Physiology of the World’s Second-Most Popular Drug

Kevin T. Strang, PhD
Department of Physiology
1. Cellular mechanism of alcohol effects

2. Effects on the nervous system
I. Mechanism of Alcohol Effects
Alcohol Structure

Methanol
\[ \text{H} - \text{C} - \text{OH} \]

Ethanol
\[ \text{H} - \text{C} - \text{C} - \text{OH} \]

Propanol
\[ \text{H} - \text{C} - \text{C} - \text{C} - \text{OH} \]
Alcohol Structure

Methanol

Ingestion → blindess

Ethanol

THE alcohol

Propanol

Most “other” alcohols are highly toxic to the body
• Clear, colorless liquid, miscible with H2O and Organics

Carbon-Hydrogen chains dissolve in lipids (hydrophobic)

This end interacts and dissolves in water (hydrophilic)
Basic Structure of Body Cells

Our bodies are made of 75 trillion specialized cells with phospholipid membranes, and aqueous environments inside and out.
Cell membranes are essentially oily bubbles formed from a bilayer of phospholipid molecules.
Proteins are the machinery that determine the function of different cell types; they’re found floating free and within membranes.

**Basic Structure of Body Cells**

- Ion channels (Na+, K+, Ca+2)
- Enzymes
- Receptors
- Signals
Proteins are made of amino acid chains:

20 different amino acids have unique “R” groups:

- Some are hydrophilic
- Some are hydrophobic
Proteins are made of amino acid chains:

The “R”-group sequence determines the complex folding and final shape of a protein.
Ethanol’s unique chemistry makes it a skeleton key that can interact with protein machinery of cells throughout the body.

**Ethanol**

\[
\text{H} - \text{C} - \text{C} - \text{OH} \quad \text{(hydrophilic)}
\]

\[
\text{H} \quad \text{H} \\
\text{H} \quad \text{H}
\]

\[
\text{H} \quad \text{H}
\]

\[
\text{H} \quad \text{H}
\]
e.g., Ethanol can alter gating properties of many different types of ion channels...
Why Does Whiskey “Burn”? 
Why Does Whiskey “Burn”?

“Vanillin Receptor 1” (mouth, throat)
Why Does Whiskey “Burn”?  

Heat, capsaicin….and Ethanol!
Why Does Whiskey “Burn”? 

Heat, capsaicin….and Ethanol!

Nerve signal to brain

“HOT!!”
“Drug” isn’t a four-letter-word....
“Drug” isn’t a four-letter-word….

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What do all “drugs” (and ethanol) have in common?
1. Sought-after effects
2. Unintended side-effects
3. The dose determines the effect/side-effect ratio
“Drug” isn’t a four-letter-word….

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“Alcohol is a pharmacological hand grenade.”

Stephen Braun--*Buzz*
Ethanol Affects All Body Systems

Cardiovascular  Gastrointestinal  Urinary

Endocrine/Reproductive

Today’s Focus: Nervous System
Ethanol affects synapses

Neuron signals and networks (x 100 billion!)

Synapses, Neurotransmitters and Receptors
Why was the drinking age raised from 18 to 21?
Normal cognition depends on a balance of excitatory and inhibitory synaptic activity:

- 50% of the brain’s synapses use Glutamate
- 40% use GABA (gamma-aminobutyric acid)
Well-documented pharmacological effects of ethanol include stimulation of GABA signaling and inhibition of glutamate signaling.

Overall effects are dose and situation dependent.
"Alcohol Myopia" Can Explain Variable Neural Effects

The basic idea:

Ethanol globally suppresses cognition, reducing the mental focus of an individual to immediate internal thoughts or external stimuli.
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Ethanol globally suppresses cognition, reducing the mental focus of an individual to immediate internal thoughts or external stimuli.

Example: Study demonstrating that ethanol is NOT a good anti-anxiety drug....
Alcohol, Anxiety, and Public Speaking

Volunteer subjects invited to a party

“In 15 minutes, you have to go on stage and give an impromptu speech:”
*What I dislike most about my body and physical appearance*

ANXIETY

<table>
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<th>Sit and think</th>
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<td>Easy slide sorting task</td>
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<tr>
<td>Moderate difficulty slide sorting task</td>
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ANXIETY
Alcohol, Anxiety, and Public Speaking

The chart illustrates the change in stress levels for placebo and alcohol subjects under different conditions:
- **No Slides**: The stress level remains unchanged.
- **Low Demand Slides**: The stress level decreases slightly.
- **Moderate Demand Slides**: The stress level decreases moderately.
- **High Demand Slides**: The stress level increases moderately.

The chart shows that alcohol subjects experience a higher increase in stress compared to placebo subjects under high demand slides conditions.
Myopia can also boost self-esteem!
Other Neurotransmitters: Ethanol stimulates brain “reward” centers.
THIS EXPLAINS:
Short-term: Drinking leads to more drinking
Chronically: Addiction
Both related to “Rising Phase Effect”
Rising Phase Effect

Moderate Dose and Rate

Elevated Dopamine: Reward/Euphoria

Depressed Dopamine: Craving/Dependence

Blood Alcohol Content

Time

Increasing Dose/Side Effects
Moderate Dose/Effects
Rising Phase Effect

Blood Alcohol Content

Time

Increasing Dose/Side Effects
Moderate Dose/Effects

Binge Drinking
Rising Phase Effect

Blood Alcohol Content

Time

Binge Drinking
Optimized Drinking

Increasing Dose/Side Effects

Moderate Dose/Effects
OTHER SIDE EFFECTS:
Impaired memory formation (low doses!)
Amnesia/Blackout (higher doses)
Bar Skanks Announce Plans To Kiss

COLUMBUS, OH—In an announcement that received wide attention throughout Wolverine’s tavern Tuesday, bar skanks Stephanie Fletcher and Jessica Keneally stated that they would share a passionate kiss at an unspecified time that evening.

“Steph and I are totally hot for each other,” Keneally said over the loud music to several unspecified bar patrons. “We’re going to make out. We don’t care who’s watching.”

According to eyewitnesses who looked up the second they walked in the door, the 22-year-old skanks arrived at the bar at approximately 10 p.m., dressed in their usual skank attire of low-cut tank tops paired with either low-rider jeans or a short skirt, and exposed, brightly colored thongs.

After downing their third cosmopolitans, the two skanks stood up and began grinding to the R. Kelly song “I’m a Flirt,” which caused a nearby conversation about the Cleveland Indians to come to a sudden halt.

“Quit staring,” Keneally said to the approximately 25 male patrons in the immediate vicinity, all of whom were by that time involuntarily ogling the skank-ass pair. “Oh my God, you guys are such pervs.”

Fletcher would neither confirm nor deny that the kiss would involve tongue, saying that bargoers “would just have to wait.”

“Who knows what will go down,” Fletcher said as she reached into Keneally’s tight top and tweaked her left breast with her thumb and middle finger in front of seven rapt onlookers. “Possibly us.”

In previous months, Keneally and Fletcher have, either separately or together, on SKANKS, page B.
WHAT IS LEARNING?

Short-Term Memory
("Working memory")
(RAM)

Assimilation

Long-Term Memory
("Learning")
(Hard-drive)
Short-Term Memory → Long-Term Memory

NEW LEARNING RESEARCH

SLEEP
WHAT IS LEARNING?

ETHANOL

Short-Term Memory

Long-Term Memory
WHAT IS LEARNING?

ETHANOL

Short-Term Memory

Long-Term Memory

SLEEP

THE GRAND DELUSION...
SIDE EFFECT: Depression of motor output and sensory input
1. Loss of coordination (see drunk driving stats)
SIDE EFFECT: Depression of motor output and sensory input
1. Loss of coordination (*see drunk driving stats*)
2. 8th Cranial Nerve especially sensitive
   ("Dude, turn it up")  (Field sobriety test)
GI SYSTEM TO THE RESCUE
Normally:

Vomit: to puke, purge, barf, hurl, yak, chunky exhale, yawn in Technicolor®, worship the porcelain god, talk to Ralph on the big white phone…

stretches → stomach
bacteriotoxin wall → receptors
excess acid → brainstem → vomit
Side Effect: High ethanol concentrations cause vomiting
BEER ADVERTISING
Since 1955 Americans have enjoyed Busch's smooth, refreshing taste. Busch, the leading subpremium-priced brand, also has a clean and snappy character.

Busch. Smooth going down, extra tasty the second time around.

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QUESTIONS?