IJNLS
INTERNATIONAL JOURNAL OF NATURE AND LIFE SCIENCES
Review article

International Journal of Nature and Life Sciences (IJNLS)
https://www.dergipark.gov.tr/ ijnls
e-ISSN: 2602-2397
Vol. 3(2), December 2019, pp. 40-51

A Review of Anti-diabetic Activity of *Gymnema sylvestre* and *Pterocarpus marsupium*: Special Emphasis on its Combination in 4DM

Aminul Islam*[1], Leroy Rebello[2], Sreesudha Chepyala[3]

[1]*Biotex Life Solutions Private Limited, Hyderabad, India, orcid.org/0000-0003-2977-2234*
[2]*Biotex Life Solutions Private Limited, Hyderabad, India, orcid.org/0000-0002-1570-3417*
[3]*Biotex Life Solutions Private Limited, Hyderabad, India, orcid.org/0000-0002-6317-760X*
**Corresponding author: lab@biotex.in*

Received: *27 April 2019,* ***Revised:*** *25 May 2019,* ***Published Online:*** *01 December 2019*

Abstract

Gymnema sylvestre is a significant herb in traditional system of medicine and as well as in Ayurveda. The triterpene saponins which includes gymnemic acids, gymnosaponins and a polypeptide gurmarin are the main bioactive principle of *Gymnema sylvestre* and these phytoconstituents are mainly responsible for its antidiabetic property; *Gymnema sylvestre* also exhibits a wide range of therapeutic actions like anti-inflammatory, anti-hypercholesteromia, cardioprotective activity etc. It also is used in arthritis, diuretic, anemia, osteoporosis, asthma, indigestion etc. *Pterocarpus marsupium* is also a medicinal plant which is well known for its anti-diabetic property and other various therapeutic usages. This is a woody tree, mainly the heart wood contains the bioactive principle pterostilbene, (-) epicatechin, pterosupin, marsupin, tannins etc. which are responsible for its anti-diabetic activity. 4DM is a combination of *Gymnema sylvestre* and *Pterocarpus marsupium* - a product of Biotex Life Solutions (India). The preparation is equally proportionate, i.e. in a 1:1 ratio. *Gymnema sylvestre* and *Pterocarpus marsupium* extraction has been done in a specific standardized condition to obtain 25% Gymnemic acid and 5% Pterostilbene respectively.

Key words: Anti-diabetic activity, *Gymnema sylvestre, Pterocarpus marsupium*

1. Introduction

Diabetes mellitus is a major endocrine disorder affecting nearly 10% of the population worldwide (Brook et al., 2003) and a key issue of concern.

The rate of rise of this affliction- the type 2 Diabetes Mellitus among people of all ages even including children is alarming. Type 2 diabetes is a metabolic disorder which is characterized by hyperglycemia resulting from defective insulin secretion, resistance to insulin action or both (Jarald et al., 2008; Vasi et al., 2009; Khan et al., 2012).

The word "Gymnema" is evolved from the word "Gurmar" ("destroyer of sugar") and it is believed that it might neutralize the excess of sugar present in the body in people with Diabetes mellitus. *Gymnema sylvestre* is an important herb in the treatment of type 2 Diabetes Mellitus due to the presence of oleanane, dammarane types of secondary metabolites and the antioxidants present in flavonoids, cinnamic acid, folic acid, ascorbic acid etc. along with potential health benefits and few side effects (Sujin et al., 2008).

1.1. Gymnema sylvestre R.Br. (Asclepiadaceae)

Latin name: *Gymnema sylvestre* R.Br. (Asclepiadaceae)

English Name: Destroyer of sugar, Periploca of woods

Sanskrit/Indian name: Madhunashini, Gurmar, Meshashringi, Vishani, Merasingi.

Parts used: Leaves, stems, roots

Taxonomic classification:

Kingdom: Plantae – Plants

Subkingdom: Tracheobionta – Vascular plants

Superdivision: Spermatophyta – Seed plants

Division: Magnoliophyta – Flowering plants

Class: Magnoliopsida – Dicotyledons

Subclass: Asteridae

Order: Gentianales

Family: Asclepiadaceae – Milkweed family

Genus: *Gymnema* R. Br. – gymnema

Species: *Gymnema sylvestre* (Retz.) Schult.

Figure 1. *Gymnema sylvestre* plant.

Description of *Gymnema sylvestre*: This is a large, stout, woody climber (Fig. 1), with densely covered branch lets. Leaves are obovate-acute in shape, rarely pubescent above. Flowers are small, crowded umbelliform cymes type. Fruits are slender, glabrous with follicles. Seeds are pale brown in color flattened, ovoid-oblong with a broad wing. The flowering time is during July-September and the fruit matures during October-December.

Distribution of *Gymnema sylvestre*: The plant originates from Central and Western India, Tropical Africa, Australia, Malaysia and Sri Lanka (Gurav et al., 2007).

Gymnema sylvestre is a slow growing perennial climber found in dry forests up to 600 m height. It is mainly present in the tropical forest of Central and Western India. It is also found in Banda, Konkan, Western Ghats, Deccan extending to the parts of Southern and Northern India.

***1.2. Pterocarpus marsupium* Roxb.** is widely used in the traditional system of medicine for the treatment of diabetes mellitus. It is also used in Ayurveda as Rasayana for the management of other metabolic disorders including hyperlipidemia.

Taxonomic Classification:

The taxonomic position and the local and scientific name of *Pterocarpus marsupium* are as follows.

Kingdom: Plantae – Plants

Subkingdom: Tracheobionta – Vascular plants

Superdivision: Spermatophyta – Seed plants

Division: Magnoliophyta – Flowering plants

Class: Magnoliopsida – Dicotyledons

Sub-class: Rosidae

Order: Fabales

Family: Fabaceae – Pea family

Genus: *Pterocarpus*

Species: *Pterocarpus marsupium* Roxb.

Common Names of *Pterocarpus marsupium*

Pterocarpus marsupium has different names in various language as below:

- Vijayasara, Vijaysar, Bija, Beejaka, Asana (Hindi)
- Indian Kino tree, Malabar Kino tree, Red sandalwood (English)
- Vegai, Venga katal, Vengai (Tamil)
- Vegisa, Peddagi, Yegi (Telegu)
- Biyo (Gujarati)
- Piashala, Piasal (Oriya)
- Bijasar (Urdu)
- Venga (Malayalam)
- Banga, Bange mara, Kempu honne, Bijasara, Asana (Kannada)
- Peetashal, Piyasal, Piyasala, Pitasala, (Bengali)
- Chandan Lal, Channanlal (Punjabi)
- Vivala, Bibala (Marathi)
- Bijaysaar Siddha, Tamil-Vengai (Unani)
- Biyo, Asana, vijaysar, Pitasara, Asanam, bijasal (Ayurvedic)

Sanskrit & Indian name of Vijaysar Bijaka, Pitasara, Pitashalaka

Description of *Pterocarpus marsupium*: This is a tree, of medium to large height which varies from 10 to 30 meters (Fig. 2). The stem is stout and crooked with widely spreading branches. The bark is thick and dark brown to grey in color (Fig. 3). Leaves are compound and glabrous on both surfaces, flowers are very numerous, white, with a small tinge of yellow. Stamens are united near the base and formed the androecium; anthers are 2-lobed and globular. Ovary is hairy, oblong, pedicelled and style is ascending position. The legume, which is borne on a long petiole, is three-fourths orbicular, the upper remainder, which extends from the pedicel to the remainder of the style, is straight, the whole surrounded with a waved, veiny, downy, swelled, rugose, woody in the centre, where the seed is lodged and not opening; generally one but sometimes 2-celled. Seeds are single.

Distribution of *Pterocarpus marsupium:* In India *Pterocarpus marsupium*. grows in deciduous and evergreen forests of central, western and southern region, mostly found in the states of Madhya Pradesh, Chhattisgarh, Bihar, Gujrat, Orissa.

Figure 2. *Pterocarpus marsupium*.

Figure 3. Heart wood of *Pterocarpus marsupium*.

2. Antidiabetic Compounds

Here we have summaries the bioactive principles of *Gymnema sylvestre* and *Pterocarpus marsupium* those are responsible for the anti-diabetic activity of these two species.

2.1. Antidiabetic compounds of Gymnema sylvestre

The leaves of *Gymnema sylvestre* contain triterpene saponins belonging to oleanane and dammarene classes. Oleanane saponins are gymnemic acids (Fig. 4) and gymnemasaponins. Gymnimasaponins consist of two aglycone saponins like gymnemagenis and gymnestrogenin. Dammarene saponins include gymnemasides (I-VII) (Sinsheimer et al., 1970; Foster et al., 2002; Khramov et al., 2008; Potawale et al., 2008). All these secondary metabolites have anti-diabetic properties. The leaves also contain resins, albumin, chlorophyll, carbohydrates, tartaric acid, formic acid, butyric acid, anthraquinone derivatives, inositol alkaloids, organic acid (5.5%), parabin, calcium oxalate (7.3%), lignin (4.8%), cellulose (22%) etc which also shows anti-diabetic activity (Dateo et al., 1973).

The triterpenoid glycoside gymnemic acid (Yoshikawa et al., 1989; Manohar et al., 2009) is not a pure compound, it has a unique structure which is comprises of various types compounds with similar molecular formula. The aglycone part (Fig. 5) is located centrally in this molecule, which has a sugar moiety (e.g. glucuronic acid) or conjugated with several ester groups. Gymnemic acid A includes A1, A2, A3 and A4.

The aglycone fragment (gymnemagenin) is a D-glucoronide of hexa-hydroxytriterpene. Gymnemasaponin III is another anti-sweet compound with twenty-three hydroxy longispinogenin as the aglycone moiety (Yoshikwa et al., 1989; Tiwari et al., 2014).

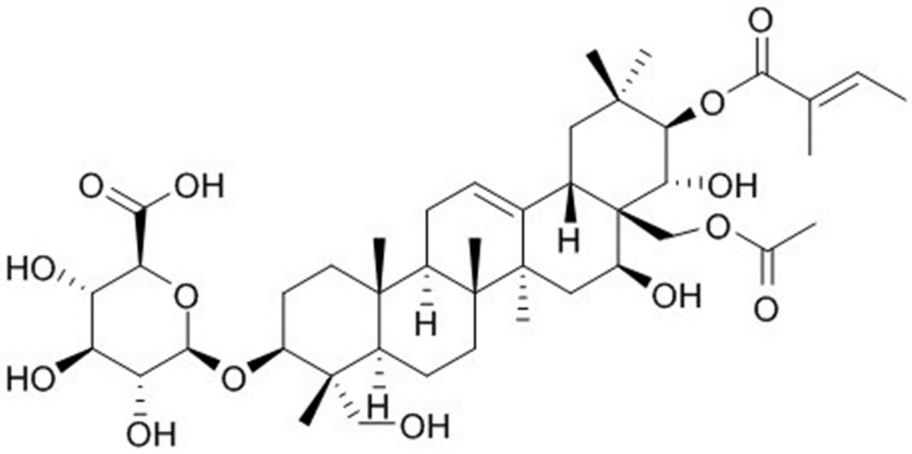


Figure 4. Gymnemic acid.

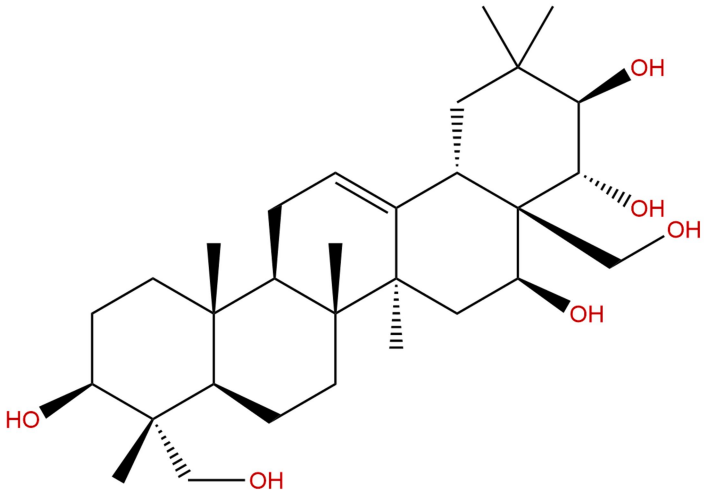


Figure 5. Gymnemagenin.

2.2. Anti-diabetic activity of Gymnema sylvestre

Gymnema sylvestre popularly known as 'gurmar', means the destroyer of sugar, which controls the cravings for sugars and regenerates the growth of pancreas tissues. After ingestion of Gymnemic acid the pancrease tissue increases the secretion of insulin which promotes the regeneration of Islet cells of Langerhans and enhances the utilization of glucose, the phoporylase activity also intensify for utilization of glucose by insulin dependent pathway. This molecule also inhibits the absorption of glucose from the intestine by binding with the receptors of intestine and prevents the glucose molecule to bond with the receptors, thus glucose absorption does not occur in the intestine.

The aglycone part of gymnema saponins contains Acyl group which is responsible for anti-sweet activity.

2.3. Anti-diabetic compounds of Pterocarpus marsupium.

Pterocarpus marsupium is a rich source of polyphenolic compounds. The standardized extract of powdered dried heartwood of *Pterocarpus marsupium* contains pterostilbene, (-)-Epicatichin, Liquirtigenin, Marsuposide, Marsupsin, Pteroside,pterosupin, Vijayoside, Propterol, 7-O-α-L-rhamnopyranosyl-oxy-4'-methoxy-5-hydroxy isoflavone (Fig. 6-15), (2S)-7-hydroxyflavanone, isoliquiritigenin, liquiritigenin, 7,4'-dihydroxyflavone, p-hydroxybenzaldehyde, (2R)-3-(phydroxyphenyl)-lactic acid and pm-33 (Maurya et al., 1984).

2.4. Anti-diabetic activity of Pterocarpus marsupium

The anti-diabetic effects of *Pterocarpus marsupium* heartwood and bark have been studied extensively, and several preclinical and clinical studies proved the potentiality of the above-mentioned compounds as a hypo glycemic agent. Some of these studies have addressed the mechanism of action of the extracts and the evidence of the β-cell regeneration in the pancreas (Chakravarthy et al., 1980; Chakravarthy et al., 1982), insulin release and insulin-like action (Mohankumar et al., 2012; Mishra et al., 2013; Anandharajan et al., 2005; Gayathri et al., 2005; Gaster et al., 2012). Many investigations have focused on pterostilbene and (-)-epicatechin which were recognized as two major compounds responsible for the anti-diabetic effects of heartwood and bark respectively.

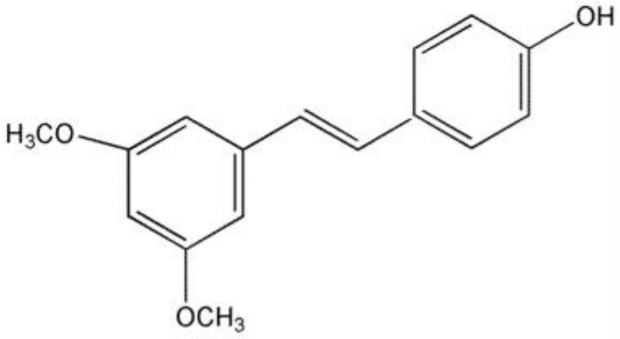


Figure 6. Pterostillbene.

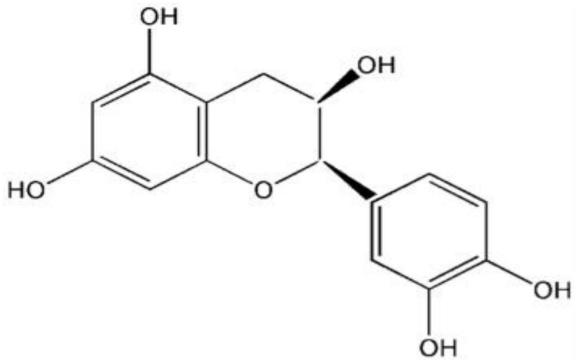


Figure 7. (-)-Epicatichin.

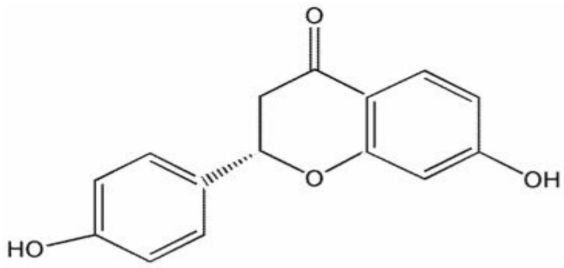


Figure 8. Liquirtigenin.

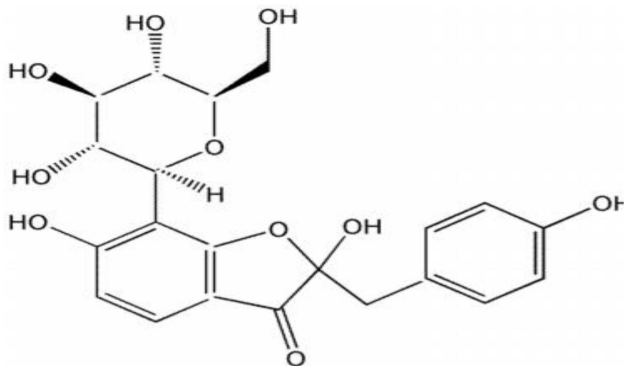


Figure 9. Marsuposide.

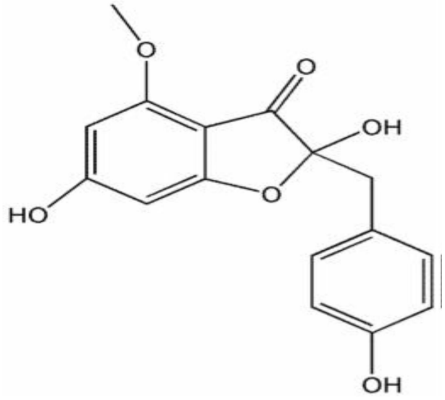


Figure 10. Marsupsin.

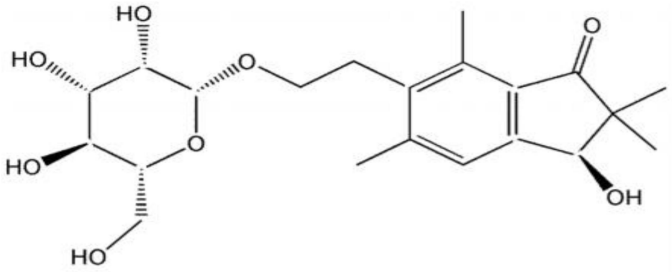


Figure 11. Pteroside.

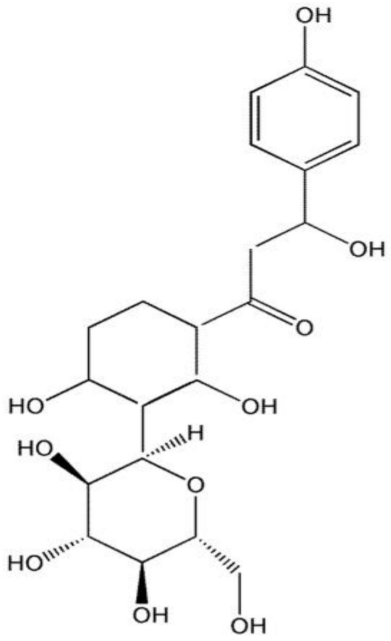


Figure 12. Pterosupin.

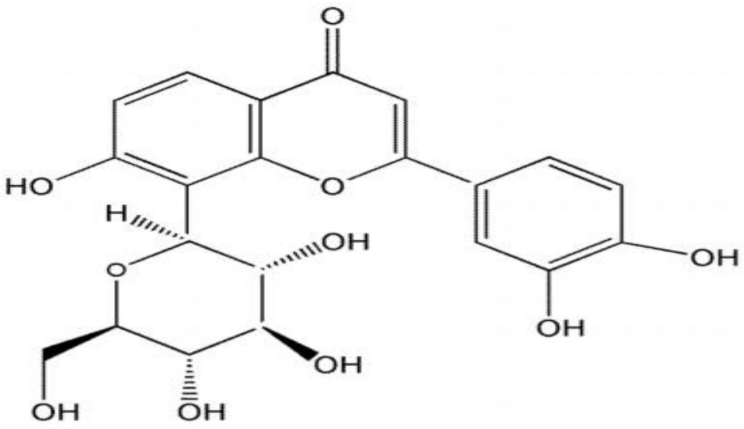
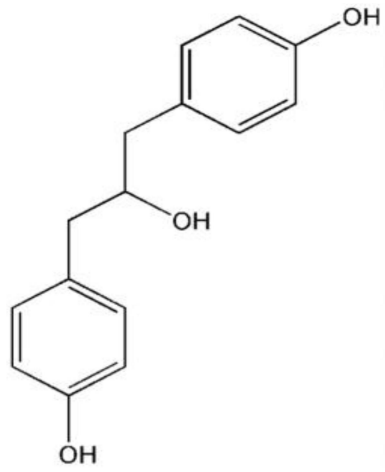


Figure 13. Vijayoside.



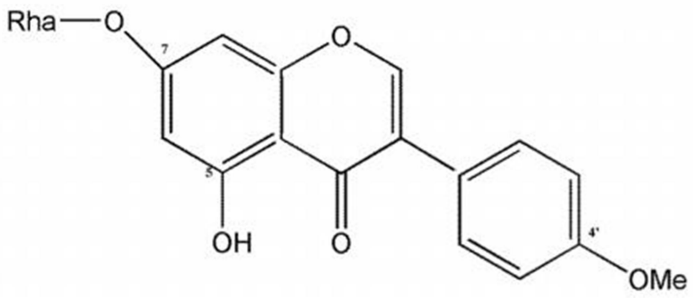


Figure 14. Propterol. **Figure 15.** 7-O-α-L-rhamnopyranosyl-oxy-4'-methoxy-5-hydroxyisoflavone.

3. Discussion

4DM is a combination of *Gymnema sylvestre* and *Pterocarpus marsupium* -a product of Biotex Life Solutions (India). Each capsule contains 250mg of *Gymnema sylvestre* and 250mg of *Pterocarpus marsupium* extracts. Both the extractions have been done in a specific standardized condition to obtain 25% Gymnemic acid and 5% Pterostilbene respectively.

4. Conclusion

It has been proven that both the extracts have anti-diabetic activity. Therefore, the combination of the two extracts also provide the synergistic effects in the management of the diabetic conditions.

References

Anandharajan, R., Pathmanathan, K., Shankernarayanan, N. P., Vishwakarma, R. A., Balakrishnan, A. (2005). Upregulation of GLUT-4 and PPARγ by an isoflavone from *Pterocarpus marsupium* on L6 myotubes: A possible mechanism of action. *Journal of Ethnopharmacology, 97,* 253-260.

Burke, J. P., Williams, K., Narayan, K. M. V., Leibson, C., Hafener, S. M., Stern, M. P. (2003). A population perspective on diabetes prevention: whom should we target for preventing weight gain? *Diabetes Care, 26,* 1999-2004.

Chakravarthy, B. K., Gupta, S., Gode, K. D. (1982). Functional beta cell regeneration in the islet of pancreas in alloxan induced diabetic rats by (-)-epicatechin. *Life Sciences, 31,* 2693-2697.

Chakravarthy, B. K., Saroj, G., Gambhir, S. S., Gode, K. D. (1980). Pancreatic beta cell regeneration–A novel anti-diabetic mechanism of *Pterocarpus marsupium* roxb. *Indian Journal of Pharmacology, 12, 123*-127.

Dateo Jr, G. P., Long Jr, L. (1973). Gymnemic acid, the anti-saccharine principle of *Gymnema sylvestre*. Studies on the isolation and heterogeneity of gymnemic acid A1. *Journal of Agricultural and Food Chemistry, 21* (5), 899-903.

Foster, S., (2002). *Gymnema sylvestre in Alternative Medicine Reviews Monographs*. Thorne Research Inc, 205-207.

Gaster, M., Nehlin, J. O., Minet, A. D. (2012). Impaired TCA cycle flux in mitochondria in skeletal muscle from type 2 diabetic subjects: Marker or maker of the diabetic phenotype? *Archives of Physiology and Biochemistry, 118,* 156-189.

Gayathri, M., Kannabiran, K. (2010). Studies on the ameliorative potential of aqueous extract of bark of *Pterocarpus marsupium* Roxb in streptozotocin- induced diabetic rats. *Journal of Natural Remedies, 10,* 36-43.

Gurav, S., Gulkari, V., Duragkar, N., Patil, A. (2007). Systemic review: Pharmacognosy, phytochemistry, pharmacology and clinical applications of *Gymnema sylvestre* R Br. *Pharmacognosy Review, 1,* 338-343.

Jarald, E., Joshi, S. B., Jain, D. C. (2008). Diabetes and herbal medicines. *Iranian Journal of Pharmacolgy and Therapy, 7,* 97-106.

Khan, V., Najmi, A. K., Akhtar, M., Aqil, M., Mujeeb, M., Pillai, K. K. (2012). A pharmacological appraisal of medicinal plants with antidiabetic potential. *Journal of Pharmacy and Bioallied Sciences, 4,* 27-42.

Khramov, V. A., Spasov, A. A., Samokhina, M. P. (2008). Chemical composition of dry extracts of *Gymnema sylvestre* leaves. *Pharmaceutical Chemistry Journal*, *42,* 30-32.

Manohar, S. H., Naik, P. M., Praveen, N., Murthy, H. N. (2009). Distribution of gymnemic acid in various organs of *Gymnema sylvestre*. *Journal of Forestry Research, 20,* 268-70.

Maurya, R., Ray, A. B. (1984). Constituents of *Pterocarpus marsupium*. *Journal of Natural Product, 47,* 179-181.

Mishra, A., Srivastava, R., Srivastava, S. P., Gautam, S., Tamrakar, A. K., Maurya, R. (2013). Antidiabetic activity of heart wood of *Pterocarpus marsupium* Roxb. and analysis of phytoconstituents. *Indian Journal of Experimental Biology, 51,* 363-374.

Mohankumar, S. K., O'Shea, T., McFarlane, J. R. (2012). In-sulinotrophic and insulin-like effects of a high molecular weight aqueous extract of *Pterocarpus marsupium* Roxb. hardwood. *Journal of Ethnopharmacology, 141,* 72-79.

Potawale, S. E., Shinde, V. M., Anandi, L., Borade, S., Dhalawat, H., Deshmukh, R. S. (2008). *Gymnema sylvestre*: a comprehensive review. *Pharmacologyonline*, *2,* 144-157.

Sinsheimer, J. E., Rao, G. S., McIlhenny, H. M. (1970). Constituents from *Gymnema sylvestre* leaves. V: isolation and preliminary characterization of the gymnemic acids. *Journal of Pharmaceutical Sciences, 59* (5), 622-628.

Sujin, R. M., Subin, R. M., Mahesh, R., Mary, R. V. J. (2008). Antidiabetic effects of *Gymnema sylvestre* (Asclepiadaceae) powder in the stomach of rats. *Ethnobotanical Leaflets, 1,* 158-67.

Tiwari, P., Mishra, B. N., Sangwan, N. S. (2014). Phytochemical and Pharmacological Properties of *Gymnema sylvestre*: An Important Medicinal Plant. Biomedical Research Institute.

Yoshikawa, K., Amimoto, K., Arihara, S., Matsuura, K. (1989). Gymnemic acid V, VI and VII from gurma, the leaves of *Gymnema sylvestre* R.Br. *Chemical and Pharmaceutical Bulletin, 37,* 852-854.

Yoshikawa, K., Amimoto, K., Arihara, S., Matsuura, K. (1989). Structure studies of new anti-sweet constituents from *Gymnema sylvestre*. *Tetrahedron Letters, 30,* 1103-1106.

Vasi, S., Austin, A. (2009). Effect of herbal hypoglycemic on oxidative stress and antioxidant status in diabetic rats. *The Open Diabetes Journal, 18,* 48-52.