

Hangover drug shows wider benefits in research

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A well-known hangover drug not only helps soothe pounding headaches but also triggers profound changes that protect the liver, USC scientists report in new findings that could help prevent alcohol-related harm.

The study focuses on dihydromyricetin (DHM), also known as

ampelopsin, an over-the-counter herbal remedy. When researchers at the USC School of Pharmacy sought to understand how it works, their investigation revealed a sequence of metabolic changes responsible not only for easing headaches but also benefitting the liver.

"We know DHM helps the body to metabolize alcohol faster, but how does it work? We found it activates a cascade of mechanisms that erase alcohol from the body very quickly," said Jing Liang, a research professor of clinical pharmacy and the corresponding author of the study.

The study appears today in *Alcoholism: Clinical and Experimental Research*.

The findings support the utility of DHM as a dietary supplement to offset acute alcohol-related effects as well as long-term risks. In addition, the authors say the substance likely has wider applications to help people cope with binge drinking, alcoholism and liver damage.

Alcohol use disorders constitute the most common form of substance abuse. About 88,000 people die of alcohol-related deaths annually—the third leading preventable cause of death in the United States, according to the U.S. Centers for Disease Control and Prevention. Globally, [alcohol consumption](#) contributes to 3 million deaths each year and is responsible for 5.1% of the global burden of disease, according to the World Health Organization. There is no effective therapeutic agent for the disorder without major side effects.

Meanwhile, [excessive alcohol consumption](#) is a significant cause of chronic liver disease, accounting for nearly half of the cirrhosis-associated deaths in the United States, according to the study.

DHM is derived from fruit from the Japanese raisin tree (*Hovenia*

dulcis), which is native to Japan, Korea and Southeast Asia and now commercially grown. It's been used in China for liver ailments for 500 years, but how the substance works is unclear.

To better understand what the drug does inside the body, the scientists fed 36 mice a daily diet of alcohol for two months, gradually increasing doses to 30% of their total food intake for an average of 39.4 g/kg of ethanol per day per mouse. Then, they assessed their livers for injury and markers of stress.

The researchers focused on the liver, Liang said, because when you take a drink, alcohol circulates through the bloodstream. Though the alcohol affects the brain, it is metabolized primarily by the liver, which is significantly harmed by long-term, high levels of alcohol consumption.

"It's like stepping on a tack; your brain says it hurts. During a hangover, the fogginess in your brain is an acute reaction to what's going on in your body," said Daryl Davies, a study co-author and professor of clinical pharmacy in the USC School of Pharmacy.

Among other significant effects, the scientists found that DHM:

- Triggered the liver to produce more ethanol-gobbling enzymes, including alcohol dehydrogenase (ADH) and acetaldehyde dehydrogenase (ALDH).
- Boosted the efficiency of ADH and ALDH, enabling the enzymes to convert ethanol into simpler forms the body can eliminate easier.
- Reduced lipid (fat) accumulation in liver tissue. Heavy doses of alcohol can negatively affect the liver's metabolism, leading to an accumulation of fat, increased stress and the eventual progression to liver diseases such as cirrhosis.
- Reduced inflammatory agents, called cytokines. Excessive

alcohol leads to the release of cytokines in the liver, which contributes to cellular damage to the liver and other organs.

"In total, these findings support the utility of DHM as a dietary supplement to reduce ethanol-induced liver injury via changes in lipid metabolism, enhancement of ethanol metabolism and suppressing inflammation responses to promote liver health," the study said. "This line of research suggests that DHM acts on multiple pathways to promote liver health and counteract ethanol injury."

Davies, who is also director of the Alcohol and Brain Research Laboratory at USC, said the findings also help explain how DHM works as a hangover treatment. The liver converts alcohol into an aldehyde with properties like formaldehyde, which contribute to headache and nausea. Since it takes about one hour for the body to metabolize one drink, a night of heavy drinking causes the liver to keep churning out the chemicals that make people feel woozy for so long.

"We now know what [DHM] is doing and how it's doing it mechanically, activating a cascade of energy-regulating mechanisms that speed metabolism of ethanol and its byproducts," said Joshua Silva, a doctoral student at the USC School of Pharmacy and study co-author.

The findings have important implications for helping prevent liver damage and harm from alcohol abuse.

For example, binge drinkers could use DHM for its liver protection properties, extending the function of the organ long enough for the person to get help and stop their bad drinking habit. "We may not be able to fix their problem overnight, but we can give them step-by-step improvements to help them drink less and gain health protection," Davies said.

Binge drinking is a serious problem for young adults, especially college students. About 37% of students engage in binge drinking—five or more drinks on a single occasion for men or four or more drinks for women—and about 10% engage in heavy alcohol use—[binge drinking](#) on 5 or more days in the past month. Those rates are much higher than among non-college peers, according to a recent survey by the National Institutes of Health.

Excessive alcohol consumption significantly contributes to higher rates of [alcohol](#)-related liver disease at a younger age.

Excessive drinking has high social and economic costs, leading to heart disease, high blood pressure, unplanned pregnancies, violence and vehicle crashes. The CDC estimates the total economic cost at \$249 billion annually.

DHM could potentially help patients who go to the doctor with early warning signs of [liver damage](#). The substance could be used to help restore and prolong their liver function and delay the onset of liver disease while waiting for a transplant. DHM could also prove useful for [liver](#) transplant patients to help the new organ perform better so patients could enjoy a better quality of life.

"There's hope here. It could be a new lease on life for a lot of people," Davies said.

More information: *Alcoholism: Clinical and Experimental Research* (2020). [DOI: 10.1111/acer.14326](https://doi.org/10.1111/acer.14326)

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