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Yuliany NN · Farhan AM · Ziyaroh PL · Dwinianti EF · Nihayah H · Su'udi M

Morphology and bioactive compounds of gurmar (*Gymnema sylvestre*) with potential as antidiabetics

Abstract. The medicinal plant *Gymnema sylvestre* is widely known for its ability to lower blood sugar levels. This study reviewed the physical characteristics and bioactive compounds of *G. sylvestre* sourced from different regions, emphasizing its potential as an antidiabetic agent. Morphological analysis includes leaf structure, trichome presence, and other anatomical features, which can influence the plant's chemical profile. Phytochemical analysis, performed using techniques like GC-MS, identifies key bioactive compounds such as saponins, flavonoids, and gymnemic acids, which contribute to its hypoglycemic effect. The findings indicate that regional variations can affect the concentration and presence of these compounds, suggesting that environmental factors and genetic diversity play significant roles. This comprehensive characterization supports the use of *G. sylvestre* as a natural antidiabetic treatment, which supports its potential as a source of antidiabetic-related bioactive compounds. Further research is recommended to explore the pharmacological mechanisms and optimize the extraction methods for maximum efficacy.

Keywords: Antidiabetic potential · Gymnemic acids · Medicinal plants · Morphological analysis · Phytochemical profiling

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Yuliany NN[1] · Farhan AM[1] · Ziyaroh PL[1] · Dwinianti EF[1] · Nihayah H[1] · Su'udi M[1]*
[1] Department of Biology, Faculty of Mathematics and Natural Sciences, University of Jember. Jalan Kalimantan No. 37, Tegalboto, Jember 68121, East Java, Indonesia
*Correspondence: msuudi.fmipa@unej.ac.id

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Introduction

Gymnema sylvestre is one of the plants of the Apocynaceae family that is spread across India, Africa, Australia, and China (Khan et al., 2019). *G. sylvestre* lives in several tropical forest areas and tends to like areas that are quite dry, on the surface *G. sylvestre* can be found at a maximum altitude of 600 meters above sea level. This plant has woody stems and is characteristic of its flower shape, so it is a differentiator between *G. sylvestre* and other plants (Vimala et al., 2023). Studies on the morphological characterization of *G. sylvestre* can be developed, this is due to the diverse morphological variation of *G. sylvestre* according to its habitat (Srivastava et al., 2019; Kalariya et al., 2021). One of the different variations of *G. sylvestre* is the morphology of its leaves. *G. sylvestre* leaves are green, oval, and elliptical in shape, and can grow up to 5 cm in length (Tripathi et al., 2024). The morphological diversity of *G. sylvestre* leaves, including their size and color, is believed to be influenced by environmental factors.

The leaves *of G. sylvestre* physiologically have their own uniqueness, because they are often used as traditional medicine in India and China (Khan et al., 2019). Local residents use *G. sylvestre* leaves to make herbal tea. *G. sylvestre* leaves are suspected to have bioactive compounds that have the potential to provide a certain health naturally, one of these properties is as an anti-diabetes mellitus (Gayathri et al., 2018; Thennarasi et al, 2024). *G. sylvestre* leaves contain active compounds such as pentriacontan, phytine, d-queritol, and gymnemic acid, which are known to have anti-sweet properties (Jamadagni et al., 2021). Phytochemically, *G. sylvestre* contains bioactive compounds such as saponins, flavonoids, and terpenoids which are natural remedies and have the potential to be anti-diabetic (Subramanian et al., 2020). The use of the GC-MS chromatography method is one of the recommended methods to identify volatile compounds in *G. sylvestre* (Subramanian et al., 2020).

The research of *G. sylvestre* mostly used samples from India, with the main active compound in the form of gymnemic acids having β-glucuronic groups in C-3 and hydroxyl in C-23 in the oleana triterpene framework (Pham et al., 2018). Gymnemic acids were successfully isolated and purified from *G. sylvestre* revealed that all related molecules exhibit anti-diabetic activity (Kashif et al., 2023). Kashima et al. (2017), suggested that *G. sylvestre* lowers the perception of sweetness and plays a role in slowing down gastrointestinal blood flow as well as gastric emptying, which can affect glycemic metabolism. *G. sylvestre* according to previous studies was identified to have functional proteins, namely, aldose reductase, glucokinase, fructose 1,6-bisphosphatase, cytochrome 450, dipeptidyl peptidases, 11β-hydroxysteroid dehydrogenase, and glutamine fructose-6-phosphate amido transferase. All of these proteins play an active role in sugar reduction, so *G. sylvestre* has the nickname as the "killer of sugar" (Kalariya et al., 2021; Rathore et al., 2016). There are several names for *G. sylvestre* in various languages, including *Periploca of the Woods* in English, *Meshashringi* and *Madhunashini* in Sanskrit, *Kavali* and *Kalikardori* in Marathi, *Dhuleti* and *Mardashingi* in Gujarati, *Adigam* and *Cherukurinja* in Tamil, *Podapatri* in Telugu, and *Sannagerasehambu* in Kannada (Mandal et al., 2024). *Gymnema* comes from the Hindu word "gurmar," which means "sugar killer," because Indians believe that plants of this genus can balance high blood sugar levels in people with diabetes (Ditchou et al., 2024).

Diabetes mellitus (DM) is one of the diseases caused by high sugar levels in the human body, followed by insulin deficiency (Parveen et al., 2019). Diabetes mellitus occurs when the body does not produce enough insulin or cells do not respond well to insulin, causing blood glucose levels to rise (Kumar et al., 2017). Diabetes mellitus is also said to be a chronic hyperglycemia condition characterized by disturbances in lipid, carbohydrate, and protein metabolism (Ditchou et al., 2024). Symptoms of this metabolic disorder include polyuria (frequent urination), polydipsia (excessive thirst), and polyphagia (excessive appetite) (Shanmugam et al., 2023). The interaction between genetic factors, environmental conditions, and modern lifestyle habits also influences the development of metabolic disorders, especially in type 2 diabetes (Dar et al., 2024). According to WHO data, diabetes mellitus is one of the deadly diseases with a total of 347 million people, with an estimated 7th cause of death in 2030 (Parveen et al., 2019). Based on previous research, the use of the herb *G. sylvestre* is very potential in the future to limit the use of pharmacological drugs on a regular basis. This study aims to comprehensively examine the morphological character and profile of bioactive compounds of *G. sylvestre* which have the potential as antidiabetic agents by emphasizing the relationship between morphological variations, environmental factors, and phytochemical content. The novelty of this study lies in an integrative approach based on the latest literature review that

combines morphology, anatomy, and bioactive compound profile analysis to provide a systematic understanding of the geographic variation of *G. sylvestre* and its implications for potential antidiabetic activity.

Materials and Methods

The research method approach used in this study is systematic scientific review and meta-analysis, starting with topic determination, followed by literature search, journal selection, interpretation of results, and analysis of the impact of conclusions on related fields. The literature search was conducted on scientific databases, namely PubMed, Scopus, and Google Scholar, using a combination of keywords *Gymnema sylvestre*, morphology, anatomy, phytochemical, GC-MS, bioactive compounds, and antidiabetic activity, with a publication period limit between 2015 and 2025. The inclusion criteria include original research articles and review articles that report on morphological or anatomical characters, bioactive compound profiles, phytochemical analysis, as well as the antidiabetic activity of *G. sylvestre* through in vitro, in silico, in vivo, or clinical approaches. In contrast, the articles that are irrelevant, unavailable in full text, or lack adequate scientific data were excluded from the analysis. Articles that meet the criteria were then selected in stages based on titles, abstracts, and complete texts, then descriptive data processing and integration of scientific findings to formulate conclusion that are in accordance with the research objectives. The various effects of *G. sylvestre* species extracts as antidiabetic drugs have been made an overview of newly discovered chemicals isolated from *Gymnema* species over the past five years have also been given (Kahksha et al, 2022). The study selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, which consist of identification, screening, eligibility, and inclusion (Figure 1). The literature selection process was conducted in accordance with the PRISMA principle to ensure transparency and reproducibility.

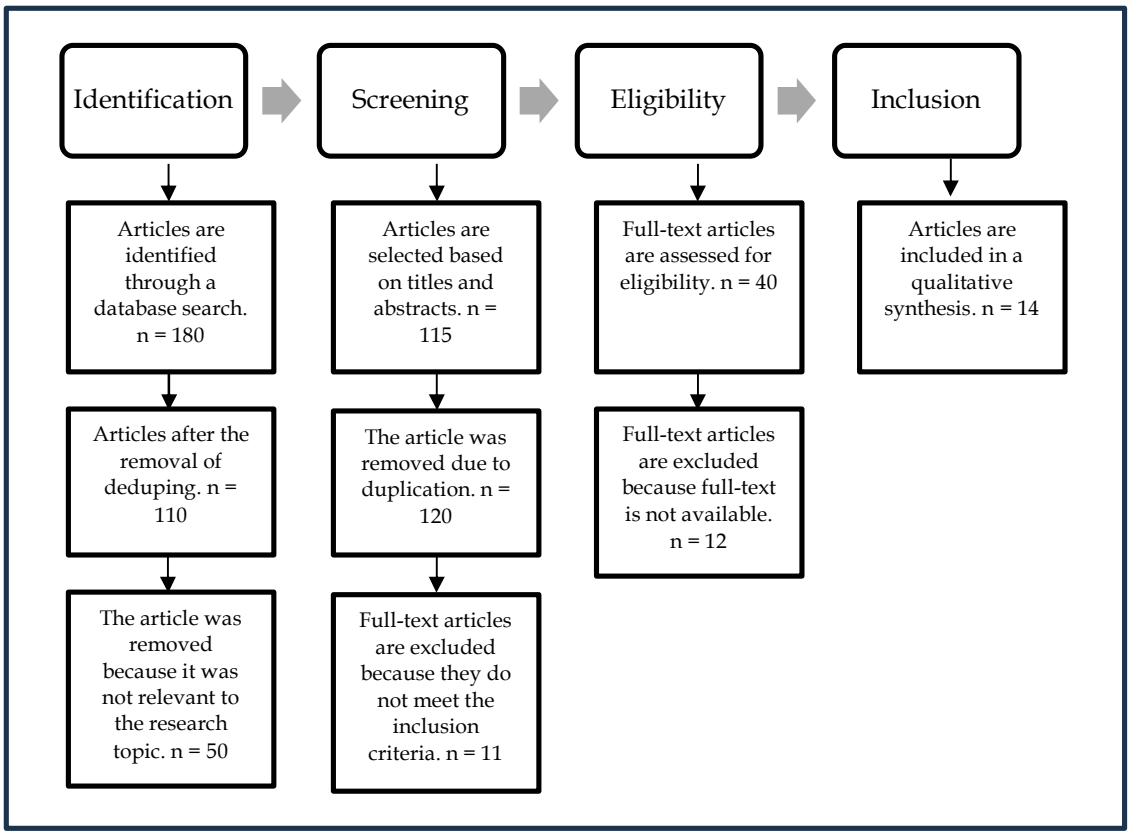

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) study flow diagram

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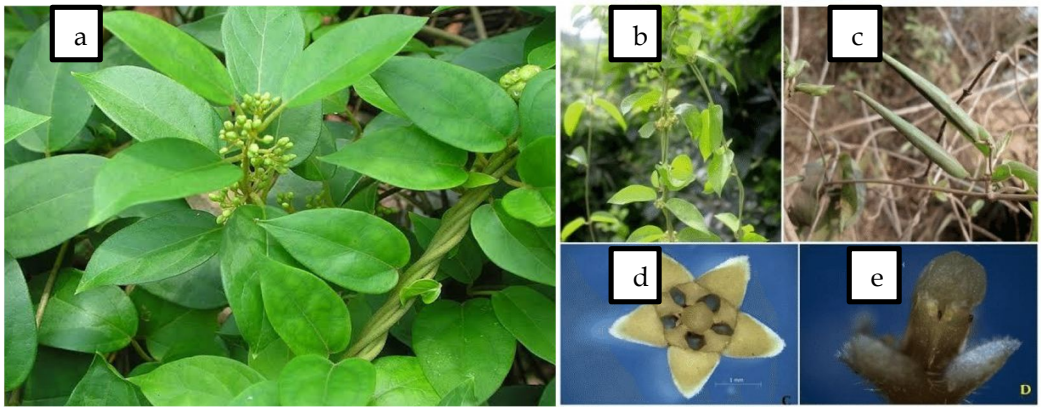

Figure 2. The morphological of *Gymnema sylvestre*. (a) Habitus; (b) Flowering twigs; (c) Fruiting twigs; (d) Light microscope (LM) images of flowers; (e) Gynostegium flowers (Source: Buddhiwant & Mali, 2022; Sinha and Mondal, 2017).

Results and Discussion

Characteristics of *G. sylvestre* *G. sylvestre* has stem organs, flowers, roots, and leaves. The trunk of *G. sylvestre* is long, slender, can creep on surrounding trees, and has a fairly hard texture in old age. The flowers in *G. sylvestre* are yellow, in multiples of 5, and have a slight trichome on the sepals. The leaves are elliptical to tapered, the upper surface is smooth, while the lower surface can be sparsely hairy to tight. Its reproductive structure is characterized by the presence of five fleshy scales on the crown, two upright pollinias, two carpels with one ovarian space, many seeds, and fruits in the form of long fusiform-shaped follicles. The following is a morphological picture of *G. sylvestre* (Figure 2).

G. sylvestre is an annual woody liana that grows in the tropical forests of central and southern India, rooted in the trunk, has elliptical to tapered leaves with varied hairy adaxial and abaxial surfaces, small pale yellow flowers in axillary or lateral umbrella-shaped inflorescences, as well as a distinctive reproductive feature in the form of a campanulate crown with five fleshy scales, two erect polynya, two single-chambered ovarian carpels with many seeds, and fruit in the form of elongated fusiform-shaped follicles (Buddhiwant and Mali, 2022). The morphological and reproductive structure characteristics of *G. sylvestre* belonging to the family Asclepiadaceae are shown through the observation of vegetative organs and flowers (Figure 2). This plant is a perennial woody climber with elliptical to oval face-to-face leaves, small pale-yellow flowers arranged in axillary inflorescences, and fruits in the form of a pair of elongated lanceolate follicles. The structure of the flower shows the characteristic of Asclepiadaceae, namely a bell-shaped crown with a single crown that has five fleshy scales, stamens with modified connectives, and a complex gynostegium (Sinha and Mondal, 2017).

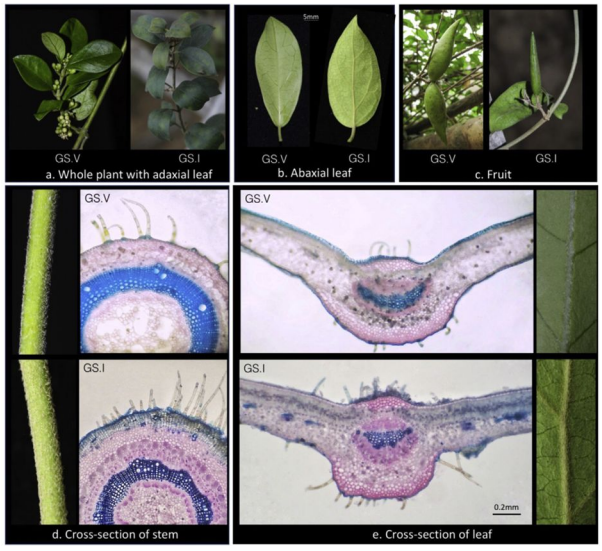

Figure 3. Morphological and anatomical characteristics of 2 varieties of *Gymnema sylvestre*. (Source: Pham et al., 2019).

Comparison of morphological and anatomical characters of *G. sylvestre* from two

geographical varieties, namely Vietnam (GS. V) and India (GS. I) (Figure 3). External morphological characters indicate differences in the overall shape of the plant, the leaf surface of the adaxial and abaxial parts, as well as the characteristics of the fruit, which indicate phenotypic variation due to differences in geographical origin. Analysis of stem anatomy through transverse incisions showed variations in the thickness of epidermal tissue, the presence and density of trichomes, and the arrangement of vascular tissue between the two varieties. In addition, the cross-sectional slices of the leaves show differences in the structure of the mesophyll and the vascular system, so the anatomical character can be used as a scientific basis for distinguishing the varieties of *G. Sylvestre* (Pham et al., 2018).

The morphological differences of *G. sylvestre* between varieties of Vietnamese and Indian origin are indicated by variations in leaf color, greenishness, and surface character of vegetative organs. The Vietnamese variety tends to have more intense green leaves and fresher-looking tissues, while the Indian variety shows relatively paler to yellowish leaves, which are related to the different growing environmental conditions, particularly temperature, humidity, and light intensity. These morphological variations reflect the physiological response of plants to changes in temperature and microclimatic conditions that affect chlorophyll content, photosynthesis efficiency, and primary metabolic processes, as reported in various plant species (Bae & Kim, 2023; Jing et al., 2016). Light intensity, light spectrum quality, and photoperiod are known to play an important role in regulating plant morphological development, photosynthetic activity, and carbon metabolism, so these differences in environmental factors are the main basis for *G. sylvestre* morphological variation between Vietnamese and Indian varieties (Tang et al., 2022).

Based on this morphology, it appears that *G. sylvestre* in areas of brighter sunlight intensity has more trichomes (Karabourniotis et al., 2020). The presence of trichomes is very important for *G. sylvestre*, they can functionally help the adaptation process of the plant to the environment (Guan et al., 2022; X. Wang et al., 2021). Theoretically, plants living in warmer regions have a higher number of trichomes, which is in line with the function of trichomes, namely to minimize water evaporation in plants (Wang et al., 2021), so that *G. sylvestre* in areas with fairly high sunlight intensity does not lose too much water. The presence of water in a plant is very important to be used in metabolic processes such as photosynthesis, this also applies to *G. sylvestre* (Wu et al., 2022). The difference in the number of trichomes in *G. sylvestre* is unique in itself to be studied in more depth. Trichomes are functionally intended to prevent water evaporation in plants, but trichomes also have a correlation with the activity of bioactive compounds in plants (Guan et al., 2022).

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Table 1. The list of major bioactive compounds identified in *G. sylvestre* from India was determined using GC-MS analysis

Peak	Compound	RT (min)	%total	Activity	Reference
1.	n-Hexadecanoic acid	28.814	5.186	Anticancer, antidiabetic	(Aslam et al., 2024; Ravi & Krishnan, 2016)
2.	Phytol	30.763	10.294	Antioxidant, anticancer, antimicrobial, anti-inflammatory	(Kumosani et al., 2024)
3.	Squalene	39.274	10.282	Antioxidant and Anti-inflammatory	(Micera et al., 2020)
4.	Tetratriacontane	44.315	9.570	Antioxidants and antimicrobials	(Hepokur et al., 2020)
5.	Stigmasterol	48.979	2.484	Antidiabetic	(Bakrim et al., 2022; Wang et al. 2017)

(Source : Subramanian et al., 2020).

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Bioactive Compound Content of *G. sylvestre* and Its Potential. Based on the literature studies that have been conducted, there are several factors that affect the existence of a bioactive compound contained in a plant extract, one of which is environmental factors. In the study that has been conducted by Subramanian et al., (2020) is the analysis of GC-MS on two samples of *G. sylvestre* from India (representative of the abundant number of trichomes and located in the contours of higher light intensity) (Table 1)

The results of the GC-MS analysis identified that the *G. sylvestre* extract sample from India had bioactive compounds with different percentages of total ingredients. The dominant bioactive compounds found in *G. sylvestre* are squalene (10%), phytol (10%), tetratriacontane (9%), n-hexadecanoic acid (5%), and stigmasterol (2%). All of these bioactive compounds have their own activities. The detected bioactive compounds have a dominant total percentage, have potential biological activity as antioxidants, antimicrobials, anti-inflation, anticancer, and antidiabetics. Squalene and phytol are bioactive compounds that have the highest percentage of total (10%), according to the literature squalene has the ability of biological activity as an antioxidant and anti-inflammatory. Squalene (SQ) is a metabolite compound that belongs to the triterpene group. The compound has the chemical formula C30H50 and is high in antioxidants. The activity of squalene as an antioxidant, if applied in the medical field has potential as a prevention of hypertension and hypercholesterolemia. Squalene in the GC-MS *G. sylvestre* test can be found at the 31st peak (Micera et al., 2020).

Phytol is one of the bioactive compounds detected in *G. sylvestre* at the 23rd peak. Phytol compounds are one of the potential compounds that have anticancer properties (Kumosani et al., 2024). The mechanism of phytol compounds as anticancer is to inhibit ROS production through NADH oxidase, this is because if ROS production is too excessive, it can support the growth of foreign cells or cancer. Phytol also inhibits the proliferation and regulation of genes, that is, affects protein kinase pathways such as ERK1/2 and JNK. Disruption of these gene pathways can prevent the proliferation and growth of cancer cells. Theoretically, phytols are also able to perform apoptosis in foreign cells, namely by increasing the release of cytochrome C (CYP-C) in the mitochondrial pathway, so that it can activate the enzyme capase-3 which functions as an executor in the apoptosis pathway (Alencar et al., 2018).

The molecular mechanism of phytol compounds as anticancer agents through cellular signaling pathways. Phytol interacts directly with transmembrane receptors such as RTK (receptor tyrosine kinase), GPCR (G protein-coupled receptor), and CKR (chemokine receptor), activating the PI3K and PKC signaling pathways, as well as influencing the activation of transcription factor NF-κB to regulate gene expression related to cancer cell survival and cellular migration via MMPs (matrix metalloproteinases). The production of reactive oxygen species (ROS) is increased through the activation of NADPH oxidase, causing oxidative stress and mitochondrial damage, which triggers the release of cytochrome c (CYP-c). The activation of this mitochondrial pathway induces caspase 9 and caspase 3, which directly initiate apoptosis. This apoptotic pathway is reinforced by the inhibition of anti-apoptotic proteins such as Bcl-xL and increased expression of pro-apoptotic proteins such as Bax. Gene regulation is affected through the ERK1/2 and JNK signaling pathways, which can modulate gene transcription, stop cell cycles, or induce apoptosis depending on the context. Activation of the p53, p38, p21, and p16 proteins also contributes to the control of cancer cell proliferation. An additional mechanism involves the activation of the RIP and MLKL proteins, which trigger non-programmed cell death through necrosis (Alencar et al., 2018).

Tetratriacontane is one of the dominant bioactive compounds found in *G. sylvestre* with a total percentage of 9%. Tetratriacontane biologically has potential, one of which is activity as an antimicrobial (Hepokur et al., 2020). The compound may support *G. sylvestre* as an antimicrobial. According to the results of research by Gayathri et al. (2018) *G. sylvestre* proved to have potential as an antimicrobial by being able to inhibit the growth rate of specific microbes of gram-positive bacteria, namely *Bacillus subtilis*, *Staphylococcus aureus* and *Micrococcus luteus*, in addition to gram-positive bacteria, *G. sylvestre* can inhibit gram-negative bacteria, namely *Escherichia coli bacteria*, *Shigella flexneri* and *Proteus vulgaris*. The presence of a clear zone in the bacterial culture medium indicates inhibition.

The compounds n-Hexadecanoic acid (peak-20) and Stigmasterol (peak-35), are both potential compounds in *G. sylvestre* that have the

same biological activity, namely as an antidiabetic. Hexadecanoic acid is one of the compounds of hexane, which is often found in plant samples including *G. sylvestre*. Research on specific n-Hexadecanoic acid applied to antidiabetes has not been widely done and needs to be further developed (Aslam et al., 2024). Stigmasterol compounds have begun to be developed in the application of antidiabetic mellitus. Stigmasterol has potential as an antidiabetic with evidence it can help improve the regulation of glucose levels in the blood and improve insulin sensitivity. Research shows that the administration of stigmasterol increases the translocation of GLUT4 (glucose transporter type 4) and the regeneration of cells β the pancreas, which plays a role in insulin secretion. This effect helps lower fasting glucose levels and improves oral glucose tolerance, which is important for the management of type 2 diabetes (Wang et al., 2017). The potential of *G. sylvestre* as an antidiabetes is unique, because in several Asian countries it has taken a traditional approach to use *G. sylvestre* as an antidiabetic drug, one of these countries is India (Rathore et al., 2016).

Overall, the bioactive compound content in *G. sylvestre* has different biological activity capabilities, but further research needs to be conducted in order to confirm the primary data regarding the profile of each bioactive compound.

Potential of *G. sylvestre* as an Antidiabetes. *G. sylvestre* in India is believed to be an herbal alternative medicine as an antidiabetes mellitus. Scientifically, according to Laha & Paul, (2019), *G. sylvestre* contains secondary metabolites that are characteristic of the plant, namely gymnemic acid. The GC-MS test has been carried out by (Subramanian et al., 2020) but has not been able to detect the presence of gymnemic acid. Gymnemic acid is specifically a member of the triterpenoid group. Gymnemic acid has several types, namely, gymnemic acid (I-XVIII) homologue, gymnemic acid A1 and its derivatives, and there may still be several others (Laha & Paul, 2019). Gymnemic acid is suspected to be able to prevent the occurrence of diabetes mellitus because it can inhibit sugar absorption, so in countries such as India and China the process of developing the research (Gaytán Martínez et al., 2021). The research stage starts from in silico gymnemic acid testing. The results of the study of Shenoy et al., (2021) indicate that Gymnemic acid I has an interaction with the enzyme Sucrase α-glucosidase (one of the sugar-binding enzymes). The in silico interaction can be continued in the in vitro stage, because gymnemic acid I can produce binding affinity. (Table 2).

Table 2. In silico molecular docking analysis of gymnemic acid

Enzyme	Compounds in *Gymnema*	Residue	Binding Affinity
Sucrase α-glucosidase	Gymnemic Acid I	PHE140,PHE244 ARG278,ASP280	-95.8172
	Gymnemic acid IV	VAL325,ASP392, HIS443, ARG515	-101.119

(Source : Shenoy et al., 2021).

The chemical structure of gymnemic acid I and gymnemic acid IV, the two main triterpenoid glycoside compounds isolated from *G. sylvestre* (Figure 4). Both compounds have a hydrophobic oleanane-type triterpene base structure and are conjugated to sugar groups through glycosidic bonds, which contribute to increased solubility and biological activity. Gymnemic acid I is composed of gymnemagenin aglicon containing several hydroxyl and carboxyl groups, which play an important role in forming molecular interactions with target enzymes of carbohydrate metabolism. Gymnemic acid IV has differences in the amount, position, and type of sugar substituents as well as functional groups, resulting in variations in molecular conformation and chemical properties. These structural differences affect the binding affinity of the compounds to the enzymes α-glucosidase and sucrase, which is indicated by a higher binding affinity value in gymnemic acid IV than in gymnemic acid I.

Kumar et al. (2010) reported the results of a study on patients with type 2 diabetes mellitus treated with *G. sylvestre* 500 mg per day for three months. Treatment results showed a decrease in fasting blood glucose levels, postprandial blood glucose, and glycated hemoglobin, as well as improvements in symptoms of fatigue, polyphagia, and lipid profile. Devangan et al. (2021) conducted a systematic review and meta-analytical study that included 10 studies with a total of 419 patients with type 2 diabetes. This study showed that the treatment of *G. sylvestre*

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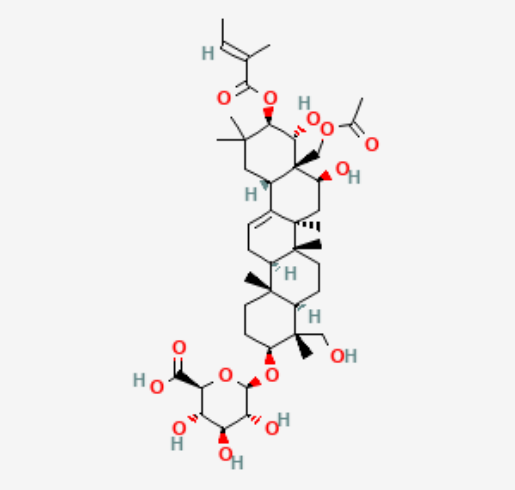
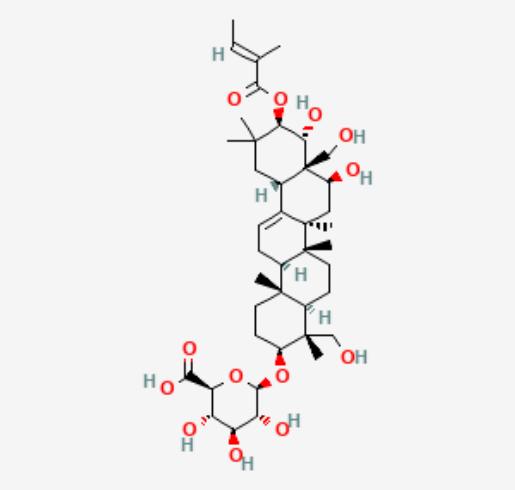
was associated with a decrease in fasting blood sugar ($P < 0.0001$), postprandial blood sugar ($P < 0.0001$), and glycosylated hemoglobin ($P < 0.0001$). Treatment also significantly lowers blood triglycerides ($P < 0.0001$), and cholesterol ($P < 0.0001$). The available evidence suggests that *G. sylvestre* is a hypoglycemic agent and lipid lowering agent. However, the available evidence research also shows the usefulness of several other supplements including fenugreek, cinnamon, and lipoic acid in the management of diabetes. Therefore, the choice of diabetes supplements depends to some extent on availability and cost. It appears that *G. sylvestre* is the most available and cost-effective diabetes supplement in India, however, it is not present in any other country in the world including Iraq (Alam et al., 2022).



Gymnemic acid I



Gymnemic acid IV

Figure 4. Structure of gymnemic acid compounds I and IV (PubChem, 2025)

Conclusion

This overview highlighted that *G. sylvestre* exhibits morphological variation across different countries, as reported in the reviewed literature, with differences in vegetative traits descriptively linked to environmental factors, particularly light intensity. However, since this study relies on secondary data regardless controlled experimental observations, the relationship needs to be interpreted carefully and requires further confirmation through supporting experimental studies. *G. sylvestre* has great potential as a natural medicinal agent, this is due to the content of bioactive compounds in *G. sylvestre* which are abundant and have biological activities such as antioxidants, anticancer, antimicrobials, and natural antidiabetics. One of the potential ingredients of *G. sylvestre* is gymnemic acid which provides hypoglycemic effects as an antidiabetic. This report was constructed as a literature-based synthesis study that integrates the latest findings regarding the morphological character, bioactive compound content, and antidiabetic potential of *G. sylvestre*, thus providing a comprehensive framework of understanding as a scientific basis for further research. This study is expected to be a conceptual reference in the development of experimental research and pharmacological applications of *G. sylvestre* in the future.

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