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Therapeutic properties of Madhunashini

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Abstract: Madhunashini is a prodigy shrub for diabetic cure. The chief bioactive compound of Madhunashini is a group of oleanane type triterpenoid saponin known as "gymnemic acids". Apart from that, auxillary plant constituents are flavones, anthraquinones, hentriacontane, pentatriacontane, chlorophylls a and b, phytin, resins, dquercitol, tartaric acid, formic acid, butyric acid, lupeol, jamyrin related glycosides and stigmasterol. The plant extract also tests positive for alkaloids. Among these bioactive compounds of the plant gymnemic acids, gymnemagenin and gurmarin have antidiabetic, and anti inflammatory activities. Gymnemic acid molecules fill the receptor site in the absorptive upper coverings of the bowels so suppressing the absorption of sugars by the intestine and that results in lower blood sugar level thereupon enormous anti-diabetic potential. Other uses included as a panacea for rheumatism, abdomen ailments, cold, pustule, jaundice, nausea, anti-obesity. The root of the herb is a remedy for snake bite used by tribes. As a result of these exclusive qualities the shrub has been over exploited.

Keywords: Madhunashini, gymnemic acids, alkaloids, and overexploited.

INTRODUCTION

This review paper is the agglomeration of literature updates on ethnobotany, phytochemistry and pharmacological activities of a rare medicinal plant *Gymnema sylvestre* R. Br., (madhunashini or sugar destroyer). *Gymnema sylvestre* with compelling therapeutic properties has played a significant part in Indian conventional system of community medicine; Ayurveda and homeopathic system of medicine.

The binomial name of the plant is *Gymnema sylvestre* is a vital remedial woody climber belonging to family Asclepiadaceae- 'The Milk Weed Family'. One appropriate name of this plant species is 'Miracle fruit'. It is endemic to central and western India and can be also found in tropical Africa and in Australia.

Gymnema sylvestre is a large woody twinning shrub flourishing 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 for few hours.

Madhunashini plant.

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Anti-diabetic Activity

The first scientific acceptance of *G. sylvestre* use in human diabetics came around a century back when it was confirmed that the leaves of *G. sylvestre* lessen urine glucose in diabetics. Indians first used Gymnema to treat diabetes almost 2,000 years ago. The jungle Irulas inhabitants (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.

Other relevant characteristic of the oral consumption of leaves of *Gymnema sylvestre* suppress the taste of sugar upon chewing and also suppresses to detect sweet tastes (Thakur et al., 2012; Yeh et al.,2003; Sudhanshu et al., 2012; Tiwari et al.,2014). Therefore, leaf plant material is also used to lower the intense desire of consuming sugary products (Saneja et al.,2010; Rani et al.,2012; Thakur et al.,2012; Gupta and Solanki, 2015; Tiwari et al., 2014). The reduced sensitivity to sweet substances produced by *Gymnema sylvestre* might resulted from the competition at the receptor sites between glycosides and the sweet substances (Tiwari et al.2014; Thakur et al.,2012; Yeh et al.,2003)

In an animal study, Paliwal et al have investigated that Madhunashini 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 leaf powder of the plant is effective in lowering the fasting as well as postprandial blood glucose levels. Moreover, Pankaj Kishor Mishra et. al. has investigated the anti-diabetic and hypolipidemic activity in Alloxan induced diabetic rats by using aqueous leaf extract at variable dosage. 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* . 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 at 2 and 4 hr after the glucose load in glucose tolerance test.

In a study in fasted individual half were given *G. sylvestre* extract those who received supplement had less appetite for sweet foods at a subsequent meal and were more likely to limit their food intake compared to those not taking the extract.

Gymnemic acids in *G. sylvestre* can block the sugar receptors on tongue decreasing the ability to taste sweetness; this can lead to reduced sugar carvings. (P.M. Brala et al, 1983).

G. sylvestre can increase the activity of enzymes which are insulin dependent including hexokinase, glycogen synthase, glyceraldehyde 3 phosphate dehydrogenase and glucose- 6- phosphate dehydrogenase and decrease the activity of insulin independent enzymes such as glycogen phosphorylase, gluconeogenic enzymes, glucose- 6-phosphatase which also increases phosphorylase activity.(Shanmugasundaram et al, 1990).

Madhunashini Vati strengthens metabolic processes by stabilizing the endocrine system. One research finds that sugar-based molecules weaken the impact of beta-defensin peptides that fight against infections. It also promotes improved immunity to minimize the possibility of the arrival of any adverse diabetic complications.

2. **Hypolipidemic 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.

In 2014 study involving moderately obese people showed that Gymnema extract decreased bad cholesterol (LDL) by over 20% and increases good cholesterol (HDL) by 22% (Preuss H G et al, 2004).

3. 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 inflammation. The aqueous extract of *Gymnema sylvestre* leaves (GSE) tested on inflammatory models showed anti inflammatory activity by inhibiting carrageenan-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.

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. 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

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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. Hexane fraction of *Gymnema sylvestre* used for the treatment of induced obesity in Sprague dawley rats. A significant reduce in increased body weight 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 extract.

Antimicrobial activity

Naidu et al., 2013 investigated the antibacterial activity and phytochemical screening of the hexane, chloroform and methanol extracts of leaves of *Gymnema sylvestre*. The antibacterial activity was evaluated by agar well diffusion method against four Gram-negative (*Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus vulgaris*) and five Gram-positive bacteria (*Bacillus subtilis, Enterococcus faecalis, Micrococcus luteus, Staphylococcus aureus, Streptococcus pneumoniae*). Methanol extract showed good antibacterial activity with the high inhibition zones, while chloroform extract exhibited mild to moderate activity and hexane extract was found to be less active. Phytochemical screening revealed the presence of various secondary metabolites like steroids, alkaloids, phenols, flavonoids, coumarins, saponins, tannins and triterpenoids. The results of the present study suggest that leaves of *Gymnema sylvestre* can be used to treating infectious diseases caused by *Escherichia coli* and *Staphylococcus aureus.*

Anticancer activity (Cytotoxicity)

Anticancer potential of gymnemagenol on He La cancer cell lines in vitro conditions was determined. These experimental results confirmed that the isolated bioactive constituent showed high degree of inhibition of He La cancer cell lines (Tiwan et al, 2014). These activities may be due to the strong occurrence of polyphenolic compounds.

The biosynthesized silver nanoparticles and gold nanoparticles of *G. sylvestre* leaf extract exhibited substantial in vitro cytotoxic effects against Hep2 cells. Among the two nanoparticles synthesized, silver showed better cytotoxic effects in cancer cells than gold nanoparticles [13]. The gymnemagenol at 50 µg/ml showed a good cytotoxic activity (63%) in HeLa cells at 48 hrs. [14]. *G. sylvestre* extract reported a significant reduction in tumor incidence, tumor burden and cumulative number of papillomas along with a significant increase in average latent period [15].

Ethanol extract of *G. sylvestre* showed cytotoxic activity in A375 cells (human skin melanoma).

It was revealed to have significant inhibitory effect against intestinal breast cancer resistance protein (BCRP). (Tomaki et al 2010).

In a study the administration of flavonoids was found to be inhibiting BCRP and subsequently improving multidrug resistance of BCRP substrates that was induced by it (Imai et al.2004). Thus it can be suggested that inhibition of this protein by *G. sylvestre* may improve the activity of BCRP substrates, methotrexate, topotecan, and epirubicin and so on by increasing the systematic availability and absorption (Mao, 2018).

Antioxidant activity

Gymnema sylvestre exhibited potent antioxidant activity by inhibiting DPPH free radicals (Vani et al, 2016). Therefore the root and leaf extract of the plant can be used as accessible source of natural antioxidant agent. It might be due to the presence of saponins, flavonoids, phenols, and alkaloids. The ability of gymnemic acid fraction to quench nitric oxide radicals was tested in-vitro. The results indicated that gymnemic acid fraction exhibited IC_{50} 229.8µg/ml. compared with standard ascorbic acid IC_{50} value of 69.41µg/ml.

CONCLUSION

The WHO report has estimated that in developing countries more than 80% of the population depends on herbal medicines for their basic healthcare needs [11]. Synthetic medicines acquire resistance day by day for the many microorganisms and therefore it desirable to move toward herbal medicines and their combinations. Plant origin drugs have established much attention of the world for their efficacy and whispered to be safe for human use. Herbal medicine has good scope in the field of new drug therapy as well as nutraceuticals [12]. *G. sylvestre* is a multipurpose potential medicinal plant having a high market potential worldwide. *G. sylvestre* has an important place with its diverse ethanobotanical, traditional uses and economic uses in different systems of medicine not only in India but also throughout the world. It exhibits enormous hypoglycemic activity along with hypolipidemic and antioxidant property. *G. sylvestre* has clinical evidences to treat diabetes and tradition antidiabetic formulation showed their hypoglycemic potential by any one or all the mechanism of increase secretion of insulin promotes regeneration of islet cells and increase utilization of glucose. As the synthetic agents act by only one pathway but the herbal remedies have to show the various pathways due to their phytochemicals to treat diseases. This review will be beneficial to the scientists and researchers to further investigation and development of the new drug from the relevant studies.

So *Gymnema sylvestre* is a good plant for further studies in alternative medicine due its multifunctional medical properties.

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