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METHANOL TOXICOLOGY

- **1. Introduction**

Methanol (methyl alcohol) is produced by the distillation of wood (carbinol, wood spirit). It is the simplest and most important alcohol and should not be confused with ethanol (drinkable alcohol).

- **2. Chemical Structure**

A hydroxyl group (–OH) is attached to a saturated carbon atom, which is bonded to three hydrogen atoms (methyl group).

- **3. Physicochemical Properties**
- Colorless, volatile liquid with a mild odor (less intense than ethanol)
- Melting point: −97.8°C
- Boiling point: +64.7°C (more volatile than ethanol)
- Miscible with water and most organic solvents (ketones, ethers)
- Dissolves fats, plastics, and mineral salts
- Chemically stable
- Highly reactive (OH group is very mobile)
- Esterifiable with organic and inorganic acids
- Oxidizable by oxidizing agents ($K_2Cr_2O_7$, $KMnO_4$) and enzymes
- Highly flammable: vapors can form explosive mixtures with air (flames are barely visible in daylight)

- **4. Uses**
- Fuel
- Windshield washer fluids and de-icers
- Antifreeze
- Cleaners
- Paints, varnishes, solvents

- **5. Sources of Exposure**

a. Natural

- Oxidation of methane

b. Industrial

- Organic synthesis (methylating agent, formaldehyde, acetic acid)
- Paints, varnishes, inks, adhesives, textiles, footwear industry
- Automotive industry

c. Non-professional (domestic)

- Household products
- Fuel for lamps
- Adulterated alcohol ingestion

- **6. Toxicokinetics**

a. Absorption

- Ingestion (suicide attempts, substitution for ethanol)
- Inhalation: ~58%
- Cutaneous: rare

b. Distribution

- Rapid distribution in tissues
- Diffuses in total body water
- Volume of distribution: 0.7 L/kg (formate: 0.6 L/kg)
- Half-life: 3 h (increases with dose and ethanol co-ingestion)

c. Metabolism

- Mainly in the liver
- Also in retinal cells (rods and cones)

d. Elimination

- Expired air (methanol and CO_2)
- Urine (methanol 3–10% and formates)
- Formaldehyde is not detectable (rapidly oxidized to formic acid)

- **7. Mechanism of Toxic Action**

Direct toxicity

- CNS depression (anesthetic effect)

Indirect toxicity (metabolites)

A. Formaldehyde

- Acts on –SH groups (enzymes)
- Inhibits retinal and hepatic hexokinase
- Inhibits anaerobic glycolysis → ↓ ATP
- Inhibits retinol → retinal conversion (Vitamin A)

B. Formic Acid (major toxic metabolite)

Accumulation leads to:

1. **Metabolic acidosis + increased anion gap**
2. **Inhibition of cytochrome c oxidase → ↓ ATP → oxidative stress**
3. **Altered Na^+/K^+ ATPase activity**

Ocular toxicity

- Low cytochrome oxidase in optic nerve → cellular anoxia
- Leads to:
    - Impaired nerve conduction
    - Axoplasmic stasis
    - Intra-axonal edema
    - Papilledema

Neurological toxicity

- Damage to basal ganglia → bilateral putamen hemorrhage
- Parkinsonian syndromes

- **8. Acute Toxicity**

a. Ingestion

- 30–100 mL may be lethal

Symptoms (after latency)

- Digestive: nausea, vomiting, epigastric pain
- Neurological: headache, dizziness, coma
- Ocular: mydriasis, blindness
- Hemodynamic: hypotension
- Metabolic: acidosis, lactate accumulation, hypokalemia

Sequelae

- Blindness
- Extrapyramidal syndrome

Toxic levels

- Neurological signs: >200 mg/L
- Ocular signs: >1 g/L
- Fatal: 1.5–2 g/L

b. Inhalation (rare)

- Respiratory irritation
- Neurological symptoms
- Visual disturbances

- **9. Diagnosis**
- **Metabolic acidosis + high anion gap + osmolar gap → suspect methanol or glycol poisoning**
- Visual symptoms + normal renal function → methanol

Confirmation

- Methanolemia (toxic ≥ 0.25 g/L)
- Formate level (better severity marker)

Important: Measure ethanol level (delays toxicity, affects treatment)

Key findings

- pH < 7.2 (coma if ~6.6)
- Osmolar gap correlates with methanol level

- **10. Treatment**

Evacuation

- Early gastric decontamination
- Activated charcoal ineffective

Symptomatic

- Maintain vital functions
- Correct hydro-electrolyte balance

Specific treatment

α. Ethanol

- Competitive inhibitor of alcohol dehydrogenase (ADH)
- Therapeutic level: 1–1.5 g/L

β. 4-methylpyrazole (Fomepizole)

- ADH inhibitor
- More effective and safer

γ. Folic acid

- Enhances formic acid metabolism

Hemodialysis

Indicated if:

- Methanol > 500 mg/L
- Metabolic acidosis
- Visual symptoms
- Renal failure
- Ingestion > 30 mL

- **11. Chronic Toxicity**
- Visual disturbances
- Headache, dizziness
- Mucosal irritation

- **12. Analysis**

Atmosphere

- Oxidation → formaldehyde → colorimetry
- Gas chromatography

Biological samples

- Methanol in blood/urine
- Formic acid (HPLC)

- **13. Prevention**
- Proper storage
- Protective equipment
- Ventilation
- Monitoring
- Immediate washing in case of exposure