ETHANOL
Chemistry & Physiology of the World’s Second-Most Popular Drug

Personal Notes from Prof. Shakhashiri

• Serious impediments to learning, personal growth and development, and responsible behavior can be caused by alcohol and substance abuse. The notorious national reputation of the UW-Madison campus in this regard is shameful. I urge you to follow the guidance provided by the Chancellor’s Advisory Group on Alcohol and Other Drugs and other officials to help achieve a drug-free environment and to exercise responsible and lawful use of alcoholic beverages.

• WISL Fellow Dr. Kevin Strang presents an excellent lecture on “Ethanol: Chemistry and Physiology of the World's Second-Most Popular Drug.” I invite you to view a recording of this very popular lecture.

Ethanol (ethyl alcohol, grain alcohol) is a clear, colorless liquid with a characteristic, agreeable odor. In dilute aqueous solution, it has a somewhat sweet flavor, but in more concentrated solutions it has a burning taste. Ethanol, CH₃CH₂OH, is an alcohol, a group of chemical compounds whose molecules contain a hydroxyl group, –OH, bonded to a carbon atom. The word alcohol derives from Arabic al-kuhul, which denotes a fine powder of antimony used as an eye makeup. Alcohol originally referred to any fine powder, but medieval alchemists later applied the term to the refined products of distillation, and this led to the current usage.

Ethanol melts at –114.1°C, boils at 78.5°C, and has a density of 0.789 g/mL at 20°C. Its low freezing point has made it useful as the fluid in thermometers for temperatures below –40°C, the freezing point of mercury, and for other low-temperature purposes, such as for antifreeze in automobile radiators.

Ethanol has been made since ancient times by the fermentation of sugars. All beverage ethanol and more than half of industrial ethanol is still made by this process. Simple sugars are the raw material. Zymase, an enzyme from yeast, changes the simple sugars into ethanol and carbon dioxide. The fermentation reaction is represented by this simple equation:

\[ C_{6}H_{12}O_{6} \rightarrow 2 \text{CH}_3\text{CH}_2\text{OH} + 2 \text{CO}_2 \]

But it is actually very complex, and impure cultures of yeast produce varying amounts of other substances, including glycerine and various organic acids. In the production of beverages, such as whiskey and brandy, the impurities supply the flavor. Starches from potatoes, corn, wheat, and other plants can also be used in the
production of ethanol by fermentation. However, the starches must first be broken down into simple sugars. An enzyme released by germinating barley, diastase, converts starches into sugars. Thus, the germination of barley, called malting, is the first step in brewing beer from starchy plants, such as corn and wheat.

The ethanol produced by fermentation ranges in concentration from a few percent up to about 14 percent. Above about 14 percent, ethanol destroys thezymase enzyme and fermentation stops. Ethanol is normally concentrated by distillation of aqueous solutions, but the composition of the vapor from aqueous ethanol is 96 percent ethanol and 4 percent water. Therefore, pure ethanol cannot be obtained by distillation. Commercial ethanol contains 95 percent by volume of ethanol and 5 percent of water. Dehydrating agents can be used to remove the remaining water and produce absolute ethanol.

Much ethanol not intended for drinking is now made synthetically, either from acetaldehyde made from acetylene, or from ethylene made from petroleum. Ethanol can be oxidized to form first acetaldehyde and then acetic acid. It can be dehydrated to form ether. Butadiene, used in making synthetic rubber, may be made from ethanol, as can chloroform and many other organic chemicals. Ethanol is used as an automotive fuel by itself and can be mixed with gasoline to form gasohol. Ethanol is miscible (mixable) in all proportions with water and with most organic solvents. It is useful as a solvent for many substances and in making perfumes, paints, lacquer, and explosives. Alcoholic solutions of nonvolatile substances are called tinctures; if the solute is volatile, the solution is called a spirit.

Most industrial ethanol is denatured to prevent its use as a beverage. Denatured ethanol contains small amounts, 1 or 2 percent each, of several different unpleasant or poisonous substances. The removal of all these substances would involve a series of treatments more expensive than the federal excise tax on alcoholic beverages (currently about $20 per gallon). These denaturants render ethanol unfit for some industrial uses. In such industries undenatured ethanol is used under close federal supervision.

When an alcoholic beverage is swallowed, it passes through the stomach into the small intestine where the ethanol is rapidly absorbed and distributed throughout the body. The ethanol enters body tissues in proportion to their water content. Therefore, more ethanol is found in the blood and the brain than in muscle or fat tissue. The ethanol is greatly diluted by body fluids. For example, a 1-ounce shot of 100-proof whiskey, which contains 0.5 fluid ounces of ethanol (about 15 mL), is diluted 5000-fold in a 150-pound human, producing a 0.02 percent blood alcohol concentration.

Ethanol is toxic, and the body begins to dispose of it immediately upon its consumption. Over 90 percent of it is processed by the liver. In the liver, the alcohol dehydrogenase enzyme converts ethanol into acetaldehyde, which is itself toxic.

\[
\text{CH}_3\text{CH}_2\text{OH} \rightarrow \text{CH}_3\text{C} \equiv \text{H} + 2 \text{H}
\]

Acetaldehyde is destroyed almost immediately by the aldehyde dehydrogenase enzyme, which converts it to acetate ions.
The hydrogen atoms represented by these equations are not unattached, but are picked up by another biologically important compound, nicotinamide-adenine dinucleotide (NAD), whose function is to carry hydrogen atoms. NAD is involved in both of the above processes, being converted to NADH.

\[
\text{NAD} + \text{H} \rightarrow \text{NADH}
\]

NADH must be recycled to NAD for the disposal of ethanol to continue. If the amount of ethanol consumed is not great, the recycling can keep up with the disposal of ethanol. The ethanol disposal rate in a 150-pound human is about 0.5 ounce of ethanol per hour, which corresponds to 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of hard liquor. The figure (at right) shows how the blood alcohol level changes with time for various doses of ethanol.

Ethanol acts as a drug affecting the central nervous system. Its behavioral effects stem from its effects on the brain and not on the muscles or senses themselves. It is a depressant, and depending on dose, can be a mild tranquilizer or a general anesthetic. It suppresses certain brain functions. At very low doses, it can appear to be a stimulant by suppressing certain inhibitory brain functions. However, as concentration increases, further suppression of brain functions produce the classic symptoms of intoxication: slurred speech, unsteady walk, disturbed sensory perceptions, and inability to react quickly. At very high concentrations, ethanol produces general anesthesia; a highly intoxicated person will be asleep and very difficult to wake, and if awakened, unable to move voluntarily.

Alcohol levels in the brain are difficult to measure, and so blood alcohol levels are used to assess degree of intoxication. Most people begin to show measurable mental impairment at around 0.05 percent blood alcohol. At around 0.10 percent, mental impairment will show obvious physical signs, such as an unsteady walk. Slurred speech shows up at around 0.15 percent. Unconsciousness results by 0.4 percent. Above 0.5 percent, the breathing center of the brain or the beating action of the heart can be anesthetized, resulting in death. Reaching this level of blood alcohol by ingestion is unlikely, however. In a 150-pound human, it would require rapid consumption of a fifth gallon of a 100-proof spirit.

**Resources:**

Alcohol and Cancer: A Statement of the American Society of Clinical Oncology
Journal of Clinical Oncology, 11/7/2017

Low-Risk Alcohol Drinking Guidelines, Canadian Centre on Substance Use and Addiction, 2017