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THE ROLE OF *TRIKATU GUTIKA* IN THE MANAGEMENT OF *MADHUMEHA* WITH SPECIAL REFERENCE TO DIABETES MELLITUS TYPE II: A REVIEW

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ABSTRACT

Diabetes mellitus (*Madhumeha*) is one amongst the refractory disease conditions recognized by *Ayurveda* scholars of ancient India. It is becoming fastest considerable diseases in the world. The Diabetes mellitus is equated with *Madhumeha* due to similarity in etiology, pathology, symptoms and prognosis. In the present study we planned to evaluate the role of *Trikatu Gutika* in the management of *Madhumeha* with special reference to diabetes mellitus type II. Based on the many review articles, *Trikatu Gutika* could have potential active ingredients to treat *Madhumeha* and could provide preliminary data for further investigations which could possibly lead in the development of novel drugs with little or no side effects and transferring it to future generation. Furthermore, such evidence based herbo-mineral medicine which is generated based on their intimate experience accumulated over many generations could be helpful in rescuing disappearing knowledge and invention of new drugs of many diseases.

KEYWORDS: *Trikatu Gutika, Madhumeha*, Diabetes Mellitus.

INTRODUCTION

Diabetes Mellitus (DM) is one of the lifestyle related and non communicable diseases. Diabetes mellitus (DM) is a clinical syndrome characterised by hyperglycaemia due to absolute or relative deficiency of insulin. Several distinct types of Diabetes Mellitus are caused by a complex interaction of genetics and environmental factors. Factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization and increased glucose production. Diabetes Mellitus can be classified into two broad categories: Type I DM and Type II DM. Type I DM is a result of absolute deficiency of insulin while type II DM is a heterogeneous group of disorders characterised by variable insulin resistance, impaired insulin secretion and increased glucose production. Diabetes Mellitus usually presents with symptoms like polyuria, polydypsia and polyphagia.

Prevalence of Diabetes Mellitus (DM) has been significantly raised over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013. Based on this trend, the International Diabetes Federation Projects that 592 million individuals will have diabetes by the year 2035. The countries with the greatest number of individual with diabetes in 2013 are China (98.4 million), India (65.1 million), United States (24.4 million), Brazil (11.9 million), and the Russian Federation (10.9 million). Even though both type I and type II DM are common, the prevalence of type II DM is rising much more rapidly, probably due to increasing obesity, reduced activity levels, etc.

Diabetes Mellitus can be correlated with *Madhumeha* in *Ayurveda*. *Madhumeha* is a condition in which patient passes urine resembling honey in appearance and taste. It has been described under *Vataj Prameha*. *Acharya Sushruta* has mentioned that *Madhumeha* is the consequence of untreated *Prameha*. *Prameha* is a condition in which patient passes excess and turbid urine. It is a *Tridoshaj* condition with dominance of *Kapha*. It affects *Meda, rakta, Shukra, Jala, Mamsa, Vasa, Lasika, Majja, Rasa, Oja* esp. *Meda. Prameha* is caused by day sleeping, sedentary life style, excessive intake of curd, *Gramya, Audak* and *Anupa* M*amsarasa*, milk and milk products, new grains, jaggery and all kinds of *Kapha* aggravating factors. The prodromal features of *Prameha* are excess *Mala* in tooth, palate and tongue, burning sensation of hands and feet, oiliness in the body, excess thirst, sweet sensation in mouth according to *Madhavnidan* while additional features like sweetness in

urine, foul breathe are mentioned in *Sushrutasamhita*. Similarly *Acharya Charak* has mentioned gathering of ants towards the site of urination as one of the prodromal features of *Prameha*. The main clinical features of *Prameha* are excessive micturition and turbid urine. However according to predominance of *Dosha* and the associated *Dushya* there is difference in the colour, smell of urine thus producing 20 types of *Prameha*.

Rationale

Despite the immense investment in drugs and therapeutics for the management of *Madhumeha*, its prevalence is increasing at an alarming rate. *Madhumeha* does not come alone; it brings with itself the various metabolic complications of hyperglycaemia both acute and chronic affecting every organ from head to toe. Once an individual is diagnosed with *Madhumeha* the dosage of medicine is ever increasing and ultimately insulin has to be given for glycaemic control. As *Madhumeha* is often associated with obesity, dyslipidaemia, hypertension, insulin resistance, known as metabolic syndrome, an intervention capable of handling all these associated conditions is necessary.

Ayurveda has a great potential in treating diabetes and its associated complications. Among the wide varieties of drugs mentioned in *Ayurveda* text books *Trikatu Gutika* has been chosen for the study. The contents of this drug are easily available and cheaper. It is easy to use as there is no special measure or precaution that needs to be taken during its administration.

AIMS AND OBJECTIVES

- To evaluate the role of *Trikatu Gutika* in the management of *Madhumeha* with special reference to diabetes mellitus Type II.

MATERIALS AND METHODS

- *Ayurvedic* textbooks were referred to collect the relevant materials.
- The index, non-index medical journals were referred to collect relevant information.

DRUG REVIEW

Even the ancient sages were well aware about the disease '*Madhumeha*' and various descriptions regarding the disease have been mentioned in different classical text books by different *Acharya*. Moreover, the *Acharya* have mentioned several herbs and formulations in the management of *Madhumeha*. They all are potent in its own way in the management of *Madhumeha*. Out of many such drugs, one formulation '*Trikatu Gutika*' has been selected for the study.

This drug has been mentioned in *Pramehapidka* chapter of *Bhavaprakash* (*Uttarardha*).

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Table No. 1: Contents of *Trikatu Gutika.*

S. N.	Name of the drug	Latin Name	Parts Used	Quantity
1.	*Maricha*	*Piper nigrum* L.	Fruit	1 part
2.	*Shunthi*	*Zingiber officinale* Roscoe	Rhizome	1 part
3.	*Pippali*	*Piper longum* L.	Fruit	1 part
4.	*Haritaki*	*Terminalia chebula* Retz.	Fruit	1 part
5.	*Bibhitaki*	*Terminalia bellirica* (Gaertn.) Roxb.	Fruit	1 part
6.	*Amalaki*	*Phyllanthus emblica* L.	Fruit	1 part
7.	*Gokshura*	*Tribulus terrestris* L.	Fruit	As per requirement
8.	*Guggul*	*Commiphora wightii* (Arn.) Bhandari	Resin	6 parts

Table No. 2: *Ayurvedic* Properties, Chemical Composition and Parts Used.

Name of Drug	Chemical Composition	*Rasa*	*Guna*	*Virya*	*Vipaka*	*Doshakarama*	Parts Used
Maricha	Piperine, Piperidine, Piperettine, Chavicine, volatile oil, protein, carbohydrate, calcium, phosphorus, iron, thiamine, riboflavin, nicotinic acid, vitamin A, etc	*Katu*	*Laghu, Tikshna*	*Ushna*	*Katu*	*Kapha shamak*	Fruit
Sunthi	Zingiberene, zingiberol, gingerin, oleoresin, gingerol, shogaol	*Katu*	*Laghu, Snigdha*	*Ushna*	*Madhur*	*Kapha-vata shamaka*	*Kanda*
Pippali	Piperine, piplartine,	*Katu*	*Laghu, Snigdha,*	*Anush-*	*Madhur*	*Kapha-vata*	Fruit

	sesamin, piplasterol, Piperlongumin		*Tikshna*	*nashita*		*shamak*	Root
Haritaki	Chebulagic acid, Chebulinic acid, Corilagin	*Pancha-rasa (*except *Lavana) Kashaya pradhan*	*Laghu, Ruksha*	*Ushna*	*Madhur*	*Tridosha-hara*	Fruit
Bibhitaki	Tannin, B sitosterol, gallic acid, elaigic acid, ethyl gallate, chebulaigic acid, mannitol, glucose, galactose, fructose, raminose, etc	*Kashaya*	*Ruksha, Laghu*	*Ushna*	*Madhur*	*Tridosha-hara* Esp. *Kaphashamak*	Fruit
Amalaki	Galic acid, tannic acid, sugar, albumin, cellulose, vitamin C, elaigic acid, calcium, phosphorus	*Pancha rasa (*except *Lavana) Amla rasa pradhan*	*Guru, Ruksha, Shita*	*Shita*	*Madhur*	*Tridosha-hara* Urinary system: *Pramehaghna*	Fruit
Guggulu	Moisture, volatile oil, resin, gum	*Tikta, Katu*	*Laghu, Ruksha, Tikshna, Vishada, Sukshma, Sara, Sugandh, Snigdha, Picchil*	*Ushna*	*Katu*	*Kapha-Vata shamak*	*Niryas* (resin)
Gokshura	Alkaloid, volatile oil, resin, tannin, glycoside, sterol, nitrate, Harman, Harmine, saponin	*Madhur*	*Guru, Snigdha*	*Shita*	*Madhur*	*Vata- Pitta shamak*	Fruit, root

Probable mode of action of *Trikatu Gutika*

Madhumeha has been mentioned under *Vataj Prameha*. *Vata* is aggravated either due to *dhatu kshaya* or due to *margavarodh*. *Dhatu kshayajanya Madhumeha* can be correlated with type I Diabetes Mellitus while *margavarodhjanya Madhumeha* can be correlated with Type II Diabetes Mellitus.

Due to excessive intake of *kapha vardhak aahaar-vihaar, kapha* gets aggravated. This increases *meda* due to similarity in *guna*. *Kapha prakopa* causes *mandagni* leading to the formation of *ama dosha*. This causes *margaavarodh* which in turn increases *vata*. Aggravated *vata* causes *oja dushti* and *ojo ksharan* ultimately leading to a condition known as *Madhumeha*. It means there is involvement of both *vata* and *kapha* in the pathogenesis of *Madhumeha. Dushya* involved in it are mainly *meda, mamsa, kleda, shukra, shonita, vasa, majja,* etc. are all *kapha vargiya*. Most of the drugs in *Trikatu Gutika* have *vata-kapha shamaka* properties. So the contents of this drug have ability to break the pathogenesis of the disease. Due to *katu, tikta rasa, laghu, ruksha guna, ushna virya* of most of the drugs of *Trikatu Gutika*, the aggravated *kapha* subsides resulting in proper functioning of *agni* and hence preventing *margaavarodhjanya vata prakopa* thereby breaking the pathogenesis of the disease.

Various studies have also been conducted to show the antidiabetic effect of these drugs.

Amalaki

As per the research, aqueous fruit extract of *P. emblica* has a potent antidiabetic activity. It showed a significant fall in blood glucose level of diabetic rats treated with aqueous fruit extract at 200 mg/kg body weight. Maximum decrease in blood glucose level was observed after 1 and 2 hours of treatment. As diabetes was induced by alloxan in experimental rats (Qureshi and Hasnain, 1997), the antidiabetic effect of aqueous fruit extract might be extra-pancreatic either by inhibiting glycogenolysis, hepatic gluconeogenesis and glucose absorption from intestine or by increasing glucose absorption in cells of peripheral tissues (muscles and adipose tissues) and hepatic glycogenesis (Kamanyi et al., 1994). Few Phyllanthus species, were found to involve in regeneration and rejuvenation of ß - cells leading to an increased insulin production and secretion (Daisy et al., 2004).

Haritaki

Oral administration of 75% methanolic extract of *Terminalia chebula* (100 mg/kg body weight) reduced the blood sugar level in normal and alloxan diabetic rats significantly within 4 h. Continued daily administration of the drug produced a sustained effect. The chloroform extract of *T. chebula* seeds (100, 200 and 300 mg/kg body weight) produced dose-dependent reduction in blood glucose of diabetic rats in both short term and long term study (300 mg/kg body weight for 8 weeks). Further, remarkable renoprotective activity was also observed in *T. chebula* treated rats. Oral administration of ethanolic extract of fruits of *T. chebula* (200 mg/kg body weight for 30 days) reduced the levels of blood glucose and glycosylated hemoglobin in streptozotocin (STZ)-induced experimental diabetic rats. In a similar study, aqueous extract of *T. chebula* (200 mg/kg body weight for two months) reduced the elevated blood glucose and increase in glycosylated hemoglobin. The same dose also showed a marked improvement in

controlling the elevated blood lipids as well as decreased serum insulin levels. The in vitro studies with pancreatic islets showed that the insulin release was nearly two times more than that in untreated diabetic animals. The treatment did not have any unfavorable effect on liver and kidney function tests.

Bibhitaki

A study showed that *Terminalia bellirica* fruit extract possessed anti-diabetic and anti-oxidant activity and these activities may be interrelated. Administration of *Terminalia bellirica* extract did not have any significant effect on serum glucose level in alloxan diabetic rats during first five days. However, as compared with untreated control animals treated with *Terminalia bellirica* showed much lowered serum glucose in extract treated animals found to be reduced to 54% ($P<0.001$) when compared with that of control diabetic animals.

Shunthi

Administration of an aqueous extract of raw ginger daily (500 mg/kg, intraperitoneally) for a period of 7 weeks to streptozotocin (STZ)-induced diabetic rats showed significant effect in lowering serum glucose, cholesterol and triacylglycerol levels compared with the control diabetic rats. The ginger treatment also resulted in a significant reduction in urine protein levels. In addition, the ginger-treated diabetic rats sustained their initial weights during the treatment period. Moreover, ginger decreased both water intake and urine output in the STZ-induced diabetic rats. The result indicated that raw ginger possesses hypoglycaemic, hypocholesterolaemic and hypolipidaemic potential. Additionally, raw ginger is effective in reversing the diabetic proteinuria observed in the diabetic rats. Thus, ginger may be of great value in managing the effects of diabetic complications in human subjects.

Pippali

Oral administration of *Piper longum* dried fruits (PLEFet) has shown significant antihyperglycemic, antilipidperoxidative and antioxidant effects in diabetic rats**.** PLEFet also corrected the metabolic alterations observed by the activities of several carbohydrate metabolizing enzymes (hexokinase, glucose-6-phosphatase, glucose-6-phosphate dehydrogenase, fructose 1.6-bisphosphatase and glycogen phosphorylase) in alloxan induced diabetic rats. The antihyperglycemic effect of PLEFet is comparable to that of the standard reference drug, glibenclamide. The study results indicated that PLEFet has potent antihyperglycemic and antilipidperoxidative effects in alloxan induced diabetic rats**.** PLEFet can therefore be used as an alternative remedy for diabetes and oxidative stress associated diabetic complications.

Maricha

Aqueous extract (0.5 ml/day) of *Piper nigrum* seeds was administered orally to alloxan-induced diabetic on male albino wistar rats once a day. After 4 weeks of experiment, blood glucose levels by treatment with the extract-treated group was 129 mg/100 ml compared to the insulin treated (120 mg/100 ml), diabetic control (270 mg/100 ml) and normal control (102 mg/100 ml) groups. The study suggested potential hypoglycaemic effect of aqueous extract of *P. nigrum* seeds via antioxidant property.

Four alkamides piperidine, pipernonaline, piperrolein B and dehydropipernonaline, isolated from chloroform extract of P. nigrum fruits inhibited acyl CoA diacylglycerol acyltransferase (DGAT) in vitro. Inhibition of DGAT is associated with improved insulin sensitivity in vivo.

Guggulu

As per a study the administration of *Commiphora mukul* ethalonic extract 200 mg/kg/day daily for 60 days in high-fructose induced diabetic rats reversed the parameter significantly designed for study.

Increase in plasma glucose, total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), hepatic LPO and PO levels with decrease in plasma high density lipoprotein cholesterol (HDL-C), insulin, hepatic reduced glutathione (GSH) content and activities of antioxidant enzymes namely, glutathione peroxidase (GPX), glutathione reductase (GR), glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT) were the salient features observed in diabetic rats. On the other hand, oral administration of CMEEt at a dose of 200 mg/kg for 60 days resulted in the prevention of above mentioned abnormalities. The results suggested that CMEEt could be beneficial in the treatment of diabetes, characterized by atherogenous lipoprotein profile, aggravated antioxidant status and impaired glucose metabolism and in their prevention.

Gokshura

A study suggested that Harmine present in *gokshura* decreases the blood glucose level and thus is useful in the treatment of diabetes mellitus.

CONCLUSION

Currently diabetes is a burning problem as its incidence and prevalence is skyrocketing. A potent medicine for its cure is today's requirement. *Trikatu Gutika* mentioned in *Bhavaprakash* could play this role. It is composed of *Haritaki, Bibhitaki, Amalaki, Maricha, Sunthi, Pippali, Guggulu* and *Gokshura*. All these contents have properties through which it can break the pathogenesis of *Madhumeha*. Further, various researches have already been conducted in favour of their anti-diabetic properties. So we can use this medicine for the treatment of *Madhumeha*. However, more clinical researches should be carried out to establish the antidiabetic action of *Trikatu Gutika* as a whole as well as its mode of action.

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