Gymnema Sylvestre Plant
2.0 LITERATURE REVIEW OF GYMNEMA SYLVESTRE:

_Gymnema sylvestre_ is a well known antidiabetic plant. The antidiabetic activity has been mentioned in several herbal treatises and claimed to possess potent activity by the therapists of folk and traditional systems of medicine. A monograph on _Gymnema sylvestre_ is also given in Ayurvedic Pharmacopoeia. There are several antidiabetic formulations of _Gymnema sylvestre_ either alone or in combination with other herbal products. The detailed literature on various aspects of _Gymnema sylvestre_ has been reviewed and reported here:

2.1 Pharmacognosy & Botany

(Nadakarni, 1976; Wealth of India, 1956; Indian medicinal plants, 1995) _Gymnema sylvestre_ belongs to _Angiospermae_ division in plant kingdom. It is placed in the _Dicotyledoneae_ class under _Contortae_ order. It belongs to _Asclepiadaceae_ family. The botanical synonyms are _Asclepias geminata_ Roxb, _Periploca sylvestris_ Retz.

The _Gymnema sylvestre_ is called as _Gudmar_ in Hindi, _Periploca of the woods_ in English. In Kanada and Malyalam it is named as _Kadhasige_ and _Cakkarakkolli_ respectively. In Tamil and Sanskrit it is termed as _Sakkaraikkolli_ and _Madunashini_ respectively. In Telugu it is known as _Podapatra_. The leaves of _Gymnema sylvestre_ are used for various medicinal properties.
Gymnema sylvestre is a lengthy creeper possessing roots at nodes. The leaves are elliptical in shape and have acuminate tip. The base of the leaves is acute and occasionally acuminate. The upper surface is glabrous and lower surface is densely tomentose. It bears flowers which are small in axillary and with long pedicels. The calyx has lengthy lobe which is oval and obtuse in shape. The petals are light yellow in color. It has a single corona with five fleshy scales. The scales are adnate up to neck of corolla tube between lobes. Anther connection is formed into a membranous tip. There are two pollinia which are erect. There are two carpels which are unilocular. The locules are many ovuled. The follicle is long and fusiform.

Gymnema sylvestre is geographically distributed all over India and covered throughout dry forests up to 600 meters. It is vividly found in the Deccan peninsula and North and Western parts of India. The plant is widely spread in Asian countries, tropical African countries, Malaysia and Ceylon.

2.2 Phytochemistry

The important phytochemical constituents of Gymnema sylvestre include oleanane class of triterpenoids called as “gymnemic acids” (Hong-Min et al., 1992). These are acylated (tigloyl, methylbutyroyl etc.,) derivatives of deacylgymnemic acid (dAGA) which is 3-O-β-D-glucuronide 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 (Masayuki et al, 1997). It also contains flavones, anthraquinones, pentatriacontane, hentriacontane, resins, d-Quercitol, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin and its related glycosides and stigmasterol (Kuzuko et al 1989).

2.3 Pharmacology:

*Gymnema sylvestre* has been investigated by various scientists for various pharmacological activities. Among these antidiabetic activity is exhaustively studied and many reports are available.

Shanmugasundaram studied the insulinotropic activity of *Gymnema sylvestre* leaf powder in alloxan induced diabetic rabbits (RadhaShanmugasundaram et al., 1981). It was observed that there was an increase in circulating insulin levels. It was also found that the hypoglycemic action of leaf powder was not abrupt and severe but it was slow. *Gymnema sylvestre* therapy revealed that blood glucose homeostasis is associated with lowering of the serum lipid levels. The study revealed that *Gymnema sylvestre* is useful to correct metabolic derangements in rabbit liver, kidney and muscle. The same group has also studied the effect of *Gymnema sylvestre* on enzymatic levels and glucose uptake in diabetes induced rabbits. This study revealed that *Gymnema sylvestris* produced homeostasis of the blood and enhanced enzymatic activities that utilize glucose by insulin dependent pathways. There was an increase in levels of
dehydrogenase, phosphorylase and gluconeogenic enzymes. In *Gymnema sylvestre* treated animals, $^{14}$C Glucose uptake and incorporation into glycogen and protein was found to increase in muscle, kidney and liver and in comparison to control diabetic animal. (Shanmugasundaram, 1983).

Anti-diabetic effect of a leaf extract from *Gymnema sylvestre* was studied in non-insulin dependent diabetes mellitus patients by Bhaskaran, wherein a study on 22 Type-II diabetic patients was carried out using conventional oral hypoglycemic agents. GS4,- extract of *Gymnema sylvestre* leaves, at a dose of 400 mg/ day, was administered orally for 18-20 months, as a supplement to the oral conventional drugs. There was a substantial fall of glucose in the blood, glycosylated plasma proteins and glycosylated hemoglobin. This led to a decrease in the conventional drug dosage. Five out of 22 volunteers could stop the drug without disturbing the blood glucose levels in the body by using only GS4. This study suggests that GS$_4$ supplementation regenerated the beta cells of pancreas which was evident by increased insulin levels in serum. (Bhaskaran *et al.*, 1990)

Tominaga reported the effects of Seishin-renshi-in and *Gymnema sylvestre* on insulin resistance in streptozotocin induced diabetic rats. This group had also studied the anti-sweet properties of *Gymnema sylvestre* in human volunteers. The study was carried out to find the effect of an
aqueous decoction of *Gymnema sylvestre* on two amino acids, glycine and d-alanine and also on sucrose. It was found to produce the expected depression of sweetness for all three chemicals (Tominaga et al., 1995).

Gymnemoside b and gymnemic acids III, V, and VII show a little inhibitory activity against glucose absorption, but the principal constituents, gymnemic acid I and gymnemasaponin V, lacked this activity in oral glucose-loaded rats (Yoshikawa, 1997). *Gymnema sylvestre* was found to stimulate insulin release in vitro by increased membrane permeability. (Persaud et al., 1999).

Triterpene glycoside gymnemic acid IV, from *Gymnema sylvestre* at doses of 3.4-13.4mg/kg reduced blood glucose levels by 13.5-60% 6hr. after administration which was comparable to potency of glibenclamide & 13.4 mg/kg dose also increased plasma insulin levels in streptozotocin-diabetic mice. (Sugihara, 2000).

Two water soluble fractions of *Gymnema sylvestre* extract were thoroughly studied for the possible regeneration of the islets of langerhans in streptozocin-induced diabetic rats by Shanmugasundaram. It was reported that both the fractions were capable of doubling the islet number and beta cell number (Shanmugasundaram et al., 2002).

Dianex, a polyherbal formulation consisting of the aqueous extracts of 8 drugs including Gymnema sylvestre, Eugenia jambolana, etc. produced
significant hypoglycemic activity in both normal and streptozotocin induced diabetic mice (Mutarik, 2005).

Gymnemic acid IV isolated from Gymnema sylvestre leaves has antisweet, antihyperglycemic, glucose uptake inhibitory and gut glycosidase inhibitory effects. (Kimura, 2006).

John et al., reported the reduction of sucrose preference in hamsters by gymnemic acid. This study included the treatment of tongue of hamster with gymnemic acid and 0.04M sucrose with water. There was a significant decrease in sucrose preference when compared to a control treatment. This effect was similar to magnitude of electrophysiological gustatory response produced after gymnemic acid administration (John et al., 1971).

Hypolipidemic and anti atherosclerotic effects of Gymnema sylvestre were studied in experimentally induced hyperlipidemic rats. The leaf extract was administered orally at a dose of 25-100 mg/kg for 2 weeks and tested for TG, TC, VLDL and LDL levels. There was a reduction in the elevated serum triglyceride (TG), total cholesterol (TC), very-low density lipoprotein (VLDL), and low-density lipoprotein (LDL)-cholesterol in a dose dependent manner. The decreased HDL-Cholesterol and antiatherogenic index (AAI) in hyperlipidemia had become normal. The effects of the extract at 100 mg/kg dose were similar to that of standard lipid lowering drug – Clofibrate (Anupam Bishayee et al., 1994). Harry G Preuss reported the comparative
effects of Chromium, Vanadium and Gymnema sylvestre on sugar induced Blood Pressure Elevations in SHR (Harry G Preuss et al., 1998).

*Gymnema sylvestre* extracts, when administered orally to rats at 0.05-1.0 g/kg for 22 days, increased fecal excretion of neutral steroids and bile acids. The response was dose-dependent and correlated with fecal gymnemagenin. There was a significant decrease in food intake and body weight and at higher doses two animals were found to be dead (Nakamura, 1999). Jitender K Malik et al studied the anti-inflammatory activity of *Gymnema sylvestre* leaves extract in rats at a dose 200, 300 and 500 mg/kg in carrageenan induced paw oedema and cotton pellet method. The aqueous extract has shown significant activity, which is comparable to the standard drug Phenybutazone (Jitender K Malik et al., 2008).

The effect of long term-administration with *Gymnema sylvestre* on plasma and liver lipid in rats was studied by Shigematsu et al wherein they have found that oral administration of leaf extracts to rats fed with high fat diet and to rats on normal fat diet, for 3 weeks did not increase in serum cholesterol and triglyceride levels. The drug was not having any influence on bodyweight and feed intake (Shigematsu et al., 2001). Extract of *Gymnema sylvestre* with & without chitosan (C) on plasma & liver lipids (LL) & on fat accumulation in rats receiving either high or normal fat diet revealed that within the high fat diet groups, extract suppressed body weight gain & accumulation of LL to same extent as chitosan C & combined use (Shigematsu et al., 2001). The ethyl acetate extract of leaves of *Gymnema*
*Gymnema sylvestre* was found to show antimicrobial activity against *Bacillus pumilis*, *B. subtilis, Pseudomonas aeruginosa & Staphylococcus aureus* (Satdive, 2003).

Harry G Preuss et al reported the efficacy of *Gymnema sylvestre* extract in combination with (-) hydroxyl citric acid (HCA-SX) and niacin bound chromium in weight management in human volunteers (Harry G Preuss et al., 2004).

The antioxidant activity of six teas, including the aqueous extracts of green tea & Gymnema sylvestre, against DPPH radicals and LDL oxidation was assessed which revealed that Green tea showed strongest antioxidant activity among the six different teas (Ohmori et al., 2005).

Leishmanicidal activity was also reported for the saponins isolated from the leaves of *Eclipta prostrata* and *Gymnema sylvestre*. Gymnemagenol of *G. sylvestre* had shown 52% parasitic death at 1000 μg/mL concentration. The activity on other *Leishmania species, L. aethiopica* and *L. tropica* promastigotes, was not considerable (Venkateshan Gopiesh Khanna et al., 2009).

Gymnemagenol from Gymnema sylvestre and dayscyphin C from *Eclipta prostrate* have shown cytotoxic activity on HeLa cells at 50μg/mL at 48 hrs. The cell death was maximum after 96 hrs. (Venkateshan Gopiesh Khanna et al.,2009).
2.4 Patents:


3. Glucose inhibition by (3 beta, 4 alpha,16 beta)-16,23,28-trihydroxyolean-12-ene-3-yl-beta-D-glucopyranonic acid from Gymnema inodorum leaves and the preparation by aqueous acid, 1-butanol and using HPLC US Patent 5,843,909

4. Suppressing the absorption of saccharides with a Gymnema inodrum extract prepared by roasting the leaves or extracting with hot water or an alcohol US Patent 5,484,593


6. Inhibition of glucose assimilation by G. sylvestre US Patent 4,761,286
2.5 Traditional Herbal Formulations & Uses:

_Gymnema Sylvestre_ leaves are traditionally used by the South Indians as an antidiabetic and the following are some of the antidiabetic formulations of _Gymnema sylvestre_. (www.diabetes-herbs.com; www.bioporex.com)

a. DIABET GUARD – Ingredients: _Gymnema sylvestre_ Extract

b. ALFASULIN - Ingredients: _Gymnema sylvestre_ Extract and Banana Extract

c. ULTRADIA - Ingredients: _Gymnema sylvestre_ Extract and Banana Extract

d. DIABOHILS Ingredients: _Gymnema sylvestre_ Extract

e. HYPONIDD- Ingredients: _Gymnema sylvestre_ Extract Pterocarpus marsupium