Pharmacology of Alcohol (Ethanol)

Samar Hunaiti

Introduction

- Alcohol (ethanol) has historical and social significance.
- Widely consumed globally; has both recreational and medical relevance.
- Understanding its pharmacology is critical for clinical practice.

Chemical Properties

- Simple alcohol with high water and lipid solubility.
- Molecular formula: C2H5OH.
- Rapidly absorbed in the GI tract.

Pharmacokinetics

- Absorption: Mainly in stomach and small intestine.
- Distribution: Crosses blood-brain barrier and placenta.
- Metabolism: Via ADH, MEOS (CYP2E1), and ALDH.
- Excretion: Primarily lungs, also urine and sweat.

Pharmacodynamics

- CNS depressant: enhances GABA_A receptor activity.
- Inhibits NMDA (glutamate) receptors.
- Activates mesolimbic dopamine system (reward pathway).

Acute Effects

- Dose-dependent CNS depression.
- Euphoria → impaired coordination → stupor → coma.
- Also causes vasodilation, nausea, hypoglycemia.

Chronic Effects

- Neurotoxicity: cognitive deficits, neuropathy.
- Liver damage: steatosis, hepatitis, cirrhosis.
- Cardiovascular: hypertension, arrhythmias.
- Endocrine/reproductive disruption.

Alcohol Use Disorder (AUD)

- Chronic, relapsing brain disease.
- DSM-5 diagnostic criteria: 2+ symptoms in 12 months.
- Tolerance and withdrawal present.
- Withdrawal: tremors, anxiety, seizures, delirium tremens.

Therapeutics

- Withdrawal: benzodiazepines, thiamine, hydration.
- Long-term: disulfiram (aversion), naltrexone (craving), acamprosate (relapse prevention).

Toxicology

- Alcohol poisoning: respiratory depression, risk of death.
- Methanol and ethylene glycol toxicity: metabolic acidosis, visual loss.
- Ethanol used as antidote for competing enzyme binding.

Legal and Forensic Considerations

- BAC determines level of intoxication.
- Legal limits vary by country (e.g., 0.08% in many regions).
- Breath, blood, and urine tests used in detection.

Clinical Case Studies

- Case 1: Acute intoxication and management.
- Case 2: Chronic alcoholic liver disease.
- Case 3: Withdrawal management in hospitalized patient.

Methanol Intoxication

Introduction

- Methanol is a toxic alcohol with serious systemic effects.
- Found in industrial products: antifreeze, solvents, adulterated alcohol.
- Toxicity primarily due to its metabolites: formaldehyde and formic acid.

Chemical and Physical Properties

- Simple alcohol (CH_3OH).
- Colorless, volatile, polar solvent.
- High absorption from gastrointestinal and respiratory tracts.

Pharmacokinetics

- Absorption: Rapid via GI and lungs.
- Distribution: Widely distributed in body water compartments.
- Metabolism: Hepatic conversion by alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH).
- Elimination: Primarily renal and pulmonary.

Toxic Metabolism Pathway

- Methanol → (ADH) → Formaldehyde → (ALDH) → Formic Acid.
- Formic acid causes metabolic acidosis and optic nerve toxicity.
- Accumulation leads to cellular hypoxia and organ damage.

Pharmacodynamics

- Methanol itself is not highly toxic.
- Formic acid inhibits mitochondrial cytochrome c oxidase.
- Results in lactic acidosis, retinal toxicity, CNS depression.

Clinical Manifestations

- Latency period: 6–30 hours post-ingestion.
- Visual disturbances: 'snowfield' vision, photophobia, blindness.
- CNS symptoms: headache, dizziness, seizures, coma.
- Severe metabolic acidosis (high anion gap).

Diagnosis

- History of exposure, suspicious symptoms.
- Anion gap and osmolal gap calculation.
- Definitive: Serum methanol level (if available).

Treatment Overview

- Stabilization: airway, breathing, circulation.
- Antidotes: Fomepizole (preferred) or Ethanol.
- Correct acidosis: Sodium bicarbonate infusion.
- Hemodialysis: Removes methanol and formic acid.

Mechanism of Antidotes

- Fomepizole: Competitive ADH inhibitor, blocks toxic metabolism.
- Ethanol: Competes with methanol for ADH binding, delays formic acid formation.
- Both reduce formate accumulation and toxicity.

Role of Hemodialysis

- Indications: High methanol level, visual changes, severe acidosis.
- Effectively removes methanol and corrects acidosis.
- Used alongside antidotal therapy.

Prognosis and Outcomes

- Early intervention leads to full recovery.
- Delayed treatment can result in permanent blindness or death.
- Public education and prevention crucial in high-risk areas.

Ethanol vs. Fomepizole

- Ethanol: competes for alcohol dehydrogenase.
- Fomepizole: direct inhibitor of alcohol dehydrogenase.
- Both prevent formation of toxic metabolites.

Summary -1

- Methanol toxicity is pharmacologically driven by its metabolites.
- Early recognition and intervention are critical.
- Fomepizole and ethanol are key pharmacologic agents.
- Dialysis plays a major role in severe cases.

Summary-2

- Alcohol affects multiple organ systems, primarily CNS and liver.
- Understanding PK/PD is essential for safe management.
- Important in emergency, psychiatry, internal medicine.

Blood Alcohol Content (BAC)

Here's how different BAC levels can affect the body physically and mentally:

- **BAC 0.0%**: No alcohol in your blood (sober).
- **BAC 0.02%**: Altered mood, relaxation, and slightly impaired judgment.
- **BAC 0.05%**: Uninhibited and lowered alertness and impaired judgment.
- **BAC 0.08%**: Reduced muscle coordination, difficulty detecting danger, and impaired judgment and reasoning.
- **BAC 0.10%**: Reduced reaction time, slurred

THANK YOU