

# ORGANIC SOLVENTS I I

Prof. Dr. Benay Can E

METHYL ALCOHOL/ Methanol

- Methanol used as a solvent in printing and copy solutions, adhesives, paints, polishers and stabilizers.
- It is also used for window cleaners, antifreeze, as a fuel in alcohol lamp and as an additive in gasoline.
- Methyl alcohol (methanol) is obtained by distillation of wood .
- It is used in the construction of materials such as paint thinner, antifreeze, glass cleaner.
- The most common cause of methanol poisoning is adulteration of alcoholic drinks. These alcoholic drinks are illicit liquor produced by unauthorized persons .
- It is cheaper than ethanol, which makes it suitable for mixing.
- The other subset of patients with methanol poisoning presents as suicidal or accidental ingestion.
- Chronic poisoning occurs as a result of inhalation of vapor in the workplace.
- It is also possible to remove the methyl alcohol, which is abundantly contaminated with clothing, through the skin.

- **Absorption, Distribution and Metabolism**

Methanol is rapidly absorbed through gastro-intestinal tract,

- so the average absorption half - life is 5 minutes and reaches maximum serum concentration within 30 – 60 minutes and well dissolves in body water.
- Methanol is not toxic by itself, but its metabolites are toxic.....

- Methanol is metabolized in different phases mainly in the liver. The initial enzyme in its metabolism is alcohol dehydrogenase.

**Methanol**



*Alcohol Dehydrogenase (ADH)*



(-)

**Fomepizole (Antizol)  
or Ethanol**

(both competitive inhibitors)

**Formaldehyde**



*Aldehyde Dehydrogenase (ALDH)*

**Formic Acid**



*Folic Acid (Vit B9)*

**CO<sub>2</sub> + H<sub>2</sub>O**

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- 20 mg / dl. are considered toxic,
- 40 mg / dl. causes serious disorders,
- The level of 80-100 mg / dl is generally considered to be the limit lethal level.

## **Poisoning symptoms:**

- Signs of poisoning begin in 10-25 h after methyl alcohol intake.
- Toxicity depends on the severity of acidosis



Symptoms are .....

- Congestion, balance and movement disorder
- Nausea, vomiting, severe pain in the abdomen, throat, arms and limbs, visual impairment and blindness, metabolic acidosis, coma, and respiratory arrest, death
- 4-15 ml -----blindness
- 15-100 ml..... death

# Treatment

- It is not recommended to induce vomiting with ipeka or apomorphine
- After taking methyl alcohol, gastric lavage is appropriate but not if a long period has occurred ( Active charcoal?? )

# Treatment

- **Sodium Bicarbonate:**
- Life threatening complication of methanol intoxication is severe metabolic acidosis
  
- **Correction of electrolyte imbalance:**
- Hyperkalemia and hypokalemia should be detected and corrected.

- **Ethanol administration**
- Ethyl alcohol is used as a systemic antidote for methyl alcohol intoxication.
- 7-10 ml / kg i.v. in 30-60 minutes
- During treatment with ethyl alcohol hypoglycemia may be occurs, 5% dextrose should be given to patient.
- **Fomepizole**
- **Folic Acid**
- **Hemodialysis:** Patients with severe metabolic acidosis will require hemodialysis for rapid correction of acidosis and elimination of methanol.
- **If necessary, diazepam** should be given by 5-10 mg iv to patient.

- **Treatment of Methanol Poisoning**
- Maintenance of Airway, Breathing, Circulation.
- Sodium Bicarbonate for acidosis.
- Ethanol i.v., - a competitive inhibitor of Alcohol Dehydrogenase.
- **4- Methyl Pyrazole** – a competitive inhibitor of Alcohol Dehydrogenase.
- **Folate** to metabolize and eliminate Formic acid.
- Hemodialysis.

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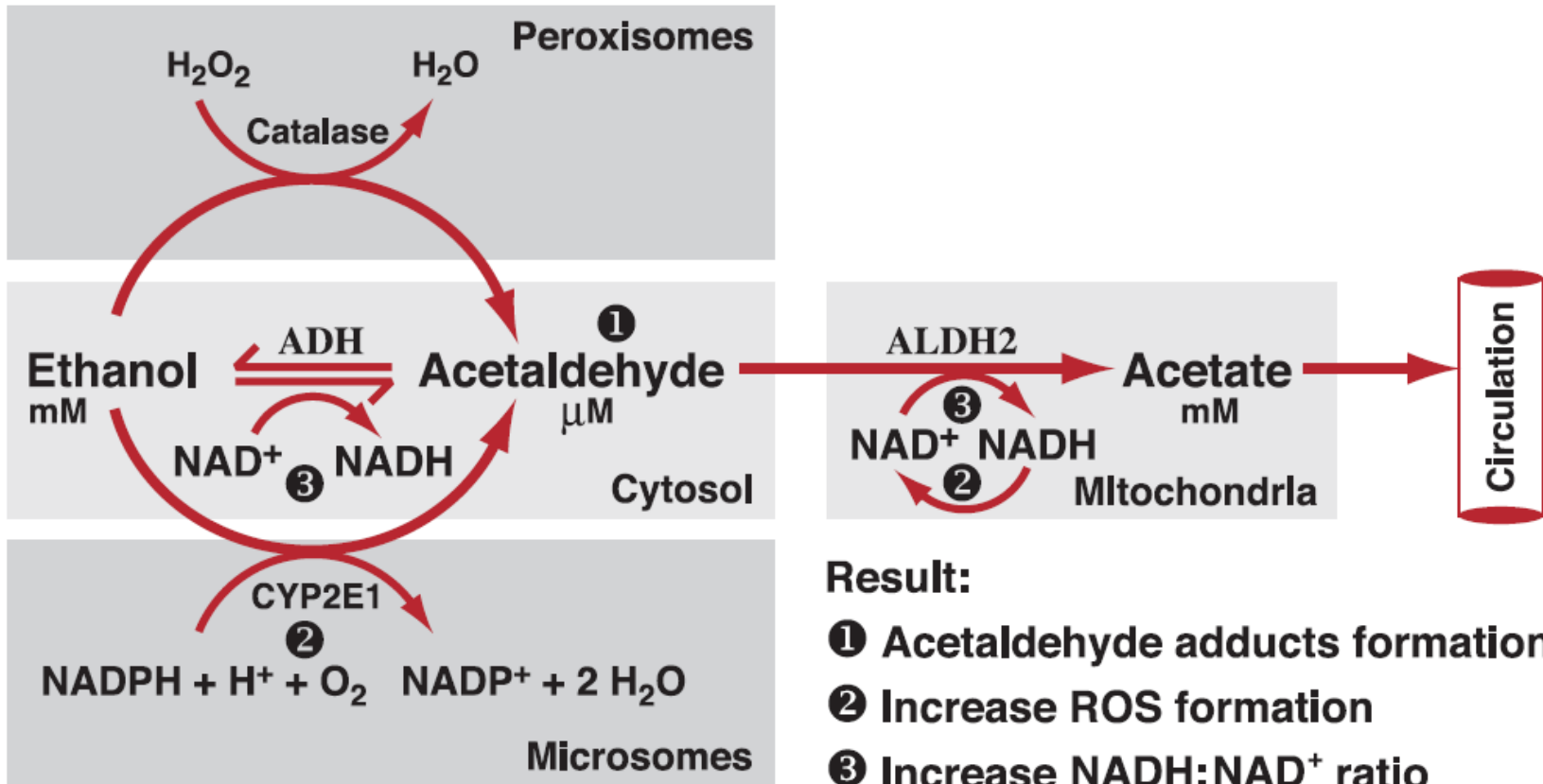
**CO<sub>2</sub> + H<sub>2</sub>O**

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ETHYL ALCOHOL/ ALCOHOL

- Ethanol can be produced synthetically or naturally through fermentation (grains, fruits, vegetables); fermentation is the chemical action of yeast on sugars.
- Ethyl alcohol used in beverages.





- **Absorption**
- rapid and complete through the gastric mucosa
- **Distribution**
- rapid distribution to tissues
- **Metabolism**
- Ethanol is 90% oxidised by the liver, with the remainder excreted through the kidneys and the lungs
- Ethanol is metabolized by the cytoplasmic enzyme alcohol dehydrogenase to acetaldehyde (mainly)
- The microsomal ethanol oxidizing system (MEOS) is an alternate pathway of ethanol metabolism that occurs in the microsome and results in the oxidation of ethanol to acetaldehyde.
  - minor role in ethanol metabolism in average individuals
  - requires the CYP2E1 enzyme (a cytochrome P450 enzyme) to convert ethanol to acetaldehyde
  - Ethanol's affinity for CYP2E1 is lower than its affinity for alcohol dehydrogenase
  - MEOS activity increases after chronic alcohol consumption, correlating with an increase in CYP2E1

# Factors that influence alcohol's effects

- Intoxication- the state in which the body is poisoned by alcohol or another substance
  - Body size
  - Gender
  - Food
  - Rate of intake
  - Amount
  - Medicine

# Short Term Effects

- Effects on the brain:
  - Development
  - Memory
  - Judgment and control
  - Risk of stroke
- Effects on the heart:
  - Increase heart rate and blood pressure
  - Heart rhythm becomes irregular
  - Decreased body temperature

# Short Term Effects

- Effects on Liver and Kidney:
  - Chemicals that are metabolized can cause inflammation and scarring of the liver.
  - Increase urine output and increase the chance of dehydration.
- Effects on Stomach:
  - Nausea and vomiting
  - Disrupt the absorption of nutrients (pancreas)

- CNS
- effects are dependent on blood ethanol level, but varies greatly according to individual variation and tolerance
  - chronic high ethanol consumers appear less intoxicated at higher blood concentrations – they may even appear sober at levels that would seriously affect alcohol naive patients
  - females tend to have less tolerance than males
- typical
  - <50 mg/dL: may be asymptomatic
  - 50-100 mg/dL: relaxation, sedation, prolonged reaction time, euphoria
  - 100-200 mg/dL: impaired motor function and coordination, dysarthria, ataxia
  - 200-300 mg/dL: emesis, stupor
  - 300-400 mg/dL: coma
  - >500 mg/dL: respiratory depression, death

# Long Term Effects

- Damage to brain cells
- Increase in blood pressure (heart attack, stroke)
- fat cells in the liver
- ulcers and cancer
- Destruction of the pancreas
- liver cirrhosis

# Fetal Alcohol Syndrome

- Fetal Alcohol Syndrome is a group of alcohol-related birth defects that include physical and mental problems. (Alcohol dehydrogenase)
- Problems can include:
  - Small head, deformities to face, hands, and feet.
  - Heart, liver, and kidney defects
  - Vision and hearing problems
  - CNS problems and developmental delays
  - Short attention span
  - Hyperactivity, anxiety, and social withdrawal



- **Acute Alcohol Poisoning**
- CNS depression (dose-dependent)
- Anxiety, anesthesia, narcosis
- Coma, respiratory failure and death
- Acidosis, electrolyte disorders
- Bleeding
- Teratogenic.

## Treatment

- Patient should be hospitalized
- Avoid excessive movements
- Gastric lavage
- Apomorphine should not be used due to depressant effect
- Acidosis ( $\text{NaHCO}_3$ )
- Caffeine

- **Chronic Alcohol Poisoning**
- **Dependence** (Physical, psychological dependence, tolerance)
- Nutritional disorders
- Nourishment (forgetfulness, dementia)
- Cardiovascular diseases
- Degradation of liver functions
- Gastrointestinal bleeding
- Esophageal vascular enlargement, pancreatic dysfunction
- Repeated exposure to skin causes skin contact.
- Delirium tremens

# Alcoholism

- **Alcoholism** is a disease in which a person has a physical or physiological dependence on alcohol.
- Alcoholism can lead to alcohol abuse which is an excessive use of alcohol.

- Treatment☹️ (Alcoholism)
- Apomorphine or ipeka syrup, the patient is vomited)
- Disulfiram (antabus): AD<sub>2</sub>H inhibitor

- promil
- promil; The amount of alcohol in 100 milliliters of blood. (milligram / 100 milliliters)
- 1 promil = 100% mg
- = 1g / 1000ml blood

- Risk factors for traffic accidents according to the World Health Organization (WHO):
- alcoholic beverage
- Fast driving
- Do not use safety equipment such as seat belt

- Casarett & Doull's Toxicology: The Basic Science of Poisons, 9th edition, 2018
- Toksikoloji , Prof. Dr. Nevin VURAL , Ankara Üniversitesi Eczacılık Fakültesi Yayınları No: 73, 2005