



The Effect of Chamomile Tea versus Black Tea on Glycemic Control and Blood Lipid Profiles in Depressed Patients with Type 2 Diabetes: A Randomized Clinical Trial

Sahar Kermanian; MSc¹, Hassan Mozaffari-Khosravi; PhD^{*1,2}, Ghasem Dastgerdi; MD³,
Javad Zavar-Reza; PhD⁴ & Masoud Rahmanian; MD²

¹ Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

² Yazd Diabetic Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

³ Department of General Psychiatry, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

⁴ Department of Biochemistry, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

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*Corresponding author:

mozaffari.kh@gmail.com

Department of Nutrition,
School of Public Health
Shahid Sadoughi University
of Medical Sciences
Shohaday Gomme BLV,
Yazd, Iran.

Postal code: 8915173160

Tel: +98 35 38209143

ABSTRACT

Background: According to traditional beliefs, chamomile products have anti-depression effect. The aim of this study was to investigate the effects of chamomile tea on glycemic control, depression status and lipid profiles in type 2 diabetes (T2D) with depression. **Methods:** This randomized clinical trial was carried out on 74 depressed patients with T2D. Participants were randomly divided into two 37-people groups, chamomile tea (CG) and black tea group (BG). The CG received 3 cups of chamomile tea daily and the BG received 3 cups of black tea daily half an hour after meals for 12 weeks. To examine the status of depression, Beck II test was utilized. Anthropometric measurements, 24-h dietary recalls, glycosylated hemoglobin A1c (HbA1c) and blood lipids profile were measured at the baseline and at the end of the intervention. **Results:** The HbA1c mean was significantly reduced in CG after the intervention, when compared with BG ($7.15 \pm 1.23\%$ vs. $7.98 \pm 1.76\%$, $P = 0.02$). In the same vein, the mean changes in CG and BG were -0.74 ± 1.29 and 0.04 ± 1.07 ($P = 0.006$), respectively. No significant changes were observed in mean of serum lipids within and between groups. The Beck score also showed a significant reduction in the CG after the intervention ($P < 0.001$) and also, the mean changes showed a significant difference between the two groups. **Conclusions:** The results of this study demonstrated that drinking three cups of chamomile tea daily for 12 weeks by T2D suffering from depression lead to improve glycemic control and depression state. Therefore, drinking this kind of tea by these patients is recommended.

Keywords: Chamomile; Depression; Diabetes mellitus; Serum lipids

Introduction

The prevalence of diabetes is growing rapidly in the world, and this condition has reached epidemic proportions (Liu *et al.*, 2015).

Meanwhile, type 2 diabetes (T2D) is more common both in developed and developing countries (Yeghiazaryan *et al.*, 2012). Currently,

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according to the statistics of the International Diabetes Federation (IDF), worldwide prevalence of diabetes is 8.3% and 3818 million people. It is predicted that by 2035, the number of people suffering from this disease will increase to 591.9 million (Guariguata L, 2014). T2D is associated with long term complications such as macrovascular and microvascular disease, nephropathy, neuropathy and retinopathy (Wang *et al.*, 2014).

Studies have shown a high prevalence of depression in patients with T2D, and its prevalence has been reported to be two times higher in these patients than in non-diabetic patients. This have caused many dysfunction in patients who fail to control their disease (Ali *et al.*, 2006). Good glycemic control is considered as the cornerstone of diabetes-related complications in patient with diabetes (Lind *et al.*, 2012). In spite of various medications utilized to reduce hyperglycemia in patients with diabetes, diabetes and its complications are still the main health challenges faced by majority of the population (Nolte and Karam, 2004). . The use of herbal medicines for the treatment and control of blood sugar in patients with diabetes has been in use for a long time, and it has already been accepted as an alternative therapy (Eddouks *et al.*, 2005).

Chamomile belongs to Asteraceae family and is one of the widely used plants in Europe and west Asia (Kolodziejczyk-Czepas *et al.*, 2015). The use of chamomile due to its therapeutic properties can be dated back to ancient Greece and Rome (Amsterdam *et al.*, 2012). The rate of Chamomile tea consumption is about a million cups per day (Khan *et al.*, 2014). Moreover, chamomile is a safe plant and the Food and Drug Administration (FDA) has recognized it as a safe plant (Shoara *et al.*, 2015). This plant is mainly used because of its anti-inflammatory, analgesic, antispasmodic (Avallone *et al.*, 2000, Blumenthal *et al.*, 2000), wound-healing, anti-microbial and sedation effects (Blumenthal *et al.*, 2000). Different studies have demonstrated the antioxidant, anti-parasitic, anti-aging and anti-cancer effects of chamomile (Lee and Shibamoto, 2002, Srivastava and Gupta, 2011,

Zemestani *et al.*, 2015). The healing property of chamomile is attributed to its components. The major bioactive compounds in chamomile are sesquiterpenic compounds such as α -bisabolol, bisabolol oxides A and B and chamazulene and farnesene, and phenolic compounds namely the flavonoids apigenin, quercetin, patuletin, and luteolin, and their glucosides, and also coumarins (Petronilho *et al.*, 2012).

Several studies have demonstrated the hypoglycemia (Khan *et al.*, 2014, Rafrat *et al.*, 2014, Weidner *et al.*, 2013) and hypolipidemia (Al-Jubouri *et al.*, 1990, Najla *et al.*, 2012) effects of chamomile. Rafrat *et al.*, in a study indicated the hypoglycemia, hypolipidemia and antioxidant efficacy of chamomile tea on patients with T2D (Rafrat *et al.*, 2014). On the other hand, Eddouks *et al.* demonstrated that oral administration of aqueous extracts of chamomile at a dose of 20 mg/kg caused an improvement in glucose homeostasis in normal and streptozotocin-induced diabetic rats (Eddouks *et al.*, 2005, Rafrat *et al.*, 2014). Moreover, Cemek *et al.* in a study demonstrated the hypoglycemic and antioxidant effects of alcoholic extract of chamomile in diabetic rats (Cemek *et al.*, 2008).

Although several studies have demonstrated the effects of chamomile on glycemic control in animal models (Cemek *et al.*, 2008, Darvishpadok *et al.*, 2012, Eddouks *et al.*, 2005, Kato *et al.*, 2008, Khan *et al.*, 2014, Najla *et al.*, 2012, Ramadan and Emam, 2012); only one study was found using human model (Rafrat *et al.*, 2014). Moreover, according to the survey, no study has been carried out in depressed patients with T2D. Hence, this study was carried out to assess the effects of chamomile tea consumption on glycemic control, including HbA1c and blood lipid profiles in T2D patients suffering from depression.

Methods

Study Design and Participants: This study was a randomized controlled clinical trial in which 74 depressed patients with T2D participated. They were selected from patients who referred to Yazd Diabetes Research Center under the supervision of

an endocrinologist and a psychiatrist and via the use of Beck II questionnaire from January 2015 to September 2015. Inclusion criteria included duration of diabetes between 5-15 years, Beck test scores between 11-30, no disorders and diseases of the kidney, liver, heart, and thyroid, bleeding disorders and malignancies, autoimmune diseases, and degenerative diseases of the central nervous system, no history of hospitalization for mental illness, not using nutritional and antioxidant supplementation and sedative and diuretics during the last 3 months. Exclusion criteria included having allergy to chamomile, major depression (Beck test score greater than 30) which requires special treatment, people that nurtured the thoughts of suicide during the interview, history of events such as loss of job, divorce or death of their relatives during the last 3 months and preferring not to drink tea. Participants received their routine treatment under the supervision of an endocrinologist.

To estimate the sample size, by considering α equal 0.05, test power of 80% and based on previous study (Amsterdam *et al.*, 2012), a sample size of 32 was computed accounting for 15% of attrition, and finally, 37 patients were obtained in each group. Using table of random numbers, patients were divided into two groups; chamomile tea (CG) and black tea group (BG). CG received 3 bags containing 2.5 g of chamomile tea, while BG received 3 bags containing 2.5 g of black tea. Both tea bags were purchased from the Iranian Institute of Medicinal Plants and the amount of tea polyphenols presented in the sample was tested.

Tea preparation directions: At the beginning of the intervention, the method of tea preparation, the dosage and other information were communicated to the patients; for every use, each tea bag was placed in 150 cc boiled water. The time needed to put the tea bag in a cup of boiling water was similar for the two groups. Both groups consumed tea daily for at least half an hour after meals for 12 weeks. The patients were asked to mark their consumption of chamomile or black tea in a special

registration sheet at the same time. The patients were also asked not to consume another tea during the intervention. They were also requested not to change their physical activity, diet, pharmaceutical and lifestyle as much as possible during the intervention. Follow-up of patients was carried out to control their consumption trend of tea bags and prevalence of attrition and also give answers to some questions asked by the patients via phone every week and every 4 weeks when patients referred to receive the next packets of tea.

Measurements: At baseline, a questionnaire containing general information such as age, height, weight, occupation, marital status, duration of disease, type and dose of medications was completed for each of the participants. Moreover, anthropometric measurements were conducted for each individual and recorded in a special form. To study anthropometric indices, weight was measured utilizing a digital scale, without shoes and with minimal covering. Height also was measured using stadiometer and without shoes. At baseline and at the end of the study, a 24-h recall of the questionnaire was completed to estimate the energy and macronutrients and micronutrients intake and as well as to assess whether individual's food habits have changed during the study or not.

The Beck II was utilized to determine the presence and severity of depression. Based on this, test score of 0-10 are considered normal, 11-16 mild depression, 17-20 need psychological counseling, 21-30 relatively depressed, 31-40 severely depressed, and more than 40 have very severe depression (Dabson and Mohammad, 2007). The depression of the individuals was measured using the Beck questionnaire at the beginning, at the end of the sixth week and at the end of the study.

At beginning and at the end of the study, 5 cc venous blood samples were collected from each individual after at least 12 h fasting by a lab technician. Serum samples were isolated from blood by centrifugation and were frozen at -70 °C until final analysis. Ion exchange chromatography method was used for the measurement of HbA1c.

The measurement of total cholesterol, triglyceride and HDL-c were carried out with enzymatic method using test kits (Pars Tehran – Iran) and autoanalyzer (Italy). LDL-c concentration was carried out using the Friedwald formula (Friedewald *et al.*, 1972). All the anthropometric measurements, dietary intake, blood samples and biochemical measurements were re-evaluated at the end of the study in both groups.

Data analysis: All data were analyzed using SPSS 16 software. Dietary data were analyzed using Nutritionist 4 software. Kolmogorov-Smirnov test was used to investigate normality of data. For comparison of mean variables that were normally distributed within and between groups, Paired t-test and Student t-test were used, respectively. P-value was considered less than 0.05.

Ethical considerations: This clinical trial was approved by the ethical committee on research of the Shahid Sadoughi University of Medical Sciences. It was registered on the Iranian Registry of Clinical Trials (<http://www.irct.ir>, identifier: IRCT2014112820132N1). Written informed consents were also obtained from all participants in the study.

Results

All 74 patients who met the inclusion criteria participated in the study. The patients were randomly divided into two groups: 37 patients in the intervention group and 37 patients in the control group. Finally, 64 patients completed the study. Among 10 people who were excluded from the study, 5 patients were in chamomile tea group and 5 patients were in black tea group. These people could not complete the study due to disease, travel and the lack of desire to cooperate (**Figure 1**). The compliance with tea consumption in patients was 90% in both groups; which shows that all of the patients complied with the protocol as well. No certain side effects were reported by the

patients during the study.

The average age of participants in the CG group was 51.95 ± 10.69 years while it was 52.30 ± 5.85 years in the BG group. Baseline characteristics and anthropometric measurements of patients are presented in **Table 1**. As it be shown, none of the variables of age, sex, height, weight, body mass index (BMI), and duration of diabetes were statistically significant in the two groups. After 12 weeks of intervention, there were no statistically significant differences between the two groups in terms of weight and BMI.

Table 2 shows patients' daily intake of nutrients. According to the results, there were significant changes in the mean energy and protein intake in the BG group after intervention and only the mean change of protein showed significant difference between the two groups.

The findings related to lipid profiles, HbA1c and Beck score are presented in **Table 3**. It can be seen that significant differences were observed between mean serum total cholesterol, triglycerides, LDL-c, HDL-c and LDL-c/HDL-c ratio in each group at the beginning and end of the study as well as between the two groups.

The HbA1c mean and Beck score and their changes within and between groups are presented in **Table 3**. The results showed that the HbA1c mean was significantly lower in the CG group before and after intervention ($P = 0.04$). On the other hand, the mean change showed a significant difference between the two groups, and this variable had a significant reduction when compared with the BG group. The Beck mean score was significantly reduced in CG group when compared with BG group ($P = 0.02$). The Beck score also showed a significant reduction in the CG group before and after the intervention ($P < 0.001$) and also, the mean changes showed a significant difference between the two groups.

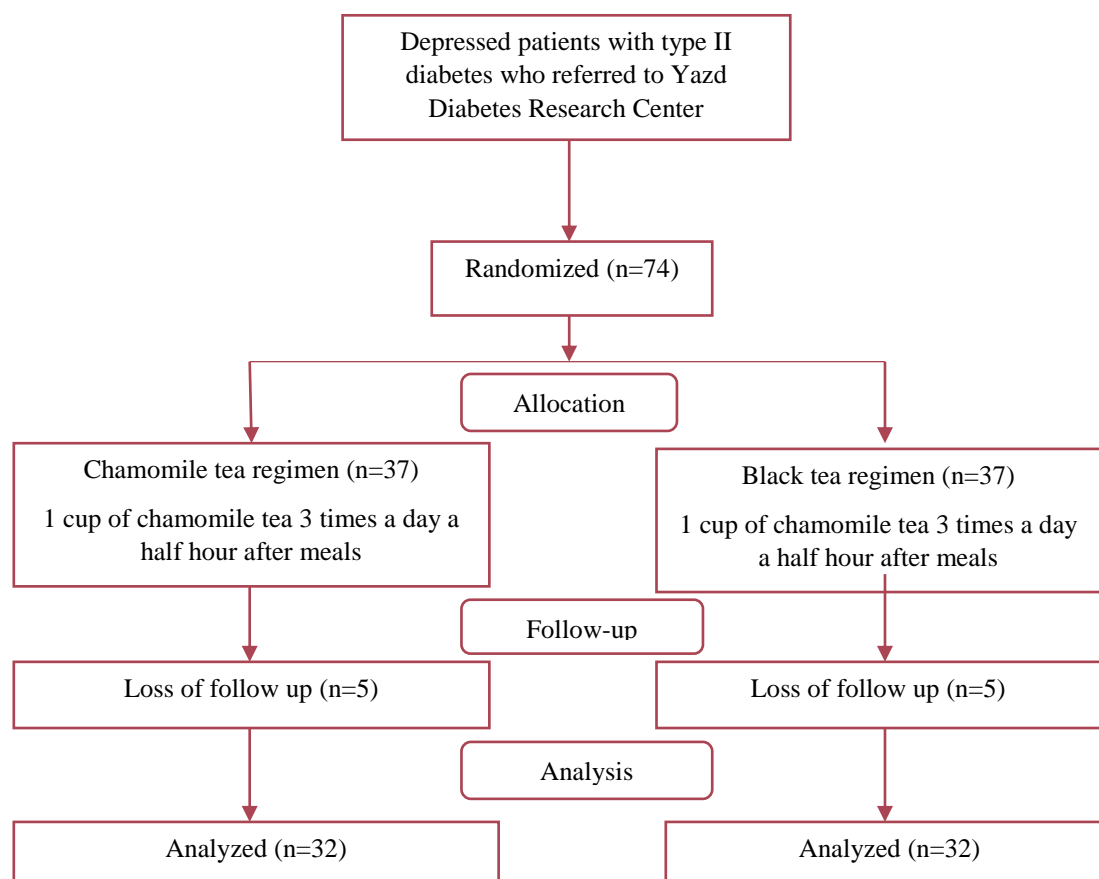


Figure 1. Flow chart of the study

Table 1. Comparison of quantitative and qualitative variables between the two groups before intervention

Variables	Chamomile group	Black tea group	P-value ^a
	Mean \pm SD	Mean \pm SD	
Age (year)	51.95 \pm 10.69	52.30 \pm 5.85	0.86
Height (cm)	163.38 \pm 8.97	163.20 \pm 8.21	0.93
Weight (kg)	76.65 \pm 11.48	75.95 \pm 13.28	0.80
Body mass index (kg/m ²)	28.81 \pm 4.43	28.44 \pm 3.94	0.70
Duration of diabetes (months)	99.14 \pm 69.87	83.57 \pm 65.00	0.32
Sex	N (%)	N (%)	
Male	13 (35.1)	15 (40.5)	0.63 ^b
Female	24 (64.9)	22 (59.5)	

^a: Student t-test; ^b: chi square test

Table 2. Comparison of the mean daily dietary intake in both Chamomile tea and Black tea groups before and after intervention

Variables/groups	Before	After	P-value ^a	Changes
Energy (kcal)				
Chamomile tea group	1586.4 ± 547.37	1510.6 ± 313.18	0.56	-68.15 ± 605.95
Black tea group	1797.7 ± 610.43	1559.2 ± 445.87	0.01	-2.66 ± 619.25
P-value ^b	0.12	0.61		0.21
Carbohydrate (g)				
Chamomile tea group	216.16 ± 68.498	215.03 ± 52.98	0.83	-3.41 ± 84.80
Black tea group	238.55 ± 89.69	217.97 ± 58.65	0.14	-25.55 ± 99.27
P-value	0.23	0.84		0.36
Protein (g)				
Chamomile tea group	60.62 ± 23.18	59.78 ± 18.15	0.85	0.89 ± 24.86
Black tea group	77.64 ± 38.91	62.56 ± 22.44	0.009	-14.74 ± 30.80
P-value	0.02	0.60		0.03
Total fat (g)				
Chamomile tea group	53.24 ± 28.53	45.69 ± 16.23	0.27	-6.44 ± 30.29
Black tea group	59.21 ± 28.60	48.56 ± 28.31	0.07	-11.73 ± 36.46
P-value	0.37	0.62		0.54

^a: Paired t-test; ^b: Student t-test**Table 3.** Comparison of lipid profiles, HbA1c and Beck score at the beginning and end of the study in both groups

Variables/groups	Before	After	P-value ^a	Changes
Total cholesterol (mg/dL)				
Chamomile tea group	172.03 ± 41.48	182.34 ± 45.91	0.24	-8.0 ± 36.45
Black tea group	166.81 ± 44.36	170.97 ± 30.36	0.83	-1.84 ± 50.95
P-value ^b	0.60	0.25		0.59
TG (mg/dL)				
Chamomile tea group	212.41 ± 116.27	246.66 ± 152.29	0.41	-17.44 ± 113.14
Black tea group	195.54 ± 79.73	201.34 ± 90.46	0.38	-10.96 ± 70.41
P-value	0.46	0.15		0.78
Low density lipoprotein cholesterol (mg/dL)				
Chamomile tea group	83.54 ± 35.20	86.44 ± 37.48	0.58	-3.55 ± 31.14
Black tea group	77.73 ± 31.25	82.49 ± 20.47	0.71	-2.87 ± 41.19
P-value	0.46	0.64		0.94
High density lipoprotein cholesterol (mg/dL)				
Chamomile tea group	48.27 ± 5.60	48.79 ± 5.95	0.87	-0.17 ± 5.95
Black tea group	48.14 ± 15.06	47.44 ± 7.50	0.68	1.21 ± 16.57
P-value	0.95	0.44		0.67
Low density lipoprotein cholesterol (mg/dL)/ High density lipoprotein cholesterol (mg/dL)				
Chamomile tea group	1.72 ± 0.65	1.78 ± 0.65	0.65	0.06 ± 0.65
Black tea group	1.69 ± 0.59	1.80 ± 0.61	0.65	0.08 ± 0.99
P-value	0.82	0.89		0.92
HbA1c (%)				
Chamomile tea group	7.90 ± 1.37	7.15 ± 1.23	0.04	-0.74 ± 1.29
Black tea group	7.94 ± 1.33	7.98 ± 1.76	0.78	0.04 ± 1.07
P-value	0.90	0.02		0.006
Beck score				
Chamomile tea group	17.46 ± 6.36	11.75 ± 6.06	< 0.001	5.75 ± 6.24
Black tea group	17.97 ± 6.07	15.11 ± 6.63	0.05	2.55 ± 7.67
P-value	0.72	0.02		0.05

^a: Paired t-test; ^b: Student t-test

Discussion

The present study showed that drinking 3 cups of chamomile tea daily by T2D patients suffering from depression in duration of 12 weeks significantly reduced the HbA1c mean compared to baseline values and black tea. These results are consistent with findings from previous studies. There were several animal studies on the effect of chamomile on diabetes (Cemek *et al.*, 2008, Darvishpadok *et al.*, 2012, Eddouks *et al.*, 2005, Kato *et al.*, 2008, Khan *et al.*, 2014, Najla *et al.*, 2012, Ramadan and Emam, 2012, Weidner *et al.*, 2013). However, there was only one study that used human model (Rafrat *et al.*, 2014); therefore the present study was the second study using human model.

Rafrat *et al.* investigated the antidiabetes and anti hypercholesterolemic effects of chamomile tea in type 2 diabetes patients (Rafrat *et al.*, 2014). The results of this study show that consumption of 3 g of chamomile tea in 150 ml boiling water 3 times per day for eight weeks, could significantly reduce blood glucose and lipid profile in patients with diabetes. Khan *et al.* showed that chamomile tea (1 g chamomile flowers in 150 ml boiling water) reduces fasting blood glucose, postprandial blood glucose levels and glycosylated hemoglobin in diabetic rats (Khan *et al.*, 2014). In a study by Weidner *et al.* chamomile flower extract was given for 6 weeks at a dose of 200 mg/kg per day to obese mice (Weidner *et al.*, 2013). After 2 weeks, fasting blood glucose was reduced to 13% and fasting insulin levels were reduced to 23%.

A study of Ramadan *et al.* showed that oral administration of 100 mg/kg chamomile extract per day for 21 days on streptozotocin-induced diabetic rats could significantly reduce blood glucose and serum insulin levels in rats (Ramadan and Emam, 2012). A study of Najla *et al.* was carried out on diabetic rats, showed that oral administration of aqueous extract of chamomile (200 mg/kg) for 21 days in diabetic rats reduced fasting blood glucose at a rate of 62.2% (Najla *et al.*, 2012). The study of Darvishpadok *et al.* was carried out on fertile female diabetic rats (Darvishpadok *et al.*, 2012). Alcoholic extracts of chamomile was administered

in three doses; 100, 300 and 500 for 17 days. All three doses of chamomile extract led to significant reduction in blood glucose and glycosylated hemoglobin in female rats. Another study by Kato *et al.* found that aqueous extracts of chamomile (500 mg/kg/day) and its major compounds have the effect of reducing blood glucose in streptozotocin-induced diabetic rats (Kato *et al.*, 2008).

Moreover, a study carried out by Cemek *et al.* on streptozotocin-induced diabetic rats showed that oral administration of 20-100 mg/kg/day of ethanol extract of chamomile (MCE) for 7-14 days resulted in a significant reduction in blood glucose levels in diabetic rats (Cemek *et al.*, 2008). Eddouks *et al.* indicated that oral administration of aqueous extract of chamomile (20 mg/kg/day) for 2-15 days to streptozotocin-induced diabetic rats resulted in a significant reduction in blood glucose in healthy and diabetic rats (Eddouks *et al.*, 2005). The findings in this study are consistent with the results of the above mentioned studies.

In this study, a significant reduction in the concentration of HbA1c in the intervention group at the end of the study was observed. Chamomile seems to have a beneficial effect on glycemic control via the inhibition of key enzymes involved in gluconeogenesis and glycogenolysis and also stimulates peripheral glucose utilization, especially in muscle and adipose tissue (Eddouks *et al.*, 2005). Esculetin, the main component of chamomile, inhibits intestinal alpha-glucosidase and thus reduces blood glucose levels in streptozotocin-induced diabetic rats (Kato *et al.*, 2008). Chamomile also reduces digestion and the rate of carbohydrate absorption (Eddouks *et al.*, 2005). Kato *et al.* showed that inhibition of phosphorylation of glycogen causes a reduction in the degradation of glycogen, and one of the mechanisms behind the hypoglycemic effect of chamomile and quercetin is the inhibition of glycogen degradation (Kato *et al.*, 2008).

Several studies have shown the beneficial effects of consuming chamomile on blood lipids (Al-Jubouri *et al.*, 1990, Najla *et al.*, 2012, Rafrat *et al.*, 2014, Weidner *et al.*, 2013). In a study by

Al-Jubouri et al. aqueous extracts of chamomile reduces total cholesterol in rat with blood lipid (Al-Jubouri *et al.*, 1990). Several studies have reported that chamomile intake reduces serum levels of TC, TG, and LDL-c in patients with type 2 diabetes (Chang and Chen, 2015). It causes 16% reduction in the serum levels of TC and TG in obese mice and also reduces serum levels of TC, TG and LDL-c in diabetic mice (Najla *et al.*, 2012). But in this study, the effect of consuming chamomile on lipid profile was not observed.

The study also showed the beneficial effects of chamomile on depression. Chang et al. had observed such an outcome (Chang and Chen, 2015). Their study shows that consumption of German chamomile tea for two weeks resulted in significant improvement in physical-symptoms-related sleep inefficiency and the symptoms of depression after delivery. The sedative effect may be due to the apigenin present in the chamomile because the central benzodiazepine receptors tend to have a mild sedative effect (Anjaneyulu *et al.*, 2003).

Another study showed the antidepressant effect of quercetin (100 and 50 mg/kg) for 6 weeks in diabetic depression mice (Anjaneyulu *et al.*, 2003). Quercetin reduces depression by inhibiting monoamine neurotransmitter oxidase (MAO) and catechol-O-methyltransferase (COMT), it also increases the concentrations of catecholamines in the synaptosomes in diabetic depression mice (Anjaneyulu *et al.*, 2003).

This study is the second human study on diabetic patients. Some conflicting results were obtained in this study which may be due to special conditions of patients suffering from various degrees of depression. In this study, the sample size was large when compared to other similar

studies that have been carried out in this field. Assessing the effect of chamomile tea consumption on depressed patients with diabetes was one of the limitations of this study. Therefore, the findings of this study cannot be generalized to the entire population. The other limitation of this study was lack of measurement of other parameters of glucose levels in the subjects. For better identification of the effects of chamomile, some further human studies are required.

Conclusions

The results of this study showed that drinking three cups of chamomile tea daily for 12 weeks by depressed patients with diabetes reduced the concentration of HbA1c and improved depression status when compared with baseline values and drinking black tea in these patients. However, a further study is needed to detect the effects of chamomile tea on lipid indicators.

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Authors' contribution

The study was designed by Mozaffari-Khosravi H and Kermanian S. statistical analysis was performed By Mozaffari-Khosravi H. Data collection and writing manuscript were performed by all authors. All authors reviewed the paper and confirmed it.

Conflicts of interest

None declared.

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