
The Biochemistry of Alcohol Toxicity

B Ramachandra Murty

A dependency on alcohol causes life shattering addiction that leads to physical illness, severe malnutrition and demoralizing erosion of self esteem. The following discussion highlights some of the harmful effects of alcohol.

How Alcohol Enters the System

From the moment an alcoholic drink is swallowed the body pays special attention to it. Unlike foods which require digestion before they can be absorbed, the tiny ethanol molecules can diffuse right through the walls of an empty stomach to reach the brain in no time. Ethanol is a toxin and too high a dose of it triggers one of the body's primary defences against poison, namely vomiting. Many times, alcohol is taken gradually and in a dilute form and thereby the vomiting reflex is delayed and the alcohol is absorbed.

One can become intoxicated almost immediately when alcohol is consumed on an empty stomach. But, when the stomach is full of food, alcohol molecules have less chance of coming in contact with the stomach walls and alcohol affects the brain more slowly.

If one drinks slowly enough, the alcohol, after absorption, will collect in the liver and get processed without much effect on other parts of the body. If one drinks rapidly, however, some of the alcohol will bypass the liver and flow for a while through the rest of the body and the brain.

Alcohol is metabolized mainly in the liver in two stages and catalyzed by alcohol and aldehyde dehydrogenases, with NAD^+ as a hydrogen acceptor.

As can be seen from the pathway shown in *Figure 1*, the presence of alcohol within the cell makes a heavy demand on a limited



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Keywords

Alcohol, metabolism, health.

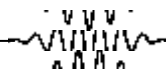
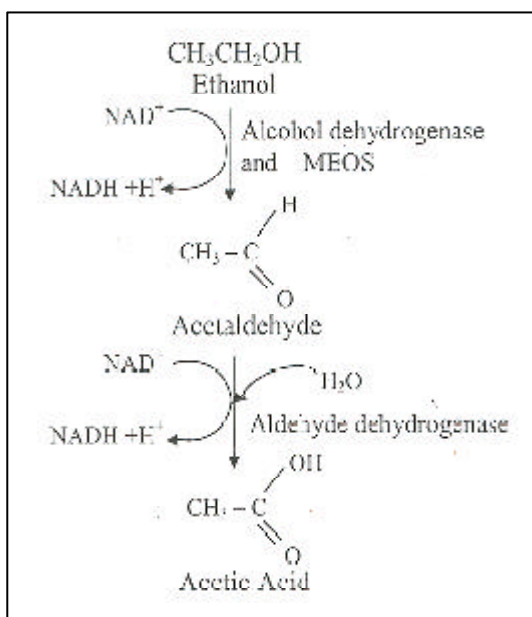
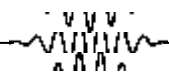


Figure 1. Metabolism of alcohol in the liver. Apart from alcohol dehydrogenase which oxidises 90% of the alcohol in the body, a chain of enzymes known as microsomal ethanol oxidizing system (MEOS) oxidizes not only alcohol but also several classes of drugs. The second enzyme that converts acetaldehyde to acetate i.e., aldehyde dehydrogenase is present not only in the liver but also in the peripheral tissues.



supply of NAD^+ , (a niacin-derived coenzyme) and consequently the NAD^+/NADH ratio falls. Other reactions that depend on NAD^+ will thus be curtailed. In particular, the oxidation of lactate to pyruvate will become much slower than the reverse reaction, which accounts for the observed accumulation of lactate. Other redox reactions depending on NAD^+ that occur in the tricarboxylic acid cycle (Figure 2) also similarly become slower in the presence of alcohol. The maximum rate of oxidation of acetate may not be more than 25% of the normal. Therefore acetate is diverted into the fatty acid synthetase system accounting for the *fatty liver* condition commonly found in alcoholics.

The hypoglycemia (a low blood glucose level) observed is the result of the failure of a metabolic pathway called *gluconeogenesis* i.e., production of glucose from non-carbohydrate sources like lactate, glycerol and amino acids. All these precursors require NAD^+ for the synthesis of glucose and since NAD^+ is in short supply, gluconeogenesis is greatly reduced. Lactate when present in an abnormally high concentration in the blood competes in the renal mechanism for the excretion of uric acid. Therefore the



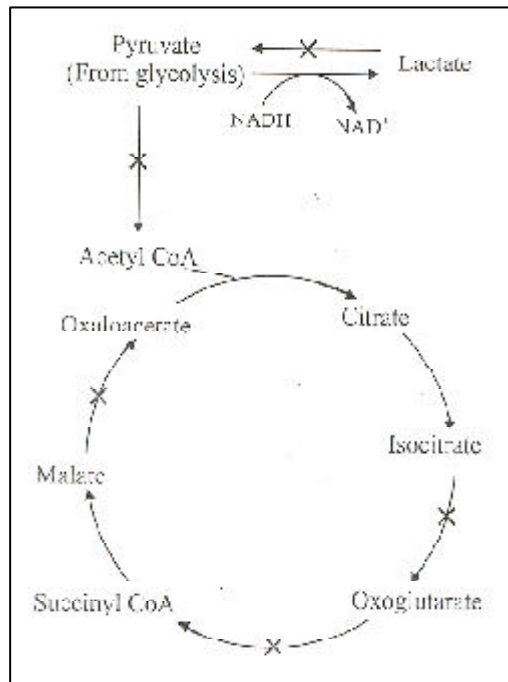


Figure 2. Effect of alcohol on the metabolism of pyruvate, the end product of glycolysis. The rates of reactions marked 'X' are reduced as a result of the lack of NAD^+ in the tricarboxylic acid cycle.

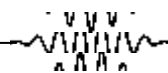
kidney is unable to fully excrete this end product of nucleic acid metabolism and its accumulation leads to the symptoms of the disease *gout*.

Alcohol in the Brain

Alcohol is often used as a social anesthetic to relax or to relieve anxiety. This gives the impression that alcohol is a stimulant. But it actually works by sedating the inhibitory nerves, thus allowing the excitatory nerves to take over. This is however temporary and ultimately alcohol acts as a depressant and sedates all the nerve cells.

Brain cells are particularly sensitive to excessive exposure to alcohol. The brain shrinks even in persons who drink moderately. The extent of shrinkage is proportional to the amount consumed. Abstinence together with good nutrition can reverse some of the brain damage. However, prolonged drinking beyond an individual's capacity can cause severe and irreversible damage to vision, memory and learning ability.

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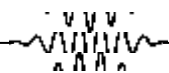


Alcohol increases urine output. This is because alcohol depresses the pituitary gland's production of the antidiuretic hormone *vasopressin*. The resulting loss of body water leads to thirst. The only fluid that can relieve dehydration is water, but if alcoholic beverages are the only drinks available, then each drink will only worsen the thirst. The water takes with it important minerals such as potassium, magnesium, calcium and zinc. These minerals are vital to the maintenance of the body's fluid balance, nerve and muscle action and coordination. They must be replenished immediately to prevent deficiency. An awful feeling of headache, pain, unpleasant taste in the mouth and nausea that one experiences in the morning after drinking too much is called a hangover. Alcohol not only causes the body to lose water but actually reduces water content in the brain cell. When these cells take in water and rehydrate in the morning, pain accompanies their swelling back to their normal size.

Another more serious consequence of ethanol consumption is the effect on the development of the embryo and fetus *in utero* [1]. The so-called *Fetal Alcohol Syndrome* (FAS) is characterized by mental deficiency, microcephaly (meaning small head) and irritability. These infants are generally smaller and demonstrate poor muscular coordination. The severity of the symptoms appears to be related to the extent of alcohol consumption by the mother during pregnancy. The interference of ethanol with membrane functions, the possibility that acetaldehyde can escape the damaged liver of the alcoholic mother and reach the developing fetal brain, and alcohol-induced hypoglycemia are some of the factors responsible for FAS.

Alcohol in the Liver

The capillaries that surround the digestive tract merge into veins that carry the alcohol-laden blood to the liver. Here the veins branch and rebranch into capillaries that touch every living liver cell. The liver being situated at this point along the circulatory system enables it to remove toxic substances before they reach other body organs such as the heart and brain.



The liver is the only organ that can dispose of significant quantities of alcohol, but its maximum rate of alcohol clearance is fixed. This explains why only time will restore sobriety and exercise does not help because muscles cannot metabolize alcohol.

When alcohol is consumed the liver speeds up the synthesis of fatty acids. Fat accumulation has been observed in the livers of young men after a single night of heavy drinking [2]. If the condition persists for more than a day, *fatty liver*, the first stage of liver deterioration starts. It interferes with the distribution of nutrients and oxygen to the liver cells. If the condition lasts long enough, fibrous scar tissue invades the liver. This is the second stage of liver deterioration called *fibrosis*. Fibrosis is reversible with abstinence from alcohol and good nutrition, but the next and the last stage, *cirrhosis* is not. In cirrhosis, liver cells harden, turn orange and lose function forever as they die.

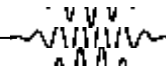
Long Term Effects of Alcohol

If the doses of alcohol are heavy and if the time between them is short, complete recovery cannot take place and repeated onslaughts of alcohol gradually take a toll on the body. For example, alcohol is directly toxic to skeletal and cardiac muscles causing weakness and deterioration in a dose related manner [3]. Alcoholism makes heart disease more likely, probably because chronic alcohol use raises the blood pressure [4]. Upon autopsy, the heart of an alcoholic appears bloated and weighs twice as much as a normal heart. Alcoholism also leads to cancers of the mouth, throat, esophagus and lungs. Some reliable sources rank daily exposure to ethanol high among possible carcinogenic hazards [5,6,7].

Long term effects of alcohol also include

- Diabetes (non insulin dependent)
- Ulcers of the stomach and intestines
- Severe psychological depression

Upon consuming alcohol, the liver accelerates fatty acid synthesis. Fat accumulates in the liver which interferes with the distribution of nutrients and oxygen to the liver cells. If this condition persists, liver deteriorations called fibrosis occurs.



Nutritional deficiencies are virtually inevitable consequences of alcoholism, not only because alcohol displaces food but also because alcohol directly interferes with the body's use of nutrients, making them ineffective even if they are present.

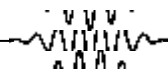
- Impaired immune response
- Central nervous system damage
- Malnutrition
- Bone deterioration and osteoporosis.

Alcohol causes the stomach cells to over-secrete both an acid and an agent of the immune system, *histamine*, that produces inflammation. These changes make the stomach and esophagus linings vulnerable to ulcer formation. Intestinal cells fail to absorb important vitamins. Liver cells lose their efficiency in activating vitamin D and in the excretion of bile. Rod cells in the retina which normally process vitamin A (retinol) to the form needed in vision, find themselves processing ethanol instead.

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Alcohol and Barbiturates

Barbiturates and alcohol both interact with the γ -aminobutrate (GABA)-activated chloride channel. Activation of the chloride channel inhibits neuronal firing, which explains the depressant effects of both these compounds. This drug-alcohol combination is very dangerous and normal prescription doses of barbiturates have potentially lethal consequences in the presence of ethanol. Ethanol inhibits the metabolism of barbiturates, thereby



prolonging their effective time in the body, causing increased depression of the central nervous system.

A chronic alcoholic, when sober, has trouble falling asleep even after taking several sleeping pills, because the liver has developed an increased capacity to metabolize barbiturates contained in the pills. In frustration more pills are consumed followed by alcohol. Sleep results, but may be followed by respiratory depression and death because the alcoholic although less sensitive to barbiturates when sober, remains sensitive to the synergistic effects of alcohol.

This discussion highlights some of the ways alcohol affects metabolism and health. Even though alcohol is legal, it alters one or more bodily functions and is medically defined as a depressant drug. In addition to deaths due to health problems, many die each year in alcohol-related traffic accidents. As new methods of personality development advise us to switch over to more enthusiastic ways of living, it is certainly not advisable to cultivate a habit that breeds depression. With all these aspects in view, the best way to escape the harmful effects of alcohol might be to abstain from it altogether.

Suggested Reading

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