ISSN: 2322 - 0902 (P)
ISSN: 2322 - 0910 (O)

International Journal of Ayurveda and Pharma Research

Review Article

A SCIENTIFIC EVALUATION OF AYURVEDIC DRUGS IN THE MANAGEMENT OF DIABETES MELLITUS TYPE 2: AN EVIDENCE BASED REVIEW

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ABSTRACT

Diabetes Mellitus (DM) is a major challenging health problem of the 21st century. Prevalence of DM is rapidly rising throughout the globe where India leads with largest number of diabetics and became "Diabetes capital of the world". It refers to a heterogenous chronic metabolic disorder that shares the phenotype of hyperglycaemia. DM is caused by a complex interaction of genetic, behavioural and environmental factors. It results due to impaired insulin secretion or insulin resistance, decreased glucose utilization and increased glucose production. It is characterized by polyuria, polydipsia, weight loss, fatigue, Dryness of mouth and throat, constipation and instance itching. Diabetes mellitus is of two types- Type I - IDDM (*Jata pramehi* or *Sahajapramehi*) Type II - NIDDM (*Sthula pramehi* and *Apathyanimittaja pramehi*).

Ayurvedic management strategy of *Apathayanimittajaprameha* (type-2 diabetes mellitus) include *Snehana* (oleation), *Shodhan* and shaman treatments accompanied with suitable dietary and life style modification which has been found very effective. In Ayurvedic system of medicine various single herbs, herbal formulations, herbominerals and minerals are using popularly and very effectively in the treatment of *Madhumeha* i.e., Diabetes Mellitus type- 2. Many Ayurvedic drugs revalidated to having anti-diabetic and anti-hyperglycaemic activity by clinical and experimental study but many are awaited. In this study, the initiation have been taken to collect and compiled all the related information regarding Ayurvedic drugs used therapeutically that may facilitate further research works.

KEYWORDS: Diabetes Mellitus, Anti-hyperglycaemic activity, Ayurvedic drugs, Herbomineral compound.

INTRODUCTION

Diabetes Mellitus (DM) is a major challenging health problem of the 21st century. It is one of the life style disorders whose prevalence is growing rapidly throughout the world, where India leads with largest number of diabetics and consider as "Diabetic capital of the world" by international diabetic federation.[1] WHO estimated that diabetics are 19.4 million in India and these increases79.9 million diabetics by 2030[2]. There is a wide rural and urban difference in the prevalence of type 2 diabetes mellitus. The prevalence is 2.4% in rural and 11.6% in the urban populations. A quarter of the income is devoted to diabetic care for a low income Indian family that WHO said.[3]

Diabetes mellitus is a group of metabolic disease marked by high level of blood glucose resulting from defects in insulin production, insulin action or both.[4] It is characterized by polyuria, polydipsia, weight loss, fatigue, Dryness of mouth and throat, constipation and instance itching. It may leads to serious complication in multiple organ systems.[5] Commonly occurring complications are of retina, kidney, and nervous system.

Diabetes mellitus is of two types- Type I - Insulin Dependent Diabetes Mellitus (IDDM) or juvenile diabetes mellitus. Complete or near total insulin deficiency is found in type I. In Ayurveda it is comparable with *Jata pramehi* (Charaka) or *Sahaj pramehi* (Sushruta). It is not curable. Type II-Non-Insulin Dependent Diabetes Mellitus (NIDDM) or adult onset diabetes. It is characterized by variable degree of insulin resistance, impaired insulin secretion and increased glucose production. In Ayurveda it is comparable with *Sthula pramehi* (Charaka) and *Apathya-nimittaja pramehi* (sushruta). It is curable.

Despite of recent progression in medical science, several challenges still exist in the management of diabetes that requires special attention to develop un-explored fields of medical knowledge. Modern medicine systems have developed medicines to control and treat diabetes but are unable to provide complete relief. In addition, they are associated with adverse effects or hypoglycaemia.[6] Ayurveda through its armamentarium can become a potential source of hypoglycemic drugs that may be relatively safe, significantly potent with negligible side effects and can

improve quality of life.[7] WHO has also identified importance of herbal remedies in the management of diabetes mellitus type - 2. Based on similarities in signs and symptoms, DM type‑2 can be compared with *Madhumeha* in Ayurveda.

Ayurvedic management strategy include *Snehana* (oleation), *Shodhan* (purification) and *Shaman* treatments (*Aushdha*) accompanied with *Pathya*‑*Apathya* (compatible diet and lifestyle), in the management of diseases.[8] In Ayurvedic system of medicine various single herbs and minerals, herbal and herbo-minerals formulations are using popularly and very effectively in the treatment of *Madhumeha* i.e., Diabetes Mellitus type- 2. These Ayurvedic formulations are combination of different herbs and minerals. Many of these were revalidated to having anti-diabetic and anti-hyperglycaemic activity by clinical and experimental study but many are awaited. In this review authors summarized those Ayurvedic herbs and minerals which having proven anti-hyperglycemic effect in experimental study.

Material and Methods

Single herbs described in Ayurveda having hypoglycemic activity. These were classifieds on the bases of useful parts.

Leaves

***Bilva* (*Aegel marmelos*)** -Biochemical studies in streptozotocin-induced diabetic rats confirmed the potent hypoglycaemic activity of an aqueous extract of leaves[9].It showed the anti-diabetic effect which was more effective along with the oral hypoglycemic therapy. Beal leaves can be combined in high dose with oral hypoglycemic agents to bring the blood glucose to normal levels in patients whose diabetes is not in control with these agents or in those patients in whom these drugs produce adverse effects on dose increments.[10]

***Nimba* (*Azedirechta indica*) -**In the study it was shown that hydro alcoholic extracts of this plant has anti-hyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemi diaphragm.[11]

***Tejapatra* (*Cinnamomum tamala*) -** Ethanolic (50%) extract of *Cinnamomum tamala* leaves significantly lowered the plasma glucose levels in normoglycemic and streptozotocin-induced hyperglycaemic rats while given orally. The extract also showed antihyper-cholesterolaemic and anti-hypertriglyceridaemic activity in streptozotocin-induced diabetic rats.[12]

***Bimba* (*Coccinia indica*)-** The juice and decoction of leaves and stems of *Coccinia indica* (20ml/kg) showed significant hypoglycemic response in fasting rabbits. The decoction of the fruits of the plant also showed similar activity.[13] While the plant-extract reduced the blood sugar levels of fasted, glucose-loaded and streptozotocin-induced diabetic albino mice to different degrees, root extract reduced the blood sugar only of glucose-loaded animals. [14]

***Ghritkumari* (*Aloe barbidensis*) -** The aqueous extract of *Aloe vera* has the hypoglycemic property which was given orally at a dose of 150mg/kg of body weight. Whole study was performed on the alloxan induced male albino rats.[15]

***Meshasringi* (*Gymnema sylvestre*) -** Administration of *Gymnema sylvestre* extract decreased serum glucose concentration in dexamethasone induced hyper-glycaemic animals. The effects were comparable to the standard corticosteroid-inhibiting drug, ketoconazole. [16]

***Cashew plant* (*Anacardium occidentale*)-** Methanolic leaf extract of *Anacardium occidentale* was investigated in streptozotocin induced diabetic rats. Oral administration of methanolic extracts at doses of 35, 175 and 250 mg/kg significantly reduce blood glucose levels in diabetic rats. In another study it was investigated that methanolic stem bark extract of cashew plant shows anti-diabetic activity in fructose-fed (diabetic) rats. [17]

***Arhar* (*Cajanus cajan*) -** The methanolic leaves extract of *Cajanus cajan* has antidiabetic activity which was studied in alloxan induced diabetic and oral glucose loaded rats. It was investigated that the extract (400 and 600 mg/kg) significantly reduced fasting blood sugar of alloxan induced diabetic rats in a dose-related manner, with maximum hypoglycemic effect at 4-6 hr. The extract also significantly suppressed the peak postprandial rise in blood glucose of normal rats by 101.8 and 57.40% respectively.[18]

***Kasamarda* (*Cassia occidentalis*)** -Methanolic fraction of leaves was tested against streptozotocin induced diabetic rats. Treatment with this plant extracts at different doses and times following in normal and diabetic rats significantly reduced blood glucose level to normal in diabetic rats. Histopathological examination showed that methanolic extract protects the pancreatic tissue from STZ induced damage.[19]

Barks

***Tvak* (*Cinnamomum zeylanicum*) -** Aqueous extract of *Cinnamomum zeylanicum* bark significantly reduced blood glucose value at 1h during glucose tolerance test. When diabetic animals with fasting blood glucose were treated with cinnamon extract (200mg/kg, b.w.) once daily for 2 weeks, the fasting blood glucose level came down. [20]

***Vijayasar* (*Pterocarpus marsupium*) -** Administration of ethyl acetate-soluble fraction of ethanol extract of *P. marsupium* wood to alloxan-induced diabetic rats for 5 days significantly reduced the blood sugar levels along with an increase in insulin levels. [21] The effect of the anti-diabetic plant, *Pterocarpus marsupium*on the development of cataract was assessed in rats. Administration of the plant extract exerted a favourable

effect on body weight, blood glucose and anti-cataract effect as evident from decreased opacity index. [22]

***Daruharidra* (*Berberis aristata*) -**Antidiabetic activity of methanolic extract of this plant has been observed in streptozotocin induced diabetes in adult male wistar rats. [23]

***Arjuna* (*Terminalia arjuna*)-** Stem bark of *Terminalia arjuna* has the antidiabetic activity which was studied on alloxan induced diabetic rats. Ethanolic extract of bark was given at a dose of 250 and 500mg/kg which significantly decrease the blood glucose and decrease in the activities of glucose-6-phosphatase, fructose-1, 6-disphosphatase, aldolase and an increase in the activity of phosphor glucoisomerase and hexokinase in tissues. [24]

***Udumbar* (*Ficusra cemosa*) -**Ethanolic extract of bark showed antihyperglycemic and hypolipidemic activities in alloxan induced diabetic rats. The dose of 100-500 mg/kg of extract showed significantly lowered blood glucose level. [25]

Roots

***Haridra* (*Curcuma longa*) -** Rhizome powder of curcuma longa in the dose of 200mg/Kg was identified as the most effective dose with significant decrease in the levels of blood glucose & lipid profile. [26]

***Tinospora cordifolia* (*Guduchi*)** - Oral administration of the root extract of *Tinospora cordifolia* for 6 weeks resulted in significant reduction of blood and urine glucose and of lipids in serum and tissues in alloxan-induced diabetic rats. [27]

***Vidarikanda* (*Ipomoia digitata*)** - The antidiabetic effect of various fractions of *Ipomoia digitata* was studied on alloxan induced diabetic rats. Extract was used in the dose of 100 mg/kg, medium dose 200 mg/kg, high dose 400 mg/kg of body weight. glibenclamide (10mg/kg body weight) was used as a standard reference. [28]

***Teak* (*Tectona grandis*)** - Methanolic extract of *Tectona grandis* root has antidiabetic activity which was performed on alloxan induced diabetic albino rats. Its hypoglycemic action was compared with glibenclamide. [29]

***Sitaphala* (*Annona squamosa*) -** The aqueous extract of roots of *Annona squamosa* at a dose of 250 mg/kg and 500 mg/kg body weight respectively was reported for antidiabetic activity in Streptozotocin (STZ) induced hyperglycemic rats. It reduces the blood glucose level and effects were compared with the glibenclamide. [30]

***Arka* (*Calotropis procera*) -** The root extracts of *Calotropis procera* were investigated for its anti-diabetic effect in streptozotocin induced diabetic male wister albino rats. The different extracts like ether, methanolic and aqueous extracts of roots were tested for anti-diabetic activity on rats. [31]

SEEDS

***Methika* (*Trigonella foenum*-graecum) -** Oral administration of an alcoholic extract of *Trigonella foenum*-graecum seeds significantly reduced the blood sugar levels of normal as well as of alloxan-induced diabetic rats. [22]

***Gunja* (*Abrus precatorius*) -** The antidiabetic effect of chloroform methanol extract of *Abrus precatorius* seed was studied in alloxan induced diabetic rabbits. Its anti-diabetic property was found to be similar to that of chlopropamide. [32]

***Rajika* (*Brassica juncea*) -** Its aqueous seed extract has a potent hypoglycemic activity which was investigated in STZ induced diabetic male albino rat. [33]

***Papita* (*Carica papaya*)** - Hypoglycemic activity was seen in aqueous seed extract of *Carica papaya* in normal male wistar rats. It was found that crude extract significantly and progressively lowered fasting blood sugar. [34]

***jamun* (*Syzium cumini*) -** Seed extract of *Syzium cumini* has shown the antidiabetic activity against streptozotocin induced diabetic rats. The compound 'Mycaminose' and ethyl acetate and methanol extract was found to reduce the blood glucose level. [35]

FRUITS

***Karavellaka* (*Momordica charantia*)** -Experimental and clinical studies revealed anti-diabetic and adaptogenic properties of the aqueous extract of *Momordica charantia*. The aqueous extract of the fruit was more effective in diabetes than the powder of the dried fruit.[36]

***Amalki* (*Embellica officinalis*) -** The aqueous fruit extract of *Phyllanthus emblica* showed effect on type-II diabetes, triglycerides and liver specific enzyme, alanine transaminase. It was shown that aqueous fruit extract in a dose of 200mg/kg body weight, significantly decreased the blood glucose level. [37]

Whole Plant /Bulb/ Aerial part

***Palandu* (*Allium cepa*) -** Its ethenolic extract show hypoglycemic effect which was carried on alloxan induced male albino rats. The most effective percentage reduction in blood glucose level, total serum lipids and cholesterol is observed at 300 mg/kg. [38]

***Rason* (*Allium sativum*) -**Hypoglycemic study was performed on the STZ induced diabetic rats. Simple garliac extract and ethanolic extract shows significantly antidiabetic activity. Raw garlic possesses a beneficial potential in reversing proteinuria in addition to reducing blood sugar, cholesterol and triglycerides in diabetic rats.[39]

***Bhumyamalki* (*Phyllanthus niruri*) -** Methanol extract of aerial parts of *Phyllanthus niruri* has antidiabetic activity. It was evaluated in normal and alloxan diabetic rats.[40]

Single Minerals (Metal *Bhasma*)

***Yasad bhasma* (Zn) –** The *Yasad bhasma* (Zinc ash) 3-30mg/Kg has anti-diabetic activity was assessed in STZ induced diabetic rat. 4 wks treatment with zinc ash resulted in improved glucose tolerance, lowered blood glucose levels and reduced serum insulin levels. [41]

***Vangabhasma* (Sn) –** *Vangabhasma* at a dose of 25-50mg/Kg showed a dose dependent decrease in glucose level in alloxan induced hyperglycemic rats. It did not influence the blood glucose in normal rats. Metformin was used as reference standard. [42]

***Naga bhasma* (Pb)–**Treatment with *Nagabhasma* showed no change in blood glucose level in normal rats but normalized the impaired glucose tolerance and alloxan induced hyperglycemia on long term treatment. Glibenclamide was as used as reference standard.[43]

***Swarnamakshika* (Copper pyrite) –** *Swarnamakshika bhasma* showed marked decrease in blood sugar level from 7th day onwards of treatment. The result was comparable with standard drug glibenclamide. [44]

Ayurvedic Compound Formulations Used in Diabetes Mellitus Type -2

A number of Compound formulations described in different Ayurvedic literature for the treatment of *Madhumeha* (DM Type-2)[45,46]. Most of these are given below.

Table 1: Name of Compound and Ingredient Used in *Madhumeha*

S.No.	Name of Compound	Ingredient (contains metal & minerals in *Bhasma* & *Shodita* form)	Dose with Anupana
1.	*Trivanga Bhasma*	*Naga, Vanga, Yashad*	125mg, Honey, Butter
2.	*Mehakalanal Rasa*	*Rasasindoor, Vanga*	250 mg, *Gunjamool-kwath*, cow milk
3.	*Panchanan Rasa*	*Parada, Gandhak, Abhrak, Lauha, Vanga*	250 mg, Cold water
4.	*Chadrakala Rasa*	*Shilajatu, Rasasindoor, Abhrak, Lauha, Vanga, Ela, Nagakeshar, Shalmali Karpur, Jatiphala, Amalki,*	250mg, Honey
5	*Mehamudgara - Rasa*	*Lauha, Trikatu, Triphala, Guggulu, Rasanjana, Devadaru, Vidlavana, Gokshur, Bilva, Dadim, Bhunimb, Trivrita, Pipalimula*	500mg, Honey
6.	*Pramehakulantaka Rasa*	*Shilajatu, Parada, Gandhak, Abhrak, Vanga, Trikatu, Triphala, Rasanjana, Devadaru, Vidlavana, Gokshur, Bilva, Dadim, Pipalimula*	500mg, Cow & Goat milk
7.	*Vasantkusumakar Rasa*	*Swarna, Rajat, Kantlauha, Naga, Vanga, Abhrak, Praval, Mukta, Kasturi*	125mg, Honey, Ghee, milk
8.	*Swarnavanga*	*Parada, Gandhak, Vanga, Nausadar*	125-250mg, Honey
9.	*Vangeswar Rasa*	*Rasasindoor, Vanga*	125mg, Honey
10.	*Vangeswar Rasa (Y.R.)*	*Kantlauha, Vanga, Abhrak, Nagakeshar*	250mg, Honey
11.	*Brihat Vangeswar Rasa*	*Parada, Gandhak, Swarna, Kantlauha, Naga, Vanga, Abhrak, Mukta, Swarnamakshik*	250mg, Cow & Goat Milk, Curd
12	*Mehavajra Rasa*	*Shilajatu, Rasasindoor, Kantlauha, Swarnmakshik, Manahashila Trikatu, Triphala, Bilva, Jeerak, Kapith, Haridra*	500mg, *Nimbachurna*, *Ghrita*, Rice washed water
13.	*Yogeshwar Rasa*	*Parada, Gandhak, Lauha, Naga, Vanga, Abhrak, Tamra, Varatika, Ela, Tejapatra, Mustak, Vidang, Nagakeshar, Amalki, Reduka, Pipalimula*	250 mg, Honey
14.	*Vasant Tilaka Rasa*	*Swarna, Rajat, lauha, Vanga, Abhrak, Praval, Mukta, Javitri, chaturjata, Swarnamakshik*	250 mg, Honey
15.	*Harishankar Rasa*	*Rasasindoor, Abhrak*	125mg, Honey
16.	*Bhrita Harishankar Rasa*	*Parada, Gandhak, lauha, Vanga, Swarna, Swarnamakshik*	125mg, Honey
17.	*Pramehasetu Rasa*	*Rasasindoor, Abhrak*	375 mg, *Triphala-churna*, Honey
18.	*Megnada Rasa*	*Rasasindoor, Abhrak, Shilajatu, Kantlauha, Swarnmakshik, Manahashila, Trikatu, Triphala, Ankhoth, Jeerak, Karpas, Haridra*	375 mg, Honey
19.	*Anandabhairb Rasa*	*Rasasindoor, Vanga, Swarna*	125mg, *Gunjamula-churna*, Honey
20.	*Mehantak Rasa*	*Parada, GandhakSwarna, Lauha, Rajat, Abhrak, Vanga, Talamuli*	250mg, Honey, warm milk

21.	*Mehakesari Rasa*	*Rasasindoor, Swarna, Kant Lauha, Vanga, Mukta, Ela, Nagakeshar, Tejpatra, Twak,*	250mg, milk
22.	*Sarweshwar Rasa*	*Swarna, Lauha, Rajat, Abhrak, Shilajatu, Mukta, Swarnmakshik, Trikatu, Madhuyashti*	250mg, Honey
23.	*Apoorvamalinvasant Rasa*	*Rasasindoor, Abhrak, Rajat, Praval, lauha, Swarnmakshik, Tamra, Vaikrant, Vanga, Tankan, Ksudhrasankh, Kasturi, Karpur*	375mg, Honey, *Guduchi churna, Pipali churna*
24.	*Pramehachintamani Rasa*	*Rasasindoor, Swarna, Lauha, Vanga, Abhrak, Praval, Mukta, Swarnamakshik*	250mg, Honey, *Triphala kwath*
25.	*Brihat Somnath Rasa*	*Parada, Gandhak, Swarna, Lauha, Rajat, Abhrak, Vanga, Swarnamakshik, Kharpar*	250mg, Honey
26.	*Vidangadi Lauha*	*Lauha, Vidang, Triphala, Pipali, Shunthi, Mustak, Jirak, Krishna jirak*	250-500mg, Honey
27.	*Chandraprabhavati*	*Lauha, Shilajatu, Swarnamakshik, Triphala, Trikatu, Lavantraya, Kshardaya, Dhanyak, Chutrajata, Haridra, Chavya, Chitrak, Ativisha, SarivaKachur, Devdaru, Gugulu, Vacha*	500mg, Honey, *Ghrita*
28.	*Indravati*	*Rasasindoor, Vanga*	125mg, Honey
29.	*Vangastak Rasa*	*Parada, Gandhak, Lauha, Rajat, Abhrak, Vanga, Tamra, Kharpar*	250mg, Honey, *Haridrachurna*
30.	*Shilajatwadilauha*	*Shilajatu, Trikatu, Swarnamakshika, Lauha*	500mg, Honey
31.	*Phalatrikadikwath*	*Amalki, Haritaki, Vibhitak, Daruharidra, Indrayana, Nagarmotha*	30-40 ml, Honey
32.	*Nisha-Amalkichurna*	*Haridra, Amalki*	3-6 mg, *Triphala kwath*
33.	*Chaturbijachurna*	*Methi, Ajmoda, Chandrasur, Kalazazi*	3-6 mg *Triphala kwath*
34.	*Triphlachurna*	*Amalki, Haritaki, Vibhitak*	3-6 mg, warm water
35.	*Triyushnadigutika*	*Sunthi, Pippali, Maricha, Trphala, Guggulu*	3-6 mg, water

DISCUSSION

Conventional modern medicine is not always successful to control DM in all cases. Insulin is not always indicated due to the development of insulin resistance and generation of insulin antagonists in the body, whereas the OHD are found to be limited use in many cases due to the major side effects. Therefore search for better remedies from Ayurvedic resources continue. Ayurvedic drugs not only have hypoglycemic effect but also corrects metabolic derangements, helps in maintaining the *Agni* and *Ojas* status i.e., metabolic stability and immune strength in diabetic patients and retard the complications of DM & OHA and having less side effects.

CONCLUSION

Almost all the ingredients of Ayurvedic formulations (as shown above in the table) shown anti-hyperglycaemic or Anti-diabetic activity in experimental study as reviewed above. These effort may provide treatment for all and justify the role of Ayurvedic treatment in DM Type-2.

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Cite this article as:
Garg Richa, SachdevKamal, Dharmendra. A Scientific Evaluation of Ayurvedic Drugs in the Management of Diabetes Mellitus Type 2: An Evidence Based Review. International Journal of Ayurveda and Pharma Research. 2017;5(11):21-27.

Source of support: Nil, Conflict of interest: None Declared

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