



Ethnopharmacological Importance of *Gymnema sylvestre*

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Author's contribution

This work was carried out by author VK, she designed the study, managed the literature searches, performed the statistical analysis, wrote the protocol, and wrote the manuscript. The author read and approved the final manuscript.

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Review Article

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ABSTRACT

Gymnema sylvestre is one of the valuable medicinally important herbs that belong to family Apocynaceae. *G. Sylvester* is a woody climber mostly found in India, Srilanka, China, Indonesia, Malaysia and Tropical Africa. Traditionally the leaf of the herb is used as antidiabetic, antihelmentic, antiobesity, anti-inflammatory, hypolipidaemic, antivenom and antimicrobial. The herb is used by some ethnic community 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.

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1. INTRODUCTION

"*Gymnema sylvestre* R. Br. is an important herb belongs to the family Apocynaceae or previously called Asclepiadaceae. The herb 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" [16, 29]. 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 [42]. "Gymnemic acid is the most important constituent present in the leaves and roots of *G. sylvestre* used in the treatment of diabetes or lowering and balancing of blood sugar" [13]. Tribal people of India generally use the bark and roots of the herb as an emetic, expectorant, and analgesic for body ache and juice from the root has been acclaimed as a useful treatment for snakebite. In addition, the plant is traditionally used as hepatoprotective [55], anti-hypercholesterolemic, antimicrobial and anti-inflammatory properties [52, 34], and prevention from dental caries [20]. "It is also used in the treatment of asthma, eye complaints, digestive problems, inflammations, snake bite" [31].

"There are a large number of phytochemical constituents have been isolated from *G. sylvestre*, these are gymnemic acid, saponins, stigmasterol, quercitol and amino acid derivatives betaine, choline, and trimethylamine" [26]. 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 [76]. 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 β -amyrin" [60]. 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, the herb has significant role in most important health problems like diabetes, obesity, cardiovascular problems, osteoporosis, and asthma as well as a popular medication for number of other health ailments [64].



Fig. 1. Flowers and seeds of *G. sylvestre*

2. GEOGRAPHICAL AND BOTANICAL DESCRIPTION

G. sylvestre flourish well from 100 to 1000 m of altitude [56]. 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 [71]. "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" [35]. "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" [18]. Seeds are cotyledons, ovate, margined, ending in a silky coma, elliptic and radicle is cylindrical [41]. Flowering occurs in March to August and the fruiting season is from October onwards. The *Gymnema* species are diploid with a chromosome number of $2n = 22$ [59].

3. PHYTOCHEMICAL CONSTITUENTS

The bioactive components found in different parts including leaves of *G. sylvestre* contain gymnemic acids, gymnemasaponins, gymnemosides, gurmarin, gymnemanol, stigmasterol, d-quercitol, β -amyryn 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 gymnemasides [24]. The major phytochemicals such as gymnemic acids and gymnema saponins are parts of oleanane type of saponins while gymnemasides are dammarane saponins [30]. Acidic glycosides and anthraquinones and their derivatives are extracted from the leaves of the plant [10]. Other phytochemicals such as flavones,

anthraquinones, hentriacontane, pentatriacontane, phytin, resins, tartaric acid, formic acid, butyric acid, lupeol, β -amyryn related glycosides, stigmasterol, and calcium oxalate are found in the leaves [65]. "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*" [73]. The derivatives of gymnemic acids are several acylated tigloyl, methylbutyryl group substituted members, derived from deacylgymnemic acid (DAGA) which is a 3-O- β -glucuronide of gymnemagenin (3 β , 16 β , 21 β , 22 α , 23, 28-hexahydroxy-olean-12-ene). Gymnemic acid A comprises of gymnemic acids A₁, A₂, A₃, and A₄ and named gymnemagenin. This constituent is a D-glucuronide of hexahydroxy-triterpene that esterifies with acids [67]. Other five gymnemic acids, namely, VIII, IX, X, XI, and XII, were isolated and characterized later [74]. Gymnemasaponins III is isolated from the plant function as an antisweet compound consists of 23 hydroxylogispinogenin as the aglycone moiety glycosylated with either one or two glucose molecules at both the 23 and 28 hydroxyl groups [43]. These compounds exhibited lesser antisweet effect than those of gymnemic acids [75]. Gurmarin is extracted from *G. sylvestre*, an important 35 amino-acid peptide [21]. This polypeptide has antisweet effect on tongue because of change in pH [8]. Gymnemasins A, B, C, D and alkaloids are the other valuable bioactive constituents found in the leaves of the herb [69]. Similarly different kinds of saponins including gymnemagenin, gymnestrogenin, gymnemic acid, deacyl gymnemic acid, and 23-hydroxylogispinogenin are isolated from *G. sylvestre* [57, 72]. 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* [40]. 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 [65]. 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* [57].

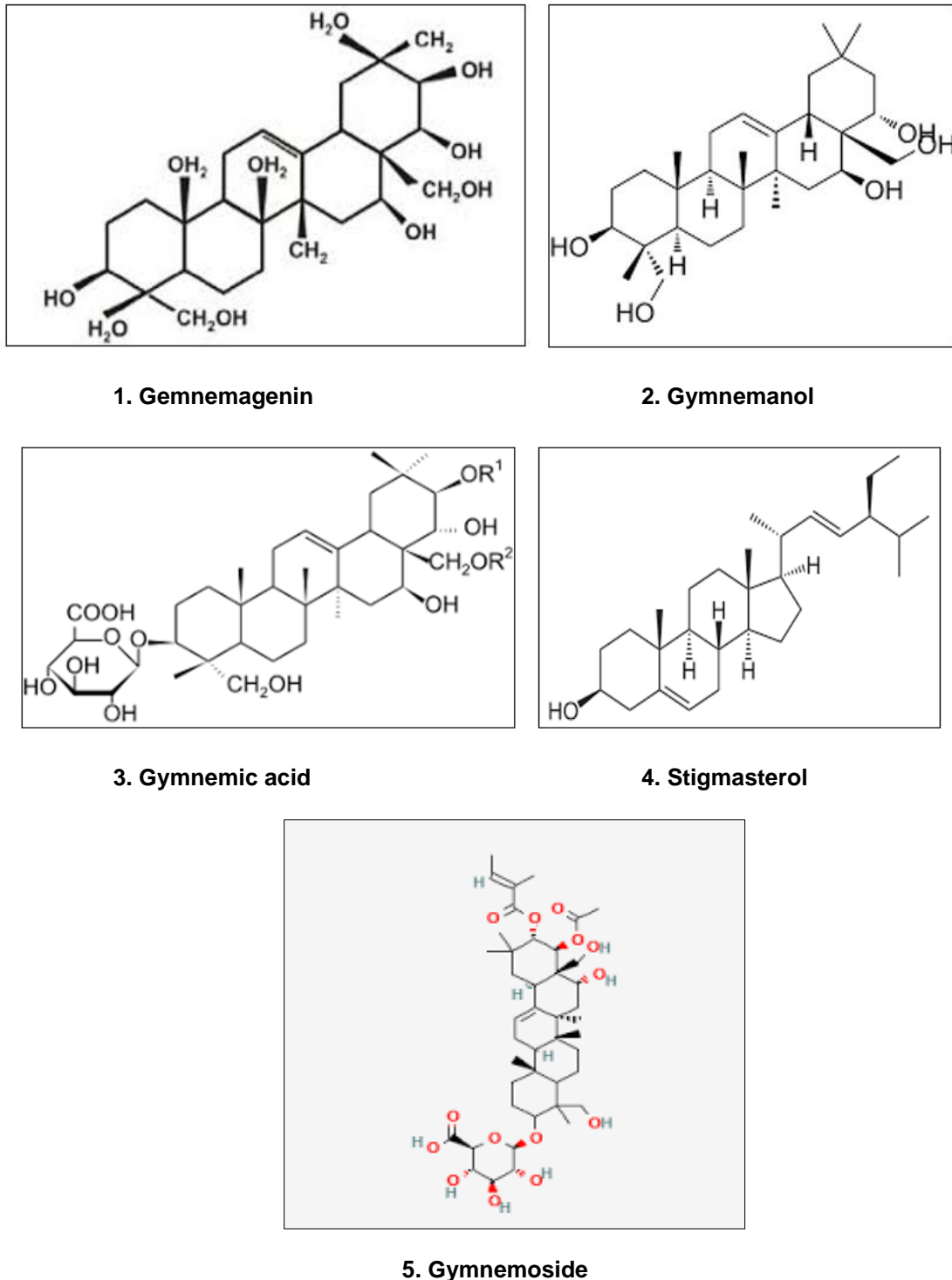


Fig. 2. Structural composition of phytochemical constituents

4. ETHNOPHARMACOLOGICAL IMPORTANCE

G. sylvestris is well described in Ayurveda and Sushruta as neutralizing excess sugar in body and curing of urinary diseases [45]. Ethnic

peoples traditionally use the leaves of the plant for the treatment of piles and diabetes and root is applied in insect bites [33]. Juice extracted from the leaf of the plant help in pancreatic stimulation to release insulin [50]. The plant is effectively used as digestive, cardiotoxic, diuretic, laxative,

anthelmintic and antipyretic [77]. 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 [33, 9]. In Siddha and Unani systems of medicine, the *Gymnema* leaves are used as an ingredient of different antidiabetic formulations [4, 9, 44]. Some ethnic community used the plant root in snake bite [63]. 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 [28]. The herb is advised to the patient suffering from Parkinson disease [3]. 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 [14, 1, 33]. Some of the important ethnopharmacological properties of *G. sylvestre* are mentioned below.

5. 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 [61, 7, 46, 48]. The important phytochemicals of the plant such as gurmarine, crude saponin and five triterpene have antihyperglycemic effect without any adverse effect [68]. These phytochemicals keep delayed in the absorption of glucose in the blood. Gurmarin 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 [57]. 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 [68, 25]. 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 [6].

Antiobesity: *G. Sylvestre* has antiobesity properties because of Gurmarin peptide which block the sweet taste ability and controlling of blood sugar levels [51]. 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 [53].

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* [58]. 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* [49]. The aqueous leaves extract is highly effective against the *Salmonella* species [47].

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 [38]. The phytoconstituents isolated from the plant is effective against the joint cartilage and bone damage in chronic arthritic [38]. 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 [15].

Anti-Inflammatory: The aqueous extract of leaf of *G. sylvestre* was observed effective against inflammations in rat [37]. Saponins and tannins isolated from the plant are used as anti-inflammatory agents [12].

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 [39, 11].

Antihyperlipidemic: *G. sylvestre* has the properties of antihyperlipidemic that protect heart from coronary artery disease and atherosclerosis by reducing the level of serum cholesterol [19, 27]. 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 [54, 5].

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 [66].

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 [70]. Leaves of *G. sylvestre* have the properties of immunostimulation [17]. Aqueous extracts of the leaf has remarkable immunostimulatory property [36].

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 [2, 32, 36].

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 [22]. It was not toxic to the growth of normal cells under *in vitro* conditions [23].

6. 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 [62].

7. 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.

8. 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.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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