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# *GYMNEMA SYLVESTRE:* A REVIEW OF ITS PHYTOCHEMISTRY, PHARMACOLOGICAL ACTIVITY

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**ABSTRACT**

*Gymnema sylvestre*, a plant belonging to the Apocynaceae family, is native to various regions of Asia, Africa, and Australia. It has long been used in traditional medicine and is currently popular as a dietary supplement owing to its numerous health benefits. G. sylvestre is commonly used in both traditional and Ayurvedic medicine, primarily because of its ability to lower blood glucose levels. This glucose-lowering effect is attributed to its phytochemical content, which includes compounds such as gurmarin, gymnemic acid, and gymnemasaponins. In addition to its role in managing diabetes, the plant is also used to treat a variety of conditions, such as arthritis, diuretic issues, anemia, osteoporosis, high cholesterol, heart disease, asthma, constipation, infections, indigestion, and inflammation. Additionally, *Gymnema sylvestre* is recognized for its antioxidant, antibiotic, antiviral, gastrointestinal, and liver-protective properties, as well as its anticancer and lipid-lowering effects. This review provides a comprehensive overview of the pharmacological and clinical benefits of *Gymnema sylvestre*, along with the chemical components linked to these therapeutic properties.

**KEYWORDS:** *Gymnema sylvestre*, phytomedicine, herbal medicine, traditional medicine, immunomodulation.

## INTRODUCTION

Naturopathic treatments for various diseases have been extensively explored since ancient times and have continued to gain popularity. India is home to approximately 45,000 plant species, many of which are pharmacologically significant. Plants play a crucial role in drug discovery and are a major source of modern medicine. Approximately 25% of contemporary medications are derived from plants; however, yet only 5-15% of plant species have been studied for their medicinal properties.[1] Currently, there is significant global research on natural plants, herbal medicines, phytomedicines, and functional foods, leading to promising therapeutic benefits such as antidiabetic[2], anticancer[3], immunomodulatory, antiobesity, lipid-lowering, anti-inflammatory, and antibacterial activities.[2]

*Gymnema sylvestre*, a plant from the Apocynaceae family, has been traditionally used to treat a variety of ailments. It is a wild herb found in India, Africa, Australia, and China.[4] It is also referred to as 'Gurmur' because of its sugar-lowering properties. *Gymnema sylvestre* has long been recognized as a key botanical in the Ayurvedic system for treating diabetes and is included in the Indian Pharmacopoeia as an anti-diabetic plant. It has a long history of use, especially in Ayurveda, where it is used to treat various conditions such as diabetes, malaria, and snakebites.[5] Various formulations of this plant are available in products such as tea bags, health tablets, and food supplements because of its effectiveness against major diseases, such as cardiovascular conditions, asthma, cancer, diabetes, and obesity.[6]

This review provides an update on *Gymnema sylvestre*, a rare herb with notable medicinal properties. It covers the herb's ethnobotanical uses, an in-depth analysis of its phytochemistry, and the bioactivity of its compounds. This review also discusses the potential of *Gymnema sylvestre* in modern therapeutic development, aligning with current trends in pharmacology and drug development.[6]

## PLANT PROFILE

**Synonym**: This plant is also known as 'Gurmur' because of its ability to lower sugar levels.[6]

## VARNACULAR NAME[7]

This plant is known by several names, including
Sanskrit: Meshashringi
Kannada: Sannagerasehambu,
Hindi: Merasingi,
Marathi: Kavali, Kalikardori, Vakundi,
Gujrathi: Dhuleti, Mardashingi,
Telugu: Podapatri,
Tamil: Adigam, Cherukurinja,
Chigengteng Australian Cowplant (in German), Waldschlinge Periploca of the Woods (in English).



**Fig. 1: *Gymnema Sylvestre* plant.**

## TAXONOMY OF *GYMNEMA SYLVESTRE*[8]

| | |
|---|---|
| Kingdom | Plantae |
| Subkingdom | Tracheobionta |
| Superdivision | Spermatophyta |
| Division | Magnoliophyta |
| Class | Magnoliopsida |
| Super class | Asteridae |
| Order | Gentianales |
| Family | Asclepidaceae |
| Genus | *Gymnema* |
| Species | *sylvestre* |

## BOTANICAL DESCRIPTION

*Gymnema sylvestre* is a slow-growing perennial woody climber found throughout India, especially in dry forests up to 600 m above sea level. It thrives in tropical forests across Central and Southern India, as well as in areas such as Banda, Konkan, the Western Ghats, Deccan, and parts of Western and Northern India. The plant was large, woody, and slightly pubescent.[9]

The leaves are opposite, usually elliptical or ovate, ranging from 1.25 to 2.0 inches in length and 0.5 to 1.25 inches in width. The flowers are small, yellow, and grouped in the axillary and lateral umbels within cymes. The follicles were cylindrical and lance-shaped, growing up to 3 inches in length. The corolla is pale yellow and bell-shaped, with valvate petals and a single corona consisting of five fleshy scales. These scales were attached to the throat of the corolla tube between lobes. The anther connective has a membranous tip, with two erect pollinia. The plant has two carpels that are unilocular and contain many ovules in each locule.[1][10]

This shrub is a pubescent variety with young stems and branches. It has a taproot system. The stems are cylindrical, branched, hard, and twining, with terete internodes ranging from 0.7 to 17.2 cm in length and 2 to 10 mm in diameter.[11] The leaves are arranged in a distichous, opposite pattern, typically 2.5 to 6 cm long, and are usually ovate or elliptical and simple in structure.[7] The venation was both transverse and

reticulate, with a marginal vein present. The seeds are flat, 1.3 cm long, with a thin marginal wing, and have a narrowly ovoid-oblong shape. The calyx is 5-lobed, ovate, obtuse, and ciliated, while the corolla is campanulate, yellow, and also 5-lobed.[12] Flowering occurred between August and March. Propagation via seeds is challenging due to low seed viability; therefore, an alternative method is planting root cuttings in June and July or terminal cuttings in February and March.[8]

## TRADITIONAL USES

*Gymnema sylvestre* is mentioned in the ancient medical text, Shushruta, as a treatment for glycosuria and urinary disorders. This herb is known for its wide therapeutic applications in folk medicine, Ayurveda, and Homeopathy.[7] It has a long history of use, especially in Ayurveda, where it has been employed to treat various conditions such as diabetes, malaria, and snakebites.[5] In Ayurvedic practice, it is commonly prescribed for ailments, such as dyspepsia, constipation, jaundice, hemorrhoids, kidney and bladder stones, heart diseases, asthma, bronchitis, amenorrhea, and leukoderma. Additionally, different parts of the plant, roots, stems, andleaves are utilized as cardiotonic, digestive aid, diureti c, laxative, stimulant, stomachic, and uterine tonic in traditional medicine. The leaves are used to treat obesity, dental issues, stomach pain, blood problems, and rheumatism.[13]

## PHYTOCHEMISTRY OF *GYMNEMA SYLVESTRE*

The stems of ***Gymnema sylvestre*** have been studied using chromatographic methods, revealing the presence of several therapeutically significant compounds, including stigmasterol and triterpenoid saponins. Stigmasterol is known for its various therapeutic properties, including antidiabetic, hypoglycemic, antioxidant, and anticancer activities. Triterpenoid saponins have demonstrated antitumor, antifungal, hepatoprotective, and antidiabetic effects in several studies.[14-15] The leaves of this plant contain saponins, anthraquinones, and cardiac glycosides. Additionally, the plant contains tannins, quinones, flavonoids, and phenols.[16] The leaves contain resins, albumin, chlorophyll, carbohydrates, tartaric acid, formic acid, butyric acid, anthraquinone derivatives, inositol alkaloids, organic acids (5.5%), parabin, calcium oxalate (7.3%), lignin (4.8%), and cellulose (22%).[17] The primary chemical constituents of ***Gymnema sylvestre*** are gymnemic acids and gymnemasaponins, which are oleanane saponins. Both oleanane and dammarane saponins are found in plant's leaves.[18]

*Gymnema* contains a group of nine related acidic glycosides, the primary ones being gymnemic acids A–D, which are found in all parts of the plant. The highest concentration of gymnemic acid was found in the shoot tips, whereas the lowest was found in the seeds. Gymnemic acids A2 and A3 contain both glucuronic acid and galactose, whereas gymnemic acid A1 only includes glucuronic acid.[19] Gurmarin, a 35-amino-acid peptide with a molecular weight of 4209, was isolated from G. sylvestre.[20] Additionally, a series of gymnemic acids (I, II, III, IV, V, VI, and VII) were identified and characterized in a hot water extract of the dry leaves of G. sylvestre.[21] Gymnemic acid A is composed of A1, A2, A3, and A4 and is referred to as gymnemagenin. This compound is a d-glucuronide of hexahydroxy-triterpene, which is esterified with acids.[22]

### Mechanism of action of Gymnemic acid

The drug works by stimulating insulin secretion from the β-islets of Langerhans and helps lower blood sugar levels by delaying glucose absorption.[23] The atomic structure of gymnemic acids resembles that of sugar molecules, allowing them to fill receptors on taste buds and prevent activation by sugars in food. Similarly, in the intestine, gymnemic acids bind to receptors on the outer layer of the intestine, blocking the absorption of sugar molecules and reducing blood sugar levels.[24] The hypoglycemic effect of gymnemic acids triggers a series of events, starting with modulation of incretin activity, which promotes insulin secretion and release. It also supports the regeneration of pancreatic islet cells, enhances enzyme-mediated glucose uptake, and reduces absorption of glucose and fatty acids in the small intestine. Additionally, it disrupts the ability of the receptors in the mouth and intestine to detect sweetness. Previous studies have suggested that gymnemic acid acts similar to incretin-mimetic mechanisms.[25] Gymnemic acid also interacts with glyceraldehyde-3-phosphate dehydrogenase (GAPDH), a key enzyme in the glycolysis pathway.[26] This research suggests that the acyl groups in gymnemic acids play a crucial role in GA-induced inhibition of GAPDH and G3PDH, contributing to the antihyperglycemic effects of GA derivatives.[27]

### Pharmacological Activities of Extracts and Pure Compounds Isolated from *Gymnema sylvestre*

Although Gymnema sylvestre is commonly used as a natural treatment for diabetes, it also shows potential for treating conditions such as obesity, arthritis, high cholesterol, Parkinson's disease, high blood fat levels, and other diseases. Plant bioactive compounds have antimicrobial, anti-inflammatory, and anticancer effects.[28-31]

### 1. Antidiabetic Activity

*Gymnema sylvestre* is well known for its ability to help manage diabetes. Studies have shown that different extracts of this plant can reduce the blood glucose levels. For example, ethanol extract reduces glucose by 46%, water extract by 26%, and methanol extract by 12%.[32] In rats that were insulin-resistant to dexamethasone, the aqueous extract improved glucose, insulin, and lipid levels.[33] When administered to diabetic animals, *Gymnema sylvestre* helped lower blood glucose, insulin, triglycerides, cholesterol, and protein levels and even reduced body weight while improving liver histopathology.[34]

In one study using alloxan-induced diabetic rats, *Gymnema sylvestre* significantly lowered fasting blood glucose, cholesterol, and triglycerides while raising "good" HDL-cholesterol levels. It also brought urea, uric acid, and creatinine levels closer to normal.[35] Both acute and long-term use of methanol extract in rats reduced blood glucose levels. In rats with streptozotocin-induced diabetes induced by Streptozotocin (STZ), this plant helped reduce high blood glucose, liver enzymes, and harmful fats (such as triglycerides and low-density lipoprotein cholesterol), while boosting insulin, HDL-cholesterol, and a protective antioxidant enzyme, superoxide dismutase. It also helps to regenerate insulin-producing cells in the pancreas.[36]

The active compounds in *Gymnema sylvestre*, called gymnemic acids, lower blood glucose levels and increase insulin levels in diabetic mice. Even small doses of the plant (like 0.2 g/kg) helped reduce blood sugar raised by sucrose. However, in another study, no antidiabetic effect was observed when the plant was administered to alloxan-treated animals.[37]

**2. Anticancer Activity**

*Gymnema sylvestre* has been shown to have anticancer properties in several studies. One of its key components, gymnemagenol, demonstrated significant anticancer effects in HeLa cancer cells.[38] It was found to strongly inhibit intestinal breast cancer resistance protein (BCRP), which is linked to multidrug resistance in cancer treatment. By blocking BCRP, *Gymnema sylvestre* may enhance the effectiveness of certain cancer drugs, such as methotrexate, daunorubicin, and epirubicin, by improving their absorption and availability in the body.[39]

*In vitro* studies of gymnemagenol showed cytotoxicity against HeLa cells. The MTT cell proliferation assay revealed that different concentrations of gymnemagenol (5, 15, 25, and 50 µg/mL) were effective, with an IC50 of 37 µg/mL. After 96 h, 50 µg/mL of the extract resulted in a 73% reduction in HeLa cell growth. Importantly, gymnemagenol did not harm normal cells, suggesting that it may be a promising anticancer treatment. Given the increasing incidence of cancer, herbal formulations such as *Gymnema sylvestre* could offer potential in cancer therapy.[40]

**3. Anti-Inflammatory Activity**

The methanolic extract of *Gymnema sylvestre* has demonstrated anti-inflammatory effects in Wistar rats. When inflammation was induced using carrageenan, the methanol extract significantly reduced paw swelling ($P < 0.05$). In another study, the aqueous extract also showed inhibitory effects on carrageenan-induced paw swelling and peritoneal ascites in mice.[41] Additionally, the ethanolic extract of *Gymnema sylvestre* exhibits anti-inflammatory activity by inhibiting TPA-induced inflammation in mice.[42]

**4. Antiarthritic Activity**

The leaf extract of Gymnema sylvestre has been studied for its anti-arthritic effects in albino rats. Both water-soluble and petroleum ether (40–60°C) extracts were found to be highly effective in controlling arthritis. This suggests that the potent anti-arthritic activity may be due to the presence of triterpenoids, steroids, and saponin glycosides in the leaves.[29] The aqueous and petroleum extracts showed significant ($p < 0.01$) anti-arthritic effects, possibly by reducing the release of inflammatory mediators, which helps prevent bone damage in arthritis. Additionally, another study found that the ethanolic root extract of Gymnema sylvestre significantly reduced carrageenan-induced paw swelling ($p < 0.01$) and inhibited 39-75% of histamine-induced paw edema.[43]

**5. Antioxidant Activity**

The ethanol extract of this plant exhibited significant ($p < 0.05$) DPPH radical scavenging activity, demonstrating a stronger antioxidant effect than those of A. bilimbi and C. frutescens.[44] *Gymnema sylvestre* has also been shown to possess antioxidant properties, particularly DPPH radical scavenging, surpassing butylated hydroxytoluene (BHT).[45] Additionally, previous studies have indicated that it can be reduced. In another study, *Gymnema sylvestre* demonstrated both hydroxyl free radical scavenging activity and impressive antioxidant potential, with DPPH inhibition reaching 87.3% and hydroxyl free radical inhibition at 59.8%.[46] Furthermore, this plant was found to exhibit significant radical scavenging activity against ferric ions ($p < 0.05$), superoxide ($p < 0.05$), and hydrogen peroxide ($p < 0.05$).[47] *Gymnema sylvestre* has shown antioxidant effects under various conditions, including high-fat diets, hydrogen peroxide exposure, and oxidative stress induced by nitric oxide and superoxide radicals in rats.[48]

**6. Antiobesity Studies**

*Gymnema sylvestre* may aid in weight loss, potentially by reducing cravings for sweets and helping regulate blood sugar levels. The gurmarin peptide in plants is known to block the ability to taste sweet or bitter flavors, which could help diminish sweet cravings.[49-50] A standardized extract of *Gymnema sylvestre*, when combined with niacin-bound chromium and hydroxycitric acid, has been studied for its anti-obesity effects. The study tracked changes in body weight, BMI, appetite, lipid profiles, serum leptin, and urinary fat metabolites. The results indicated that this combination could be an effective and safe weight loss formula, helping to reduce excess body weight and BMI while also supporting healthy blood lipid levels.[51]

**7. Treatment of Dental Caries**

Dental caries is an infection of the tooth caused by various gram-positive cariogenic bacteria such as *S. aureus*, *S. mitis*, and *S. mutans*, along with the fungus *Candida albicans*. These microorganisms adhere to the tooth surface by releasing extracellular polysaccharides from sucrose and metabolizing sugars into organic acids,

primarily lactic acid, leading to the demineralization of tooth enamel.[52] Chloroform, petroleum ether, and methanolic leaf extracts of *Gymnema sylvestre* were tested at concentrations of 25, 50, and 100 mg/mL against microbial dental infections. These extracts demonstrated significant effectiveness, especially the methanolic extract, which showed the highest activity, even at the lowest concentration. The promising results of the hydroalcoholic extract have led to the development of gurmar-based dental products, such as "Gurmar Herbal Toothpaste" and "Gurmar Herbal Tooth Powder." These herbal formulations hold potential as new treatments for dental caries, pending clinical approval from the scientific community.[53]

**8. Antibiotic and Antimicrobial Activity**

The antibiotic and antimicrobial properties of various extracts of *Gymnema sylvestre* were evaluated against several pathogens, including *S. aureus*, *E. coli*, and *B. subtilis*, with no significant activity observed against gram-negative bacteria. The leaf extracts of *Gymnema sylvestre* showed promising potential as a herbal remedy for bacterial infections.[54] Further studies revealed that both *Gymnema sylvestre* extracts and gymnemic acid exhibited notable antimicrobial effects against *E. coli* and *B. cereus.*[55] When the methanolic extracts of *Gymnema sylvestre* were tested separately for aerial and root parts, the results showed that the methanol extracts, particularly in an acidic environment, displayed good antimicrobial activity against a broad range of pathogens. In another study, ethanolic extracts of *Gymnema sylvestre* demonstrated significant antimicrobial effects against *Bacillus pumilus*, *B. subtilis*, *P. aeruginosa*, and *S. aureus*. Based on these findings, it can be concluded that the methanolic and ethanolic leaf extracts of *Gymnema sylvestre* possess considerable antibiotic and antimicrobial activity.[56]

**9. Hepatoprotective Activity**

In an *in vitro* study, a hydroalcoholic extract of *Gymnema sylvestre* was found to exhibit anti-hepatotoxic effects in isolated rat hepatocytes in a dose-dependent manner, where hepatotoxicity was induced using D-galactosamine. The study showed a significant increase in the levels of ASAT, ALAT, ALP, total bilirubin, and direct bilirubin ($p < 0.001$).[57] Additionally, the methanolic extract of *Gymnema sylvestre* was reported to reduce urea and creatinine levels following both acute and chronic administration in Wistar rats.[58] In another study, a methanolic polyherbal preparation containing *Gymnema sylvestre* demonstrated the ability to reverse hepatotoxicity in albino rats induced by paraffin and carbon tetrachloride.[59]

**10. Immunostimulatory Activity**

Immunomodulation refers to the regulation or control of the immune system, and can involve either enhancing or suppressing immune responses. The body's response to a specific condition can be adjusted by agents that either stimulate or inhibit activity. *Gymnema* sylvestre is an immunostimulatory plant and its leaves are reported to have immune-boosting effects.[60] The immunostimulatory properties of the aqueous leaf extract were tested using several methods, including neutrophil movement, chemotaxis assays, phagocytosis of killed Candida albicans, and nitroblue tetrazolium tests. The results demonstrated significant immunostimulatory activity of the aqueous leaf extract of *Gymnema* sylvestre at concentrations of 10, 25, 50, 100, and 1000 µg/mL in human neutrophils *in vitro*.[29]

**11. Wound Healing Activity**

The alcoholic extract of Gymnema sylvestre leaves showed notable wound healing activity in rats.[61] The hydroalcoholic extract demonstrated better wound-healing properties than the control group. The synergistic effect of the plant extracts was supported by thin-layer chromatography (TLC) analysis, wound contraction studies, and qualitative tests. The enhanced wound healing effect of the hydroalcoholic extract is likely due to its free radical scavenging ability and the presence of phytoconstituents, particularly flavonoids, which may act alone or in combination to promote wound healing. Flavonoids in the alcoholic extract were identified using TLC and phytochemical analyses.[62]

**12. Lipid-Lowering Activity**

*Gymnema sylvestre* leaf extract has shown potent lipid-lowering effects in studies involving female Wistar rats. When these rats were fed a high-fat diet, the extract significantly reduced cholesterol, LDL, and triglyceride levels ($p < 0.01$) and increased HDL levels ($p < 0.001$).[63] In another study, after seven days of a high-cholesterol diet, rats were treated with the extract, which lowered cholesterol, triglycerides, and LDL, while increasing HDL levels.[30] This lipid-lowering effect is attributed to compounds such as flavonoids, saponins, and tannins in plants. Similar results were observed in diabetic rats, with reductions in triglyceride, cholesterol, VLDL, and LDL levels.[64]

**CONCLUSION**

*Gymnema sylvestre*. contains several important phytochemicals, such as flavonoids, alkaloids, tannins, saponins, flavonols, glycosides, gymnemanol, and gurmarin, which contribute to its life-saving therapeutic effects and are responsible for a wide range of pharmacological properties, including anti-metastatic, anti-diabetic, hypoglycemic, antioxidant, hepatoprotective, anti-inflammatory, antibacterial, antifungal, antiviral, anti-obesity, immunostimulatory, lipid-lowering, and dental caries treatment. Different parts of the plant, such as the leaves and roots, have medicinal properties, and are used in Ayurvedic medicine to treat various diseases.

In developing countries, approximately 80% of people have faith in natural medicine to address health issues. However, despite their high demand and therapeutic potential, only approximately 10% of plants have been

studied for their medicinal properties, and the review also discusses the potential of *Gymnema sylvestre* in modern therapeutic development, aligning with current trends in pharmacology and drug development.

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