Journal of Pharmaceutical Research International

33(58A): 365-376, 2021; Article no.JPRI.78327
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Pharmacognostical Profile of *Gymnema sylvestre* and its Anti-Hyperglycemic Activity

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i58A34128

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/78327

Review Article

Received 10 October 2021
Accepted 14 December 2021
Published 15 December 2021

ABSTRACT

In this paper explored the pharmacognostical profile of *gymnema sylvestre* and its anti-hyperglycemic activity has been documented well with references. The importance of the species in Ayurveda has been highlighted. The bioactive components like *gymnema sylvestre* has a variety of secondary metabolites, including oleanane, gymnemic acid, gymnemasides (A-F), gymnemic acid (IXVIII) homologue, gymnemic acid A1 and its derivatives, triterpenoidsaponin, al has been clearly includedin the review kaloid (Conduritol-A), polypeptide (Gurmarin), and gymnemasaponins. This study has provided the groundwork for developing a pharmacognostical profile of medicinal plant growers and collectors. The goal of this review study is to provide a regional profile of the indigenous knowledge system for medicinal plant usage and cultural behaviors related to healing. This study aids in the identification of novel ethnomedicinal plant species in the study region, which may lead to the development of new medicines. The plant toxicity test results indicated that it may be used as an alternative to diabetes therapy with no or little adverse effects. This study confirms the conventional use of indigenous plant-derived natural medicine for treating diabetes mellitus. The study also highlighted the efficacy of "Ayurveda" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable. I hope that this kind of research will be useful to future researchers as per their needs.

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Keywords: Pharmacognostical profile; gymnema sylvestre; anti-hyperglycemic activity.

1. INTRODUCTION

Natural treatments such as Ayurveda, Yunani, and Siddha have all come from the Indian subcontinent. Researcher can discover not only novel medicines, but also new lead compounds, using such systems. Despite of encouraging results of clinical studies, further research and comprehensive clinical trials are needed. Plant medications are mostly secondary plant metabolites that don't play a part in plant metabolism but are thought to be important in plant defense. The fundamental metabolic processes in plants and animals, on the other hand, show little variation. *G. sylvestre* plant preparation may be one of the alternative treatments for diabetes and obesity, though it is recognized to also have a positive effect for treating diabetes through impeding sugar binding sites also and stopping glucose molecule from collecting in the body.

Naturopathic medicine has indeed been thoroughly studied since prehistoric times and also is gaining popularity today. The Indian flora has around 45,000 plant species, many of which are medicinal [1]. Type 2 diabetes resulting in increased blood glucose after every meal. It is caused by insulin shortage or dysfunction [2]. Diabetes, in its most severe form, disrupts key bodily processes, resulting in multiorgan problems. Oral hypoglycemic medicines such as sulphonylureas and biguanides are the most common pharmaceuticals used for therapy, however these treatments have a number of negative side effects. In comparison to marketed medications and much more effective treatment and usage of health complications, herbal therapies are becoming increasingly popular due to superior results and safe use [3]. Ethnobotanists are interested in plants having anti-diabetic properties since they are regarded to offer medicinal advantages in various places and a variety of them have showed various levels of anti-hyperglycemic activity [1].

Several plant species have bioactive compounds that can be extracted and used as medicines, lead compounds, and pharmacological agents. These age-old remedies may hold the secret to resolving diabetes issues in a natural way [4]. Phytomolecules' molecular structures play a crucial role in their anti-diabetic activities. Many plant species high with terpenoids, coumarins, phenolics, flavonoids, as well as other bioactive compounds have indeed been discovered to aid in the reduction of blood sugar levels [5,6]. People from both developed and developing countries have reported all use of medicinal herbs as a cure for numerous diseases or infections, as per World Health Organization (WHO). Herbal treatments are also noted for having no side effects, being affordable, and being widely available [7]. Throughout Indian, Egyptian, Chinese, Roman, Greek, as well as Syrian literature, the first crude documented proof of the use of herbal treatment dates back about 5000 years [8,9]. The use of medicinal herbs is described in the Rigveda, Atharvaveda, Charak Samhita, and Sushruta Samhita, among other ancient Indian treatises. This implies that herbal or traditional medicines were drawn from ancient civilizations' rich practices and scientific heritage. In poor nations, the use of economic drug usage has been established as a platform for overcoming unpleasant effects and substantially limiting drug usage [10]. Identifying of medicinal herbs as well as the extracting of drugs from them is significant in the medical field. As a result, researchers have been heavily engaged in bioactive natural chemical screening. Morphoanatomical investigations and pharmacological evaluation have been proven to be significant techniques in the regular quality control of novel medicinal plants [11-13]. To establish a reasonable connection between the chemical, biological, and medicinal actions of traditional plants, valuable scientific information has been added to the choice of these herbal screening methods [14]. Furthermore, ethnomedical herbal data provide not only a novel avenue for drug development, but also significant socioeconomic advantages [15,16]. In India, there are about 17,000-18,000 blooming plant species, with 6000-7000 having therapeutic qualities. For this study, we focused on *Gymnema sylvestre* medicinal plant.

2. PHARMACOGNOSTICAL PROFILE OF *Gymnema sylvestre* AND ITS USES

2.1 Vernacular Name

Other names for *gymnema sylvestre (g. sylvestre),* Sanskrit*: Meshashringi, Madhunashini,* Hindi*: Gur-mar, Merasingi,* Marathi*: Kavali, vakundi, kalikardori,* Gujrathi: *Dhuleti, mardashingi,* Kannada*:*

Sannagerasehambu, Telugu: Podapatri, Tamil: Adigam, cherukurinja.

2.2 Botanical Description

G. sylvestre (*gymnema sylvestre*) is just a wood, growing plant which is indigenous to India and relates to Chyoanpyase group. Madhumeha (glycosuria) and other urinary diseases are destroyed by *G. sylvestre*, according to Sushruta. It was given the name gur-mar, which means sugar killer, because of its ability to eliminate the taste of sugar, and it is thought to be able to counteract excess sugar in diabetics.

A vulnerable species, *G. sylvestre* (*asclepiadaceae*), is indeed a slow-growing perennial medicinal wood climber endemic to central and peninsular India. A 5-year-old parental plant is shown in Fig. 1. It's a powerful anti-diabetic plant that's been used in ancient, ayurveda, as well as homoeopathic medicine for millennia. Asthma, eye problems, inflammations, family planning, and snakebite are all treated with it. Hepatoprotective, antihypercholesterolemic, antibacterial, as well as sweet-suppressing activities too are present. It's also been used in skin treatments, as just a feed intake inhibitor for caterpillar Prodenia eridania, and also to minimize Streptococcus mutans-caused dental caries.

G. sylvestre is a big, woody climber that is more or less pubescent. It is sometimes grown for medical purposes. Leaves are either elliptic or ovate, and also frequently elliptic/ovate (1.25–2.0 inches, 0.5–1.25 inches). The umbellate cymes of the flowers are tiny as well as yellow. Follicles can be terete or lanceolate, and can be up to three inches in length. The leaves of *G. sylvestre* have indeed been demonstrated to lower blood glucose levels, strengthen the heart, uterus, as well as cardiovascular system, and also have anti-sweet and hepatoprotective activities. In animal models, *G. sylvestre* leaf extract also had a lipid-lowering and antioxidant effect (Kang et al., 2012). These effects may also be observed in humans [17]. It is one of the most often used medicinal plants as an antidiabetic agent, either alone or in combination with other herbs.

The drug similarity of a natural or synthetic molecule is screened using in silico docking or molecular docking. In silico drug target identification covers a variety of methods for locating target proteins (Liu et al., 2010). Furthermore, researches on cell lines provide an animal-free way to study the physiology or biochemistry of cells, as well as evaluate the effects of different chemical compounds or medicines on particular cell types. They may also aid in the discovery of the drug mechanism of action.

2.3 Pharmacognostic Evaluation

Agnihotri et al. [18] performed a pharmacognostic evaluation of aerial sections of *G. sylvestre* was discovered in three different Indian sites. The foaming index, alcohol, and water soluble extractives of local samples showed minimal variance, but the botanical and physico-chemical characteristics of all the samples were quite comparable. Horseshoe-shaped petiole with three amphicribal vascular bundles, well-developed sieve tubes, anomocytic stomata only on the leaf abaxial surface, amphicribal vascular bundle fan-shaped, intraxylary phloem presence, anomocytic stomata only on the leaf abaxial surface, amphicribal vascular bundle fan-shaped, intraxylary. The only difference was in the amount of several of the chemicals. All of the samples had a TLC fingerprint profile that was almost identical.

Fig. 1. *G. sylvestre* parent plant

Patel [19] performed pharmacognostic standardization and physicochemical analysis on G leaves. Sylvestre's macro and microscopic qualities, and also particular insoluble ash as well as sulphated ash, alcohol, including water soluble extraction values for phytochemical analyses, were also investigated. A proximal powder assessment was conducted on the leaves, which also included determining extraction values, ash value, foreign material, moisture levels, dryness losses, as well as foam indices, as well as applying the soxhlet extraction method using ethanol to execute sequential solvent extraction.

2.4 Uses

The plant has showed potential to treat for overweight, Parkinsonism, hyperlipidemia, arthritis, as well as hypercholesterolemia [Malik et al., 2006], yet it is most widely seen as a naturopathic diabetic treatment [20]. Anti-inflammatory, antibacterial, as well as cancer-fighting activities are also found in plant bioactive compounds. Dental cavities, obesity, stomachaches, antibiotics, blood cleansers, in addition to rheumatism have all been treated with plant leaves [21]. Gurmarin, gymnemic acids, and gymnemasaponins, which are triterpene saponins, are responsible for the herb's pleasant inactivation. *G. sylvestre* hypoglycemic effect has been confirmed in research [Patil et al., 2012], for beryllium nitrate as well as streptozotocin-treated rats. The antihyperglycemic effects of the crude saponin component including 5 triterpene glycosides (gymnemic acids I-IV as well as gymnemasaponin V) isolated from leaf methanol extract have also been demonstrated [Sugihara et al., 2002]. A dried leaf powders possesses anti-diabetic properties as well as the ability to inactivate sugar [22]. Sylvestre is well-known for its bitterness, caustic, thermogenic, gastrointestinal, anodyne, liver medicinal, as well as anti-inflammatory leaves [Kokate, 1999].

G. sylvestre leaf has historically been used to control diabetes as well as other disorders, whereas the flowers with bark are being used to heal phlegm-related diseases [23]. Gurmar is referenced in Sushruta, an ancient Hindu medical text, as a reliever of madhumeha (glycosuria) and some other bladder disorders. The extract is designated by the letter G. Gastrointestinal, anti-inflammatory, emetic, liver restorative, diuretics, stomachic, thermogenic, anthelmintic, stimulants, cardiotonic, laxative, antipyretic, expectorant, even uterus tonic activities have been recorded for Sylvestre. Jaundice, cardiopathy, constipation, bronchitis, asthma, conjunctivitis, amenorrhea, vesical and renal calculus, dyspepsia, Parkinsonism, and leucoderma are all treated with the plant [24]. Among several medical properties documented in historical texts are antipyretic, antihelminthic, alexipharmic, astringent, cardiotonic, anodyne, diuretic, intestinal, haemorrhoids, cough dyspepsia, hepatosplenomegaly, stimulant, laxative, stomach, intermittent fever, uterine tonic, leucoderma, and jaundice. For physical pain, the bark extract is being used as an expectorant, emetic, as well as analgesic, while the root juice is being used to cure snakebite [25]. Leaf extracts can also aid with piles, colic pain, drops, phlegm, eye problems, cardiac problems, and breathing issues.

3. PHYTOCHEMISTRY AND ITS MECHANISM OF GYMNEMIC ACIDS IN ANTIDIURETIC ACTIVITY

Leaves of *G. sylvestre* comprises of inositol alkaloids, albumin, resins, carbohydrates, chlorophyll, formic acid, tartaric acid, anthraquinone derivatives, butyric acid, paraben, calcium oxalate (7.3 percent), organic acid (5.5 percent), cellulose (22percent)and lignin (4.8 percent) (Sinsheimer and Rao, 1970). Further parts of the plant include anthraquinones, flavones, pentatriacontane, hentri-acontane, as well as formic acid, chlorophylls, resins, phytin, tartaric acid, butyric acid, and also amyrin associated glycosides [26]. Gymnemic acid is also an organic acid glycoside with antisaccharide properties. It's a sophisticated mix of acidic glycosides which are all related together. The primary ingredient substance is gymnemic acid. Gymnemic acids comprise saponins having triterpenoid composition (Fig. 2).

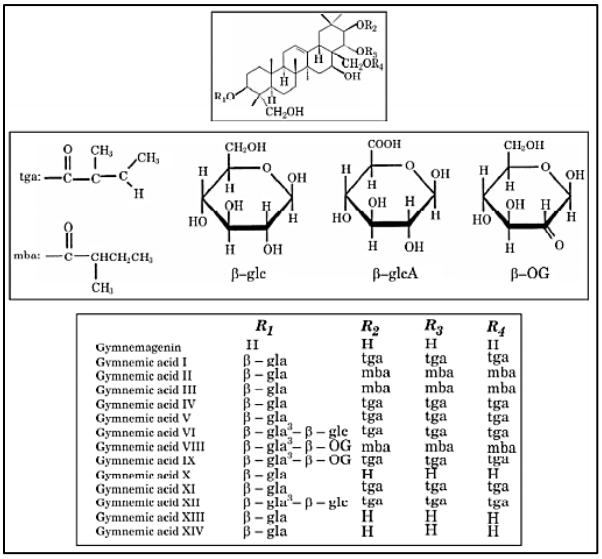
More than ten different types of gymnemic acid and related chemicals have been discovered [27]. Every gymnemic acid within leaves contains 0.0050–0.012%, as per Murakami et al. (1996). Gymnemic acid, (-) amyrin, (+) quercitol, lupeol, as well as stigma sterol have all been found in *G. sylvestre*. Kaempferol 3-O-beta-D-glucopyranosyl-(1–>4) is a novel flavonol glycoside. -(1—>6) alpha-L-rhamnopyranosyl *G. sylvestre* aerial portions have also been discovered to contain -beta-D-galactopyranoside [28]. beta- O- benzoyl- sitakisogenin3- O- betaD-glucopyranosyl (1—>3) are three oleanane-type triterpene glycosides. -beta-D-glucuronopyranoside, longispinogenin 3-O-beta-

Dglucopyranosyl (1–>3)- beta-Dglucuronopyranoside, and 29-hydroxylongispinogenin 3-O- beta-Dglucopyranosyl (1—>3)-beta- Dglucopyranosyl (1—>3)-beta-Dglucopyranosy.-beta-D-glucurono-pyranoside and the sodium salt of alternoside II were obtained from an ethanol extracts of *G. sylvestre* leaves. (Ye et al.,2001). *G. sylvestre* alcoholic excavation contains saponins. Four new triterpenoid saponins extracted from leaf of *gymnema sylvestre* have also been named as Gymnemasins A, B, C, and D which are 3-O-[beta-Dglucopyranosyl(1—>3)-beta-D-glucuronopyranosyl] 3-O-[beta-D-glucopyranosyl (1—>3)-beta-D-glucuronopyranosyl] -22-O-tigloylgymnemanol 3-O-beta-Dglucuronopyranosyl-22-O-tigloylgymnemanol, 3-O-beta-Dglucuronopyranosyl-gymnemanol, and 3-O-beta-Dglucuronopyranosyl-gymnemanol. Gymnemanol, also known as 3 beta-16 beta-22 alpha-23-28 pentahydroxyolean-12-ene, is a discovery of a new aglycone [29]. Gymnestrogenin is indeed a pentahydroxy triterpene discovered in *G. sylvestre* leaves [30]. Moreover, the 35-amino-acid peptide grumarin has also been linked to inhibitors of sweetness [31].

3.1 Gymnemic Acids Mechanism of Action

Gymnemic acids are a collection of at least 17 distinct saponins that make up gymnema's primary constituents [32]. Antidiabetic, antilipidemic, and anti-inflammatory effects have been discovered in gymnemic acids [33]. The phytochemical prevents glucose from being absorbed into the bloodstream. Gymnemic acid molecules have the same atomic configuration as glucose molecules. Consequently, gymnemic acids clog up tastes bud receptor, keeping the glucose molecule throughout the food from stimulating them. Moreover, the acids attach to receptor inside the gut's absorptive outer layers, blocking the intestine from absorbing sugar [33]. Low blood sugar is the consequence of this.

Furthermore, the acids have been discovered to stimulate the pancreas to generate insulin, which is necessary for glycemic management and the treatment of adult onset diabetes [34]. The acids may also function as a laxative, cough suppressant, and diuretic by increasing cholesterol excretion in the faeces [33]. Gymnemic acids have been shown to affect the capability of tasting receptor on the tongue to distinguish between sweet and bitter tastes. Researchers think that since the acids may block the sweet sensation, they can also block the absorption of glucose. This, however, has not been proven by study [33]. In conclusion, the phytochemical promotes antidiabetic responses by boosting insulin production, enhancing glucose consumption, encouraging pancreatic islet cell regeneration, and inhibiting glucose absorption in the small intestines (Fig. 3). Gymnemic acids are also antioxidants that may scavenge reactive oxygen species and other free radicals [35,36].



	R_1	R_2	R_3	R_4
Gymnemagenin	H	H	H	H
Gymnemic acid I	β – gla	tga	tga	tga
Gymnemic acid II	β – gla	mba	mba	mba
Gymnemic acid III	β – gla	mba	mba	mba
Gymnemic acid IV	β – gla	tga	tga	tga
Gymnemic acid V	β – gla	tga	tga	tga
Gymnemic acid VI	β – gla^3– β – glc	tga	tga	tga
Gymnemic acid VIII	β – gla^3– β – OG	mba	mba	mba
Gymnemic acid IX	β – gla^3– β – OG	tga	tga	tga
Gymnemic acid X	β – gla	H	H	H
Gymnemic acid XI	β – gla	tga	tga	tga
Gymnemic acid XII	β – gla^3– β – glc	tga	tga	tga
Gymnemic acid XIII	β – gla	H	H	H
Gymnemic acid XIV	β – gla	H	H	H

Fig. 2. Gymnemic and Gymnemagenin acids share structural similarities [27]

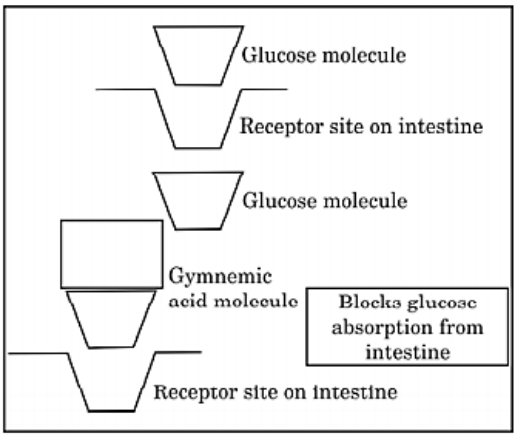


Fig. 3. Gymnemic acid competes with a gut receptor site (adopted from [33])

The hypoglycemic acid impacts of *G. sylvestre* leaf extracts (Gymnemic acid) are manifested in the three places:

1. It helps in promoting the regeneration of cell.
2. It increases insulin secretion.
3. It prevents the intestines from absorbing glucose.
4. It improves glucose consumption by boosting the activity of enzymes involved in insulin-dependent glucose consumption, including phosphorylase activities, gluconeogenic enzyme, as well as sorbitol dehydrogenase [28].

3.2 Antidiabetic Activity

This botanical main therapeutic use is as an antidiabetic drug. Since the 1930s, Gymnema has been the subject of extensive study, so both diabetes that is type 1 and type 2 have shown positive results. The leaf of *G. sylvestre* had been found to lower urinary sugar in diabetics approximately 80 years ago, which was the first scientific proof of its usage in humans. A series of research on *G. sylvestre* extract published in 1990 elevated this herb from intriguing to revolutionary. Diabetic mice were given *G. sylvestre* extract that not only enhanced glucose homeostasis, however it also led in pancreas regeneration of cell [37]. G. According to scientific studies, sylvestre medication increased the activity of enzyme which enables sugar to be utilised via insulin-dependent systems through regulating phosphorylase concentrations, gluconeogenic enzyme, as well as sorbitol dehydrogenase. This therapeutic plant seems to correct metabolic abnormalities in the liver, kidneys, and muscles of diabetic rabbits (Shanmugasundaram et al., 1983). For rats, oral feeding powders *G. sylvestre* leaves (500 mg/rat) for ten days prevented and brought injectable beryllium nitrate-induced hyperglycemia to normal in 4 days, contrasted to ten days in untreated rats. G was given to normal rats. No significant hypoglycemia was observed after 25 days of consuming sylvestre leaves (Prakash et al., 1986). Between 20 and 60 days, oral therapy with aqueous extraction from *G. sylvestre* leaf (20 mg/day) normalized the level of blood sugar on STZ diabetic rats through regeneration of cell (Shanmugasundaram et al., 1990b). Singular or chronic (32-35 days) orally oral administration extract and perhaps *G. sylvestre* leaves (1 g/kg) with non-diabetic as well as STZ (30 mg/kg) generated modest diabetic mice resulted in a significant reduction in blood sugar on the OGTT (1 g/kg), with no effect on immuno-reactive insulin (IRI) densities [38]. Different doses containing aqueous extract from 50, 100, 200, as well as 500 mg/kg administered orally to ordinary as well as a strong dose–dependent hypoglycemia impact was observed in STZ diabetic rats [39].

3.3 Antioxidant Activity

Researchers believe that oxidative stress plays a key role in the progression of diabetes and associated consequences. Non-enzymatic glycation with proteins, oxidative glucose, as well as oxidative degradation of glycated proteins all produce free radicals [40]. Consequently, a powerful anti-drug must also have antioxidant properties. In research, *gymnema sylvestre* was revealed to also have strong antioxidant activity. According to Rachh et al., this phytochemical suppresses 2,2- diphenyl-1-picrylhydrazyl

(DPPH), scavenges superoxide in addition to hydrogen peroxide, and it has an antioxidant potential of 17.54 mg/g expressed as ascorbic acid (2009). While combined with the other phytochemicals, Kaskoos et al. [36] reported however that *gymnema sylvestre* extraction had mild antioxidant property via an IC50 of 45 g/ml. If given individually or in conjunction with another phytochemical, Gymnema has also been shown to protect animals against lipid peroxidation [41]. This shows that the phytochemical can inhibit lipid peroxidation, indicating that it possesses antioxidant capabilities.

3.4 Hypolipidemic Activity

Type 2 diabetes is linked to obesity and excessive lipid levels in the body. As a result, an effective antidiabetic medication must also have hypolipidemic properties. Leaves extract given orally to hyperlipidemic rats at a dose of 25-100 mg/kg for two weeks lowered high blood TG (triglycerides), TC (total cholesterol), LDL (low density lipoprotein), and VLDL (very low density lipoprotein) cholesterol in a dose-dependent manner. With 100 mg/kg, the ability of extraction to lower TG as well as TC also in blood, as well as its antiantheroscelrotic potential, remained virtually equal to those of clofibrate, a common lipid-lowering medication [42]. For three weeks, rats were fed a *G. sylvestre* leaf extraction followed by a standard or high fat diet, there was a decrease in evident digestive enzymes as well as an improvement in acidic and neutral sterol excretion. Triglycerides as well as overall serum cholesterol too were significantly lowered [43]. Following ten weeks, *gymnema*-fed rats had lower plasma triglycerides than control, The variations of total cholesterol in plasma, on the other hand, would no longer be visible [43].

3.5 Weight Control

Gymnema may aid weight reduction by reducing sweet cravings and regulating blood sugar levels. Gurmarin is indeed a peptide which adheres to the bitter and sweet tonguereceptor, temporarily inhibiting taste and thereby lowering sweet cravings [44]. Height and weight of the body, BMI, hunger, serum lipids, serum leptin, as well as urinary fat metabolites excretion were tracked to determine the antiobesity effectiveness of a concentrated *G. sylvestre* extraction in conjunction plus niacin bound chromium as well as hydroxycitric acid. Sixty significantly obese people (ages 21-50, BMI>26 kg/m) actively participated in an 8-week randomized, double-blind, placebo-controlled human research in Elluru, India. The topics all were provided a 2000-calorie regular intake and had been instructed to walk under surveillance. After eight weeks, every individuals' body mass as well as BMI had decreased around 5-6 percent. Triglycerides, cholesterol level, lipoproteins with a low density, as well as serum leptin levels all fell, whereas high density lipoprotein concentrations as urinary fatty metabolites excretion rose. This research found that combining Gymnema extract with HCA-SX, NBC may be used as a safe and effective weight loss solution that can help people lose weight and improve their BMI while also supporting healthy blood lipid levels [45,46].

3.6 Toxicity of *Gymnema sylvestre* (*asclepiadaceae*)

While injected i.p. to rats, their LD50 of water and ethanol extraction of *G. sylvestre* been found to also be 375 mg/kg [47]. A 52-week investigation of orally recurrent dose toxicities using *G. sylvestre* extract dust been conducted for both gender in wistar rats. This research found that rats fed up to 1% *G. sylvestre* in their diet for 52 weeks had no harmful effects. With 1% *G. sylvestre*, approximately 504 mg/kg/day in male as well as 563 mg/kg/day in female as average daily intake during 52 weeks, there was no noticeable effect [48]. There were no obvious behavioral, neurologic, or autonomic effects in a mouse acute toxicity investigation. 3990 mg/kg was the acute LD50. Its safety ratio (LD50/ED50) for normal and diabetic rats has reached to 11 and 16, significantly [39]. There have been no documented instances of human toxicity linked to the plant. However, certain over-the-counter (OTC) medications may induce a detectable hypoglycemia response in people with as little as 12 pills. Patients taking *G. sylvestre* supplements in addition to their regular antidiabetic medicine had normal blood urea, uric acid, and hemoglobin levels, indicating that there was no hepato or nephrotoxicity at reasonable dosages [39]. *G. sylvestre* usage in humans over a period of 20 months has not been linked to any major adverse pharmacological responses, according to studies [17]. It has been shown in the past that *G. sylvestre* may be used safely for years (Talbot, 2003). *G. sylvestre* must be administered with medical guidance and blood sugar levels should also be evaluated on a daily basis in nursing as well as women who are pregnant, as much as anyone with serious liver and renal ailment [49].

4. AN OVERVIEW OF ADMINISTRATION, DOSAGE OF *Gymnema sylvestre* AND CONTRAINDICATIONS

Ayurvedic medicine prescribes a daily dose of 6 to 60 g of dried or powdered leaves as an infusion [50]. Adults should take 25 to 75 cc of *G. sylvestre* liquid extract each week. Some diabetic patients react rapidly, however the greatest benefits are seen after 6 to 12 months of consistent usage. Because *G. sylvestre* is available in tablet form, 8 to 12 grams of leaves equivalence per day is advised. Tablets should be swallowed whole rather than crushed since they are enterically coated. 1 to 2 ml of liquid extract per day, split into divided doses, should be administered directly to the tongue by dropper and washed off after one minute for sweet desire and sweet taste depression. This may be repeated every 2 to 3 hours. As per widely accessible scientific and medical research, the dietary supplement must be normalized at 25percent of gymnemic acids each intake, as well as the most common intake is a standard extraction of 250 mg twice each day [51].

As a nutritional supplement, the herbal extract should be taken orally. The extracts do not have a particular dosage, although an amount that does not cause toxicological consequences is advised [52]. The phytochemical is contraindicated for surgical patients, pregnant and nursing moms, and those with cardiovascular problems since it affects blood sugar, which may impede wound healing. This is due to the phytochemical's ability to decrease blood pressure [53]. People who are sensitive to *asclepiadaceae* plants may also be allergic to *G. sylvestre*. Gymnema seems to be quite safe when taken in proper doses, but no comprehensive research have been conducted. One apparent concern is that if *gymnema* is effective, it may cause severe hypoglycemia by lowering blood sugar levels too low. As a result, medical monitoring is required. As a result, diabetic individuals on hypoglycemic medicines should take *G. sylvestre* with caution. Hypoglycemia may, however, develop in non-diabetic individuals [54]. Too far, no harmful consequences linked to foetal development during pregnancy or breast-fed babies have been documented in the medical literature. As a result, owing to a lack of safety information, it is not advised [49]. While *G. sylvestre* may help reduce blood sugar levels, it can also cause hypoglycemia when used with other blood sugar-lowering herbs. Eleuthero, Fenugreek, Ginger (in large doses), Kudzu, and Panax Ginseng are herbals that may help lower blood sugar [49]. *G. sylvestre* may improve the blood glucose management impacts for insulin as well as oral diabetes drugs like glyburide, glipizide,glimepiride, as well as metformin. *Gymnema sylvestre* may enhance the cholesterol-lowering benefits of medicines including Crestor, lovastatin, Lipitor, pravastatin, and simvastatin. Antidepressants, herbal therapies including St. John wort, as well as salicylates (aspirin/white willow) may boost *G. sylvestre* blood sugar lowering advantages, but stimulant include ephedra (Ma Huang) may reduce *G. sylvestre* effectiveness [49]

5. ANTI-HYPERGLYCEMIC ACTIVITY OF *Gymnema sylvestre*

Gymnema sylvestre extract reduce blood glucose levels, although not statistically significant, according to Mulkalwar et al. [55]. *Gymnema sylvestre* extract improved the regeneration of the pancreas, liver, and kidney. *Gymnema sylvestre* has a variety of secondary metabolites, including oleanane, gymnemic acid, gymnemasides (A-F), gymnemic acid (IXVIII) homologue, gymnemic acid A1 and its derivatives, triterpenoidsaponin, alkaloid (Conduritol-A), polypeptide (Gurmarin), and gymnemasaponins, according to Laha and Paul [56].

Gymnemagenin and Gymnestrogenin, for example, have anti-hyperglycemic properties. Gymnemic acid hypoglycemic effect could be attributed to enhance pancreatic insulin output as well as islet cell regeneration. Gymnemic acid interacts to the intestinal receptor and inhibits glucose molecules from attaching to the receptor, limiting excessive glucose absorption. Gymnemic acid binds to the Na^+ glucose symporter in the intestine, limiting glucose absorption. Gymnemasaponins have anti-sweet action owing to the presence of the Acyl group, and thus they are classified as aglycone saponins. It also raises the quantity of insulin in blood plasma. [56] Gymnemagenin possesses antihyperglycemic properties.

6. CONCLUSION

Over 20 triterpene saponins have been discovered in *G. sylvestre* that form molecular complexes involving sterols, proteins, sterols, and tannins. *G. sylvestre* is very well for the

capacity to block sweet taste, and has been demonstrated to be beneficial in the treatment of obesity and diabetes. *G. sylvestre* leaf extracts have been shown to inhibit glucose absorption all through the intestinal tract and also glucan production via glucosyltransferase. Gymnema products have been developed, comprising capsule, tea, bioshape®, as well as diaxinol®, that are used to treat various types of ailments. Despite the differences in hypoglycemic impact and precise mode of action and extracts of *gymnema sylvestre* are regarded as a viable option in diabetes. The plant toxicity test results indicated that it may be used as an alternative to diabetes therapy with no or little adverse effects. This study also confirmed the conventional use through indigenous plant-origin natural remedy to treat of diabetes mellitus. *Gymnema sylvestre* has been demonstrated to have strong antidiabetic effect by reducing sugar levels, boosting insulin secretion, as well as preventing pancreatic cells from oxidative stress damages. Grover et al. [1] discovered that providing insulin-treated people solubility in water extraction of *gymnema sylvestre* leaves lowered fasting blood glucose levels and boosted insulin secretion. Further research by Bnouham et al. [57] indicated that supplementing with *gymnema sylvestre* boosts serum insulin levels, implying that the phytochemical promotes the regrowth of pancreatic beta cells for type 2 diabetes patients. The study highlights the efficacy of “Ayurveda” which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable. I hope that this research will be useful to future researchers.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
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https://www.sdiarticle5.com/review-history/78327