





# ***Ethanol Metabolism***

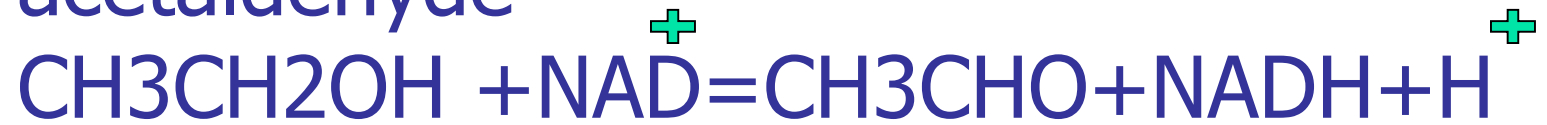
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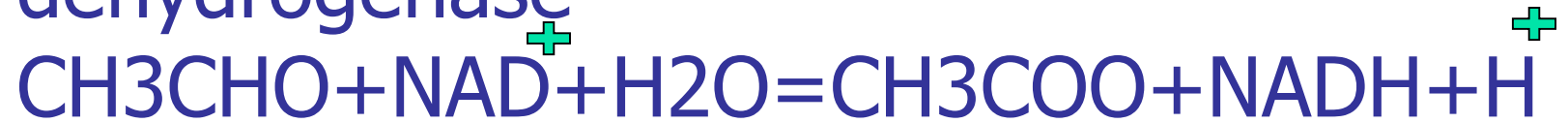
Ethanol is a small two carbon alcohol that, due to its small size and alcoholic hydroxyl group is soluble in both aqueous and lipid environments .



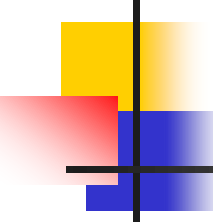
- Ethanol is oxidized in the liver by cytosolic alcohol dehydrogenase to form acetaldehyde



-Acetaldehyde is further oxidized to acetate by a mitochondrial aldehyde dehydrogenase



-Much of the acetate produced from ethanol leaves the liver and is converted to acetyl CoA which enter TCA cycle and convert into ATP , CO<sub>2</sub> and H<sub>2</sub>O .



- Acetyl CoA may also be formed in the liver and used as a precursor for lipid biosynthesis .

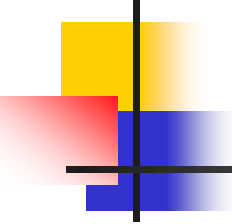
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- The increased  $\text{NADH}/\text{NAD}^+$  ratio causes a shift to left in the equilibrium :

( malate = oxaloacetate )


which may reduce activity of the CAC .

- The increased  $\text{NADH}/\text{NAD}^+$  ratio also causes an increased the formation of lactate from pyruvate that result in hyper lactic acidemia which turn decrease the capacity of the kidney to extract uric acid .

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- Other effect may include increased cholesterol synthesis from acetyl CoA .
  - The net effect of inhibiting FA oxidation by ethanol is to causes increased esterification of fatty acid in triacylglycerol which appears to be the cause of the fatty liver .
  - Ethanol also inhibit the metabolism of some drug (i.e: barbiturates) and prolong the time remain effective in the body . (Hydroxylation of barbitual in liver cell is inhibited by ethanol ) .

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- Acute and chronic ethanol metabolism results in impaired gluconeogenesis leading to severe hypoglycemia .
  - Alcohol consumption can cause a loss of calcium in the body by increasing urinary calcium excretion .
  - Studies have shown that alcohol consumption will affect vitamins A ,B12 and folate levels .

Note :



Disulfiram is a drug use in treatment of ethanol , it inhibited aldehyde dehydrogenase by competing with NAD<sup>+</sup> for binding site of the enzyme , so increase the level of acetaldehyde in the blood causing symptoms of vomiting , thirst , sweat and head achalasia .

Q : The person who drink alcohol become fat ? Why

This because acetyl CoA convert to fat and accumulate in the body .

Acetaldehyde is a highly unstable compound and quickly forms free radicals structures which are highly toxic . Some metabolic effects of acetaldehyde are :

1. Inhibition of protein synthesis .
2. Decreased protein secretion ( e.g. albumin ) from liver .
3. Promotion of radical - mediated reactions.
4. Inhibition of pyridoxal – 5 – phosphate ( vitamin B6 ) metabolism .
- 5 . Impaired cell division(e.g. in bone marrow).
6. Inhibition of glycoprotein and testicular steroid synthesis .



## ( Toxicity of methanol )

Methanol is oxidized by liver alcohol dehydrogenase to give formaldehyde and this is oxidized to formic acid .

Formaldehyde causes retina damage and blindness while formic acid causes acidosis ( coma and death ) .

Methanol toxicity is treated by giving ethanol as an antidot . It complex with methanol at the dehydrogenase enzyme causing a delay of methanol metabolism and its excretion in urine is increased .

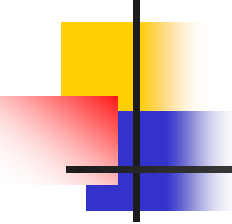


## ( Notes )

1. Adult hemoglobin ( Hb A ) consists of four polypeptide chains ( two alpha and two beta chains ) , each containing a molecule of heme . Each molecule of hemoglobin contain four molecules of heme while myoglobin contain one molecule of heme .

2 . In sickle cell anemia the B-chain of hemoglobin contain a valine instead of glutamate at position 6 .

RBCs that contain large complexes of ( Hb S ) molecules can assume a sickle shape . These cells undergo hemolysis and an anemia result .



3 . Proteins can be denatured by agents such as heat and urea that causing unfolding of polypeptide chains without causing hydrolysis of peptide chains .

If a denatured proteins returns to its native state after the denaturing agent is removed , the process is called renaturation .