REVIEW ON GYMNEMA: AN HERBAL MEDICINE FOR DIABETES MANAGEMENT

Vaidya S.*
Dr. H.S.Gaur University, Sagar (M.P.)

Abstract

Diabetes has been recognized by western medicine since the early 1800 s as being one of the most prevalent and controllable conditions affecting a large portion ofthe population. Gymnema Sylvestre, an Ayurvedic herb, came to be known as "destroyer of sugar" because, in ancient times, Ayurvedic physicians observed that chewing a few leaves of Gymnema sylvestre suppressed the taste of sugar. It is used today all over India for controlling blood sugar. Several bioactives has been isolated from that herb for diabetes cure. The present review elaborate the bioactives and some facts and mechanism which make this herb an effective remedy for the same.

Introduction

Gymnema Sylvestre is a woody, climbing plant of tropical forests of central and southern India and in parts of Africa. Distribution is worldwide and it is recognized in the traditional medicinal literature of many countries including Australia, Japan, and Vietnam. Gymnema has been referred to in some texts as *Asclepias geminata, Gymnema melicida,* and *Periploca sylvestris.* Gymnema has played an important role in Ayurvedic medicine for centuries. Its use has been confined primarily to the management of diabetes mellitus and similar hypo/hyperglycemic conditions. Despite the part used being the leaf, another common name of this species is miracle fruit,[1][2][3] which is shared by two other species: *Synsepalum dulcificum and Thaumatococcus daniellii* [1].

Vernacular name

English : Periploca of the woods
Hindi : Gudmar
Kannada : Kadhasige
Malayalam : Cakkarakkolli, Madhunasini
Tamil : Sirukurunkay, Sakkaraikkolli
Sanskrit : Mesasrngi
Telugu : Podapatra

Geographical Distribution

G. sylvestre is native to the tropical forests of central and southern India had wider distribution and it grows in the plains fromthe coast, in scrub jungles and in thickets at an altitude ranging from 300 - 700 m. The genus Gymnema comprises 40 species distributed from Western Africa to Australia. 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. sylvestre R.Br., G. tingens W&A, G. indorum, G. yunnanse and G. spartum are some of the important species of genus Gymnema.. They are mainly distributed in the Deccan peninsula parts of northern, western India, Tropical Africa, Australia, Vietnam, Malaysia and Sri Lanka.

*Address for Correspondence
Shivani Vaidya
L.N.C.P. , Bhopal (M.P.) e-mail : shivani_vdy@rediffmail.com

Phytochemistry

The major class of phytochemical belongs to G. sylvestre leaves contains triterpene saponins belonging to oleanane and dammarene classes. Oleanane saponins are gymnemic acids and gymnemasaponins, while dammarene saponins are gymnemasides. The other chemical constituents are flavones, anthraquinones, hentri-acontane, pentatriacontane, α and β-chlorophylls, phytin, resins, d-quercitol, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin related glycosides and stigmasterol, some alkaloids and anthroquinones [4].

Gymnemic acids have antidiabetic, antisweetener and anti-inflammatory activities. The antidiabetic array of molecules has been identified as a group of closely related gymnemic acids [5, 6].

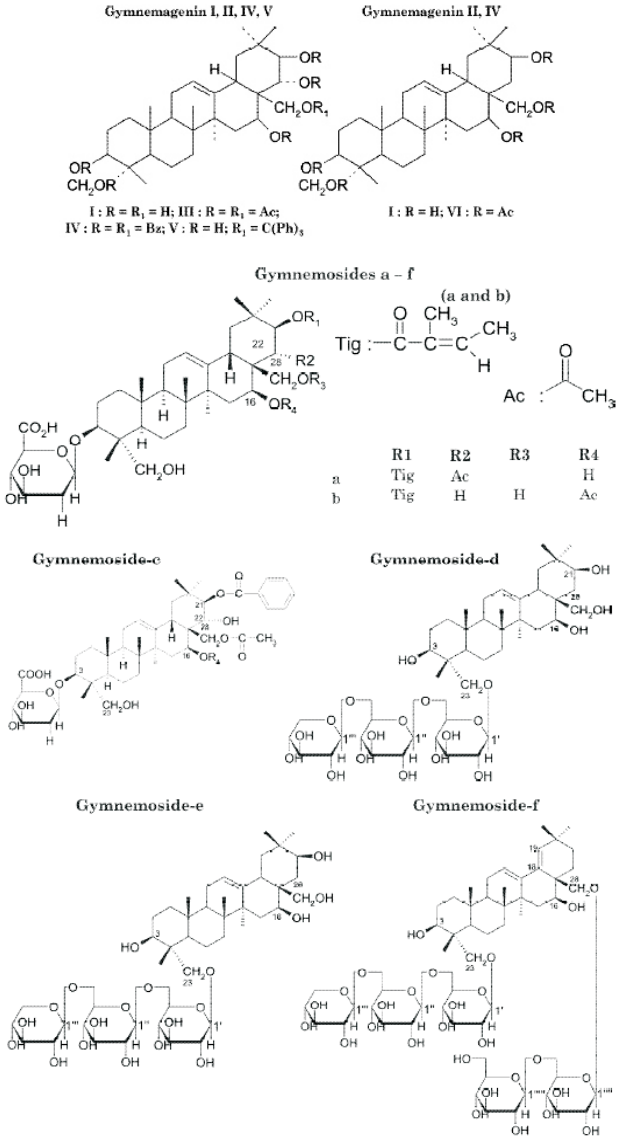

Fig.1 Structure of Gymnemagenin and Gymnemosides a-f

Some of many phytochemicals found in G. sylvestre are and their pharmacological actions [7] have been given in Table 1:

Phytochemical	Pharmacological activity
Ascorbic-Acid	Acidulant, Aldose-Reductase-Inhibitor, Angiotensin-Receptor-Blocker, AntiAGE, AntiCrohn's, Antiaging, Antiatherosclerotic, Antidecubitic, Antidepressant, Antidote (Aluminum), Antidote (Paraquat), Antiedemic, Antigingivitic, Antihepatotoxic, Antihistaminic, Antihypertensive, Antiinflammatory, Antimeasles, Antimigraine, Antimutagenic, Antiobesity, Antiorchitic, Antioxidant, Antiparkinsonian, Antiseptic, Apoptotic, Beta-Adrenergic Receptor Blocker, Beta-Glucuronidase-Inhibitor, Collagenic, Fistula-Preventive, Hypotensive, Immunostimulant, Mucolytic, Urinary-Acidulant, Vulnerary
Beta-Carotene	AntiPMS, Antiacne, Antiaging, Antihyperkeratotic, Antilupus, Antimastitic, Antimutagenic, Antioxidant, Antiphotophobic, Antiporphyric, Antiproliferant, Antistress, Antitumor, Antixerophthalmic, COX-1-Inhibitor, Colorant, Immunostimulant, Interferon-Synergist, Phagocytotic, Prooxidant, Thymoprotective
Betaine	Antigastritic, Antihomocystinuric, Ethanolytic, Hepatoprotective
Choline	Antialzheimeran, Antichoreic, Anticystinuric, Antidementia, Antidyskinetic, Antimanic, Cardiodepressant, Cerebrotonic, Hepatoprotective, Hypotensive, Memorigenic
Conduritol-A	Aldose-Reductase-Inhibitor, Antidiabetic, Antihistaminic, Antiinflammatory, Antipyretic, Antiseptic, Antitesticular, Cyclooxygenase-Inhibitor, Fungicide, Gastrostimulant, Hypoglycemic, Hypotensive, Hypothermic, Immunostimulant, Molluscicide, Mutagenic, Nematicide, Progesteronigenic, Ribosome-Inactivator, Sedative, Serotoninergic, Thyrotropic
Gymnemic-Acid	Antiflu, Antihistaminic, Antiinflammatory, Antiobesity, Antipyretic, Antiseptic, Antiviral, Cyclooxygenase-Inhibitor, Fungicide, Gastrostimulant, Hypotensive, Hypothermic, Immunostimulant, Molluscicide, Mutagenic, Nematicide, Progesteronigenic, Sedative, Serotoninergic, Thyrotropic
Gymnemic-Acid-B	Antiflu, Antihistaminic, Antiinflammatory, Antiobesity, Antipyretic, Antiseptic, Antiviral, Cyclooxygenase-Inhibitor, Fungicide, Gastrostimulant, Hypotensive, Hypothermic, Immunostimulant, Molluscicide, Mutagenic, Nematicide, Progesteronigenic, Sedative, Serotoninergic, Thyrotropic
Niacin	AntiMeniere's, Antiacrodynic, Antiallergic, Antiamblyopic, Antianginal, Antichilblain, Anticonvulsant, Antihistaminic, Antiinsomnic, Antineuralgic, Antiparkinsonian, Antipellagric, Antiscotomic, Hepatoprotective, Sedative, Serotoninergic

Table 1: phytochemicals found in G. sylvestre are and their pharmacological actions

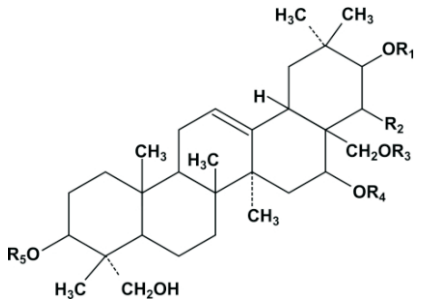

Fig.2 Basic structure of gymnemic acid.

The antidiabetic ability of gymnemic acids is due to retardation of glucose absorption in the blood. The atomic arrangement of gymnemic acid molecules is similar to that of glucose molecules. These molecules fill the receptor locations on the taste buds thereby preventing its activation by sugar molecules present in the food, thereby curbing the sugar craving. Similarly, Gymnemic acid molecules fill the receptor location in the absorptive external layers of the intestine thereby preventing the sugar molecules absorption by the intestine, which results in low blood sugar level.

After examination of the results of several investigations it is found that G. sylvestre leaves have been found to cause hypoglycemia in laboratory animals to treat onset of diabetes mellitus (NIDDM). When Gymnema leaf extract is administered to a diabetic patient, there is stimulation of the pancreas which results in increased insulin secretion [8]. These compounds have also been found to increase fecal excretion of cholesterol [9]. Other uses for Gymnema leaf extract are its ability to act as a laxative, diuretic, and cough suppressant. These other actions would be considered adverse reactions when Gymnema is used for its glucose lowering effect in diabetes.

Gymnema leaf extract, notably the peptide 'Gurmarin', has been found to interfere with the ability of the taste buds on the tongue to taste sweet and bitter. Gymnemic acid has a similar effect. It is believed that by inhibiting the sweet taste sensation, it will limit their intake of sweet foods, and this activity may be partially responsible for its hypoglycemic effect [10].

There are some possible mechanisms by which gymnemic acids exert its hypoglycemic effects by several ways like, it increases secretion of insulin, promotes regeneration of islet cells, increases utilization of glucose: it is shown to increase the activities of enzymes responsible for utilization of glucose by insulin-dependant pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase, and it causes inhibition of glucose absorption from intestine by binding the glucose binding sites on transport receptors [10].

One of the mechanisms responsible for adult onset diabetes mellitus is a form of insulin resistance, which is attributed to the inability of insulin to enter cells via the insulin receptor. Should this effect be proven, Gymnema may prove useful in both adult onset (NIDDM) and juvenile onset diabetes mellitus (IDDM) to help insulin enter cells [11].

The leaves are also noted for lowering serum cholesterol and triglycerides. The primary chemical constituents of Gymnema include gymnemic acid, tartaric acid, gurmarin, calcium oxalate, glucose, stigmasterol, betaine, and choline. While the water-soluble acidic fractions reportedly provide the hypoglycemic action, it is not yet clear what specific constituent in the leaves is responsible for the same. Some researchers have suggested gymnemic acid as one possible candidate, although further research is needed [12]. Both gurmarin (another constituent of the leaves) and gymnemic acid have been shown to block sweet taste in humans. The major constituents of the plant material 3B glucuronides of different acetylated gymnemagenins, gymnemic acid a complex mixture of at least 9 closely related acidic glucosides [13-15].

The following figure could provide a diagrammatic representation for explaining the action of gymnemic acids on the intestinal receptors. The basic function of the acids is to bind to the receptor on the intestine, and stop the glucose molecule from binding to the receptor. Thus, gymnemic acids prevent the absorption of excess glucose.

Pharmacodynamic and clinical studies suggest that the hypoglycaemic activity of Gymnema may be mediated through stimulation of insulin release (and possibly by pancreatic regeneration or repair), stimulation of enzymes responsible for glucose uptake and utilisation and/or inhibition of intestinal absorption of glucose. [16-19]

Gymnema extract and some isolated constituents have inhibited glucose uptake in isolated small intestinal tissue. [20,21] Gymnema extract and gymnemic acids inhibited the intestinal absorption of glucose in humans and rats. [22-23]. In evidence of this, two fractions obtained from Gymnema (containing gymnemic acids) suppressed potassium-induced contraction of isolated ileal longitudinal muscle, interfered with the increase in transmural potential difference induced by glucose and inhibited the elevation of blood glucose in vivo (route unknown) [24]. Two gymnemic acids suppressed the contraction of smooth intestinal muscle, most likely by inhibiting glucose uptake [22].

Oral administration of Gymnema extract reduced postprandial serum glucose and improved glucose tolerance in mildly diabetic rats. Pancreas weight and content of insulin were not changed [25]. Gymnema corrected hyperglycaemia in mild alloxandiabetic rats and significantly prolonged lifespan in severe alloxandiabetic rats (i.e. with completely destroyed pancreatic tissue). The authors suggested that the prolonged survival time was due to the adaptogenic activity of Gymnema [26].

The crude saponin fraction of Gymnema and gymnemic acid IV reduced blood glucose levels in streptozotocin-diabetic mice when administered by injection. Gymnemic acid IV also increased plasma insulin levels. Gymnemoside b and gymnemic acids III, V and VII (route unknown) produced some inhibitory activity on glucose absorption after oral glucose loading in rats, but gymnemic acid I and gymnemasaponin V were inactive.

Conclusion

Although there are many phytoconstituents that could combat diabetes and obesity, a single phytoconstituent that could be used in the treatment of both the diseases simultaneously would be a welcome addition. Gymnemic acid fulfills this criterion. The common masses do not avail of the fact that obesity can also be caused due to over-accumulation of sugar molecules specially sucrose, along with fat molecules. The common man needs to be made aware of these facts, since they are posing a big threat after cardiac problems and cancer. This review paper aimed at putting forth a molecular perspective of the medicinal aspect of gymnemic acids, and also a possible linkage between obesity and diabetes via a potential common medicine.

References:

1. Wiersema, John Harry; León, Blanca. World Economic Plants: A Standard Reference. CRC Press 1999. p. 661. ISBN 0-8493-2119-0. http://books.google.com/books?id=hQL-2sdxgDAC.

2. Rehm, Sigmund (ed) (1994). Multilingual dictionary of agronomic plants. Springer. p. 91. ISBN 0-7923-2970-8. http://books.google.com/books?id=qIgY_I_6WpoC.

3. Duke, James A., (ed) . Handbook of medicinal herbs (2nd ed.). CRC Press 2002. p. 855. ISBN 0-8493-1284-1. http://books.google.com/books?id=8AJkBmPDRUUC.

4. Dateo GP, Long L. Gymnemic acid, the antisaccharine principle of Gymnema sylvestre. Studies on isolation and heterogenesity of gymnemic acid A1. *J. Agric. Food Chem.* 21; 1973: 899–90.

5. Liu H.M., Kiuchi F., Tsuda Y. Isolation and structure elucidation of Gymnemic acids, antisweet principles of Gymnema sylvestre. *Chem. Pharm.* Bull. 40; 1992: 1366–1375.

6. Sinsheimer JE, Manni PE. Constituents from Gymnema sylvestre leaves. *J. Pharm. Sci.*; 54; 1965: 1541–1544.

7. Kanetkar PV, Laddha KS, Kamat MY. Poster presented at the 16th ICFOST meet organized by CFTRI and DFRL. Mysore, India: 2004. Gymnemic acids: A molecular perspective of its action on carbohydrate metabolism. http://www.ayurgold.com/plant_phytochemistry.htm?plantid=1080

8. Persaud SJ, Al-Majed H., Raman A, Jones PM. Gymnema sylvestre stimulates insulin release in vitro by increased membrane permeability. *J. Endocrinol.*; 163; 1999: 207–212.

9. Nakamura Y., Tsumura Y., Tonogai Y., Shibata T. Fecal steroid excretion is increased in rats by oral administration of gymnemic acids contained in Gymnema sylvestre leaves. *J. Nutr.* 129; 1999:1214–1222.

10. Agarwal S.K, Singh S.S., Verma S, Lakshmi V., Sharma A. Chemistry and medicinal uses of Gymnema sylvestre (gurmar) Leaves: A Review. *Indian Drugs*. 37; 2000: 354–360.

11. Khare A.K, Tondon R.N., Tewari J.P. Hypoglycemic activity of an indigenous drug Gymnema sylvestre in normal and diabetic persons. Ind. *J. Physiol. Pharmacol.* 27; 1983: 257–261.

12. Maeda M., Iwashita T., Kurihara Y. Studies on taste modifiers II: Purification and structure determination of gymnemic acids, antisweet active principle from Gymnema sylvestre leaves. *Tetr. Lett.* 30; 1989: 1547–1550.

13. Manni P.E., Sinsheimer J.E. Constituents from Gymnema sylvestre leaves. *J. Pharm. Sci.* 54; 1965: 1541–1544.

14. Sinsheimer J.E., Subbarao G. Constituents from Gymnema sylvestre leaves VIII: Isolation, chemistry and derivatives of gymnemagenin and gymnestrogenin. *J. Pharm. Sci.* 60; 1971:190–193.

15. Shanmugasundaram K.R ., Enzyme changes and glucose utilisation in diabetic rabbits: the effect of Gymnema sylvestre, R.Br. *J Ethnopharmacol.* 7(2); 1983: 205-34.

16. Shanmugasundaram E.R., Possible regeneration of the islets of Langerhans in streptozotocin-diabetic rats given Gymnema sylvestre leaf extracts. *J Ethnopharmacol.* 30(3); 1990: 265-79

17. Shanmugasundaram E.R., Use of Gymnema sylvestre leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. *J Ethnopharmacol.* 30(3); 1990: 281-94.

18. Baskaran K. Antidiabetic effect of a leaf extract from Gymnema sylvestre in non-insulin-dependent diabetes mellitus patients. *J Ethnopharmacol.* 30(3); 1990: 295-300

19. Kyremateng P.H., cited in Prendergast HDV (ed.) Plants for Food and Medicine, Royal Botanic Gardens, Kew, 1998.

Yoshikawa M., *Chem Pharm Bull*; 45; 1997: 2034

20. Shimizu K. Inhibitory effects of glucose utilization by gymnema acids in the guinea-pig ileal longitudinal muscle. J Smooth *Muscle Res.* 32; 1996: 219

21. Wang L.F. *Can J Physiol Pharmacol* . 76; 1998: 1017

22. Shimizu K., Suppression of glucose absorption by some fractions extracted from Gymnema sylvestre leaves. *J Vet Med Sci.* 59; 1997: 245

23. Okabayashi Y., Effect of Gymnema sylvestre, R.Br. on glucose homeostasis in rats. Diabetes. *Res Clin Pract.* 9(2); 1990: 143-8.

24. Srivastava Y., Nigam S., Bhatt H. Hypoglycemic and life- prolonging properties of Gymnema sylvestre leaf extract. Int *J Crude Drug Res.* 24; 198: 6171

25. Chattopadhyay R.R. A comparative evaluation of some blood sugar lowering agents of plant origin. *J Ethnopharmacol.* 67; 1999: 367

26. Yoshikawa M., et al, Medicinal foodstuffs. IX. The inhibitors of glucose absorption from the leaves of Gymnema sylvestre R. BR. (Asclepiadaceae): structures of gymnemosides a and b. *Chem Pharm Bull* (Tokyo). 1997 Oct; 45(10):1671-6