ABSTRACT

Diabetes mellitus (DM) can be correlated as Madhumeha in Ayurveda. There is wide number of herbal drugs are mentioned in Ayurvedic texts in the treatment of Madhumeha (DM). Among many herbs known for their anti-diabetic properties, Haridra (Turmeric – Curcuma longa Linn.) stands the leader. Modern studies too have proven the efficacy of turmeric in the treatment of DM especially Type 2 DM. Its rhizomes exhibit anti-inflammatory, anti-human immunodeficiency virus, antibacterial, antioxidant effects, anti-arthritic, hypoglycemic, and wound healing activities etc. This article provides a comprehensive summary of medicinal properties with review of recent literature on the therapeutic applications of Curcuma longa in the treatment of DM according to Ayurveda and modern science. Another relevant experimental and clinical research works are also reviewed here. Different formulations of Curcuma longa mentioned in different ayurvedic texts are also included in this paper.

KEYWORDS: Curcuma longa Linn., Madhumeha, Haridra, Zingiberaceae.
INTRODUCTION

In Ayurveda, Madhumeha is considered as chronic and distressing disease, where there is involvement of Tridosha (three humors- vata, pitta, kapha), major Dhatu (tissues) such as Rasa (nutritional fluid plasma), Asrula (blood), Mamsa (muscle tissue), Meda (adipose tissue/fat), Majja (bone marrow), Shukra (semen), Ambu (watery portion of body), Vasa (oily part of flesh), Lasika (lymph) and Oja (essence of all the tissues). The features of Madhumeha mentioned in Ayurveda can be compared with NIDDM (Non insulin dependent Diabetes Mellitus), type II diabetes, a multifaceted metabolic disorder characterized by common feature of chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism whereas Madhumeha is a type of Vatika Prameha in which person passes Kashaya (astrigent), Madhura (sweet) and Panduvarna (pale colour) character urine.

Current Indian diabetic scenario is very astonishing, calculating a prevalence rate of approximately 20% in urban populations and approximately 10% in rural populations. The hazardous side effects of the hypoglycemic agents after long term use have further created problems and hence an ideal therapy is still obscure. There are large numbers of herbal drugs mentioned in Ayurvedic texts, which are advised for treatment of Diabetes mellitus (DM). Haridra (Curcuma longa Linn.) is one of them very well known drug mention in the management of DM. Curcuma longa Linn. is an Indian spice derived from the rhizomes of the plant commonly known as ‘Haldi’ in Hindi is also an important dietary spice. It is extensively used in Ayurveda, Unani and Siddha systems of medicine as home remedy for various diseases including biliary disorder, anorexia, diabetic wounds etc.

This review seeks to briefly summarize the ancients as well as contemporary scientific literatures related role of Curcuma longa Linn. in DM and its associated complications. Particular attention is given to comprehend the antidiabetic property of curcuma longa. Authors have also compiled Ayurvedic properties of Haridra from different Nighantu (Ayurvedic materia medica) such as Bhavaprakasha Nighantu, Dhanvantari Nighantu, Raja Nighantu, Kaiyadev Nighantu. Ample formulations of Haridra are mentioned reffering a variety of ancient texts such as Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, Madhava Nidana, Bhaishajya Ratnavali, Harita Samhita, Kashyapa Samhita , Sharngadhara Samhita and Yogaratnakara. Moreover, informations were collected from contemporary textbooks, electronic journals, E-library & other research materials.
DESCRIPTION OF CURCUMA LONGA LINN.

Curcuma longa Linn. (Turmeric) is a perennial member of the Zingiberaceae family and is cultivated in India and other parts of Southeast Asia. The rhizome of turmeric, the portion of the plant used medicinally, yields a yellow powder. (Fig.1, 2) Dried Curcuma longa is the source of turmeric, the ingredient that gives curry powder its characteristic yellow color. Turmeric is used extensively in foods for its flavor and color, as well as having a long tradition of use in the Chinese and Ayurvedic systems of medicine, particularly for the treatment of flatulence, jaundice, menstrual difficulties, hematuria, hemorrhage, liver disorders, diabetes and colic. Turmeric can also be applied topically in poultices to relieve pain and inflammation.

Current research has focused on turmeric’s antioxidant, hepatoprotective, anti-inflammatory, anticarcinogenic, and antimicrobial properties, including hypoglycemic property. However, reports on its antidiabetic properties are limited and therefore this review study the effect of C. longa on diabetes mellitus is selected for review study.

Active Constituents: Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. The Curcumin is a lipophilic polyphenol that is nearly insoluble in water but is quite stable in the acidic pH of the stomach. The best-researched active constituent is curcumin, which comprises 0.3-5.4 percent of raw turmeric. Curcumin, has caught scientific attention as a potential therapeutic agent in experimental studies as well as human studies diabetes and for the treatment and
prevention of diabetes patients, primarily because it is effective in reducing glycemia and hyperlipidemia in rodent models and is relatively inexpensive and safe.

Curcumin has been shown to possess several pharmacological activities i.e. antioxidant, anti-spasmodic, anti-arthritis, hypoglycemic, anti-bacterial, cardioprotective, wound healing etc. in animal studies as well as in human studies.

This article focuses on one of the best-explored actions, the antidiabetic activity of curcumin. Curcumin has been since extensively studied in experimental animal models of diabetes and in a few clinical trials of type 2 diabetic patients to treat their complications.

Properties: Screening the various classical texts, Rasa (taste), Virya (potency), Vipaka (post digestion effect) and Guna (property) of Haridra are mentioned in the table 1.

Table 1: Properties of Haridra (Curcuma Longa Linn.)

<table>
<thead>
<tr>
<th>Text</th>
<th>Rasa (Taste)</th>
<th>Guna (property)</th>
<th>Virya (potency)</th>
<th>Vipaka (post digestion effect)</th>
<th>Doshaghnata (pacification of Dosha)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Katu (pungent)</td>
<td>Tikta (bitter)</td>
<td>Ruksha (dry)</td>
<td>Ushna (hot)</td>
<td>Katu (pungent)</td>
</tr>
<tr>
<td>A.S.</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B.P.</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>D.N.</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>R.N.</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>K.N.</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>


Toxicity
No significant toxicity has been reported following either acute or chronic administration of turmeric extracts at standard doses. At very high doses (100 mg/kg body weight), curcumin may be ulcerogenic in animals, as evidenced by one rat study. In human clinical trials, curcumin has been found to be safe and efficacious, and the U.S. Food and Drug Administration has approved curcumin as a “generally regarded as safe” compound.

Contraindications
Contraindications have not been determined.

HARIDRA AS AN ANTIDIABETIC IN AYURVEDA
Haridra is mentioned as a best drug among the drugs in the treatment of Prameha. There are many herbs which cure Diabetes, but nothing in comparison to Haridra (turmeric). This reference clearly suggests Haridra as the drug of choice in effectively tackling Diabetes mellitus. Moreover, Amalaki (Embellica officinalis) and Haridra (Curcuma Longa) were considered as the best medicines for treating Prameha in Ashtanga Hridaya.

One finding of an experimental study done by Rao G. et al. support the above traditional view that combination of turmeric and Indian gooseberry can provide benefit to diabetic patients. In combination, these two plant products probably potentiate the actions of each other. The hypoglycemic effect of turmeric has been suggested to be due to increased peripheral glucose utilization, decreased hepatic glucose synthesis and/or increase in insulin secretion.

In this study, mixture of powdered rhizome of Curcuma longa (turmeric) and the dried fruits of Emblica officinalis (Indian gooseberry) was studied for its effect on glycemic control and erythrocyte parameters of oxidative stress in rats with streptozotocin - induced diabetes mellitus. Nishamalaki treatment resulted in significant lowering of plasma glucose and glycated hemoglobin in diabetic rats (p<0.001 NT- Nishamalaki treated vs DC- Diabetic control) comparable to that of the GT (glyburide treated-4 mg/kg) and TT (troglitazone-36 mg/kg) groups.

On analyzing different texts of Ayurveda, we come across different formulations of Haridra cited in the treatment of DM, which are mentioned as below.

Table 2: Different formulations of Haridra (Curcuma longa Linn.)

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Name of formulation</th>
<th>Mode of administration</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Churna (Powder) preparation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Haridra Mixed with Amalaki Juice</td>
<td>Orally</td>
<td>C.S. Chi. 6/26, p. 447</td>
</tr>
<tr>
<td>2</td>
<td>Haridra mixed with Honey with Amalaki Juice</td>
<td>Orally</td>
<td>S.S. Chi.11/8, p. 60</td>
</tr>
<tr>
<td>3</td>
<td>Khadiradi Churna</td>
<td>Orally</td>
<td>H.S. 3rd sthana 28/44, p. 389</td>
</tr>
<tr>
<td>4</td>
<td>Kushthadi Churna</td>
<td>Orally</td>
<td>H.S. 3rd sthana 28/45, p. 389</td>
</tr>
<tr>
<td>Kwatha (Decoction) preparation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Haridrudi Kashaya</td>
<td>Orally</td>
<td>C.S. Chi. 6/27, p. 447</td>
</tr>
<tr>
<td>No.</td>
<td>Preparation</td>
<td>Route</td>
<td>Source</td>
</tr>
<tr>
<td>-----</td>
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<tr>
<td>6</td>
<td><em>Nimba-arjunadi Kashaya</em></td>
<td>Orally</td>
<td>C.S. Chi. 6/31, p. 447</td>
</tr>
<tr>
<td>7</td>
<td><em>Mustadi Kwatha</em></td>
<td>Orally</td>
<td>B.R., 37/18, p. 697</td>
</tr>
<tr>
<td>8</td>
<td><em>Vidangadi Kwatha</em></td>
<td>Orally</td>
<td>Y.R. Prameha chikitsa/71, p. 530</td>
</tr>
<tr>
<td><strong>Ghrita-taila (Oil) preparation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td><em>Trikantakadi Taila</em></td>
<td>Orally</td>
<td>C.S. Chi. 6/38, p. 447</td>
</tr>
<tr>
<td>10</td>
<td><em>Trikantakadi Ghrita</em></td>
<td>Orally</td>
<td>C.S. Chi. 6/38, p. 447</td>
</tr>
<tr>
<td>11</td>
<td><em>Haridradi Taila</em></td>
<td>Orally</td>
<td>Y.R. Prameha chikitsa/117, p. 535</td>
</tr>
<tr>
<td><strong>Asava- Arishta (Fermented Liquor) preparation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td><em>Kanakabindu Arishta</em></td>
<td>Orally</td>
<td>C.S. Chi. 7/76-79, p. 340 (Vol.III)</td>
</tr>
<tr>
<td>13</td>
<td><em>Devadarvyadyarishta</em></td>
<td>Orally</td>
<td>Sha.S. Madhyaama Khanda 10/ 53-59, p. 142</td>
</tr>
<tr>
<td><strong>Vati (Pill)</strong></td>
<td></td>
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<tr>
<td>14</td>
<td><em>Chandraprabha Vati</em></td>
<td>Orally</td>
<td>Sha. S. Madhyaama Khanda, 7/40-49, p. 200</td>
</tr>
<tr>
<td><strong>Rasa (Herbomineral) preparation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td><em>Abhrakabhasma Yoga with Madhu</em></td>
<td>Orally</td>
<td>Y.R. Prameha chikitsa/148, p.538</td>
</tr>
<tr>
<td>16</td>
<td><em>Bangabhasma Yoga with Madhu</em></td>
<td>Orally</td>
<td>Y.R. Prameha chikitsa/144, p.538</td>
</tr>
<tr>
<td>17</td>
<td><em>Nagbhasma Yoga with Madhu</em></td>
<td>Orally</td>
<td>Y.R. Prameha chikitsa/149, p.538</td>
</tr>
<tr>
<td>18</td>
<td><em>Meghanad Rasa</em></td>
<td>Orally</td>
<td>Y.R. Prameha chikitsa/120-121, p.536</td>
</tr>
<tr>
<td>19</td>
<td><em>Mehabadhha Rasa</em></td>
<td>Orally</td>
<td>Sha.S. Madhyaama Khanda 12/204-207, p. 176</td>
</tr>
<tr>
<td>20</td>
<td><em>Vasantsukamakara Rasa</em></td>
<td>Orally</td>
<td>Sha.S. Madhyaama Khanda 12/143-147, p. 171</td>
</tr>
</tbody>
</table>


PROBABLE MODE OF ACTION OF TURMERIC (CURCUMA LONGA) IN DIABETES MELLITUS

Detail description regarding mode of action of Haridra in the breaking down of pathogenesis of DM is mentioned as below. (Flow chart:1)
Flow Chart 1: Probable Mode of action of Haridra in DM:

SCIENTIFIC EVIDENCE BASED HYPOGYCEMIC POTENTIAL OF CURCUMA LONGA LINN.

The efficacy of Ayurvedic interventions have been demonstrated through various experimental and clinical studies and few illustrations are as follows.

Experimental Studies: The hypoglycemic effect of turmeric and its constituent curcumin has been reported in a variety of animal models. A research study done by Arun and Nalini et al. investigated the efficacy of turmeric in alloxan-induced diabetes in rat and it shows decrease in blood sugar level, glycosylated hemoglobin, free fatty acids, total cholesterol, triglyceride and lipid peroxidation levels while increasing plasma insulin. Curcumin treatment can induce hypoglycemia in rats with streptozotocin (STZ)-induced diabetes has been confirmed by others.
Curcuma longa freeze dried rhizome powder dissolved in milk shows an effective and safe antidiabetic dietary supplement of high potential.\textsuperscript{[42]} Hamsters fed a high fat, high cholesterol diet treated with curcumin exhibited a normalization of lipoprotein profile together with a reduction in leptin levels and attenuated insulin resistance.\textsuperscript{[43]}

Another study done by Srinivasan et al. revealed that turmeric reduced the blood sugar and glycosylated hemoglobin levels significantly.\textsuperscript{[44]} In one study done on genetically diabetic mice, turmeric was found to be a promising ingredient of functional food for the prevention and/or amelioration of type 2 diabetes mellitus by the same biological mechanism as the thiazolidinedione derivatives \textsuperscript{[45]} Moreover, study done by P K Rai et al reveals the antidiabetic, hypolipidemic and hepatoprotective effects of C. longa freeze dried rhizome powder dissolved in milk which could be used as an effective and safe antidiabetic dietary supplement of high potential.\textsuperscript{[46]}

In male Sprague Dawley rats with Type 2 DM induced by a high fat diet were treated with curcumin and their glucose lowering effect was studied, it exhibited hypoglycemic activity and improved insulin sensitivity.\textsuperscript{[47]} Besides this study, the effect of curcumin on pancreatic cells has been extensively studied by K. Meghana et al. and they revealed that curcumin increased islet viability and delayed islet ROS production in STZ-induced islet damage.\textsuperscript{[48]}

In addition to ameliorating diabetes, curcumin have been shown to reduce diabetes complications including ophthalmologic, nephrologic and cardiovascular complications. In rats with streptozotocin [STZ] -induced diabetes, turmeric and curcumin delayed cataract maturation\textsuperscript{[49]} and reduced renal lesions.\textsuperscript{[50]} In atherosclerotic rabbits fed a high fat diet, curcumin reduced plasma lipid peroxides, increased antioxidant α-tocopherol and coenzyme Q levels, and reversed atherosclerotic damage to the thoracic and abdominal aorta.\textsuperscript{[51]} Sajithal et al. concluded that Curcumin decreases advanced glycation end products induced complications in diabetes mellitus.\textsuperscript{[52]}

\textbf{Clinical Studies:} Few clinical trials of turmeric, curcumin or others of its bioactive components have been conducted by various researchers. Wickenberg et al.\textsuperscript{[53]} studied the effects of turmeric on postprandial plasma glucose and insulin in healthy subjects; they found out that the ingestion of 6g C. longa increased postprandial serum insulin levels, while reducing plasma glucose levels. The results indicate that C. longa may have an effect on insulin secretion.
In adults with type 2 diabetes and diabetic nephropathy, short-term turmeric supplementation attenuated proteinuria, TGF-β and IL-8.\textsuperscript{[54]}

In another clinical trial, the effects of NCB-02 (a standardized preparation of curcuminoids), atorvastatin and a placebo on endothelial function and its biomarkers in patients with type 2 diabetes mellitus were evaluated. 72 patients with type 2 diabetes were randomized to receive NCB-02 (two capsules containing curcumin 150 mg twice daily), atorvastatin 10 mg once daily or a placebo for 8 weeks. An endothelial function assessment was performed at baseline and post-treatment. NCB-02 had a favorable effect, comparable to that of atorvastatin, on endothelial dysfunction in association with reductions in inflammatory cytokines and markers of oxidative stress.\textsuperscript{[55]}

In a open clinical trial, Nanda et al. studied Nishamalaki powder in NIDDM patients (n=100) in the age range of 31-70 years with normally blood sugar elevated cases i.e. 100mg or more in FBS. patients were put on the drug Nishamalaki 1 gm twice daily with water for 6 weeks between. The results showed that the drug has got moderately good hypoglycemic effect.\textsuperscript{[56]}

Khati Y. J. et al. studied the effect of Madhumehari Ghanvati in patients of Diabetes mellitus and concluded that Madhumehari Ghanvati possess hypoglycemic effect particularly in Kapha-Pitta Prakriti patients of Diabetes and showed significant improvement in signs and symptoms of DM.\textsuperscript{[57]} Katiyar V.C. et al. observed insignificant decrease in fasting and post prandial blood sugar level with Haridra amalaki choorna and Devadarvyadi Ghana vati in the patients of Mahumeha (Diabetes mellitus).\textsuperscript{[58]}

**Efficacy of Curcuma longa in Prevention of DM**

Modern researches also have shown that Type 2 DM can be effectively prevented if Haridra (Turmeric) and its active principle (extract) Curcumin is regularly given in those having Pre-Diabetes.

A remarkable human clinical study\textsuperscript{[59]} revealed that turmeric extract was 100% successful at preventing prediabetic patients from becoming diabetic over the course of a 9-month intervention. The researchers concluded that a 9-month curcumin intervention in a prediabetic population significantly lowered the number of prediabetic individuals who eventually developed T2DM. In addition, the curcumin treatment appeared to improve overall function
of β-cells, with very minor adverse effects. Therefore, this study demonstrated that the curcumin intervention in a prediabetic population may be beneficial.

CONCLUSION

It can be concluded that Curcuma longa has a lot of potentials as a medicinal usage in Madhumeha (NIDDM). Curcumin, an active constituent of Curcuma longa exhibited various pharmacological activities which are helpful to manage DM. Ancient Acharyas have already mentioned the use of Haridra (Curcuma longa) in management of Madhumeha (NIDDM) thousands year back. Various researches have proved its antidiabetic activity in experimental models as well as in clinical studies which confer a strong scientific base. Moreover, Curcuma longa is proved to be effective in preventing type-2 Diabetes and also in delaying the progression of pathology. Only a few works are attributed to its antidiabetic activity in human study, so, there is a large scope to explore its immense potential in the management of Diabetes mellitus in human studies which are need of the hour.

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