

Is This a Natural Option for Harmful 'Skinny' Injections?

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✓ Fact Checked

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STORY AT-A-GLANCE

- › Some are calling berberine "nature's Ozempic," a once-weekly injectable diabetes medication that has grown in popularity as a weight loss product. Semaglutide is marketed as Ozempic for diabetes and in higher doses as Wegovy for weight loss
- › Data show adverse side effects include anxiety, confusion, depression, nightmares, seizures and slurred speech. The tablet form has a boxed warning as it's known to increase the risk of thyroid growths and data show that after withdrawal of the drug, most people regain at least two-thirds of their weight loss
- › Berberine works by helping to regulate blood sugar and to improve insulin sensitivity and gut microbiome diversity that may contribute to weight loss. Data show berberine has a positive effect on lipid profile, fasting blood glucose, obesity parameters and systolic blood pressure
- › Berberine helps prevent diarrhea, lowers the risk of leaky gut, nourishes beneficial microbes and improves symptoms of fatty liver disease. Other beneficial effects include easing symptoms of anxiety and depression, improving symptoms of PTSD in an animal model and easing symptoms of opioid withdrawal

Berberine is a naturally occurring compound found in certain plants, which some are calling "nature's Ozempic."¹ It is a once-weekly injectable diabetes medication that has grown in popularity as a weight loss product. However, as popularity has grown, so have shortages.² In response, some are posting information about alternatives, such as other diabetic drugs, generic Ozempic (semaglutide) made at compounding pharmacies or berberine.

Prescriptions for semaglutide have doubled since mid-2021, rising to more than 1.2 million. In April 2023, a spokesperson for Novo Nordisk, maker of semaglutide, said the drugs are now available in pharmacies nationwide. Semaglutide is sold under the name Ozempic as a diabetes drug and under the name Wegovy as a weight loss prescription drug.

Berberine has received a lot of media attention as it gains momentum on social media as a weight loss supplement. Berberine is a compound that's extracted from goldenseal, barberry, Oregon grape and tree turmeric. It has traditionally been used in Ayurvedic medicine and traditional Chinese medicine³ for nearly 2,000 years.⁴

Recent research has analyzed the effect berberine may have on hypertension and insulin resistance. The yellow-colored alkaloid has antibacterial, anti-inflammatory, antiproliferative, antidiarrheal, antineoplastic, antidiabetic and immune-enhancing properties.⁵

However, the property that appears to have piqued people's interest is the weight loss potential. While the news media does offer some information about berberine in relation to Ozempic and Wegovy, the vast majority of the information cautions readers.⁶

The list of potential issues includes that supplements are not reviewed or approved by the FDA, may not be safe for consumption and that people who experience weight loss with berberine should stop immediately and consult with their physician as it suggests the supplement may have been adulterated.

Berberine Helps Regulate Blood Sugar and Aids Gut Microbiome

Research data shows that berberine helps to regulate blood sugar and may help with weight loss. A 2022 systematic review of the literature⁷ evaluated randomized controlled trials of adults who were given berberine supplementation. The pooled results demonstrated that berberine did reduce insulin levels and the optimal dose given in these studies was 1 gram per day.

The researchers concluded that supplementing with berberine had a positive effect on lipid profile, fasting blood glucose, obesity parameters and systolic blood pressure. One objection to berberine as a potential assistant to weight loss is that it may help insulin resistance, but evidence that it helps with weight loss is "patchy and preliminary."⁸

Yet, insulin resistance and weight loss are strongly associated, and the evidence suggests it may be bidirectional. Research⁹ has shown that insulin sensitivity improves after an individual loses weight and integrates an exercise program into their daily activities. However, the study also showed that exercise training was not enough to prevent insulin resistance and weight loss was required to improve sensitivity.

Other studies¹⁰ have also demonstrated a strong association between insulin resistance and weight gain. A 2020 study¹¹ also showed that how sensitive a person's brain is to insulin may determine weight loss, weight gain and where in the body the weight is lost or gained.

When a person's brain is sensitive to insulin, they can lose a significant amount of weight, including visceral fat, and the weight loss can be maintained.¹² The same study showed that when a person's brain is insulin resistant, they often regain weight quickly and in the long term, their visceral fat also increases.

In other words, if you are insulin resistant, you can improve insulin sensitivity through weight loss, but weight loss is more difficult when you are insulin resistant.

The data from the systematic review in 2022¹³ showed that berberine could help improve insulin sensitivity and may therefore influence weight loss. According to Dr. Yufang Lin,¹⁴ integrative medicine specialist at Cleveland Clinic, the antimicrobial properties in berberine may help improve your gut microbiome and your gut microbiome plays a strong role in your ability to lose weight and maintain that weight loss.^{15,16}

In a 2022 paper¹⁷ in *Frontiers in Cellular and Infection Microbiology*, the researchers wrote that "Studies have shown that BBR [berberine] can alleviate the pathological conditions of metabolic disorders, and the mechanism is related to the regulation of gut

microbiota ... meanwhile, the structure and function of gut microbiota also changed after intervention by berberine."

Berberine supports a healthy gastrointestinal tract in several different ways, which can also have a beneficial impact on your mood and mental health. Studies have shown that berberine helps:

- Prevent diarrhea by delaying the amount of time it takes for food to pass through your small intestine¹⁸
- Lower your risk of leaky gut¹⁹
- Preferentially nourish microbes that produce beneficial short-chain fatty acids, known to have many health benefits²⁰
- Improve symptoms of fatty liver disease by normalizing the gut microbiome²¹

Semaglutide: Long-Term Results and Adverse Effects

Ozempic and Wegovy are both semaglutide, but Wegovy, which is approved for weight management, is a higher dose. The drug is a GLP-1 agonist that is available as a prefilled pen injector used once weekly. It stimulates the pancreas to release insulin, slows the gastrointestinal tract so you feel full longer and may directly affect appetite control in your brain.²²

It can take a few months to reach your personalized target dose to manage the side effects of the drug.²³ During this time there can be some weight loss but for most people weight loss begins after several weeks. During clinical trials, people who took a 0.5 mg dose lost 3.73 kilograms (8.2 pounds) over 30 weeks. If a higher a dose is required it must be increased slowly in four-week intervals.

In another study²⁴ published in the New England Journal of Medicine, researchers administered 2.4 mg of semaglutide in a double-blind trial involving 1,961 adults with a body mass index of 30 or greater. The change in body weight from baseline at 68 weeks

was a loss of 14.9% in the treatment group and 2.4% body weight loss in the placebo group.

In another study²⁵ published in Nature Medicine, a cohort of adults with obesity or overweight and one related comorbidity, were administered 2.4 mg of semaglutide subcutaneously for 104 weeks. In that time, the intervention group lost 15.2% of their body weight versus 2.6% body weight loss in those taking a placebo.

It's also important to note that the pharmaceutical company designed semaglutide as a chronic-use drug, in other words, regularly over a long period. A study²⁶ funded by Novo Nordisk and published in Diabetes, Obesity and Metabolism also found that one year after withdrawing the drug, participants regained two-thirds of the weight lost and the researchers concluded that "ongoing treatment is required to maintain improvements in weight and health."

Most studies also recorded significant side effects with short-term treatment²⁷ that caused participants to withdraw from the studies.²⁸ Serious and common side effects of semaglutide^{29,30} include anxiety, confusion, depression, difficulty swallowing, nightmares, seizures and slurred speech.

Both medications have a boxed warning when used in tablet form as the drug is known to increase the risk of thyroid C-cell tumors in rodent testing. Because of this, the drug is contraindicated in patients with a personal or family history of Multiple Endocrine Neoplasia syndrome type 2 or medullary thyroid carcinoma.

In a two-year trial, patients who had Type 2 diabetes had an increased risk of diabetic retinopathy complications and some individuals developed antibodies to the drug.³¹ While there are precautions while using berberine discussed below, they don't include cancer or neurological disorders.

In addition to the physical side effects, the drug can have a significant impact on your pocketbook or insurance policy. According to GoodRx, a month's prescription costs from \$1,300 to \$1,500, depending on where you purchase it.³²

Berberine Affects Insulin Resistance in the Liver

Recent evidence has suggested that trimethylamine-N-oxide (TMAO) is a therapeutic target for insulin resistance and gastrointestinal cancers. A 2017 scientific review³³ noted that gut bacteria form metabolites that contribute to developing cancer and insulin resistance and TMAO is one molecule that may be a biomarker or an independent risk factor for insulin resistance.

In a 2019 paper³⁴ led by James DiNicolantonio, Pharm.D., the team showed that elevated levels of TMAO are linked to increased risk for Type 2 diabetes and metabolic syndrome and that TMAO serves as a marker for hepatic insulin resistance.

TMAO is created when gastrointestinal bacteria metabolize choline and carnitine. According to DiNicolantonio, a key factor in significantly elevating TMAO appears to be insulin resistance in the liver. He writes:³⁵

"TMAO arises when dietary choline and carnitine is metabolized by gastrointestinal bacteria to yield trimethylamine, which is then absorbed and oxidized to TMAO by hepatic flavin monooxygenases (FMO), primarily FMO3 ... subnormal hepatic insulin activity, as found in those with hepatic [liver] insulin resistance, boosts hepatic FMO3 expression and hence TMAO levels."

If elevated TMAO reflects hepatic insulin resistance, which in turn raises your risk of cardiovascular disease and Type 2 diabetes, what can you do to correct it and lower your risk?

Berberine is a supplement that is beneficial in the treatment of hepatic insulin resistance and research shows that it functions like metformin,³⁶ a commonly used medication in the treatment of diabetes. At least in part, both activate adenosine monophosphate-activated protein kinase (AMPK), which is known as the "metabolic master switch."³⁷

AMPK is an enzyme that controls how energy is produced in your body³⁸ and how it's used by the cells. By activating the enzyme, berberine and metformin help regulate the

biological activities that normalize lipid, glucose and energy imbalances. Traditional Chinese medicine practitioners have used berberine to treat diabetes³⁹ and it has also been shown to have a therapeutic effect on Type 2 diabetes, hyperlipidemia and hypertension.⁴⁰

Anxiety, Depression and Drug Withdrawal

Berberine has other beneficial health effects, including easing symptoms of anxiety and depression. This function may again be related to low levels of AMPK, which is linked to mitochondrial dysfunction, neurodegeneration and chronic inflammation. These lay the groundwork for a wide variety of serious chronic diseases.

In a 2008 study,⁴¹ researchers confirmed that berberine has antidepressant effects in a rodent model and concluded, "Taken together, these findings demonstrate that berberine exerted antidepressant-like effect in various behavioral paradigms of despair possibly by modulating brain biogenic amines (norepinephrine, serotonin and dopamine)."

Another study⁴² found berberine helpful in treating post-traumatic stress disorder (PTSD). In this animal model, the rats exposed to prolonged stress exhibited significantly reduced anxiety-driven behaviors after receiving berberine and were better able to complete an elevated plus maze test. The researchers concluded:

"These results suggest that BER had anxiolytic-like effects on behavioral and biochemical measures associated with anxiety. These findings support a role for reduced anxiety altered DAergic transmission and reduced anxiety in rats with PTSD. Thus, BER may be a useful agent to treat or alleviate psychiatric disorders like those observed in patients with PTSD."

Berberine has also been shown to activate Sigma1 receptors, a subclass of opioid receptors that react to morphine and similar substances – including those produced naturally in your body – and inhibit glutamate, thereby improving anxiety and depression.⁴³ Sigma1 receptors play a role in oxidative stress, the functioning of your

nervous system and the survival of neurons, and as such are believed to influence neuropsychiatric problems.⁴⁴

A 2012 study⁴⁵ assessed berberine's effect on not just depression and anxiety but also on the noradrenergic system. Here, they used morphine-addicted rats to see whether berberine might ease morphine withdrawal – symptoms of which often include depression and anxiety.

The results of the study demonstrated that berberine could significantly reduce withdrawal-associated behaviors from morphine after the drug was discontinued. They hypothesized that this potentially was by modulating the hypothalamic corticotrophin-releasing factor and the central noradrenergic system. They proposed that berberine could be useful for treating or alleviating withdrawal symptoms and preventing morphine use relapse.

According to many studies, berberine is well-tolerated.⁴⁶ However, it can interfere with some medications, including oral chemotherapy, high blood pressure medications, blood thinners, cholesterol medications, immunosuppressive drugs, and pharmaceutical diabetes treatments. Women who are pregnant or breastfeeding should avoid berberine. Other side effects can include constipation, diarrhea, low blood sugar, nausea and vomiting.

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