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Madhunasini (*Gymnema sylvestre*): A miracle plant for diabetes

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Abstract
Diabetes mellitus (DM) results from the inability of the pancreas to produce sufficient insulin or weakened cellular response to the insulin produced, which leads to hyperglycemia. Current treatments of DM focus on the use of oral hypoglycemic drugs such as acarbose, alphaglucose inhibitors, sulphonylureas, thiazolidinediones, and biguanides to control blood glucose levels. However, these medications are known to have various side effects in addition to their bioavailability, efficacy, and safety concerns. These drawbacks have increased interest in the anti-diabetic potential of plant-derived bioactive compounds. Madhunasini (*Gymnema sylvestre,* Asclepiadaceae) is regarded as one of the plants with potent anti diabetic properties. This plant is also used for controlling obesity in the form of Gymnema leaf powder. The active compound of the plant is a group of acids termed as gymnemic acids. It has been observed that there could be a possible link between obesity, Gymnemic acids and diabetes. Gymnema is most often consumed in Western medicine in the form of pills or tablets, making dosage easier to control and monitor. It can also come in the form of leaf powder or extract.

Keywords: Diabetes, madhunasini, *Gymnema*, gymnemic acids, anti-diabetic, tannin

Introduction
Diabetes mellitus (DM) is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycaemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels. The number of people with diabetes rose from 108 million in 1980 to 537 million in 2021. Prevalence has been rising more rapidly in low- and middle-income countries than in high-income countries. Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. Between 2000 and 2016, there was a 5% increase in premature mortality from diabetes. In 2021, diabetes was the ninth leading cause of death with an estimated 6.7 million deaths directly caused by diabetes and 1in every 5seconds (IDF 2021) [9].

Current treatments of DM focus on the use of oral hypoglycemic drugs such as acarbose, alphaglucose inhibitors, sulphonylureas, thiazolidinediones, and biguanides to control blood glucose levels. However, these medications are known to have various side effects in addition to their bioavailability, efficacy, and safety concerns. These drawbacks have increased interest in the anti-diabetic potential of plant-derived bioactive compounds.

Madhunasini (*Gymnema sylvestre,* Asclepiadaceae) is a woody climbing shrub that's native to the tropical forests of India, Africa and Australia. Its leaves have been used in the ancient Indian medicinal practice Ayurveda for thousands of years. It has been a traditional remedy for various ailments, including diabetes, malaria and snakebites (Kanetkar *et al.,* 2007) [11]. This herb is thought to inhibit sugar absorption and thus has become a popular study subject in Western medicine. There are several impressive health benefits of Madhunasini.

1. Reduce sugar cravings by making sweet foods taste less appealing
Madhunasini can help reduce sugar cravings. One of the primary active components in this plant is gymnemic acid, which helps suppress sweetness (Brala and Hagen 1983, Kanetkar *et al.,* 2007) [4, 11]. When consumed prior to a sugary food or beverage, gymnemic acid blocks the sugar receptors on your taste buds (Kanetkar *et al.,* 2007) [11]. Research shows that Madhunasini extracts can reduce the ability to taste sweetness and thus make sweet foods less appealing (Brala and Hagen 1983, Kanetkar *et al.,* 2007) [4, 11]. In a study in fasted individuals, half were given *Gymnema* extract.

Those who received the supplement had less appetite for sweet foods at a subsequent meal and were more likely to limit their food intake, compared to those not taking the extract (Brala and Hagen 1983) [4].

2. Helps lower blood sugar levels

According to the IDF, more than 537 million people worldwide have diabetes, and this number is expected to increase to 643 million by 2030 and 783 million by 2045 (IDF 2021) [9]. Diabetes is a metabolic disease characterized by high blood sugar levels. It's caused by the inability of human body to produce or use insulin effectively.

Madhunasini is considered to have anti-diabetic properties. As a supplement, it has been used in combination with other diabetes medications to lower blood sugar. It's also called gurmar, which is Hindi for "destroyer of sugar" (Tiwari *et al.*, 2017) [24]. Similar to its effects on human tongue taste buds, Madhunasini can also block receptors in human intestines and thus sugar absorption, lowering our post-meal blood sugar levels.

Scientific proof of *Gymnema*'s ability to lower blood sugar is insufficient to recommend it as a standalone diabetes medication. However, research shows strong potential. Studies suggest that consuming 200–400 mg of gymnemic acid reduces the intestinal absorption of the sugar glucose (Tiwari *et al.*, 2017) [24].

In one study, *Gymnema* appeared to improve blood sugar control in people with type 2 diabetes by lowering blood sugar levels (Anonymus, 2001). The study concluded that reducing blood sugar after a meal resulted in a decrease in average blood sugar levels over time. This could help decrease long-term complications of diabetes. For people with high blood sugar or a high HbA1c, Madhunasini can help reduce fasting, post-meal and long-term blood sugar levels. Hence Madhunasini has anti-diabetic properties and may lower your blood sugar levels after a meal.

3. May contribute to favorable insulin level by increasing insulin production

Gymnema's role in insulin secretion and cell regeneration may also contribute to its blood sugar lowering capabilities. Higher insulin levels mean that sugar is cleared from blood at a faster rate. If humans have prediabetes or Type 2 diabetes, body tends to not make enough insulin, or your cells become less sensitive to it over time. This results in consistently high blood sugar levels. Madhunasini may stimulate insulin production in human pancreas, promoting the regeneration of insulin producing islet cells. This can help lower human blood sugar levels (Al-Romaiyan, 2012, Pothuraju *et al.*, 2014) [2, 18]. Many traditional drugs help increase insulin secretion and sensitivity. However, herbal therapies are gaining momentum in drug development. Interestingly, metformin, the first anti-diabetic drug, was an herbal formulation isolated from *Galega officinalis* (Pragya Tiwari, 2014) [19].

4. Improves cholesterol and triglyceride levels, reducing heart disease risk

Madhunasini may help lower "bad" LDL cholesterol levels and triglycerides. While *Gymnema* gets its fame from lowering blood sugar levels and reducing sugar cravings, research shows that it may also influence fat absorption and lipid levels. In one study in rats on a high-fat diet, *Gymnema* extract aided weight maintenance and suppressed the accumulation of liver fats. Also, animals fed the extract and a normal fat diet experienced lower triglyceride levels (Shigematsu *et al.*, 2001) [23]. Another study found that *Gymnema* extract had an anti obesity effect on animals fed a high-fat diet. It also decreased blood fat and "bad" LDL cholesterol levels (Kumar *et al.*, 2013) [13].

In addition, a study in moderately obese people showed that *Gymnema* extract decreased triglycerides and bad "LDL" cholesterol by 20.2% and 19%, respectively and interestingly it increased "good" HDL cholesterol levels by 22% (Preuss, 2004) [20]. High levels of "bad" LDL cholesterol and triglycerides are risk factors for heart disease. Therefore, the positive effects of Madhunasini on LDL and triglycerides levels may contribute to a lower risk of heart conditions (Pothuraju *et al.*, 2014, Pragya Tiwari, 2014) [18, 19]. Research supports that *Gymnema* can play a role in lowering "bad" LDL cholesterol and triglyceride levels, which can decrease human risk of heart disease.

5. Aid in weight loss

Madhunasini extracts have been shown to aid in weight loss in animals and humans. One three week study showed reduced body weight in rats given a water extract of Madhunasini. In another study, rats on a high fat diet that were fed a *Gymnema* extract gained less weight (Luo 2007, Kumar *et al.*, 2013) [5, 13]. Moreover, a study in 60 moderately-obese people taking a *Gymnema* extract found a 5–6% decrease in body weight, as well as reduced food intake (Preuss 2004) [20]. By blocking sweet receptors on human taste buds, Madhunasini may cause human to eat fewer sweet foods and consume fewer calories. A consistent calorie deficit can result in weight loss. Madhunasini may play a role in weight loss and prevent weight gain. It may promote reduced calorie intake.

6. Helps reduce inflammation due to its tannin and saponin content

Inflammation plays an important role in your body's healing process. Some inflammation is good, such as when it helps protect your body from harmful organisms in cases of injury or infection. Other sides, inflammation may be caused by the environment or the food. However, chronic low grade inflammation can contribute to various health issues (Schultz *et al.*, 2015, Hu *et al.*, 2014, Jiang *et al.*, 2016, Ma *et al.*, 2011) [21, 8, 10, 16]. Studies have confirmed the link between excessive sugar intake and increased inflammatory markers in animals and humans (Frazier *et al.*, 2011, Aeberli *et al.*, 2011, Bruun *et al.*, 2015) [7, 1, 5].

The ability of Madhunasini to reduce sugar absorption in your intestines may also allow it to decrease inflammation caused by excess sugar intake. Moreover, *Gymnema* appears to have anti-inflammatory properties of its own. This is thought to be due to its content of tannins and saponins, which are beneficial plant compounds. Madhunasini leaves are considered immunostimulatory, meaning they can regulate the immune system, reducing inflammation (Pragya Tiwari, 2014) [19]. People with diabetes not only suffer from high blood sugar and insulin resistance but may also have decreased antioxidant levels, which can contribute to inflammation (Pothuraju *et al.*, 2014) [18]. Due to its anti-inflammatory properties, Madhunasini can help those with diabetes and high blood sugar in a variety of ways, including by fighting inflammation. The tannins and saponins

in *Gymnema* have anti-inflammatory properties that help fight inflammation.

Phytochemistry of *G. sylvestre*

G. sylvestre leaves contain triterpene saponins belonging to oleanane and dammarene classes. Oleanane saponins are gymnemic acids and gymnemasaponins, while dammarene saponins are gymnemasides. Besides this, other plant constituents are flavones, anthraquinones, hentri-acontane, pentatriacontane, α and β-chlorophylls, phytin, resins, dquercitol, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin related glycosides and stigmasterol. The plant extract also tests positive for alkaloids. Leaves of this species yield acidic glycosides and anthroquinones and their derivatives (Dateo and Long 1973) [6]. Gymnemic acids have antidiabetic, antisweetener and anti-inflammatory activities. The antidiabetic array of molecules has been identified as a group of closely related gymnemic acids after it was successfully isolated and purified from the leaves of *G. sylvestre* (Liu *et al.*, 1992) [14].

Dosage

Madhunasini is traditionally consumed as a tea or by chewing its leaves. In Western medicine, it's typically taken in pill or tablet form, making it easier to control and monitor dosage. It can also be ingested in extract or leaf powder form. The recommended dosage for Madhunasini depends on the form in which humans consume it (Shanmugasundaram *et al.*, 1990, Baskaran *et al.*, 1990):

- **Tea:** Boil leaves for 5 minutes and then let steep for 10–15 minutes before drinking.
- **Powder:** Start with 2 grams, increasing to 4 grams if no side effects occur.
- **Capsule:** 100 mg, 3–4 times daily.

Bhaskran *et al.*, 1990 suggested that the beta cells may be regenerated/repaired in Type 2 diabetic patients on GS4 (400mg) supplementation. This is supported by the appearance of raised insulin levels in the serum of patients after GS4 supplementation. If humans want to use Madhunasini as a way to block the sugar receptors on tongue, take a supplement with water 5–10 minutes before a high-sugar meal or snack.

Conclusion

Madhunasini is considered safe for most people, but it should not be taken by children or women who are pregnant, breastfeeding or planning to get pregnant. Moreover, though it appears to improve blood sugar and insulin levels, it's not a substitute for diabetes medication. Gymnema is a supplement that has been used as a complementary treatment for both Type 1 and Type 2 diabetes as well as it also prevents the all other complication of diabetes. Hence Madhunasini is a miracle plant for diabetes.

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