha- 1 Antitrypsin	Deficiency and Emphysema
Serratopeptidase	Pain killer and Anti inflammatory

Table 4.3 Some important therapeutic enzymes

Enzyme	Reaction	Therapeutic use
Asparaginase	$L\text{-Asparagine} + H_2O \rightarrow L\text{-aspartate} + NH_3$	Leukaemia
Collagenase	Collagen hydrolysis	Skin ulcers
Glutaminase	$L\text{-Glutamine} + H_2O \rightarrow L\text{-glutamate} + NH_3$	Leukaemia
Hyaluronidase	Hyaluronate hydrolysis	Heart attack
Lysozyme	Bacterial cell wall hydrolysis	Antibiotic
Ribonuclease	RNA hydrolysis	Antiviral
$\beta$ -Lactamase	Penicillin $\rightarrow$ penicilloate	Penicillin allergy
Streptokinase	Plasminogen $\rightarrow$ plasmin	Blood clots
Trypsin	Protein hydrolysis	Inflammation
Uricase	$Urate + O_2 \rightarrow$ allantoin	Gout
Urokinase	Plasminogen $\rightarrow$ plasmin	Blood clots

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### Enzymes as therapeutic agents

- Streptokinase:** prepared from streptococcus and used in **clearing blood clots** in MI. Streptokinase activates **plasminogen forming plasmin**  $\rightarrow$  cleaves **fibrin** into several soluble components.
- Asparaginase:** **used in adult leukemia**. Decreases asparagine level which is needed for tumor cells.

## ENZYMES IN THERAPY

- **Substitution of missing production of digestive enzymes – digestive enzymes – pepsin trypsin...**
- **Removal of deposits of death tissue or fibrin (e.g. in lungs, eyes), treatment of skin defects – proteinases, nucleases, collagenase**
- **Acceleration of fibrinolysis in lungs embolization (activation of plasmin and plasminogen) –**
- **streptokinase, urokinase**

## Conclusion

Enzyme therapy has improved the lives of many patients, by reducing the burden of their disease. Several studies have sought to determine to what extent optimal clinical outcomes are a function of the prescribed enzyme dose and its resultant costs. Goals of treatment should include important clinical end points, such as enhanced quality of life and reduced the diseases.

## Applications of Immobilized Enzymes:

### General Concepts:

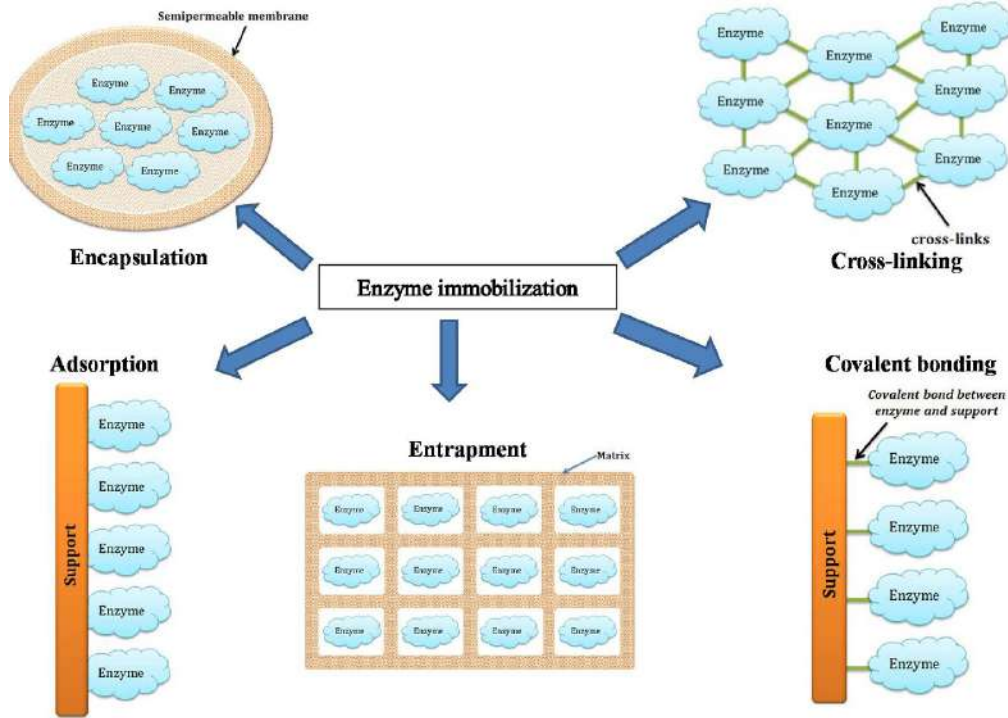
- The immobilized enzyme system - should fit the requirements in terms of stability, activity, pH optimum and other characteristics should all be considered
- The property of immobilized enzymes - greatest industrial importance is the ease with which they can be separated from reaction mixtures
- Hence, in contrast to systems involving soluble enzymes - the reaction can be stopped by physical removal of the immobilized enzyme - without requiring such procedures as heat inactivation which might affect the products of the reaction
- Furthermore, the enzyme will still be active and largely uncontaminated, so can be used again

## Enzyme immobilization

□ Immobilized enzymes are enzymes which are attached to an inert , material, that will prevent loss of enzyme activity by not changing chemical nature of the reactive groups in the binding site of the enzyme.

### Need for Immobilization

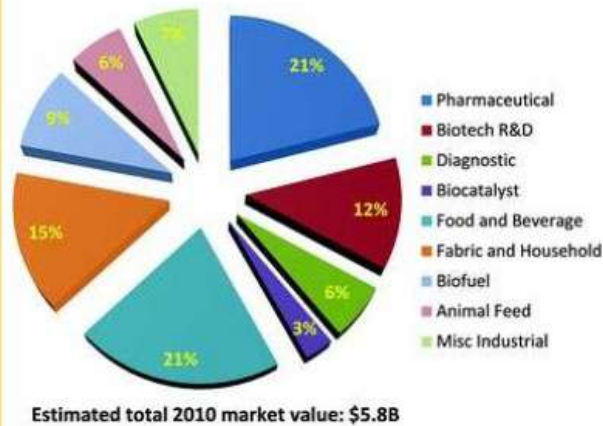
- **Economical:** continuous use of biocatalyst is possible
- **Convenience:** separation of biocatalyst and product is much easier than conventional batch process.
- **Stability:** Immobilized enzymes typically have greater thermal and operational stability than the soluble form of the enzyme



2.5.U5 Immobilized enzymes are widely used in industry.

Common uses of enzymes in industry include:

1. Detergents
2. Biofuels
3. Textiles
4. Brewing
5. Medicine & Biotechnology
6. Juice yield
7. Paper production



## Applications of immobilization

1. **Industrial production:** Industrial production of **antibiotics, beverages, amino acids** etc. uses immobilized enzymes.
2. **Biomedical applications:** Immobilized enzymes are widely used for **diagnosis and treatment of many diseases** such as inborn disorder.
3. **Food industry:** Enzymes like pectinases and cellulases immobilized on suitable carriers are successfully used in the **production of jams, jellies and syrups from fruits and vegetables**.
4. **Research:** The use of immobilized enzyme allow researcher **to increase the efficiency of different enzymes** such as different proteases for cell and organelle lysis.
5. **Biodiesel production** from vegetable oils.
6. **Textile industry:** **Scouring, bio polishing and desizing of fabrics**.
7. **Waste water management:** **Treatment of sewage and industrial effluents**.
8. **Detergent industry:** **Immobilization of lipase enzyme for effective dirt removal from cloths**.

### 2.5.5 Immobilized enzymes are widely used in industry

#### *Enzymes: A multi-billion dollar industry...*

**Detergents** contain proteases and lipases to help breakdown protein and fat stains

Enzymes are used to breakdown the starch in grains into **Biofuels** that can be combusted

In the **Textiles** industry enzymes help in the processing of fibers, e.g. polishing cloth to make it appear more shiny

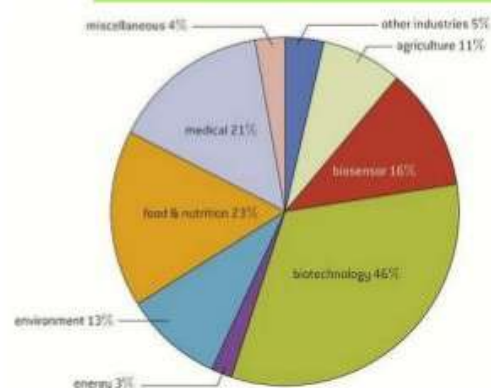
In the **Brewing** industry enzymes help a number of processes including the clarification of the beer

In **Medicine & Biotechnology** enzymes are widely used in everything from diagnostic tests to contact lens cleaners to cutting DNA in genetic engineering.

Enzymes are widely used in the **Food** industry, e.g.

- fruit juice, pectin to increase juice yield from fruit
- Fructose is used as a sweetener, it is converted from glucose by isomerase
- Rennin is used to help in cheese production

**Paper production** uses enzymes to helping in the pulping of wood



▲ Figure 13

## Application of the Immobilized Enzymes:

### **Biomedical Application:**

- Immobilized enzymes are used in medicine from 1990
- immobilized enzymes are used for **diagnosis and treatment of diseases** in the medical field.
- The inborn **metabolic deficiency can be overcome** by replacing the **encapsulated enzymes** (i.e, enzymes **encapsulated by erythrocytes**) instead of waste metabolites
- The **enzyme encapsulation through the electroporation** is a easiest way of immobilization in the biomedical field and

it is a reversible process for which enzyme can be regenerated

## Enzymes in Food Industry

- **Pectinase** break down substances in apple cell walls and enable greater juice extraction.



- **Lactase** breaks down **lactose** in milk into **glucose** and **galactose**. This makes milk drinkable for lactose intolerant people.



## Other immobilized enzymes in industries

Immobilized enzyme	Substrate	Product
Raffinase	Raffinose in sugar beet juice, soybean and milk	Raffinose free solutions
Glucomylase	Dextrin produced by $\alpha$ -amylase	D-Glucose
Invertase	Sucrose	Invert sugar (artificial honey)
Lactase (in cellulose triacetate fibres)	Milk and whey	Lactose free milk (baby foods)
Aspartate ammonia lyase	Fumarate and Ammonia	L-Aspartic acid

### Reference

1. [www.google.com](http://www.google.com)