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Subject :	Alchol metabolism
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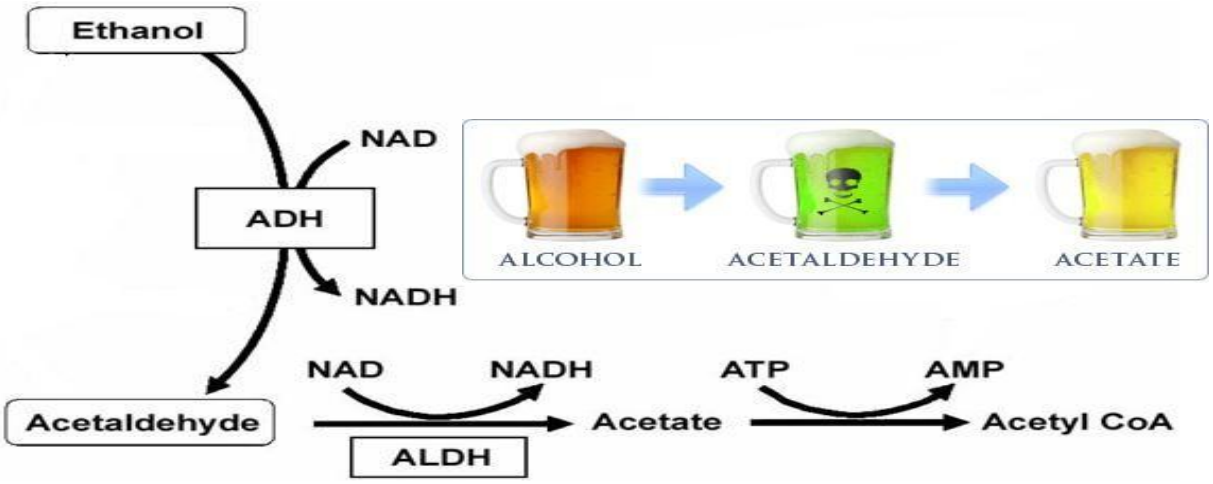
Alcohol metabolism

-As we know alcohol it is a high-energy compound, and it's consumed by many people so we have to study its metabolism.

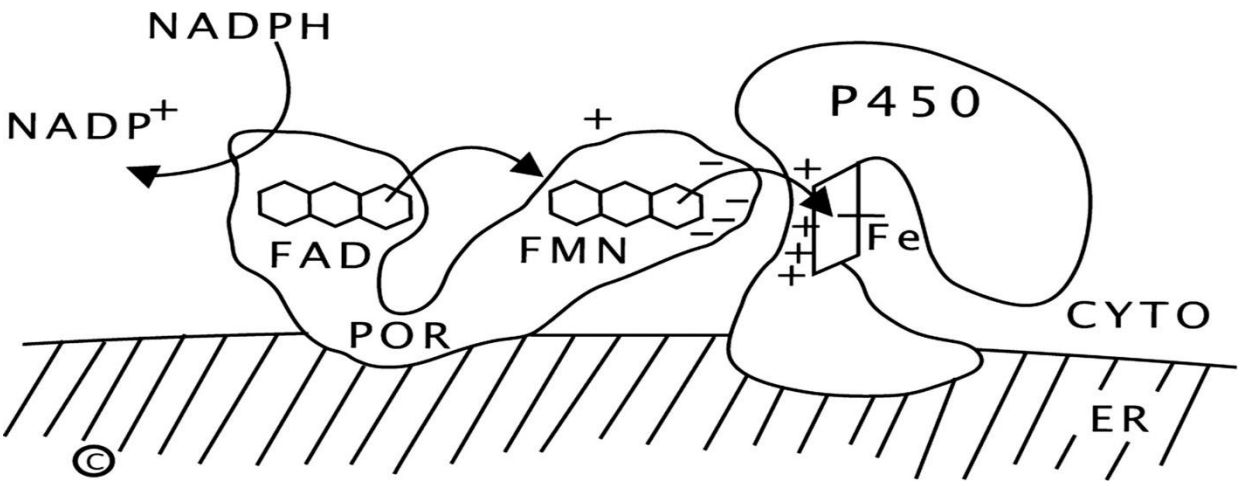
-Alcohol (ethanol) is metabolized in the **liver** by an enzyme called **ethanol dehydrogenase**, which metabolizes ethanol into acetaldehyde and NADH, a small amount of acetaldehyde escapes to the blood. Fortunately, 90% of acetaldehyde enters the mitochondria and is converted by **aldehyde dehydrogenase** into acetate and NADH. Acetate is a safe compound so we don't have a problem with it. Acetate then enters the blood and is taken by various tissues mainly the muscles and it's activated either in the cytosol or in the mitochondria to acetyl CoA by the enzyme **acetyl CoA synthetase** (two high energy bonds are being spelled to get the acetyl CoA); if this conversion happens in the cytosol, the acetyl CoA may be used for fatty acid or cholesterol synthesis, but if it happens in the mitochondria acetyl CoA will enter TCA cycle to produce energy.

-90% of the ingested alcohol is metabolized by the previous pathway, what about the remaining 10%?

It escapes to the blood and enters the lungs; that's why **it can be smelled in the breath (breath test)**, or it can be excreted by the kidneys.



*** As it's mentioned earlier, the majority of ethanol is metabolized by **alcohol dehydrogenase**, but there is another enzyme that is also involved in its metabolism which is **CYP2E1 (which is a microsomal enzyme from cytochrome P450 family)**, this enzyme oxidizes ethanol and requires NADPH (as a source of energy) and O2, and yields acetaldehyde. The contribution of this enzyme is about 20%; because **its KM is high**; which means that its affinity is low. This contribution increases in the case of chronic alcoholics or in massive intake of alcohol.



The structure of cytochrome P450 enzymes (including CYP2E1) contains:

1-Reductase

2-Heme

-O2 binds to the P450 Fe-heme in the active site and is activated to a reactive form by accepting electrons, the electrons are donated by the cytochrome P450 reductase, which contains an FAD plus an FMN or Fe-S center to facilitate the transfer of single electrons from NADPH to O2 and ethanol (O2 will be converted to H2O and ethanol to acetaldehyde).

Acute effects of alcohol ingestion principally arise from:

١-acetaldehyde (the bad compound):

-As we mentioned earlier, there is a small amount of acetaldehyde that escapes to the blood.

-For that, we treat alcoholics by giving a drug that inhibits acetaldehyde dehydrogenase, so the acetaldehyde will accumulate in the body, causing vomiting, and as a result the person will hate the alcohol at the end.

2-The generation of NADH:

-Which greatly increases the NADH/NAD ratio of the liver. As a consequence, fatty acid oxidation is inhibited, and ketogenesis may occur. The elevated NADH/NAD ratio may also cause lactic acidosis and inhibit gluconeogenesis.

**If someone is ingesting alcohol and not eating food, he'll necessarily need gluconeogenesis, therefore if someone drinks alcohol and eats at the same time is better that drinking alcohol alone (because it inhibits gluconeogenesis).

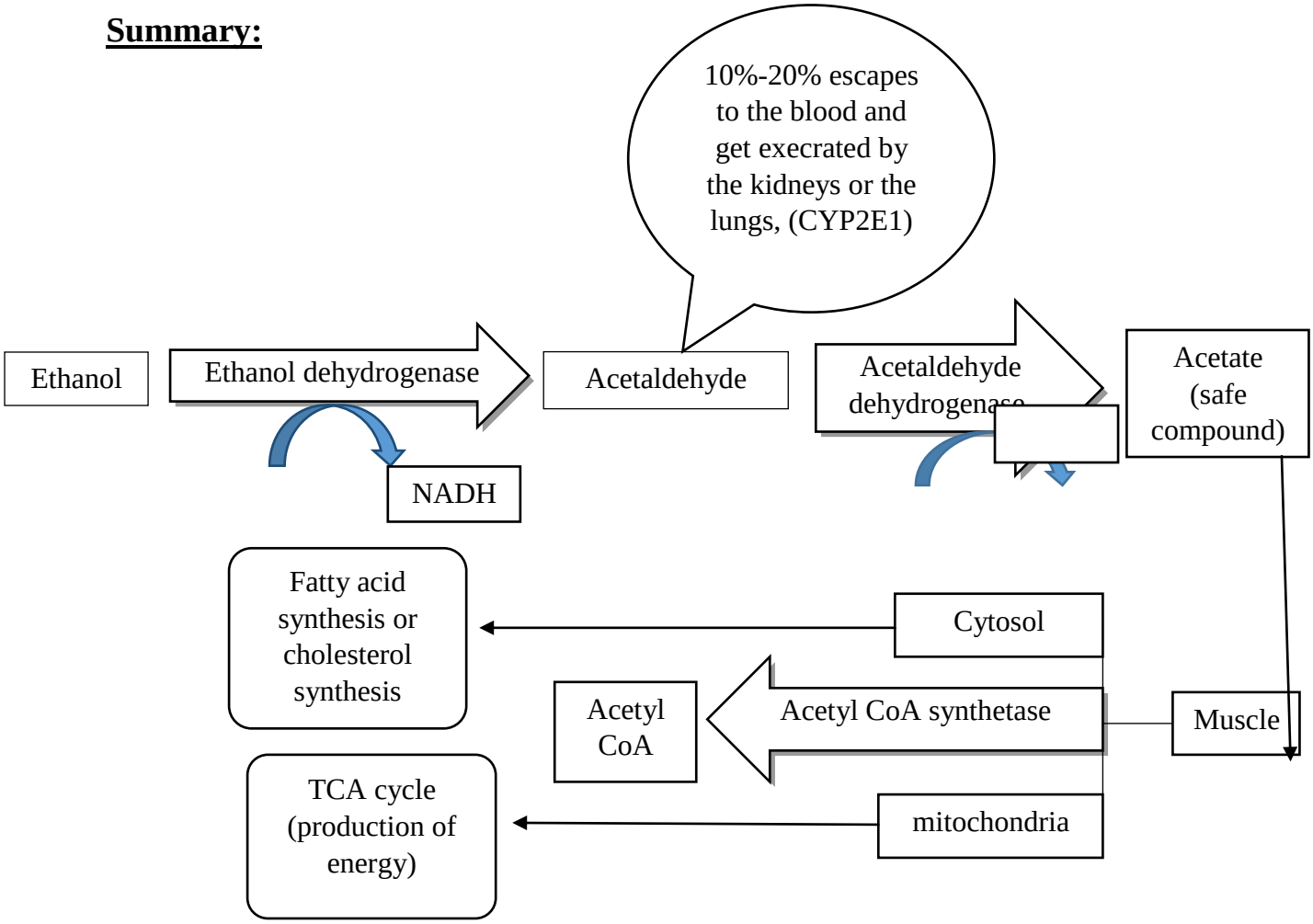
Notes:

**Ethanol metabolism may result in alcohol-induced liver disease, including hepatic steatosis (fatty liver), alcohol-induced hepatitis, and cirrhosis.

**The principal toxic products of ethanol metabolism include acetaldehyde and free radicals. Acetaldehyde forms adducts with proteins and other compounds.

**Genetic polymorphisms in the enzymes of ethanol metabolism may be responsible for individual variations in the development of alcoholism or the development of liver cirrhosis.

Summary:



GOOD LUCK