HYPOGLYCEMIC AND HYPOLIPIDEMIC EFFECT OF THE SIDDHA MEDICAL PREPARATION 'MATHUMEHA CHOORANAM' IN PATIENTS WITH TYPE II DIABETES MELLITUS

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Abstract:

Diabetes is a chronic disorder in metabolism of carbohydrates, proteins, and fat due to absolute or relative deficiency of insulin secretion with / without varying degree of insulin resistance. It is a disease where the body produces little insulin/ ceases to produce insulin, or becomes progressively resistance to its action. During the last twenty years, the prevalence of diabetes has increased dramatically in many parts of the world and the disease is now a worldwide public health problems. In the Siddha system of Medicine there are several chooranams are used to cure the *Mathumeham* (Diabetes mellitus). Amoung the chooranams,the Different verities of *Mathumeha chooranam* are used in Siddha system. *Mathumeha chooranam* contains *Terminalia chebula, Phyllanthus embelica, Murrya keonigii ,and Gymnema sylvestrae.* This *chooranam* is widely used in Siddha Hospitals and Dispensaries of North and Eastern Provinces of Srilanka. The objective of this study was to determine the hypoglycemic and antioxidant activity of the Siddha Medical preparation of *MMC* in patients with type II diabetes mellitus. 63 subjects of age range between 40 - 70 years with fasting plasma glucose (FPG) between 140-300mg/dl were included in the study. Fasting plasma glucose, glycosylated hemoglobin, lipid profile, renal and liver function test were estimated at baseline and at the end of twelfth week. A paired t-test was used to assess the statistical significance between baseline and final measurements. Paired t-test revealed that the fasting ($p<0.001$) and HbA1c ($p<0.001$) significantly reduced after *MMC* administration. Renal and liver function test were well within the normal range. The results suggest MMC to be beneficial for the treatment of type II diabetes.

KEYWORDS: Diabetes mellitus, Cholesterol, *Mathumeha chooranam*,[*M M C*] ,

Introduction

Oxidative stress has significant effect in the causation of diabetes as well as diabetic related complains in human beings (Wilson, RL.1998). Antioxidants are vital substances which possess the

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ability to protect the body from damages caused by free radical induced oxidative stress. Free radicals are fundamental to any biochemical process and represent an essential part of aerobic life and metabolism (Twani,A. 2001). Both exogenous and endogenous antioxidants (whether synthetic or natural) can be effective in the prevention of the free radical formation by scavenging or promoting the decomposition and suppression of such disorders. (Maxwell,SRI. 1995) Diabetes mellitus is characterized by Hyperglycemia, Hypercholesterolemia, and Hypertriglyceridemia resulting from defects in insulin secretion or reduced sensitivity of the tissue to insulin (insulin resistance) and / or combination of both (M. Shra Akansha et al 2009). It is a serious endocrine syndrome with poor metabolic control and responsible for increased risk of cardio vascular diseases including atherosclerosis, renal failure, blindness or diabetic cataract worldwide (Prasad et al 2009, Shas Shweta et al 2006). Recent overwhelming attention to plant products and alternative medicine has encouraged plant chemist, pharmacologist, biochemist and molecular biologist to combine their efforts in a search for natural agents that can limit diabetes mellitus and its complications. (Hosseinzadeh et al 2005) Management of diabetes without dyslipidemia and side effects is still a challenge to the medical community for thousands of year's plants and their derivatives are being used for treatment of diabetes mellitus. Although herbal medicines have long been used effectively in treating diseases throughout the world and frequently considered to be less toxic and free from side effects as compared to synthetic ones (M.Shra Akansha et al 2009, Prasad et al 2009,Kim Jong et al 2006.) Sri Lanka having a rich heritage of traditional medicine constituting with its different components like Ayurvedha, Siddha and Unani. The development of these traditional systems of medicines with the perspectives of safety, efficacy and quality will help not only to preserve the traditional heritage but also to rationalize the use of natural products in the health care (Subbarayappa, 1997)

2.1 Materials and Method

All chemicals and reagents used were of Analytical grade and purchased from Hemsons International (Pte) Ltd. Hemas Bulding, 36, Sir Razik Fareed Mw, Colombo 01. The plasma glucose, glycosylated hemoglobin (HbA1C), Serum lipid profile, serum creatinine, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), Alkaline phosphatase, standard kits were purchased from P & T Trading (Pvt)Ltd. No.30/1, Thimbirigasyaya Place, Colombo - 05.

2.2 Plant material

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Leaves of *Gymnema sylvesrae* , leaves *Murrya keonigii*, Seeds of the *Terminalia chebula* and Fruit of *Phyllanthus emblica* were collected from Karaveddy and Meesalai of Jaffna peninsula.

2.3 Preparation of Mathumeha Chooranam

Leaves of *Gymnema sylvestre*, leaves *Murrya keonigii*,skin of the seeds of the *Terminalia chebula* and fruits of *Phyllanthus emblica* were cleaned, washed and dried under shade at room temperature for 10 days. The individual parts were powered by a multi fine grinder and kept in airtight containers. *Mathumeha chooranam* was prepared from the above powders in 0.5:1:1:1 ratio respectively. This *choornam* was repeatedly prepared every three months.

2.4 Inclusion criteria

Subjects suffering from Diabetes mellitus type II Adult patients either gender of 40-70 Yrs, Among the selected patients 63 patients were selected whose blood glucose level above 140 mg/dl (FBG Test) were included in the study

2.4 Exclusion criteria

The Subjects who had more suffering from other illness such as GIT, Hepatic, Renal, Endocrine disorders, Those who took allopathic drugs and those including the complication of the Diabetes mellitus, Insulin dependent diabetes mellitus, Those unwilling to come for regular follow - up for the entire duration of the study and any subjects considered not eligible according to the researcher's discretion. Women who are pregnant, lactating and having childbearing potential were excluded from the study.

2.5 Research ethics

The study design was approved by the Ethical Review Committee, Faculty of Medicine, University of Jaffna and It was registered in Sri Lanka Clinical Trials Registry (Registration No: SLCTR/ 2015/ 008) on 8th April 2015.All patients were informed about the aim of the study and were included in the study after written consent.

The clinical trial was conducted at the Rural Free Ayurvedic Hospital/ Karaveddy, and Free Ayurvedic Dispensary/ Point Pedro, Free Ayurvedic Dispensary, Manthihai, Free Ayurvedic Dispensary, Alvai, Free Ayurvedic Dispensary, Udupiddy, under the Vadamaradchy South East Piradesa Sabbah. Prior to the clinical trial, a written permission was obtained from the Provincial commissioner, Provincial Dept. of Indigenous Medicine, Northern Province.

2.6 Data collection

The researcher did it after verifying the identity and eligibility of the diabetic subjects. Researcher Before taking Measurements subjects were explained well about the study. Totally 63 subjects of age range between 40-70 years with fasting blood glucose above 140 mg /dl were included in this study. At the enrollment, each subject was requested to complete the Self-administered Questionnaire to

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collect the data. A full medical history, , details of their food habits and life style of each subjects, were collected by the researcher. After that, Fasting blood sample was collected, after an overnight fast of at least 10 hours. From each subject 7 ml of blood was collected from the anticubital vein at selected Ayurvedic Hospitals under the Vadamaradchy South East Piradesa Sabbah. The blood specimens were transported to Dept of Biochemistry, Faculty of Medicine, University of Jaffna, used appropriate cold storage precautions. The samples were used to analyzed the plasma glucose, glycosylated hemoglobin (HbA1C), Serum lipid profile, serum creatinine, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), Alkaline phosphates, were done using the standard kits.The maximum prescribed dose is 2.5g twice a day to be taken with hot water before meals. The dose will be titrated according to the blood glucose level (if blood glucose <200mg/dl, 5g of the product to be taken once daily and if blood glucose is >200mg/dl, 2.5g of the product to be taken once daily). Total duration of treatment is 3 months. And end point evaluation will be made at baseline at $10^{th,}$ 20^{th} 30^{th}, 40^{th}, 50^{th} 60^{th} days and 90^{th} day of intervention and then follow - up measures after completion of prescribed dosage of first and 3^{rd} month. Blinding not done as the biochemical values of baseline (or initial) values compared with different points of time as bellow all subjects were followed at every 10 days, 60^{th} and 90th day for analyzing blood glucose level. At the end of 12 weeks along with blood glucose, HbA1C, Lipid profile, renal, and liver function test were performed during each visit, body weight, blood pressure, Cardio vascular and respiratory system were examined during each visit.

2.7 STATISTICAL ANALYSIS

All data were analyze using the SPSS 16.0 (Chicago, 1L, USA) and presented as means and standard deviation. The significance of the difference between the baseline and after 12 weeks of administering '*MMC*' was tested using the paired't' test. A probability value of < 0.05 was considered statistically significant

RESULTS AND DISCUSSION

There were 63 subjects of whom 38 (60%) were males and 25 (40%) females. The mean (± SD) age was 54.7(±8.5) years. The mean Body Mass Index at baseline is 26.31(±3.6) kg, after 12 weeks there was25.97 (±3.7).and p value is 0.000.

Table 1: Blood glucose concentration before and after *MMC* intervention

	Initial visit	After 12 weeks	P value
FBG	184.4±51.8	114.5±9.8	< 0.000
HbA1C	7.2 ±1.0	5.7±0.64	< 0.000

FBG; Fasting blood glucose; HbA1C; glycosylated hemoglobin; MMC; *Mathumeha Chooranam*

Table 2: Lipid profile in the study participants

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	Initial visit	After 12 weeks	P value
Cholesterol (mg/dl)	196.4±38.9	169.0±39.2	0.000
TG(mg/dl)	133.9±50.4	119.1±47.9	0.000
HDL (mg/dl)	46.7±9.2	40.2±9.2	0.000
LDL(mg/dl)	137.5±46.7	117.4±42.7	0.000
Chol/HDL ratio	4.4±0.9	4.2±1.1	0.220

TGL; Triglyceride HDL; High-density lipoprotein; LDL; Low-density lipoprotein; Chol/HDL Cholesterol to HDL Cholesterol

Table 3: Liver and renal function parameters in the study participants

	Initial visit	After 12 weeks	P value
SGOT (U/L)	26.4±14.3	22.7±13.6	0.000
SGPT(U/L)	24.9±114.4	22.4±15.3	0.000
Alkaline Phosphate(U/L)	75.6±23.0	65.6±20.5	0.000
Serum Creatinine (mg/dl)	0.83±0.16	0.80±0.18	0.351

SGOT; serum glutamic oxaloacetictransaminace; SGPT; serum glutamic pyruvic transaminace

Paired t- test revealed that the Fasting blood glucose and HbA1C levels (Table1), Cholesterol TGL LDL and HDL were significantly lowered after administration of 'MMC'compared to the baseline values (Table:2).

Analysis of variables related to liver function tests in the study participants between baseline and after administration of 'MMC' showed significant reduction in SGOT, SGPT, Alkaline phosphate function was (Table:3).
And renal function tests in the study participants between baseline and after administration of 'MMC' showed No statically significant difference was observed between baseline, follow-up serum creatinine levels (Table: 3) values were still well within the normal range(Table; 3).

Discussion

In the present study, there was were significant decreased in the blood glucose level when diabetes mellitus type II subjects were treated with '*MMC* ' (Table 1). From the proceeding results it can be concluded that the *MMC*' possesses the best hypoglycemic and hypolipidemic actions along with

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improved renal and hepatic functions. Therefore, it may have beneficial effects in type II diabetes mellitus and the hope of new generation oral hypoglycemic drugs. A number of poliherbal formulations are available in Govt Ayurvedha Siddha and Unani Hospitals and Dispensaryin Sri Lanka for the treatment of diabetes like Mathmeharani , Lippa kathalyathi decoction, Aavarai panchangam..... Reduction of the FBG and HbAIc is expected, because the individual herbs are known to have hypoglycemic action,Incorporation of *Murrya keonigii*, leves(10%w/v) in the diet of normal rats for 60 days resulted in hypoglycemia associated with increased hepatic glycogencontents due to increased glycogenesis and decreased glycogenolysis and gluconeogenesis (Khan et al., 1995). Liubo2009 reported that *Gymnema sylvesrae* posses Insulinotrophic activity of Human islets of langerhans. Shanmugasundram et al 1990 reported that *Gymnema sylvesrae* has regeneration of the islets of langehans in streptozotocin diabetic rats. Terminalia chebula contains maltase inhibitory principles and exhibited significant antidiabetic and renoprotective effects (Gaoet al., 2008), (Anam et al 2009). Analysis of ∞ glucosidase inhibitory activity in vitro revealed that the *Terminalia chebula* acts as a potential ∞ glucosidase inhibitor and exhibit antidiabetic prpperties(Rao et al 2006).In streptozotocin-induced type II diabetes rats, the dose of 300mg/ kg of aqueous *Embelica officinalis* seed extract produced a maximum fall of blood glucose.(Mehta et al 2009). *MMC* also demonstrated a significant reduction in the lipid profile of the study participants. Reduction of the lipid profile is expected. Because the individual herbs are known to have hypolipidemic action, several biological activities of *M. keonigii* have been reported for its anti- hypercholesterolemic (Khan et al., 1996a,) and reported anti diabetic activity and some physiological parameters like weight loss and cholesterol lowering effects at prolonged administration of fruit juice of. *M keonigii* (Tembhurne and Sakarkar2009a, b) Yokozawa et al (2007) reported that it prevents dyslipidaemia and oxidative stress in the ageing process. Analysis of variables related to liver function tests in the study participants between baseline and after administration of '*MMC*' showed significant reduction in SGOT, SGPT, Alkaline phosphate function (Table:3) Hepatotoxicity is another risk factor associated to oral hypoglycemic on long term use. This risk factor was minimized by use of MMC. It exhibited better results for SGPT, SGOT levels (Table3)

.And renal function tests in the study participants between baseline and after administration of '*MMC*' showe. No statically significant difference was observed between baselines, follow-up serum creatinine level. (Table÷ 3) Values were still well within the normal range (Table; 3). It has been reported that *T. chebula* has antioxidant status in the liver and kidney of young and aged rats (Mahes *et al.*, 2009).

CONCLUSION

MMC significantly reduced the fasting blood glucose and HbA1C. MMC also demonstrated a significant reduction in the lipid profile of the study participants. A significant reduction in SGOT, SGPT, and alkaline phosphates were observed. Renal function was well within the normal range, demonstrating the safe use of MMC as anti diabetic medication. Further follow-up studies with larger samples are warranted to confirm the safety aspects of MMC.

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