

Consumption of Mixed Spices and Herbs and General Well-Being Observed in Case Controlled Type 2 Diabetes Mellitus (T2DM)

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Abstract. Herbs and spices are believed to possess hypoglycemic effects in Type 2 Diabetes Mellitus (T2DM) patients. Twenty patients were recruited from the Medical Outpatient Department of Hospital Tengku Ampuan Afzan (HTAA) Kuantan Pahang, Malaysia. Informed consent was obtained and the study protocol was approved by the International Islamic University Malaysia Research Ethical Committee (IREC) & Clinical Research Committee (CRC) Ministry of Health Malaysia. Ten patients were provided with placebo while the other 10 patients received 4 gram of mixed herbs and spices. The total duration of the trial was 30 days. Blood samples were collected before and at the end of the - placebo and mixed herbs & spices feeding period. These were analyzed for parameters namely fasting glucose, glycosylated haemoglobin (HbA1c) and lipid (profile) concentrations. The result shows that there was significant reduction ($p < 0.05$) in the fasting blood glucose and HbA1c. There were no changes in the blood lipid profile. The present study indicates that the mixed herbs & spices tested in this clinical trial have some efficacy for hyperglycemia control and general well-being, as during the feeding period, the patients felt more energetic.

Keywords: Herbs, Spices, Diabetes Mellitus, HbA1c, Lipid Profile.

1. Introduction

Diabetes mellitus (DM) is the most severe metabolic pandemic of the 21st century, affecting essential biochemical activities in almost every cell in the body and increasing the risk of cardiovascular problems. It was estimated that in the year 2000, 171 million people had diabetes, and this is expected to double by the year 2030 [1]. Changes in human behaviour and lifestyle over the last century have resulted in a dramatic increase in the incidence of DM worldwide. The epidemic is mainly of T2DM and its associated conditions known as 'diabetes' and 'metabolic syndrome' [2], [3]. Conventionally, insulin-dependant diabetes mellitus is treated with exogenous insulin [4] and non insulin-dependant diabetes mellitus with synthetic oral hypoglycemic agents like sulphonylureas and biguanides [5]. The preventive activity of medications against the progressive nature of diabetes and its complications was the modest but not always effective. Insulin therapy affords glycemic control in type 1 diabetes, yet its shortcomings such as; ineffectiveness on oral administration, short shelf life, the requirement of constant refrigeration, fatal hypoglycemia in event of excess dosage, reluctance of patients to take insulin injection and above all the resistance due to prolonged administration, limits its usage [6]. Similarly, treatment of type 2 diabetes patients with sulphonylureas and

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biguanides is always associated with side effects [7]. For various reasons in recent years, the popularity of alternative medicine has increased. Surveys conducted in Australia and United States indicate that almost 48.5% and 34% of the respondents respectively had used at least one form of unconventional therapy, including herbal medicine [8]. Natural materials like herbs and spices today seem to be used widely as traditional remedies for certain diseases. Spices which are added during preparation of foods for taste and aroma have been shown to be effective in the control of hyperglycemia both in animals and human studies. Khan, et al. (1990) [9] reported that these spices have insulin potentiating factor and enhanced chromium contents. According to some published research, a few herbs and spices are effective in improving blood glucose control in T2DM patients. For instance, the consumption of cinnamon to improve glucose and lipids of patients with T2DM was investigated. The results show that daily intake of cinnamon reduces serum glucose, triglyceride, LDL cholesterol, and total cholesterol in subjects with T2DM [10]. Therefore, it was suggested that the inclusion of cinnamon in the diet of patients with T2DM will reduce risk factors associated with DM and cardiovascular diseases [10]. There are several studies conducted throughout the world, recognizing the facts e.g. coriander has been used for many years to lower blood glucose in traditional herbal medicine. It has been reported that streptozocin induced diabetic mice were fed with coriander in feed or drinking water caused a significant reduction in blood glucose [11]. Bunching Onion is a flavour and taste enhancer and contains many health promoting compounds that can lower Low Density Lipoprotein cholesterol (LDL-C) and raise high density lipoprotein cholesterol (HDL-C) level, prevent cancer, and stabilize blood sugar levels [12]. Curry Leaves is an inhibitor of pancreatic enzyme alpha-amylase. This enzyme degrades starch to glucose, which is then released to the blood stream. So by reducing the availability of the pancreatic alpha-amylase enzyme, the leaves are able to inhibit the degradation of starches to sugar which can help to treat DM effectively [13]. According to Hassan (2007), Holy Basil contains an essential oil that possess antibacterial, antioxidant, anti-inflammatory, immune stimulating effects, and blood sugar lowering properties in diabetic patients [12]. Heimes, et al. (2009) [14] investigated the effects of ginger extracts known to interact with serotonin receptors, which inhibit insulin release. The authors found that this condition can be reversed by two different ginger extracts, spissum and an oily extract. After treatment, the researchers found that blood glucose was decreased by approximately 35 percent, and plasma insulin level was increased by approximately 10 percent. The authors concluded that serotonin receptor systems are involved in modulating insulin release and that various ginger extracts can be used to improve diabetic symptoms. Similarly two studies [15], [16] conducted to determine the hypoglycemic properties of lemongrass (*Cymbopogon proximus*) in alloxan induced diabetic rats. Both studies showed that lemongrass restore glucose levels to normal in four weeks of treatment in rats. Onion (*Allium cepa*) is a common vegetable. Onion bulb and leaves are part of diet. Ether soluble fraction of onion (0.25mg/kg, orally) has been observed to lower blood sugar level in normal rabbits and exhibited potent antioxidant activity [17]. In a clinical study, treatment of diabetic patients by juice of *Allium cepa* bulb, controlled the blood sugar level [18]. Dipropyl-disulphi-deoxide and onion oil produced significant hypoglycemic effect [19]. A sulphur containing amino acid, S-methyl-cystein-sulphoxide (at a dose of 200mg/kg for 45 days) from onion showed potent hypoglycemic activity in alloxan induced diabetic rats [20]. S-allyl-cystein-sulphoxide from onion significantly reduced blood glucose level of alloxan induced diabetic rats [21]. Prolonged administration of freeze dried onion powder (3%) with a diet produced anti-hyperglycemic, hypolipidaemic and antioxidant activity in STZ-diabetic rats [22]. *Allium cepa* juice (0.4g/100g between 4 weeks) exhibited anti-hyperglycemic and antioxidant effect in alloxan induced diabetic rats, it also repaired hepatic and renal damage caused by alloxan [23]. The anti-diabetic, hypolipidaemic and antioxidant activities of aniseeds (star anise) and coriander seeds were compared in T2DM patients. The seed powders (5 g/day) were administered to two groups of T2DM patients for 60 days. The results indicated 36% decrease in fasting blood glucose in aniseed treated, and 13% decrease in coriander treated T2DM patients, while 11% rise of fasting blood glucose in the control group. Significant decrease in serum cholesterol and triglycerides in aniseed treated and coriander seed treated patients was also observed. Both seeds have anti diabetic, hypolipidaemic and antioxidant effects in diabetic patients [24].

Like other tropical countries, Malaysia has also its own treasure of nature including herbs and spices. The most commonly used herbs and spices by all the communities in Malaysia, in the preparation of their own

specific cuisines, were selected to be processed and fed to the patients with established T2DM and having their regular follow-up at Medical Outpatient Department (M-OPD) at Hospital Tengku Ampuan Afzan (HTAA) Kuantan, Malaysia.

2. Material and Methods

This study was conducted at Medical Department, HTAA, Kuantan, and Department of Nutrition Sciences, Kulliyah of Allied Health Sciences, International Islamic University Malaysia (IIUM), Kuantan. In the present study, 20 established T2DM patients were recruited from the M-OPD, HTAA, Kuantan. These patients were either fed with placebo (maize starch) or four gram/d mixed spices & herbs (on dry weight basis). The patients having established T2DM, adult, both sexes were included in the study and patients having T1DM, allergy or intolerant to herbs/spices, consuming other herbal supplements, pregnant women with/without gestational diabetes mellitus (GDM) and or having any other disease were excluded from the study. Informed consent was obtained prior to the commencement of the clinical/experimental trial from each patient. This study was submitted to the Kulliyah Postgraduate and Research Committee (KPGRC) for approval and subsequently to the IIUM Research Ethics Committee (IREC) and Clinical Research Committee (CRC). The four types of spices namely, ginger (*Zingiber officinale*), onion (*Allium cepa*), cloves (*Syzygium aromaticum*) & lemongrass (*Cymbopogon citratus*) and the four types of herbs namely coriander leaves (*Coriandrum sativum*), bunching onion (*Allium fistulosum* L.), curry leaves or Bay Leaves (*Murraya koenigii*), and holy basil leaves (*Ocimum tenuiflorum*, also known as *Ocimum sanctum*). The spices and herbs were purchased from the local market/supplier, and thoroughly cleaned. These were then weighed and freeze-dried, weighed again and the weight loss was determined. After having weighed, the spices and herbs were ground with coffee mill and appropriate amounts were encapsulated in the capsules to be offered to the patients. The dry powder of mixed spices and herbs were equal to the wet weight of 4 gram/day of spices and herbs which were offered to the subjects. The spices and herbs contributed 12.5% in the mixture to be fed to the patients. The consumption of the capsules was spread over the day and the numbers of capsules to be consumed per day were tailored to four gram of spices and herbs. The spices and herbs tested in this clinical trial are not new to consumers; however, the only thing which was new is the dose which was investigated. Among the 20 patients, 10 patients were allocated to the placebo group and the other 10 were allocated the afore mentioned dose of the mixture of mixed spices and herbs. The total duration of the trial was 30 days.

2.1. Data Collection

The data were collected based on personal information and biochemical or blood analysis as described in the following sections; all data pertaining to the patient were compiled from the patient's file and were recorded in the proforma for the use of this clinical trial. All the patients were requested to provide the blood samples on Day 0, and Day 31, for the analysis of various parameters, to assess any possible changes induced by the consumption of mixed spices and herbs.

2.2. Blood Sample Analysis

The blood sample collected was immediately processed in HTAA for appropriate analysis and storage. Then, blood was analyzed for HbA_{1c} concentration using the "Bio-Rad D-10 Hemoglobin-A_{1c} Program". This program was intended for the percent determination of hemoglobin-A_{1c} in human whole blood using ion-exchange high-performance liquid chromatography (HPLC). For lipid profile, "Beckman Coulter AU analyzer" was used with the "required lipid reagent" using appropriate kits for the listed parameters.

2.3. Statistical Analysis

The current study design was Quasi-experimental study design on registered T2DM patients. Two-way ANOVA was used for statistical analysis. Furthermore, the data was expressed as mean \pm SD and the difference in the means was ascertained at 95 % confidence interval ($P < 0.05$).

3. Results and Discussion

3.1. General Well-Being of the Patients

As stated before, in this study, 20 subjects with established T2DM were recruited and no subject withdrawn from this study. The mean age of the subjects was 52.7 ± 19.7 years. This study was started immediately after the holy month of Ramadan and that is the period whereby Muslims generally celebrate Eid and this duration is longer in Malaysia compared to other Muslims countries in the world. During these days there are open houses arranged by the Muslims families and these open houses offer variety of delicacies based on high carbohydrates and higher fats contents. According to the patients the effect was prominent on their general well-being. However, this effect was not quantified on scale(s). The patients in the follow up showed encouraging signs of controlling their hyperglycemia and took the advantage to enjoy the open houses. In most cases the response was that they felt more energetic with the consumption of the herbs and spices. This finding is of clinical importance and would be re-evaluated on the hedonic scale.

3.2. Effect on Blood Glucose and Lipid Profile

The blood glucose status was assessed by FBS, 2HPP and HbA1c as indicated in the Fig. 1. The herbs and spices consumption caused significant ($P < 0.05$) reduction in FBS and HbA1c concentrations in the test group as compared to the placebo. When the reduction was calculated on the basis of percent reduction, it appears to be 16.58, 20.32 and 14.28 % for FBS, 2HPP and HbA1c respectively. As mentioned before, the effect was also evaluated on the lipid profile i.e. total cholesterol, triglyceride, high density lipoprotein-cholesterol, and low density lipoprotein-cholesterol. In general, mean blood lipid parameters showed positive changes (improvement) as compared to the placebo group, but the effect was not statistically significant as indicated in the Fig. 2. The mean TC and LDL of the test group showed reducing pattern and reduction in total was 10.08 and 6.83 % respectively whereas there was increasing trend in the HDL-c concentration of 10.92. Similarly, when the mean TG of the test group compared with placebo it also showed reducing trend from 2.04 ± 1.06 to 1.68 ± 0.65 which is 17.64 % respectively. The ratios of the total cholesterol to HDL-c, HDL-c to LDL-c and TG/HDL-c were improved after feeding the herbs and spices to the diabetic patients as shown in the Table 1.

Table 1. The ratios between the total cholesterol (TC), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), and triglyceride (TG) before and after the intervention.

Lipid Ratios					
TC/HDL-c		HDL-c/LDL-c		TG/HDL-c	
Pre Intervention	Post Intervention	Pre Intervention	Post Intervention	Pre Intervention	Post Intervention
4.17	3.38	0.420	0.557	3.924	2.896

Glucose is the primary factor to be studied in diabetic patients followed by lipid profile and related hormones. The present study results may be of clinical interest to the clinicians and researchers involved in diabetic and cardiovascular diseases related studies. In type 2 diabetes, additional environmental factors, including hormones, increased caloric intake, decreased physical inactivity, and high lipid profile have a marked influence on the disease. As increased levels of FFAs are positively correlated with both insulin resistance and the deterioration of β -cell function in the context of concomitant hyperglycemia. These latter effects may result from oxidative stress. There is evidence that oxidative stress, defined as a persistent imbalance between the production of highly reactive molecular species (chiefly oxygen and nitrogen) and antioxidant defenses, leads to tissue damage and late complications associated with T2DM [25]. Dietary manipulation in the form of mixed herbs and spices in our study not only improved the means FBS, HbA1c but also the TC, LDL-c, HDL-c and TG along with their ratios as noted above (Table 1). Furthermore, the spices and herbs used in this trial are well known for their antioxidant properties, thus having the potential in reducing the macro and micro vascular complications in the long run. The current study was limited to 30 days and the effect may be more significant if the clinical trial is extended to 120 days. Therefore, in future studies the total duration of the trial will be tailored to the life-cycle of red blood cells (RBCs). It is hoped that in future this study will shed some light on the efficacy of the mixed spices and herbs on glycosylated haemoglobin in the entire life cycle of RBCs in the patients.

The observed effects in the present study have been attributed to various components of herbs and spices possesses. It has been proposed that spices have insulin higher amount of chromium which enhance the insulin sensitivity [9]. This effect is particularly observed in case of cinnamon in the human subjects [10]. In traditional herbal medicines, similar effects have been reported eg; the effects of coriander on the lowering of blood glucose both in human and rats [11, 26]. Similarly, bunching onion, a flavour & taste enhancer contains health promoting compounds which lower Low Density Lipoprotein cholesterol (LDL-c) and raise high density lipoprotein cholesterol (HDL-c) concentrations [12]. Some herbs, like curry leaves is an inhibitor of pancreatic enzyme alpha-amylase and lower the starch degradation and help to improve glucose regulation [13]. Some of the herbs like holy basil leaves contains essential oils which are anti-hyperglycemic, antibacterial, antioxidant, anti-inflammatory and immune modulating [12]. Another spicy ingredient ginger has inhibitory effect on the enzymes α -glycosidase & α -amylase that masks the glucose availability [14] and may increase insulin secretion via blocking the serotonin receptors and releasing the inhibitory effect of serotonin on insulin release and therefore having modulating effect on insulin [15]. Similarly, another two studies on the hypoglycemic properties of lemongrass (*Cymbopogon proximus*) in alloxan induced diabetic rats restored glucose concentrations to normal [15,16].

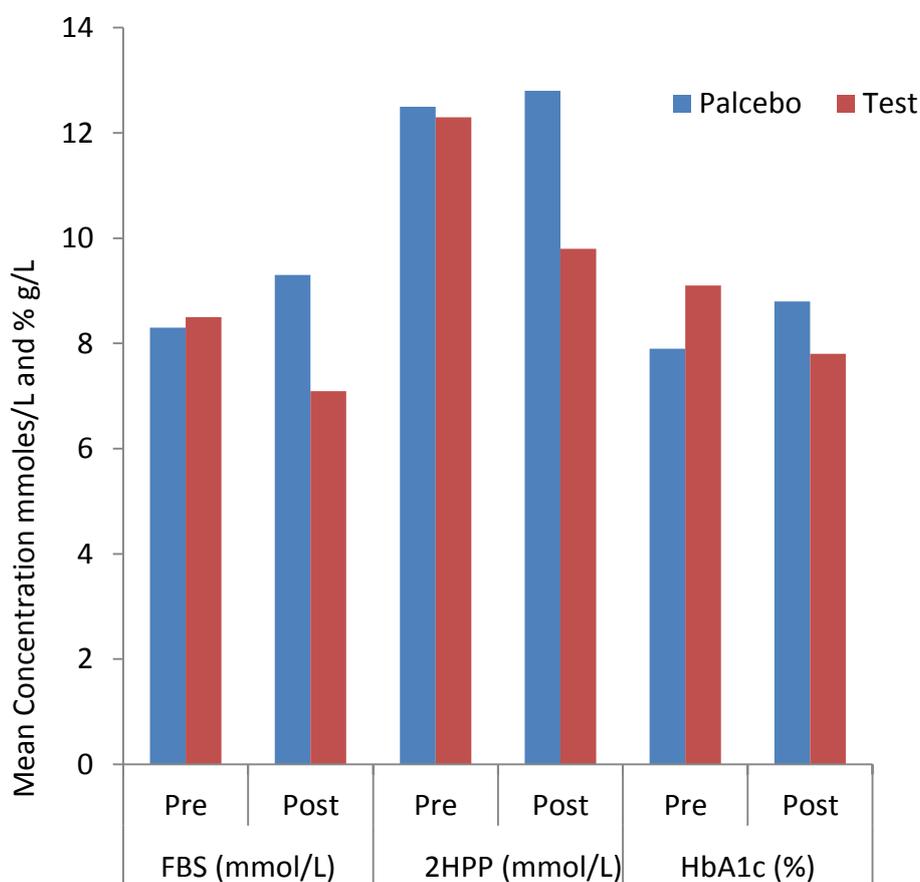


Fig. 1: Comparison of the effect of mixed herbs and spices on the fasting blood glucose, two hours postprandial blood glucose and glycosylated haemoglobin concentrations.

Onion bulb and leaves are the important part of our daily routine diet have been shown to lower blood glucose in normal rabbits [17, 20, 21] and onion have hypolipidaemic effect [18] and this is probably brought through dipropyl disulphide oxide and essential oils in it [26], through S-allyl cystein sulphoxide [22] or through antioxidant activity [23]. Similarly, it also has hypolipidaemic effect and these effects might be through antioxidant activities [23]. The present study indicates that the mixed herbs & spices tested in this clinical trial have some efficacy for the control of hyperglycemia, hyperlipidaemia and during the feeding period, the patients felt more energetic.

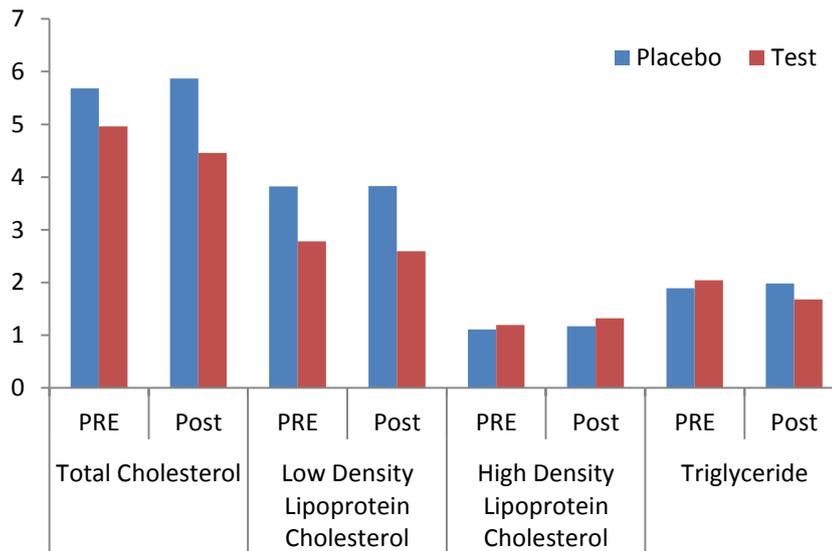


Fig. 2: Comparison of the effect of mixed herbs and spices on the Total Cholesterol, Low Density Lipoprotein Cholesterol (LDL-c), High Density Lipoprotein Cholesterol (LDL-c) and Triglyceride concentrations.

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