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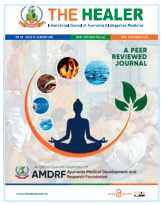

REVIEW ARTICLE

Potential Role of Darvyadi Kwatha in the Management of Diabetes- A Review

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ABSTRACT:

Introduction: Diabetes is a clinical condition characterized by a spike in blood glucose in plasma. It is one of the 21st century's greatest public health crises and is among the top 10 causes of death worldwide. Although new drugs and therapeutics are emerging for its management but the prevalence is increasing at an alarming pace; thus, every system must contribute for effective management. **Objectives:** To review and explore the efficacy and safety evaluation of the individual herbs of *Darvyadi Kwatha* (DK), (an Ayurvedic formulation) mentioned in *Charaka Samhita.* **Methodology:** The literature review was performed using the relevant search terms in classical Ayurveda textbooks and various databases, which were then evaluated on the basis of the function or impact on diabetes. **Results:** The constituents of the DK has some strong efficient antidiabetic/ hypoglycaemic chemical principle having insulin-triggering and insulin-like behaviors which increases the activity of glucose-6-phosphate dehydrogenase (G6PD) and glucokinase and decreases glucose-6-phosphatase activity, reduce oxidative stress and prevention of glutathione reductase, superoxide dismutase, and catalase activity play a critical role in glucose homeostasis. DK also improve biochemical parameters such as SGPT, SGOT, cholesterol and triglycerides and is found to be safe in animal experiments. **Conclusion:** The various evidences clearly indicates that DK has definite hypoglycemic potential as well as anti-diabetic activity.

Keywords: Ayurveda, Darvyadi Kwatha, Diabetes, Insulin, Madhumeha, Prameha,

INTRODUCTION:

Diabetes is a clinical condition characterized by a spike in blood glucose in plasma.[1] It's because the body can't efficiently manufacture any or enough of the hormone insulin or use insulin. Hyperglycemia can lead to damage to different body organs with health problems that are debilitating and life-threatening, such as cardiovascular disease, nephropathy, neuropathy, retinopathy, etc. Type

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1 diabetes, type 2 diabetes and gestational diabetes are the three primary forms of diabetes.[2] Diabetes being itself a disease it carries different acute and chronic metabolic complications of hyperglycemia with itself that affect every organ from head to toe. The dosage of medication is ever growing after a person is diagnosed with diabetes and eventually insulin has to be provided for glycemic control in most cases. It is one of the 21st century's greatest public health crises and is among the top 10 causes of death worldwide. India is the second largest and it is estimated that by the year 2045 it will be the lead.[2,3] So, there is a need to prevent new cases and to cure a diabetic person. Although new drugs and therapeutics are emerging for its management but the prevalence is increasing at an alarming pace; thus, every system must contribute for effective management. According to aetiological factors and clinical features, Diabetes can be correlated with *Prameha* or *Madhumeha* in Ayurveda science. There are many texts mentioning drug for *Prameha* and *Madhumeha* which need to be tested and validated scientifically. In this article, we intend to evaluate the assessment of the efficacy and safety of individual *Darvyadi Kwatha* (DK) (an Ayurvedic formulation) herbs in diabetes management.

METHODOLOGY

The classical text books of Ayurveda and various databases like PubMed, Scopus, Google Scholar, Research Gate has been searched with the terms Diabetes, *Madhumeha, Prameha, Triphala, Darvyadi Kwath*, and the Sanskrit, English and Scientific name of each individual herbs. The material collected then has been analyzed based on the role or effect upon Diabetes.

Darvyadi Kwatha:[4]

दार्वी सुराह्वां त्रिफलां समुस्तां कषायमुत्क्वाथ्य पिबेत् प्रमेहि ।

क्षौद्रेण युक्तामथवा हरिद्रां पिबेद्रसेनामलकिफलानाम् ।।२६।।

METHODS OF PREPARATION:

At first *Daarvi, Devadaaru, Haritaki, Bibhitaki, Amalaki* and *Naagarmothaa* must be taken in equal parts and prepare their *Yavakuta* (Coarse Powder). Then the *Kwatha* (decoction) of those *Yavakuta* drugs must be prepared according to the instruction of method given in *Kwatha Kalpana (Shaarangdhar Samhita*) i.e. the drugs in *Yavakuta* form will be boiled with 16 times of water under low heat and reduced to 1/8th and filtered. Dose: 50ml

REVIEW OF INDIVIDUAL HERBS

1. Daruharidra (Berberis aristata):

In a study, repetitive administrations of *Daruharidra* (BA) stem methanolic extracts (250 & 500 mg/kg) significantly lowered blood glucose level (BGL) in diabetic rats ($p<0.05$) and also reported a substantial decrease in serum total cholesterol and triglyceride levels and a significant increase in HDL cholesterol levels.[5] Likewise, in addition to being safe, BA root extract (250 mg/kg) significantly reduced BGL without any hypoglycemic impact on its control counterparts, increased activity of glucokinase and G6PD and decreased activity of glucose-6-phosphatase (G6P) in diabetic rats, which play a key role in glucose regulation.[6] In another study, petroleum ether extract of BA (100 & 400 mg/kg, body wt.) showed substantial decreases in BGL.[7]

The addition of BA to insulin therapy in type 1 diabetic patient has been found to contribute to a decrease in the insulin dose required for sufficient glycemic control.[8] The combination of berberine and silymarin has been shown to be more effective in reducing HbA1c than berberine alone when given at the same dose and in the form of standardized extracts.[9] It is evident that the roots and their methanol and aqueous extracts induced substantial decreases in BGL at two, four and eight hours in normal rabbits and even in diabetics ($P<0.05$ & 0.001). Compared to the diabetic control group, the ethanol extract of the BA root showed a substantial reduction in serum glucose level (SGL) in alloxan-induced diabetic rats at day 15. BA ethanol extract improves glucose tolerance in oral glucose tolerance tests.[10]

2. Devdaru (Cedrus deodara)

Devdaru (CD) is rich with antidiabetic active constituents like flavonoids, tannins and embelin. Streptozotocin-induced diabetes mice were exposed to ethanolic CD extract at doses of 250 and 500 mg/kg body weight, which exhibited substantial anti-hyperglycemic activity and also reduced biochemical parameters (SGPT, SGOT, cholesterol and triglycerides). The 500 mg/kg bw dosage was found to be more effective in decreasing the BGL, almost similar to the effect of the standard drug.[11] Powdered woods of CD defatted with petroleum ether and extracted from ethanol played a vital role in the management of diabetes.[12] The other analysis of CD heart wood aqueous extract efficiently and substantially reduced alloxan-induced oxidative stress and produced a decrease in BGL.[13]

3. Haritaki (Terminalia chebula)

For 30 days, oral administration of ethanolic fruit extract (EETC) (200 mg/kg bw/rat/day) stimulated insulin and significantly reduced BGL and HbA1c levels in rats with diabetes. A drop in the amount of secretory β-cell granules was observed and stabilized after treatment with *Haritaki* (TC) extract in Streptozotocin (STZ)-induced diabetic rats.[14] The treatment with EETC reduced the histopathological changes like the granular cytoplasm, dilatation, shrunken nuclei, excess epithelium proliferation and inflammation caused by induction of alloxan.[15] In normal rats, TC demonstrated substantial anti-hyperglycemic effects ($P<0.01$) without hypoglycemic action, and efficacy was lower in the alloxan model than glibenclamide but higher in the adrenaline-induced model. The ethanol pulp extract of TC fruit is likely to have substantial anti-diabetic activity due to insulin-like component action and insulin release promotion.[16] In the rat model of metabolic syndrome, the TC fruit extract exerts a substantial and dose-dependent glucose reducing effect.[17]

In comparison to untreated diabetic animals, oral administration of aqueous extract (200 mg/kg bw) once daily for two months lowered elevated blood glucose levels, substantially reduced the rise in HbA1c and the decreased levels of serum insulin were regulated. An in-vitro study with islets of pancreas showed that the release of insulin was almost twice as high as that of untreated diabetic animals and is safe with LD-50 above 3 g/kg bw, suggesting a high safety margin.[18]

4. Vibhitaki (Terminalia bellerica):

Vibhitaki (TB) prevents alloxan-induced hyperglycaemia and oxidative stress; increases the level of superoxide dismutase, glutathione reductase and the activity of catalase decreased by alloxan.[19] By reducing lipid peroxidation, hydroxyl radical scavenge and superoxide radicals, it has been used for its lower serum glucose level and antioxidant activity.[20] Methanolic TB extract and Emblica officinalis can serve as a potent inhibitor of α-glucosidase and α-amylase and have demonstrated substantial antiglycation activity and inhibited LDL oxidation under in vitro conditions.[21]

Gallic acid of TB helps for the regeneration of β-cells and normalization of all biochemical parameters, as it significantly reduced the amount of plasma glucose in a dose-dependent manner, decreased triglycerides, total serum cholesterol, LDL-cholesterol, uric acid, creatinine, urea, and increased the level of plasma insulin, C-peptide, and glucose tolerance markedly.[22] By upregulating the levels of cAMP and intracellular calcium in the β cells, octyl gallate of TB can enhance insulin secretion.[23]

5. Amalaki (Emblica offcinalis):

In order to evaluate its glycaemic potential, standardized doses of 100, 200, 300, and 400 mg/kg bw of the *Amalaki* (EO) extract were given orally to diabetic and normal rats. During fasting blood glucose trials, a median fall of 27.3 percent ($p < 0.001$) in the BGL of normal rats was observed at 6 hours, with a dose of 300 mg/kg bw reported as the most effective.[24] Oral administration of EO leaf extract hydro-methanolic (20:80) in the same standard doses daily for 45 days showed a substantial decrease in fasting blood sugar and other biochemical parameters (serum creatinine, serum urea, SGOT, SGPT and lipid profile). Compared to diabetic rats, therapy substantially raises the insulin level and also increase the levels of reduced glutathione, superoxide dismutase, glutathione peroxidase and catalase and decrease LPO level in the kidney and liver of diabetic rats.[25]

6. Nagarmotha (Cyperus rotundus)

Administration of 500 mg/kg of Nagarmotha (CR) extract once daily orally for 7 days substantially reduced the high BGL caused by alloxan in rats.[26] In terms of the fluorescence strength of glycated bovine serum albumin, the hydroalcoholic extract of CR at different concentrations from 25 µg/ml to 250 µg/ml significantly reduced the formation of advanced glycation end products (AGEs). It also prevented oxidative protein damage, including the effect on the formation of protein carbonyl and thiol oxidation, which are believed to form under the glycoxidation method.[27]

Administration of ethanolic rhizome extract to STZ induced diabetic swiss mice for 3 weeks at doses of 250 and 500 mg/kg bw showed important antidiabetic activity, increase in body weight and decrease in elevated biochemical parameters.[28] CR rhizomes have inhibitory activities against alpha-amylase and alpha-glucosidase in phytochemical investigations using in vitro enzyme inhibition assays.[29] Gallic acid, Quercetin and 4-hydroxyl cinnamic acid derivatives of CR have demonstrated important anti-diabetic activities.[30]

Review of *Triphala* as a whole

The methanolic extract of a preparation consisting of dried fruits of *Triphala* (EO, TB and TC) and seeds of Trigonella foenum graecum when administered orally to glucose-loaded Swiss albino mice at doses of 50, 100, 200, and 400 mg/kg bw is safe and significantly lowered BGL by 35.5, 46.8, 49.2, and 51.6 percent respectively, whereas Glibenclamide for the same at a dose of 10 mg/kg bw dropped BGL by 62.1%.[31] In another study, the supplementation of the *Triphala* powder (TP) to NIDDM subjects for a period of 45 days showed substantial decrease in the BGL.[32]

TP therapy substantially improved the level of urine parameters such as glucose, albumin, creatinine, plasma proteins, and BUN and decreased oxidative stress and damage to the kidney. ELISA, Immunohistochemistry, and western blotting studies have shown that TP therapy has reduced TGF-β expression in kidney tissues, showing a major nephro-protective effect.[33]

Review of *Darvyadi Kwatha* as a Whole

The 0.01 µg/ml dose of this formulation in C elegans (CE) was able to increase the mean lifespan by 16.09 percent. In addition, in both wild type and stress hypersensitive mev-1 mutant, this formulation treated worms demonstrated oxidative stress resistance along with upregulation of sod-3 and gst-4 stress response genes.[34]

DISCUSSION:

Ayurveda has a great potential in the management of Prameha and *Madhumeha* and its associated complications. It has two ways of treatment viz. *Sodhana* (Purification) and S*hamana Chikitsa* (Pacificatory management). Keeping in mind the etio-pathogenesis of *Madhumeha, Shamana Chikitsa* must be done with such drugs that possess *Agni Deepana* (digestion and metabolism enhancing) and *Kleda nasaka* (moistness removing) properties along with the pacifier of the aggravated D*osha.* Drugs having *Tikta* (bitter)*, Kashaya* (astringent) and *Rooksha* (dry) properties are mostly used in the management of *Madhumeha*. *Darvyadi Kwatha* possess above mentioned properties required for the management of *Madhumeha* (Diabetes).

Without any hypoglycemic effect on their counterparts, the essential dose of the alcoholic, aqueous and petroleum extract of BA substantially reduced the BGL. In addition, reduces the insulin dose in type 1 diabetes. It increases the activity of glucokinase and G6PD and decreases the activity of G6P in diabetic rats that play a critical role in glucose homeostasis. Therefore, it is conceivable that BA contain some strong efficient antidiabetic/hypoglycemic chemical principle having insulin-triggering and insulin-like behaviors.[35] Also, the myriad CD extracts not only exhibit substantial anti-hyperglycemic activity, but also reduce oxidative stress and reduce biochemical parameters such as SGPT, SGOT, cholesterol and triglycerides. In addition to providing anti-diabetic activity with the promotion of insulin release, TC also raises the amount of β-cell secretory granules and avoids epithelium proliferation in the pancreas. Alloxan-induced hyperglycemia, decreased oxidative stress, and increased glutathione reductase, superoxide dismutase, and catalase activity were significantly prevented by TB. This various evidences about the role of EO clearly indicates that its' extract has definite hypoglycemic potential as well as anti-diabetic activity. The statistical evaluation about the effect of *Triphala* showed significant reduction in the BGL and improved the blood and urine parameters such as glucose, plasma proteins, albumin, creatinine, and BUN levels.[36,37] Due to its capacity to inhibit oxidative stress and TGF-β in diabetes, TP has a substantial nephro-protective impact.[36] The CR extract demonstrates inhibitory activities against α-amylase and α-glucosidase, reduces AGEs and prevents damage to oxidative proteins, showing important antidiabetic activity of CR.

The Ayurveda analysis on the basis of the properties against *Madhumeha* and *Prameha* and the in-vitro and phytochemical analysis of each single herbs shows they have significant anti-diabetic role. Although there are no published research papers on the involvement of this formulation in humans, one research activity carried out in CE indicates that the formulation of Darvyadi could play an important role in controlling aging and associated complications such as diabetes.[33]

CONCLUSION:

This analysis of different studies of the constituents in a single or in compound form shows that *Darvyadi Kwatha*, along with its histologically regenerative and physiologically insulin-promoting function, has important anti-diabetic properties. For more validation, there is a need for further experimental and clinical trials.

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CONFLICT OF INTEREST: Author declares that there is no conflict of interest.

SOURCE OF SUPPORT: None

Table 1 : Contents and their *Rasa-Panchaka* of *Darvyadi Kwatha:*

SN	Name of the drug	Latin Name	Rasa	Guna	Veerya	Vipaka	Dosakarma	Parts Used	Quantity
1	Darvi	*Berberis aristata DC.*	*Tikta, Kashaya*	*Laghu, Ruksha*	*Ushna*	*Katu*	*Kaphaghna*	Root	1 part
2	Devadaru	*Cedrus deodara (Roxb.) Loud.*	*Tikta*	*Laghu, Snigdha*	*Ushna*	*Katu*	*Kapha Vata Shamaka*	Heartwood	1 part
3	Haritaki	*Terminalia chebula Retz.*	*Madhura, Amla, Katu, Tikta, Kashaya*	*Laghu, Ruksha*	*Ushna*	*Madhura*	*Tridoshahara Esp. Vatashamaka*	Fruit	1 part
4	Bibhitaki	*Terminalia bellirica Roxb.*	*Kashaya.*	*Ruksha, Laghu*	*Ushna*	*Madhura*	*Tridoshahara Esp. Kaphashamaka*	Fruit	1 part
5	Amalaki	*Emblica officinalis Gaertn*	*Madhura Amla, Katu, Tikta, Kasaya*	*Guru, Ruksha, Sheeta*	*Sheeta*	*Madhura*	*Tridoshahara Esp. Pittashamaka*	Fruit	1 part
6	Nagarmotha	*Cyperus rotundus Linn.*	*Tikta, Katu, Kashaya*	*Laghu, Ruksha*	*Sheeta*	*Katu*	*Kapha Pitta Shamaka*	Root/Rhizome	1 part

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