Jundishapur Journal Chronic Disease Care
Quarterly Journal of Ahvaz Faculty of Nursing and Midwifery

Evaluation of standardized ginseng extract Panax (G115 ®) effect on fasting blood glucose levels, glycated hemoglobin and lipid profile in patients with diabetes type 2

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Abstract

Introduction: Despite enormous efforts to search for cure, diabetes mellitus still remains as a formidable challenge for public health. This project was designed to evaluate effect of standardized ginseng extract Panaxs (G115®) on fasting blood glucose levels, glycated hemoglobin and lipid profiles in patients with diabetes type 2.
Materials & Methods: In this randomized, double blind placebo controlled clinical trial, 30 patients with type 2 diabetes were contributed. They were divided into two groups (n=15 each), the randomized and placebo groups, the former received300 mg/day G115 and placebo received300 mg/d wheat flour. FBS, Hb_{A1c} and lipid profile were determined at baseline and at the end of study. SPSS version 18.0 (SPSS Inc, Chicago, IL, USA) was used for data analysis. Independent and paired samples T-test was applied for comparison.
Results: Subjects randomized to G115, as compared to the placebo group, had a significant decrease in Hb_{A1c} (t= -2.593,p=0.015)) and FBS levels (t=-2.13,p=0.042). There was no improvement lipid profiles of subjects randomized to G115, compared to controls.
Conclusion: Results of this study suggest that G115 supplementation in subjects with type 2 diabetes may improve glucose control but it has no significantly effect on lipid profiles.
Keywords: Panax ginseng, Fasting blood glucose, Glycated hemoglobin, Lipid profiles

Introduction

Diabetes mellitus is a chronic and progressive disease that can lead to disability and premature mortality and type 2 is non-insulin dependent and high blood sugar in it usually caused by reduce insulin secretion or the body's resistance to this hormone(1).Due to the effects of insulin and oral hypoglycemic agents, increasing interest has created among this group of patients on the use of natural products with anti- diabetic activity (2).Medicinal herbs are rich sources of natural antioxidant and are applied in traditional medicine to control and cure many diseases including diabetes. Glucose-lowering effects of many of medicinal plants in animal models and clinical trials, has been reviewed and approved(3).Many studies have shown that more than 400 plant species are have lowering blood sugar activity and several laboratories are working to isolate the oral hypoglycemic compounds of herbs (4).Herbal impact on the treatment or prevention of certain diseases such as diabetes, are still controversial because its mechanism of action of the compounds present in these plants is not clear (5-6).

Among some species of medicinal plants such as Ginseng plant has been important due to its effect on blood sugar(7-10).To investigate the effects of ginseng on diabetes 3

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Received:5Aug2012 Accepted: 11Jan 2013

issue should be developed: 1) Ginseng root be standardized because different batches have different concentrations of ginsenosoid. 2) Further clinical trials should be performed to confirm the effects of ginseng on both types of diabetes. 3) Mechanisms of each of the active ingredients of ginseng which have therapeutic properties be tested (11).It should also be noted that due to the effect of diabetes on lipid profiles and prone these patients for cardiovascular diseases, effect of this plant on Lipid complications caused by diabetes should also be examined. This necessity of perform this study can be sought in the increasing use of herbal medicines to improve blood glucose and lipid levels. According to the above – mentioned the present study aimed to evaluate effect of standardized ginseng extract Panaxs (G115®) on FBS(Fasting blood sugar) levels, HbA_{1c}(Glycosylated haemoglobin) and lipid profiles in patients with diabetes type 2.

Materials and Methods

This study was designed as a randomized, double-blind, placebo-controlled, and parallel group trial in type 2 diabetes patients. The study population included patients with type 2 diabetes that referred to the endocrinology clinic of Razi Hospital in Ahvaz March to May 2012.

Inclusion criteria including fasting blood glucose greater than or equal to 126 mg/dL, at least 40 years of age, at least two years history of diabetes type 2, consumption of oral hypoglycemic medicine (metformin, glibenclamide) with no history of other diseases (such as cardiovascular diseases-cardiovascular, hepatic, renal and metabolic) and body mass index between 25 to 35 kg/m^2.Exclusion criteria including: allergies to ginseng extract, ketonuria symptoms and the need for insulin injections.

Few clinical trial performed on effect of ginseng on diabetic patients, also not used standardized ginseng extract. To calculate sample size a pilot study was performed on 5 patients. We have observed that the glycosylated hemoglobin before and after 8 weeks intervention was 7.41±0.28 % and 6.81±0.37 %, respectively. Considering the $\alpha = 0.05$ and power of 0.95 % the sample size of 15 patients per each group was calculated. The subjects were randomly divided into two groups, one group received ginseng extract and the other group received placebo (capsules containing 1 gram flour). The code of groups a (extract) and B (placebo) were recorded by the clerk and physicians, researchers and statistical consultants were unaware of this division. Before the intervention, fasting blood glucose, glycosylated hemoglobin, VLDL(Very-low-density lipoprotein), LDL-c(Low-density lipoprotein), HDL-c(High-density lipoprotein), TG(Triglycerides) and TC(Total cholesterol) were measured in patients. Group A were receive standardized ginseng extract (G115) 300 mg daily (100 mg three times a day), 30 minutes before breakfast, lunch and dinner. The placebo group received placebo for the same protocol described above. In order to ensure the intake of capsules, patients received a telephone call at the end of each week. The intervention lasted for 8weeks and then variables were measured again. To reduce the effect of confounding factors, patients were asked not change diet and physical activity during study. To compare diet, three 24 hour food recall for three days (two week days and one weekend)at baseline and also at end of study

was completed by face to face interviews by the researcher. To evaluate the level of physical activity the International Physical Activity Questionnaire (IPAQ) was completed before and after of intervention. Data analysis was conducted by using the Statistical Package for Social Science (SPSS 18). Descriptive analysis was carried out to obtain mean and standard deviation for all continuous data. The data gathered from the 24 hour recall questionnaire, analyzed using the Iranian food processing software. For between-group comparisons, Independent T-test was used to determine differences in mean among the intervention and control groups. For within group comparison, the Paired-t test was applied. The level of significance was set at ($p< 0.05$) for all statistical analyses.

Ethical considerations

This study was conducted after obtaining the confirmation of the Ahvaz Jundishapur Ethics Committee and the informed consent from all subjects participating in the study.

Results

A total of 30 patients, 14 were male and 16 were female There was no significant difference between the groups studied for variables of age, sex and BMI (Table 1-3).Consumption of oral hypoglycemic medications were recorded at baseline, and this was no statistically significant difference between the two groups (Table 1).

According to the results in Table 2 it can be seen that the diet of patients in both groups had no significant difference between baseline and end of study. In other words, a change in diet was not considered as a confounding factor in this study. Physical activity was unchanged in both groups before and after intervention and base on the International Physical Activity Questionnaire were classified in the light level.

Independent t tests showed that glycated hemoglobin, fasting blood glucose and lipid profiles between the two groups before the intervention were not statistically significant difference. After administration of ginseng extract, fasting blood glucose and glycosylated hemoglobin levels significantly decreased in extract group ($p= 0.001$), whereas administration of placebo did not result in a significant reduction in these two variables. However, the levels of lipid profiles before and after treatment showed no significant difference between patients of two groups (Table 3).

Discussion

The findings of this study showed that daily administration of 300 mg of standardized ginseng extract for 8weeks reduces fasting blood glucose and glycosylated hemoglobin significantly ($p=0.001$). Double-blind and clinical studies of ginseng extract in patients with type 2 diabetes was limited. The power potentiality of lowering blood sugar level using ginsenosids and their metabolites was strongly evidenced through in vitro and in vivo studies using animal models. Results extracted from Sotaniemiet al, Tetsutani et al and Vuksanet alstudies on type 2 diabetic patients were consistent with the present study (12-14).Pre-clinical data suggest that ginsenosides improved insulin secretion via increasing ATP(Adenosine triphosphate) production by enhancing the activity of glycolytic enzymes (15). Ginsenosideshave important role in controlling the ATP

dependent potassium channels in the membrane by binding to the sulphonylurea receptor, which leads to insulin secretion.

Table 1: Demographic and characteristics of participant

	Case(G115)	Control(placebo)	Pvalue*
Age(year)	48.1±5.7	46±4.5	0.267
Sex (male/female)	(8/7)	(6/9)	0.464
BMI(Kg/m^2)	29.9±3	30.6±2.8	0.529
Metformin(mg/day)	1500	1500	1
Glibenclamide(mg/day)	10	10	1

* Independent samples T-test

Table 2: Food intake of the subjects before and after the intervention

	Case(G115)	Control(placebo)	P value*
Energy(kcal)			
before intervention	1952±542	2012±486	0.77
after intervention	1891±421	1963±519	0.72
p value**	0.36	0.58	
Carbohydrate(g)			
before intervention	244±42	246±65	0.81
after intervention	239±47	242±57	0.44
p value**	0.27	0.33	
Protein(g)			
before intervention	59±15	60±12	0.63
after intervention	61±18	61±10	0.75
p value**	0.25	0.36	
Fat(g)			
before intervention	71±13	72±14	0.76
after intervention	70±18	71±16	0.65
p value**	0.59	0.70	
Saturated fat(g)			
before intervention	9±4	11±4.5	0.14
after intervention	8.5±2	10±4	0.15
p value**	0.22	0.18	

* Independent samples T-test

** Paired samples T-test

Table 3: Blood glucose , glycosylated hemoglobin and lipid profiles in both groups

	Stages	Case(G115)	Control(placebo)	p value*
HbA1C(%)	before intervention	8.10±0.23	7.9±0.33	0.068
	After intervention	7.56±0.21	7.8±0.32	0.015
	p value**	0.001	0.31	-
FBS(mg/dL)	before intervention	166.13±9.56	160.32±8.55	0.091
	After intervention	150.73±12.88	161±13.51	0.042
	p value**	0.001	0.819	-
TG(mg/dL)	before intervention	163.93±14.43	161.86±12.33	0.677
	After intervention	161.86±15.78	161.06±12.66	0.869
	p value**	0.132	0.614	-
Chol(mg/dL)	before intervention	196.73±23.02	190.73±30.05	0.469
	After intervention	195.53±23.55	188±32.01	0.781
	p value**	0.07	0.163	-
LDL-c(mg/dL)	before intervention	117.06±26.52	111.53±27.29	0.578
	After intervention	115.66±27.85	109.20±24.97	0.509
	p value**	0.07	0.106	-
HDL-c(mg/dL)	before intervention	49.53±11.41	50.66±10.66	0.781
	After intervention	50.33±11.92	51±10.27	0.871
	p value**	0.09	0.503	-

* Independent samples T-test
** Paired samples T-test

This reflects the effect of Ginsenosides in increasing insulin secretion that are very similar to conventional drug therapy (Glibenclamide) (16).This observation is supported by evidence that ginsenosides can inhibit free fattyacid-mediated apoptosis and regulate the activity and expression of pro- and anti-apoptotic factors, such as caspase 9 and Bcl-2 (B-cell lymphoma 2), respectively(17). Preclinical research has demonstrated that ginsenosides may inhibit enzymes such as JNK (c-Jun NH 2 Terminal Kinase) and NFκB (Nuclear Factor kappa B) that are involved in incorrectly phosphorylating the IRS proteins (insulin receptor substrate proteins) (18). In addition, it was reported that ginsenosides regulate down stream effects of insulin action; they can increase the expression and translocation of the glucose transporter, GLUT4(Glucose transporter type 4), to the plasma membrane in order to facilitate glucose uptake (19). In a study by Chang et al, the potential of ginseng to lower glucose levels was demonstrated via reduced expression and activity of the sodium/glucose co-transporter (20). In this study, changes were observed in lipid profiles in order to improve their levels, but these changes were not statistically significant. Lack of significant changes in lipid profiles could

be due to short intervention period or low concentrations of prescribed supplement. Yoo and colleagues examined the effects of 16-week administration of 1 g American ginseng root extracts per day on the lipid profiles of patients with dyslipidemia and reported HDL-C was markedly elevated from the beginning through test period while TG is conversely decreased and TC and LDL-C revealed the tendency to decrease but not significant in degree (21). Effects of ginseng on cholesterol is dose-dependent and is associated with an improvement in the antioxidant efficiency (22). Improvements to lipid profile through ginseng administration have also been associated with activation and increased expression of peroxisome proliferator-activated receptors, transcription factors regulating expression of proteins involved in lipid metabolism and adipocyte differentiation (23). Leeand colleagues investigated the effect of Rg3 ginsenosid on the accumulation of fat in the HepG2(a human liver carcinoma cell line) cells. They suggested that ginsenoside Rg3 reduces hepatic lipid accumulation with inhibition of SREBP-2(sterol regulatory element-binding protein-2) and 3-hydroxy-3-methyl-glutaryl-CoA reductase expression and stimulation of AMPK(5' AMP-activated protein kinase) activity in HepG2 cells and may be beneficial as a food ingredient to lower the risk of cardiovascular disease by regulating dyslipidemia (24).

Conclusion

Based on the findings of this study it can be concluded that administration of 100 mg of standardized extract of Korean red ginseng (G115) before the three main meals (breakfast, lunch and dinner) is effective on blood sugar and glycosylated hemoglobin and can significantly reduce those values .In this study it was observed that administration of the G115 extract, despite the lack of significant changes in lipid profiles, these profiles could orient towards the improvement. With regard to the above-mentioned and non-report specific complications in patients, this extract can be used, alongside other drugs, to control diabetes and its associated complications.

Acknowledgments

The source of data used in this paper was master sciences on nutrition thesis of Reza Malihi; and financial support was provided by Ahvaz Jundishapur University of Medical Sciences (thesis no. B-90/302). This study was registered in Iranian Registry of Clinical Trials (IRCT No. IRCT201103196090N1) of the Ministry of Health and Medical Education.

References

1. World Health Organization: Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. Issue 5: What diagnostic tests should be used to define glycaemic status? Geneva: World Health Org, 2006.

2. Holman RR, Turner RC. Oral agent and insulin in the treatment of NIDDM. In: Pickup J, Williams G, editors . Textbook of diabetes. Oxford: Blackwell 1991. 467 -79.

3. Omar EA, Kam A, Alqahtani A, Li KM, Razmovski V, Nammi S, et al. Herbal medicines and nutraceuticals for diabetic vascular complications: mechanisms of action and bioactive phytochemicals. Curr Pharm Des. 2010; 16: 3776-807 .

4. Rai MK. A review on some antidiabetic plants of India .Ancient Science of Life 1995; 14: 42-54 .
5. Tripathi A, Bhoyar P, Baheti J, Biyani D, Mayuresh M, Yogesh M. Herbal Antidiabetic. International Journal of Research in Phamaceutiucal. 2011; 2(1):30-37.
6. malviya N, jain S, Malviya S. Antidiabetic potential Of Medicinal Plants. Actapoloniaepharmaceutica-Dryg Research, 2010;67: 113-118
7. National Institute of Diabetes and Digestive and Kidney Diseases. National Diabetes Statistics fsB, MD: U.S. Department of Health and Human Services ,National Institutes of Health. 2008:20-30.
8. Kim W, Khil LY, Clark R, Bok SH, Kim EE, Lee S, et al. Naphthalenemethyl ester derivative of dihydroxyhydrocinnamic acid, a component of cinnamon, increases glucose disposal by enhancing translocation of glucose transporter 4. Diabetologia. 2006; 49(10):2437-48.
9. Al-Achi A. Herbs That Affect blood glucose levels. Womens Primary Care. 2005 ;8 :12-18.
10. Xie J, Mehendale S, Yuan C. Ginseng and Diabetes. The American Journal of Chinese Medicine. 2005; 33(3): 397–404.
11. John ZL, LuguangL . Ginseng on Hyperglycemia: Effects and Mechanisms. eCAM 2009; 6(4): 423–427.
12. Sotaniemi EA, Haapakoski E, Rautio A. Ginseng therapy in non-insulin-dependent diabetic patients. Diabetes Care. 1995;18:1373-75.
13. Tetsutani T, Yamamura M, Yamaguchi T, Onoyama O, Kono M. Can red ginseng control blood glucose in diabetic patients. Ginseng Rev. 2000; 28:44-47.
14. Vuksan V, Xu Z, Jenkins AL, Beljan-Zdravkovic U, Sievenpiper JL, Leiter LA, et al. American Ginseng (Panax Quinquefolius L.) Improves Long Term Glycemic Control in Type 2 Diabetes: A Double-blind Placebo-controlled Crossover Trial. American Diabetes Association Annual Meeting. 2000; Abstract No. 384.
15. Han GC, Ko SK, Sung JH, Chung SH. Compound K Enhances Insulin Secretion with Beneficial Metabolic Effects in db/db Mice. J Agric Food Chem. 2007; 55(26):10641-10648.
16. Charpentier G. Oral Combination Therapy for Type 2 Diabetes. Diabetes Metab Res Rev. 2002;18 (Supplement 3): S70-S76.
17. Kim K, Park M, Kim HY. Ginsenoside Rg3 Suppresses Palmitate-Induced Apoptosis in MIN6N8 Pancreatic Beta-Cells. J Clin Biochem Nutr. 2010; 46(1): 30-35.
18. Zhang Z, Li X, Lv W, Yang Y, Gao H, Yang J, et al. Ginsenoside Re Reduces Insulin Resistance Through Inhibition of c-Jun NH2-Terminal Kinase and Nuclear Factor kappa B. Mol Endocrinol. 2008; 22(1):186-195.
19.Shang W, Yang Y, Zhou L, Jiang B, Jin H, Chen M. Ginsenoside Rb1 Stimulates Glucose Uptake Through Insulin-like Signaling Pathway in 3T3-L1 Adipocytes. J Endocrinol. 2008;198(3):561-569.
20. Chang TC, Huang SF, Yang TC, Chan FN, Lin HC, Chang WL. Effect of Ginsenosides on Glucose Uptake in Human Caco-2 cells is Mediated Through Altered Na+/glucose Cotransporter1 Expression. J Agric Food Chem. 2007;55(5):1993-1998.
21. Yoo WS, Ko IH, Ko I. Effect of ginseng extract on blood lipids and atherosclerosis. The Korean Circulation Journal.1981;11(2):143-146
22. Kaneto H, Nakatani Y, Kawamori D, Miyatsuka T, Matsuoka T, Matsuhisa M, Yamasaki Y. Role of Oxidative Stress, Endoplasmic Reticulum Stress, and c-Jun N-terminal Kinase in Pancreatic Beta-Cell Dysfunction and Insulin Resistance. Int J Biochem Cell Biol. 2005;37(8):1595-1608.
23. Ni H, Yu N, Yang X. The Study of Ginsenoside on PPAR gamma Expression of Mononuclear Macrophage in Type 2 Diabetes. MolBiol Rep. 2010;37(6):2975-2979.
24. Lee S, Lee M, Kim C, Kim I, Kim Y. Ginsenoside Rg3 Reduces Lipid Accumulation with AMP-Activated Protein Kinase (AMPK) Activation in HepG2 Cells. Int J Mol Sci. 2012; 13: 5729-39.