

Enzymes

1. Define enzyme Specificity? Give example.
enzyme Specificity refers to tendency for enzymes to catalyze a specific set of chemical reactions.

Specificity depends on active site orientation.

Three types of enzyme Specificity are well recognized

- i) Stereospecificity
- ii) Reaction Specificity
- iii) Substrate Specificity.

i) Stereospecificity :- Stereoisomers are the compounds which have the same molecular ~~weight~~ formula, but differ in their structural configuration.

The enzymes act only on one isomer and exhibit Stereospecificity.

Eg:- hexokinase acts on D-hexoses,
glucokinase acts on D-glucose

ii) Reaction Specificity :- The same substrate can undergo different types of reactions, each reaction is catalyzed by different enzymes.

Eg:- Amino acid can undergo Transamination, oxidative decarboxylation, decarboxylation etc.

iii) Substrate Specificity - The substrate specificity varies from enzyme to enzyme.

Eg:- glucokinase acts on glucose to give glucose-6-phosphate, urease cleaves urea to ammonia & carbon dioxide.

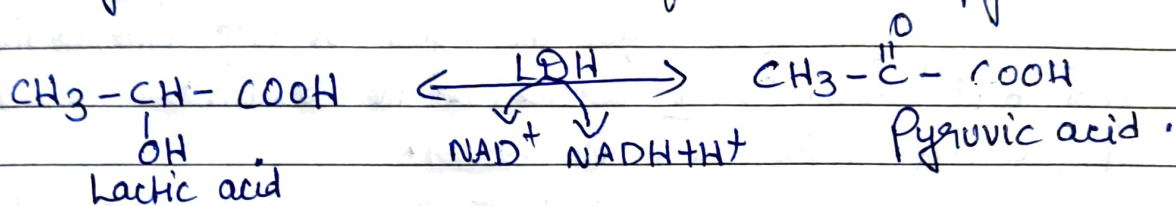
Isoenzymes

The multiple forms of an enzyme catalysing the same reaction are isoenzymes or isozymes.

They differ in their physical & chemical properties like structure, pH optimum, K_m & V_{max} etc.

Isoenzymes of Lactate Dehydrogenase (LDH)

LDH Systemic name is L-Lactate - NAD^+ oxidoreductase catalyses the interconversion of lactate and pyruvate



LDH has five isoenzymes - It is a tetrameric enzyme made up of 4 subunits. Two types of subunits M (muscle) & H (heart) are produced by genes.

LDH ₁ - H ₄ - Heart & RBC	are produced by genes.
LDH ₂ - H ₃ M - Heart & RBC	
LDH ₃ - H ₂ M ₂ - Brain & Kidney	
LDH ₄ - H ₃ M - Liver & Skeletal Muscle	
LDH ₅ - M ₄ - Skeletal Muscle & Liver	

➔ Diagnostic importance of LDH:- Isoenzymes of LDH have an important role in the diagnosis of heart & liver related disorders.

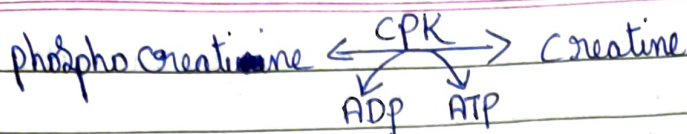
→ In healthy individuals, LDH₂ is higher than LDH₁ in Serum.

→ In the case of myocardial infarction, LDH₁ is much greater than LDH₂ & this happens within 12 to 24 hrs after infarction.

→ Increased levels of LDH₅ in Serum is an indicator of liver disease.

Isoenzymes of Creatine Phosphokinase:-

Creatine Kinase (CK) or creatine phosphokinase (CPK) catalyses the inter-conversion of phosphocreatine to creatine.



CPK exists as three isoenzymes. Each isoenzyme is a dimer composed of two subunits - M (Muscle) (B) B (brain) (B) both.

CPK ₁ - BB	Brain
CPK ₂ - MB	Heart
CPK ₃ - MM	Skeletal Muscle
<u>Isoenzyme</u>	<u>Sub unit</u>
	<u>Tissue of origin</u>

Diagnostic Importance: - After the myocardial infarction, within the first 6-18 hours, CPK₂ increases in the Serum.
CPK₂ is not elevated in muscle disorder.
Estimation of CPK₂ is the earliest reliable indication of Myocardial Infarction.

Isoenzymes of alkaline phosphatase: -

Six isoenzymes of alkaline phosphatase have been identified. The most important ALP isoenzymes are α_1 -ALP, α_2 -ALP (heat labile), α_2 -ALP (heat stable), pre β -ALP, Γ -ALP etc

→ Increase in α_2 -heat labile ALP suggests hepatitis whereas pre β -ALP indicates bone disease.

Isoenzymes of alcohol dehydrogenase: -

Alcohol dehydrogenase has two isoenzymes. α B₁ isoenzyme is predominant in white Americans & Europeans while α B₂ is present in Japanese & Chinese.

α B₂ rapidly converts alcohol to acetaldehyde. Accumulation of acetaldehyde is associated with tachycardia & flushing (facial).

Co-enzymes

The non-protein, organic, low molecular weight and dialysable substance associated with enzyme function - Coenzyme

Co-enzymes participate in various reactions involving transfer of atoms & groups like hydrogen, aldehyde, keto, amino, acyl, methyl, carbon dioxide etc.

Co-enzymes from B-Complex vitamins:-

Most of the co-enzymes are the derivatives of water soluble B-Complex vitamins.

①

Biochemical role & deficiency symptoms of Thiamine

Thiamine has a specific coenzyme, Thiamine pyrophosphate (TPP) & is mostly associated with carbohydrate metabolism.

Biochemical functions

TPP or CoCarboxylase is intimately connected with energy releasing reactions of carbohydrate metabolism.

1. pyruvate dehydrogenase catalyses irreversible conversion of pyruvate to Acetyl CoA. This pyruvate dehydrogenase is dependent on TPP.
2. α -Ketoglutarate dehydrogenase an enzyme of citric acid cycle requires TPP for its catalytic activity.
3. Transketolase an enzyme of HMP Shunt pathway is dependent on TPP.
4. α -Keto acid dehydrogenase catalyses oxidative decarboxylation of branched chain amino acids (valine, leucine & isoleucine) to the respective keto acids. This enzyme also requires TPP.
5. TPP plays an important role in the transmission of nerve impulse.

Deficiency Symptoms:-

1) Beri-Beri - Commonly seen in people having polished rice as staple food.

Symptoms include - loss of appetite, weakness, constipation, Nausea, Mental depression, peripheral neuropathy, irritability etc.

In adults 2 types of Beri-Beri occurs.

1) Wet beri-beri - characterized by edema of legs, face, trunk & serous cavities, Breathlessness, palpitation, Systolic B.P. increases.

2) Dry beri-beri - Associated with neurological manifestations resulting in peripheral neuritis, Edema is not seen, patient depends on support to walk.

3) Infantile Beri-Beri:- Seen in infants born to mothers due to thiamine deficiency. Breast milk contains low thiamine & is characterized by sleeplessness, restlessness, vomiting, convulsions & cardiac dilatation.

4) Wernicke-Korsakoff Syndrome:- (Cerebral beri-beri)
→ Seen in alcoholics, where the body demands of high thiamine. Characterized by loss of memory, apathy, to & fro motion of eye balls.

(2) Biochemical Role & deficiency of B_2 (Riboflavin)

Flavin ^{Mono}nucleotide (FMN) & Flavin adenine dinucleotide (FAD) are the two coenzyme forms of riboflavin. The ribitol (5 carbon) is linked to a phosphate in FMN. FAD is formed from FMN by the transfer of an AMP moiety from ATP.

Biochemical Functions:-

The flavin coenzymes (FAD, FMN) participate in many redox reactions responsible for energy production. The functional unit of both FAD & FMN is isoxanthine ring which accepts 2 hydrogen

atoms (with electrons) forming FMNH₂ (80) FADH₂.

Enzymes that use flavin coenzymes are called flavoproteins. Many flavoproteins contain metal ion (iron, molybdenum etc) and are called as metalloflavoproteins.

The coenzymes FAD & FMN are associated with enzymes involved in carbohydrate, lipid, protein and purine metabolisms, beside electron transport chain.

Deficiency Symptoms:- Riboflavin deficiency is usually uncommon.

- ① cheilosis - fissures at the corners of the mouth.
- ② glossitis - tongue smooth & purplish
- ③ dermatitis -

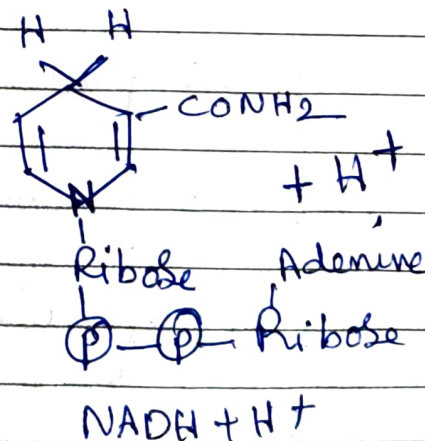
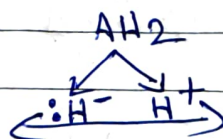
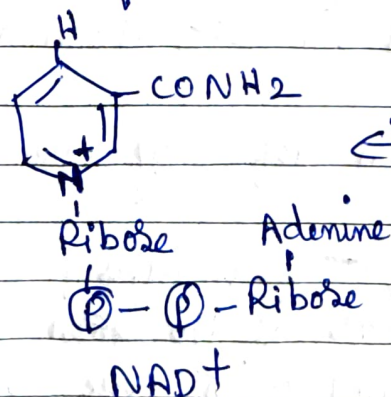
Chronic alcoholics are susceptible to B₂ deficiency.

③ Biochemical role & deficiency of Niacin (B₃)

Niacin (80) nicotinic acid is also known as pellagra preventive factor of Goldberg.

The coenzymes of Niacin are NAD⁺ & NADP⁺
Nicotinamide adenine dinucleotide ← Nicotinamide adenine dinucleotide phosphate.

Biochemical functions:-

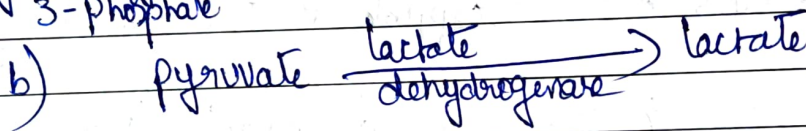
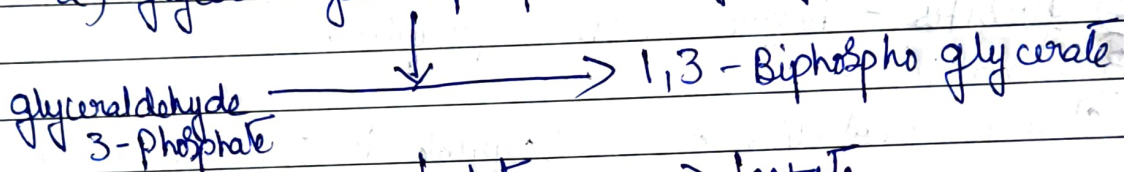


The coenzyme NAD^+ & NADP^+ are involved in many oxidation reduction reactions. They accept hydride ion (C:H^-) and undergo reduction in the pyridine ring. This results in neutralization of positive charges. While one of the hydrogen atom (AH_2) is accepted while the other one is released into surroundings.

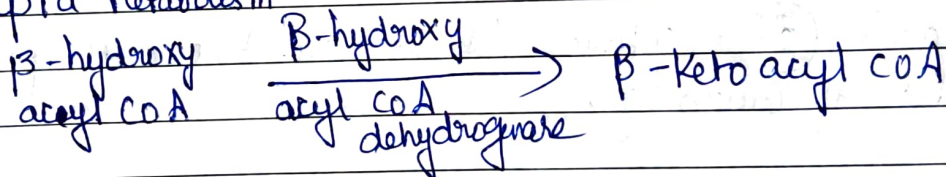
A large number of oxidoreductases (40) are dependent on NAD^+ & NADP^+ . They participate in almost all the metabolic reactions.

1. Carbohydrate Metabolism

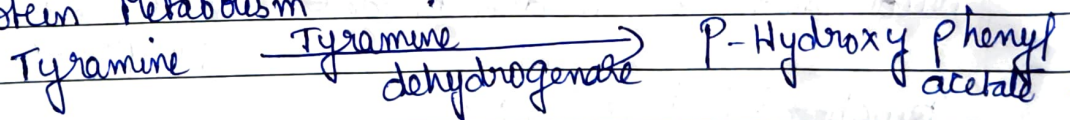
a) glyceraldehyde 3-phosphate dehydrogenase



2. Lipid Metabolism



3. Protein Metabolism



NADH produced is oxidized in ETC chain to generate ATP.

Deficiency Symptoms: - Niacin deficiency results in

1) Pellagra (Italian rough skin) - dermatitis, diarrhoea, dementia. Dermatitis is seen in areas of the skin exposed to sunlight. Dementia is associated with degeneration of nervous tissue. Symptoms of dementia include anxiety, irritability, poor memory, sleeplessness etc.

Pellagra is seen in people whose staple food is maize. B_3 available in maize is in bound form & unavailable to the body.

Therapeutic uses of niacin:-

- 1) niacin inhibits lipolysis in the adipose tissue & decreases the circulatory free fatty acids.
- 2) Triacylglycerol Synthesis in the liver is decreased.
- 3) Serum levels of LDL, VLDL, triacylglycerol & cholesterol are lowered.

Hence Niacin is used in the treatment of Hyperlipoproteinemia type IIb