

**Abstract**

*Gymnema sylvestre* is one of the valuable medicinally important herbs belongs to family Apocynaceae. *G. Sylvester* is a woody climber herb generally found in India, Srilanka, China, Indonesia, Malaysia and Tropical Africa. Traditionally the plant is used as antidiabetic, antihelmentic, antiobesity, anti-inflammatory, hypolipidaemic, antivenom and antimicrobial. The ethnic community use parts of the plants in constipation, haemorrhoids, jaundice, leucoderma, asthma, bronchitis, cardiac problems and dyspepsia. Most important phytochemicals of the plant are gymnemic acid, deacyl gymnemic acid and gymnemagenol which help in the controlling of blood cholesterol, triglyceride levels, inflammation and body weight. The present review aims to document the traditional and modern pharmacological uses of the plant to provide better scope for further experiments and future application. The botanical description, cultivation practices, phytochemical constituents and safety issues of the plant has also been described in the chapter.

**Keywords:** *Gymnema sylvestre*, Medicinal Plant, Ethnopharmacology, Phytoconstituents, Traditional and Modern Uses

**Introduction**

*Gymnema Sylvestre* R. Br. is an important herb belongs to the family Apocynaceae (or previously called Asclepiadaceae). The plant is native to India, Australia and Tropical Africa commonly known as miracle plant in English and Gurmar (slayer of sugar) in Hindi as chewing the leaves causes a loss of sweet taste for a short time (Gloria et al., 2003; Keshavamurthy and Yoganarasimhan, 1990). Ethnomedicinally it is a popular plant mostly used in Homeopathic, Ayurvedic, Unani and Siddha systems of traditional medicine advised to the diabetic and toothache patients (Mitra et al., 1996). Gymnemic acid is the key constituent found in the leaves and roots of *G. sylvestre* used in the treatment of diabetes or lowering and balancing of blood sugar (Duke et al., 1997). Tribal people of India use the plant bark and roots as an emetic, expectorant, and analgesic for body ache and juice from the root has been acclaimed as a useful treatment for snakebite (Sastry, 2005). In addition, the plant is traditionally used as hepatoprotective (Rana and Avadhoot, 1992), anti-hypercholesterolemic, antimicrobial and anti-inflammatory properties (Potawale et al., 2008; Kumar et al., 2008), and prevention from dental caries (Hiji, 1990). It is also used in the treatment of asthma, eye complaints, digestive problems, inflammations, snake bite (Kini and Gowda, 1982). There are a large number of phytochemical constituents isolated from *G. sylvestre*, these are gymnemic acid, saponins, stigmasterol, quercitol and amino acid derivatives betaine, choline, and

trimethylamine (Kapoor, 1990). Similarly the plant leaves contains albumin, resins, chlorophyll, carbohydrates, tartaric acid, formic acid, butyric acid, anthraquinone derivatives, inositol alkaloids, organic acid, paraben, calcium oxalate, lignin, and cellulose. The leaves also contain triterpene classes of oleanane saponins such as gymnemic acids, gymnemasaponins, and dammarane saponins such as gymnemasides and terpenoids as 6-octen 1-ol, 3,7-dimethyl, isophytol, squalene, nerolidol, and  $\beta$ -amyrin (Srinivasan and Kumaravel, 2016). The present review on *G. sylvestre* is a research update with important medicinal traits and significant ethnopharmacological importance. It also searches the reality and prospects of its development into modern and efficient therapeutic trends of pharmacology and drug development. Moreover, it holds significant views in most important health problems like diabetes, obesity, cardiovascular problems, osteoporosis, and asthma as well as a popular medication for number of other health problems.

### Geographical and Botanical Description

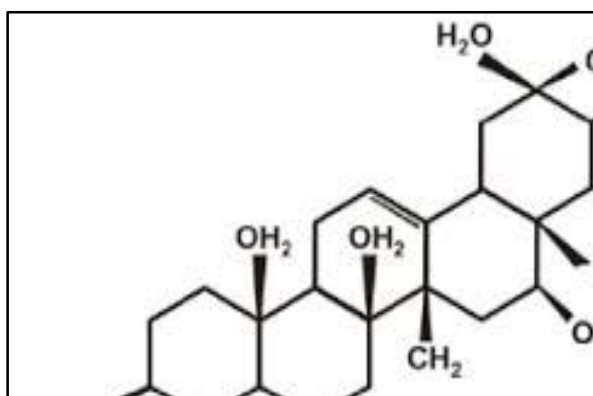
*G. sylvestre* flourish well from 100 to 1000 m of altitude (Sabitha et al., 2012). It is generally found in tropical and subtropical and humid climatic zone and hills of evergreen forests in India, Srilanka, China, Malaysia, Indonesia, Australia, Japan, Vietnam and tropical Africa (Yadav et al., 2001). It is a perennial, upward growing, woody climber (up to 8 m length), and cylindrical, light brown, pubescent herb. The leaves are simple, green, reticulate venation, petiolate, entire, opposite, acute apex, elliptical to ovate, 2-6 cm in length, 1-4 cm in width and pubescent on both the surfaces. Leaf is astringent and bitter having remarkable characteristic of paralyzing the sense of the taste buds for sweet substances (Madhurima et al., 2009). Flowers of the plant are small, yellow, auxiliary and lateral umbel in cymes. The follicles are lanceolate and terete length is about 3 inches. The Calyx-lobes are ovate, pubescent, long and obtuse. The Corolla is pale yellow, valvate, campanulate, corona single, with 5 fleshy scales. Scales adnate to throat of corolla tube between lobes, anther connective produced into a membranous tip, pollinia 2, erect, carpels 2, unilocular having many ovuled in locules (Gurav et al., 2007). Seeds are cotyledons, ovate, margined, ending in a silky coma, elliptic and radicle is cylindric (Mathew and Rani, 1983). Flowering occurs in March to August and the fruiting season is from October onwards. The *Gymnema* species are diploid with a chromosome number of  $2n = 22$  (Sredeeivi and Namboodiri, 1977).



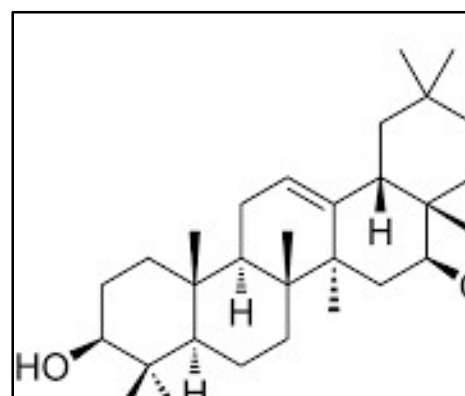
Fig 1.

## Phytochemical Constituents

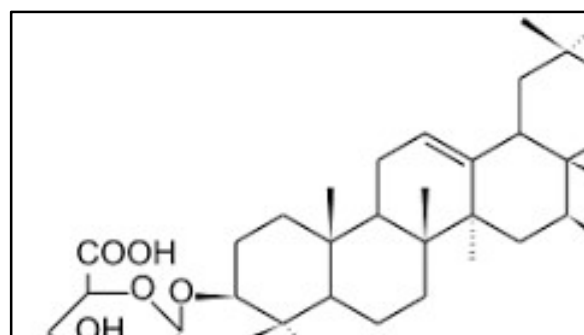
The bioactive components found in different parts including leaves of *G. sylvestre* contain gymnemic acids, gymnemasaponins, gymnemosides, gurmarin, gymnemanol, stigmasterol, d-quercitol,  $\beta$ -amyrin related glycosides, anthraquinones, lupeol, hydroxycinnamic acids, and coumarols group. Triterpene saponins are come under oleanane and dammarene classes. Oleanane saponins are gymnemic acids and gymnemasaponins, while dammarene saponins are gymnemosides (Khramov et al., 2008). The major phytochemicals such as gymnemic acids and gymnemasaponins are parts of oleanane type of saponins while gymnemosides are dammarane saponins (Khramov et al., 2008). Acidic glycosides and anthraquinones and their derivatives are extracted from the leaves of the plant (Dateo and Long, 1973). Other phytochemicals such as flavones, anthraquinones, hentriacontane, pentatriacontane, phytin, resins, tartaric acid, formic acid, butyric acid, lupeol,  $\beta$ -amyrin related glycosides, stigmasterol, and calcium oxalate are found in the leaves (Sinsheimer et al., 1970). The most important secondary metabolites in *G. sylvestre* comprises a group of nine closely related acidic glycosides, most important are gymnemic acid A–D which found in whole parts of the plant. In addition, a series of gymnemic acids (gymnemic acid I, II, III, IV, V, VI, and VII) are present in dry leaves of *G. sylvestre* (Yoshikawa et al., 1989). The derivatives of gymnemic acids are several acylated tigloyl, methylbutyryl group substituted members, derived from deacylgymnemic acid (DAGA) which is a 3-O- $\beta$ -glucuronide of gymnemagenin (3 $\beta$ , 16 $\beta$ , 21 $\beta$ , 22 $\alpha$ , 23, 28-hexahydroxy-olean-12-ene). Gymnemic acid A comprises of gymnemic acids A<sub>1</sub>, A<sub>2</sub>, A<sub>3</sub>, and A<sub>4</sub> and named gymnemagenin. This constituent is a D-glucuronide of hexahydroxy-triterpene that esterifies with acids (Stocklin et al., 1967). Other five gymnemic acids, namely, VIII, IX, X, XI, and XII, were isolated and characterized later (Yoshikawa et al., 1992). Gymnemasaponins III is isolated from the plant function as an antisweet compound consists of 23 hydroxylongispinogenin as the aglycone moiety glycosylated with either one or two glucose molecules at both the 23 and 28 hydroxyl groups (Murakami et al., 1996). These compounds exhibited lesser antisweet effect than those of gymnemic acids (Yoshikawa et al., 1991). Gurmarin is extracted from *G. sylvestre*, an important 35 amino-acid peptide (Imoto et al., 1991). This polypeptide has antisweet effect on tongue because of change in pH (Chattopadhyay, 1999). Gymnemasins A, B, C, D and alkaloids are the other valuable bioactive constituents found in the leaves of the herb (Suttisri et al., 1995). Similarly different kinds of saponins including gymnemagenin, gymnestrogenin, gymnemic acid, deacyl gymnemic acid, and 23-hydroxylongispinogenin are isolated from *G. sylvestre* (Sahu et al., 1996; Yoshikawa et al., 1997). Kaempferol 3-O-beta-D-glucopyranosyl-(1-->4)- alpha-L-rhamnopyranosyl-(1-->6)-beta-D-galactopyranoside are a flavonol glycoside present in aerial parts of *G. sylvestre* (Masayuki et al., 1997). Leaves of *G. sylvestre* contain carbohydrates, resins, lignin, cellulose, anthraquinone, tartaric acid, organic acid, formic acid, butyric acid, albumin, parabin, inositol alkaloids and calcium oxalate (Sinsheimer et al., 1970). The new compounds gymnemanol and aglycone have been characterized as 3 beta-16 beta-22 alpha-23-28-pentahydroxyolean-12-ene. A new pentahydroxytriterpene called gymnestrogenin has been obtained from the leaves of *G. sylvestre* (Sahu et al., 1996).



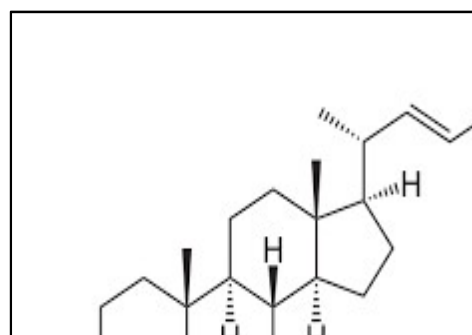
1. Gemnemagenin



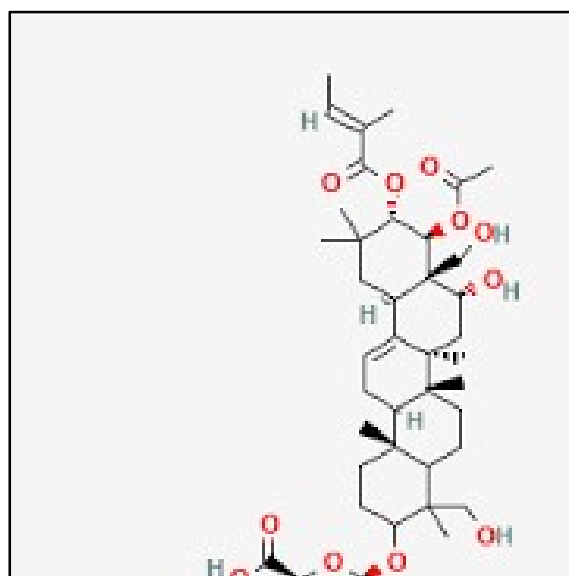
2. Gymnemanol



3. Gymnemic acid



4. Stigmasterol



5. Gymnemoside

Fig 2.

## Ethnopharmacological Importance

*G. sylvestre* is well described in Ayurveda and Sushruta as neutralizing excess sugar in body and curing of urinary diseases (Nadkarni, 1986). Ethnic peoples traditionally use the leaves of the plant for the treatment of piles and diabetes and root is applied in insect bites (Kirtikar and Basu, 1975). Juice extracted from the leaf of the plant help in pancreatic stimulation to release insulin (Persaud et al., 1999). The plant is effectively used as digestive, cardi tonic, diuretic, laxative, anthelmintic and antipyretic (Sastry, 1994; Sastry, 2005). The root bark is used as expectorant, emetic and analgesic and snakebite. In Ayurveda the plant leaf is given the patients of jaundice, glycosuria, urinary disorder, leukoderma and inflammation (Kirtikar and Basu, 1975; Chopra, 1956). In Siddha and Unani systems of medicine, the *Gymnema* leaves are used as an ingredient of different antidiabetic formulations (Anonymous, 1997; Chopra et al., 1992; Nadkarni, 1993). Some ethnic community used the plant root in snake bite (Singh et al., 2008). A herbal formulation is prepared by mixing of *Galega officinalis*, *Trigonella foenum-graecum*, *Cynara cardunculus* and *Azadirachta indica* which is effective in the treatment of diabetes and weight loss (Kerry, 2007). The herb is advised to the patient suffering from Parkinson disease (Anis et al., 2000). The extracts of root and flower are traditionally used in dysentery, vomiting and cold, and the paste prepared from fresh leaves mixed with mother milk is applied in the treatment of mouth ulcer (Ekka and Dixit, 2007; Agnihotri et al., 2004; Kirtikar and Basu, 1975). Some of the important ethnopharmacological properties of *G. sylvestre* are mentioned below.

### Antidiabetic Properties:

The scientific study of ethnopharmacological properties of *G. sylvestre* has confirmed that the plant parts are useful in diabetes and effective in the balancing of blood glucose level. The bioactive constituents of the plant stimulate to enhance insulin level by regenerating the pancreas and maintaining of homeostasis of the blood glucose (Shanmugasundaram et al., 1990; Charpurey, 1926; Paliwal et al., 2009; Patel et al., 2009). The important phytochemicals of the plant such as gurmarmine, crude saponin and five triterpene have antihyperglycemic effect without any adverse effect (Sugihar et al., 2000). These phytochemicals keep delayed in the absorption of glucose in the blood. Gurmarmine differentiates sweet and bitter tastes by interfering with the ability of taste buds on the tongue. Likewise, it attaches to the receptor present in external layer of intestine and preventing the absorption of sugar molecules in blood (Sahu et al., 1996). The hypoglycemic effect of Gymnemic acid adjoins a flow of actions starting from modulation of incretion activity that stimulates insulin secretion. The pancreatic islet cells regenerated through the stimulation of insulin to increase enzyme mediated uptake of glucose. Gymnemic acid fused with glyceraldehyde-3-phosphate dehydrogenase which is a key enzyme in glycolysis pathway (Sugihara et al., 2000; Kanetkar et al., 2007). This process reduced glucose and fatty acid assimilation in the small intestine and intervenes in the capacity of receptors in mouth and intestine to sensation of sweetness (Bone, 2002).

**Antiobesity:** *G. Sylvestre* has antiobesity properties because of Gurmarin peptide which block the sweet taste ability and controlling of blood sugar levels (Pierce, 1999). The plant extracts, hydroxycitric acid and niacin-bound chromium are helpful in antiobesity activity. Body weight is also controlled by the hexane extract of the plant (Preuss et al., 2004).

**Antimicrobial:** The ethanolic extract of leaf of *G. sylvestre* is effective against some microbes such as *Bacillus pumilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *B. subtilis* (Satdive et al., 2003; Yogisha and Raveesha, 2009). The ethanolic, ethyl acetate and chloroform extract of the aerial part of the plant are effective against *S. aureus Klebsella pneumonia*, *P. vulgaris*, *E. coli* and *P. aeruginosa*. The methanolic extract showed fair effect against *S. typhi*, *S. typhimurium* and *Salmonella paratyphi* (Paul and Jayapriya, 2009). The aqueous leaves extract is highly effective against the *Salmonella* species (Pasha et al., 2009).

**Antiarthritic:** It was reported that the aqueous and petroleum leaves extract of *G. sylvestre* are effective in joint pain and arthritis due to saponin glycosides, triterpenoids and steroids (Malik et al., 2010). The phytoconstituents isolated from the plant is effective against the joint cartilage and bone damage in chronic arthritic (Malik et al., 2010). Paw swelling is reduced because of blocking the response of inflammatory cells or inhibiting the release of mediators like cytokines (IL-1b and TNF-a), GM-CSF, interferons and PGDF from petroleum ether extracts of the plant. It also control the pain of damaged of bone and cartilage (Eric and Lawrence, 1996).

**Anti-Inflammatory:** The aqueous extract of leaf of *G. sylvestre* was observed effective against inflammations in rat (Malik et al., 2007). Saponins and tannins isolated from the plant are used as anti-inflammatory agents (Diwan et al., 1995).

**Anticaries:** Different scientific study show that methanolic, chloroform and petroleum ether leaf extracts of *G. sylvestre* at a range of concentrations are effective in dental caries caused by various kinds of gram positive cariogenic bacteria. Ethnic people used leaves of *Gymnema sylvestre* or Gurmar as a tooth powder as an anticaries (Marsh and Martin, 1992; Devi and Ramasubramaniraja, 2010).

**Antihyperlipidemic:** *G. sylvestre* has the properties of antihyperlipidemic that protect heart from coronary artery disease and atherosclerosis by reducing the level of serum cholesterol (Hardman et al., 2010; Kaushik et al., 2011). The hydroalcoholic extract of the plant leaves notably reduce the levels of lipids with increase in HDL-C as compared to high cholesterol diet control given to rats. It was observed that the hexane leaf extract of the plant improve the good cholesterol, triglyceride, LDL, and HDL levels. The hexane extract have the potential to treat the heart diseases (Rachh et al., 2010; Bishayee and Chatterjee, 1994).

**Hepatoprotective:** A study was conducted in rat where it was observed that the hydroalcoholic extract of fresh leaf of *G. sylvestre* was effective as a hepatoprotective and reduces the D-galactosamine-induced hepatotoxicity. The cells showed revival of the altered biochemical parameters towards the normal when compared to D-galactosamine treated groups in a dose-dependent manner (Srividya et al., 2010).

**Immunostimulation:** Regulation or control of the immunity which involves the enhancement or reduction in the immune responses is called immunostimulation. It is regulated by agent that enhances or suppresses its action (Trease and Evans, 1983). Leaves of *G. sylvestre* have the properties of immunostimulation (Gupta et al., 2010). Aqueous extracts of the leaf has remarkable immunostimulatory property (Malik et al., 2009).

**Wound Healing:** Flavonoids of the leaf of *G. sylvestre* has wound healing properties. It was observed in rat that the alcoholic extract of leaves heal wounds (Alam et al., 2011; Kiranmai et al., 2011; Malik et al., 2009).

**Anticancer:** Some of the studies revealed that phytoconstituents such as saikosaponins, soyasaponins and ginsenosides of *G. sylvestre* show significant anticancer activity. The same anticancer potential was reported by applying gymnemagenol of *G. sylvestre* on *HeLa* cancer cell lines in *in vitro* conditions (Jain et al., 2007). It was not toxic to the growth of normal cells under *in vitro* conditions (Khanna and Kannabiran, 2009).

### Drug Safety

*G. sylvestre* has no any toxic effect when it was taken in adequate dose. High doses of the drug may cause any side effects such as hypoglycemia, shakiness, muscular dystrophy and weakness. It was reported by few researchers that drug-induced liver injury or toxic hepatitis is cause by the crude plant materials. Gymnemic acid has complex structure and poor lipid solubility; therefore it is hard to pass through the bio-membranes for its absorption in circulatory system (Shiyovich et al., 2010).

### Conclusion

Medicinal plants are one of the important sources of basic healthcare in the developing countries as these are safer for human use. *G. sylvestre* has diverse ethnopharmacological importance in the world because of high market value and efficacy. The plant has various clinical evidences in effective treatment of diabetes and other diseases. The tradition formulations of the plant has hypoglycemic potential that increases secretion of insulin, regenerate islet cells and enhance utilization of glucose. The phytochemicals present in the plant have different pathways to treat different ailments. The different secondary metabolites have increased pharmacological potential of the plant. This review will be useful to the scientists and researchers in further investigation and development of new drugs for diabetes and other diseases.

### Future Remarks

*Gymnema sylvestre* has been used as valuable medicinal plant for ancient Ayurveda and Siddha periods by the ethnic communities. The plant species needs to be conserved as it is a source of important phytochemical constituents. The research on the large scale production of secondary metabolites and bioactive substances of the plant through cell culture will provide new dimensions to this area of research and innovation. The plant accounts for different pharmacological significance because of its use for the treatment different ailments including of diabetes. A number of clinical trials and experimental studies reported that *G. sylvestre* is a very useful source of bioactive compounds and phytoconstituents such as gymnemic acids that could be a good source of drug development in future.

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