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A REVIEW: ANTI-DIABETIC MEDICINAL PLANTS FROM TORANMAL REGION OF MAHARASHTRA

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ABSTRACT

In the past few decades, diabetes mellitus is emerged as major public health issue across the globe. The chronic hyperglycemia of diabetes can inflict various organ damages and result in alarming secondary complications. There are ample of therapeutic approaches available to address the rising need of diabetes control. However, these are costly and associated with adverse effects both in short and long run. The ancient medical literature well documented the hypoglycemic and insulin release stimulatory effect of medicinal plants. Moreover, the cost benefits ratio makes them suitable drugs, particularly for under-privileged people. Plants extract show a significant hypoglycemic effect in preclinical studies, which is comparable to currently available therapeutic agents. From the future perspective, these plant extract can be considered as an excellent candidate in diabetes drug development in pharmaceutical industries. In view of above aspect, this review aims at scanning literature for previous studies confirming the usage and mechanism of action of medicinal plants widely available in Toranmal region of Maharashtra for controlling diabetes and associated complications.

KEYWORDS: Diabetes, Phytochmicals, Blood glucose level, Medicinal plant, Antidiabetic activity, Hypoglycemic activity.

INTRODUCTION

Diabetes mellitus (DM) is chronic metabolic condition characterized by a persistent increase in blood glucose level. Globally, DM affect large segment of the population. The disease is gaining a status of "global diabetes epidemic" due to continuous increase in newly diagnosed

cases every year. Global diabetes burden is predicted to rise from 366 million people in 2011 to 552 million by 2030.[1] DM is multifactorial in origin where genetic factors coupled with environmental influences play a significant role in initiation and progression of disease.[2] Prevention and control of diabetes is the global need of mankind. The disease has been linked with co-morbidities including obesity, hyperlipidemia and cardiovascular diseases which usually complicate effective diabetes management.[3] The currently available therapeutic approaches are usually associated with adverse effects both in short and long run.[4] Moreover, most people with diabetes are from low- and middle-income countries.[1] Hence, the cost factor is important aspect that prevents effective utilization of these therapeutic agents.

In this scenario, opting for alternative therapies can be helpful to overcome the limitations of conventional agents. Plant and plant products have been utilized for the medicinal purpose in human cultures over millennia.[5] Harbal medicines are popular since centuries due to safety, efficacy and ample availability.[6] Cost benefits ratio makes them suitable drugs, particularly for under-privileged people from India. Most of these plants have been extensively studied for antidiabetic activity in various animal models. These plants contain various active principles, which exert significant antidiabetic activity. During last few decades, major insight has been achieved on these active principles from medicinal plants. However, there is no general agreement on the antidiabetic potential of these medicinal plants. The exact mechanism of action and long-term effect is still a mystery. This is due to either lack of or inconsistent data from preclinical and clinical studies.

In view of above aspect, the current review was undertaken to summarize the updated information on antidiabetic properties of medicinal plants commonly found in Toranmal region of the Maharashtra. This review briefly involves the discussion and consolidation of data on the potential medicinal plants with antidiabetic activity and their possible mechanism of action.

BIODIVERSITY AT TORANMAL REGION OF MAHARASHTRA

Toranmal is one of the highest elevation plateaus of Satpuda mountain range in Nandurbar district. It is situated in the northern part of Maharashtra state. The most part of Toranmal plateaus is covered by dense forest which is enriched with variety of plants. Plants grown in Toranmal area are very popular from ethno-medicinal aspect. The tribal population residing in this area used these plants not only as a food but also for treating various diseases.[7]

Medicinal plants claiming antidiabetic potential in preclinical setting are also found in Toranmal area. In this review, we try to identify and discuss 15 such plants from Toranmal area proved to possess significant hypoglycemic activity. These plants are summarized with possible mechanism of action. (Table no.1).

ANTI-DIABETIC MEDICINAL PLANTS FROM TORANMAL REGION OF MAHARASHTRA

Aloe barbadensis miller

Aloe barbadensis miller, commonly known as aloe vera, is a member of Asphodelaceae (Liliaceae) family. Throughout the history, the plant has shown a wide range of therapeutic applications in the field of cosmetology. This shrubby or arborescent plant mainly grows in dry regions as shown in fig.no.1. The plant is known as a storehouse of 75 potentially active constituents, including various vitamins, enzymes, minerals, sugars, lignin, saponins, salicyclic acids and amino acids.[8]

Fig 1: *Aloe barbadensis miller*

In a recently conducted study, ethanolic extract of fresh leaf gel of aloe vera was found to elicit significant reduction in fasting blood glucose level in streptozotocin (STZ) induced diabetic rats. The mean reduction in fasting blood glucose level was noted to be profound at higher doses, i.e.44% reduction with 300 mg/kg dose and 73% with 500 mg/kg dose. The possible hypoglycemic activity was due to inhibition of hepatic glucose production and increase of muscle glucose uptake. The antioxidant properties of extract were thought to prevent death of β-cells of pancreas or may induce recovery of partially destroyed β-cells, which improves the insulin release. Additionally, the presence of active principles like lophenol, 24-methly-lophenol, 24-ethyl-lophenol,cycloartanol and 24-methylene-cycloartanol may also play a role in improvement in hypoglycemic status.[9]

Similarly, another study proved the hypoglycemic role of aqueous extract of aloe vera leaves in reduction of blood glucose level in alloxan induced diabetic rats. This supports the role of aloe vera in initiation of pancreatic β-cell proliferation.[10]

Azadirachta indica

Azadirachta indica, very popularly known as Neem, has significant ethnomedicinal value in several cultures. It is a fast growing evergreen plant belonging to family Meliaceae (Fig.no.2). Almost every part of the plant possesses medicinal properties. In Sanskrit the plant is known as 'Arishtha' meaning 'reliver of sickness'.[11]

Fig. 2: *Azadirachta indica*

70% alcoholic neem root bark extract was noted to produce both antihyperglycemic and hypoglycemic activity at the dose of 800 mg/kg body weight. In initially conducted oral glucose tolerance test (OGTT) in different groups of rats, a delay in the rise of blood glucose was noted in group receiving alcoholic extract. Moreover, in the same study 800 mg/kg dose of extract produced significant reduction in blood glucose level in alloxan induced diabetic rats. However, this effect is not significant compared to glibenclamide, a standard oral hypoglycemic agent. The antidiabetic activity was attributed due to presence of active ingredient nimbidin, a mixture of tetranortriterpenes. The antihyperglycemic activity of nimbidin makes neem extract as a suitable prophylactic agent in delaying the onset of diabetes.[12]

In another *in vivo* study choloroform extract of leaves of *Azadirachta indiaca* improves glucemic control by reducing fasting blood glucose in STZ induced diabetic mice. It was

possibly due to extract induced regeneration of insulin-producing cells and increase in plasma insulin level.[13]

Allium sativum

Allium sativum, commonly known as garlic, is one of the most widely used cooking spice in every Indian kitchen. This bulbous plant is easy to grow in mild climate (Fig. no.3). It belongs to Lillaceae family.[14] Rich phytochemistry of garlic offers a wide range of medicinal applications and knows to promote good health.

Fig. 3: *Allium sativum*

Garlic has been documented for its antidibetic effect since long time. Garlic has been claimed to possess antidiabetic activity, and many studies support this finding. In this relation, an aqueous extract of raw garlic confirmed the hypoglycaemic effect in STZ induced diabetic rat model. Additionally, the same study evaluated the hypocholesterolaemic and hypotriglyceridaemic potential of garlic. Moreover, it was noted that the garlic extract reduces protein levels in urine and reverses proteinuria, a symptom suggesting glomerular injury and kidney damage associated with chronic hyperglycemia. Thus, the study concluded the garlic as an effective remedy for both diabetes control and management of associated pathologies. The garlic induced favorable effect may be due to presence of allicin (S-allyl cystein sulphoxide), a sulphur containing amino acid, which increases section of insulin from pancreatic bets cells, releases bound insulin and enhance the insulin sensitivity.[15]

A synergistic effect has been recorded when garlic was co-administered with metformin, an oral hypoglycemic agent. Thus, garlic was found to enhance the hypoglycemic effect of metformin in diabetic rats. This property of garlic is useful in reducing the dose of metformin and minimizing metformin associated side effects.[16]

Senna auriculata

Senna auriculata is a native plant found in India and belongs to family Fabaceae. It grows as a branched shrub or small tree as shown in fig.no.4. Its synonym is *Cassia auriculata* L and commonly known by other names as avaram senna, matara tea, styptic weed or tanner's cassia.[17]

Fig.4: *Senna auriculata*

The oral administration of ethanolic extract of *S. auriculata* leaves at the dose of 150mg/kg body weight was found to produce significant reduction in blood glucose level in alloxan induced diabetic rats. The reduction in blood glucose level was associated with the rise in serum insulin level by inducing pancreatic beta cells by leaf extract. Moreover, The study also observed significant reduction in lipid parameters, including total cholesterol (TC), triglyceride (TG) and low density lipoprotein-cholesterol (LDL-c). Apart from this, the same found significant increase in high density lipoprotein-cholesterol (HDL-c) along with the rise in antioxidant enzymes. This means *S. auriculata* is the not only effective anti-diabetic agent but also helpful to reduce associated complications. The antidiabetic effect of extract is potentially due to presence of phytochemicals like flavonoids, terpenoids, glycosides, steroids, saponin and phenols.[18]

Coriandrum sativum

Coriandrum sativum, also known *as* coriander, is an annual herb used principally for seasoning purpose. Flavor of freshly cut leafs of coriander makes it a common ingredient in culinary purposes. It is grown all over the world and a member of family Apiaceae (Umbelliferae) (Fig.no.5). It contains all essential oil, vitamin K, α-tocopherol and polyphenols.[19]

Fig.5: *Coriandrum sativum*

A preclinical study testing the effect of aqueous extract of fruit of coriander found reduction in blood glucose level. The effect was more pronounced at dose of 500 mg/kg as compared to 250 mg/kg. Additionally, there was reduction of total cholesterol and rise in level of HDL suggesting improvement in lipid profile. The presence of linalool (coriandrol) as an active agent may be responsible for medical properties of coriandrum.[20] Thus, coriander may have a role in improving glucose and lipid metabolism and alleviating diabetes associated complications.

Zingiber officinale

Zingiber officinale Rosc, popularly known as ginger, belongs to the family Zingiberaceae. Ginger is a natural herb and used as cooking spice and condiment to add favor to food (Fig.no.6). It is better known for its anti-inflammatory and anti-oxidative properties. The rhizome of ginger offers the wide range of benefits to maintain digestive health.[21]

Fig.6: *Zingiber officinale Rosc*

The aqueous extract of raw ginger was found to produce considerable hypoglycemic activity in STZ-induced diabetic rats. Moreover, ginger was found to improve lipid profile by reducing total cholesterol, LDL-c and triglyceride. It also increases antioxidant capacity by

improving activity of super-oxide dismutase (SOD) and glutathione peroxidase (GSH-Px) enzymes. The hypoglycemic role of ginger was attributed to its serotonin receptor blocking activity. Serotonin was found to induce hyperglycemia in experimental rats. Inhibition of lipid peroxidation by ginger additionally provides benefit in reducing secondary complications of diabetes.[22]

The anti-diabetic effect of ginger was also noted in clinical setting. In a randomized placebo-controlled clinical trial, a ginger supplementation was found to reduce the levels of fasting blood glucose in type 2 diabetic patients. The same study noted the effect of ginger in reduction of hemoglobin A1c, apolipoprotein B, apolipoprotein A-I, the ratio of apolipoprotein B to apolipoprotein A-I and malondialdehyde. Thus, suggest the role of ginger in reducing diabetes associated chronic complications.[23]

Mentha piperita

Mentha piperita L.is a natural hybrid of *M.aquatica* and *M.spicata*. It is very widely consumed as peppermint. The plant shown evergreen and shown as in fig.no.7. Its synonym is *M.balsamea* and belongs to family Lamiaceae. It is a popular flavoring agent in chewing gum. Usefulness of *Mentha piperita* is also found in cosmetics and pharmaceutical products.[24]

Fig.7: *Mentha piperita* L.

Oral administration of juice extracted from peppermint leaves for 21 days produces significant reduction in blood glucose in alloxan induced diabetic rats. This is due to presence of menthol and flavonoids and phenolic compounds, which improves abnormalities in glucose metabolism.[25]

Carica papaya

Carica papaya is a popular fruit tree in tropical and subtropical areas of the world (Fig.no.8). Papaya is a widely consumed as fresh fruit due to its delicious taste and health benefits. It is high in Vitamin A,B,C and proteolytic enzymes like papain and chymopapain. *Carica papaya* is identified as multipurpose commercial fruit plant and has a valuable nutraceutical status as almost all parts of plant offer medicinal benefits. It belongs to the family Caricaceae.[26]

Fig.8: *Carica papaya*

The aqueous extract of leaves of *Carica papaya* significantly decreases blood glucose level in STZ induced diabetic rats. The study also recorded reduction in cholesterol and triacylglycerol. There was regeneration of islet cells as indicated by preservation of cell sizes in diabetic rat treated with extract. However, the possible mechanism of action is thought to be the release of more insulin by stimulation of remaining pancreatic β-cells.[27]

Panax ginseng

Ginseng is a root of *Panax ginseng* Meyer, belonging to the family Araliaceae. The roots of ginseng are shown in fig. no.9. It is a storehouse of various pharmacological components like ginsenosides, polyacetylenes, polyphenolic compounds and acidic polysaccharides.[28] Ginseng is well documented for its healing and restorative properties.[29]

Fig.9: *Panax ginseng*

Orally administered root powder of ginseng reduces blood glucose level in STZ induced diabetic rat. Along with it, ginseng aided in reduction of cholesterol, triglyceride, LDL and VLDL cholesterol levels. It also improved liver antioxidant levels. Antihyperglycemic action of ginseng was considered due to presence of ginsenosides, which modulates glucose transport, glucose disposal and insulin secretion.[30]

Euphorbia hirta

Euphorbia hirta is also known as *E.pilulifera* linn or dudhi. It is an annual growing, slender-stemmed hairy plant as shown in fig.no.10. It belongs to family Euphorbiaceae and distributed throughout the hotter part of India and Australia. Presence of white milky latex is the characteristic of Euphorbiaceae family. It is the rich source of flavanoids, triterpenoids, alkanes, amino acids and alkaloids.[31] It is widely used in clinical practice for curing gastrointestinal and respiratory disorders.[32]

Fig.10: *Euphorbia hirta*

Ethanolic and petroleum ether extracts of *Euphorbia hirta* flower exhibited the dose dependent fall in blood glucose level in alloxan induced diabetic mice. The maximum

antidiabetic effect was noted after 15 days and remains constant in third week. Flower extract also produced significant antioxidant acitivity in diabetic mice. This antidiabetic effect was attributed due to presence of flavanoids, tannins and other phenolic compounds and free radical scavenging effect of extract.[33]

Ficus pumila

Ficus is a tropical, evergreen tree consisting of more than 800 species. *Ficus pumila* is one of the species of ficus. *Ficus pumila*, synonyms ficus repens, is commonly known as creeping fig as shown in fig.no.11. It belongs to the family of Moraceae. It is enriched source of polyphenolic compounds and flavanoids, which produce strong antioxidant activity.[34]

Fig.11: *Ficus pumila*

The ethanolic leaf extract of *Ficus pumila* was found to reduce blood glucose level in the dose dependent fashion in STZ induced diabetic rats. Blood glucose level reduces slowly at the dose of 200mg/kg and rapid depletion was noted at 400mg/kg of extract. Moreover, the same extract showed the reduction in triglyceride and LDL level. The hypoglycemic effect is attributed due to increase in glycogenesis, reduction in glycogenolysis or increase in entry of glucose molecules to various skeletal muscles.[35]

Glycine max

Glycine max, synonym *glycine angustifolia* is a regularly cultivated legume in India (Fig.no.12). It is very commonly known as soybean or soy and enriched source of essential amino acids. It comes under Fabaceae family and classified as oilseed.[36]

Fig.12: ***Glycin max***

Methanolic seed extract of soybean was found to deplete blood sugar level in dose dependent manner in STZ induced diabetic mice on 21st day post treatment. Along with it, there is a reduction in cholesterol, TG, LDL and VLDL. This activity was may be due to restoration of normal cells of islets and enlargement in size of endocrine islets as manifested by hyperplasia. Furthermore, there was a reduction in serum urea and creatinine, indicating the role of extract role kidney health.[37]

Ipomoea batatas

Ipomoea batatas, commonly known as white skinned sweet potato, is a delicious vegetable with high nutritional value. It belongs to family Convolvulaceae. It is typically grown worldwide in tropical and subtropical areas as shown in fig.no.1. It is high in potassium and magnesium and beneficial to nerve and muscle health.[38]

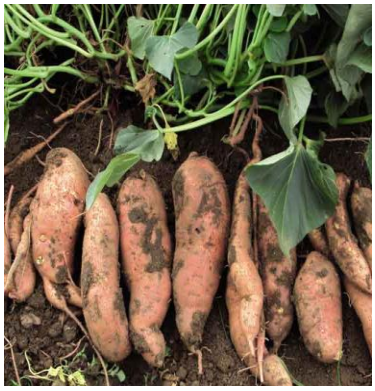

Fig.13: ***Ipomoea batatas***

When the flour suspension of sweet potato was tested in STZ induced diabetic rats, it found to lower blood glucose level significantly. This may be due to increase in the number of

pancreatic beta cells and insulin expression in a dose dependent manner. Sweet potato is effective in both insulin-deficient and insulin-resistant diabetic model suggesting the new anti-diabetic agent with unique mechanism of action. It may be due to presence of high-molecular weight component or presence of vitamin A and C that makes it a good healing agent to regenerate beta cells.[39]

Ocimum sanctum

Ocimum sanctum commonly known as Tulsi is cultivated for the religious purpose in Indian tradition. It is also known as *Ocimum tenuiflorum*. The plant is popular for diverse healing properties with almost all parts having therapeutic potential. It belongs to family Lamiaceae. It is an erect and herbaceous plant grows in the tropical region as shown in fig.no.14.[40]

Fig.14: *Ocimum sanctum*

Ethnolic extract of leaves of *Ocimum sanctum* was found to produce significant and sustained oral hypoglycaemic activity in alloxan induced diabetes rats. The effect was comparable to standard hypoglycaemic drug glibenclamide. The possible hypoglycaemic activity is due to increase in intracellular calcium of beta islet cells of pancreas and increase in insulin secretion.[41]

***Curcuma longa* Linn**

Turmeric is very popular indigenous medicine due to its health promoting perspective. It is commonly known as haridra and one of the oldest spices used in Indian kitchen as shown in fig.no.15. Rhizome of turmeric is commonly used to treat cough and cold and it is very popular in the field of cosmetology due to its healing properties. It belongs to the family Zingiberaceae and synonym is *Curcuma longa* Linn.[42]

Fig. 15: *Curcuma longa* Linn

Ethanolic extract of rhizomes of turmeric produce significant reduction in blood glucose level in alloxan induced diabetic rats. The effect was noted on seven days onward and its takes longer duration for the onset of action. The effect may be due to presence of constituents like Curcumin, dimethoxy Curcumin, Bis-demethohoxy Curcumin and Arturmerone having PPAR-γ ligand binding activity which enhances the transcription of several insulin responsive genes and improves insulin resistance.[43]

Table 1: Medicinal plants with anti-diabetic activity found in Toranmal region of Maharashtra

Sr. No.	Botanical Name	Common Name	Family	Part used	Type of extract used	Possible mechanism of action	Activity observed	Reference number
1.	*Aloe barbadensis miller*	Aloe Vera	Asphodelaceae (Liliaceae)	Leaf	Ethanol	Due to presence of lophenol,24-methly-lophenol,24-ethyl-lophenol,cycloartanol and 24-methylene-cycloartanol	Hypoglycemic	[9]
2.	*Azadirachta indica*	Neem	Meliaceae	Rootbark	Alcoholic	Due to presence of Nimbidin	Antihyperglycemic and hypoglycemic	[12]
3.	*Allium sativum*	garlic	Lillaceae	Garlic	Aqueous	Due to presence of Allicin	Hypoglycaemic effect	[15]
4.	*Senna auriculata*	Matata Tea	Fabaceae	Leaf	Ethanol	Due to presence of Flavonoids, terpenoids, glycosides, steroids, saponin and phenols	Hypoglycaemic effect	[18]
5.	*Coriandrum sativum*	coriander	Apiaceae (Umbelliferae)	Fruit	Aqueous	Due to presence of linalool (coriandrol)	Hypoglycaemic effect	[20]
6.	*Zingiber officinale Rosc*	Ginger	Zingiberaceae	Ginger	Aqueous	Serotonin receptor blocking activity	Hypoglycemic activity	[22]
7.	*Mentha piperita* L	Peppermint	Lamiaceae	Leaves	Aqueous	Presence of menthol, flavonoids and phenolic compounds	Hypoglycemic activity	[25]
8.	*Carica papaya*	Papaya	Caricaceae	Leaves	Aqueous	Stimulation of remaining β-cells of pancreas and release of more insulin	Hypoglycemic activity	[27]
9.	*Panax ginseng*	*Ginseng*	Araliaceae	Root	Powder	Ginsenosides modulates glucose transport, glucose disposal and insulin secretion	Hypoglycaemic effect	[30]
10	*Euphorbia hirta*	Dudhi	Euphorbiaceae	Flower	Ethanolic and	Presence of flavanoids,	Hypoglycaemic	[33]

					petroleum ether	tannins and other phenolic compounds and free radical scavenging effect of extract	effect	
11	*Ficus pumila*	Creepig fig	Moraceae	Leaf	Ethanol	Increase in glycogenesis, reduction in glycogenolysis or increase in entry of glucose molecules to various skeletal muscles	Hypoglycemic effect	[35]
12	*Glycin max*	Soybean	Fabaceae	Seed	Methanolic	Restoration of normal cells of islets and enlargement in size of endocrine islets as manifested by hyperplasia	Hypoglycemic effect	[37]
13	*Ipomoea batatas*	White skinned sweet potato	Convolvulaceae	Sweet potato	Flour suspension	Increase in number of pancreatic beta cells and insulin expression	Hypoglycemic effect	[39]
14	*Ocimum sanctum*	Tulsi	Lamiaceae	Leaves	Ethanolic	Increase in intracellular calcium of beta islet cells of pancreas and increase in insulin secretion	Hypoglycaemic effect	[41]
15	*Turmeric*	Haridra	Zingiberaceae	Turmeric	Ethanolic	Presence of constituents like Curcumin, dimethoxy Curcumin, Bis-demethohoxy Curcumin and Arturmerone having PPAR-γ ligand binding activity which enhance the transcription of several insulin responsive genes and improve insulin resistance	Hypoglycemic effect	[43]

CONCLUSION

The results of the preclinical studies demonstrated the potential antidiabetic activity of plants found in Toranmal region of Maharashtra. Thus these plant extract must be considered as an excellent candidate in diabetes drug development in pharamaceutical industry. However, the potential antidiabetic benefits are yet to be explored. Moreover, some ambiguities in results of various studies necessitate further research to better claim efficacy and safety of these medicinal plants. Large scale controlled trials are warranted to confirm the preliminary findings about the efficacy and to elucidate the mechanism of action of all these plants extract in clinical setting. Thus, medicinal plants from Toranmal regions may represent a new area of research with promising results.

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