

Can B Vitamins Help Prevent Nonalcoholic Fatty Liver Disease?

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STORY AT-A-GLANCE

- > Vitamin B12 and folic acid were found to significantly impact nonalcoholic steatohepatitis (NASH), for which there is no pharmaceutical treatment option
- NASH is the second stage of nonalcoholic fatty liver disease (NAFLD); a few potential causes of which include consuming high fructose corn syrup, low-level exposure to glyphosate or choline deficiency
- > Although NAFLD may have no symptoms it can progress to NASH, fibrosis and finally cirrhosis, with a higher risk of liver cancer. Supplementation with B12 and folic acid appeared to slow the progression of NASH and reverse fibrotic tissue changes in the liver
- > Iron overload is also associated with liver damage and high iron levels are found in individuals with alcoholic liver disease and NAFLD
- > Consider protecting your liver by eliminating high-fructose corn syrup from your diet, don't use Roundup, and make sure to purchase organic, non-GMO produce. Also, take care to get enough B vitamins and choline from your food

According to the American Liver Foundation,¹ approximately 100 million people in the U.S. have nonalcoholic fatty liver disease (NAFLD). Research² published by Duke-NUS Medical School³ revealed that two B vitamins may have a significant effect on an advanced form of the disease, for which there is no pharmaceutical treatment.⁴

Your liver weighs just over 3 pounds and is located on the right side of your abdomen, protected by your rib cage.⁵ It's the largest solid organ in your body and one of the largest glands, carrying out over 500 essential tasks to maintain optimal health.⁶

The liver has two main lobes and each of those has eight segments. Every segment is made up of approximately 1,000 lobules that are connected to small ducts. The liver filters your blood, regulates many chemical levels and excretes bile into your intestines to help break down fat. The liver also produces cholesterol, stores and releases glucose and regulates blood clotting.⁷ Each of these vital functions is impacted by the four stages of NAFLD.

NAFLD is a serious liver condition caused by excess fat in the liver, and not from being exposed to alcohol. The medical term is hepatic steatosis, and it is the most common chronic liver disease in developed countries.⁸ In one population-based study,⁹ 18.9% of the participants had confirmed NAFLD, which was more prevalent in men than women.

Risk factors in this study were being over age 40, male, and being diagnosed with central obesity and elevated fasting blood sugar, aspartate transaminase (AST) and alanine transaminase (ALT). Dietary fructose is a significant link in the development of NAFLD,^{10,11,12} chronic hepatic inflammation and an increased risk of developing the next stage of liver disease, nonalcoholic steatohepatitis (NASH).

The results of one study¹³ presented at the 2022 Endocrine Society annual meeting found a significant link between those whose diet contained the most fructose and the development of NAFLD. In a press release, one researcher on the study, Dr. Theodore Friedman from Charles R. Drew University, said:¹⁴

"We found that when adjusting for the demographics and behavioral factors (smoking, modest alcohol consumption, diet quality and physical activity), high fructose consumption was associated with a higher chance of NAFLD among the total population and Mexican Americans."

Vitamin B12 and Folic Acid May Reverse NASH

The researchers in the featured study¹⁵ were studying the effect that vitamins B12 and B9 might have on NASH. After years of inflammation from NAFLD and fatty deposits on the liver, it is possible to develop NASH.¹⁶

Dr. Madhulika Tripathi, a senior research fellow with the Laboratory of Hormonal Regulation at Duke-NUS' Cardiovascular & Metabolic Program, said in a press release, 17 "While fat deposition in the liver is reversible in its early stages, its progression to NASH causes liver dysfunction, cirrhosis and increases the risk for liver cancer."

The researchers were seeking to understand the relationship between hyperhomocysteinemia and NASH. Using an animal model, they administered vitamin B12 and folic acid, attempting to reverse the cellular features of NASH. While evaluating preclinical models, 19 they discovered that homocysteine attaches to a protein called syntaxin 17 and blocks the protein. This in turn appears to induce the development and progression of NASH.

However, when mice were supplemented with vitamin B12 and folic acid, the levels of syntaxin 17 rose, which slowed the progression of NASH and reversed fibrosis. One of the scientists in the study, Dr. Brijesh Singh, said:²⁰

"Our findings are both exciting and important because they suggest that a relatively inexpensive therapy, vitamin B12 and folic acid, could be used to prevent and/or delay the progression of NASH. Additionally, serum and hepatic homocysteine levels could serve as a biomarker for NASH severity."

The researchers were excited by the possibilities since the early stages of NAFLD often have no symptoms and don't usually cause any harm.²¹ Yet, without identification, the condition can progress to NASH or fibrosis. This can lead to extreme tiredness, unexplained weight loss and weakness.

There are four stages of NAFLD which begin with simple fatty liver steatosis.²² This can progress to NASH, then fibrosis and finally cirrhosis. In the latter stages, patients are also at higher risk for liver cancer.²³ During all stages of NAFLD, a person has a higher risk of developing cardiovascular diseases.

Vitamin B12 and Choline Deficiencies?

One reason there is such a high prevalence of individuals with NAFLD and NASH may be a deficiency or insufficiency in Vitamin B12, folic acid and/or choline. According to the National Institute of Diabetes and Digestive and Kidney Diseases,²⁴ NAFLD is more common in individuals who are obese or have obesity-related conditions, such as Type 2 diabetes.

The National Institutes of Health²⁵ reports that the rate of vitamin B12 deficiency is close to 20% in those who are older than 60. This data is from the National Health and Nutrition Examination Survey (NHANES) from 2015 to 2016. Data from another large, nationally representative sample²⁶ demonstrated that serum levels of B12 are inversely associated with obesity.

In other words, people who are obese have a higher risk of NAFLD. A vitamin B12 deficiency may allow NASH to progress and the rate of vitamin B12 deficiency is close to 20% in those older than 60 and higher in those who are obese.

Vitamin B12 is also called cobalamin.²⁷ It's found in animal food and is a key component in the function and development of the central nervous system. A second essential nutrient for human health that is also associated with central nervous system health and the risk of NAFLD is choline. Choline was identified in 1862²⁸ and officially recognized as an essential nutrient by the Institute of Medicine in 1998.²⁹

Choline plays a significant role in human health, from neurotransmitter synthesis to cell structures and has a large impact on the development of NAFLD, atherosclerosis³⁰ and neurological disorders.³¹ The body can produce some choline endogenously in the liver but not enough to meet human needs. There is an interrelationship between folic acid and choline deficiencies as both are methyl donors.³²

When the diet is deficient in folic acid, choline becomes the primary methyl donor, creating greater insufficiency or deficiency of the nutrient. Nearly 12 years ago,³³ Chris Masterjohn, who has a Ph.D. in nutritional science, wrote that choline insufficiency or

deficiency may play a more significant role in the development of fatty liver disease than fructose.

According to Masterjohn,³⁴ your body uses choline to rid itself of excess fat. Without enough choline, it can trigger fatty liver. Yet, the most significant culprit remains excessive fructose, as it must be metabolized by the liver and is primarily converted into body fat as opposed to being used for energy like glucose. Without enough choline, the fat is deposited in the liver.

The Importance of Iron Levels for Liver Health

Another factor that is associated with liver damage is iron overload. Iron may be one of the most common nutritional supplements that can be found as a single supplement or added to multivitamins and processed foods. However, damage from too much iron may be greater than that from iron deficiency anemia.³⁵

Although it is necessary for biological functions, too much can do tremendous damage. Nearly all adult men and postmenopausal women are at risk for iron overload since there are no efficient means for the body to excrete excess iron. In other words, these populations do not lose blood on a regular basis.

Blood loss is a primary way to lower excess amounts of iron which, if left untreated, can contribute to neurodegenerative diseases, diabetes, heart disease and cancer.

Additionally, high iron levels are found in individuals with alcoholic liver disease and NAFLD.³⁶

Low-Levels of Roundup Exposure Damage the Liver

Glyphosate, which is the active ingredient in the herbicide Roundup, is also linked to NAFLD and NASH. Researchers³⁷ from the University of California San Diego School of Medicine³⁸ found patients with NASH had higher residues of glyphosate in their urine, an association that held true regardless of other factors in liver health, such as body mass index, diabetes, age or race.

Exposure to glyphosate may lead to more severe forms of liver disease, and subsequently an increased risk of liver cirrhosis, liver cancer and higher mortality rates than the general population from liver-related and non-liver-related causes.³⁹

In a UC San Diego news release, study researcher Paul J. Mills, Ph.D., explained, "There have been a handful of studies, all of which we cited in our paper, where animals either were or weren't fed Roundup or glyphosate directly, and they all point to the same thing: the development of liver pathology. So, I naturally thought: 'Well, could it be exposure to this same herbicide that is driving liver disease in the U.S.?'"⁴⁰

Glyphosate is also known to trigger the production of reactive oxygen species, leading to oxidative stress. As noted in Scientific Reports, "Elevation in oxidative stress markers is detected in rat liver and kidney after subchronic exposure to GBH [glyphosate-based herbicides] at the United States' permitted glyphosate concentration of 700 μ g/L in drinking water."⁴¹

Researchers from King's College London also showed an "ultra-low dose" of glyphosate-based herbicides was damaging.⁴² The study involved glyphosate exposures of 4 nanograms per kilogram of body weight per day, which is 75,000 and 437,500 times below EU and U.S. permitted levels, respectively.⁴³

After a two-year period, female rats showed signs of liver damage, specifically NAFLD and progression to NASH. The researchers noted⁴⁴ that glyphosate may bring about toxic effects via different mechanisms, depending on the level of exposure, including possibly mimicking estrogen and interfering with mitochondrial function.

Consider These Tips for Liver Support

There are several steps you can take to protect your liver. Among those are eliminating high-fructose corn syrup from your diet, not using Roundup or other glyphosate-based herbicides in your garden, purchasing organic, non-GMO produce and foods, lowering your risk of iron overload and taking care to ensure you get enough B vitamins and choline.

However, we would need to live in a perfect world to ensure our liver is not inundated with a ubiquitous chemical assault commonly found in our industrialized world. As the featured research pointed out, even those with NASH, an advanced form of NAFLD, can benefit from supplementing with vitamins B12 and folic acid.

While the focus of the featured study was NAFLD, overconsumption of alcohol also drives liver damage, cirrhosis and death. Data⁴⁵ gathered between 1999 and 2016 revealed a 65% increase in annual deaths from cirrhosis, with 25- to 34-year-olds experiencing the greatest relative increase in mortality driven entirely by alcohol-related disease.

Milk thistle is an herb that has been used for thousands of years to support liver, kidney and gallbladder health. In modern times, silymarin, the active ingredient in milk thistle, has been used to treat alcoholic liver disease and hepatitis.⁴⁶ Silymarin may help suppress cellular inflammation⁴⁷ and inhibit the mammalian target of rapamycin (mTOR), a pathway that, when overactivated, increases your risk of cancer.⁴⁸

Coenzyme Q10 (CoQ10) is the third-most consumed supplement,⁴⁹ yet many people don't realize how clinically effective it is, including the role it plays to protect your liver. In one study,⁵⁰ 44 patients were divided into two groups. One group was given 100 mg of CoQ10 each day, while the other was given a placebo.

After four weeks, the group taking CoQ10 dropped weight and had lower levels of serum AST, a blood marker that indicates liver disease and/or damage. The reduced version of CoQ10 is ubiquinol. As you age, the body's ability to absorb and utilize CoQ10 drops, but it can still use ubiquinol.⁵¹ Ubiquinol is absorbed three to four times better than CoQ10.⁵²

N-acetylcysteine (NAC) is a precursor needed to produce glutathione, also called the "master antioxidant." NAC helps support liver health in those with hepatitis C and other chronic liver diseases. 54

An animal study showed NAC could effectively minimize damage associated with alcohol consumption⁵⁵ and is used as an antidote for acetaminophen toxicity, which causes liver damage by depleting glutathione.^{56,57} Research published in Hepatitis

Monthly⁵⁸ has also shown NAC supplementation helps improve liver function in patients with NASH.

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