

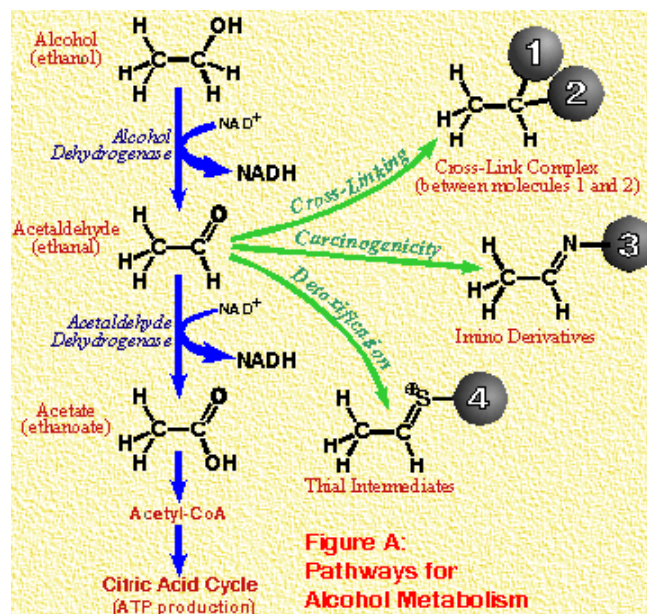
## Living with Alcohol by Steven Wm. [Fowkes](#)

Alcohol is everywhere within Western culture. Since the dawn of recorded history, the art of fermenting fruit and grain into wine and beer has been a much-prized skill. As technology advanced, distillation of alcoholic beverages into refined spirits became quite popular. The high alcohol content of refined spirits made them exceptionally stable for long-term storage and commerce.

Along with fermentation technology came *drunkenness*, *hangovers* and *alcoholism*. Drunkenness is caused by alcohol's pharmacological effect on the human central nervous system. This effect causes incoordination, slowed reaction time, muscle relaxation, behavioral disinhibition and impaired judgment, all of which last for several hours after alcohol is consumed. There is no simple and effective way to prevent drunkenness other than to avoid alcohol consumption in the first place.

Hangovers are the result of alcohol's toxicity. Hangover symptoms include headaches, dehydration, irritability, sleep disturbances, liver toxicity, nerve and tissue hypersensitivity, etc. These symptoms can be prevented or significantly reduced by simple interventions that will be discussed in this article. These interventions augment *natural detoxification mechanisms* that would otherwise be overwhelmed by the sheer volume of alcohol intake.

Alcoholism can result from any one or combination of addictive mechanisms created by alcohol's powerful pharmacological effect on the body. Some of these mechanisms are psychological and some are physiological. This article will discuss primarily physiological mechanisms. Although the majority of people consuming alcoholic beverages do not have problems with regulation of their intake, a significant minority of users do. Some learn to control their intake through adaptive behaviors. Many learn to cope through a strategy of abstinence. And some become alcoholics.



## Acetaldehyde Toxicity

Alcohol's effects are not limited to those of alcohol alone. Alcohol is metabolized in a multi-step process into various metabolites which have unique biochemical effects of their own. The first step in this process is the conversion of alcohol to acetaldehyde [see Figure A]. Since acetaldehyde is approximately 30 times more toxic than alcohol, acetaldehyde is a major cause of alcohol-associated side effects. If acetaldehyde is not efficiently converted into acetic acid (the second step in the metabolism of alcohol), severe toxicity can result. This is a common problem among certain people of Asian extraction (notably Inuit and American Indians) who have a genetic weakness in the *acetaldehyde dehydrogenase* enzyme [see Figure A]. Even in people who do not have this genetic trait, acetaldehyde dehydrogenase is often unable to fully keep up with the production of acetaldehyde during alcohol intoxication.

## Cross-Linking

One of the most significant mechanisms of alcohol toxicity is the powerful *cross-linking* activity of acetaldehyde. Cross-linking is a process by which “molecular bridges” are formed between “reactive sites” on different molecules. These cross-links “tie up” the affected molecules and interfere with their normal function. In some circumstances, molecular function can be completely blocked by cross-linking.

A good example of the effect of cross-linking in action is the “tanning” of leather. The tanning process involves applying large amounts of a cross-linking agent (like tannic acid) to animal hides to cross-link the flexible collagen and elastin proteins in the animal skin to produce tough, inflexible, abrasion-resistant leather. This same process happens — at a slower rate — in people. Cross linking is largely responsible for age-related changes in human skin that make it inflexible, wrinkled and dry. Some of the most leathery skin you will ever see is found on alcoholics who stay outdoors a lot of the time. The ultraviolet (UV) and near-ultraviolet components of sunlight activate the cross-linking process.

There are many substances that can act as cross-linking agents. Aldehydes are one class of cross-linker, of which acetaldehyde is a member. Acetaldehyde is used in making plastics, adhesives and fabrics. The closely related chemical *formaldehyde* is used in insulating foams, plywood, particle board and embalming fluid.

## Stewed, Not Pickled

The primary detoxification mechanism for scavenging unmetabolized acetaldehyde is sulfur-containing antioxidants [see Figure A]. The two most important are *cysteine*, a conditionally essential amino acid, and *glutathione*, a cysteine-containing tripeptide (a three-amino-acid polymer) [see Figure B]. Cysteine and glutathione are active against acetaldehyde (and formaldehyde) because they contain a reduced (unoxidized) form of

sulfur called a *sulfhydryl group*, which contains a sulfur atom bonded to a hydrogen atom (abbreviated SH).

Sulfhydryl groups interact with aldehydes to render them incapable of forming cross links. This “mops up” or scavenges any stray acetaldehyde that is not properly metabolized into acetate (acetic acid) [see Figure A]. Although this is a powerful aldehyde detoxification mechanism, it is easily overwhelmed by the relatively large amounts of alcohol that are typically consumed with alcoholic beverages as compared to the amounts of alcohol and acetaldehyde that are produced through normal metabolism. Fortunately, sulfhydryl antioxidants can easily be fortified through dietary supplementation.

In one experiment with rodents [Sprince *et al.*, 1974], a LD-90 dose of acetaldehyde (the dose that would normally kill 90% of the animals) was *completely* blocked by pretreatment of the animals with cysteine and vitamins B-1 and C. In other words, *none* of the cysteine-treated animals succumbed to the lethal dose of acetaldehyde! N-Acetylcysteine (NAC) protected almost as well as cysteine.

In another rodent experiment [Busnel & Lehman, 1980], alcohol’s ability to inhibit swimming *after* the alcohol had been completely metabolized was blocked by vitamin C. What this and the previous study suggests is that the pharmacologic and toxic effect of alcohol are different. The pharmacological effect (*i.e.*, intoxication or drunkenness) is *not* inhibited by vitamin C or cysteine, but the *toxic* effect (*e.g.*, the hangover, nervous irritability, swimming difficulty) *is* inhibited. This suggests that, with alcohol, you can “have your cake and eat it too.”

## Dosage Suggestions

Typical doses of cysteine that are sufficient to block a major portion of the toxic effect of alcohol/acetaldehyde are about 200 mg per ounce of alcohol consumed. However, the rapid assimilation and metabolism of alcohol requires both prior and concurrent dosing of cysteine to maintain protection. Furthermore, a multifold excess of vitamin C is required to keep the cysteine in its reduced state and “on the job” against acetaldehyde. I use capsules (because they dissolve fast) containing 200 mg cysteine plus 600 mg of vitamin C (with or without extra B-1). I take one before I start drinking, one with each additional drink and one when I’m finished. It works remarkably well.

## Additional Nutrients

There are several other nutrients which may synergize with cysteine and vitamin C. Glutathione, the predominant sulfhydryl antioxidant in the human body, should be considered. Although it is probably quite effective, it is many times more expensive than cysteine and it is not as concentrated; it contains only 10% sulfur compared to 26% sulfur in cysteine. Much larger doses of glutathione must be taken to get the same sulfhydryl concentration, and a significant but unknown amount of glutathione is broken down in

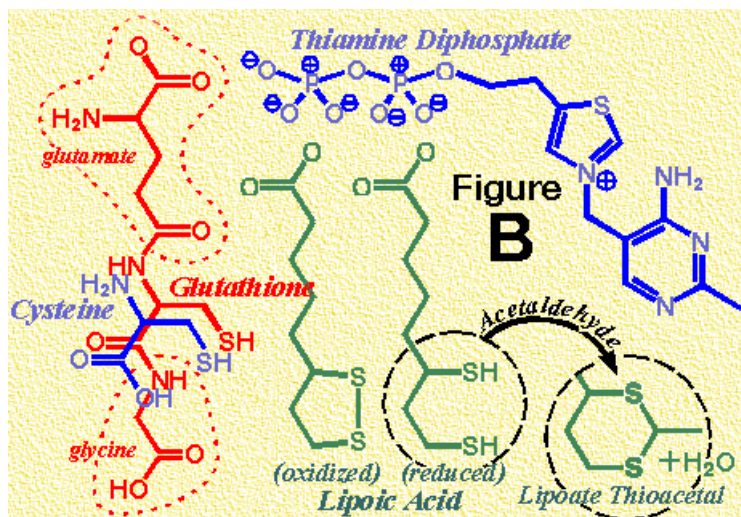
the stomach into its component amino acids (glutamate, cysteine and glycine). So while glutathione is a great idea, it's an expensive great idea.

Thiamine (vitamin B-1) and lipoic (thioctic) acid are key sulfur-containing nutrients that may be depleted by alcohol and/or may help with acetaldehyde detoxification. Thiamine was tested by Sprince and colleagues [1974] and found to offer protective benefit to acetaldehyde toxicity when combined with C and cysteine. Whether this is due to a direct interaction between acetaldehyde and the thiamine-bound sulfur or an enhancement of cellular energy production by the active thiamine cofactor (thiamine pyrophosphate) is not known. Alcoholics are known to be thiamine depleted, but whether this depletion is caused by diminished intestinal absorption of thiamine by alcohol or by destruction of thiamine by acetaldehyde is not known. Even under normal circumstances, intestinal absorption of thiamine is not very efficient.

In its reduced form, lipoic acid is a powerful sulfhydryl antioxidant. Due to lipoic acid's twin sulfhydryl groups, it should scavenge aldehydes even more effectively than either cysteine or glutathione (see Figure B). However, supplemental lipoic acid is commercially available only in its oxidized form which contains no sulfhydryl sulfur. It is converted into the reduced form within the mitochondria after absorption from the bloodstream into the cell. So while lipoic acid may be a good cellular protector, it is not as efficient at scavenging acetaldehyde from the bloodstream as cysteine and glutathione. Lipoic acid is also fairly expensive.

Within the cells of the liver, however, lipoic acid and acetaldehyde may be readily interacting. The liver metabolizes the largest percentage of ingested alcohol and acetaldehyde levels may be quite high in liver cells. Acetaldehyde may bind to reduced lipoamide (the active lipoic acid factor) to render it inactive (see Figure B). Due to this potential problem, it may be a good idea *not* to take one's *regular* dose of lipoic acid near when one drinks alcohol but rather several hours before and after.

Two combination formulas are available: Twin Labs and Vitamin Research Products make a C-and-cysteine formula, and VRP makes a B-1, C and N-acetylcysteine formula.



## Addiction Mechanisms

The toxicity of acetaldehyde is mitigated to a significant extent by alcohol itself. This provides a strong incentive for people who *start* drinking alcohol to *keep* drinking alcohol. When they stop drinking, the toxic effects of acetaldehyde increase as the alcohol is rapidly cleared from the body. This mechanism reinforces “binge” drinking.

## Blood Sugar Regulation

Alcohol also causes the liver to convert glycogen (a sugar-storage carbohydrate) into sugar. For people with blood-sugar regulation problems (primarily reactive hypoglycemia), alcohol can offer a “quick fix” to normalize blood sugar. This is why brandy is given to revive people who have fainted. The brain relies upon blood sugar for its primary energy supply.

For people with low blood sugar, alcohol can temporarily relieve their physiological and psychological symptoms. This provides a quick reward for alcohol consumption. If the effect of the alcohol is allowed to wear off, the symptoms return even stronger, providing additional incentive for further drinking. When alcohol consumption eventually stops, blood sugar tends to crash, severely aggravating symptoms and distress. This might be described as “drinking one’s self into unconsciousness.” This problem leads to binge drinking behaviors.

The high prevalence of blood sugar-related alcohol addictive behaviors is supported by the high percentage of former alcoholics who have become “sugar junkies.” It is probably no accident that Alcoholics Anonymous meetings and 12-step programs usually feature ample availability of sweet snack foods (cookies, cakes, candy, soft drinks, *etc.*).

The solution to this problem is improved glycemic control. This can be accomplished by such dietary changes as eating *complex carbohydrates* instead of simple carbohydrates, eating less carbohydrates (*carbohydrate restriction*) to activate fat-burning enzymes, and eating smaller, more frequent, *high-protein meals*. It can also be addressed with supplements. The amino acid *glutamine*, for example, provides an alternative source of fuel for the brain. Supplemental glutamine can make the brain less sensitive to low blood sugar. Typical doses are 1-3 g.

The trace mineral *chromium* is an essential part of *glucose tolerance factor* (GTF), which is necessary for efficient transport of blood sugar into the insulin-sensitive cells of the body. Chromium is slow to absorb and accumulate, so extended use is required. Chromium chloride, chromium nicotinate and chromium picolinate are commonly available as supplements. Typical high-potency chromium supplements are in the 200 mcg range, although many physicians will recommend that their diabetic and diabetic-prone patients take 1000 mcg. Typical maintenance doses are in the 25-50-100 mcg range.

## The NADH Connection

When alcohol is metabolized, it has a powerful effect on cellular energy production pathways. The conversion of alcohol into acetaldehyde by *alcohol dehydrogenase* and acetaldehyde into acetate by *acetaldehyde dehydrogenase* results in the generation of NADH (reduced nicotinamide adenine dinucleotide). NADH is the hydrogen-transfer chemical (*i.e.*, *electron transporter*) that enables *oxidative phosphorylation* to take place (*i.e.*, the production of ATP energy within the mitochondria through the utilization of oxygen). This process is too complex to discuss in detail here, but an extensive review article can be found in *Smart Drug News* Volume 5, No. 2.

Suffice it to say that NADH production generates lots of energy. This is why drinking alcohol warms people up. The extremely rapid NADH production from the alcohol dramatically increases energy availability and body temperature, especially in people who are chilled. After alcohol has been converted into acetate, the acetate enters the citric acid cycle to generate even more NADH. Vinegar is about 5% acetic acid (acetate).

For people with compromised mitochondrial function, alcohol may provide a temporary shot of energy that can energize the brain for dealing with stressful circumstances. This increased energy, combined with muscle relaxation and behavioral disinhibition, can be perceived as a valuable aid to social interaction.

Mitochondrial energy production can be supported through diet and supplements instead of alcohol. NADH is now available as a supplement in 2.5 and 5 mg doses. Dosages range from 2.5 mg to more than 10 mg. NAD (the oxidized form of NADH) is also available as a supplement. NAD is made in the human body in two ways: primarily from the essential amino acid *L-tryptophan*, and secondarily from niacinamide (vitamin B-3). Both of these can be taken supplementally.

In addition to making NAD, tryptophan also makes serotonin, a brain neurotransmitter involved in the regulation of carbohydrate feeding behaviors, mood and emotional control. Elevated serotonin levels suppress the appetite for carbohydrates (“sugar cravings”) and promote calmness and equanimity. Low serotonin levels increase carbohydrate appetite, aggressive and violent behaviors, and depression. Maybe this factor is involved in the difference between “happy” and “angry” drunks.

The natural production of NADH (in the absence of alcohol) depends on lipoic acid, thiamine and riboflavin. Since lipoic acid and thiamine contain sulfur which may become bound to acetaldehyde, I wonder whether the use of alcohol compromises the very energy pathways it stimulates.

That’s it for the lesson. Now it’s time to practice. Have fun! But, please, don’t forget the designated driver.