

Full Length Research Paper

Efficacy and safety of Ziabites (an Iranian traditional medicine compound) on glycemic control in type 2 diabetic patients

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This study was designed to evaluate the efficacy and safety of Ziabites on glycemic control in type 2 diabetic patients. The samples consisted of 31 subjects and the doses of Ziabites were equally administered orally in the form of capsule before the breakfast, lunch and dinner. The doses were given for 4 weeks. Ziabites capsule contains *Portulaca oleracea* L., *Rhus coriaria* L. and *Punica granatum* L. The efficacy was assessed on the basis of the following parameters: fasting blood glucose (FBG), 2 h postprandial plasma glucose (2hppG), serum fructosamine, triglyceride (TG) and total cholesterol (Tc) levels. Also, side effects were assessed by history and physical and biochemical examinations. All of the assays were performed on the starting day of study and after 4 weeks. After 4 weeks of treatment with Ziabites capsule, there was a significant decrease ($P < 0.05$) in mean FBG and 2hppG levels when compared with its levels on starting day. Data of mean serum fructosamine levels, showed no significant different between the starting day and after 4 weeks. Also, the reductions of mean serum TG and Tc levels after treatment, were not significant ($P > 0.05$). This study indicated that Ziabites capsule is effective in decreasing fasting and postprandial plasma glucose levels among type 2 diabetic patients without any side effects.

Key words: Ziabites, *Portulaca oleracea* L., *Rhus coriaria* L., *Punica granatum* L., diabetes mellitus.

INTRODUCTION

"Diabetes mellitus (DM) is a chronic disorder characterized by the impaired metabolism of glucose and other energy-yielding fuels as well as the late development of vascular and neuropathic complications" (Goldman and

Ausiello, 2008). "The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 285 million in 2010. Based on current trends, the International Diabetes

Federation projects that 438 million individuals will have diabetes by the year 2030" (Longo et al., 2012).

Various studies in herbal medicine or phytotherapy have shown beneficial effects of medicinal plants to treatment of diabetes disease (Naseri et al., 2010; Mirghazanfari et al., 2010; Al Jamal, 2009). Also, study on herbal combinations and polyherbal formulations have been considerable for some researchers (Lu et al., 2012; Viswanathan et al., 2011; Ahmad et al., 2010; Keche et al., 2010; Naseri et al., 2009). Recently, some studies described the perspective of Iranian traditional medicine in prevention and treatment of diseases (Asghari et al., 2012; Emtiyazi et al., 2012; Chooapani et al., 2012; Khodadoost et al., 2011; Shahabi et al., 2008).

Herbal combinations are also important for Iranian traditional medicine physicians to treat diseases. A number of herbal combinations have a long history of traditional use in treating diabetes. One of them that have been long recommended is Ziabites (Avicenna, 1999; Razi, 2000; Jorjani, 2006; Kermani, 2008).

With this background and according to World health Organisation (WHO) traditional medicine guideline that "prolonged and apparently uneventful use of a substance usually offers testimony of its safety" (WHO, 2000), the present study was designed to evaluate the efficacy of Ziabites on glycemic control in type 2 diabetic patients and to know the side effects during the study period.

MATERIALS AND METHODS

This study is a before and after clinical trial that was carried out on type 2 diabetic patients. Thirty-one subjects of both sexes (11 males and 20 females) were recruited from Iranian Traditional Medicine Clinic of Shahed University and Diabetes Clinic of Shahid Mostafa Khomeini Hospital in Tehran during the year 2011. Patients were eligible for enrollment in the study if they met the following inclusion criteria: 1, Age 30 to 70 years; 2, HbA1C >7% (Uncontrolled type 2 diabetes); 3, being treated with oral diabetes medications (one or more pharmaceutical group); 4, absence of any alteration in consumption of anti-diabetic drug, at last month. The main exclusion criteria included the following: 1, glomerular filtration rate (GFR) < 60 ml/min; 2, serum albumin < 4 g/dl; 3, aspartate transaminase (AST) or alanine transaminase (ALT) levels > 40 U/L (more than upper limit of normal). The investigation was performed in accordance to the principles of Helsinki Declarations (WMA, 2002). All patients gave informed consent to a protocol that was approved by medical ethical committee of Shahed University. Also, the clinical trial was registered in Iranian Registry of Clinical Trials with registry number IRCT201108107286N1. A questionnaire for demographic variables and the results from history and physical and biochemical examinations was used for data collection.

Ziabites is an Iranian traditional medicine compound that contains powder of three medicinal plants. This herbal combination was packed in inert gelatin capsules and each capsule contains *Portulaca oleracea* L. seed (300 mg), *Rhus coriaria* L. fruit (100 mg) and *Punica granatum* L. flower (20 mg) (Avicenna, 1999; Razi, 2000; Jorjani, 2006; Kermani, 2008). These capsules were prepared in Shahed University of Traditional Medicinal Pharmacy. Type 2 diabetic patients were allowed to take their routine diet and usual diabetic medicine.

Each patient was asked to take orally one capsule immediately before breakfast, lunch and dinner (3 capsule/day) for 4 weeks. In

this study, no alterations was suggested in other aspects of the subject's medical care, diet, or exercise. Compliance was monitored by weekly contact with the patients and study was conducted for 4 weeks. Efficacy was assessed on the basis of the following parameters: fasting blood glucose (FBG), 2 h postprandial plasma glucose (2hppG), serum fructosamine, triglyceride (TG) and total cholesterol (Tc) levels. Also, side effects were assessed by history and physical examination and the checking of complete blood count (CBC), AST, ALT, blood urea nitrogen (BUN), serum albumine, creatinine, sodium and potassium levels. Measurement of glycated hemoglobin (HbA1C) was only for entering the patients in the study. All other assays were performed on the starting day of study and after 4 weeks.

Biochemical estimations

Blood samples were collected after 8 h overnight fasting in the morning. The glucose levels were measured by the glucose oxidase method on a BT3000 autoanalyzer (Biotecnica instrument, Italy). HbA1C was measured by the immunoturbidometry method on a BT3000 autoanalyzer from whole blood immediately after obtaining the sample.

The fructosamine assay (measuring glycated albumin) that is a short term glycemic indicator and reflects the glycemic status over the prior 2 weeks (Longo et al., 2012; Youssef et al., 2008) was performed by the colorimetric method on a Hitachi 717 autoanalyzer (Roche instrument, Germany and Japan) using Diazyme kit (USA). Serum samples were kept at -70°C temperature and serum fructosamine assay for all patients were performed simultaneously at one day.

TG, Tc, CBC, AST, ALT, BUN, serum albumine, creatinine, sodium and potassium levels were measured by routine methods. For measuring sodium and potassium levels, Roche kit (Germany) was used and all other assays were performed using Diagnostic systems kit (Germany). The blood elements were counted using automatic cell counter KX21E (Sysmex, Japan). Except for serum fructosamine test, which was measured at private center called Gorgan Laboratory, all other assays were performed at the Laboratory of Shahid Mostafa Khomeini Hospital in Tehran. Finally, body mass index (BMI) and GFR were measured according to the following equations:

BMI = weight (kg)/length² (m²) and

GFR = (140-Age) weight (kg)/72 Cr_p(Meq/L).

Statistical analysis

Data are presented as means ± standard deviations (SD) and proportions (%). At the level of significance α = 5% and 80% power, and using pilot study data of 8 patients, the sample size of 31 was calculated by Altman's nomogram. Mean values of fasting blood glucose and HbA1C at starting day of the pilot study and after 4 weeks were used for calculation of sample size. In this study, mean values at starting day and after 4 weeks were compared by using paired Student's t-test, while value of P<0.05 was considered to be statistically significant (using SPSS statistics program, version 11.5).

RESULTS

Demographic characteristics of 31 type 2 diabetic patients are shown in the Table 1. For assessment of efficacy, FBG, 2hppG, serum fructosamine, TG and Tc levels on the starting day and after 4 weeks were measured and

Table 1. Demographic characteristics of type 2 diabetic patients.

Characteristic	No. of patient
Male (%)	35.5
Female (%)	64.5
Age (y)	53 ± 7
Employed (%)	41.9
Unemployed (%)	58.1
BMI	29 ± 5
Duration of diabetes (y)	7 ± 5

Data are means ± SD.

Table 2. Effect of Ziabites capsule on glycemic control and lipid levels.

Test	Starting day	After 4 weeks
n (%)	31 (100)	31 (100)
FBG (mg/dl)	195.8 ± 75.3	174.6 ± 52.6*
2hppG (mg/dl)	262 ± 91.2	236.9 ± 73.3*
Fructosamine (micromol/L)	439 ± 165	450 ± 187
Triglyceride (mg/dl)	166.9 ± 82.6	159.7 ± 73.2
Cholesterol (mg/dl)	182.6 ± 49.8	176.4 ± 40.4

Data are means ± SD or percent. *P ≤ 0.05.

are shown in Table 2. All patients were under treatment with oral anti-diabetic drugs (treated with Glibenclamid: 12.9%, Metformine: 25.7% and both: 61.3%) and 11 patients (35.4%) were under treatment with Atorvastatin tablet (10 mg/day). After 4 weeks of the treatment with Ziabites capsule, there was a significant decrease (P<0.05) in mean FBG and 2hppG levels when compared with its levels on the starting day. The data of mean serum fructosamine levels showed no significant different between the starting day and after 4 weeks. The mean serum TG and Tc levels decreased after treatment as compared to the starting day, but these reductions were not significant (P>0.05). The mean HbA1C levels was 8.5 ± 1.4 (%) on the starting day.

According to the assessment of side effects by history and physical examination and the checking of CBC, AST, ALT, BUN, serum albumine, creatinine, sodium and potassium levels, no side effect was indicated and was not reported hypoglycemia.

DISCUSSION

In the present study, the effects of Ziabites capsule on glycemic control in type 2 diabetic patients were evaluated when administered orally one capsule immediate before breakfast, lunch and dinner (3 capsules/day) for 4 weeks. We observed the lowering effects of Ziabites capsule on mean fasting blood glucose levels (10.8%),

and mean postprandial plasma glucose levels (9.5%) that were significant at (P<0.05) as compared to their mean values at the starting day of study.

The lowering effects of Ziabites capsule on fasting blood glucose and postprandial plasma glucose are confirmed by some studies about components of Ziabites. El-Sayed (2011) investigated the effects of *P. oleracea* L. seeds in treatment of type 2 diabetes mellitus patients. In this study, patients received 10 g/day of *P. oleracea* seed powder in 40 ml of skimmed yogurt subdivided equally into two doses for 8 weeks. The study results showed a significant decrease in serum levels of fasting and postprandial blood glucose, triglyceride and total cholesterol.

Also, Gao et al. (2010) indicated that *P. oleracea* extract would alleviate the blood glucose and lipid rising associated with diabetes, in alloxan-induced diabetic rats. This study showed that oral consumptions of 200 and 400 mg/kg body weight of *P. oleracea* extracts, decreased glucose levels by 36.58 and 46.17%, respectively.

According to the review articles made by Miguel et al. (2010) and Li et al. (2008), is indicated that *P. granatum* flower was already prescribed in Unani and Ayurvedic medicines for the treatment of diabetes.

Also, Li et al. (2005) showed that oral administration of *P. granatum* flower extract markedly lowers plasma glucose levels in diabetic rats and also *in vitro*, PGF extract demonstrated a potent inhibitory effect on α -glucosidase activity.

In addition, Jafri et al. (2000) indicated significantly blood glucose lowering with oral administration of *P. granatum* flower extracts in diabetic rats. Maximum effect of the extract was at 400 mg/kg body weight. Also, Giancarlo et al. (2006) reported that ethyl acetate extract of sumac (*R. coriaria* L.) may be effective in the treatment and prevention of hyperglycemia with an inhibition of glycoside hydrolase: α -amylase.

According to the mentioned studies, antihyperglycemic activity of components of Ziabites capsule was shown. Despite some studies and findings about anti-diabetic drugs that have reported gastrointestinal symptoms, especially flatulence (Lam et al., 1998; Longo et al., 2012), in the present study according to the assessment of side effects by history and physical and laboratory examination, no side effect was observed.

This study was the first research about Ziabites capsule and due to low compliance of patients, there were some limitations. The main limitations include the following: small sample size, short period of follow up, low dose of drug administration and absence of control group.

Conclusively, this study indicated that Ziabites capsule is effective in decreasing of fasting and postprandial plasma glucose levels among type 2 diabetic patients without any side effects. However, controlled clinical trials with correction of limitations are necessary to confirm these effects.

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