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Gymnema Sylvestre (Gurmar): A Review

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Abstract

Gymnema Sylvestre R. Br. (Asclepiadaceae) is a herb distributed throughout the world. The leaves of the plant are widely used for the treatment of diabetes and as a diuretic in Indian proprietary medicines. Gymnemic acid is the main active chemical constituent isolated from the *Gymnema Sylvestre* plant. The plant is documented to possess beneficial effects as digestive, anti-inflammatory, diuretic, hypoglycemic and antihelmentic. It is believed to be used in dyspepsia, constipation, jaundice, haemorrhoids, cardiopathy, asthma, bronchitis and leucoderma. A scrutiny of literature revealed some notable pharmacological activities of the plant such as antidiabetic, antiobesity, hypolipidaemic, antimicrobial, free radical scavenging and anti-inflammatory. The present review is an attempt to highlight the various ethnobotanical and traditional uses as well as phytochemical and pharmacological reports on *G. sylvestre*.

Keywords: *Gymnema sylvestre*, ethnobotanical uses, pharmacognosy, pharmacological activities, phytochemistry

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Introduction

Gymnema Sylvestre R. Br. is a valuable herb belonging to the family Asclepiadaceae, and widely distributed in India, Malaysia, Srilanka, Australia, Indonesia, Japan, Vietnam, tropical Africa and the southwestern region of the People's Republic of China. The plant is commonly known as *Periploca of the woods* (English); *Gurmar* (Hindi); *Meshashringi, madhunashini* (Sanskrit); *Kavali, kalikardori* (Marathi); *Dhuleti, mardashingi* (Gujrathi); *Adigam, cherukurinja* (Tamil); *Podapatri* (Telgu) and Sannagerasehambu (Kannada)[1-5]. The word "Gymnema" is derived from a Hindu word "Gurmar" meaning "destroyer of sugar" and it is believed that it might neutralize the excess of sugar present in the body in Diabetes mellitus [6]. The taxonomy of the plant is described in table 1 [7].

Table 1: Taxonomy of *Gymnema sylvestre*

Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Gentianales
Family	Asclepiadaceae
Genus	*Gymnema*
Species	*sylvestre*

Plant description

G. sylvestre is a slow growing, perennial, woody climber, distributed throughout the India, in dry forests upto 600 m height. It is mainly present in the tropical forest of Central and Southern India. It is also found in Banda, konkan, Western Ghats, Deccan extending to the parts of western and northern India [6-8]. The plant is a large, more or less pubescent, woody climber. The leaves are opposite, usually elliptic or ovate (1.25 – 2.0 inch x 0.5-1.25 inch). Flowers are small, yellow, in axillary and lateral umbel in cymes; Follicles are terete and lanceolate upto 3 inches in length. The Calyx-lobes are long, ovate, obtuse and pubescent. Corolla is pale yellow campanulate, valvate, corona single, with 5 fleshy scales. Scales adnate to throat of corolla tube between lobes; Anther connective produced into a memberanous tip, pollinia 2, erect, carpels 2, unilocular; locules many ovuled [5,7, 9,10].

G. sylvestre is a potent antidiabetic plant and used in folk, ayurvedic and homeopathic systems of medicine. It is also used in the treatment of asthma, eye complaints, family planning, snakebite, urinary complaints, stomach problems, piles, chronic cough, breathing troubles, colic pain, cardiopathy, constipation, dyspepsia and hemorrhoids, hepatosplenomegally. In addition, it also possesses antimicrobial, antihypercholesterolemic, anti- inflammatory and sweet suppressing activities and it also acts as feeding deterrents to caterpillar [5, 7, 9, 11-12]

Literature surveys reveal that, *G. sylvestre* is a popular plant used in treating various ailments and used as one of the important ingredient in several ayurvedic formulations, very little efforts have also been made to verify its efficacy through scientific screening in animal models and clinical trials. The present review highlights the various folk, ayurvedic uses and pharmacognostical, phytochemical and pharmacological studies conducted on *G. sylvestre*.

Pharmacognostical Studies

Leaves of *G. sylvestre* are widely used for the treatment of diabetes and as a diuretic in Indian proprietary medicines and in most of herbal drug market of the country, leaves are being sold along with the aerial parts as Gurmarbuti [13]. Therefore, macroscopic and microscopic characters of the aerial parts are described below:

Macroscopic Characteristics

Leaves of *G. sylvestre* are green in colour and stem is hairy and light brown. Leaf is 2-6 cm in length and 1-4 cm in width. The leaves are simple, petiolate, rounded to cordate base, margin entire, opposite with acute apex, reticulate venation, pubescent on both the surfaces. The odour is characteristic and taste of leaf is slightly bitter and astringent. It also possesses remarkable property of paralyzing the sense of the taste for sweet substances for few hours [13-14].

Microscopic Characteristics

Petiole

Transverse section of petiole is horse shoe shaped. The epidermis is barrel shaped single layered, thick walled covered with uniseriate, multicellular, non-glandular trichomes. The cortex is collenchymatous and vascular bundles are amphicribal and three in number. Well developed phloem consists of sieve tubes, companion cells and phloem parenchyma. The xylem consists of vessels, tracheids and tracheidal fibres. The starch grains are polygonal, simple or compound in two or many groups. The rosette crystals of calcium oxalate are present more towards the centre [13-15].

Lamina

The epidermal cells of lamina are square shaped with outer convex wall and thin cuticle. When viewed transversally, epidermal cell surface are interrupted with trichomes, which are uniseriate, multicellular with 2 to 5 celled, present in abundance on both the surfaces. Single layered closely arranged palisade cells are present just below the adaxial epidermis. Vascular bundles are amphicribal and the mesophyll is 3-5 celled thick [13-15].

Stem

The transverse section of stem is circular in outline. The epidermis is barrel shaped and thick walled. Trichomes are multicellular, uniseriate and 185-485 µ long and 9-25 µ broad. The cork is 3 to 5 layered thick, and cortical cells are latterly elongated and collenchymous. The phloem well developed consists of large sieve plates, companion cells and phloem parenchyma. The xylem is in the form of a continuous cylinder transverse by narrow medullary rays. The endodermis is conspicuous and the pericycle is broad [13-14].

Powder

The powdered material is slight yellowish green in colour, bitter in taste with pleasant aromatic odour. On microscopic examination, it shows thick walled, uniseriate multicellular trichomes, anomocytic stomata, idioblast with rosette crystals of calcium oxalate, starch grains, remnants of collenchymatous and parenchymatous cells; vessels, tracheids, tracheidal fibres, bast fibres and sieve plates [9, 13-14].

Identification Tests

When powder is treated separately with 1 N aqueous NaOH and 50% KOH, shows green fluorescence under UV 254 nm and orange colour with 50% HNO_3 in daylight. General identification tests for *G. sylvestre* hydro-alcoholic extracts are as given below: The dilute solution suppresses the sweet taste buds, it gives copious foam appearance when shaken with water and on addition of dilute acid, it forms a voluminous precipitate [9, 15-16].

Purity Test

Purity test of *G. sylvestre* depicts the following characteristics: 1) Maximum moisture content should not more than 6 percent, 2) Total ash content should not more than 12 percent, 3) Heavy metal content in leaves or leaves extract should not more than 40 ppm and in the final dosage form, it should not more than 10 ppm [13,17].

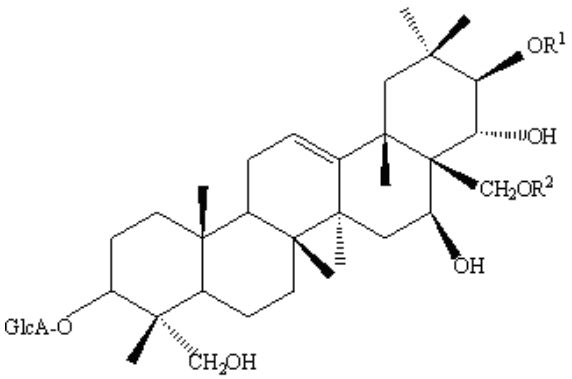
Phytochemistry

The leaves of *G. sylvestre* contain triterpene saponins belonging to oleanane and dammarene classes. Oleanane saponins are gymnemic acids and gymnemasaponins, while dammarene saponins are gymnemasides [18-20]. The leaves also contain resins, albumin, chlorophyll, carbohydrates, tartaric acid, formic acid, butyric acid, anthraquinone derivatives, inositole alkaloids, organic acid (5.5%), parabin, calcium oxalate (7.3%), lignin (4.8%), cellulose (22%) [21].

The gymnemic acids contain several acylated (tiglolyl, methylbutyroyl etc.) derivatives of deacylgymnemic acid (DAGA) which is a 3-O-β-glucouronide of gymnemagenin (3β, 16β, 21β, 22α, 23, 28-hexahydroxy-olean-12-ene). The individual gymnemic acids (saponins) include gymnemic acids I-VII, gymnemosides A-F, gymnemasaponins. The presence of gymnemic acids, (+) quercitol, lupeol, (-) amyrin, stigma sterol etc. have been reported from *G. sylvestre.* A new flavonol glycoside namely kaempferol 3-O-beta-D-glucopyranosyl-(1-->4)- alpha-L-rhamnopyranosyl-(1-->6)-beta-D-galactopyranoside has also been found in aerial parts of *G. sylvestre* [22-25].Three new oleanane type triterpene glycosides i.e. beta-O-benzoylsitakisogenin 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucuronopyranoside, the potassium salt of longiospinogenin 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucopyranoside and the potassium salt of 29- hydroxylongispinogenin 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucopyranoside along with sodium salt of alternoside II were isolated from an ethanol extract of the leaves of *G. sylvestre* [26]. Four new triterpenoid saponins, gymnemasins A, B, C and D isolated from the leaves of *G. sylvestre* were identified as 3-O-[beta-D-glucopyranosyl(1-->3)-beta-D-glucopyranosyl]-22-O-tiglyol-gymnemanol,3-O-[beta-D-glucopyranosyl(1-->3)-beta-D-glucuro - nopyranosyl]- gymnemanol, 3-O-beta-D-glucuronopyranosyl-22-O-tigloyl-gymnemanol and 3-O-beta-D-glucopyranosyl-gymnemanol respectively. The aglycone, gymnemanol, which is a new compound, was characterized as 3 beta-16 beta-22 alpha-23-28-pentahydroxyolean-12-ene. Gymnestrogenin, a new pentahydroxytriterpene from the leaves of *G. sylvestre* has been reported [27, 28].

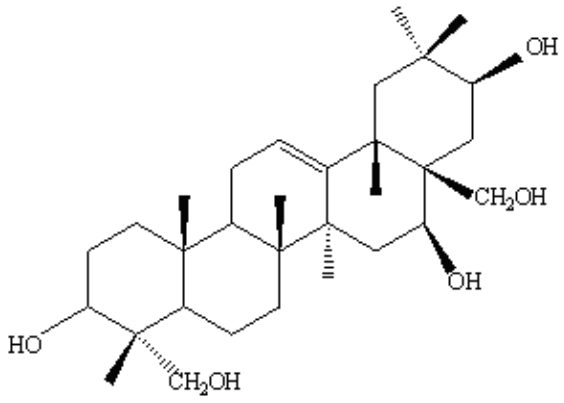
Mechanism of action of *G. Sylvester* (Gymnemic Acid)

G. Sylvester leaves have been found to cause hypoglycemia in laboratory animals and shown a use in herbal medicine to treat diabetes mellitus in adults. When leaf extract of plant, administered to a diabetic patient, there is stimulation of the pancreas by virtue of which there is an increase in insulin release. These compounds have also been found to increase fecal excretion of cholesterol [29, 30]. There are some possible mechanisms by which the leaves extract of *G. Sylvester* or (Gymnemic acid) possess its hypoglycemic acid effects are: 1) It promotes regeneration of islet cells, 2) It increases secretion of insulin, 3) It causes inhibition of glucose absorption from intestine, 4) It increases utilization of glucose as it increase the activities of enzymes responsible for utilization of glucose by insulin-dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase [2].

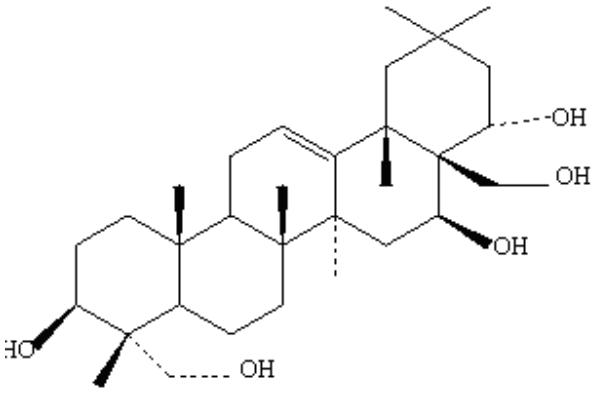


Gymnemic acid

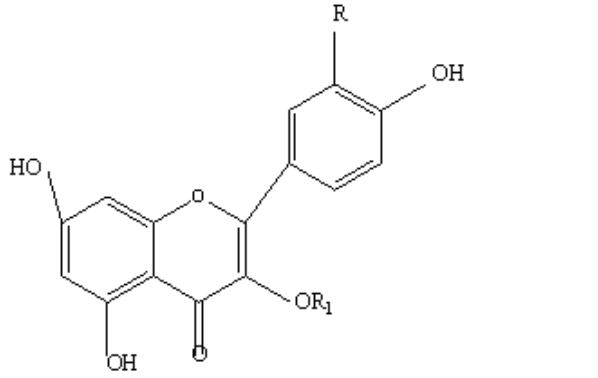
Gymnemic acid types	**R^1**	**R^2**
Gymnemic acid 1	Tigloyl	Ac
Gymnemic acid II	2-methylbutyroyl	Ac
Gymnemic acid III	2-methylbutyroyl	H
Gymnemic acid IV	Tigloyl	H



Gymnestrogenin



Gymnemanol



R = H, R_1 = beta-O-Glcp-(1--> 4)- alpha-L-Rhap-(1-->6)-beta-O-Galp

Kaempferol 3-O-beta-D-glucopyranosyl-(1-->4)-alpha-L-rhamnopyranosyl- (1-->6)-beta-D galactopyranoside

Figure 1. Structures of some phytoconstituents isolated from *Gymnema sylvestre*

Uses

Traditional Uses

Susruta describes *G. sylvester*, as a destroyer of madhumeha (glycosuria) and other urinary disorder. It is also reported to be bitter, astringent, acrid, thermogenic, anti-inflammatory, anodyne, digestive, liver tonic emetic, diuretic, stomachic, stimulant, anthelmenthics, laxative, cardiotonic, expectorant, antipyretic and uterine tonic. It is useful in dyspepsia, constipation and jaundice, haemorrhoids, renal and vesicle calculi, cardiopathy, asthma, bronchitis, amenorrhoea, conjunctivitis and leucoderma [12, 31-32]. The drug is also used in the composition of ayurvedic preparations like *Ayaskri*, *Varunadi kasaya*, *Varunadighrtam*, *Mahakalyanakaghrtam* [33].

Ethnobotanical Uses

There are over four hundred different tribal and other ethnic groups in India. Each tribal group is having their own tradition, folk language, beliefs and knowledge about the use of natural resources as medicines. The plant is reported to be useful in ethnobotanical surveys conducted by ethnobotanists. It has been documented that the Jungle Irulas inhabitants of Nagari Hills of the North Arcot District, Bombay and Gujarat from India have the habit of chewing a few green leaves of *G. sylvestre* in the morning in order to keep their urine clear and to reduce glycosuria. Bourgeois classes of Bombay and Gujarat also chew fresh leaves for the same effect. In Bombay and Madras, 'Vaids' are known to recommend the leaves in the treatment of furunculosis and madhumeha. The juice obtained from root is used to treat vomiting and in dysentery and plant paste is applied with mother milk to treat mouth ulcer. [7, 13, 34].

Pharmacological Uses

Following the folk and traditional uses of the plant, it has been investigated scientifically to validate the potential of plant in cure of variety of ailments.

General Pharmacological Activities

The LD_{50} of ethanolic and water extract of *G. sylvestre* administered intraperitoneally in mice was found to be 375 mg/kg [35]. In an acute toxicity study in mice, no gross behavioral, neurologic, or autonomic effects were observed. The safety ratio (LD_{50}/ED_{50}) was 11 and 16 in normal and diabetic rats, respectively [36]. The pharmacological activities of *G. sylvestre* are desribed below:

1. Antiobesity Study

G. Sylvestre helps to promote weight loss possibly through its ability to reduce cravings for sweets and control blood sugar levels. It has been reported that the gurmarin peptide block the ability to taste sweet or bitter flavors and thus reduces sweet cravings [37-38]. A standardized *G. sylvestre* extract in combination with niacin-bound chromium and hydroxycitric acid has been evaluated for antiobesity activity by monitoring changes in body weight, body mass index (BMI), appetite, lipid profiles, serum leptin and excretion of urinary fat metabolites. This study showed that the combination of *Gymnema Sylvestre* extract and hydroxycitric acid, niacin bound chromium can serve as an effective and safe weight loss formula that can facilitate a reduction in excess body weight and BMI while promoting healthy blood lipid levels [39].

2. Antidiabetic Activity

The first scientific confirmation of *G. sylvestre* use in human diabetics came almost a century back when it was demonstrated that the leaves of *G. sylvestre* reduce urine glucose in diabetics [40]. In an animal study, Paliwal *et al* have investigated that gurmar leaf powder had positive and encouraging effects over blood glucose levels. No adverse effect was observed on the health status of the subjects and thus, it can thus be concluded that gurmar powder is effective in lowering the fasting as well as postprandial blood glucose levels [3]. Moreover, Sugihar *et al* have investigated the antihyperglycemic action of a crude saponin fraction and five triterpene glycosides derived from the methanol extracts of *G. sylvestre* [41].

3. Hypolipidaemic Activity

The administration of leaf extracts to hyperlipidaemic rats for two weeks have been found to show reduction in elevated serum triglyceride (TG), total cholesterol (TC), very low density lipoprotein (VLDL) and low density lipoprotein (LDL) – cholesterol in dose dependent manner. The efficiency of this drug was almost similar to that of a standard lipid lowering agent clifibrate [42, 4].

4. Antimicrobial Activity

The ethanolic extract of *G. sylvestre* leaves showed good antimicrobial activity against *Bacillus pumilis, B. subtilis, Pseudomonas aeruginosa* and *Staphylococcus aureus* and no activity was found against *Proteus vulgaris and Escherichia coli* [43]. The aqueous and methanolic extract of *G. sylvestre* leaves also showed moderate activity against the three pathogenic *Salmonella* species (*Salmonella typhi, S. typhimurium* and *S. paratyphi*). Out of the two extracts used, aqueous extract showed higher activity against the *Salmonella* species [44]. Ethanolic, Chloroform and Ethyl acetate extracts of the aerial parts of *G. sylvestre* also reported to have antibacterial effects against *P. vulgaris, E. coli, P. aeroginosa, Klebsella pneumoniae* and *S. aureus* [45].

5. Anti-Inflammatory Activity

The aqueous extract of *G. sylvestre* leaves was investigated for evaluation of anti-inflammatory activity in rats at a dose 200, 300 and 500 mg/kg in carrageenin-induced paw oedema and cotton pellet method. The aqueous extract at 300 mg/kg decreased the paw oedema volume by 48.5% with in 4 h after administration, while the standard drug phenylbutazone decreased the paw oedema volume by 57.6% when compared with the paw oedema volume of control. The aqueous extract at the dose of 200 mg/kg and 300 mg/kg produced significant reduction in granuloma weight, when compared to control group [46].

6. Free Radical Scavenging Activity

In vitro, the inhibitory effects of DPPH radicals and LDL oxidation were found with aqueous extract of *G. sylvestre*. *G. sylvestre* require 32.1 µl, for scavenging 50% of the DPPH radicals [47].

Dosage Forms

In market, *G. sylvestre* is available in the form of crude plant, powder, extract paste and solid in standardized form. The plant material is also available in the form of capsule or tablets in combination with other herbal plants [48].

Adult dose: In liquid form (extract), 25 to 75 ml per week is recommended. Best results of this medicine will come after 6 to 12 months of continuous use. It is also prescribed in tablet form, in this case 8 to 12 g per day of leaf equivalent is recommended.

Pediatric dose: In this case, there is insufficient evidence about its uses for pediatric population, so it can not be recommended for them [49].

Suggested Combinations with Other Herbs

G. sylvestre can be taken along with fenugreek, goat's rue and neem leaves for the treatment of diabetes, and with globe artichoke or blue flag for weight loss. In case of hypercholesterolaemia, *G. sylvestre* recommended with turmeric, hawthorn, Silybum, globe artichoke and garlic [49].

Discussion

In recent years, ethnobotanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. They obviously deserve scrutiny on modern scientific lines such as physiochemical characterization, biological evaluation, toxicity studies, investigation of molecular mechanism of action(s) of isolated phytoprinciple and their clinical trials. These are necessary classical approaches in search of new lead molecule for management of various diseases. Diabetes is now becoming a common disease through the world and a lot of new drugs are being synthesized for the same. Many Indian herbs are being used in traditional practices to cure diabetes. *Gymnema sylvestre*, has an important place among such antidiabetic medicinal plants, it can also be used in treating dyspepsia, constipation and jaundice, haemorrhoids, renal and vesicle calculi, cardiopathy, asthma, bronchitis, amenorrhoea, conjunctivitis and leucoderma. Furthermore, in future study, the isolated principles from Gurmar needs to be evaluated in scientific manner using various innovative experimental models and clinical trials to understand its mechanism of action, in search of other active constituents, so that its other therapeutic uses can be widely explored.

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