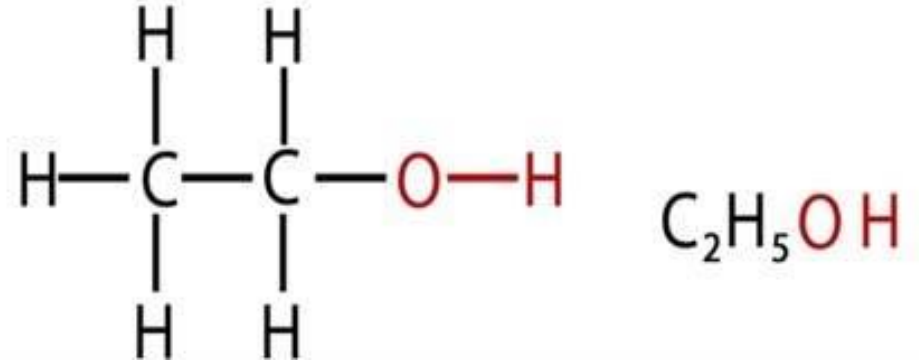




Ethanol

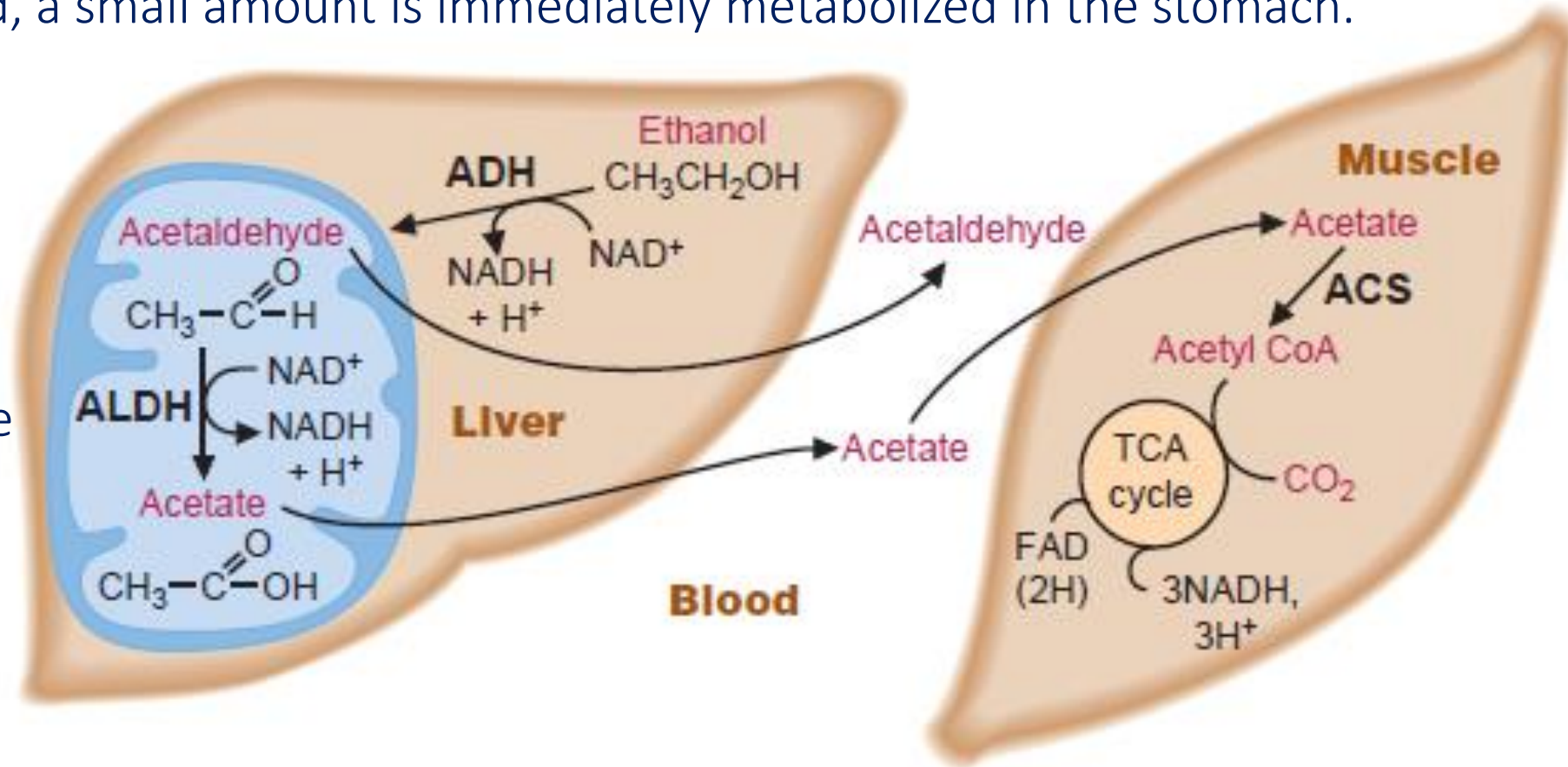


Alcohol Metabolism

Dr. Diala Abu-Hassan

Metabolism of Alcohol

- ✓ When alcohol is ingested, a small amount is immediately metabolized in the stomach.
- ✓ Most of the remaining alcohol is subsequently absorbed from the gastrointestinal tract, primarily the stomach and upper small intestine



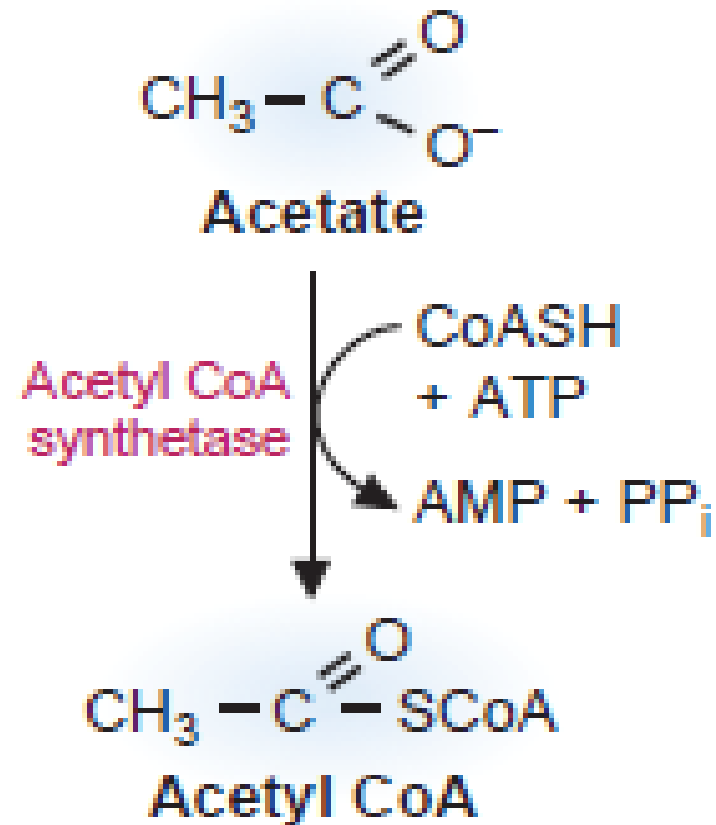
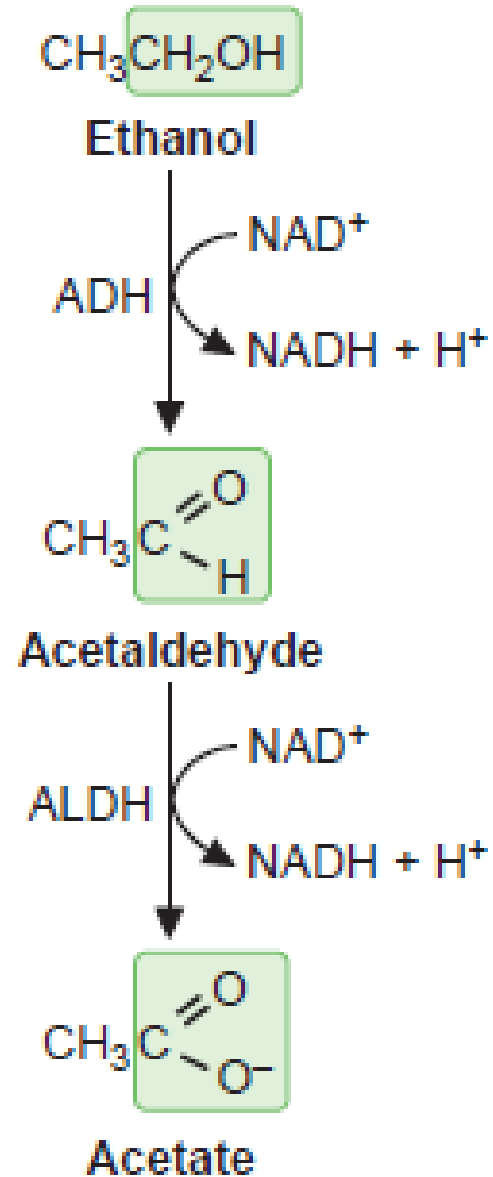
How do you prepare acetic acid from ethanol in organic chemistry?

ADH: Alcohol Dehydrogenase

ALDH: Acetaldehyde Dehydrogenase

ACS: Acetyl CoA Synthetase

Metabolism of Alcohol-Steps

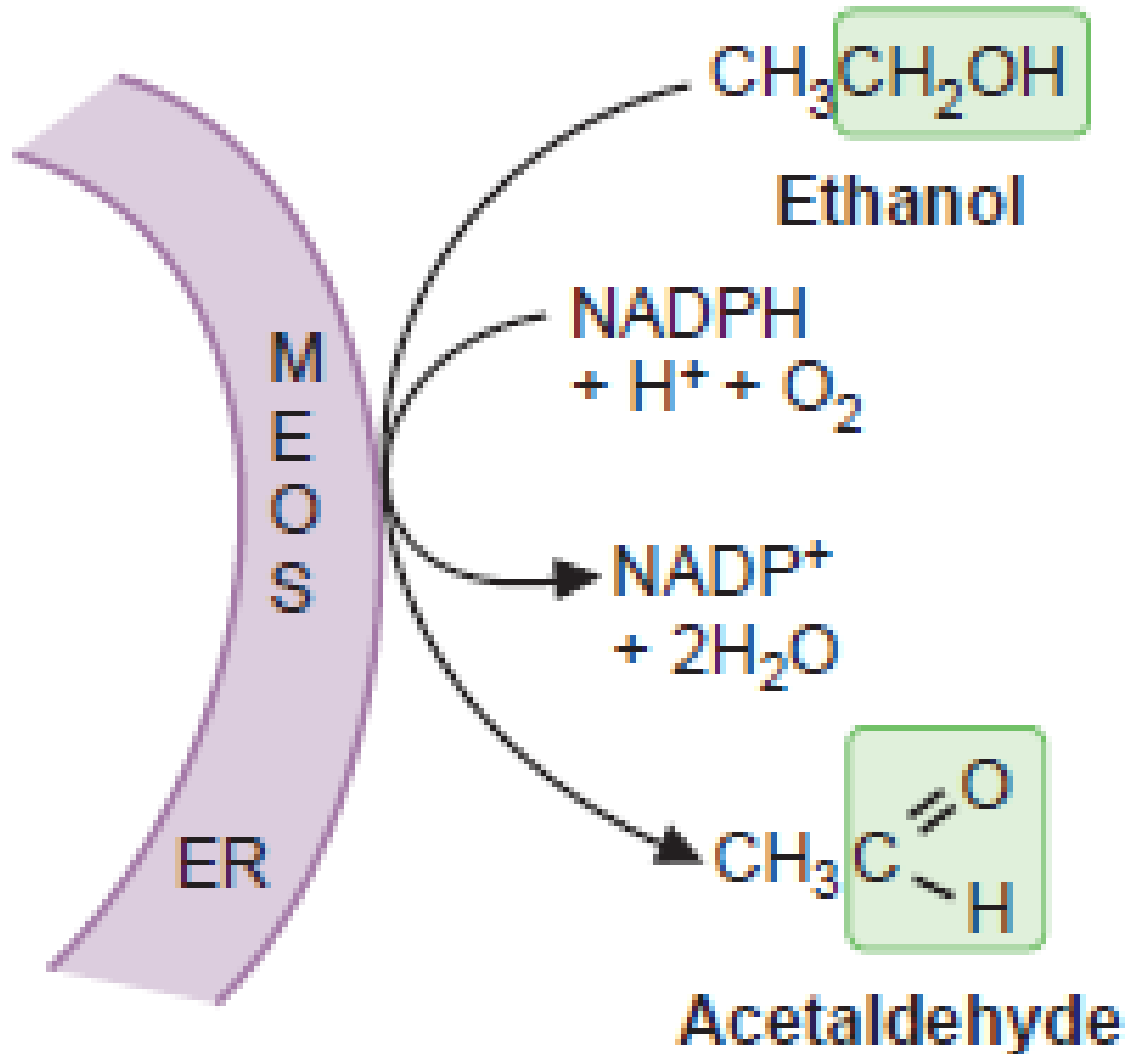


What happens when a high amount of Ethanol is metabolized?

- ✓ High NADH/NAD⁺
- ✓ Inhibition of FA oxidation
- ✓ Inhibition of gluconeogenesis
- ✓ Lactic acidosis

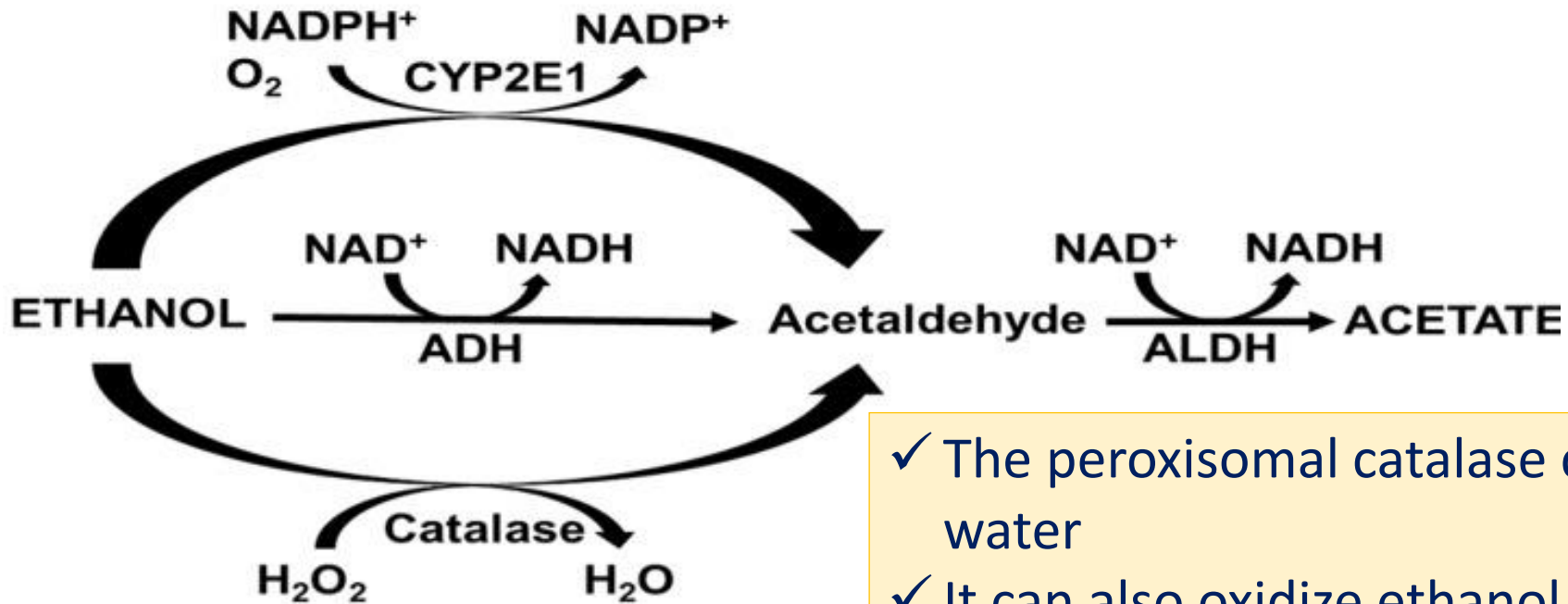
Metabolism of Alcohol

MEOS: Microsomal Ethanol Oxidizing System



- ✓ An alternative pathway for ethanol metabolism
- ✓ 10-20% of the ingested ethanol
- ✓ Involves primarily the cytochrome P450 2E1 (CYP2E1)
- ✓ CYP2E1 is associated with NADPH-cytochrome P450 reductase in the
- ✓ High K_m for ethanol
- ✓ Inducible by ethanol
- ✓ CYP2E1 is a major contributor of oxidative stress in the hepatocytes by generating several reactive oxygen species (ROS) such as hydrogen peroxide (H_2O_2), hydroxyethyl radical ($\text{HER}\cdot$), hydroxyl radical ($\text{OH}\cdot$) and superoxide (O_2^-)

Metabolism of Alcohol-Catalase



- ✓ The peroxisomal catalase converts H_2O_2 to oxygen and water
- ✓ It can also oxidize ethanol to acetaldehyde
- ✓ Is not a key pathway for ethanol elimination
- ✓ Catalase is ubiquitously expressed in almost all tissues
- ✓ Catalase is also expressed by colonic floras which may lead to acetaldehyde production in the lower gastrointestinal tract
- ✓ Catalase activity relies on the cellular level of H_2O_2

Ethanol Metabolism Application

- ✓ ADH has 5 classes or isoenzymes
- ✓ Different isoforms are expressed in different tissues such as liver, lung, stomach and esophagus.
- ✓ People with different races inherit different sets of ADH isoenzymes, for example African Americans have an isoform with a high maximal velocity resulting in fast ethanol metabolism