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***Gymnema sylvestre* : A miracle fruit for Diabetes cure**

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ABSTRACT

Gymnema sylvestre R.Br. is a perennial shrub found over the tops of woody trees in tropical forest of India. It is a miracle plant having great anti-diabetic potential. Apart from this it has various traditional uses like in the treatment of urinary complaints, stomach problems, piles, chronic cough, breathing troubles, asthma, eye complaints, cardiopathy, constipation, jaundice, and bronchitis. An inspection of literature revealed some extraordinary pharmacological activities of this plant such as anti-obesity, anti-inflammatory, anti-microbial, hypolipidemic and anti-arthritic activity. *Gymnema* leaves have many bioactive compounds like Gymnemic acid which is responsible for its tremendous activity specially its blood glucose lowering capacity. The present review is an effort to emphasize the various traditional use as well as pharmacological uses on *G. sylvestre*.

Keywords: *Gymnema sylvestre*, Gymnemic acid, Hypolipidemic, anti-diabetic potential.

INTRODUCTION

During the last decade, the changes in life style and junk food habits have resulted in obesity and diabetes in large area of population. For the treatment of such diseases market is flooded with many synthetic anti-diabetic medicines but the long term use of these drugs has resulted in many side effects. So that natural plant based products are gaining importance. *Gymnema sylvestre* R. Br. is one of the important medicinal plants of India widely used in the treatment of *diabetes mellitus*.

Gymnema sylvestre R.Br. is an imperative remedial woody climber belonging to family Asclepiadaceae- 'The Milk Weed Family'. One special name of this plant species is 'Miracle fruit'. The name '*Gymnema*' probably derives from the Latin word meaning 'naked' and *sylvestre* means 'from the forest'.

It is native to central and western India and can be also found in tropical Africa and in Australia. The leaves are opposite, usually elliptic or ovate. Flowers are small, yellow, in auxiliary and lateral umbel in cymes. The leaves of *Gymnema* are reported to be bitter, astringent and acrid. They temporally paralyze the sensory perception of sweet and for this amazing property it is known as "GUDMAR". It is also known as 'Sugar Destroyer'. *Gymnema* leaves have the mixture of bioactive constituent's tri-terpines and saponins viz. Gymnemic acids, Gymnemagenin and Gurmarin due to them this plant represents anti-diabetic property.

Its leaves are also used in food additives against obesity. *G. sylvestre* also has Stomachic, diuretic and cough suppressant properties. The root of this plant is an antidote for snake bite used by tribals. It was traditionally used in Ayurveda. Due to these unique qualities the plant has been overexploited and the species became endangered.

Fig. 1

TAXONOMIC POSITION:

Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Gentianales
Family	Asclepiadaceae
Genus	<i>Gymnema</i>
Species	<i>sylvestre</i>



English name- Periploca of the woods, Ram's Horn

Hindi name- Gudmar

Sanskrit name- Meshashringi, Madhunashini

Vernacular name- Kavali, kalikardori (Marathi); Dhuleti, mardashingi (Gujarati); Adigam, cherukurinja (Tamil); Podapatri (Telgu) and Sannagerasehambu (Kannada) etc.

DISTRIBUTION:

Gymnema sylvestre R.Br. is distributed in whole Asia, tropical Africa, Malaysia and Srilanka. In India it grows in open wood lands and bush lands at an altitude of 100-1000 m. It is found in the Deccan peninsula, extending to parts of northern and western India.

It is abundantly found in Kota district of Rajasthan. Some area like Mukundara Hills National Park and Garadiya Mahadeva serves as a bank for this plant.

MORPHOLOGY:

Gymnema sylvestre is a large woody twinning shrub growing wildly running over the tops of high trees in forests. Stem is aerial, hard, twinning and branched. The young stems, branches are smooth and cylindrical. Leaves are elliptic, base acute to acuminate, glabrous and opposite. The 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.

FLOWERING SEASON:

April and November.

FRUITING SEASON:

Winter (December- March)

CHROMOSOME NUMBER:

$2n = 22$

BOTANICAL SYNONYMS:

Asclepias geminate Roxb., *Periploca sylvestris* Retz., *Marsdenia sylvestris* (Retz.)

MECHANISM OF ACTION (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^{2,3}. There are some possible mechanisms by which the leaves extract of *G. Sylvester* or (Gymnemic acid) possess its hypoglycemic acid effects are: 1) It initiates regeneration of islet cells of pancreas, 2) It may increases the

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 dehydrogenase¹.

PROPAGATION:

G. sylvestre is propagated naturally by seed germination. But at the time of release of seeds from their pods, seeds have low moisture content together with dry environment and less endosperm result in very low germination, thus the natural production of this plant species is very poor. Therefore, it is very essential to make an artificial propagation protocol to maintain the existence of this valuable plant. To prevent its extinct plant tissue culture technique is utilizing at large scale. (Pratibha Gupta, 2012)

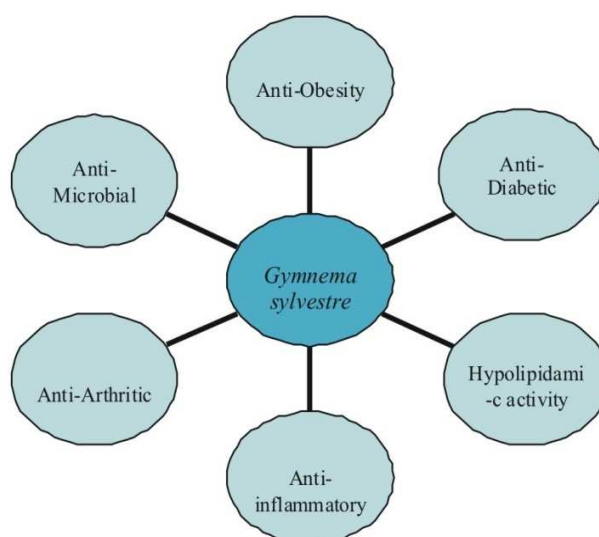
TRADITIONAL USES:

G. Sylvestre is used in folk, Ayurvedic system to treat type 1 and 2 diabetes. It is also used in the treatment of urinary complaints, stomach problems, piles, chronic cough, breathing troubles, asthma, eye complaints, cardiopathy, constipation, jaundice, and bronchitis^{4,5,6}. It is also used by trials to treat to neutralize the toxin of snake bite⁷.

PHARMACOLOGICAL USES:

G. sylvestre is one of the crucial medicinal plants, which is well known for its anti-sweetening activity. It used by Ayurveda for the treatment of Diabetes and as well as for various diseases described below (Fig. 2):-

Fig.2- Pharmacological properties of *G. sylvestre*



1. Anti-obesity activity:

G. sylvestre helps in weight loss possibly due to its ability to control blood sugar levels. It has been reported that the constituent Gurmarin peptide block the ability to taste sweet or bitter flavors and thus reduces sweet cravings^{8,9}. A standardized *G.sylvestre* extract in combination with niacin-bound chromium and hydroxycitric acid has been evaluated for anti-obesity activity by monitoring changes in body weight, body mass index (BMI), appetite, serum leptin, lipid profiles 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 levels¹⁰. Hexane fraction of *Gymnema sylvestre* used for the treatment of induced obesity in Sprague dawley rats. A significant ($P>0.001$) reduce in increased body weight, temperature due to obesity was observed after 45 day of treatment. The extract also improved the triglyceride, LDL, HDL, Cholesterol level. Observed data was found significant reduction in obese rat treated with *Gymnema* extract¹¹.

Use of *G. sylvestre* in combination with fenugreek, chitosan and vit. C was investigated on obese adults (body mass index 30 kg/m² or more) and found significant loss in body weight¹².

2. Anti-diabetic Activity:

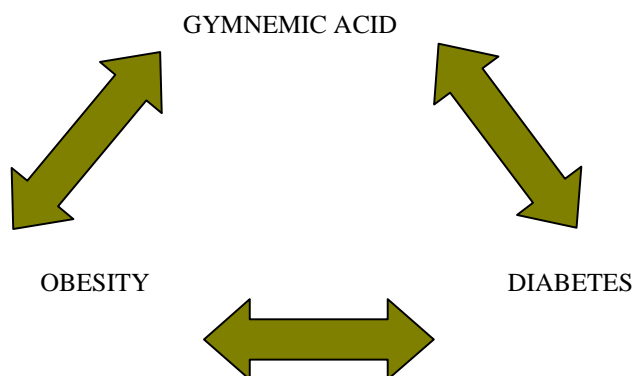
The first scientific confirmation of *G. sylvestre* use in human diabetics came almost a century back when it was demonstrated that the leaves of *G. sylvestre* reduce urine glucose in diabetics¹³. In an animal study, Paliwal *et al* have investigated that Gudmar leaf powder had positive and encouraging effects over blood glucose levels. No harmful effect was observed on the health status of the subjects and thus, it can thus be concluded that Gudmar powder is effective in lowering the fasting as well as postprandial blood glucose levels [14]. Moreover, Pankaj kishor mishra *et. al.* has investigated the anti-diabetic and hypolipidaemic activity in Alloxan induced diabetic rats by using aqueous leaf extract at variable dosage¹⁵. Similarly R. Mary Sujin *et. al.*, also checked the effect of *G. sylvestre* powder in the stomach of rats and investigated the anti-hyperglycemic action of a crude saponin fraction and five triterpene glycosides derived from the methanol extracts of *G. sylvestre*¹⁶.

N. Verma *et. al.* was evaluated Alcoholic extract of *G. sylvestre* leaf for anti diabetic activity in streptozotocin induced diabetic rats. Isolated glycoside content of this plant compared with glibenclamide reference drug at hypoglycemic level. *Gymnema* decrease blood glucose ($p < 0.05$) at 2 and 4 hr after the glucose load in glucose tolerance test¹⁷.

Linkage between Obesity, Diabetes and Bioactive compound Gymnemic acid-

The exact cause of Diabetes are still not fully understood, it is known that factors up the risk of developing different types of diabetes. For type 2, this includes being overweight or obese (having a body mass index of 30 or greater). In fact, obesity is believed to account for 80-85% of the risk of developing type 2 diabetes, while recent research suggests that obese people are up to 80 times more likely to develop type 2 diabetes. This point shows the interdependence of obesity and diabetes and suggests new term 'Diabesity'. To cure Obesity and Diabetes many scientist did various trials by using *Gymnema sylvestre*. They showed that *G. sylvestre* has Gymnemic acid with control the weight and as well as it help in the re-synthesis of insulin. The diagrammatic representation shown below will give an idea as to how the three are interconnected with each other (fig.3). Hence, it is clear that same medicine can be used for curing of both the disease. Obesity is the main consequence from the accumulation of the carbohydrates and fats. Gymnemic acids cure the binding of carbohydrates to the receptors in the intestine and hence, the "empty calories" are taken care of so that the body does not go into obese stage. The acids are also useful in curbing of diabetes by a similar mechanism as mentioned above for carbohydrate. Currently, Gymnemic acids are being sold in the form of *Gymnema* Tea, for curing obesity¹⁸.

Fig..3: Interlinking between Obesity, Diabetes and Gymnemic acid



3. Hypolipidaemic Activity:

Gymnema sylvestre possess hypolipidemic activity. Adequate doses of Leaf extract of *G. sylvestre* was given to hypolipidemic rats for two weeks. It has been found that leaf extract help in the reduction in serum triglyceride (TG), total cholesterol (TC), very low density lipoprotein (VLDL) and low density lipoprotein (LDL). The efficiency of this drug was almost similar to that of a standard lipid lowering agent^{20,19,21}.

4. Anti-Inflammatory Activity:

The aqueous extract of *G. sylvestre* was investigated for the detection of anti-inflammatory activity in rats. It observed that *G. sylvestre* produced significant role to reduce inflammation²².

The aqueous extract of *Gymnema sylvestre* leaves (GSE) tested on inflammatory models showed anti-inflammatory activity by inhibiting carrageenin-induced rat paw oedema and peritoneal ascites in mice. GSE elevated liver enzymes (Superoxide dismutase (SOD) and γ -glutamyl transpeptidase) showing protection against the release of slow- reacting substances. GSE appeared less gastro anti-inflammatory agent when compared with other anti- inflammatory agents^{23,24}.

5. Anti-arthritis activity:

The anti-arthritis activity of *Gymnema sylvestre* leaves was studied in Freund's adjuvant induced arthritic rat. In this study Diclofenac sodium was used as a standard drug. The study revealed that the aqueous extract and petroleum ether extract of *Gymnema* possessed anti-arthritis activity. This anti-arthritis activity of *G. sylvestre* leaves may be due to nature of saponin, triterpenoids and steroids²⁵.

6. Anti-microbial activity:

The aqueous and methanol leaf extract of *G. sylvestre* showed significant antibacterial and antifungal activities against the most prevalent microbes like *Staphylococcus aureus* , *Bacillus cereus*, *Candida krusei*, *Klebsiella pneumoniae*, *Candida tropicalis*, *Escherichia coli* , *Candida albicans* and *Candida kefyr*²⁶.

The aqueous methanolic extract of *G. sylvestre* leaves also showed moderate activity against the three pathogenic *Salmonella* species (*Salmonella typhi*, *S. paratyphi* and *S. typhimurium*). Out of the two extracts used, aqueous extract showed higher activity against the *Salmonella* species²⁷. Ethanolic, Chloroform and Ethyl acetate extracts of the aerial parts of *G. sylvestre* also reported to have antibacterial effects against *P. vulgaris*, *E. coli*, *Klebsella pneumoniae*, *P. aeruginosa* and *S. aureus*²⁸.

Ant- bacterial activity of hexane, chloroform and methanol extract of leaves of *Gymnema sylvestre* was evaluated against *Escherichia coli*, *Klebsiella pneumoniae*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Proteus vulgaris*, *Micrococcus luteus*, *Streptococcus pneumoniae*, *Staphylococcus aureus*. Methanolic extract showed good activity with maximum zone of inhibition while chloroform exhibited mild to moderate activity and hexane extract was found to be less active²⁹.

The antibacterial activity was determined in petroleum ether, chloroform, acetone, methanol and aqueous extracts of *G. sylvestre* using disc diffusion method. Methanol and chloroform extract showed significant activity against these microbes than petroleum ether and acetone³⁰.

ECONOMIC BENEFIT:

India is the native producer of *Gymnema sylvestre*. Now a day it became a bulk exporter of *Gymnema* products like Leaf extract and leaf powder. India supplies these products to USA, Canada, South Africa, Europe, Middle East, Taiwan, South East Asia countries. Diabetes is a fast growing disease of world so the diabetic products are in large demand. An herb from India has enabled diabetics to lower or stop taking insulin.

India is bulk exporter of *Gymnema* extract and *Gymnema* leaf powder. India supply it to various manufacturers, traders and distributors of Canada, USA. The quality of our product meet the requirement of food industry, the product specification meets the requirement of FAO/WHO standard. Big market, an herb from India has enabled diabetics to lower or stop taking insulin; about 1,395 products from 430 stores are available.

FUTUR's NEED:

Gymnema Leaves has been used by Ayurvedic clinics in India for centuries to support healthy blood sugar levels. *G. sylvestre* is a marvelous anti- diabetic plant. . It has shown experimental or clinical anti-diabetic activity and it boosts our insulin level. This plant is of greater value in the field of medicines so that the knowledge about it must be given to the generation. It must be grown on a large scale via governmental or non-governmental companies. Since each part of *G.sylvestre* has some medicinal property, so it is very much commercially exploitable. During the last few decades considerable progress has been achieved regarding its biological activity and medicinal applications. Hence, it can be chosen as a source for the development of drug for treatment of diabetes mellitus. And this use of plant will also give economical strength to India.

CONCLUSION AND DISCUSSION

In present years, traditional as well as pharmacological uses of herbal products received much attention because it is believed that they are safe for human use. So, they obviously deserve study on biotechnological scientific lines such as phytochemical isolation, characterization, toxicity level evaluation, Investigation of mechanism of action of isolated phytochemical and their clinical trials on various cell lines. These are necessary approaches in search of new treatment of diseases. Diabetes is now becoming a hazardous and most common disease of world and lot of drugs are being synthesized for its control. Many Indian medicinal herbs are being used from ancient time to control diabetes. *Gymnema sylvestre*, has an important place among such anti diabetic medicinal plants because of its good scientific evidences that it actually work in diabetes. And apart from diabetes it also work in constipation, jaundice, cardiopathy, asthma etc. so, furthermore in future study, the isolated compounds from Gudmar needs to be evaluated in scientific manner using various innovative methods 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. And further studies also required for the development of its *in-vitro* micro propagation for the conservation of this plant because of over use they have reached to endangered level.

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