

## A REVIEW ON PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES OF MILKWEED FAMILY HERBS (ASCLEPIADACEAE)

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### ABSTRACT

*Calotropis procera* and *Gymnema sylvestre* are a perennial shrub and woody climber, respectively, and belonging to the family Asclepiadaceae. They are commonly known as milkweed family herbs. The *Calotropis* commonly have two species, i.e., *C. procera* and *C. gigantean*. All parts of plant exude white milky latex when cut. It has been widely used in traditional medicine due to its pharmacological active compounds found in all parts of plants such as bark, roots, and leaves and especially its latex which exudes from damaged or broken stem and leaves. *G. sylvestre* an ayurvedic herb came to be known as “destroyer of sugar” because in ancient times Ayurveda physicians observed that chewing a few leaves of *G. sylvestre* suppressed the taste of sugar. It also reported to possess antidiabetic, antioxidant, and immunomodulatory, antiulcer, and anticancer potential. The gymnemic acid is the main constituent which is responsible for number of pharmacological activities. The present review assembles the data on pharmacognostic and pharmacological potential of *C. procera* and *G. sylvestre*.

**Keywords:** *Calotropis procera*, *Gymnema sylvestre*, Milkweed, Gymnemic acid.

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### INTRODUCTION

To make disease free healthy life medicinal plants are the nature's gift to human beings. It plays a very important role to conserve our health. India is one of the most diverse countries in the world, and the main traditional systems of medicine include Ayurveda, Unani, and Siddha [1]. From ancient times in India, different parts of medicinal plants have been used for curing various diseases. In this regard, *Calotropis procera* and *Gymnema sylvestre* are the herbs of milkweed family have reported number of pharmacological activities from antique times. The recent review represents pharmacognostic characteristics and the pharmacological potential of *C. procera* and *G. sylvestre*.

### C. PROCERA

*C. procera* (Aiton) R.Br. is a small shrub belonging to family Asclepiadaceae, and commonly known as milkweed or giant weed. It is commonly grown in wastelands and roadside area. It is frequently known as “Rui” in Marathi, “Mudar” in Hindi, and “Sodom of apple” in English (Fig. 1). There is a number of species of *Calotropis* but most commonly available species include *C. sussuela*, *C. acia* Buch, *C. gigantean* (Linn), and *C. procera*. However, *C. gigantean* and *C. procera* are mostly found in the region of India [2]. *C. procera* is drought resistant, salt tolerant and it disperse seeds through wind and animals. It quickly becomes recognized as a weed along degraded roadsides and overgrazed native pastures [3,4]. *C. procera* is resident to India, Pakistan, Nepal, Afghanistan, Algeria, Iran, Iraq, Israel, Kenya, Kuwait, Nigeria, Saudi Arabia, United Arab Emirates, Yemen, and Zimbabwe [5].

The *C. procera* traditionally used in Ayurveda and other medicine systems from prehistoric time. These are useful to treatment various diseases such as diabetes, rheumatism, and inflammation. All parts of these plant used traditionally and the leaves possess anti-inflammatory and hepatoprotective potential. Table 1 summarizes the vernacular names of *C. procera* [6,7].

### Systemic classification of *C. procera* [8]

- Kingdom: Plantae - Plants
- Subkingdom: Tracheobionta - Vascular plants
- Super division: Spermatophyta - Seed plants
- Division: Magnoliophyta - Flowering plants
- Class: Magnoliopsida - Dicotyledons
- Subclass: Asteridae
- Order: Gentianales
- Family: Asclepiadaceae - Milkweed family
- Genus: *Calotropis* R.Br.
- Species: *C. procera* (Aiton).

### Pharmacognostic studies

*C. procera* is a single or many branched, soft-wooded shrub, and irregularly a tree reaching to 6 m length. The monarch butterflies are the highly insects through which it pollinated. Both animals and wind disperse the seeds, flowering and fruiting takes place throughout the year. When cut all parts of the plant exude white milky latex [9]. Soils of all texture but prefer disturbed sandy soils, as well as soils with high sodium saturations, are tolerated. The characteristics plant [10,11] parts of *C. procera* are depicted in Table 2. The biophysical limits for *C. procera* are:

- Altitude: Up to 1300 m
- Mean annual rainfall: 300-400 mm
- Mean annual temperature: 20-30°C.

### Phytochemistry

*C. procera* has been investigated by various researchers and found to possess number of chemical constituents.

### Whole plant

Phytochemistry revealed that *C. procera* has several types of compounds such as cardenolide, triterpenoids, alkaloids, resins, anthocyanins and proteolytic enzymes in latex, flavonoids, tannins, sterol, saponins, and cardiac glycosides [12].



Fig. 1: Flowers and leaves of *Calotropis procera*

#### Leaves

The leaves enclose mainly the amyirin, amyirin acetate,  $\beta$ -sitosterol, ursolic acid, cardenolides, calotropin, and calotropagenin. The leaves of plant contain mudarine as the principal active constituent [13].

#### Latex

The latex of plant has calotropin, calotoxin 0.15%, calactin 0.15%, uscharin 0.45%, trypsin, voruscharin, uzarigenin, syriogenin, and proceroside [14].

#### Flowers

The flavonoids, quercetin-3-rutinoside, sterol, calactin, calotoxin, calotropagenin, terpenes, multiflorenol, and cyclisadol and calotropin, polysaccharides with D-arabinose, glucose, glucosamine, and L-rhamnose isolated from the flowers. Flowers also contain enzymes 3-proteinase and calotropain (protease). *C. procera* flowers other chemical constituents are lupeol, uscharin, proceroside, proceragenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3-pentenoate), 3-thiazoline cardenolide, gigantol, giganteol, isogiganteol, uscharidin, uzarigenin voruscharin a-calotropeol, 3-epimoretenol, alactuceryl acetate, and a-lactuceryl isovalerate [15].

#### Root bark

*C. procera* root bark has triterpenes, a new norditerpenyl ester, named calotropterpenyl ester, and two unknown pentacyclic triterpenoids, namely, calotropursenyl acetate and calotropterfiedelenyl acetate, akundarol isovalerate, mundarol isovalerate, and quercetin -3- rutinoside. The benzoyllineolone, benzoyllisolineolone, calotropterpenyl ester, calotropursenyl acetate, and calotropterfiedelenyl acetate also found to include in root bark (Fig. 2) [16].

#### Traditional uses

In Ayurveda system of medicine, the plant is known as Arka and leaves are fried in oil for medicinal purpose. Sometimes it referred to as vegetable mercury because the latex is said to have mercury like effects on the human body. The root bark was earlier used as a substitute of ipecacuanha and has a digitalis-like an effect on the heart.

The various diseases has been treated by plant and widely used in the Ayurvedic, Unani, Arabic, and Sudanese-Indian traditional system of medicine. It has been utilized as a purgative, anthelmintic, digestive, stomachic, emetic, expectorant, sedative, blood purifier, and an antidote for snake bite. The treatment of ulcers, tumors, leprosy, asthma, boils, dysentery, eczema, piles and disease of liver, abdomen, and spleen also exploited by the plant parts [17]. The plant has been traditionally used as an antifungal, analgesic, and antipyretic agent. The migraine also treated by tender leaves of the plant. It acts as an abortifacient and for the treatment of piles. It is mentioned as bitter tonic, laxative, anthelmintic, expectorant and to cure ulcer in Ayurveda. The abdomen pain is cured by applying hot leaves, while the flowers are described as tonic, appetizer, and stomachic, and to cure asthma [18]. The Ayurvedic preparations such as Dhanvantari Ghrita, Mahanarayan taila, Arka lavana, and Chitrakadi taila prepared using roots of the plant [19].

All the parts of *C. procera* have been documented to attain medicinal desirable quality in ethno botanical surveys. The leaves used for the cure of cold, cough in Uttar Pradesh and latex for toothache and

Table 1: Vernacular names of *Calotropis procera*

Language	Common name
English	Calotropis, Rooster tree, Mudar plant
Marathi	Rui, Mandara
Hindi	Aaka, Aanaka
Urdu	Madar, Aak
Sanskrit	Arka, Alaka, Ravi
Gujarati	Akado
Arabic	Oshar
Kannada	Ekka, Ekkada gida
Telugu	Jilledu
Panjabi	Ak
Tamil	Vellerukku
Bengali	Akanda, Akone
Malayalam	Erikku

Table 2: Characteristics of plant parts of *Calotropis procera*

S.No.	Plant parts	Description
1	Bark and branches	Thick, rough, corky and yellow-brown color; twigs are green and fleshy
2	Leaves	Opposite-decussate, simple, ovate to obovate, quite large about 30 cm×25 cm
3	Flowers	White at the base and purple at the tips and 5 purple tipped stamens, 5 thick ovate petals
4	Fruits	Green, spongy ovoid, up to 15 cm long by 10 cm wide
5	Inflorescence	Arise from the base of the leaves in pedunculate cymes of 3-20
6	Root bark	Cracked, yellowish gray outside and yellowish white inside. Dried bark is bitter to taste
7	Roots	Grayish white in color and exhibit sap exudations at the places where bark has been cut
8	Corolla	Regular, gamopetalous, pale rose-purple or lilac, with a short tube and five broad ovate spreading lobes

scorpion bite. The treatment of dropsy, rheumatism, leprosy, and taeniasis using latex carried out in districts of Madhya Pradesh. The latex used for application on wounds in rural areas of Jammu was reported [16].

#### Pharmacological activities

Different parts of *C. procera* have been used for their biological activities since anciently, and some of them have an experimental opinion for their acceptance. Apart from their use in folk medicine, there are several reports on the biological activities and pharmacological actions of *C. procera* based on modern scientific investigation.

#### Antimicrobial activity

*C. procera* latex was evaluated for antimicrobial activity against *Escherichia coli*, *Streptococcus pneumoniae*, *Bacillus cereus*, *Staphylococcus saprophyticus*, and *Staphylococcus aureus* using disc diffusion method. Plant latex gives activity against most of the microorganisms [20]. Antimicrobial activity of solvent extracts and flavonoids of *C. procera* were reported using agar well-diffusion method. The flavonoids fraction of methanolic extract confirms the highest antimicrobial activity and quercetin-3-O-rutinoside have superior activity over the rest of flavonoids. The Gram-positive bacteria were more vulnerable than the Gram-negative, and the yeast species were more susceptible than the filamentous fungi [21].

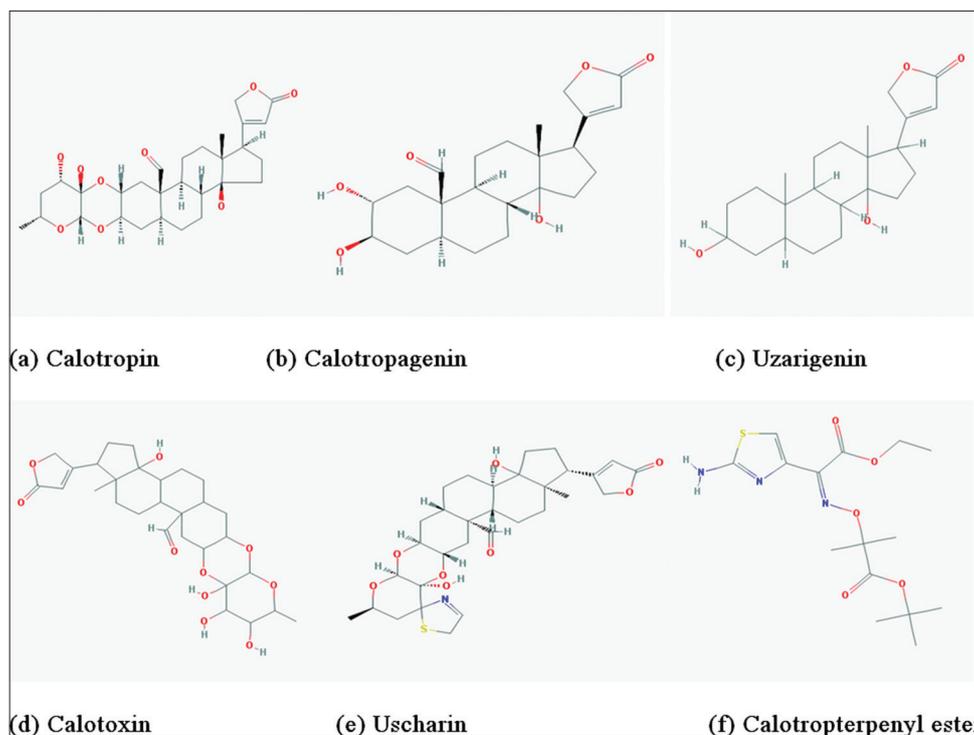


Fig. 2: (a) Calotropin (b) Calotropagenin (c) Uzarigenin (d) Calotoxin (e) Uscharin (f) Calotropterpenyl ester

#### Insecticidal activity

The larvicidal potential against *Musca domestica* was reported for ethanol extract of *C. procera* leaves by dipping method for 48 hrs. The leaf extract of *C. procera* was originated to be more active in terms of insecticidal potential. The data point out that the leaf extracts of these plants may be utilized as safer and economic alternatives to the synthetic insecticides [22].

#### Antibacterial activity

The aqueous and ethanolic extracts of root and leaves of *C. procera* evaluated for antibacterial potential using disc method. The ethanolic extract of leaves and roots was reported to possess higher antibacterial potential than the aqueous extract [23]. The antibacterial effect of extracts of leaf was reported and determined using agar well diffusion method, and minimum inhibitory concentration was determined using serial dilution method. The study revealed the significant antibacterial activity of all extracts [24].

#### Antioxidant activity

Methanolic extract of leaves, flowers, and root investigated to has antioxidant activity by radical (1,1-diphenyl-2-picrylhydrazyl [DPPH]) scavenging, reducing power; ferric reducing ability of plasma assay and metal chelating activity assay. The higher antioxidant potential reported for leaves of *C. procera* with inhibitory concentration 50% values of 0.21  $\mu\text{g/ml}$  for DPPH scavenging, 0.98 mg/ml for metal chelating [25]. The plant extract showed promising source of antioxidant due to the presence of phenolics and tannins [26].

#### Analgesic activity

The methanolic extract of *C. procera* exhibited a dose-dependent analgesic action in acetic acid writhing method. *C. procera* extract confirmed outstanding response in comparison to aspirin [27]. Ethanolic extract of the leaf of *C. procera* confirms the prominent analgesic potential and investigated for its analgesic activity using acetic acid-induced writhing and tail flick tests in mice [28].

#### Anti-inflammatory activity

The anti-inflammatory effect of methanolic extracts of *C. procera* was tested for formalin-induced paw edema in white albino mice and exhibited a dose-dependent anti-inflammatory potential [27]. Ethanolic extract of the leaf of *C. procera* was reported anti-inflammatory potential using formalin-induced paw lick, carrageenan-induced paw edema in Wistar rats. The extract showed inhibition of formation of paw edema significantly higher than of indomethacin [28]. The dry latex of *C. procera* was demonstrated anti-inflammatory activity using acute and chronic model of inflammation. Inhibition of fluid exudation, possibly due to its effect on vascular permeability was performed by DL significantly [29]. The potent anti-inflammatory activity was reported for methanolic extract of plant *C. procera* against acute and chronic model in albino Wistar rats. The methanolic extract of roots illustrated very close activity to the inhibitory effect of diclofenac sodium [30].

#### Hepatoprotective activity

Hepatoprotective activity of ethanolic extract of flowers of *C. procera* was illustrated, and it may be recognized to the quercetin related flavonoids present in flower [31]. Ethanolic and water extract of flowers also reported their hepatoprotective activity. The coadministration of antituberculosis drugs with CP has reduced levels of alanine amino transferase, aspartate amino transferase, and bilirubin within the normal range [32].

#### Antidiabetic activity

The petroleum ether, methanol and aqueous extracts of leaves of *C. procera* at a dose of 250 mg/kg were accounted for its anti-hyperglycemic potential. The investigation established pharmacological evidence to support the folklore claim that it is an antidiabetic agent [33]. The antidiabetic activity of hydroalcoholic extract of the leaves was investigated and illustrated the inhibition of level of blood glucose throughout the evaluation period [34].

#### Antiulcer activity

The stem bark of *C. procera* was studied for gastro-mucosal protective effect using aspirin and ethanol model in albino rats. A significant

gastro-mucosal protective effect showed by chloroform extract at 400 mg/kg [35]. The antiulcerogenic potential of an extract of leaves and root was investigated and accounted a dose-dependent reduction of lesion formation [36].

#### Anticancer activity

The root extracts of *C. procera* were reported antitumor potential against Hep2 cancer cells. Tetrazolium bromide colorimetry was used for cellular proliferation activities [37]. A complete protection against hepatocarcinogenesis showed by dried latex treatment of mice.

#### G. SYLVESTRE

*G. sylvestre* is one of the powerful medicinal plants used from prehistoric times. It is perennial, woody climber spread through in dry forest up to height of 600 m [38]. It is commonly known as Gurmar in Hindi. The Greek words "Gymnos" means naked and "nema" means thread while the specific description "sylvestre" is of Latin origin means "of the forest" [39]. *G. sylvestre* is generally disseminated in India, Malaysia, Sri Lanka, Indonesia, Japan, Vietnam, tropical Africa, and South Western region of the people's republic of China. It is also found in Banda, Konkan, Western Ghats, and Deccan extending to the parts of Western and Northern India (Fig. 3).

The genus *Gymnema* consists of 40 species distributed from Western Africa to Australia. *Gymnema acuminatum* (Roxb.) wall, *Gymnema aurantiacum*, *Gymnema balsamicum*, *Gymnema elegans* W and A, *Gymnema lactiferum*, *Gymnema latifolium*, *Gymnema montanum* Hook. F., *G. sylvestre* R.Br., *Gymnema tingens* W and A, *Gymnema inodorum*, *Gymnema yunnanense*, and *Gymnema spartum* are some of the important species of *Gymnema* [40,41]. Ayurvedic and Homeopathic system of medicine used *G. sylvestre* as a potent antidiabetic herb. It also reported to be a bitter, astringent, diuretic, laxative, stomachic, liver tonic, stimulant, expectorant, and antipyretic agent. The vernacular names of *G. sylvestre* as depicted in Table 3.

#### Taxonomical classification of *G. sylvestre*

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Super division: Spermatophyta
- Division: Magnoliophyta
- Class: Magnoliopsida
- Subclass: Asteridae
- Order: Gentianales
- Family: Asclepiadaceae
- Genus: *Gymnema*
- Species: *G. sylvestre*.

#### Pharmacognostic studies

The plant is more or less juvenile woody climber running over the high trees. *G. sylvestre* is native to the tropical forests of Southern and Central India and grown in the plains of coast in jungles at an altitude of 300-700 m [44,45]. The pharmacognostic characteristic of the *G. sylvestre* as presented in Table 4. The *Gymnema* species are diploid with a chromosome number of  $2n=22$  [46,47].

#### Phytochemistry

A number of phytochemical constituents have been reported by several researchers. Plant comprises two resins one soluble in alcohol, saponins, gymnemic acid, stigmasterol, quercitol and amino acid derivatives betaine, choline, and trimethylamine [48]. The leaves of *G. sylvestre* contains resins, albumin, chlorophyll, carbohydrates, tartaric acid, formic acid, butyric acid, anthraquinone derivatives, inositol alkaloids, organic acid (5.5%), paraben, calcium oxalate (7.3%), lignin (4.8%), and 22% of cellulose [49]. The leaves also enclose triterpene classes of oleanane saponins such as gymnemic acids, gymneasaponins, and dammarane saponins such as gymneasides and terpenoids as 6-octen-1-ol, 3,7-dimethyl, isophytol, squalene, nerolidol, and  $\beta$ -amyryn [50,51].

Leaves of *G. sylvestre* have acidic glycosides and anthraquinones and their derivatives [50]. Gymnemic acids A2 and A3 possessed both glucuronic acid and galactose in their molecular structures while glucuronic acid was found to be the only moiety in gymnemic acid A1 [52]. Further, a gymnemic acids series (gymnemic acid I, II, III, IV, V, VI, and VII) were isolated and characterized from the hot water extract of dry leaves of *G. sylvestre* [53,54]. An important 35 amino acid peptide gurmarin having a molecular weight of 4209 was isolated from *G. sylvestre* (Fig. 4) [55].

#### Traditional uses

Sushruta describes *G. sylvestre* as destroyer of sugar and other urinary diseases and these activities due to *G. sylvestre* neutralizing excess sugar in body [56]. Leaves of gurmar used traditionally for treatment of diabetes, piles and insect bites are treated by root bark [57]. The plant is useful in treatment of dyspepsia, constipation, jaundice, hemorrhoids, renal and vesical calculi, cardiopathy, asthma, bronchitis, amenorrhea, conjunctivitis, leukoderma, and Parkinsonism [58]. In Siddha and Unani systems of medicine, the *Gymnema* leaves are used as an ingredient of different antidiabetic formulations [59].

*G. sylvestre* is considered an alexipharmic, anodyne, anthelmintic, antipyretic astringent, bitter, cardiogenic, digestive, diuretic, laxative, stimulant, stomachic, and uterine tonic and is used to treat amenorrhea, asthma, bronchitis, conjunctivitis, constipation, cough dyspepsia, hemorrhoids, hepatosplenomegaly, intermittent fever, jaundice, and leukoderma according to Indian systems of medicine. The plant leaves are useful to remove inflammation. The bark from the plant roots is useful as an emetic, expectorant, and analgesic for body ache and juice from the root has been acclaimed as a useful treatment for snakebite by Bhav Prakash Nighantu [60,61]. The various formulations used for the treatment of diabetes as predicted in Table 5 [62].

#### Pharmacological activities

*G. sylvestre* is one of the essential medicinal plants used in ayurvedic system of medicine for the treatment of diverse diseases (Fig. 5) and is well known for their sugar suppressing activity.

Table 3: Vernacular names of *Gymnema sylvestre* [42,43]

Language	Common name
Hindi	Gudmar
Kannada	Kadhasige
Malayalam	Chakkarakolli, Madhunashini
Tamil	Sirukurunja/Sakkaraikkolli
Sanskrit	Measuring, jaboli
Telugu	Podapatri
English	Periploca of the wood
Marathi	Kavali, Kalikardori, Vakundi
Gujarati	Dhuleti, Mardashingi



Fig. 3: Leaves, flowers, and fruit of *Gymnema sylvestre*

**Antidiabetic activity**

The gymnemic acid the main constituent encloses different saponins and delays the glucose absorption in the blood due to the similarity with the atomic arrangement of the glucose. The leaf extract administered to patient stimulate the pancreas and increase release of insulin [63]. The extract of *G. sylvestre* encourages release of insulin from  $\beta$ -cells and from islets in the absence of any other stimulus [64]. Clinical study of *G. sylvestre* revealed antidiabetic potential in Type II diabetic patient for blood glucose level. *G. sylvestre* capsule reduced 37% glucose, 5%

triglycerides level, 13% cholesterol, and 19% low-density lipoproteins (LDL) level in diabetic individuals [65].

Glucoscare herbal tea (GCT) consists of two plants, namely, the *G. sylvestre* and *Camellia sinensis* assessed for antidiabetic activity. The complimentary effects on HbA1c and fasting blood sugar in patients with uncontrolled Type 2 diabetes mellitus after 12 weeks showed by GCT [66]. The study revealed that *G. sylvestre* leaves aqueous extracts augmented  $\beta$ -cell expansion and potentiated glucose-evoked  $Ca^{2+}$ -regulated insulin secretion [67].

**Table 4: Morphological characteristics of plant parts of *Gymnema sylvestre***

S.No.	Plant parts	Description
1	Stem	Cylindrical, hard, twining, branched; internodes terete; rooting at nodes
2	Leaves	Opposite, elliptic or ovate, 1.0-9.5 cm×0.5-5.5 cm, acute at apex, base rounded, ciliate along margins, smooth above, densely velvety pubescent beneath, especially on the nerves
3	Flowers	Small, yellow, in axillary and lateral umbellate cymes Flowering: August-March
4	Calyx	5-lobed, ovate, obtuse, ciliated
5	Corolla	Campanulate, yellow, 5-lobed; lobes ovate-deltoid, spreading and glabrous, united at base
6	Fruits	2 or 1, dark green smooth follicular mericarps
7	Seeds	Fruiting: from October onward Ovate, margined, ending in a silky coma, cotyledons elliptic, radicle cylindric

**Antibacterial activity**

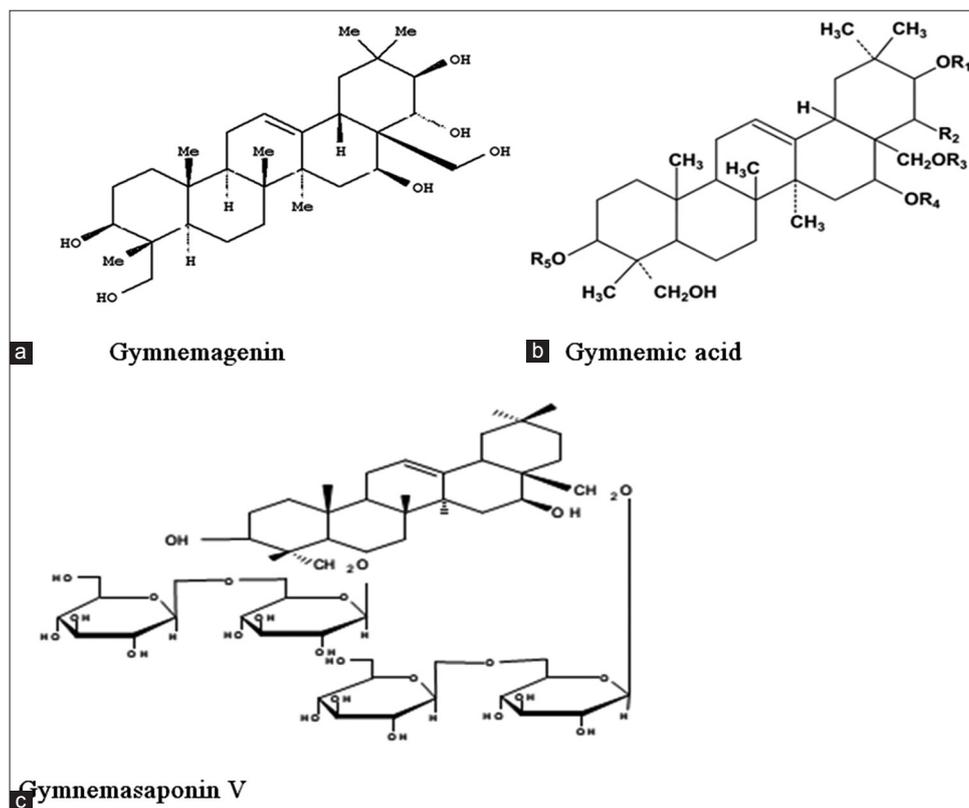
The ethanolic extract of leaves illustrated high degree of antibacterial activity [68]. The antimicrobial activity against *Bacillus pumilus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *S. aureus* demonstrated by ethanolic extract of *G. sylvestre* leaves [69]. Aqueous and methanolic leaf extracts were studied for their antimicrobial efficacy, the methanolic extract of the leaves demonstrated activity against all four tested microorganisms while aqueous leaf extracts found to be non-effective [70]. The aqueous and methanol leaf extract showed significant antibacterial activity [71].

**Antiobesity activity**

*G. sylvestre* possesses lipid-lowering potential due to inhibition of pancreatic lipase activity. The study clear that decoction of leaves is useful in obesity [72]. A decrease in food and water intake along with a body weight reduction of 57.2±6.4 and 75.5±6.3 g during 1 and 2 weeks, respectively, observed in Otsuka Long-Evans Tokushima fatty rats [73]. The narrative combination has resulted in significant body weight and fat loss in obese adults [74].

**Hypolipidemic activity**

Gymnemat extracted from *G. sylvestre* extract found to decrease the total cholesterol by about 1/3, and the LDL and very LDL cholesterol has



**Fig. 4: (a) Gymnemagenin. (b) Gymnemic acid. (c) Gymnemasaponin V**

decreased by about half [75]. The ethanolic extract study illustrated that decrease in the circulating cholesterol concentrations in spontaneously hypersensitive rats [76]. Gymnemic acids have found to increase the fecal excretion of neutral steroids and bile acids especially those of cholesterol and cholic acid derived bile acids [77]. The aqueous leaf extracts of *G. sylvestre* significantly diminished cholesterol and serum triglycerides and the treated rat's serum high-density lipoprotein cholesterol level were increased [78].

**Anticancer activity**

The biosynthesized silver nanoparticles and gold nanoparticles of *G. sylvestre* leaf extract exhibited substantial *in vitro* cytotoxic effects against Hep2 cells. Among the two nanoparticles synthesized, silver showed better cytotoxic effects in cancer cells than gold nanoparticles [79]. The gymnemagenol at 50 µg/ml showed a good cytotoxic activity (63%) in HeLa cells at 48 hrs. [80]. *G. sylvestre* extract reported a significant reduction in tumor incidence, tumor burden and cumulative number of papillomas along with a significant increase in average latent period [81].

**Antioxidant activity**

The ethanolic extract of *G. sylvestre* reported antioxidant activity by inhibiting DPPH; it might be due to the presence of saponins, flavonoids, phenols, and alkaloids [82]. The antioxidant activity of *G. sylvestre* leaves showed concentration-dependent response and it varied from 3.92% to 72.22% for 7.81-1000 µg/ml, respectively [83].

**Immunomodulatory activity**

The study designated that methanolic extract of *G. sylvestre* exhibited significant immunosuppressive activity by inhibiting the increase in

CD3 and CD19 lymphocytes and cytokines, interleukin 2, interferon-γ, and IL-4 [84]. *G. sylvestre* aqueous leaf extracts showed remarkable immunostimulatory activity on human neutrophils under *in vitro* conditions [85].

**Antiulcer activity**

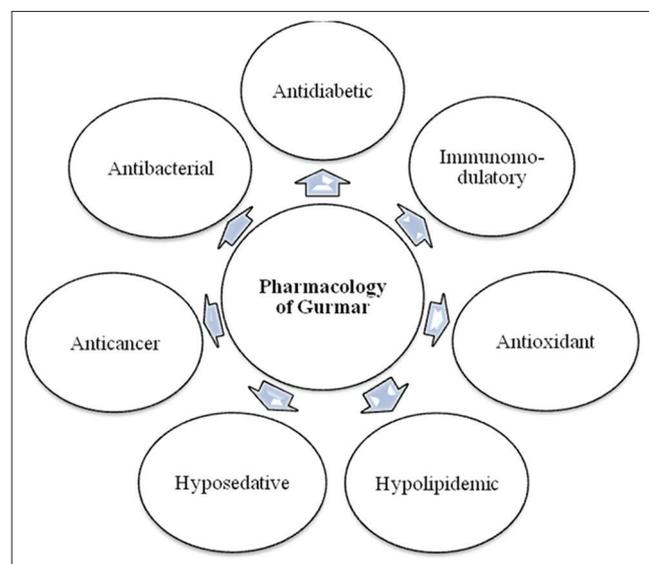
Ethanolic leaf extract reported protective effect in the experimentally induced ulcerative colitis by acetic acid in Wister rats. Long-term administration of alcoholic leaf extracts did not show any influence on hematological and blood chemical parameters. 1% in diet/52 weeks showed no observable toxic effect in rats [86]. Gymnemic acid appraised antiulcerogenic potential by the inhibition of prostaglandin synthesis and generation of ulcer [87].

**CONCLUSION**

The WHO report has estimated that in developing countries more than 80% of the population depends on herbal medicines for their basic healthcare needs [88]. Synthetic medicines acquire resistance day by day for the many microorganisms and therefore it desirable to move toward herbal medicines and their combinations. Plant origin drugs have established much attention of the world for their efficacy and whispered to be safe for human use. Herbal medicine has good scope in the field of new drug therapy as well as nutraceuticals [89]. *G. sylvestre* is a multipurpose potential medicinal plant having a high market potential worldwide. *G. sylvestre* has an important place with its diverse ethnobotanical, traditional uses and economic uses in different systems of medicine not only in India but also throughout the world. It exhibits enormous hypoglycemic activity along with hypolipidemic and antioxidant property. *G. sylvestre* has clinical evidences to treat diabetes and tradition antidiabetic formulation showed their hypoglycemic potential by any one or all the mechanism of increase secretion of insulin; promotes regeneration of islet cells and increase utilization of glucose. As the synthetic agents act by only one pathway but the herbal remedies have to show the various pathways due to their phytochemicals to treat diseases. The *C. procera* contains various secondary metabolites which are responsible for the pharmacological potential. This review will be beneficial to the scientists and researchers to further investigation and development of the new drug from the relevant studies.

**Table 5: Antidiabetic traditional formulations of *Gymnema sylvestre***

S.No.	Formulation name	Ingredients
1	Diabet guard	<i>Gymnema sylvestre</i> extract
2	Alfasilin	<i>Gymnema sylvestre</i> extract and banana extract
3	Ultradia	<i>Gymnema sylvestre</i> extract and banana extract
4	Diabohills	<i>Gymnema sylvestre</i> extract
5	Hyponidd	<i>Gymnema sylvestre</i> extract



**Fig. 5: Pharmacological activities of *Gymnema sylvestre***

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