GYMNEMA SYLVESTRE: A COMPREHENSIVE REVIEW

Potawale S.E.[1*], Shinde V.M.[2], Libi Anandi [1], Borade S.[1], Dhalawat H.[1], Deshmukh R.S.[3]

1. A.I.S.S.M.S. College of Pharmacy, Kennedy Road, Pune-411001.
2. Bharati Vidyapeeth's Poona College of Pharmacy, Pune-411037
3. Sinhgad College of Pharmacy, Wadgaon, Pune-411041.

Summary

Gymnema sylvestre R.Br, commonly known as "Gurmar" belonging to the family Asclepiadaceae and the genus *Gymnema,* native to the tropical forests of southern and central India, is a perennial, woody climbing plant. The main class of chemical constituents isolated from *G. sylvestre* is Gymnemic acids (a group of triterpenoid saponins) which are responsible for its anti-diabetic action. This herb is being widely used in the treatment of diabetes. Recent studies have shown that this plant is also has antiobesity, hypolipidaemic, antibacterial and anti-inflammatory potentials. This review pretends to contribute to the knowledge of the pharmacology, phytochemistry and pharmacognostical aspects of the plant.

Keywords: *Gymnema sylvestre*, pharmacology, phytochemistry, review

[*]**Address for correspondence:**
Mr. S.E. Potawale
Department of Pharmacognosy,
A.I.S.S.M.'S College of Pharmacy,
Kennedy Road, Pune-411001
Phone: +919881363782, +919270050808
E-mail: sachin_potawale@yahoo.co.in

Introduction

The future of medicine is rooted in the past, before chemists undertook to synthesize synthetic silver bullets for all that ails, and before pharmaceutical companies hitched our collective health to what has become for them a multibillion-dollar wagon[1]. In the past, almost all the medicines were from the plants, the plant being man's only chemist for ages. Herbs are staging a comeback , herbal 'renaissance' is happening all over the globe and more and more people are taking note of herbal therapies to treat various kinds of ailments in place of mainstream medicine. There are three main reasons for the popularity of the herbal medicines[2].
1) There is growing concern over the reliance and safety of drugs and surgery.
2) Modern medicine is failing to effectively treat many of the most common health conditions.
3) Many natural measures are being shown to produce better results than drugs or surgery without the side effects.
Also there is increasing evidence that many current drug therapies simply suppress symptoms and ignore the underlying disease process. In contrast, many natural products appear to address the cause of many diseases and yield superior clinical results. Unfortunately, most physicians and patients are not aware that these natural alternatives exist. But research in this field is a never ending process. Diabetes has almost become an epidemic in today's world. Thus, control of this disease has now attained utmost attention. And if such a disease has an herbal solution, then it is surely a boon to mankind. *Gymnema sylvestre*, commonly known as "Gurmar" in Hindi, has been reported in the ancient Aurvedic texts as an herbal solution for diabetes[3].

Synonyms [4]:-
It is known as "periploca of the woods" in **English**. The other synonyms of *Gymnema sylvestre* are; **Sanskrit:** Meshashringi (meaning "ram's horn"), madhunashini, **Hindi:** Gur-mar (The name "Gurmar" has been derived from the two hindi words "Gur" means sugar, "mar" means to kill, thus Gurmaar means "The sugar killer"), merasingi, **Marathi:** Kavali, kalikardori, vakundi, **Gujrathi:** Dhuleti, mardashingi, **Telugu:** Podapatri, **Tamil:** Adigam, cherukurinja**, Kannada:** Sannagerasehambu.

Taxonomy [5]:-
The plant *Gymnema sylvestre* belongs to the
Kingdom: *Plantae*
Subkingdom: *Tracheobionta*
Superdivision: *Spermatophyta*
Division: *Magnoliophyta*
Class: *Magnoliopsida*
Subclass: *Asteridae*
Order: *Gentianales*
Family: *Asclepiadaceae*
Genus: *Gymnema*

Morphology:-
Gymnema sylvestre is a perennial, woody climbing plant that grows in the tropical forests of central and southern India.[6,7] It is a large climber, rooting at nodes, leaves are elliptic, acuminate, the base is acute to acuminate, glabrous above sparsely or densely tomentose beneath; the flowers are small, in axillary and lateral umbel like cymes, pedicels are long; Calyx-lobes are long, ovate, obtuse, pubescent; Corolla is pale yellow campanulate, valvate, corona single, with 5 fleshy scales. Scales are adnate to throat of corolla tube between lobes; Anther is connective produced into a membranous tip, pollinia 2, erect, carpels 2, unilocular; locules many ovuled; Follicle long, fusiform (Figure Number 1).

Figure 1

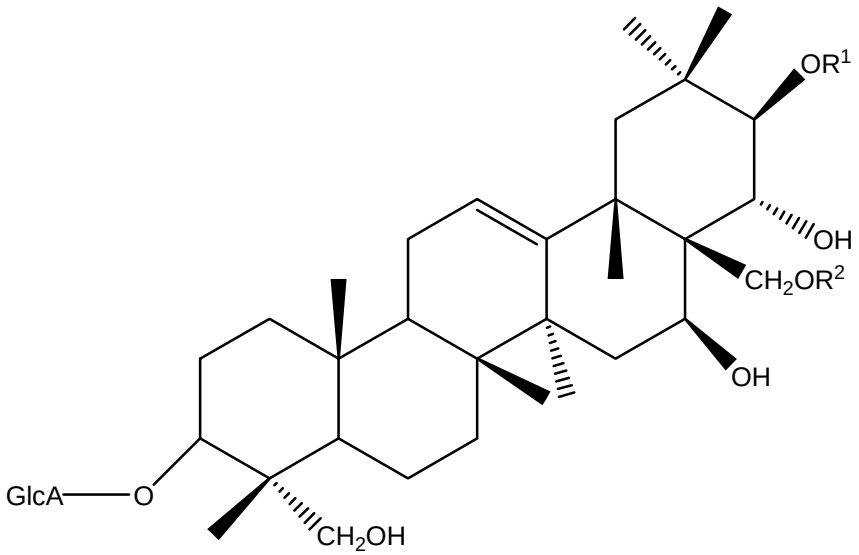
Geographical source [8]:-
It is distributed through out India, in a dry forest up to 600-meter height. It is found in Banda, Konkan, Western Ghats, and Deccan extending to the part of the northern and western India. It is distributed in Asia, Tropical Africa, Malaysia and Srilanka. It is occasionally cultivated as medicinal plant.

Phytochemistry:-
The major active components are a group of oleanane type triterpenoid saponins known as Gymnemic acid (Table number 1) [11].The latter contain several acylated (tigloyl, methylbutyroyl) derivatives of deacylgymnemic acid (DAGA) which is 3-O- b- glucuronide of gymnemagenin (3β, 16β, 21β, 22α, 23, 28-hexahydroxy-olean-12-ene [9]. The individual gymnemic acids (saponins) include gymnemic acids I-VII **(1)**, gymnemosides A-F **(2-7)** (Table number 2), gymnemasaponins1-3 **(8)**[12]. Besides six known gymnemic acids, four new tritepenoid saponins, gymnemasins A, B, C and D, isolated from the leaves of *Gymnema sylvestre* were identified as 3- O-[beta-D glucopyranosyl(1-->3)-beta-D-glucuronopyranosyl]- 22-O-tigloyl- gymnemanol, 3-O-[beta-D-glucopyranosyl (1-- >3)-beta-D-glucuronopyranosyl]-gymnemanol, 3-O-beta-Dglucuronopyranosyl- 22-O-tigloyl-gymnemanol and 3-O-beta-Dglucuronopyranosyl- gymnemanol respectively.
The aglycone, gymnemanol, **(9)** which is a new compound, was characterized as 3 beta-16 beta-22-alpha-23-28-pentahydroxyolean-12-ene[13]. Also the presence of (+) quercitol, lupeol, (-) amyrin, stigma sterol etc.

have been reported from *Gymnema sylvestre*. A new flavonol glycoside namely kaempferol 3 – O – beta - D – glucopyranosyl - (1->4) – alpha – L – rhamnopyranosyl - (1-->6) – beta - D galactopyranoside **(10)** has also found in aerial parts of *Gymnema* sylvestre[14]. The *Gymnema sylvestre* leaves contain resins, albumin, chlorophyll, carbohydrates, tartaric acid, formic acid, butyric acid, anthraquinone derivatives, inositol alkaloids, organic acid 5.5%, parabin, calcium oxalate, 7.3%; lignin, 4.8%; cellulose, 22% [15]. Leaves of this species yield acidic glycosides and anthroquinones and their derivatives[16.] Gymnestrogenin,**(11)** a new pentahydroxytriterpene from the leaves of *Gymnema sylvestre* has been reported[17]. Six oleanane-type saponins, along with two known triterpene saponins, have been isolated from the leaves of *Gymnema sylvestre*. The structures of the oleanane triterpene glycosides were characterized as longispinogenin 3-*O*-β--glucuronopyranoside, 21β-benzoylsitakisogenin 3-*O*-β- -glucuronopyranoside, 3-*O*-β--glucopyranosyl (1→6)-β--glucopyranosyl oleanolic acid 28-*O*-β--glucopyranosyl ester, oleanolic acid 3-*O*-β—xylopyranosyl (1→6) – β – glucopyranosyl (1→6) – β- glucopyranoside , 3-*O*-β—xylopyranosyl (1→6) – β – glucopyranosyl (1→6) – β - glucopyranosyl oleanolic acid 28-*O*-β-glucopyranosyl ester and 3-*O*-β-glucopyranosyl (1→6)-β-glucopyranosyl oleanolic acid 28-β-glucopyranosyl (1→6) -β- -glucopyranosyl ester[18]. Seven new dammarane-type saponins, named gymnemasides I–VII have been isolated from the leaves of Gymnema sylvestre, together with the previously known dammarane-type saponins, gypenoside XXVIII, XXXVII, LV, LXII and LXIII. Their structures were characterized by spectral data and chemical transformations[19].

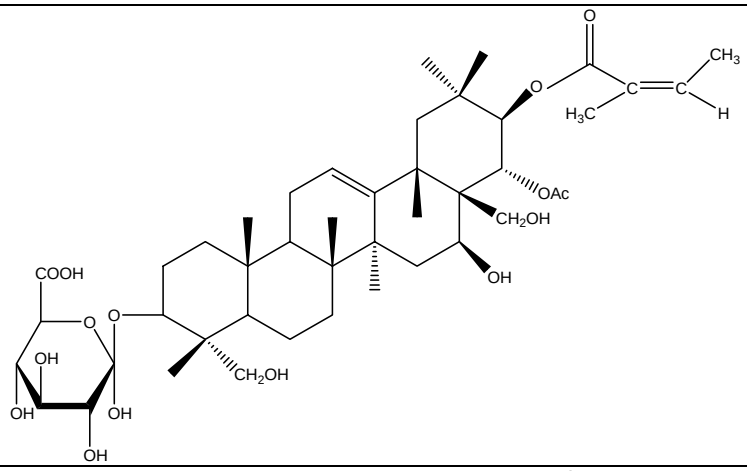
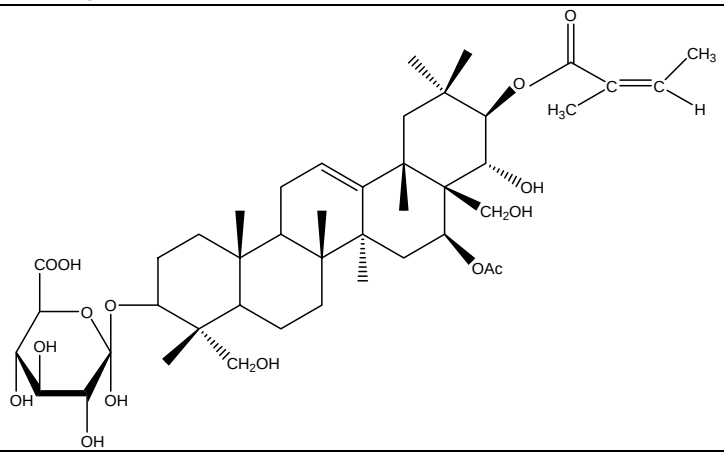
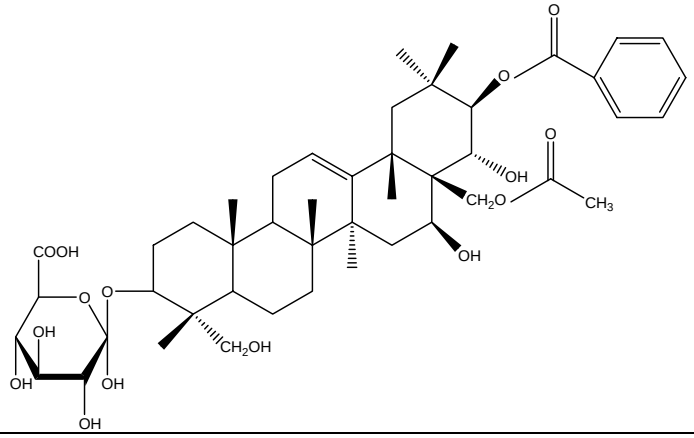
Table Number 1: Structures of gymnemic acids present in *Gymnema sylvestre*.R.Br:

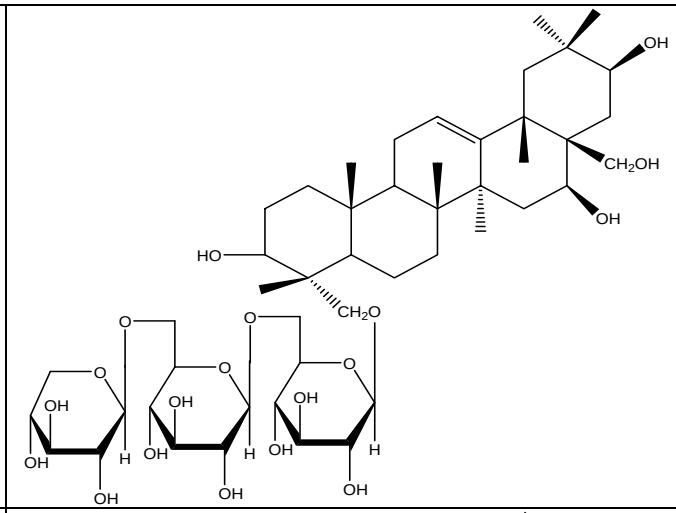
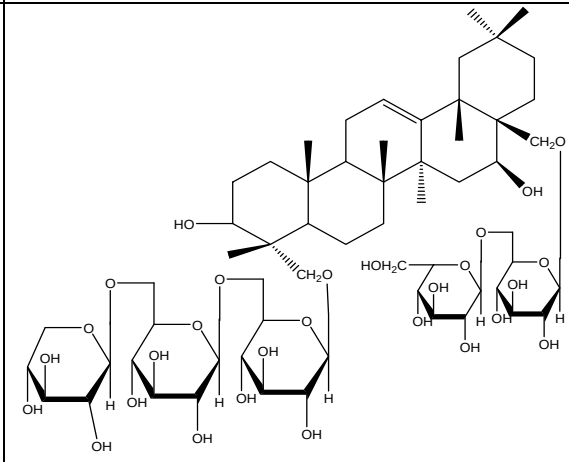
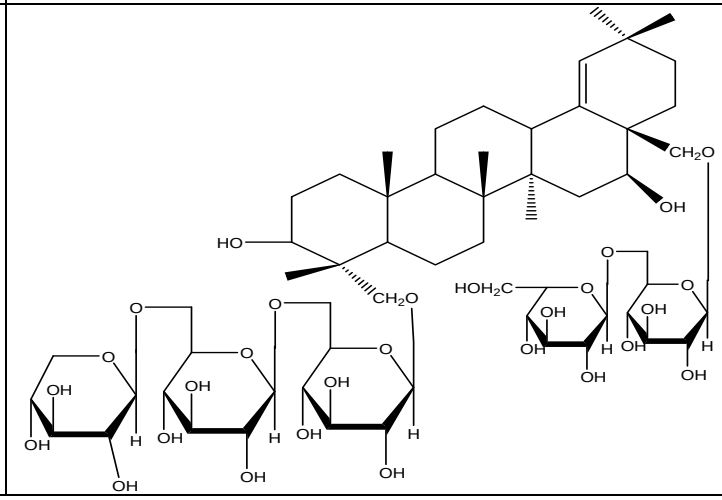
1. GYMNEMIC ACID[9]

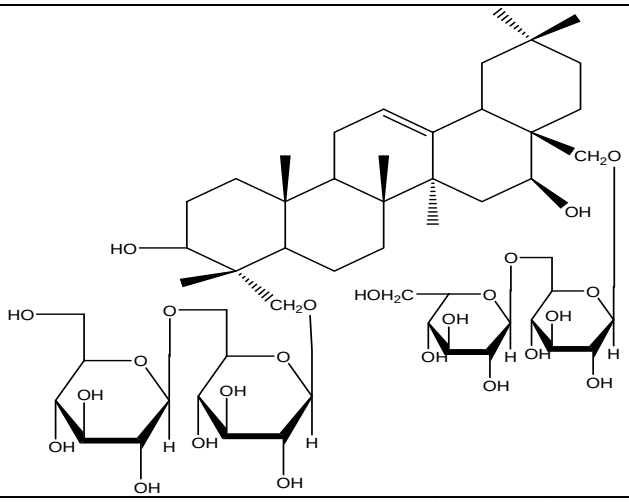
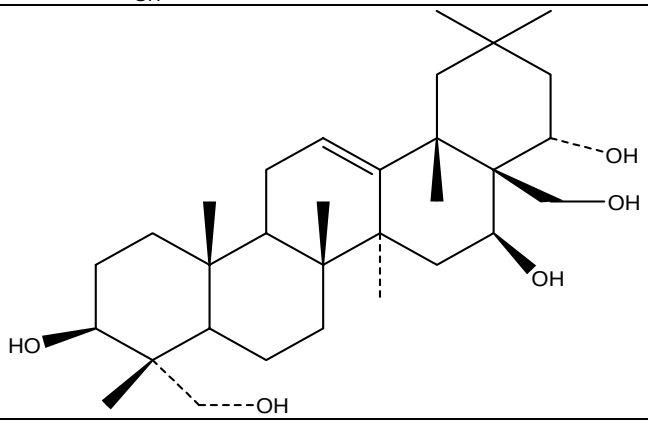
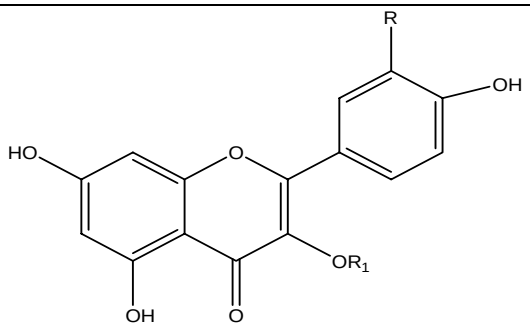
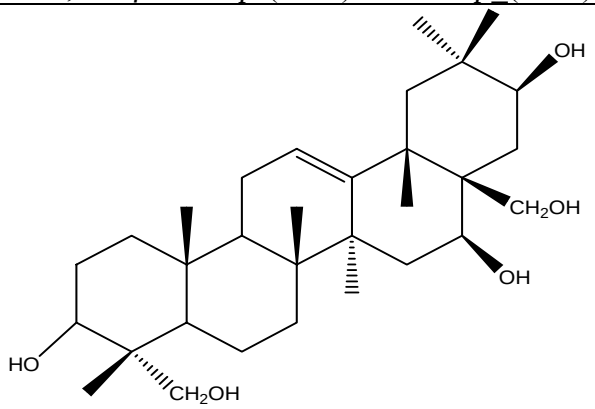


Gymnemic acid types	R^1	R^2
Gymnemic acid l	Tigloyl	Ac
Gymnemic acid ll	2-methylbutyroyl	Ac
Gymnemic acid lll	2-methylbutyroyl	H
Gymnemic acid lV	Tigloyl	H

Table 2: Structures of the chemical constituents present in *Gymnema sylvestre*.R.Br

Sr no	Chemical constituents	Structures
1.	**Gymnemoside A[10]**	
2.	**Gymnemoside B[10]**	
3.	**Gymnemoside C[10]**	

4.	**Gymnemoside D[10]**	
5.	**Gymnemoside E[10]**	
6.	**Gymnemoside F[10]**	

7.	**Gymnemasaponin V[10]**	
8.	**Gymnemanol [13]**	
9.	**Kaempferol 3-O-beta-D-glucopyranosyl-(1-->4)-alpha- L-rhamnopyranosyl-(1-->6)-beta-D galactopyranoside [14]**	 R=H, R_1=β-O-Glc*p*-(1→4)-α-L-Rha*p*_(1→6)- =β-O-Gal*p*
10.	**Gymmestrogenin[10]**	

Uses:-

Traditional uses:-

Susruta describes *Gymnema sylvestre* as a destroyer of 'Madhumeha' and urinary disorder. On account of its property to abolish the taste of sugar, it has been given the name of 'Gurmar 'meaning sugar destroyer[3].
It is bitter, astringent, acrid, thermogenic, anti-inflammatory, anodyne, digestive, liver tonic, emetic, diuretic, stomachic, stimulant, anthelmentic, alexipharmic, laxative, cardiotonic, expectorant, antipyretic and uterine tonic. It is useful in inflammations, hepatosplenomegaly, dyspepsia, constipation, jaundice, haemorrhoids, strangury renal and vesical calculi, helminthiasis, cardiopathy, cough asthma, bronchitis, intermittent fever, amenorrhoea, vitiated conditions of vata, conjunctivitis and leucoderma [20, 21].
The drug also enters into the composition of Ayurvedic preparations like *Ayaskrti, Varunadi kasaya, Varunadighrtam, Mahakalyanakaghrtam* [5].

Uses supported by animal and Clinical data:-
i) Antidiabetic activity:-
The first scientific confirmation of its use in human diabetics came almost 80 years ago when it was demonstrated that the leaves of *Gymnema sylvestre* reduced urine glucose in diabetics[22]. In 1990 a series of published studies on *Gymnema sylvestre extract* lifted this herb from interesting to revolutionary. It was shown that the administration of *Gymnema sylvestre extract* to diabetic animals not only resulted in improved glucose homeostasis, this improvement was accompanied by a regeneration of beta cells in the pancreas[21]. Studies were conducted on albino rats to establish the antidiabetic activity of *Gymnema sylvestre,* which was compared with other conventional indigenous oral antidiabetic drugs like *Coccinia indica, Pterocarpus marsupium, Momordia charantia.* The inhibitory effect was highly significant in *Gymnema sylvestre* when compared with *Pterocarpus marsupium* and *Momordia charantia* [24]. Scientific investigation of the biological effect of oral administration of the leaves revealed that *Gymnema sylvestre* therapy also increased the activities of the enzymes affording the utilisation of glucose by insulin dependent pathways: it controlled phosphorylase levels, gluconeogenic enzymes and sorbitol dehydrogenase. This valuable herb appears to correct the metabolic derangements in diabetic rabbit liver, kidney and muscle[25].
Gymnema sylvestre extract (400 mg/day) for 18-20 months was observed to reduce blood glucose in 22 non-insulin dependent diabetic patients [26].
The hypoglycaemic effect of *Gymnema sylvestre* was later studied in 16 normal subjects and in 43 mild diabetic patients. The results indicate that *Gymnema sylvestre* leaf powder has a hypoglycaemic effect comparable to tolbutamide. Serum triacylglycerol, free fatty acids and cholesterol levels was significantly decreased in diabetic patients[27]. The extended release tablet of the *Gymnema sylvestre* as a supplementary treatment in about 65 patients also showed the positive results to reduce blood glucose, glycosylated hemoglobin and glycosylated plasma proteins, thereby reducing the complications of the diabetes[28].
In vivo studies have indicated that extracts of *Gymnema sylvestre* containing gymnemic acid suppress the elevation of blood glucose levels by inhibiting glucose uptake in the intestine [29] and by increasing insulin release from the pancreas[30]. The major mode of action was proposed to be through increased permeability of the β-cell plasma membranes, leading to unregulated loss of insulin from the cells. The high saponin glycoside content of the extract is thought to be responsible for this action. In addition, a calcium $^{++}$ sensitive component is present; some degree of insulin release may occur through channel-independent calcium $^{2+}$ influx into the β-cells, perhaps through the pores formed by plasma membrane disruption[30]. Another study has indicated that the mean glycosylated hemoglobin (HbA_{1c}) decreases significantly from baseline at 6 months in a controlled trial of patients with type 1 diabetes[31].

The feeding of powdered leaves of Gymnema sylvestre in the diet of rats for 10 days prior and 15 days after i.v. Beryllium nitrate significantly protected the animals from the full fall of blood glucose seen in rats receiving beryllium nitrate alone. It as concluded that the leaves may contain a principle that could be useful as a prophylactic against beryllium toxicity[32].

Cataract is the leading cause of blindness worldwide and Diabetes has been considered to be one of the major risk factors of cataract. Agents that can inhibit aldose reductase and prevent sorbitol accumulation may be helpful to combat sugar-induced cataract. In a recently conducted study, aldose reductase inhibitory activity of Diabecon (an herbal drug used for diabetes containing *Gymnema sylvestre*) was studied together with its effect against sugar-induced lens opacity in organ culture. Diabecon aqueous extract (DAE) showed potential inhibitory activity with an IC_{50} value of 10 µg /ml against rat lens aldose reductase. It was also demonstrated that most of these effects were mainly due to *Gymnema sylvestre*[33].

ii) Antiobesity study/ Weight control:-

Gymnema helps to promote weight loss possibly through its ability to reduce cravings for sweets and control blood sugar levels. The peptide gurmarin, temporarily binds to the sweet and bitter receptors on the tongue, thereby blocking the taste sensation and thus reduces sweet cravings[34].

A standardized *Gymnema sylvestre* extract in combination with niacin-bound chromium and hydroxycitric acid has been evaluated for antiobesity activity by monitoring changes in body weight, body mass index (BMI), appetite, lipid profiles, serum leptin 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 levels[35].

Use of a dietary supplement containing *Gymnema sylvestre* in combination with glucomannan, chitosan, fenugreek, and vitamin C was investigated in obese adults (body mass index 30 kg/m^2 or more). These adults lost significantly body weight, and percentage of body fat and absolute fat mass were significantly reduced. Reduction in upper abdominal, waist, and hip circumferences also was demonstrated in this patients[36]. An increase in body weight was significantly suppressed in a long-term study of the administration of *Gymnema sylvestre* extract in rats fed a high-fat diet. However, in rats receiving a normal diet, no significant suppression of weight gain was observed[37].

iii) Hypolipidaemic activity:-

The administration of leaf extracts to hyperlipidaemic rats for two weeks have been found to have reduced the elevated serum trigylceride (TG), total cholesterol (TC), very low density lipoprotein(VLDL) and low density lipoprotein(LDL)-cholesterol in a dose dependent manner. The efficiency of this drug was almost similar to that of a standard lipid lowering agent clifibrate[38].

Also a 3-week study in rats receiving an extract of *Gymnema sylvestre* leaves and either a normal or high-fat diet showed a decrease in apparent fat digestibility and an increase in excretion of neutral sterols and acidic steroids. The Total serum cholesterol and triglycerides also were decreased significantly.[39] After 10 weeks, plasma triglycerides were lower in gymnema-fed rats than in controls, but the difference in plasma total cholesterol levels was no longer significant [37].

Other uses *Gymnema sylvestre*:-

Gymnema sylvestre leaf extract, notably the peptide 'Gurmarin', has been found to interfere with the ability of the taste buds on the tongue to taste sweet and bitter. Gymnemic acid has a similar effect. It is believed that by inhibiting the sweet taste sensation, people taking it will limit their intake of sweet foods and this activity may be partially responsible for its hypoglycemic effect[40]. Gurmarin is also reported to selectively suppress responses to sweet substances in rat [41, 42, 43] and mouse chorda tympani nerves[34, 44, 45] and gerbil taste cells[46].

The fresh leaves when chewed have the remarkable property of paralysing the sense of taste for sweet and bitter substance for some time.[5] The people from Nagari Hills of the North Arcot District, Bombay and Gujarat from India have the habit of chewing a few green leaves of *Gymnema sylvestre* in the morning in order to keep their urine clear and to reduce glycosuria. In Bombay and Madras, Vaids are known to recommend the leaves in the treatment of furunculosis and Madhumeha[47]. However the anti-sweet effect of gymnemic acid, is evident only in humans and chimpanzees but not in other experimental animals including rodents[48,49].An alcoholic extract of dried leaves have been found to exhibit antibacterial activity against *Bacillus pumilis , Bacillus subtilis , Pseudomonas aeruginosa* , and *Staphylococcus aureus* [50].
Gymnemic acids A and B have demonstrated antiviral activity against the influenza virus[37]. A possible application in the prevention of dental plaque formation has been investigated, but systematic studies are lacking to confirm this use[51].
Anti-inflammatory properties of *Gymnema sylvestre* have been demonstrated. Biochemical markers of inflammation, such as γ-glutamyl transpeptidase, superoxide dismutase, and lipid peroxides are enhanced, increasing protection against leukotrienes and free radicals and aiding rapid tissue repair and remodeling.[51.] However no clinical data is available with respect to this activity. Root has long been reputed as a remedy for snakebite. Leaves triturated and mixed with castor oil are applied to swollen glands and enlargement of internal viscera as the liver and spleen[5].

Toxicity studies:-
The LD50 of ethanol and water extract of *Gymnema sylvestre* administered intraperitoneally in mice was found to be 375mg/*kg*[52]. A 52-week study of oral-repeated-dose toxicity for the extraction powder of *Gymnema sylvestre* was conducted recently in both genders of Wistar rats. It was concluded from this study that there was no toxic effect in rats treated with *Gymnema sylvestre* at up to 1.00% in the diet for 52 weeks. The no-observable-effect level from this study is 1.00% *Gymnema sylvestre*, i.e., 504 mg/kg/day for male and 563 mg/kg/day for female as mean daily intake, for 52 weeks[53].
In an acute toxicity study in mice, no gross behavioral, neurologic, or autonomic effects were observed. The acute LD_{50} was 3990 mg/kg. The safety ratio (LD_{50} /ED_{50}) was 11 and 16 in normal and diabetic rats, respectively[54]. Systolic blood pressure was raised in spontaneously hypertensive rats fed a high sucrose diet. The clinical significance of this finding is unknown[55].The plant has not been associated with published reports of human toxicity. However, it is possible that as few as 12 tablets of some over the counter (OTC) preparations could cause a demonstrable hypoglycemic reaction in humans. Blood urea, uric acid, and hemoglobin levels remained in the normal range in patients receiving *Gymnema sylvestre* supplements in addition to their usual antidiabetic medication, suggesting the absence of hepato- or nephrotoxicity at normal doses[54]. Studies have shown that the use of *Gymnema sylvestre* for the duration of 20 months was not associated with any significant adverse drug reactions in humans[26]. Historically, it has been documented that *Gymnema sylvestre* can safely be taken for years[56]. As the safety of the *Gymnema sylvestre* is still not established in the nursing and pregnant women or the people with severe liver or kidney disorder the drug should be taken under medical supervision and it is advisable to monitor the blood glucose levels frequently[28].

Dosage:-
Pediatric Dose: No sufficient evidence is available on the use of *Gymnema sylvestre* in pediatric population. Thus, it is not recommended for pediatrics[57].
Adult Dose: The adult dosage for *Gymnema sylvestre* liquid extract is 25 to 75 ml per week [47].
In Type 1 or 2 DM patients, 200mg extract GS4 orally twice daily (or 2ml of an aqueous decoction [10g of powdered leaves per 100ml] three times daily) to be taken in conjunction with other hypoglycemic agents is recommended[58]. Currently available medical and scientific literature indicates that the dietary supplement should be standardized to 25% gymnemic acids per dose and most common dose is standardized extract of 250 mg twice a day[47].

Contraindications/ allergies:

Allergy: People allergic to plants in the Asclepiadaceae (milkweed) family may be allergic to *Gymnema sylvestre*[58]. When used in appropriate dosages, gymnema appears to be fairly safe, although extensive studies have not been performed. One obvious risk is that if gymnema is successful, it may lower blood sugar levels too far, causing a dangerous hypoglycemic reaction. For this reason, medical supervision is essential.[59] Hence; *Gymnema sylvestre* should be used cautiously diabetic patients on hypoglycemic medications. However hypoglycemia may also occur in non-diabetic patients[58].

Pregnancy and Lactation:
To date, the medical literature has not reported any adverse effects related to fetal development during pregnancy or to infants who are breast-fed. Therefore it is not recommended due to insufficient safety information[57].

Interactions:
Interactions with other herbs:
Since *Gymnema sylvestre* may decrease blood sugar levels, taking it with other blood sugar-lowering herbal products may result in hypoglycemia—blood sugar that is too low. Herbals that may reduce blood sugar include:

- Eleuthero
- Fenugreek
- Ginger (in high amounts)
- Kudzu
- *Panax Ginseng*[60]

Interactions with the prescription drugs:

Gymnema sylvestre may increase the blood sugar lowering effects of insulin and oral drugs for diabetes, such as: glimepiride, glipizide, glyburide, metformin. The cholesterol-lowering effects of drugs such as Crestor, lovastatin, Lipitor, pravastatin, and simvastatin may be increased by taking gymnema sylvestre[60]. Certain other medications, including prescription antidepressants, herbal products like St. John's wort, and salicylates (white willow and aspirin) can enhance the blood sugar-lowering effects of *Gymnema sylvestre*, whereas certain stimulants such as ephedra (Ma Huang) may reduce the effectiveness of *Gymnema Sylvestre*[61].

Standardization:-

A simple and reproducible HPTLC method for the determination of gymnemagenin in *Gymnema sylvestre* has been developed. Components were separated on pre-coated silica gel 60 F_{254} plates with chloroform: methanol (9:1) and scanned using a densitometric scanner in the UV reflectance mode at 290 nm. Linearity of determination of 1 was observed in the range 4-10 µg. The average percentage recovery of 1 from an extract was 99.09 +/- 0.29, and the content of 1 in leaves of the title plant was 1.61% (dry weight) [62]. An improved high-performance thin-layer chromatographic (HPTLC) method for the standardization of *Gymnema sylvestre* is reported. The method involves the initial hydrolysis of gymnemic acids, the active ingredients, to a common aglycone followed by the quantitative estimation of gymnemagenin[63]. A reproducible and reliable HPTLC method for the indirect determination of gymnemic acids as gymnemagenin in *Gymnema sylvestre* plant has been recently reported.

The mobile phase used was toluene: chloroform: methanol (5: 8: 3) v/v. Post-derivatzation method was used for quantification of gymnemagenin. This method was found to be more sensitive where gymnemagenin was quantified at nanogram level. The method was validated as per ICH guidelines and successfully applied for quantification of gymnemagenin from plant leaf powder, extract and poly herbal marketed formulation.[64]

Assay / Analytical methods:

Anti-saccharic assay:

It shows that 1M Gymnemic acid solution when applied to mouth completely suppresses the sense of sweetness of 0.4 M sucrose solution.[65, 66].

Foaming index:

Studies provide range of 444-333 for *Gymnema sylvestre*. In this case foaming index is calculated using formula

Foaming index = 1000/a

a= volume in ml the decoction used for preparing the dilution in the tube where foaming to a height 1 cm is observed[67].

Marker compounds of *Gymnema sylvestre*:

Gymnemic acid: Method for isolation of Gymnemic acid is available using different chemicals like petroleum ether, ethanol, 10% HCl[65, 66, 68].

HPLC methods for determination of "Total Gymnemic Acids" and Gymnemasaponins are also available.[69]

In the HPLC method for determination of gymnemasaponins a sample solution and a standard solution is prepared. Here the standard solution taken is 0.01g of gymnemagenin in 50%ethanol. Both are subjected to HPLC separately using Wakosil ll 5C18 φ4.6mm x 250mm column, Acetonitrile-water (80:20) and KH_2PO_4- water (0.1-100) as ellutents and maintaining the column at 40^0 C. Alternatively, using deacylgymnema acid dissolved in methanol as the standard, standard and the sample solutions are subjected to HPLC separately using Contrary Phase column, 0.1 % Trifluoroacetic acid: Acetonitrile mixed liquid (82:18) as ellutent [69]. TLC method for Gymnemic acid is also available in which test substance can be treated with standard on prepared silica gel 60 F_{254} plates using Chloroform : Methanol : Water (65:35:10) as solvent system. Sulphuric acid 5% solution is used as visualizing agent[65].

Trade and commerce of *Gymnema sylvestre*:

The increasing global acceptance of complimentary and alternative medicine has been the major reason in steep rise in demand for medicinal plants from countries like India, which are rich in biological diversity with 2 of 14 mega biodiversity centers of the world located within its borders. In India, the per capita annual consumption of drug is US$ 3, which is the lowest in the world since medicinal plants constitute the principle healthcare resource for the majority of population[70]. Indian exports of Gymnema extracts during 1996-1997 were reported to be Rs.65 lakhs[71].

Discussion

Since the dawn of civilization, the importance of medicinal plants in the treatment of a variety of human ailments has been immense. In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. Diabetes is now becoming a very common disease and a lot of new medicines are being synthesized for the same.

There are many popular Indian herbs used in traditional practices to cure diabetes. *Gymnema sylvestre*, commonly known as "Gurmar" in Hindi, has an important place among such antidiabetic medicinal herbs. The herb has immense potential and appears to have a broad spectrum of activity on several other ailments. It is reported in the ancient Ayurvedic texts to be a potent antidiabetic, bitter, astringent, acrid, thermogenic, anti-inflammatory, anodyne, digestive, liver tonic emetic, diuretic, stomachic, stimulant, anthelmenthics, laxative, cardiotonic, expectorant, antipyretic and uterine tonic. It is useful in jaundice, conjunctivitis, haemorrhoids, renal and vesical calculi, cardiopathy, dyspepsia, constipation, asthma, bronchitis, amenorrhoea, and leucoderma[72]. It is also important to here to highlight that *Gymnema sylvestre* extracts may be effective not only on isolation, but may actually have a modulating effect when given in combination with other herbs or drugs. G. sylvestre combines well with fenugreek, goat's rue or neem leaves for diabetes, and with globe artichoke or blue flag for weight loss. For hypercholesterolemia consider combinations of G. sylvestre with turmeric, hawthorn, Silybum, globe artichoke or garlic[47].

Although some of the uses of this herb have been studied in details to some extent, the lack of clinical trials to support its other therapeutic uses imposes several limitations for its use as a multi-purpose medicinal agent. If these traditional claims for usefulness of this plant are scientifically evaluated they may prove to be a good remedy against the same.

References

1. Duke JA. "The Green Pharmacy", Mother Earth News Online, Available at http://www.motherearthnews.com/Natural-Health/1999-12-01/Herbal-Medicine-Alternatives.aspx? (1999):page=1-8.
2. Murray ND. Natural Products vs. Drugs. Sangster's Health Centres, Natural Living Magazine Online Archives. Volume 1, Issue 1. Available at http://www.sangsters.com/nlm/natural.shtml
3. The Ayurvedic Encyclopedia, Sri Satguru Publications, Indian Book Centre, Delhi, India 1998 : 419.
4. The Wealth of India: A Dictionary of Indian Raw materials and Industrial products. Raw materials, Vol. IV, Council of Scientific and Industrial Research, New Delhi, 1956: 276–277.
5. Joy PP, Thomas J, et al. Medicinal Plants, Kerala Agricultural University, Aromatic and Medicinal Plants Research Station, 1998: 16.
6. Grover JK, Yadav S, et al. J Ethnopharmacol 2002; 81(1): 81-100.
7. Keshavamurthy KR, Yoganarasimhan SN. Flora of Coorg – Karnataka, Vimsat publishers, Bangalore; 1990:282.
8. Kirtikar K, Basu B. Indian Medicinal Plants, International Book Distributors, Deharadun, India; Vol III; 1998: 1625.
9. Hong-Min l, Fumiyuki K, et al. Chem Pharm Bull 1992; 40(6):1366-1375.
10. Masayuki Y, Toshiyuki M, et al. Chem Pharm Bull 1997; 45(12):2034-2038.
11. KuzukoY, Kayoko A, et al. Tetrahedron lett, 1989; 30(9):1130-1106.
12. Masayuki Y, Toshiyuki M, et al. Chem Pharm Bull, 1997; 45(10), 1671-1676.
13. Sahu NP, Mahato SB, et al. Phytochemistry, 1996; 41(4): 1181-5.
14. Liu X, Zhao S, et al. Carbohydrate Research. 2004; 15: 339(4):891-5.
15. Sinsheimer JE , Rao GS. J Pharm Sci 1970; 59(5): 622-28.
16. Dateo GP, Long L. J Agri. Food Chem, 1973; 21: 899–903.
17. Stocklin W. Helv Chim Acta, 1968; 51(6): 1235-42.
18. WenCai Y, Qing-Wen Z, et al. Phytochemistry, 2000; 53(8): 893-899.
19. Kazuko Y, Shigenobu A, et al. Phytochemistry, 1992; 31(1):237-241
20. Vaidyaratnam P. Indian Medicinal Plants Orient Longman Publisher, Madras, 1995; 3: 107.

21. Chopra RN, Nayar SL, et al. Glossary of Indian Medicinal plants Council of Scientific and Industrial Research, 3rd ed. New Delhi, 1992: 319-322.
22. Gharpurey KG. Indian Medical Gazette, 1926; 61: 155.
23. Shanmugasundaram ER, Gopinath KL, et al. J Ethnopharmacol 1990; 30: 265-279.
24. Gupta SS. Ind Med Res 1963; 51(4): 716-724.
25. Shanmugasundaram KR, Panneerselvam C, et al. J Ethnopharmacol 1983; 7(2): 205-234.
26. Baskaran K, Kizar B, et al. J Ethnopharmacol. 1990; 30(3): 295-300.
27. Balasubramaniam KB, Arasaratnam R, et al. J Nat Sci Coun Srilanka 1992; 20 (1), 81 – 89.
28. Joffe DJ. In Control Newsletter 2001; 76(1): 30.
29. Shimizu K, Nakajima J, et al. J Vet Med Sci 1997; 59:245-251.
30. Persaud SJ, Al-Majed H, et al. J Endocrinol 1999; 163:207-212.
31. Shanmugasundaram ER, Rajeswari G, et al. J Ethnopharmacol 1990; 30:281-294.
32. Anand OP, Mathur S. J Ethnopharmacol 1986; 18(2):143-146.
33. Moghaddam MS, Anil P, et al. J Ethnopharmacol 2005; 97(2): 397-403.
34. Ninomiya Y, Imoto T. Am J Physiol 1995; 268:1019–1025.
35. Preuss HG, Bagchi D, et al. Diabetes Obes Metab 2004; 6(3): 171-80.
36. Woodgate DE, Conquer JA. Curr Ther Res 2003 ; 64:248-262.
37. Shigematsu N, Asano R, et al. Biol Pharm Bull 2001; 24:643-649.
38. Bishayee A, Chatterjee M. Phytotherapy Res 1994; 8(2):118-120.
39. Shigematsu N, Asano R, et al. Biol Pharm Bull 2001; 24:713-717.
40. Nakamura Y, Tsumura Y, et al. J Nutr 1999; 129:1214–1222.
41. Harada S, Kasahara Y . Am J Physiol 2000;278 : 1513–R1517.
42. Imoto T, Miyasaka A, R, et al. Comp Biochem Physiol 1991; 100:309–314.
43. A. Miyasaka, T. Imoto, et al. Brain Res 1995; 676: 63–68.
44. Ninomiya Y, Inoue M, et al. Am J Physiol 1997; 272: 1002–1006.
45. Miyasaka A, Imoto T, et al. Chem Senses 1998; 23: 303–307.
46. Uchida Y, Sato T. Chem Senses 1997; 22: 163–169.
47. Gurav S, Gulkari V, et al. Pharmacog Rev 2007; 1(2): 342.
48. Hellekant G, Segerstad CH, et al. Acta Physiol Scand 1985; 124: 399–408.
49. Hellekant G, Gopal V. Acta Physiol Scand 1976; 98: 136–142.
50. Satdive RK, Abhilash P, et al. Fitoterapia 2003; 74:699-701.
51. Porchezhian E, Dobriyal RM. Pharmazie 2003; 58:5-12.
52. Bhakuni DS, Dhar ML, et al. Ind J Exp Biol 1971;9: 91-102.
53. Ogawa Y, Sekita K, et al. Shokuhin Eiseigaku Zasshi. 2004; 45(1): 8-18.
54. Chattopadhyay RR. A comparative evaluation of some blood sugar lowering agents of plant origin, J Ethnopharmacol 1999; 67:367-372.
55. Preuss HG, Jarrell ST, et al. Comparative effects of chromium, vanadium and Gymnema sylvestre on sugar-induced blood pressure elevations in SHR. J Am Coll Nutr 1998; 17:116-123.
56. Talbot SM. Gymnema/Gurmar. A Guide to Understanding Dietary Supplements. New York: Haworth Press: 2003:663-66.
57. Jellin J. Gymnema. (Drug Monograph). Natural Medicines Comprehensive Database Web site. Available at: http:www.naturaldatabase.com.
58. Basch E, Ulbricht K (eds). Gymnema (Drug Monograph). Natural Standard Web site. Available at: http:www.naturalstandard.com
59. Available at http://www.swedish.org/110912.cfm).
60. Available at http://www.drugdigest.org/DD/Interaction/ChooseDrugs/1,4109,,00.
61. Available at http://www.gymnema.net/herbal-remedies/gymnema/gymnema-side-effects.
62. Puratchimani V, Jha S. Phytochem Anal 2004; 15(3): 164-6.
63. Valivarthi SR, Raju S, et al. Phytochem Anal , 2006;17(3): 192 – 196.

64. Priti D, Kilambi P, et al. International Journal of Applied Science and Engineering 2008; 6(1): 19-28.
65. Gupta AK. Quality standards of Indian medicinal plants, Indian Council of Medical Research, Vol-I, New Delhi, 2003; 242.
66. Maeds M, Iwashita T, et al. Tetrahedron Lett 1989;30 : 1547-1550.
67. Determination of foaming index, Quality control methods for medicinal plant materials; Geneva, Switzerland, WHO, 1998, 46.
68. Toshikawa K, Nakagawa M, et al. Structure of gymnemic acids VIII-XII from *Gymnema sylvestre*, Chem Pharm Bull 1992; 40; 1779-1782.
69. Rajpal V. Standardisation of Botanicals, Vol-I, Eastern publisher, 2005; 143-146.
70. Tiwari DN. Report of the task force on conservation and suitanable use of medicinal plants, Government of India, Planning commission, 2000:90.
71. Kokate CK, Purohit AP, et al. Pharmacognosy, Nirali Prakashan, Pune, 2004; 1: 253-254.
72. Nadkarni KM. Indian Materia Medica, Popular Prakashan, Bombay, 1993; 1: 596-599.