

Ethanol is composed of two carbon atoms and one OH group.

Ethanol is an amphipathic molecule, with a polar side (the OH group) and a non-polar side (the R group).

The amphipathic property facilitates ethanol absorption through stomach cells and upper small intestine cells.

A small amount of ethanol is metabolized in the stomach cells.

A large amount of ethanol is metabolized in the liver cells.

ETHANOL METABOLISM IN THE LIVER CELLS:

STEP 1:

LOCATION: cytoplasm

REACTION: $\text{ethanol} + \text{NAD}^+ \xrightarrow{\text{ethanol dehydrogenase}} \text{acetaldehyde} + \text{NADH} + \text{H}^+$

STEP 2:

LOCATION: mitochondria

REACTION: $\text{acetaldehyde} + \text{NAD}^+ \xrightarrow{\text{acetaldehyde dehydrogenase}} \text{acetic acid} + \text{NADH} + \text{H}^+$

acetaldehyde has a significant odor and may result in cancer.

liver cells release acetic acid into the blood and muscle cells uptake acetic acid from the blood.

muscle cells convert acetic acid to acetyl-CoA by acetyl-CoA synthetase.

When a high amount of ethanol is metabolized, the NADH/NAD⁺ increase and leads to:

inhibition of the krebs cycle that result in lactic acidosis and inhibition of fatty acid oxidation.

inhibition of glycolysis that result in inhibition of gluconeogenesis.

ALTERNATIVE PATHWAYS:

1 cytochrome P450 2E1

ethanol + NADPH + O₂ + H⁺ (NADPH-cytochrome P450 reductase) acetaldehyde + NADP⁺ + H₂O

inducible by a high concentration of ethanol due to the low K_m for ethanol.

lead to oxidative stress in the liver cells due to the generation of hydrogen peroxide, hydroxyethyl radical, hydroxyl radical and superoxide.

2 peroxisomal catalase

H_2O_2 (catalase) $\text{O}_2 + \text{H}_2\text{O}$

ethanol + H_2O_2 (catalase) acetaldehyde + H_2O

the activity is dependent on the concentration of hydrogen peroxide.

peroxisomal catalase expressed in all tissues and by colonic flora.

Alcohol dehydrogenase has five isoenzymes.

The five isoenzymes are expressed in different tissues with different kinetics.

Different populations have the five isoenzymes with different velocities.