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Chamomile tea improves glycemic indices and antioxidants status in patients with type 2 diabetes mellitus

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ABSTRACT

Objectives: Oxidative stress is a major factor in the pathogenesis of diabetes complications. The objectives were to investigate the effects of chamomile tea consumption on glycemic control and antioxidant status in subjects with type 2 diabetes mellitus (T2 DM).

Methods: This single-blind randomized controlled clinical trial was conducted on 64 subjects with T2 DM (males and females) ages 30 to 60 y. The intervention group (n = 32) consumed chamomile tea (3 g/150 mL hot water) 3 times per day immediately after meals for 8 wk. The control group (n = 32) followed a water regimen for same intervention period. Fasting blood samples, anthropometric measurements, and 3-d, 24-h dietary recalls were collected at the baseline and at the end of the trial. Data were analyzed by independent *t* test, paired *t* test, and analysis of covariance.

Results: Chamomile tea significantly decreased concentration of glycosylated hemoglobin, serum insulin levels, homeostatic model assessment for insulin resistance, and serum malondialdehyde, compared with control group (all $P < 0.05$). Total antioxidant capacity, superoxide dismutase, glutathione peroxidase, and catalase activities were significantly increased by 6.81%, 26.16 %, 36.71 % and 45.06% respectively in chamomile group compared with these variables in control group at the end of the intervention (all $P < 0.05$).

Conclusions: Short term intake of chamomile tea has beneficial effects on glycemic control and antioxidant status in patients with T2 DM. A larger sample population and a longer intervention period may be required to show significant clinical improvements.

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Introduction

Type 2 diabetes mellitus (T2 DM) is a chronic metabolic disease characterized by hyperglycemia. It has significant effects on health, quality of life, and health care systems. The International Diabetes Federation (IDF) estimates that 439 million people, 7.7% of the world population, will suffer from diabetes by 2030 [1]. Chronic hyperglycemia causes complications of diabetes, such as heart disease, retinopathy, renal disease, and neuropathy [2].

Oxidative stress associated with hyperglycemia is now recognized as the driving force for the development of diabetic complications [3]. Oxidative stress in diabetes is related to activation of the polyol pathway, formation of advanced glycation end products, activation of protein kinase C, and subsequent formation of reactive oxygen species [4–8]. In the absence of a suitable condensation by antioxidant defense system, enhancement of oxidative stress leads to activation of stress-sensitive intracellular signaling pathways and the formation of gene products that cause cellular damage [9–12].

Apart from currently available therapeutic options, like oral hypoglycemic drugs and insulin therapy, which have limitations, many traditional plant medicines have been used in the treatment of diabetes [13]. Plants apparently provide effective remedies, produce only minimal or no side effects in clinical

MR was the main study investigator; MZ worked as an investigator on the study and contributed to the manuscript; MAJ worked on the statistical analysis plans and analyses the results.

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experiment, and are relatively low cost, as compared to oral synthetic hypoglycemic drugs [14].

German chamomile (Matricariachamomilla L.) is an herbaceous plant that is native to Europe and Western Asia [15]. The consumption of chamomile as tea is rated as more than one million cups per day [16]. Current studies have demonstrated its antioxidant, antiparasitic, antiaging, and anticancer properties, supporting its traditional use for treating various human ailments [17–19]. Sesquiterpenic compounds such as α-bisabolol, bisabolol oxides A and B, chamazulene and farnesene, and phenolic compounds, namely flavonoids including apigenin, quercetin, patuletin and luteolin, and their glucosides, as well as coumarins are considered to be the major bioactive compounds of this plant [20].

Antihyperglycemic and antioxidant activity of chamomile extracts have been demonstrated in experimental studies [21–23]. Cemek et al. indicated that treatment with different doses of chamomile ethanolic extract significantly lowered postprandial hyperglycemia and oxidative stress, and augmented the antioxidant system in streptozotocin (STZ)-induced diabetic rats [21]. In the study by Kholoud and Manal, chamomile aqueous extract effectively decreased blood glucose levels and oxidative stress in STZ-induced diabetic rats [22]. Namjooyan et al. determined that antioxidant activity of chamomile extract reduced the incidence of diabetic embryopathy in the STZ-induced diabetic rat model [23].

Although some experimental studies have reported effects of different extracts of chamomile on glycemic status and oxidative stress in diabetes, its possible effects on metabolic and antioxidant status of patients with diabetes have not been investigated. We hypothesized that chamomile tea consumption would ameliorate glycemic and antioxidant indices in subjects with T2 DM. To test these hypotheses, we initiated a study to evaluate the effects of chamomile tea on glycemic control (serum levels of glucose, glycosylated hemoglobin [HbA1 c], insulin, and homeostasis model assessment-insulin resistance [HOMA-IR]), and antioxidant status (total antioxidant capacity [TAC], activity of superoxide dismutase [SOD] and glutathione peroxidase [GSH-Px], and malondialdehyde [MDA]) in patients with T2 DM.

Materials and methods

Sixty-four patients with type 2 diabetes (male & female) ages 30 to 60 y with a body mass index (BMI) lower than 37 kg/m^2 were recruited for this study from the endocrinology clinic, Imam Hossien Hospital in Tehran, Iran from March 2013 to June 2013. Diagnosis of T2 DM was assessed at least six month before our examination. Exclusion criteria included insulin treatment, smoking, alcoholism, consumption of any dietary supplements, green tea, and other herbal infusion in the past 3 mo or during the study. A history of diseases including liver, kidney and cardiovascular diseases, thyroid disorders, gastrointestinal problems, cholesterol-lowering or antihypertension treatment, using corticosteroids, cyclosporine, non-steroidal antiinflammatory or immunosuppressive drugs, warfarin and antiepileptic medications, pregnancy or breast-feeding, following a specific diet and regular exercise (>2 weeks), and allergy to plants of ragweed species, and having jobs that need high level of consciousness, was taken for each subject.

The study consisted of a single-blinded randomized, controlled clinical trial with treatment and control groups running in parallel for a period of 8 wk. Ethical Committee of Tabriz University of Medical Sciences approved the study protocol, and was registered on the Iranian Registry of Clinical Trials website (http://www.irct.ir, identifier: IRCT2013012712299 N1). The study was conducted in accordance with the guidelines of the Declaration of Helsinki principles. All subjects gave written informed consent before clinical trial enrolment.

The sample size was determined based on the primary information obtained from the study by Kato et al. for blood glucose [24]. Considering 95% confidence interval and 80% power, and a change of blood glucose in 8 wk as primary outcome of the study, the sample size was computed to be 23 per group. This number was increased to 32 per group to accommodate the anticipated dropout rate. The participants were randomly allocated in two groups using a block randomization procedure (of size 4) with matched subjects in each block based on sex, age, and body mass index (BMI). The random sequence was generated using random allocation software by the statistician for the study. The endocrinologist randomly assigned participants to an intervention or control group. Whereas patients and the endocrinologist allocated to the intervention group were aware of the allocated group, outcome assessors and the statistician were blinded to the allocation.

A general questionnaire was completed for each subject. Body weight was measured using a scale (Seca, Hamburg, Germany), without shoes and wearing light clothing. Height was measured using a mounted tape without shoes. BMI was calculated as the weight in kilogram divided by the height in meters squared. Information about daily energy and macronutrient intakes were obtained by 24-h recall method for 3 d, including 2 d during the week and 1 during the weekend. A three day average for energy and macronutrient intakes of all subjects were analyzed by Nutritionist 4 software (First Databank Inc., San Bruno, CA).

Chamomile was obtained as homogenous chamomile tea bags (finished product) from the Iranian Institute of medicinal plants, Karaj Iran. The tea bag, containing approximately 3 g of chamomile tea, was manufactured on March 2013. These tea bags are a commercially available product. The intervention group ($n = 32$) consumed one cup of chamomile tea infusate (1 chamomile tea bag infused for 10 min in 150 mL hot water without milk or sugar) three times a day immediately after meals (breakfast, lunch, and dinner) for 8 wk [24,25]. The control group ($n = 32$) consumed an equivalent volume of warm water during the 8-wk period (Fig. 1). Subjects were asked to keep a record of all beverages consumed during the clinical trial and maintain their usual dietary intake and physical activity and to avoid any changes in medication, if possible. The compliance of the volunteers for the study protocol was monitored with telephone interviews once a week and counting returned tea bags in person every 2 wk.

Blood sampling and biochemical assays

Venous blood samples (5 mL) from each subject were collected between 07:00 to 09:00 h after an overnight fast at the beginning of trial. Two mL of whole blood were collected into tube contained ethylene-diamine-tetra acetic acid to measure the blood levels of HbA1 c. The serum samples were separated from whole blood by centrifugation at 3500 rpm for 10 min (Avanti J-25, Beckman, Brea, CA, USA). The serum and whole blood samples were frozen immediately at -70°C.

Serum glucose was measured using the standard enzymatic methods with commercially available Pars Azmun kit (Karaj, Iran). HbA1 c was measured in the whole blood by cation exchange chromatography with a Nycocard HbA1C kit (Oslo, Norway). Serum insulin level was measured by ELISA method using Monobind kit (Monobind Inc, Lake Forest, CA, USA) and insulin resistance was determined by HOMA index with formula: HOMA-IR = fasting insulin (μU/mL) × fasting glucose (mg/dL)/405 [26]. Serum total cholesterol, triacylglycerol, and high-density lipoprotein cholesterol were measured using the standard enzymatic methods by Pars Azmun kits (Pars Azmun Co., Kiraj, Iran). Low-density lipoprotein cholesterol concentration was determined by the Friedewald formula [27]. Measurement of TAC in serum and SOD and GSH-Px in whole blood was performed by using the colorimetric method with commercial kits (TAC, RANDOX kits; SOD, RANSOD kits; and GSH-Px, RAN–SEL kits; UK) [28–30]. The serum MDA level was estimated by using a reaction with thiobarbituric acid as a thiobarbituric acid reactive substance to produce a pink colored complex. Next, its fluorescence intensity was measured at 547 nm with excitation at 525 nm by a spectrofluorimeter (model SFM 25 A; Kontron, Milan, Italy) [31]. Catalase (CAT) activity was measured by using the method described by Aebi [32].

All anthropometric, dietary intakes, blood sampling, and biochemical measurements were assessed again at the end of intervention period in both groups.

Statistical analyses

Data were analyzed using SPSS version 16 (SPSS Inc., Chicago, IL, USA) and the results are expressed as means ± SD. The normal distribution of variables was tested and confirmed by Kolmogorov-Smirnov test. The baseline measurements and dietary intakes of subjects in two groups were compared using independent samples *t* test and chi-square test for quantitative and qualitative variables respectively. Analysis of covariance (ANCOVA) was used to identify any differences between the two groups at the end of study, adjusting for baseline values and covariates. The changes in anthropometric measurements, energy and nutrient intakes, serum levels of glucose, HbA1 c, insulin, HOMA-IR, TAC, SOD, GSH-Px, CAT, and MDA levels between the beginning and end of the study were compared by paired samples *t* test. The percentage of changes in variables after intervention was determined with the formula: [(after values–before values)/before values] × 100. Results with $P < 0.05$ were considered as statistically significant.

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