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Original article

The effect of chamomile (*Matricaria recutita L.*) infusion on blood glucose, lipid profile and kidney function in Type 2 diabetic patients: a randomized clinical trial

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Summary. *Introduction:* Chamomile is one of the medicinal herbs, frequently used in traditional medicine for treatment of diabetes. Therefore this study aimed to evaluate the effects of chamomile herbal tea on glycemic index, lipid profile and kidney function in type 2 diabetic patients. *Methods:* This randomized clinical trial was conducted on 50 diabetic patients. The intervention group received standard treatment with orally 200 ml/day of chamomile infusion (10 g/100 mL boiling water) twice a day before meals (lunch and dinner) for 4 weeks. The control group only received standard therapy. *Results:* Consumption of the chamomile infusion was accompanied by a significant reduction in total cholesterol (TC) (p= 0.02), low density lipoprotein cholesterol (LDL-C) (p= 0.04) and creatinine (Cr) (p= 0.03). Within-group comparisons showed there was a significant decrease in fasting blood sugar and 2-h postprandial glucose in the intervention group (p= 0.01), (p= 0.03), respectively. *Conclusions:* Chamomile has potential desirable effects on serum levels of TC, LDL-C and Cr in patients with type 2 diabetes taking oral hypoglycemic agent.

Key words: chamomile, Type 2 diabetes mellitus, lipid profiles, blood glucose, blood urea, creatinine

Abbreviations

T2DM, type 2 diabetes mellitus; Cr, creatinine; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; FBS, fasting blood sugar; 2hpp; 2-h postprandial glucose; M, molar.

Introduction

Diabetes is one of the most common metabolic disorders, caused by insulin deficiency or insulin resistance (1). Type 2 diabetes mellitus (T2DM) is immense increase around the world. It is estimated that until 2030, the numbers of adults with diabetes will be increased to 69% and 20% in developing and developed countries, respectively (2). A noticeable increment in the preva-

lence of T2DM has been observed in Iran (especially in Yazd) over the last decade (3-5). Prolonged hyperglycemia can cause some serious complications such as nephropathy, retinopathy, neuropathy, and cardiovascular diseases (6-8). Various oral hypoglycemic agent (biguanides, sulfonylureas and thiazolidinediones) with or without insulin therapy, have been administered for alleviating the disorder (9-11).

The use of medicinal plants and spices as a valuable alternative treatment for T2DM is on the increase in most developing countries and also in industrialized societies, despite the use of modern antidiabetic agents (12). It seems that soluble phenols constituents in hot water and sesquiterpenes are important in the hypoglycaemic and hypocholesterolaemia effects of chamomile extract in animal studies (13-15). Eddouks et al. (16) demonstrated that the consumption of aqueous extract of chamomile for 2 weeks was associated with a reduction in blood glucose levels in normal and also streptozotocin-induced diabetic rats. Some studies reported that antidiabetic activity of chamomile extract is related to its conservation effect on pancreatic beta cells in diminishing hyperglycaemia-related oxidative stress and also repressing blood glucose levels and enhancing liver glycogen concentration. On the other hand, Cemek et al. (17) observed that the chamomile extract had no significant influence on fasting blood glucose levels in normal and diabetic rats (20 mg/kg/day). Reduction of urea and creatinine was observed in streptozotocin-induced diabetic rats after administration of *Matricaria chamomilla* water extract for two weeks (18).

Several human studies have proven the effects of this plant on sleep quality and depression (19), Antiproliferative and Apoptotic in human cancer cells (20), anxiolytic activity (21), anti-inflammatory (22), hypotension in cardiac patients (23) and oral mucositis in patients undergoing hematopoietic stem cell transplantation (24). Rafraf et al. (25) demonstrated that consumption of 3 chamomile tea bags for 8 weeks is associated with reduction in total cholesterol (TC), triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) in T2DM patients. Improvement of creatinine concentration was observed with the consumption of chamomile tea in healthy volunteers (n= 14) after 2 weeks (26).

Overall, several studies have demonstrated the beneficial effects of chamomile in animals. To the best of our knowledge, there exists no accessible report which represents the effects of chamomile infusion on metabolic state and also on kidney function in patients with T2DM. The aim of this study was to determine the effects of chamomile consumption on serum lipid profiles, blood glucose, blood urea and creatinine in patients with T2DM.

Methods and materials

Study design

Study participants were randomized (using a random number table) to consume 20 g powder of chamomile flower daily, this is also known as the intervention group. Outcome assessors and the statistician, as well as laboratory technicians, were blinded to the allocation. The participants in the intervention group were asked to drink one cup of brewed chamomile (10 g of chamomile plant brewed for 10 min in 100 ml boiling water without sugar) twice a day before the meals (lunch and dinner), for 4 weeks. The control group only received standard therapy. The recommended dosage (20 g/day) was chosen as selected by previous studies (13, 19). To take 24 h dietary recalls and count returned packed sachets, participants were visited at baseline, weeks 2 and 4 of study.

Participants

Participants with type 2 diabetes who were between 30- 70 years were recruited from the Diabetes Research Center, Yazd, Iran, from March 2015 to March 2016. The calculation of the sample size was performed, considering the primitive information obtained for blood glucose from the study by Khan et al. (27), with 80% power, a significance level of 0.05, 25 subjects in each study group was determined.

The inclusion criteria included: The inclusion criteria include: subjects were confirmed the diagnosis of their T2DM based on the American Diabetes Association (ADA) guidelines (28). Also, patients who did not consume regular chamomile or other tisane within the last 1 month were also included. Exclusion criteria included: consuming less than 30% of the packed chamomile, renal failure, gastrointestinal or cardiovascular disease, hypertension, other endocrine disorders or allergic reactions to chamomile plant (self-report), pregnancy, lactation, insu-

lin therapy, following a specific diet and changing dose or type of drugs within the last 6 months or during the intervention. At baseline, all participants were asked not to change their physical activity and follow their routine diet during the study. An informed consent form was signed by each subject before beginning the study. Fifty subjects (27 males and 23 females) who met the inclusion criteria were recruited in this trial. Six subjects did not continue over the study; therefore 44 subjects (22 in each group) completed the study (Figure 1).

Plant material

The chamomile flower was procured from a local market in Yazd city (Iran) in June, 2014 and it was authenticated by Laboratories of the School of Pharmacy and Pharmaceutical sciences of Shahid Sadoughi University of Medical Sciences. The plant was weighed, added to a certain amount of distilled water (20 g/200 ml), followed by infusion for 10 min and filtration using a Buchner funnel (Whatmann No.1 filter paper) according to the reported tea brewing procedure (21).

Determination of total phenolic content

Total phenolic content was determined by Folin-Ciocalteu reagent (22), with some minor modifications.

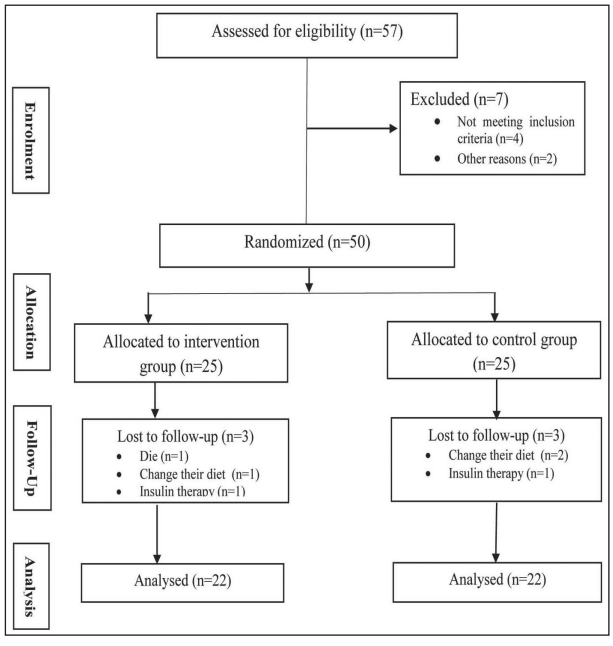

Figure 1.

The extract (200 µL) was mixed with Folin-Ciocalteu reagent (1.5 ml, 1:10 diluted with distilled water) and allowed to stand at 22˚C for 5 min; 1.5 mL of sodium bicarbonate solution (6 g/100 ml) was added to the mixture and after 90 min at 22˚C, the absorbance level was measured at 725 nm using a UV-Visible spectrophotometer. A calibration curve of gallic acid (25 to 150 µg/mL in 80% methanol) was prepared and the results were reported as milligram of gallic acid equivalents per gram of sample dry weight (mg GAE/g DW) and was reported as mean ± standard deviation (SD).

Determination of total flavonoid content

Aluminum chloride colorimetric method was used to determine the total flavonoid content in the plant (23). One mL of extract or standard solution of catechin (50, 100, 150, 200, 250 and 300 mg/L) was added separately to a volumetric flask (10 mL) containing 4 mL of double distilled water (ddH_2O) and 0.3 ml of 5 % $NaNO_2$ was added to the flask. After 5 min, 0.3 ml $AlCl_3$ (10%) was also added. At the 6th min, 2 ml of 1 M NaOH was added and topped up to a final volume of 10 mL with double distilled water. The flavonoid content was expressed as mg catechin equivalents (CE)/g dry matter.

Ferric-reducing antioxidant power (FRAP) assay

FRAP assay was conducted according to the method of Benzie and Strain (24), with slight modifications. One-hundred µL of the extract and 3 mL of prepared FRAP reagent (5 mL of 10 mM TPTZ solution in 40 mM HCl plus 5 mL of 20 mM $FeCl_3$_$6H_2O$ and 50 mL of acetate buffer (0.3 mol/L, pH 3.6) were mixed together. After an incubation period of 15 min at a temperature of 37˚C, the absorbance was measured at 585 nm. Five concentrations of $FeSO_4$ $7H_2O$ (12.5, 25, 50, 100, 200 µmol/L) were used to draw a calibration curve. In this test, ascorbic acid was used as the reference. All the measurements were carried out in triplicate and expressed as mean ± SD.

Measures

A general questionnaire was completed for each participant. Recommendations about avoiding any changes in their physical activity and usual dietary intake were evaluated using registered records through-

out the study. Height and weight were measured without shoes and with minimum clothing using a scale and non-stretched tape measure (Seca, Germany). Body Mass Index (BMI) was calculated by dividing the weight (in kilogram) by the square of the height (in meters squared).

Biochemical assays

At baseline and after 4 weeks of trial, fasting blood samples (5 mL) were taken. Blood glucose, total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), blood urea and creatinine were measured using enzymatic methods (Pars Azmoon Kit, Iran), and low-density lipoprotein cholesterol (LDL-C) levels were computed using the Friedewald formula (LDL-C = TC – (HDL-C +TG/5).

Statistical analysis

Data were analyzed using statistical package for social sciences (SPSS) statistical software (version 16.0). Kolmogorov-Smirnov test was used to evaluate the normality of data distribution. Independent sample t- test was used for two group comparisons. Paired T-test was used to compare variables at baseline and the end of study. Analysis of covariance (ANCOVA (was applied to compare differences between the two groups at the endpoint, adjusting for age, gender and baseline values as the covariates. Data were presented as means ± SD. The level of significance was considered at $p< 0.05$.

Table 1. Total antioxidant activity, phenolic and flavonoid contents of the chamomile

Variables	Mean ± SD
FRAP value, Ascorbic acid (mmol Fe2+/g DW)	155.7 ± 1.25, 649
Total phenolic (mg GAE/g DW)	5.78 ± 0.04
Total flavonoids (mg CE/g DW)	7.02 ± 1.05

Results

The total antioxidant activity, total phenolic and flavonoid contents of chamomile consumed by the study participants are shown in Table 1. Forty-four (20 women and 24 men) of the 50 enrolled patients with T2DM completed the study. Participants' age, weight, height and BMI did not differ between the two groups. Based on 24 h dietary recall, dietary intakes of energy, carbohydrate, protein and fat were not significantly different between two groups at baseline and after 4 weeks of study. These findings demonstrated patients did not change their routine diet during the study (Table 2).

Table 2. Baseline demographic characteristics and dietary intakes of the study participants [a]

Variables	Chamomile group		Control group		*p*-value[b]		
Age (year)	55.33 ± 7.85		55.22 ± 6.72		0.96		
Weight (kg)	75.72 ± 9.45		72.72 ± 10.06		0.36		
Height (cm)	166 ± 8.02		163 ± 4.71		0.18		
BMI (kg/m2)	27.51 ± 3.72		27.17 ± 3.11		0.76		
	Baseline	**After intervention**	**Baseline**	**After intervention**	**Baseline**	**After intervention**	**Group difference**
Energy (kcal/day)	1715 ± 186.11	1641.7 ± 133.24	1677.8 ± 135.07	1681.8 ± 128.53	0.46	0.36	0.30
Carbohydrate (g/day)	233.41 ± 31	226.21 ± 21.91	230.32 ± 25.59	232.41 ± 20.61	0.74	0.38	0.46
Protein (g/day)	63.45 ± 8.91	61.21 ± 5.16	62.99 ± 7.89	59.35 ± 5.65	0.87	0.30	0.62
Fat (g/day)	60.27 ± 8	58.05 ± 5.06	57.67 ± 4.70	59.45 ± 5.91	0.24	0.44	0.09

[a] *Data are expressed as mean ± SD*

[b] *Obtained from independent samples t-test for continuous variables and Chi-square for categorical ones*

The mean values of serum lipid profiles and glycemic status at study baseline and after 4 weeks of intervention are illustrated in Table 3. There existed no significant differences in TG, LDL-C, HDL-C, FBS and 2hpp between groups at baseline (p>0.05). However, there was a significant difference between the baseline values of TC (p= 0.046).

The results of ANCOVA illustrated that the TC and LDL-C significantly decreased (p<0.05), while the serum levels of TG, HDL-C, FBS and 2hpp did not differ significantly between the two groups at endpoint. After 4 weeks, TC (-4.66% vs. 4.44 % increase in control group) and LDL-C (-19.97% vs. 15.82 % increase in control group) decreased significantly in the intervention group (data not shown). A significant decrease in FBS (161.28 ± 41.57 mg/dl at study baseline vs. 146.95 ± 6.64 mg/dl after intervention; p= 0.01), as well as 2hpp (239.11 ± 67.76 mg/dl at study baseline vs 222.33 ± 10.98 mg/dl after intervention; p= 0.03), was identified in the intervention group after 4 weeks of chamomile consumption (Table 3).

No significant differences were observed in serum creatinine and urea between the two groups at baseline. However, there were significant differences in creatinine levels between the two groups at the end of the study (p= 0.03), after adjustment for confounders (age, gender and baseline values). After intervention, there were no significant differences between the two groups in urea values (p= 0.48). A significant decrease in serum levels of creatinine (p<0.04) was obtained in the intervention group in comparison to the baseline values (Table 4).

Discussion

This parallel, single-blind, randomized trial demonstrated that consumption 20 gr/day of chamomile for 4 weeks significantly reduced the TC, LDL-C, Cr levels in patients with T2DM. Furthermore, a significant decrease from baseline in FBS and 2hpp was also obtained in the intervention group. The effect of chamomile extract on serum lipid profile have already been surveyed in diabetic animals (29, 30). Najla et al. (18) indicated that the changes of serum levels of TC, TG, HDL-C and LDL-C were significantly different from

Table 3. Comparison of serum lipid profile and blood glucose at baseline and after 4 weeks of intervention*

	Chamomile group (n= 22)				Control group (n= 22)				*p*-value	
	Baseline	After intervention	Change	*p*-value[b]	Baseline	After intervention	change	*p*-value[b]	Baseline[a]	After intervention[c]
TC (mg/dL)	222.83 ± 46.44	182.68 ± 7.23	-35.55 ± 42.16	0.002	201.94 ± 32.49	211.98 ± 7.23	5.44 ± 32.07	0.48	0.046	0.008
TG (mg/dL)	230.33 ± 75.52	207.93 ± 12.24	-22.77 ± 65.60	0.1	176.38 ± 64.82	198.79 ± 12.24	-17.05 ± 38.56	0.08	0.42	0.61
LDL-C (mg/dL)	138.65 ± 39.75	102.57 ± 7.52	-34.83 ± 52.99	0.01	114.45 ± 29.60	125.12 ± 7.52	9.42 ± 32.67	0.23	0.14	0.04
HDL-C(mg/dL)	33.55 ± 7.21	40.97 ± 2.71	3.83 ± 12.70	0.21	48.80 ± 11.06	44.64 ± 2.71	-0.57 ± 8.46	0.77	0.10	0.40
FBS (mg/dL)	161.28 ± 41.57	146.95 ± 6.64	-16.94 ± 24.80	0.01	167.11 ± 57.01	162.82 ± 6.64	-1.66 ± 34.80	0.84	0.72	0.1
2hpp (mg/dL)	239.11 ± 67.76	222.33 ± 10.98	-24.22 ± 43.43	0.03	265.11 ± 81.94	237.66 ± 10.98	-20.05 ± 59.94	0.17	0.30	0.33

**The results are expressed as mean ± standard deviation (SD)*
[a] p-value is reported based on the analysis of independent sample t test
[b] p-value is reported based on the analysis of Student's paired t test
[c] p-value is reported based on the analysis of covariance (adjusted for age, gender and baseline values)

Table 4. Renal function biomarkers in diabetic patients at baseline and after 4 weeks of intervention

	Chamomile group (n= 22)				Control group (n= 22)				*p*-value	
	Baseline	After intervention	Change	*p*-value[b]	Baseline	After intervention	change	*p*-value[b]	Baseline[a]	After intervention[c]
Creatinine (mg/dL)	0.92 ± 0.16	0.90 ± 0.02	-0.45 ± 0.86	0.04	1 ± 0.27	0.98 ± 0.02	0.007 ± 0.11	0.78	0.33	0.03
Urea (mg/dL)	32.5 ± 7.77	31.17 ± 1.41	-0.94 ± 5.48	0.47	32.60 ± 8.53	32.61 ± 1.45	0.61 ± 6.18	0.68	0.96	0.48

[*] The results are expressed as mean ± standard deviation (SD)

[a] p-value is reported based on the analysis of independent sample t test

[b] p-value is reported based on the analysis of Student's paired t test

[c] p-value is reported based on the analysis of covariance (adjusted for age, gender and baseline values)

the control healthy group after administration of the water extract of chamomile in diabetic rats. The consumption of Chamomile tea in patients with T2DM resulted in a considerable decline in serum TC, TG, and LDL-C levels after 8 weeks of treatment (25). Similar effects were also reported in obese mice (31). It was suggested that the antihyperlipidemic activity of this plant might be due to the high concentration of the essential oil of chamomile (32) well as its antioxidant action (33, 34). However, the consumption of chamomile had no significant effects on HDL-C and TG levels after adjustment for confounders. In agreement with the present results, Aljubouri et al. (35) did not find a remarkable effect of the oral administration of chamomile aqueous extract on serum TG levels in hyperlipidemic rats. The same observations were observed in Guinea pigs with hyperlipidemia (36). Moreover, Weidner et al. (31), showed that the treatment with chamomile flowers extract had no effect on serum HDL-c levels in high-fat diet (HFD)-fed mice after 6 weeks intervention. This observation agreed with the result of a study which reported that the levels of HDL-C was not significantly altered after chamomile tea consumption (25). In contrast to the current findings, Ashraf et al. (37) stated that aqueous extracts of chamomile in diabetic rats for 6 weeks was associated with a significant increase in serum HDL-c levels. The presence of chlorogenic acid in chamomile flowers might be responsible for the hypolipidemic activity of this plant (26, 38). Antihyperlipidemic effect of chamomile might be due to the modulation of PPARs (13).

Although individuals in the chamomile group had a significant decline in FBS and 2hpp levels ($p<0.05$), these values did not decrease markedly in this group compared to the control group. Different effects on animals were reported previously by Khan et al. (27), Kato et al. (13), and Najla et al. (18). Cemek et al. (17) indicated that the ethanolic chamomile extract had no effect on fasting blood glucose levels in normal healthy (100 mg/kg/day) and diabetic rats treated with the extract in a dose of 20 mg/kg/day. Darvishpadok et al. (39) demonstrated that the treatment of fertile diabetic rats with 100, 300, and 500 mg/kg of chamomile ethanolic extract significantly decreased the levels of blood glucose and HbA1C, and the maximum effect was found at the dose of 500 mg/kg/day. The serum level of postprandial

glucose hyperglycemic improved significantly in high fat diet (HFD) obese mice after oral administration of chamomile aqueous extracts for 15 days (40). Esculetin, quercetin and luteolin in chamomile via inhibiting intestinal α-glucosidase activities, hepatic glycogen phosphorylase and increasing liver glycogen content, may help to decrease blood glucose (13). The inconsistencies in the findings may have partially originated from the different forms of chamomile supplement, small sample sizes, the species and growing conditions. Furthermore, a short duration of study may prohibit the proper observation of the effects of this plant on glycemic control.

The consumption of chamomile infusion led to a significant decrease in serum creatinine level (p= 0.03). Consistent with the present results, creatinine levels were reduced after administration of the chamomile extract in diabetic rats (18, 37); while these results are in contrast with the report of Shati et al. (23) who noticed the insignificant changes in the blood urea and creatinine in chamomile treated group in induced hepato-nephrotoxicity rats. The consumption of antioxidants is one of the most important treatment strategies to cause reduction in serum creatinine in diabetic patients. Therefore, the antioxidant activity of chamomile is accounted for this favorable effect.

The strengths of this study are as follows: the randomized design; the participants were advised to maintain their regular diet and physical activity habits during the study and as a result, these factors could not confound the findings. There are also some limitations to this research, including its single-blind design, differences at baseline values of some characteristics, short study duration, and small sample size. However, a placebo-controlled study with longer duration is recommended to determine the appropriate doses of chamomile in patients with T2DM and to elucidate its mechanism in more details on glucose and lipid metabolism.

Conclusion

The evidence from the current study revealed that chamomile infusion had beneficial effects on TC, LDL-C and serum creatinine in patients with T2DM. The underlying mechanisms for these desirable effects are still poorly understood. Further studies are needed to determine the antidiabetic and antihyperlipidemic effects of chamomile infusion in different doses and longer term of study.

Author contribution

F.K. contributed in conception and design and helped in analyses and interpretations of the data. Z.Y. conducted the study, wrote the manuscript, carried out the statistical analyses and contributed in the explanation of the findings. A.N.B. contributed in statistical analyses and edited the manuscript. N.B.Y. assisted in design and conducted the study. Z.Y. contributed in helped in interpretations of the findings and edited the manuscript. All authors approved the final version of manuscript.

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Ethical approval

The study protocol was approved by the Ethics Committee of Shahid Sadughi University of Medical Sciences, Yazd, Iran. It was registered at Iranian Registry of Clinical Trials website (http://www.irct.ir, identifier: IRCT 2014120918329N2). The study was performed according to declaration of Helsinki principles.

References

1. Goldenberg RM. Management of unmet needs in type 2 diabetes mellitus: the role of incretin agents. Canadian journal of diabetes. 2011 Dec 1; 35(5): 518-27.
2. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes research and clinical practice. 2010 Jan 31; 87(1): 4-14.
3. Soltanian AR, Bahreini F, Afkhami-Ardekani M. People awareness about diabetes disease and its complications among aged 18 years and older in Bushehr port inhabitants (Iran). Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2007; 1(4): 245-9.
4. Lotfi MH, Saadati H, Afzali M. Prevalence of diabetes in people aged≥ 30 years: the results of screen-ing program of Yazd Province, Iran, in 2012. Journal of research in health sciences. 2013; 14(1): 88-92.
5. Afkhami-Ardekani M, Vahidi S, Vahidi A, Ahmadieh M. The prevalence of type 2 diabetes mellitus on age of 30 years and above in Yazd province (Iranian population). Journal of Shahid Sadoughi University of Medical Sciences and Health

Services. 2001; 9(1): 22-7.
6. Abbott CA, Malik RA, van Ross ER, Kulkarni J, Boulton AJ. Prevalence and characteristics of painful diabetic neuropathy in a large community-based diabetic population in the UK. Diabetes Care. 2011; 34(10): 2220-4.
7. Frank RN. Diabetic retinopathy. New England Journal of Medicine. 2004;350(1):48-58.
8. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. New England Journal of Medicine. 1998; 339(4): 229-34.
9. Seufert J, Lübben G, Dietrich K, Bates PC. A comparison of the effects of thiazolidinediones and metformin on metabolic control in patients with type 2 diabetes mellitus. Clinical therapeutics. 2004; 26(6): 805-18.
10. Yki-Järvinen H. Thiazolidinediones. New England Journal of Medicine. 2004; 351(11): 1106-18.
11. Piedrola G, Novo E, Escobar F, Garcia-Robles R. White blood cell count and insulin resistance in patients with coronary artery disease. Annales d'Endocrinologie (Paris). 2001; 62 (1 Pt 1): 7-10.
12. UNESCO. FIT/504-RAF-48 Terminal Report: Promotion of Ethnobotany and the Sustainable Use of Plant Resources in Africa. Paris 1998. p. 60.
13. Kato A, Minoshima Y, Yamamoto J, Adachi I, Watson AA, Nash RJ. Protective effects of dietary chamomile tea on diabetic complications. Journal of agricultural and food chemistry. 2008; 56(17): 8206-11.
14. Ramadan KS, Emam MA. Biochemical evaluation of antihyperglycemic and antioxidative effects of matricaria chamomilla leave extract studied in streptozotocin-induced diabetic rats. Journal of endocrinological investigation. 2012; 2: 298-302.
15. Ganzera M, Schneider P, Stuppner H. Inhibitory effects of the essential oil of chamomile (Matricaria recutita L.) and its major constituents on human cytochrome P450 enzymes. Life sciences. 2006; 78(8): 856-61.
16. Eddouks M, Lemhadri A, Zeggwagh N, Michel J. Potent hypoglycaemic activity of the aqueous extract of Chamaemelum nobile in normal and streptozotocin-induced diabetic rats. Diabetes research and clinical practice. 2005; 67(3): 189-95.
17. Cemek M, Kağa S, imşek N, Büyükokuroğlu ME, Konuk M. Antihyperglycemic and antioxidative potential of Matricaria chamomilla L. in streptozotocin-induced diabetic rats. Journal of natural medicines. 2008; 62(3): 284-93.
18. Najla O, Olfat A, Kholoud S, Enas N, SA IH. Hypoglycemic and biochemical effects of Matricaria chamomilla leave extract in streptozotocin-induced diabetic rats. Journal of Health Sciences. 2012; 2(5): 43-8.
19. Chang SM, Chen CH. Effects of an intervention with drinking chamomile tea on sleep quality and depression in sleep disturbed postnatal women: a randomized controlled trial. Journal of advanced nursing. 2016; 72(2): 306-15.
20. Srivastava JK, Gupta S. Antiproliferative and apoptotic effects of chamomile extract in various human cancer cells. Journal of agricultural and food chemistry. 2007; 55(23): 9470-8.
21. Amsterdam JD, Li Y, Soeller I, Rockwell K, Mao JJ, Shults J. A randomized, double-blind, placebo-controlled trial of oral Matricaria recutita (chamomile) extract therapy of generalized anxiety disorder. Journal of clinical psychopharmacology. 2009; 29(4): 378.
22. Kassi E, Papoutsi Z, Fokialakis N, Messari I, Mitakou S, Moutsatsou P. Greek plant extracts exhibit selective estrogen receptor modulator (SERM)-like properties. Journal of agricultural and food chemistry. 2004; 52(23): 6956-61.
23. Gould L, Reddy CR, Gomprecht RF. Cardiac effects of chamomile tea. The Journal of Clinical Pharmacology. 1973; 13(11): 475-9.
24. Braga FT, Santos AC, Bueno PC, Silveira RC, Santos CB, Bastos JK, et al. Use of Chamomilla recutita in the prevention and treatment of oral mucositis in patients undergoing hematopoietic stem cell transplantation: A randomized, controlled, phase II clinical trial. Cancer nursing. 2015; 38(4): 322-9.
25. Rafraf M, Zemestani M, Asghari-Jafarabadi M. Effectiveness of chamomile tea on glycemic control and serum lipid profile in patients with type 2 diabetes. Journal of endocrinological investigation. 2014; 38(2): 163-70.
26. Wang Y, Tang H, Nicholson JK, Hylands PJ, Sampson J, Holmes E. A metabonomic strategy for the detection of the metabolic effects of chamomile (Matricaria recutita L.) ingestion. Journal of agricultural and food chemistry. 2005; 53(2): 191-6.
27. Khan SS, Najam R, Anser H, Riaz B, Alam N. Chamomile tea: Herbal hypoglycemic alternative for conventional medicine. Pakistan journal of pharmaceutical sciences. 2014; 27 (5 Spec No): 1509-14.
28. Gavin III JR, Alberti K, Davidson MB, DeFronzo RA. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes care. 1997; 20(7): 1183.
29. Emam MAL. Comparative evaluation of antidiabetic activity of Rosmarinus officinalis L. and Chamomile recutita in streptozotocin induced diabetic rats. Agriculture and Biology Journal of North America. 2012; 3:247-52.
30. Shati AA, El-kott AF. Phytoprotective and Antioxidant Effects of German Chamomile Extract against Dimpylate-Induced Hepato-Nephrotoxicity in Rats. Advances in Life Science and Technology. 2014;19: 33-41.
31. Weidner C, Wowro SJ, Rousseau M, Freiwald A, Kodelja V, Abdel-Aziz H, et al. Antidiabetic effects of chamomile flowers extract in obese mice through transcriptional stimulation of nutrient sensors of the peroxisome proliferator-activated receptor (PPAR) family. PLoS ONE. 2013; 8(11): e80335. http://doi.org.ololo.sci-hub.io/10.1371/journal.
32. Koch C, Reichling J, Schneele J, Schnitzler P. Inhibitory effect of essential oils against herpes simplex virus type 2. Phytomedicine. 2008;15(1):71-8.
33. Bardaweel SK, Tawaha KA, Hudaib MM. Antioxidant, antimicrobial and antiproliferative activities of Anthemis

palestina essential oil. BMC complementary and alternative medicine. 2014; 14(1): 297.
34. Kaneko T, Tahara S, Takabayashi F. Inhibitory effect of natural coumarin compounds, esculetin and esculin, on oxidative DNA damage and formation of aberrant crypt foci and tumors induced by 1, 2-dimethylhydrazine in rat colons. Biological and Pharmaceutical Bulletin. 2007; 30(11): 2052-7.
35. Al-Jubouri H, Al-Jalil B, Farid I, Jasim F, Wehbi S. The effect of chamomile on hyperlipidemias in rats. Journal of the Faculty of Medicine (Baghdad). 1990; 32(1): 5-11.
36. AL-Bayati AJ. Study the effect of chamomile on hyperlipidaemias in Guinea pigs. Kufa Journal For Veterinary Medical Sciences. 2012 Dec 15; 3(2).
37. Elbessoumy AA, Mahmoud EA. Biochemical and clinic opathological studies on some antihyperglycemic herbal preparations in alloxan induced diabetic rats. Scholars Journal of Applied Medical Sciences (SJAMS). 2013; 1(2): 48-55.
38. Guimarães R, Calhelha RC, Froufe HJ, Abreu RM, Carvalho AM, João M, et al. Wild Roman chamomile extracts and phenolic compounds: enzymatic assays and molecular modelling studies with VEGFR-2 tyrosine kinase. Food & function. 2016; 7(1): 79-83.
39. Darvishpadok MA, Namjoyan F, Khodayar M, Ahmadpour F, M Panahi A. Effect of Matricaria chamomilla L. on blood glucose and glycosylated hemoglobin in female fertile diabetic rats. Research in Pharmaceutical Sciences. 2012; 7(5): S19.
40. Lemhadri A, Eddouks M, Sulpice T, Burcelin R. Antihyperglycaemic and anti-obesity effects of Capparis spinosa and Chamaemelum nobile aqueous extracts in HFD mice. American Journal of Pharmacology and Toxicology. 2007; 2(3): 106-10.

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