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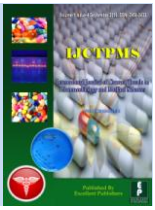

Review Article

Antidiabetic Plant, *Gymnema sylvestre* R. Br., (Madhunashini): Ethnobotany, Phytochemistry and Pharmacological Updates

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Abstract

This review paper is the collection of literature updates on ethnobotany, phytochemistry and pharmacological activities of a rare medicinal plant *Gymnema sylvestre* R. Br., (madhunashini or sugar destroyer). *Gymnema sylvestre* with significant medicinal properties has played an important role in Indian traditional system of folk medicine; *Ayurveda* and homeopathic system of medicine. Herbal preparations of *Gymnema sylvestre* are presently used in tea bags (herbal-chai), health tablets, supplements, beverages, confectioneries and in food items as an effective natural remedy for diabetes, asthma, obesity, arthritis, besides being used for osteoporosis, constipation and anti-inflammatory. All the herbal products of *Gymnema sylvestre* are available in India and international market under brand names such as Himalaya™ Pure herbs, Bangalore, India (*Gymnema*-sugar desroyer tablets), Vitamin Shoppe *Gymnema sylvestre* (sugar destroyer), Gymnema gold (Nutrigold), Novel™ Nutrients *Gymnema* tablets, Sandhus, diabetic tea (India) with *Gymnema sylvestre*, Good' N Natural (*Gymnema sylvestre* tablets), Product of China (*Gymnema* tea), Natures Plus®, The energy supplements herbal actives, *Gymnema sylvestre* (tablets), Natures Answer, *Gymnema sylvestre* (tablets), Natures way® *Gymnema sylvestre* (tablets), GNC® Herbal Plus Standardized, *Gymnema sylvestre* (tablets), Body Slatto Tea®, Gymnema®, Gymnema Diet®, Sugar Off®, Glucoset™, Cinndrome X™, and Pilisoft™. In India, rural community consume different parts (leaves, roots, stem and flowers) of fresly grown *Gymnema sylvestre* as a chief herbal medicine for the treatment of many health disorders. Therefore, herbal medicines play an important role in a primary health care sector of many developing countries. Furthermore, novel discovery of new bioactive compounds of therapeutic activity

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mimicking the synthetic drugs is another challenging aspect of pharmaceutical biotechnology. This also opens a new door of alternative chief herbal medicine (bioactive compounds) for many deadly viral, bacterial, and fungal diseases. Finally, the experimentally tested pharmaceutical activitis of *Gymnema sylvestre* also provide an opportunity for further evaluation of the proposed drugs for establishing their candidature as alternative drugs for the treatment of many human health disorders.

Introduction

Herbal medicines plays an important role in regulating human health disorders, and also served as the backbone of Indian traditional *Ayurvedic* and homeopathic system of medicine (Thakur et al., 2009a, 2009b, 2012; Malabadi et al., 2005a, 2005b; Malabadi, 2005; Malabadi and Vijayakumar, 2005, 2007, 2008; Malabadi et al., 2007; Malabadi et al., 2010; Tiwari et al., 2014; Malabadi et al., 2016a). Plants produce a large number of naturally secreted unique bioactive compounds called as secondary metabolites of pharmacological applications in addition to the primary metabolites (proteins, carbohydrates, lipids) (Malabadi et al., 2007; Tiwari et al., 2014**;** Thakur et al., 2012; Fabio et al., 2014; Gupta and Solanki, 2015; Malabadi et al., 2016a; Chalannavar et al., 2011, 2012, 2013a, 2013b, 2015a, 2015b; Narayanaswamy et al., 2013, 2014a, 2014b; Malabadi et al., 2007, 2010). Plant-based traditional knowledge has become a fundamental ethnobotanical tool in search for new sources of drugs (Ayyanar and Ignacimuthu, 2005; Malabadi et al., 2007). Therefore, herbal medicines becomes a major and chief source of bioactive compounds of therapeutic value in the drug development (Malabadi et al., 2007; Tiwari et al., 2014; Parveen et al., 2015; Malabadi et al., 2016a). Now a days there is a significant increase in the global market for plant derived pharmaceuticals. Therefore, over exploitation of medicinal plants becomes a major issue reflecting on the loss of many medicinal plants (Triveni et al., 2012; Vaidya, 2011; Tiwari et al., 2014).

Ethnobotany is the study of relationship between humans and nature (Ayyanar and Ignacimuthu, 2005; Malabadi et al., 2007). Traditional medical practices are an important part of the primary healthcare system in the developing world. The development of indigenous medicines and the use of medicinal plants for the treatment of deadly bacterial, fungal infections, and viral fever diseases such as dengue (Ganguly et al., 2013a, 2013b, 2013c, 2013d, 2014, 2015; Malabadi, 2008; Malabadi et al., 2012a, 2012b, 2012c, 2012d, 2012e, 2011, 2010; Malabadi et al., 2016c), ebola (Malabadi et al., 2016b, 2016c; Feldmann and Geisbert, 2011), zika virus, chikungunya and mosquito-borne infectious plasmodium type disease malaria becomes an important part of ethnobotanical study programme (Ayyanar and Ignacimuthu, 2005; Malabadi et al., 2007).

Herbal medicines are assumed to be of great importance in the primary healthcare of individuals and communities in rural areas of many developing countries (Ayyanar and Ignacimuthu, 2005; Malabadi et al., 2007; Malabadi et al., 2007, 2010; Malabadi et al., 2016a). Some of the indigenous medicinal plants such as insulin plant, *Costus speciosus* (Malabadi, 2002a, 2005; Malabadi et al., 2004, 2005a, 2016a), *Catharanthus roseus* (Malabadi et al., 2009), *Clitoria ternatea* (Malabadi and Nataraja, 2001, 2002; Malabadi, 2002b; Malabadi et al., 2005b) have already played an important role as a chief remedy aganist many infectious diseases. In addition to this, the first antidiabetic drug, metformin, isolated from *Galega officinalis*, was also a herbal formulation (Tiwari et al., 2014).

Gymnema sylvestre R.Br., (madhunashini or sugar destroyer) is one of the most important medicinal plant well known for many bioactive compounds of numerous pharmacological properties which include antidiabetic, antiobesity, anticarcinogenic, and neuroprotective. This review paper highlights an overview of ethnobotanical uses, phytochemistry, and recent pharmacological updates of *Gymnema sylvestre*.

Gymnema sylvestre (Madhunashini): Ethnobotany and phytochemistry

Antidiabetic plant, *Gymnema sylvestre* R.Br., (madhunashini or sannagrasehambu in Kannada) belonging to the family *Asclepiadaceae* or the "milk weed" family is a slow growing, perennial, medicinal woody climber (Thakur et al., 2012; Tiwari et al., 2014). The common name of *Gymnema sylvestre* R.Br., is periploca of the wood in English, *gurmar* in Hindi and *madhunashini* or sannagrasehambu in Kannada, Chigengteng or Australian Cowplant, *Waldschlinge* in German (Thakur et al., 2012; Tiwari et al., 2014; Gupta and Solanki, 2015; Thangavelu et al., 2012; Trivedi and Pundarikakshudu, 2008; Triveni et al., 2012; Vaidya, 2011). *Gymnema sylvestre* is native to South-Indian Western Ghat forests, and widely distributed in north and western part of India (Stocklin, 1969; Thakur et al.,

2012; Yadav et al., 2010; Tiwari et al., 2014; Yasukawa et al., 2014). *Gymnema* includes about 119 species, about 25 of them from tropical or subtropical Asia, Africa, and Australia (Parveen et al., 2015). It grows in the tropical forests of India and has been used for more than 2,000 years in traditional systems of medicine to treat madhumeha or "honey urine." (Parveen et al., 2015; Thangavelu et al., 2012; Trivedi and Pundarikakshudu, 2008; Triveni et al., 2012; Vaidya, 2011). It is popularly known as *Gurmar*, which means "sugar killer" or "destroyer of sugar" (Parveen et al., 2015**;** Tiwari et al., 2014; Wang et al., 2014; Yew et al., 2001; Thakur et al., 2012; Yogalakshmi et al., 2014; Zarrelli et al., 2013a, 2013b). Excess body sugar was reduced by *Gymnema sylvestre*, and thus called as madhunashini, meaning *destroyer of sugar* (Pednekar et al., 2011; Tiwari et al., 2014; Gupta and Solanki, 2015; Yadav et al., 2010; Yasukawa et al., 2014).

The medicinal properties of *Gymnema sylvestre* are attributed to a group of oleanane type triterpenoid saponins known as gymnemic acids and dammarenesaponins called gymnemasides (Yoshikawa et al., 1989, 1992, 1993; Thakur et al., 2012; Tiwari et al., 2014; Gupta and Solanki, 2015; Wang et al., 2014; Yew et al., 2001; Yogalakshmi et al., 2014; Zarrelli et al., 2013a, 2013b). Indian medicinal plant *Gymnema sylvestre* R.Br., (madhunashini or sannagrasehambu in Kannada) is a chief source of large number of phytochemical molecules such as resin, saponins, gymnemasine, sapogenins, anthraquinones, hentri-acontane, pentatriacontane, α and β-chlorophylls, phytin, d-quercitol, tartaric acid, formic acid, butyric acid, lupeol, *β*-amyrin related glycosides, gymnemic acids, gurmarin, gymnemosides, gymnemanol, gymnemasins, gypenoside, conduritol, gymnestrogenine, gymnemagenine, stigmasterol, vitamins, terpenoids, phenolic acids, lignins, stilbenes, tannins, flavonoids, quinones, coumarins, alkaloids, amines, betalains, and other metabolites which are rich in antioxidant and antidiabetic activities (Yoshikawa et al., 1989, 1992, 1993; Thakur et al., 2009a, 2009b, 2012; Fabio et al., 2014; Gupta and Solanki, 2015; Upendra et al., 2010; Tiwari et al., 2014;Subatra et al., 2006a, 2006b; Subatra and Srinivasan, 2008; Solanki and Gupta, 2013a, 2013b, 2013c; Luo and Shen, 1987; Luo, 1999; Luo et al., 2001a, 2001b; Luo et al., 2007; Sangeetha and Jegadeesan, 2012; Rani et al., 2012; Malik et al., 2008, 2010; Khramov et al., 2008; Komalavalli and Rao, 2000; Khanna and Kannabiran, 2009; Yadav et al., 2010; Yasukawa et al., 2014).

According to the *Ayurvedic* Pharmacopoeia of India, *Gymnema sylvestre* R. Br., (Madhunashini in Kannada) with several therapeutic applications is also a chief source of antidiabetic and antiobesity herbal drugs (Kim et al., 2016; Gupta and Solanki, 2015; Upendra et al., 2010; Tiwari et al., 2014 ; Subatra et al., 2006a, 2006b; Subatra and Srinivasan, 2008; Luo and Shen, 1987; Luo, 1999; Luo et al., 2001a, 2001b; Luo et al., 2007; Thakur et al., 2012). Leaves are reported to contain acidic glycosides, anthroquinones and their derivatives (Saneja et al., 2010; Rani et al., 2012; Gupta and Solanki, 2015; Chakraborty et al., 2013; Devi and Ramasubramaniaraja, 2010).

In addition to this, other therapeutic biomolecules are flavones, α and *β*- chlorophylls, phytin, formic acid, butyric acid, tartaric acid, hentri-acontane, lupeol, *β*-amylin related glycosides, pentatriacontane and stigmasterol (Gupta and Solanki, 2015; Tiwari et al., 2014; Hong-Min et al., 1992; Wen-Cai et al., 2000; Porchezhian and Dobriyal, 2003; Khramov et al., 2008; Sangeetha and Jegadeesan, 2012; Zhen et al., 2008; Devi and Srinivasan, 2011; Devi et al., 2006; DiFabio et al., 2015; Kiran et al., 2014; Wang et al., 2014; Yew et al., 2001; Yogalakshmi et al., 2014; Zarrelli et al., 2013a, 2013b; ; DiFabio et al., 2015; Kiran et al., 2014). It also removes cough by inducing vomiting and paste is used as an ointment in case of insect bite (Malik et al., 2008; Khanna and Kannabiran, 2009; Malik et al., 2010; Osman et al., 2010; Tiwari et al., 2014; Gupta and Solanki, 2015; Zhen et al., 2008; Devi and Srinivasan, 2011; Devi et al., 2006). Dried leaf powder, fruits, and roots of *Gymnema sylvestre* were also used in the treatment of svasa (bronchial asthma), kasa (cough), kustha (leprosy and other skin diseases), and vrana (wounds), among other conditions (Thakur et al., 2012; Wadood et al., 2007; Gupta and Singh, 2014; Sukesh et al., 2011; Arunachalam et al., 2014; Arunakumara et al., 2005; Baskaran et al., 1990; Baskaran et al., 2007). According to Charak Samhita, it removes bad odour from breast milk (Thakur et al., 2012). Bark is given in the diseases caused by vitiated kapha (phlegm) and root is useful in piles (Thakur et al., 2012; Sugihara et al., 2000; Thangavelu et al., 2012; Trivedi and Pundarikakshudu, 2008; Triveni et al., 2012; Vaidya, 2011; Tiwari et al., 2014).

The major bioactive constituents of *Gymnema sylvestre* are a group of oleanane type triterpenoid saponins known as gymnemic acids (Pednekar et al., 2011; Thakur et al., 2012; Sugihara et al., 2000; Wadood et al., 2007; Gupta and Singh, 2014; Sukesh et al., 2011; Thangavelu et al.,

2012; Trivedi and Pundarikakshudu, 2008; Triveni et al., 2012; Vaidya, 2011). The latter contain several acylated (tigloyl, methylbutyroyl, *etc*.) derivatives of deacylgymnemic acid (DAGA), which is 3-O-glucuronide of gymnemagenin (3,16,21,22,23,28-hexahydroxy-olean-12- ene) (Pednekar et al., 2011; Thakur et al., 2012; Agarwal et al., 2000; Alam et al., 2011; Aleisa et al., 2014; Al-Romaiyan et al., 2010, 2012, 2013; Arun et al., 2014; Tiwari et al., 2014). The individual gymnemic acids, (saponins) include gymnemic acids I-VII, gymnemosides A-F, gymnemasaponins are reported to lower and balance blood sugar levels (Pednekar et al., 2011; Sinsheimer and Manni, 1965; Sinsheimer et al., 1970; Tiwari et al., 2014). It blocks the sugar absorption in small intestine and stimulates the β-cells of pancreas. Gymnemic acid increases secretion of insulin, and promotes regeneration of islet cells (Thakur et al., 2012; Tiwari et al., 2014). Gymnemic acid from *Gymnema sylvestre* even rejuvenates the pancreas (Pednekar et al., 2011; Thakur et al., 2012; Tiwari et al., 2014). In clinical studies of diabetic animals, *Gymnema sylvestre* also appeared to reduce body weight, blood cholesterol and triglyceride levels (Brekhman and Dardymov,1969; Cane, 1990; Warren et al., 1969; Kim et al., 2016). Therefore, *Gymnema sylvestre* plant extracts were also used in antiobesity treatment (Pednekar et al., 2011; Thakur et al., 2012; Sinsheimer et al., 1970; Tiwari et al., 2014; Kim et al., 2016).

A major endocrine autoimmune disorder *Diabetes mellitus* is of two types, first one is called type-1 diabetes (Insulin dependent) where immune system of a type-1 diabetic patient destroys the *β*-cells that releases insulin. Therefore, insulin production is completely eliminated and unable to absorb glucose for the release of energy in type-1 diabetic patients. On the other hand, in case of type-2 diabetes, pancreas is very week and produces very less insulin. This is called as insulin deficiency and oral consumption of anti-diabetic synthetic drugs for example metformin acts as a catalyst to activate *β*-cells of pancreas to produce enough amount of insulin for the body functions. There are many commercial oral anti-diabetic drugs such as metformin (Glyciphage)® and sulfonylurea, which stimulates *β*-cells of pancreas to release insulin in type-2-diabetes by closure of B-cells K-ATP channel (Stocklin, 1969; Sinsheimer and Manni, 1965; DeFronzo, 1999; Brown et al., 2004;Thakur et al., 2012; Tiwari et al., 2014). However, longer period of consumption of synthetic drugs have side effects and affected body functions.

Recombinant insulin is now available and the technology for insulin delivery has improved in the recent past. However, there are many problems with long term insulin injection such as cutaneous complications of allergy, lipoatrophic area development, and injection abscesses (Hossain et al., 2016). Therefore, oral consumption of herbal medicines mimicking insulin action with ideal therapeutic properties plays an important role in controlling diabetic disorder (Thakur et al., 2012; Tiwari et al., 2014; Hossain et al., 2016). Furthermore, consumption of *Gymnema sylvestre* plant extracts confirmed the improvements in glycogen synthesis, glycolysis, gluconeogenesis, hepatic and muscle glucose uptake, as well as the reversal of hemoglobin and plasma protein glycosylation. Therefore, gymnema might improved glycemic control by stimulating insulin release from the pancreatic islets of Langerhans (Thakur et al., 2009a, 2009b, 2012; Tiwari et al., 2014).

Another important characteristic of the oral consumption of leaves of *Gymnema sylvestre* suppress the taste of sugar upon chewing and also suppresses to detect sweet tastes (Thakur et al., 2012; Yeh et al., 2003; Sudhanshu et al., 2012; Tiwari et al., 2014). Therefore, leaf plant material is also used to lower the intense desire of consuming sugary products (Saneja et al., 2010; Rani et al., 2012; Thakur et al., 2012; Gupta and Solanki, 2015; Tiwari et al., 2014). The reduced sensitivity to sweet substances produced by *Gymnema sylvestre* might resulted from the competition at the receptor sites between glycosides and the sweet substances (Tiwari et al., 2014; Thakur et al., 2012; Yeh et al., 2003; Sudhanshu et al., 2012; Brekhman and Dardymov,1969; Cane, 1990; Warren et al., 1969; Agarwal et al., 2000; Alam et al., 2011; Aleisa et al., 2014; Al-Romaiyan et al., 2010, 2012, 2013; Arun et al., 2014; Arunachalam et al., 2014; Arunakumara et al., 2005; Baskaran et al., 1990; Baskaran et al., 2007; Chakraborty et al., 2013; Devi and Ramasubramaniaraja, 2010). Therefore, *Gymnema sylvestre* plant is utilized as a pharmacological tool in the study of sweet-taste transduction (Thakur et al., 2012; Yeh et al., 2003; Sudhanshu et al., 2012; Tiwari et al., 2014).

According to the Indian traditional system of folk medicine-Ayurveda, *Gymnema sylvestre* is bitter cardio tonic, anti-arthritic, alexipharmic, expectorant, acrid, and stimulant. The medicinal plant *Gymnema sylvestre* is also useful in the treatment of asthma, snake bite, prevention of dental caries, cataract, acts as anticancer-

cytotoxic agent, alexipharmic, anodyne, diuretic, emetic, expectorant stimulant, stomachic, uterine tonic; useful in amennorrhoea, bronchitis, cardiopathy, conjunctivitis, antidysentery, cough, dyspepsia, haemorroids, hepatosplenomegaly, intermittant fever, laxative, cardiotonic, digestive, astringent, bitter, anthelmintic, antipyretic, anti-microbial, antiviral, antidiabetic, cardiopathy, amenorrhea, conjunctivitis, bronchitis, constipation, dyspepsia, hemorrhoids, cough, hepatosplenomegaly, lowering serum cholesterol, triglycerides, blood glucose level (hypoglycemic or antihyperglycemic), hypolipidaemic, either high or low blood pressure, aperitive, jaundice, inflammations, tachycardia or arrhythmias, water retention and liver diseases, intermittent fever, hyper cholesterolemia and leucoderma, purgative, in eye troubles, anti-inflammatory, smooth muscle relaxant, obesity, weight loss, and stomach ailments (Kim et al., 2016; Tiwari et al., 2014; Thakur et al., 2012; Gupta and Solanki, 2015; Wang et al., 2014; Yew et al., 2001; Yogalakshmi et al., 2014; Zarrelli et al., 2013a, 2013b; Brekhman and Dardymov,1969; Cane, 1990; Warren et al., 1969; Agarwal et al., 2000; Alam et al., 2011; Aleisa et al., 2014; Al-Romaiyan et al., 2010, 2012, 2013; Arun et al., 2014; Arunachalam et al., 2014; Arunakumara et al., 2005; Baskaran et al., 1990; Baskaran et al., 2007; Chakraborty et al., 2013; Devi and Ramasubramaniaraja, 2010; Hong-Min et al., 1992; Wen-Cai et al., 2000; Porchezhian and Dobriyal, 2003).

In present time, the demand of *Ayurveda,* Unani, Homoeopathy and Siddha medicine has increased considerably due to the consumption of herbal medicine extracts as a chief household remedy for the treatment of many health disorders (Thakur et al., 2012; Tiwari et al., 2014; Baskaran et al., 1990; Baskaran et al., 2007; Chakraborty et al., 2013; Devi and Ramasubramaniaraja, 2010). The commercial exploitation of *Gymnema sylvestre* plant and their secondary metabolites are some of the major prospective of this rare medicinal herb (Thakur et al., 2012; Tiwari et al., 2014; Wang et al., 2014; Yew et al., 2001; Yogalakshmi et al., 2014; Zarrelli et al., 2013a, 2013b). Therefore, the relevance of pharmacognosy in standardization of herbal drugs was long been stressed (Krishna et al., 2012; Thakur et al., 2012; Tiwari et al., 2014). Over exploitation of herbal medicine has definitely created an endangered level of medicinal plants and also a loss of gene pool too (Patel et al., 2013; Thakur et al., 2012; Tiwari et al., 2014; Malabadi et al., 2016a). Therefore, documentation, proper conservation and management of medicinal plant species is one of the important aspect of modern ethnobotanical study which gives a knowledge based sharing opportunity for the local traditional healers (Malabadi et al., 2007; Khramov et al., 2008; Aleisa et al., 2014; Al-Romaiyan et al., 2010, 2012, 2013; Arun et al., 2014; Arunachalam et al., 2014; Arunakumara et al., 2005). This also helps in the transfer of rich ethno-medicinal knowledge of plants from one generation to generation (Malabadi et al., 2007; Thakur et al., 2012;Tiwari et al., 2014; Sangeetha and Jegadeesan, 2012; Zhen et al., 2008; Devi and Srinivasan, 2011).

In vitro response of *Gymnema sylvestre* has been investigated by a number of scientists. Induction of callus, maintenance of suspension culture, micropropagation through axillary bud enhancement, somatic embryogenesis and multiplication of *in vitro* raised seedlings has been successfully achieved following gymnemic acid production in suspension culture (Ashokkumar et al., 2002; Praveen et al., 2014, 2011; Nagella et al., 2011, 2013; Gupta and Solanki, 2015; Veerashree et al., 2012; Osman et al., 2010; Kanetkar et al., 2006, 2007; Rao et al., 2015; Karthic and Seshadri, 2009; Jaybhaye and Deokule, 2010; Gopi and Vatsala, 2006; Gupta et al., 2012; Chodisetti et al., 2011, 2013; Amarasinghe et al., 2011; Aneesa et al., 2010; Arunakumara and Subasinghe, 2004; Arunakumara et al., 2013, 2006; Bakrudeen et al., 2012; Ahmed et al., 2008, 2009a, 2009b, 2010, 2011, 2012, 2013; Upendra et al., 2010; Subatra and Srinivasan, 2008; Solanki *et al.,* 2013; Solanki and Gupta, 2013a, 2013b, 2013c, Solanki et al., 2013; Singh et al., 2005; Sharma and Bansal, 2010; Reddy et al., 1998; Manonmani and Francisca, 2012; Lee et al., 2006).

In another study, Vats and Kamal (2013) evaluated phytosterols in leaves and callus cultures of *Gymnema sylvestris* (Gupta and Solanki, 2015). The highest amount of callus was obtained on MS medium with 0.5 mgl^{-1} of 2,4-D (Vats and Kamal, 2013; Gupta and Solanki, 2015). Extracts of callus and leaves were analyzed by chromatography and spectroscopy for pointing out phytosterols (Vats and Kamal, 2013; Gupta and Solanki, 2015). These extracts have confirmed the presence of beta-sitosterol, stigmasterol and campesterol in both types of extracts, while lanosterol was identified only in callus culture (Gupta and Solanki, 2015; Wen-Cai et al., 2000). Furthermore, Nagella et al., *(*2013), established hairy root cultures of *Gymnema sylvestre* and obtained 9.4 times increase in biomass with 4.7 fold increase in the gymnemic acid amount as compared to

non-transformed cultures (Nagella et al., 2013, 2011; Gupta and Solanki, 2015). Hairy root cultures of *sylvestris sylvestre* were given elicitation after 15 days of culture by oleic and linolenic acid at different concentrations and roots were harvested after 20 days (Nagella et al., 2013, 2011; Gupta and Solanki, 2015). An increase of 7.78 fold in gymnemic acid yield was obtained with 5 µM linolenic acid as compared to the non-elicited cultures (Praveen et al., 2014, 2011; Nagella et al., 2011, 2013; Gupta and Solanki, 2015; Veerashree et al., 2012; Osman et al., 2010; Kanetkar et al., 2006, 2007).

Gymnema sylvestre: Pharmacological activities

1) In one of the study, Ahmed et al., (2011) reported the hypoglycemic potential of *Gymnema sylvestre*, *Tinospora cordifolia*, *Eugenia jambolana* and *Aegle marmelos* (EI-Shafey et al., 2013). This might be due to their effect on inhibition of the activity of α-amylase resulting in the delayed digestion of the dietary carbohydrates. Therefore, the liberated glucose from the intestine lumen to the circulation decreased (Ahmed et al., 2011; EI-Shafey et al., 2013). Furthermore, Luo et al., (2007) discovered the ability of *Gymnema sylvestre* water extract to prevent the genetic obesity by improving the cholesterol metabolism and inhibiting polyphagia (EI-Shafey et al., 2013; Tiwari et al., 2014).

2) Shanmugasundaram et al., (1983) reported that administration of dried leaf powder of *Gymnema sylvestre* decreased glucose levels since plant has controlled gluconeogenic enzymes (ALT and AST) and increased glycogen levels in liver, kidney and muscle (Shanmugasundaram et al., 1983; Shanmugasundaram et al., 1990; EI-Shafey et al., 2013). In one of the treatment of 27 patients with type 1 diabetes, the use of water leaf extract of *Gymnema sylvestre* (400 mg/day) for 12 months reduced blood glucose level (up to 35%) as a direct effect of increasing exogenous insulin level (up to 50%) (Shanmugasundaram et al., 1990; EI-Shafey et al., 2013; Tiwari et al., 2014). Therefore, this study concluded that *Gymnema sylvestre* leaf extract exhibit antidiabetic activity and recommended as a complementary medicine in diabetes mellitus (Shanmugasundaram et al., 1983; Shanmugasundaram et al., 1990; EI-Shafey et al., 2013; Tiwari et al., 2014). Therefore, decrease in plasma glucose levels might be due to the increase in insulin levels after the administration of gymnemic acid. In another study, Gholap and Kar (2005) discovered that gymnemic acid was capable of reducing corticosteroid hormones in dexamethasone-induced hyperglycemia in mice (EI-Shafey et al., 2013; Saneja et al., 2010; Venkatesham et al., 2010; Tiwari et al., 2014; Brekhman and Dardymov,1969; Cane, 1990; Warren et al., 1969; Agarwal et al., 2000; Alam et al., 2011). Gymnemic acids are thought to be responsible for its antidiabetic activity and it is the major component of an extract shown to stimulate insulin release from the pancreas (Thakur et al., 2012; Tiwari et al., 2014; Devi et al., 2006; DiFabio et al., 2015; Kiran et al., 2014).

3) *Gymnema sylvestre* R. Br. (*G. sylvestre*) of the family *Asclepiadaceae* has been used as a chief herbal medicine remedy for the treatment of diabetes (Patel et al., 2012; EI-Shafey et al., 2013; Saneja et al., 2010; Venkatesham et al., 2010). Shafey et al. (2013) reported an experimental study on several physiological parameters of diabetic rats using leaf extract of *Gymnema sylvestre* (EI-Shafey et al., 2013). During this study, *Gymnema sylvestre* leaf extract (18 mg/kg body weight) was orally administered for 30 days to normal and streptozotocin (STZ) diabetic rats (EI-Shafey et al., 2013). STZ-diabetic rats exhibited a significant increase in plasma glucose, liver function enzymes [alanine aminotransaminase (ALT) and aspartate aminotransaminase (AST)], triglycerides, total cholesterol, LDL-cholesterol malondialdehyde, catalase, reduced glutathione and a significant decrease in insulin, HDL-cholesterol and erythrocyte superoxide dismutase levels (EI-Shafey et al., 2013).

Furthermore, treatment of diabetic rats with *Gymnema sylvestre* leaf extract significantly decreased plasma glucose, ALT, AST, triglycerides, total cholesterol, LDL-cholesterol, malondialdehyde and significantly increased insulin, HDL-cholesterol and erythrocyte superoxide dismutase levels compared to untreated diabetic rats (EI-Shafey et al., 2013). Therefore, this experimental study concluded that the use of *Gymnema sylvestre* leaf extract could be used as a herbal medicine for the treatment of diabetic rats' health complications including hyperglycemia, hypoinsulinemia, hyperlipidemia and oxidative stress (EI-Shafey et al., 2013; Saneja et al., 2010; Venkatesham et al., 2010). In another previous study, Chattopadhyay (1998) reported that administration of alcoholic extract of *Gymnema sylvestre* leaves to Swiss albino rats fed by glucose increases the insulin level (Chattopadhyay, 1998; EI-Shafey et al., 2013). *In vivo* leaf and *in vitro* callus methanol extract of *Gymnema sylvestre* decreased blood

glucose level (72.4%) in diabetic rats (Ahmed et al., 2008, 2011; EI-Shafey et al., 2013), and that might be due to increased liver glycogen content (Ahmed et al., 2010; EI-Shafey et al., 2013; Tiwari et al., 2014).

4) In another study, gymnemic acid extract of *Gymnema sylvestre* inhibited glucose uptake in the intestine of guinea pig which occurred due to the effect of gymnemic acid extract on the suppression of high K+ induced contraction in guinea pig longitudinal muscles (Shimizu et al., 1997; EI-Shafey et al., 2013). Fushiki et al., (1992) suggested that the *Gymnema sylvestre* leaves extract inhibited gastric inhibitory peptide (GIP) (EI-Shafey et al., 2013). Sahu et al., (1996) reported that the gymnemic acid molecules fill the receptor location in the absorptive external layers of the intestine thereby preventing the glucose absorption by the rat intestine (EI-Shafey et al., 2013). In addition to this, Ishijima et al., (2008) reported that gymnemic acid might have some pharmacological activities including antidiabetic activity and lipid lowering effects *via* the inhibition of glycerol-3-phosphate dehydrogenase activity *in vitro* (EI-Shafey et al., 2013; Saneja et al., 2010; Venkatesham et al., 2010; Tiwari et al., 2014).

5) In another study, Manish et al., (2011) reported the lipid lowering activity of flavonoids and saponins extracted from *Gymnema sylvestre* which might be due to the inhibition of pancreatic lipase activity (EI-Shafey et al., 2013; Saneja et al., 2010; Venkatesham et al., 2010). *In vitro Gymnema sylvestre* alcoholic leaf extract showed antioxidant ability by inhibiting 1,1-diphenyl-2-picrylhdrazyl (DPPH) and scavenging superoxide and hydrogen peroxide (EI-Shafey et al., 2013; Saneja et al., 2010; Venkatesham et al., 2010). In another study, the maximum scavenging activity of ethanolic extract of *Gymnema sylvestre in vitro* was 54.4% at concentration 250 lg/ml (Fazal et al., 2011; EI-Shafey et al., 2013). Some poly herbal *Ayurvedic* formulations like Hyponidd and Dihar containing *Gymnema sylvestre* extract had shown antioxidant activity by increasing superoxide dismutase, glutathione and catalase levels in rats (Mall et al., 2009; Mahajan et al., 2011; EI-Shafey et al., 2013; Saneja et al., 2010; Venkatesham et al., 2010; Tiwari et al., 2014).

6) In another study reported by Pednekar et al. (2011) a microwave assisted extraction and liquid-liquid extraction have been investigated to determine the content of gymnemic acid from leaves of *Gymnema sylvestre* R.Br (Pednekar et al., 2011). The extraction of gymnemic acid is commercially very important because it is a potent antidiabetic agent and used in various pharmaceutical products (Pednekar et al., 2011). The effect of single factors such as microwave power, microwave irradiation time, extraction solvent volume, sample size, *etc*. are evaluated and standardized (Pednekar et al., 2011). Microwave assisted extraction and liquid-liquid extraction has been comparatively evaluated for their efficiency to extract the content of gymnemic acid from leaves of *Gymnema sylvestre* (Pednekar et al., 2011). The extracts obtained by various extraction techniques were analyzed for the content of gymnemic acid by validated RP-HPLC method (Pednekar et al., 2011). In this experimental study, deacylgymnemic acid was used a reference standard and the amount of gymnemic acid was calculated by using molecular weight correction factor (Pednekar et al., 2011). Therefore, on the basis of this study, the extraction yield, extraction time, solvent and cost of extraction, better results were obtained by microwave assisted extraction (50 % methanol 5 min at 20 % power with minimum sample size) (Pednekar et al., 2011; Mandal et al., 2009; Tiwari et al., 2014). According to this study, application of microwave assisted extraction method minimized the use of organic solvents (Pednekar et al., 2011). Toxicity and comparative bio-availabilty of the microwave assisted extraction extract were also evaluated on animal model (Pednekar et al., 2011; Mandal et al., 2009; Gupta and Solanki, 2015).

7) In another study conducted by Persaud et al., (1999), gymnemic acid concentrated fractions were obtained by using a silica gel chromatography of plant extracts on the basis of size exclusion (Persaud et al., 1999; Gupta and Solanki, 2015). These fractions were tested *in vivo* on rat and *in vitro* on several pancreatic beta-cell lines and noticed the increase of insulin secretion in both cases (Persaud et al., 1999; Gupta and Solanki, 2015). The gymnemic acid plant extract has been used in traditional Ayurvedic preparations which were used to control blood sugar and cholesterol levels in diabetic animals and humans (Porchezhian and Dobriyal, 2003; Gupta and Solanki, 2015). The principal antidiabetic constituent of the plant is gymnemic acid, which is used to cure diabetes and obesity (Kanetkar et al., 2007; Gupta and Solanki, 2015). This property is attributed to increase insulin secretion by extract as noticed by Al-Romaiyan et al., (2010), in human pancreatic islets *in vivo* and *in vitro* (Gupta and Solanki, 2015). Furthermore, gymnemic acid, depresses appetite and

cause weight reduction, it restores pancreas function, and has anti-tooth decaying effect (Gupta and Solanki, 2015; Tiwari et al., 2014). Gymnemic acid possesses different therapeutic activities like suppression of taste buds activity for sweetness, inhibition of intestinal glucose absorption and lowers the plasma glucose levels (Patel et al., 2012; Nagella et al., 2011, 2013; Solanki et al., 2013; Gupta and Solanki, 2015; Tiwari et al., 2014). The broad range pharmacological activities of *Gymnema sylvestris* are due to a wide spectrum of triterpenoids found in different parts of the plant (Fabio et al., 2014; Gupta and Solanki, 2015; Upendra et al., 2010; Tiwari et al., 2014; Subatra et al., 2006a, 2006b; Subatra and Srinivasan, 2008; Solanki and Gupta, 2013a, 2013b, 2013c; Sangeetha and Jegadeesan, 2012; Luo and Shen, 1987; Luo, 1999; Luo et al., 2001a, 2001b; Luo et al., 2007; Rani et al., 2012; Malik et al., 2008, 2010; Ashokkumar et al., 2002; Khramov et al., 2008; Komalavalli and Rao, 2000; Khanna and Kannabiran, 2009).

8) Furthermore, according to Singh and Dixit, (2008), the comparative method shows that HPLC method of analysis is better than gravimetry estimation of gymnemic acids in *Gymnema sylvestres* (Singh and Dixit, 2008). In another recent study, gymnemic acid was isolated and characterized from leaf extracts of seventeen ecotypes of *Gymnema sylvestre* with different solvent systems like petroleum ether, benzene, and methanol(Krishna et al., 2012). The defatted leaves were extracted under continuous hot extraction in Soxhlet apparatus with 90% methanol gave the maximum yield of gymnemic acid (42%) from the ecotype collected from Warangal-1(Krishna et al., 2012). Gymnemic acid was purified by preparative chromatographic methods i.e., TLC and HPTLC. On the basis of this study, it was concluded that the analysis by HPTLC showed 30% purity of gymnemic acid (Krishna et al., 2012). Therefore, HPTLC method was found to be accurate, precise, and less time consuming. Hence, HPTLC could be used for analysis of gymnemic acid and for standardization of herbal drugs in general laboratory conditions (Krishna et al., 2012; Vats and Kamal, 2013; Gupta and Solanki, 2015). This study has not reported any clinical experimental study to confirm the herbal drug activity.

9) Mozersky, (1999) reported that 22 patients were given *Gymnema sylvestre* extract along with their oral hypoglycemic drugs (Mozersky, 1999). All patients demonstrated improved blood sugar control. Twenty-one out of the twenty-two were able to reduce their oral hypoglycemic drug dosage considerably, and five patients were able to discontinue their oral medication and maintain blood sugar control with the extract alone (Mozersky, 1999). In another study conducted on experimentally induced hyperlipidaemic rats, the *Gymnema sylvestre* leaf extract at a dosage of 25-100 mg/kg administered orally for two weeks reduced the elevated serum triglyceride (TG), total cholesterol (TC), very low density lipoprotein (VLDL) and low density lipoprotein (LDL)-cholesterol in a dose dependent manner (Bishayee and Chatterjee, 1994). The ability of the extract at 100mg/kg to lower TG and TC in serum and its antiantheroscelrotic potential were almost similar to that of a standard lipid lowering agent clifibrate (Bishayee and Chatterjee, 1994).

10) An increase in body weight was significantly suppressed in a long-term study of the administration of *Gymnema sylvestre* extract in rats fed a high-fat diet (Shigematsu et al., 2001a). However, in rats receiving a normal diet, no significant suppression of weight gain was observed (Shigematsu et al., 2001a). Use of a dietary supplement containing *Gymnema sylvestre* in combination with glucomannan, chitosan, fenugreek, and vitamin C was investigated in obese adults (body mass index 30 kg/m 2 or more) (Woodgate and Conquer, 2003). Compared with placebo recipients, the treatment group lost significantly more body weight, and percentage of body fat and absolute fat mass were significantly reduced. Reduction in upper abdominal, waist, and hip circumferences also was demonstrated in patients receiving active treatment (Shigematsu et al., 2001b; Woodgate and Conquer, 2003). The effect of *Gymnema sylvestre* on body weight, glucose absorption and lipid metabolism was examined by using a breed of fatty rats with genetic obese-hyperglycaemia (Woodgate and Conquer, 2003).

11) In another experimental study reported by Gupta and Singh (2014) *in vitro* antimicrobial activity against human pathogenic microorganism *(Escherichia coli, Vibrio cholera, Streptococcus mutans, Staphylococcus aureus Candida albicans and Aspergillus niger)* was assessed using gymnemic acid, the petroleum benzene, ethanol, and aqueous leaf extracts of *Gymnema sylvestre* (Gupta and Singh, 2014). During this experimental study, the *in vivo* leaf extracts were extracted from soxlate extractor and gymnemic acid was isolated from TLC method (Gupta and Singh, 2014). Different solvent extracts of *Gymnema sylvestre* leaf and isolated

gymnemic acid was assayed by *in vitro* screening for antimicrobial activity on human pathogen by using the disk diffusion method (Gupta and Singh, 2014). According to this study the aqueous extract and isolated gymnemic acid of *Gymnema sylvestre* showed the best zone of inhibition against the organisms (Gupta and Singh, 2014). A maximum zone of inhibition was obtained *Staphylococcus aureus* (9.25mm) on gymnemic acid and aqueous extract showed (8.50mm) in comparison to others but aqueous extract present large inhibition of *Escherichia coli* (9.00mm) and *Candida albicanse* (8.76mm) (Gupta and Singh, 2014; Luo and Shen, 1987; Luo, 1999; Luo et al., 2001a, 2001b; Luo et al., 2007).

The petroleum benzene extracts that showed minimum zone of inhibition or negative result against microorganisms (Gupta and Singh, 2014). On the other hand ethanol extract had performed comparatively the best inhibition on organisms than petroleum extract (Gupta and Singh, 2014). The botanical extracts showed activity against microorganisms had at least 70% of antimicrobial activity when compared to disk diffusion by the commercial antibiotic fluoroquinolone ciprofloxacin utilized as a control (Gupta and Singh, 2014). Tested plant extracts in all solvent and gymnemic acid assayed, the *Staphylococcus aureus* had the best performance, sometimes exhibiting higher activity than ciprofloxacin (Gupta and Singh, 2014). Therefore, this study concluded that *Gymnema sylvestre* plant extracts presents a strong antimicrobial properties against tested human pathogens (Gupta and Singh, 2014).

12) In another study, a novel attempt has been made for the development of *Gymnema sylvestre* plant extracts for a injectable dosage form (Ganapati et al., 2012). During this experimental study, ethanolic and water-plant extracts were used for the preparation of injection dosage (Ganapati et al., 2012). Further phytochemical and TLC study was carried out (Ganapati et al., 2012). Potassium salt of gymnemic acid was soluble in normal saline and injectables were found stable, sterile, leak proof and free from particulate matter (Ganapati et al., 2012). However, no animal or human clinical tests were conducted using this injectable plant extracts (Ganapati et al., 2012).

13) Herbal formulations offer new prospects in the treatment of dental caries (Tiwari et al., 2014; Devi and Ramasubramaniaraja, 2010). The chloroform, petroleum ether, and methanolic leaf extracts of *Gymnema sylvestre* at various concentrations of 25, 50, and 100mg/mL were tested against microbial dental infections and found to be significantly effective against these cariogenic bacteria particularly the methanolic extract which showed highest activity at minimum concentration (Tiwari et al., 2014; Devi and Ramasubramaniaraja, 2010). The good potential of the hydroalcoholic extract of the plant leads to the development and manufacture of gurmar tooth powdered marketed as "Gurmar Herbal tooth paste" and "Gurmar Herbal Tooth powder" (Tiwari et al., 2014; Devi and Ramasubramaniaraja, 2010).

14) The hydroalcoholic extract of *Gymnema sylvestre* has good wound healing property as compared with control group (Alam et al., 2011; Tiwari et al., 2014). TLC analysis, wound contraction, and qualitative tests supported the synergistic wound healing effect of the *Gymnema sylvestre* plant (Alam et al., 2011; Tiwari et al., 2014). The increased wound healing activity of hydroalcoholic extracts may be attributed to the free radical scavenging action and the presence of phytoconstituents (flavonoids) which may act individually or have additive effect (Alam et al., 2011; Tiwari et al., 2014). The flavonoids in alcoholic extract were detected by TLC and phytochemical analysis (Alam et al., 2011; Tiwari et al., 2014). Furthermore, the hexane extract of the leaves of *Gymnema sylvestre* have the potential to treat obesity (Kim et al., 2016) comparable with that of standard drug, atorvastatin (Tiwari et al., 2014; Kim et al., 2016). In another study, anticancer potential of gymnemagenol on *HeLa* cancer cell lines in *in vitro* conditions was determined. These experimental results confirmed that the isolated bioactive constituent, gymnemagenol, showed high degree of inhibition to the proliferation of *HeLa* cancer cell line (Tiwari et al., 2014).

15) Obesity is related to many health problems such as hypertension, type 2 diabetes, stroke, cardiovascular disease, osteoarthritis, asthma, and even certain types of cancer (Kim et al., 2016). Therefore, obesity-a major risk factor of various disorders is another concerning global health issue (Kim et al., 2016). Very recently, the effect of *Gymnema sylvestre* extract (GS) on initial antiobesity, liver injury, and glucose homeostasis induced by a high-fat diet (HFD) has been reported (Kim et al., 2016). The dry powder of *Gymnema sylvestre* extract (GS) was extracted with methanol, and gymnemic acid was identified by high performance

liquid chromatography as deacyl gymnemic acid (Kim et al., 2016). During this experimental study, male C57BL/6J mice were fed on either a normal diet, normal diet containing 1 g/kg *Gymnema sylvestre* extract (GS) (CON+GS), high-fat diet (HFD), or high-fat diet (HFD) containing 1.0 g/kg GS (HFD+ GS) for 4 weeks to test the initial anti-obesity effect of *Gymnema sylvestre* extract (GS) (Kim et al., 2016). In this experimental study, body weight gain and food intake, and serum levels about lipid and liver injury markers were measured (Kim et al., 2016). According to this study, the methanol extracts of *Gymnema sylvestre* (GS) exerted significant anti-obesity effects in high fat diet (HFD) + *Gymnema sylvestre* extract (GS) group (Kim et al., 2016). They decreased body weight gain, a lower food and energy efficiency ratio, and showed lower serum levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL)-cholesterol, very-low density lipoprotein (VLDL)-cholesterol and leptin compared with the HFD group (Kim et al., 2016). This study concluded that *Gymnema sylvestre* extract (GS) provide the possibility as a key role in an initial anti-obesity effects feeding with a high fat diet (Kim et al., 2016). Therefore, *Gymnema sylvestre* extract could also be used as one of the functional food additive in order to control obesity (Kim et al., 2016).

16) In another recent study, ten bioactive small compounds derived from *Gymnema sylvestre* were chosen to determine their IR binding affinity and ADMET properties using a combined approach of molecular docking study and computational pharmacokinetic elucidation (Hossain et al., 2016). Among the forty structural analogues, four compounds demonstrated considerably increased binding affinity towards IR and less toxicity compared with parent compounds (Hossain et al., 2016). Finally, molecular interaction analysis revealed that six parent compounds and four analogues interact with the active site amino acids of IR (Hossain et al., 2016). So this study would be a way to identify new therapeutics and alternatives to insulin for diabetic patients (Hossain et al., 2016). Therefore, the results of this study provide an opportunity for further evaluation of the proposed drugs *in vitro* and *in vivo* for establishing their candidature as alternative oral drugs for the treatment of diabetes (Hossain et al., 2016).

17) One of the recent study confirmed the antibacterial activity of leaf extract of *Gymnema sylvestre* (Vani et al., 2016). *Gymnema sylvestre* extracts found effective against tested bacterial strains (Vani et al., 2016). On the basis of this study, the *Gymnema sylvestre* leaf extract showed higher antibacterial activity against gram positive bacteria than gram negative bacteria (Vani et al., 2016). Hence *Gymnema sylvestre* exhibited potent antioxidant activity by inhibiting DPPH free radicals (Vani et al., 2016). Therefore, the root and leaf extracts of *Gymnema sylvestre* can be used as an accessible source of natural antioxidant agent (Vani et al., 2016). Furthermore, antibacterial potentials of ethanolic extracts from powdered leaves of *Gymnema sylvestre* were tested against bacteria *E. coli* NCIM 2065, *Pseudomonas aeruginosa* MTCC 424, *Enterococcus hirae* NCIM 2080, *Bacillus subtilis* NCIM 2063, *Micrococcus luteus* NCIM 2103, *Staphylococcus aureus* NCIM 2079 bacterial strains by disc diffusion method (Thanwar et al., 2016). Ethanol extract showed higher degree of antibacterial activity against *E. coli*, *E. hirae* and *M. luteus* and less effective against bacteria *P. aeruginosa, S. luteus* (Thanwar et al., 2016). Therefore, results of this study also confirmed the therapeutic value of *Gymnema sylvestre* for treating the diseases caused by pathogenic bacteria (Thanwar et al., 2016).

Conclusion

This review paper highlighted the collective experimental results (ethnobotany, phytochemistry and pharmaceutical activities) of the rare medicinal herb *Gymnema sylvestre* R. Br., as a potential medication for the treatment of many human health issues. *Gymnema sylvestre* R. Br., plant occupies the super most unique position in the Indian traditional folk medicine, *Ayurveda* because of its multiple pharmaceutical activities. There was also a saying in Indian ancient folk medicine *Ayurveda*, that one herbal plant *Gymnema sylvestre* for all the diseases. Now a days herbal medical treatment offers many advantages such as less expensive, and overcome side effects as compared to synthetic drugs. However, in spite of medicinal value, most of the herbal medicines including *Gymnema* species lack scientific validation and availability of standards for herbal formulations is a major limitation (Tiwari et al., 2014). On the other hand, gymnemic acid has a poor lipid solubility with complex structure resulted in the poor absorption. Toxicity studies of *Gymnema* extract have already approved the optimum dosage. Higher doses of *Gymnema* extract may lead to many health complications such as hypoglycemia, weakness, shakiness, excessive sweating, and muscular

dystropy (Tiwari et al., 2014). Furthermore treatment of diabetic patients with *Gymnema sylvestre* has been shown to cause a toxic hepatitis or drug-induced liver injury (DILI) (Tiwari et al., 2014; Shiyovich et al., 2010). *Gymnema sylvestre* 75 is a herbal preparation which contains 75% gymnemic acid from leaf extract and provides nutritional support to pancreas and maintain healthy blood sugar balance when used as a part of diet (Tiwari et al., 2014). Another major concern of many medicinal plants of commercial importance face threat of extinction due to increase in demand and destruction of their habitats due to urbanization and industrilization. Therefore, cultivation and conservation of medicinal plants of pharmacological importance is not only a challenge but a major goal of ethnobotany. Finally, till today there are many ethnobotanical and pharmacological studies have been found only on the *Gymnema sylvestre* species. Hence *Gymnema sylvestre* has been considered as a role model plant among *Gymnema* species. However, sufficient information on ethnobotanical and pharmacological activities of other species of *Gymnema* such as *G. acuminatum* (Roxb.) Wall, *G. aurantiacum*, *G. balsamicum*, *G. elegans* W&A, *G. hirsutum* W&A, *G. lactiferum*, *G. latifolium*, *G.montanum* Hook. f., *G. tingens* W&A, *G. indorum*, *G. yunnanse* and *G. spartum* is lacking. Therefore, a detailed ethnobotanical, phytochemical, and pharmaceutical study should also be conducted on other species of *Gymnema*. This will help in the identification and formulations of new bioactive compounds to be used for a novel drug discovery.

Conflict of interest statement

Authors declare that they have no conflict of interest.

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