**Alcohol Metabolism**

Alcohol metabolism takes place in the liver and has 7 kcal per gram. The alcohol you drink is not stored in the body as alcohol; instead it remains in body water until it is fully eliminated. It can also be stored as fat or used as energy. The metabolism of alcohol is higher in fast state than fasted state. This is because the ADH levels in the body are increased when fed. The average elimination of alcohol is about 170 to 240 g per day for a person weighing 70 kg. This would be equal to about 7 g/hr or 1 drink per hour.2

Ahangover is defined as when the blood alcohol concentration reaches 0 after a period of alcohol consumption. There has been no cause found for a hangover yet, but several hypotheses include alcohol withdrawal symptoms or the effect of ADH on the body. A hangover encompasses the impact on full functioning related to a decline in cognitive abilities and full physical capacity.

**Pathways to Metabolism**

There are three pathways for alcohol metabolism: elimination: alcohol dehydrogenase (ADH), microsomal ethanol oxidizing system (MEOS), and fatty acid ethyl ester synthetase (FAEE). ADH is the enzyme that is responsible for most alcohol metabolism. ADH is expressed in the liver and is located within the cytosol of the cell. MEOS is catalyzed by cytochrome P4502E1 (CYP2E1). This system contributes to the high alcohol tolerance seen in alcoholics. MEOS produces reactive oxygen species (ROS) that cause alcohol induced liver injury.3 The FAST pathway is used to eliminate the alcohol if the oxidative alcohol metabolism is blocked.2

**Alcohol Metabolism: Gluconeogenesis**

In order to limit these reactions becoming inhibited, NADH needs to be produced in the liver that require NAD+. There are several important chemical reactions in the liver and produces acetate and AMP. This AMP is the end product of the metabolic process. ADH is responsible for most alcohol metabolism. ADH is increased when fed. The average elimination of alcohol is about 170 to 240 g per day for a person weighing 70 kg. This would be equal to about 7 g/hr or 1 drink per hour.2

**Cognitive Effects and Decline**

Hangovers produce a state of cognitive deficit. In a study comparing the intoxicated and hungover states on memory, reaction time, and attention tasks, it was shown that cognitive and psychomotor skills are affected similarly during alcohol consumption and also the morning after a night’s drinking. More so during an alcoholic hangover, reaction time significantly decreased in a study where participants were required to press the space bar on a computer when an “X” appeared on the screen. In a delayed recognition test, which tested memory, it was shown that a hangover state detrimentally affects this, with subjects not being able to store information for a longer period of time. Alcohol can disrupt the transfer of information from short term to long term memory, but more so in a hangover state. Performance on tasks of delayed recognition and reaction time was worse during a hangover than during an acute intoxication. Hangover effects are evidenced mostly in sustained attention tasks. Overall, tasks that require prolonged attention and high intellectual capabilities are affected during the state of an alcoholic hangover.1,2,11

Research has shown that during a hangover, neurocognitive function declines. Neurocognitive decline is a cognitive decline seen in a specific area of the brain. The Luria-Nebraska Neuropsychological Battery (LNNB) is a test that can display brain lesions along with where the brain damage is located within the cerebral cortex. A study using the LNNB demonstrated that in the hangover state, the left frontal, left sensorimotor, and left/ right parietal-occipital failure rates increased. These parts of the brain affect vision, memory and levels of thinking, where a significant decline in function was present in participants. Specific abilities that showed a significant decrease in hungover subjects were fine motor speed, visual acuity & naming, and general verbal intelligence including reading predictable words and numbers.1,12

**Cytokines: Inflammation**

Cytokines are proteins that are released into the bloodstream to aid in communication between cells that help promote cell accumulation in sites of trauma, infection, or inflammation in the body. A recent study showed that after consumption and metabolism of ethanol, cytokines IL-10, IL-12, and IFN-y concentrations were elevated in the body of mice. IL-10 (interleukin-10) is a T helper cell that plays a role in the inhibition of cytokine production “in macrophages and cellular immunity”. IL-12 (interleukin-12) is a proinflammatory cytokine that “induces proliferation of natural killer cells and T lymphocytes and activates cytokotysis”. IL-12 (interleukin-12) and IFN-γ (interferon gamma) stimulates “natural killer cells and macrophages”. The release of these cytokines suggests that inflammation is present in the hangover state. The consumption and after effects of alcohol may have an effect on the immune system as evidenced by the activity of the cytokine pathway. In conclusion, based on studies we suggest that the deregulated cytokine pathway (IL-10, IL-12, and IFN-γ) may be associated with the hangover state.1,12

**Oxidative Stress/Mitochondria: Free Radicals**

The cellular mitochondria are the main processing components of cells. They are the powerhouse of the cell and are heavily involved in the "generation and defense against reactive oxygen species (ROS)". ROS are highly reactive ions which circle the blood and steal electrons from atoms, causing dysfunction at the cellular level. Based on studies, it has been shown that consumption of ethanol has had a negative effect on mitochondrial function by damaging the mitochondrial DNA, making it difficult for mitochondria to defend against ROS species. If these defense mechanisms are not repaired appropriately, oxidative stress is constantly imposed on the cell, leading to further impairment and a build-up of cell damage. This becomes a relentless cycle once the cell is too far damaged to repair itself. In addition to damaging DNA, continuous oxidative stress may increase cell signaling sensitivity. This means that the cell may be more receptive to damage signals which may promote apoptosis, or programmed cell death.12

Research studies have concluded that acetaldehyde, an intermediate product in the metabolism of alcohol, may be linked to hangover symptoms. It is converted to alcohol and is known to produce symptoms such as "swearing, skin flushing, nausea, and vomiting".2,10,12,13,15 The liver typically breaks down alcohol to acetaldehyde via ADH. It then combines acetaldehyde and acetaldehyde dehydrogenase and rids the tain by creating acetate. Acetate is then released or stored by the body. The effects of acetaldehyde are well felt when only drinking a moderate amount. However, when drinking in large quantities, the body tends to run out of glutathione to help metabolize acetaldehyde and there is an excess of acetaldehyde in the body. Due to its toxicity, it may result in the common hangover symptoms of nausea and vomiting.2,10,12,13,15

**Antidiuretic Hormone: Dehydration and Electrolyte Imbalance**

The amount of urine output is noticeable when drinking alcohol. This is due to the inhibition of the hormone vasopressin, also known as antidiuretic hormone. Antidiuretic hormone is released to act upon the kidneys to signal them to conserve and reabsorb water when the body is in need of it. If this hormone is inhibited there is no signal telling our bodies to conserve water, therefore, increasing urine output. This becomes a problem when urination increases excessively, causing an increased release of water and electrolytes. This ultimately leads to dehydration. During the hangover state, antidiuretic hormone levels tend to increase as blood levels decline, causing your body to release water.2,10,12,13,15 Additionally, other factors that may play into dehydration and electrolyte imbalance include “swelling, vomiting, and diarrhea” during a hangover.2,10,12,13,15

Scientists who are trying to discover a “cure” for a hangover have conducted several studies to assess different compounds that have a potential for eliminating hangover symptoms. Some of these symptoms include nausea, dry mouth and anorexia. These research articles, including “Effect of Quinata Ficus Indica on Symptoms of the Alcohol Hangover”, “Effect of Exo-Fructus Extracts on Gene Expressions Related with Alcohol Metabolism and Antioxidation in Ethanol-Loaded Mice,” “Ginsenoside-Free Molecules from Stevia rebaudiana Gymnema Berry Promote Ethanol Metabolism: An Alternative Choice for an Alcohol Hangover” and “Effects of Asparagus Officinalis Extracts on Liver Cell Toxicity and Ethanol Metabolism” were examined to determine if there are supplements that can reduce hangover symptoms. Four potential substances have been found to reduce the symptoms of an alcohol hangover; one of which reduces inflammation and the other three stimulate alcohol metabolism.

Quinata Ficus Indica (OFI) is a prickly pear fruit that was determined to have a moderate effect on lowering inflammatory responses induced by alcohol congeners, which play a significant role in the severity of an alcohol hangover.2,17 This information was concluded from a double blind, placebo-controlled, crossover trial, which included 55 subjects. The statistical analyses revealed that of the subjects studied, the number of severe hangovers when OFI was given was cut in half.2,17 This proves that OFI can be used as a potential hangover cure. Now that OFI has been proven to reduce inflammation caused by alcohol related hangovers, we will examine three other herbal substances, which “cure” alcohol related hangovers in a different way.

These three substances are exocladus fructus (EF) extract, ginsenoside-free molecules (GFM) from ginseng berries and asparagus officinalis (AOF) extracts from the leaves of asparagus plants. ADH, cytochrome P450 and catalase are important enzymes, which stimulate the metabolism of ethanol.2,13 These enzymes convert alcohol to acetaldehyde, which is then metabolized by aldehyde dehydrogenase (ALDH) and then to acetate.2,13 The issue is that the amount of acetaldehyde is the main factor that drives an alcohol hangover. High amounts of acetaldehyde can cause vasodilation, flushing of the face, nausea and headaches.2,18 The three substances, EF, GFM, and AOF have all proven to increase the amount of ADH in the body, which speeds up the metabolism of alcohol hence reducing the effects of an alcohol hangover. Although ginsenoside-free molecules concluded to have only stimulated levels of ADH, exocladus fructus extracts and asparagus officinalis extracts proved to raise levels of ADH and AOF.2,17

**Is There Actually a Cure?**

The search for a hangover cure has been something that has been extremely sought out for years. People who have been exposed to alcohol for a long period of time. The idea of a hangover has been around for over three thousand years. Research shows a hangover was found in an old Indian textbook on Vedic medicine, calling it “paramada”.2,18 Where most acute alcohol intoxication studies have been found a cure or treatment for, an alcoholic hangover is not one of them.2,18

With so many people, college students especially, regularly experiencing the negative effects of hangovers, the search for a “cure” should relatively be more prevalent. But since alcohol is a drug and it has a lack of or no alcohol consumption at all, the need for a cure may be paradoxical.2,18

According to an article that reviewed multiple clinical trials interventions for hangovers, there is no cure for hangovers, but symptoms may be reduced by lowering acetaldehyde concentrations and buildup of alcohol concentrations.2,15 This is through some of the remedies we have discussed.

The Alcohol Hangover Research Group also validated the fact that there are no effective hangover cures available. Although an alcohol hangover is a familiar concept, more research must be done on the phenomenon, and the potential for a cure.2,18

**Science of a Hangover**

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