scientific reports

Check for updates

OPEN

Cardiometabolic risk factors are affected by interaction between FADS1 rs174556 variant and dietary vegetable oils in patients with diabetes: a randomized controlled trial

Zahra Fallah[1,2,9], Azam Ahmadi Vasmehjani[1,2,9], Shiva Aghaei[3], Mojgan Amiri[4], Hamidreza Raeisi-Dekordi[5], Fatemeh Moghtaderi[1,2], Alireza Zimorovat[1,2], Ehsan Farashahi Yazd[3], Farzan Madadizadeh[6,7], Sayyed Saeid Khayyatzadeh[1,2]✉ & Amin Salehi-Abargouei[1,2,8]

FADS1 rs174556 polymorphism influences on dietary fats metabolism and type 2 diabetes (T2DM). This study aimed to compare the effect of three oils of sesame, canola and sesame-canola on cardio metabolic factors across genotypes of rs174556 variant in patients with type 2 of diabetes. This study was a randomized triple-blind three-way cross-over clinical trial. 95 Subjects with T2DM replaced their regular dietary oil with sesame oil, canola oil, or sesame-canola oil for three 9-week phases and completed the study. There were three anthropometric measurements, blood sampling and biochemical assessments at the beginning, middle, and at the end of each phase for assessments. Genotyping was conducted using the polymerase chain reaction-restriction fragment length polymorphism (PCR–RFLP) method. In the crude model, there was an interaction between consumed oils and rs174556 variant on serum concentration of Apolipoprotein A-I (ApoA-1). During intake of sesame oil, lower levels of triglycerides (TG) were observed in individuals with TT genotype compared to C allele carriers' allele, which remained significant in adjusted models. Compared to C allele carrier's, the people with TT genotype experienced significant increase and decrease in serum levels of HDL and TG, respectively in adjusted models. Also, the subjects who consumed sesame-canola oil had lower serum concentrations of fasting blood glucose than those who received sesame and canola oils, regardless of used oils and genotypes. FADS1 Gene variant (rs174556) might modify cardiometabolic changes following dietary vegetable oils. Larger longitudinal studies especially randomized clinical trials are needed to clarify these associations.

Keywords Type 2 diabetes, Sesame oil, Canola oil, Lipid profile, Fasting blood glucose, FADS1 rs174556

[1]Research Center for Food Hygiene and Safety, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. [2]Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd 8914715645, Iran. [3]Stem Cell Biology Research Center, Yazd Reproductive Sciences Institute, Yazd, Iran. [4]Department of Epidemiology, Erasmus MC, University Medical Center Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands. [5]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands. [6]Center for Healthcare Data Modeling, Departments of Biostatistics and Epidemiology, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. [7]Environmental Science and Technology Research Center, Department of Environmental Health Engineering, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. [8]Yazd Cardiovascular Research Center, Non-Communicable Diseases Research Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. [9]Equal contribution as first author. ✉email: Khayyatzadeh@yahoo.com

Type 2 diabetes (T2DM) is a growing global health challenge that needs effective management[1,2]. Modifiable environmental factors and various biomarkers are involved in T2DM[3,4]. Diets have been shown associated with metabolic condition related to T2DM[5], and nutritional interventions can play a key role in reducing the complications of T2DM[6,7]. Dietary fats which consist of fatty acids can influence on lipid profile and glycemic levels as evidenced by previous studies[8,9]. Several reports studies have suggested that unsaturated fatty acids (UFAs), which include mono- (MUFAs) and polyunsaturated fatty acids (PUFAs), are better alternatives than saturated fatty acids (SFAs)[10–14].

Plant-based oils, such as canola oil and sesame oil, are rich in UFAs, including MUFA (oleic acid), PUFAs (alpha-linolenic acid, linoleic acid), and antioxidants[15,16]. These have been shown to improve cardio metabolic markers[17,18]; however, some other studies have reported conflicting results[19–21].

Evidence has shown that genetic variants, such as single nucleotide polymorphisms (SNPs), can interact with dietary factors and influence on metabolic markers differently in subjects[22,23]. The FADS1 gene, which encodes the enzyme delta-5 desaturase (D5D), is located on the long arm of chromosome 11 (11q12–13.1). It has a SNP at position rs174556 in its promoter region, which changed the major allele G to the minor allele T[24–26]. Subjects with T allele have shown lower levels of long chain fatty acids including Eicosapentaenoic acid (EPA), Docosahexaenoic acid (DHA) and arachidonic acid (AA) than those with the G allele[27,28], this may increase their risk of coronary heart disease (CHD)[29]. Previous studies reported an interaction between the T allele and n-3 fatty acid supplementation on glucose homeostasis[30] and serum lipid and lipoprotein levels[26,31].

Since rs174556 SNP and edible vegetable oils play a role in lipid metabolism and glycemic parameters, their interaction may influence on risk factors of cardiovascular diseases (CVDs). To our knowledge, no previous studies have investigated the interaction between vegetable oils (sesame, sesame-canola, and canola) and the rs174556 variant on metabolic outcomes, hence this study aimed to examine how this interaction can influences on biochemical biomarkers, such as glycemic indices and serum lipid and lipoproteins concentration, in patients with T2DM.

Method and material

Participants

Present study that compared the effects of sesame, canola, and sesame-canola oils on cardio metabolic biomarkers in patients with T2DM, used data from a three-way cross-over clinical trial. The detailed methodology is reported in another publication[32].

All participants provided written informed consent before enrollment in the study. This trial was registered in the Iranian Registry of Clinical Trials (registration ID: IRCT2016091312571N6; in date 14/11/2016) and approved by the ethics committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (IR.SSU.SPH.REC.1399.120). All methods were carried out in accordance with relevant guidelines and regulations.

In total, 102 diabetic patients were recruited from the Yazd Diabetes Research Center and included in trail based on the following criteria; 1) having a history of type 2 diabetes for at least six months (fasting blood sugar (FBS) $\geq$ 126 mg/dL or HbA1c $\geq$ 6.5%, 2) taking oral anti-glycemic medications, 3) being between 18 and 60 years old. Exclusion criteria were; 1) history of CVDs (coronary artery disease (CAD), stroke, congestive heart disease (CHD), and coronary artery bypass grafting (CABG), cancer, kidney diseases, liver diseases, 2) insulin therapy or changing oral drug therapy to insulin, 3) adherence to a special diet 4) changes in the dosage or type of medications affect the lipid profile within the previous three months, 5) pregnancy.

Sampling size

The sample size was determined by a formula for cross-over studies[33], assuming the type one error of 5%, power of 90% and FBS as the key variable resulting a total of n = 34 participants. The formula was as follows: $n = [(z\ 1\text{-}\alpha/2 + z\ 1\text{-}\beta)^2 * s^2]/2\Delta^2$. However, in total considered a sample size of n = 100 with probability of high rate of attrition.

Method of intervention

Initially, participants underwent a four-week run-in period, which they replaced their usual cooking oils with sunflower oil, they completed three 9-week intervention periods with sesame oil, canola oil, and sesame-canola oil (a blend of sesame oil (40%) and canola oil (60%)]), separated by 4-week washout periods. The participants used sunflower oil instead of their regular cooking oils during washout periods. A person who was unaware of the study protocol labeled the oil packs was similar by three codes (S, B, and G). Specific methods for randomization, allocation concealment, and blinding described in the published protocol[32].

Dietary intake and physical activity

The participants recorded 3-day weighed food and a 3-day physical activity record (2 weekdays and 1 weekend day) at the start, middle, and end of each 9-week intervention phase. Food record trained by nutritionists and also required tools given to subjects. The daily intake of energy and nutrients calculated using Nutritionist IV software (version 3.5.2, Axxya Systems, Redmond, Washington, USA), modified for Iranian foods. Physical activities were converted metabolic equivalent (MET)-min/day.

Anthropometric and blood pressure measurements

Anthropometric parameters measured at the run in period and then at the beginning, middle, and end each treatment phase by nutritionists. They weighed on a digital scale (Omron, Japan, model: BF51) that had an accuracy of 100 g while stepped on the scale without shoes and had light clothes. Height measured using a wall-fixed tape that had an accuracy of 0.1 cm. Body mass index (BMI) calculated by dividing weight (kg) to height squared (m^2). As well, waist to hip ratio (WHR) calculated by dividing the waist circumference by

hip circumference. Visceral fat, body fat percentage, and lean mass were evaluated using a body composition analyzer (model BF51, Omron, Japan).

Blood pressure (BP) measured three times in each visit using a sphygmomanometer (Riester, model: Diplomat-presameter), after five minutes of rest in the sitting position, for the right arm with at least one-minute interval.

Laboratory

Venous blood samples collected from participants at the start and end of each intervention, after they had fasted for 10–12 h. The samples were stored at -80°C until analysis. An auto-analyzer (Alphaclassic, model: ATþþ) measured the blood levels of lipids, lipoproteins, Apolipoproteins, lipoprotein (a) [Lp (a)], fasting blood glucose (FBG), insulin and liver enzymes [alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gammaglutamyltransferase (GGT)] using Pars Azmun kits (Pars Azmun Co., Iran). The researchers used enzyme-linked immunoassay (ELISA) kits (Monobind, Inc., Lake Forest, CA, USA) to measure the fasting serum insulin concentrations. They calculated the hemostatic model assessment of insulin resistance (HOMA-IR) using suggested formulas[34].

DNA extraction and genotyping

The DNJia Blood Kit based on silica technology (Roje Technologies Inc, Iran) used to extract genomic DNA from 250 µL of whole blood samples. PCR–RFLP method used to identify the rs174556 SNP genotypes. As a 153 base pair (bp) fragment amplified by PCR. The PCR mixture was provided in a total volume of 20 µL containing; 2 µL of genomic DNA, 10 µL of Master Mix (Ampliqon, Denmark), 6 µL of water and 1 µL of each oligonucleotide primer (forward: AAG CAG GGA CCT CAA GAC and reverse: AGC CCACCA AGA ATG TAA). DNA was denatured at 94 °C for 5 min; this was followed by 40 cycles of amplification at 95 °C for 30 s, annealing at 52 °C for 30 s, extension at 72 °C for 30 s, and ended with a final extension at 72 °C for 5 min. The PCR products were digested with 1 µL of the restriction endonuclease enzyme Mbo1 (Fermentase) in a total volume of 20 µL after incubation at 37 °C overnight. The digested DNA fragments (8 µL) were loaded on 3% agarose gel (SinaClon, Iran) and subjected to electrophoresis for 2 h at 19-24 V, and were finally visualized by an ultraviolet transilluminator. The TT genotype had two bands of 97 and 56 bp, and the CC was characterized by one fragment of 153 bp in length and TC had 97, 56 and 153 bp.

Statistical analysis

Kolmogorov–Smirnov test used if the data followed a normal distribution. Analysis of covariance (ANCOVA) used to evaluate the mean values of the initial variables among different genotypes of the rs174556 polymorphism in both unadjusted and adjusted models. Linear mixed models used to compare the changes in lipid profile and glycemic indices in comparisons of the within-between periods of intervention and genotypes. Interaction between edible oils and rs174556 SNP on lipid profile and glycemic index examined by linear mixed models. Crude model and adjusted for age, gender, baseline BMI, and oil consumption, changes in energy intake and physical activity was done in each period. Data were reported as mean ± standard error (SE). Statistical analysis was performed using IBM SPSS (version 20, IBM Corporation, USA). A p-value of less than 0.05 was used as the criterion for statistical significance in all analyses.

Results

Out of 102 patients with T2DM, 94 (48 female and 46 male) followed the study protocol and entered the final analysis. Figure 1 shows the flow diagram of the participants' attendance in the trial. The genotype frequency of FADS1 rs174556 variant was for CC 59.57% (n = 56), for CT 23.40% (n = 22), and for TT 17.02% (n = 16). There was no significant difference in the mean age or gender distribution of subjects across rs174556 genotypes.

General characteristics of study participants including (demographic, anthropometric, and biochemical parameters) across genotypes of rs174556 variant were presented in Table 1. In the unadjusted model, TG and ALT levels were significantly different among the rs174556 genotypes (P = 0.02) and (P = 0.03), respectively. So that, TT carriers had higher levels of TG and ALT compared with other genotypes. No significant difference showed in levels of the other variables by the rs174556 genotypes (P > 0.05). Age- and gender-adjusted analyses showed no significant difference in the studied indices across rs174556 genotypes, except for ALT and AST levels, which were significantly higher in TT subjects than in other genotypes (P = 0.04 for both).

The effect of dietary oils on glycemic indices, lipid profile and Apolipoproteins in patients with T2DM according to the rs174556 FADS1 genotypes

In the crude model, neither the consumed oils nor the genotypes had an independent effect on the studied outcomes (P > 0.05), but their interaction significantly affected on ApoA-1 levels (P = 0.04). In unadjusted model and after controlling possible confounders (age, gender, average oil intake, baseline BMI, changes in energy intake and physical activity in each period), intra-period analyses showed no significant difference in any of the outcomes across different genotypes in all oil consumption periods. Moreover, inter-period analyses revealed no independent or interaction effects of intervention oils and genotype on any of the outcomes (P > 0.05), as shown in Tables 2, 3.

In crude model, within-period analysis showed, the TT genotype was associated with lower TG levels than those carrying C allele consuming sesame oil, which it remained significant after adjusting for potential confounders including age, gender, average oil intake, baseline BMI, changes energy intake and physical activity in each period. Between-period analysis in adjusted model diagnosed that subjects with TT genotype compared with carrier's allele C had a significant increase in levels of HDL (0.02) and also significantly had a decrease in levels of TG (0.04), other outcomes were not affected by the type of analysis in the models, nor their interaction,

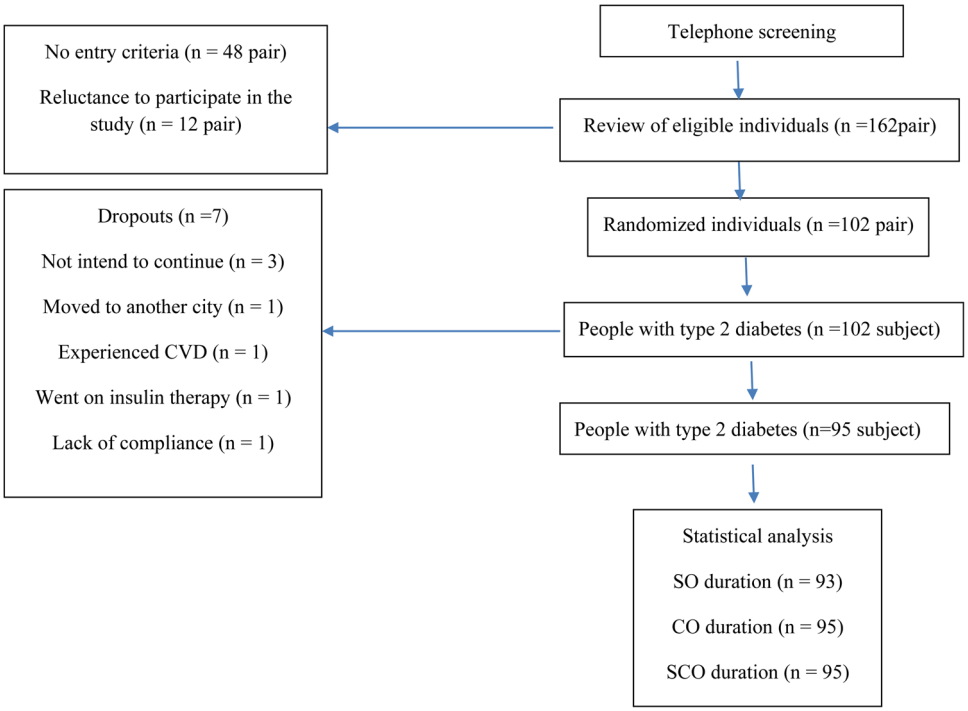

Fig. 1. The flow diagram of the attendance of study participants. CVD, cardiovascular disease; CO, canola oil; SO, sesame oil; SCO, sesame-canola oil.

as indicated in Table 4. The between-period analysis showed that the subjects who consumed sesame-canola oil had lower levels of FBS than those who consumed sesame or canola oils, regardless of their genotypes (P = 0.04). The intra-period analyses in both crude and adjusted models showed no significant differences in any of the outcomes between the T allele carriers and the CC genotype in all periods of oils consumption. Other outcomes were not affected by the type of analysis in models, nor their interaction, as presented in Table 5.

Discussion

Differences between the three triglyceride polymorphisms were observed only in the crude model. However, this significance was lost when adjusting for sex and age, indicating that the interaction between the rs174556 genotypes, and age as well as sex can influence on plasma TG concentration. We found the intervened oils and rs174556 genotypes did not affect independently on metabolic indices; however, their interaction was significant on the Apo-A1 levels only in the unadjusted model. In the adjusted model, people with TT genotype compared with carrier's allele C had a significant increase in levels of HDL and significantly a decreased level in TG while it observed independent of intervened oils. Moreover, TT genotype was associated with lower TG levels than those carrying C allele consuming sesame oil in both unadjusted and adjusted models. Subjects intervened by sesame-canola oil compared to other oils studied had significantly a decreased levels of FBG; of course, this finding was independent of genotypes.

A review study showed canola oil in comparison with olive and sunflower oils, can reduce FBS, serum lipid levels and lipoproteins ratio[35]. A clinical trial showed people with T2DM that intervened by sesame oil, compared with the control group had a decreased levels of FBS and HbA1C but increased levels of insulin[36], As sohouli et al. also indicated positive effects of sesame products on FBG and HA1C levels[37]. These differences may be related to the fatty acids profile used in the oils of the studies, as in our study, the sesame-canola oil compared to sesame or canola oils contained in different amounts of MUFA and PUFA.

In line with results of this study, a meta-analysis showed replacing SFA with PUFA lead to a favorable results in blood sugar, insulin resistance and insulin secretion capacity, while it shown less favorable changes on HbA1c and HOMA-IR levels by replacing with MUFAs[10]. It is possible that PUFAs by increasing membrane fluidity and insulin sensitivity reduce the risk of T2DM. In addition, sesame-canola oil contains MUFA, which may enhance the effects of PUFA on fasting insulin levels and insulin sensitivity[38]. Although, the exact mechanism is still unknown. Possibly, in the present study effect of canola oil or sesame on the increase of FBG, could be attributed to increased consumption of the PUFA and decreased of the MUFA that may increase pro-inflammatory markers such as prostaglandin E2 and leukotriene B4 and decrease anti-inflammatory markers including resolvins, docosatrins and proteins that is related to impaired glucose tolerance and insulin resistance[10]. However, the role of rs174556 alleles in the FADS1 gene in the observed associations remains unclear.

Khalesi et al.[19] Showed sesame oil can reduce levels of the TG but had no significant change on TC, LDL-C, and HDL-C levels. Another study[39] found daily intake of sesame oil to decrease serum levels of TC, LDL-C and TG. The evidence suggests that this effect may be mediated by inhibiting of the cholesterol intestinal absorption

Variables	Model Crude			*P*-value*	Model adjusted			*P*-value*
	FADS1 rs174556				FADS1 rs174556			
	CC	CT	TT		CC	CT	TT	
N/ Female	56/30	22/11	16/7	0.913	56/30	22/11	16/7	0.913
Age , year	49.86(0.897)	49.90(1.44)	45.80(1.74)	0.108	49.87(0.899)	49.89(1.44)	45.75(1.75)	0.103
Weight, kg	75.23(1.84)	78.15(2.96)	79.90(3.59)	0.439	75.92(1.53)	78.54(2.46)	76.72(3.04)	0.666
BMI, kg/m^2	28.52(0.502)	29.31(0.80)	29.55(0.97)	0.531	28.60(0.49)	29.41(0.78)	29.10(0.97)	0.661
WC, cm	100.21(1.21)	102.61(1.96)	101.66(2.37)	0.558	100.46(1.19)	102.82(1.91)	100.39(2.36)	0.556
Visceral fat, %	10.41(0.478)	10.97(0.770)	11.20(0.932)	0.687	10.48(0.398)	10.92(0.639)	11.01(0.790)	0.752
Body fat, %	33.04(1.28)	34.43(2.06)	34.04(2.50)	0.828	32.89(0.738)	34.70(1.18)	34.17(1.46)	0.388
Muscle mass,%	30.02(1.28)	29.22(1.11)	29.92(1.34)	0.825	30.15(0.325)	29.10(0.523)	29.61(0.646)	0.229
SBP, mm Hg	10.33(0.187)	10.43(0.301)	10.04(0.364)	0.702	10.30(0.174)	10.38(0.279)	10.24(0.345)	0.951
DBP, mm Hg	7.37(0.152)	7.31(0.24)	7.30(0.29)	0.965	7.38(0.15)	7.31(0.24)	7.27(0.30)	0.933
TC, (mg/dl)	160.47(4.24)	155.27(6.83)	173.66(8.27)	0.223	160.40(4.08)	155.72(6.56)	173.26(8.11)	0.239
HDL-C, mg/dl	39.43(1.43)	36.77(2.30)	33.80(2.79)	0.176	39.03(1.34)	36.47(2.16)	35.79(2.67)	0.418
LDL-C, (mg/dl)	80.98(2.48)	77.54(3.99)	85.10(4.83)	0.485	80.91(2.43)	77.72(3.90)	85.08(4.83)	0.501
TG, (mg/dl)	149.15(10.08)	140.47(16.23)	206.63(19.65)	**0.022**	151.03(9.86)	142.50(15.85)	196.52(19.60)	0.081
LP(a), (mg/dl)	22.70(3.19)	24.20(5.04)	18.14(4.56)	0.758	22.89(3.22)	24.32(5.08)	17.14(6.71)	0.681
LDL:HDL	2.34(0.192)	2.43(0.309)	2.80(0.374)	0.553	2.38(0.187)	2.47(0.301)	2.60(0.372)	0.858
TC:HDL	4.65(0.399)	4.91(0.642)	5.74(0.778)	0.463	4.73(0.388)	5(0.623)	5.30(0.770)	0.783
TG:HDL	5(0.858)	5.27(1.38)	7.30(1.67)	0.472	5.18(0.836)	5.44(1.34)	6.37(1.66)	0.818
Apo B, (mg/dl)	97(4.50)	88.45(7.24)	97.23(8.77)	0.585	97.31(4.54)	88.78(7.30)	95.59(9.02)	0.611
ApoA-1, (mg/dl)	152.66(3.46)	145.45(5.58)	156.66(6.76)	0.397	152.04(3.29)	145.26(5.28)	159.31(6.53)	0.249
FBG (mg/dl)	114.48(3.71)	118.70(5.97)	115.30(7.23)	0.835	114.70(3.74)	118.98(6.02)	114.04(7.44)	0.812
Insulin, (mIU/ml)	30.64(2.74)	25.18(4.62)	25.94(5.20)	0.510	30.94(2.74)	25.48(4.61)	24.48(5.30)	0.413
HOMA-IR	8.96(0.82)	7.38(1.39)	6.76(1.57)	0.366	9.05(0.828)	7.45(1.39)	6.36(1.60)	0.274
ALP, (U/L)	178.88(6.15)	205.77(9.90)	182.60(11.99)	0.073	178.67(6.16)	205.94(9.90)	183.15(12.24)	0.068
GGT, (U/L)	29.83(1.92)	27.60(3.09)	28.85(3.74)	0.825	29.99(1.90)	27.61(3.06)	28.20(3.78)	0.775
AST, (U/L)	23.20(1.57)	21.01(2.53)	29.94(3.07)	0.074	23.09(1.57)	20.83(2.52)	30.60(3.11)	**0.049**
ALT, (U/L)	25.78(2.15)	35.21(3.47)	35.59(4.20)	**0.035**	25.94(2.10)	21.29(3.38)	35.03(4.18)	**0.043**

Table 1. Demographic, anthropometric, and biochemical characteristics of type 2 diabetes patients across FADS1 rs174556 genotypes (N = 94). All data are presented as mean ± standard error. DBP, diastolic blood pressure; FBG, fasting blood glucose; GGT, gamma-glutamyltransferase; HDL-C, High-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; LDL-C, Lowdensity lipoprotein cholesterol; Lp(a), lipoprotein a; QUICKI, quantitative insulin sensitivity check index; SBP, Systolic blood pressure; TC, total cholesterol; TG, Triglyceride; WC, waist circumference. The mean initial values of the variables between genotypes measured using Analysis of Covariance (ANCOVA) test in both unadjusted and adjusted models (for age and sex adjusted).

and its synthesis, increased biliary excretion, and decreased activity of Acyl CoA reductase[16,39]. Additionally, the antioxidant compounds in sesame may prevent lipid peroxidation[40] and affect the gene expression of enzymes and proteins involved in dietary fat metabolism and fatty acid transport[41].

Wided Khamlaudi et al.[42] Showed that the minor allele in the FADS1 and FADS2 genes was associated with a decrease in TG and LDL-C levels. As, Meng-chuan huang et al.[43] Showed that the minor C allele of some polymorphisms of them can reduce the activity of delta-5 and delta-6 desaturase enzymes and lower the levels of HDL-C, which confirmed by Khathirresen[44].

A recent meta-analysis[45] in patients with T2DM showed that consumption of omega-3 fatty acids, especially EPA and DHA, can reduce serum TG levels. Evidence suggests that association the different FADS gene cluster polymorphisms with cholesterol levels related to the availability of long chain PUFAs and their effects on the homeostasis of glycerophospholipids[46].

Apo-A1, one of the most abundant components of HDL-C[47], that has not been studied in relation to the rs174556 polymorphism alleles of the FADS1 gene. A study on hypercholesterolemic subjects found that derivatives of sesame oil did not alter Apo-A1 and HDL-C levels in the treatment groups versus the control group, but they significantly lowered TG levels and the ApoB/Apo-A1 ratio[48].

A randomized crossover study showed that canola oil, compared to sesame oil, significantly improved serum Apo-A1 levels and the ApoB/Apo-A1 ratio in men. also, sesame oil compared to sesame-canola oil, , improved serum HDL-C and TG levels in women[49]. A clinical trial[50] did not show any change in Apo-A1, TG

Variable	Sesame oil			Sesame-Canola oil			Canola oil			P[1]	P[2]	P[3]
	CC	CT	TT	CC	CT	TT	CC	CT	TT			
Glycemic indices												
FBG, mg/dl	3.50(2.92)	1.52(4.62)	3.02(5.79)	-1.31(4.11)	-5.36(6.62)	0.23(8.02)	6.71(3.83)	14.38(6.16)	0.73(7.47)	0.15	0.92	0.64
Insulin, m IU/ml	-10.32(3.23)	-3.77(5.11)	-2.66(6.18)	-5.19(1.96)	-4.75(3.17)	-10.18(3.83)	-9.18(5.36)	24.58(8.62)	0.56(10.45)	0.63	0.42	0.15
HOMA-IR	-1.86(0.65)	-0.81(1.03)	-0.75(1.29)	-1.64(0.62)	-1.79(1)	-2.01(1.21)	-0.69(0.61)	-0.22(1.05)	0.12(1.18)	0.96	0.15	0.91
lipid profile and Apo lipoproteins												
TC, mg/dl	5.01(3.64)	-3.54(5.76)	-2.21(7.22)	-1.76(3.95)	0.09(6.36)	6.80(7.70)	2.12(3.43)	5.45(5.52)	-7.73(6.69)	0.91	0.85	0.29
HDL-C, mg/dl	- 0.31(1.12)	-2.19(1.76)	5.32(2.21)	0.87(1.04)	0.09(1.67)	2.82(2.03)	1.22(1.06)	1.95(1.69)	0.20(2.05)	0.97	0.13	0.28
LDL-C, mg/dl	2.04(2.05)	-2.61(3.24)	-1.17(4.06)	-1.84(2.36)	0.56(3.80)	4.83(4.61)	0.68(2.07)	1 (3.34)	-2.06(0.05)	0.88	0.90	0.46
TG, mg/dl	13.16(10.11)	12.04(16.01)	24.65(20.03)	-5.63(9.68)	6.88(15.58)	-6.10(18.86)	-0.43(8.98)	9.04(14.64)	21.36(17.51)	0.93	0.12	0.85
LP(a), mg/dl	-0.62(1.70)	-0.67(2.60)	1.23(1.51)	2.51(1.27)	-0.57(2.03)	3.04(2.68)	-0.02(1.93)	-3.36(3.04)	-1.43(3.87)	0.28	0.46	0.90
LDL:HDL	0.02(0.09)	0.10(0.15)	-0.28(0.18)	-0.41(0.28)	-0.03(0.45)	-0.07(0.55)	-0.08(0.24)	-0.30(0.39)	-0.07(0.48)	0.90	0.98	0.68
TC:HDL	0.03(0.19)	0.27(0.30)	-0.57(0.38)	-0.84(0.63)	-0.03(1.01)	-0.26(1.23)	0.17(0.53)	0.55(0.85)	-0.26(1.02)	0.88	0.94	0.76
TG:HDL	-0.17(0.47)	0.94(0.75)	-1.26(0.93)	-1.99(1.59)	0.02(2.56)	-0.68(3.10)	0.19(1.22)	-0.96(1.95)	-0.74(2.36)	0.87	0.86	0.83
Apo B, mg/dl	-0.32(2.68)	-1.34(4.28)	-1.23(5.31)	-4(5.79)	-3.88(5.31)	5.16(7.01)	0.33(2.88)	0.61(4.63)	-2.76(5.61)	0.99	0.87	0.81
ApoA-1, mg/dl	0.55(2.68)	-8.31(4.24)	2.97(5.32)	-1.64(2.66)	0.72(4.29)	4.90(5.20)	4.29(2.97)	11.43(4.78)	-5.73(5.79)	0.39	0.99	**0.04**

Table 2. Change values in glycemic indices, lipid profile, Apolipoproteins in patients with type 2 diabetes across intervention periods and FADS1 rs174556 genotypes (n = 94). All data are presented as mean ± standard error. ApoA-1, apolipoprotein A-I; ApoB, apolipoprotein B; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase, BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; GGT, gamma-glutamyltransferase; HDL-C, High-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; LDL-C, Low-density lipoprotein cholesterol; Lp(a), lipoprotein a; QUICKI, quantitative insulin sensitivity check index; SBP, Systolic blood pressure; TC, total cholesterol; TG, Triglyceride; WC, waist circumference. *P*1, Interperiod comparison of change values between the treatment oils durations using linear mixed models, in **unadjusted** model. *P*2, Interperiod comparison of change values across the genotypes using linear mixed models, in **unadjusted** model. *P*3, interaction between FADS1 rs174556 variant and treatment oils on the outcomes using linear mixed models, in **unadjusted** model.

Variable	Sesame oil			Sesame-Canola oil			Canola oil			P[1]	P[2]	P[3]
	CC	CT	TT	CC	CT	TT	CC	CT	TT			
Glycemic indices												
FBG, mg/dl	1.64(2.73)	0.69(4.31)	3.20(5.47)	1.63(4.22)	-5.42(6.78)	-3.14(8.30)	7.28(3.99)	13.92(6.40)	1.14(7.84)	0.092	0.899	0.731
Insulin, m IU/ml	-10.47(3.39)	-4.28(5.34)	-3.07(6.54)	-5.08(1.97)	-3.01(3.17)	-9.73(3.88)	-9.55(5.65)	-25.60(9.06)	0.18(11.10)	0.586	0.479	0.177
HOMA-IR	-1.99(0.67)	-1.04(1.04)	-0.874(1.33)	-1.62(0.63)	-1.34(1.01)	-2.01(1.24)	-0.68 (0.65)	-0.28(1.10)	0.065(1.25)	0.246	0.674	0.945
lipid profile and Apo lipoproteins												
TC, mg/dl	4.82(3.73)	-2.09(5.88)	-1.05(7.47)	-2.49(4.10)	2.75(6.57)	5.07(8.05)	2.48(3.51)	6.09(5.63)	-3.32(6.89)	0.95	0.96	0.54
HDL-C, mg/dl	-0.77(1.15)	-1.74(1.80)	5.62(2.29)	0.30(1.03)	-0.11(1.66)	1.99(2.03)	1.19(1.06)	1.92(1.68)	1.75(2.06)	0.76	0.06	0.50
LDL-C, mg/dl	1.86(2.12)	-2.21(3.34)	-0.56(4.25)	-2.31(2.45)	-0.57(3.93)	3.46(4.82)	1.02(2.14)	1.42(3.44)	-0.14(4.21)	0.91	0.93	0.67
TG, mg/dl	16.22(10.57)	13.33(16.67)	-23.86(21.12)	-1.13(9.53)	7.31(15.29)	-8.60(18.72)	-1.24(9.39)	10.47(15.07)	-19.78(18.45)	0.91	0.10	0.90
LP(a), mg/dl	-0.94(1.80)	-0.82(2.73)	1.75(3.76)	1.80(1.21)	-0.73(1.92)	3.11(2.59)	-0.09(2.05)	-3.50(3.22)	-1.60(4.15)	0.34	0.49	0.91
LDL:HDL	0.05(0.09)	0.09(0.15)	-0.25(0.19)	-0.42(0.29)	-0.02(0.47)	-0.03(0.58)	0.11(0.26)	-0.30(0.41)	-0.11(0.51)	0.91	0.98	0.69
TC:HDL	0.09(0.20)	0.22(0.31)	-0.52(0.40)	-0.85(0.66)	-0.02(1.06)	-0.16(1.31)	0.21(0.56)	-0.55(0.89)	0.33(1.09)	0.88	0.95	0.77
TG:HDL	-0.05(0.50)	0.95(0.78)	-1.26(0.99)	-1.95(1.68)	-0.09(2.69)	-0.65(3.29)	0.22(1.29)	-0.96(2.05)	-0.80(2.51)	0.87	0.87	0.85
Apo B, mg/dl	-0.29(2.82)	-1.19(4.44)	-0.85(5.63)	-4.65(3.70)	-4.11(5.93)	2.35(7.27)	0.88(3.01)	1.26(4.83)	-1.75(5.92)	0.87	0.94	0.92
ApoA-1, mg/dl	-0.04(0.45)	-4.14(3.86)	4.03(4.90)	-2.14(2.67)	0.81(4.28)	2.17(5.25)	4.14(3.01)	12.07(4.83)	-1.78(5.91)	0.33	0.75	0.24

Table 3. Change values in lipid profile, Apolipoproteins and glycemic indices in patients with type 2 diabetes across intervention periods and FADS1 rs174556 genotypes (n = 94). All data are presented as mean ± standard error. ApoA-1, apolipoprotein A-I; ApoB, apolipoprotein B; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase, BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; GGT, gamma-glutamyltransferase; HDL-C, High-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; LDL-C, Low-density lipoprotein cholesterol; Lp(a), lipoprotein a; QUICKI, quantitative insulin sensitivity check index; SBP, Systolic blood pressure; TC, total cholesterol; TG, Triglyceride; WC, waist circumference. *P*1, Interperiod comparison of change values between the treatment oils durations using linear mixed models, **adjusted** for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake. *P*2, Interperiod comparison of change values across the genotypes using linear mixed models, **adjusted** for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake. *P*3, interaction between FADS1 rs174556 variant and treatment oils on the outcomes using linear mixed models, **adjusted** for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake.

Variable	Sesame oil		Sesame-Canola oil		Canola oil		P[1]	P[2]	P[3]
	CC/CT	TT	CC/CT	TT	CC/CT	TT			
Crude model									
FBG, mg/dl	2.94(2.46)	3.02(5.76)	-2.44(3.48)	0.23(7.98)	8.85(3.25)	0.73(7.47)	0.54	0.71	0.61
Insulin, m IU/ml	-8.45(2.73)	-2.66(6.19)	-5.07(1.66)	-10.18(3.81)	-13.47(4.58)	0.56(10.52)	0.86	0.26	0.17
HOMA-IR	-1.56(0.55)	-0.75(1.29)	-1.68(0.52)	-2.01 (1.20)	-0.57(0.53)	0.12(1.17)	0.21	0.59	0.78
TC, mg/dl	2.55(3.09)	-2.18(7.24)	-1.24(3.34)	6.80(7.66)	3.05(2.90)	-7.43(6.66)	0.63	0.61	0.21
HDL-C, mg/dl	-0.85(0.94)	5.33(2.20)	0.65(0.88)	2.89(2.02)	1.43(0.89)	0.20(2.04)	0.69	0.05	0.11
LDL-C, mg/dl	0.70(1.73)	-1.16(0.07)	-1.48(2)	4.83(4.59)	0.77(1.75)	-2.06(4.02)	0.76	0.85	0.33
TG, mg/dl	12.87(8.50)[a]	-24.68(19.92)	-2.13(8.19)	-6.100(18.8)	2.20(7.60)	-21.36(17.44)	0.90	0.05	0.56
LP(a), mg/dl	-0.62(1.41)	1.22(3.49)	1.63(1.08)	3.04(2.69)	-0.98(1.63)	-1.43(3.87)	0.33	0.67	0.91
LDL:HDL	0.04(0.08)	-0.28(0.18)	-0.30(0.24)	-0.07(0.55)	-0.02(0.21)	-0.07(0.48)	0.92	0.86	0.67
TC:HDL	0.10 (0.16)	-0.57(0.38)	-0.61(0.53)	-0.26(1.22)	-0.02(0.45)	-0.26(1.02)	0.93	0.77	0.76
TG:HDL	0.13 (0.40)	-1.27 (0.94)	-1.41(1.34)	-0.68(3.09)	-0.13(1.03)	-0.74(2.35)	0.94	0.78	0.80
Apo B, mg/dl	-0.61(2.25)	-1.23(5.29)	-3.96(3.04)	5.16(6.97)	0.41(2.43)	-2.76(5.58)	0.93	0.60	0.46
ApoA-1, mg/dl	-1.99(2.29)	3.04(5.38)	-0.98(2.25)	4.90(5.18)	6.28(2.53)	-5.73(5.81)	0.90	0.91	0.06
Adjusted model									
FBG, mg/dl	1.37(2.29)	3.20 (5.44)	-2.69 (3.57)	-3.14 (6.26)	9.14 (3.38)	1.14 (7.38)	0.36	0.66	0.63
Insulin, m IU/ml	-8.70 (2.86)	-3.07(6.54)	-4.48 (1.57)	-9.73 (3.86)	-14.05 (4.83)	0.18 (11.18)	0.95	0.30	0.19
HOMA-IR	-1.71(0.56)	-0.87(1.32)	-1.54 (0.53)	-2.01 (1.23)	-0.58 (0.55)	0.06 (1.24)	0.27	0.66	0.74
TC, mg/dl	2.82(3.15)	-1.02 (7.47)	-1.79 (3.46)	5.07(8.01)	3.49 (2.96)	-3.32 (6.86)	0.95	0.80	0.44
HDL-C, mg/dl	-1.06 (0.97)	2.62 (2.28)[a]	0.18 (0.87)	1.99 (2.02)	1.40 (0.89)	1.75 (2.05)	0.78	**0.02**	0.22
LDL-C, mg/dl	0.68(1.79)	-0.55(4.25)	-1.82 (2.07)	3.46 (4.79)	1.14 (1.81)	-0.14 (4.18)	0.97	0.76	0.55
TG, mg/dl	15.41(8.88)[a]	-23.86 (21.00)	8.05 (0.05)	-8.60 (18.64)	2.04 (7.94)	-19.78 (18.39)	0.90	**0.04**	0.69
LP(a), mg/dl	-0.89(1.49)	1.74(3.74)	1.07 (1.03)	3.11 (2.59)	-1.09 (1.73)	-1.60 (4.15)	0.39	0.54	0.86
LDL:HDL	0.06(0.08)	-0.25(0.19)	-0.31 (0.25)	-0.03 (0.58)	-0.005(0.22)	0.11 (0.51)	0.95	0.86	0.69
TC:HDL	0.14 (0.17)	-0.52(0.40)	-0.62 (0.56)	-0.16 (1.30)	-0.002(0.47)	-0.33 (1.09)	0.95	0.78	0.76
TG:HDL	0.23 (0.42)	-1.27 (0.99)	-1.38 (1.42)	0.65 (3.28)	-0.11 (1.08)	-0.80 (2.50)	0.95	0.77	0.80
Apo B, mg/dl	-0.55(2.36)	-0.84(0.60)	-4.50 (3.12)	2.35 (7.22)	0.98 (2.54)	-1.75 (5.89)	0.99	0.72	0.64
ApoA-1, mg/dl	-1.22 (0.06)	4.07(4.90)	-1.32 (2.26)	2.17 (5.23)	6.36 (2.57)	-1.78 (5.94)	0.89	0.95	0.25

Table 4. Change values in lipid profile, Apolipoproteins and glycemic indices in patients with type 2 diabetes across intervention periods and FADS1 rs174556 genotypes (n = 94). All data are presented as mean ± standard error. ApoA-1, apolipoprotein A-I ; ApoB, apolipoprotein B; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase, BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; GGT, gamma-glutamyltransferase; HDL-C, High-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; LDL-C, Low-density lipoprotein cholesterol; Lp(a), lipoprotein a; QUICKI, quantitative insulin sensitivity check index; SBP, Systolic blood pressure; TC, total cholesterol; TG, Triglyceride; WC, waist circumference. *P*1, Interperiod comparison of change values between the treatment oils durations using linear mixed models, in **unadjusted** model and adjusted for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake. *P*2, Interperiod comparison of change values across the genotypes using linear mixed models, in **unadjusted** model and **adjusted** for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake. *P*3, interaction between FADS1 rs174556 variant and treatment oils on the outcomes using linear mixed models, in **unadjusted** model and adjusted for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake. [a] Intraperiod comparison of change values between genotypes, using linear mixed models.

Variable	Sesame oil		Sesame-Canola oil		Canola oil		P[1]	P[2]	P[3]
	TT/CT	CC	TT/CT	CC	TT/CT	CC			
Crude model									
FBG, mg/dl	2.14 (3.59)	3.49 (2.90)	-3.17 (5.15)	-1.29 (4.06)	8.70 (4.84)	6.84 (3.82)	0.06	0.90	0.89
Insulin, m IU/ml	-3.32 (3.91)	-10.32 (3.21)	-6.38 (2.48)	-5.58 (1.95)	-14.767 (6.83)	-9.04 (5.38)	0.47	0.96	0.31
HOMA-IR	-0.78(0.80)	-1.87 (0.65)	-1.77 (0.77)	-1.71 (0.61)	-0.09 (0.79)	-0.67 (0.60)	0.15	0.34	0.71
TC, mg/dl	3.17 (4.48)	5.08 (3.62)	2.72 (4.96)	-1.62 (3.90)	-0.61 (4.34)	2.61 (3.42)	0.99	0.50	0.34
HDL-C, mg/dl	0.78(1.42)	-0.33(1.16)	1.07 (1.31)	0.98 (1.03)	1.04 (1.32)	1.35 (1.05)	0.75	0.75	0.86
LDL-C, mg/dl	-2.14 (2.51)	2.09 (2.03)	1.50 (2.97)	-1.70 (2.34)	-0.71 (2.60)	0.96 (2.05)	0.99	0.67	0.32
TG, mg/dl	-2.11 (12.61)	13.15 (10.20)	2.29 (12.11)	-5.91 (9.55)	-4.02 (11.34)	-0.02 (8.94)	0.79	0.66	0.62
LP(a), mg/dl	0.04 (2.07)	-0.63 (1.69)	0.76 (1.64)	2.46 (1.26)	-2.79 (2.41)	0.02 (1.90)	0.20	0.42	0.63
LDL:HDL	-0.04 (0.11)	0.02 (0.09)	-0.05 (0.35)	-0.40 (0.27)	-0.21 (0.30)	0.08 (0.24)	0.67	0.98	0.47
TC:HDL	-0.05 (0.24)	0.04 (0.19)	-0.12 (0.79)	-0.83 (0.63)	-0.44 (0.66)	0.17 (0.52)	0.68	0.99	0.54
TG:HDL	0.08 (0.58)	-0.13 (0.47)	-0.24 (1.99)	-1.95 (1.56)	-0.89 (1.51)	0.18 (1.20)	0.69	0.81	0.63
Apo B, mg/dl	-1.31 (3.29)	-0.33 (2.66)	-0.14 (4.52)	-3.98 (3.56)	-1.25 (3.60)	0.62 (2.84)	0.89	0.89	0.74
ApoA-1, mg/dl	-3.94 (3.35)	0.54 (2.71)	3.36 (3.35)	-1.54 (2.63)	4.08 (3.82)	4.53 (3.01)	0.19	0.89	0.36
Adjusted model									
FBG, mg/dl	16.59 (3.36)	1.64 (2.72)	-4.66 (5.29)	-1.59 (4.16)	8.69 (5.05)	7.38 (3.97)	**0.04**	0.87	0.86
Insulin, m IU/ml	-3.79 (4.11)	-10.47 (3.37)	-5.05 (2.50)	-5.46 (1.96)	-15.71 (7.21)	-9.39 (5.66)	0.33	0.94	0.41
HOMA-IR	-0.96 (0.81)	-1.99 (0.66)	-1.49 (0.79)	1.69 (0.62)	-0.15 (0.83)	-0.66 (0.64)	0.22	0.32	0.84
TC, mg/dl	-1.82 (4.59)	4.89 (3.71)	1.91 (5.14)	-2.33 (4.04)	1.04 (4.42)	2.99 (3.48)	0.83	0.72	0.46
HDL-C, mg/dl	1.12 (1.46)	-0.80 (1.19)	0.53 (1.30)	0.43 (1.02)	1.65 (1.31)	1.32 (1.04)	0.53	0.41	0.77
LDL-C, mg/dl	-1.66 (2.61)	1.91 (2.11)	0.89 (3.08)	-2.16 (2.42)	0.33 (2.68)	1.31 (2.11)	0.83	0.82	0.42
TG, mg/dl	-0.83 (13.20)	16.27 (10.67)	1.66 (11.96)	-1.54 (9.41)	-2.35 (11.88)	-0.79 (9.34)	0.73	0.55	0.72
LP(a), mg/dl	0.10 (2.19)	-0.95 (1.79)	0.65 (1.57)	1.76 (1.20)	-2.97 (2.57)	-0.04 (2.02)	0.28	0.54	0.63
LDL:HDL	-0.03 (0.12)	0.05 (0.10)	-0.02 (0.37)	-0.41 (0.29)	-0.23 (0.32)	0.11 (0.25)	0.67	0.93	0.43
TC:HDL	-0.02 (0.25)	0.11 (0.20)	-0.06(0.83)	-0.84 (0.65)	-0.47 (0.69)	0.20 (0.55)	0.68	0.97	0.51
TG:HDL	0.11 (0.61)	-0.01 (0.49)	-0.21 (2.10)	-1.91 (1.65)	-0.92 (1.60)	0.21 (1.27)	0.67	0.85	0.65
Apo B, mg/dl	-1.06 (3.46)	-0.29 (2.80)	-1.48 (4.65)	-4.62 (3.65)	-0.44 (3.78)	1.17 (2.97)	0.67	0.92	0.82
ApoA-1, mg/dl	-0.99 (3.04)	-0.06 (2.46)	1.27 (3.35)	-2.03 (2.63)	6.13 (3.84)	4.43 (3.02)	0.13	0.60	0.75

Table 5. Change values in lipid profile, Apolipoproteins and glycemic indices in patients with type 2 diabetes across intervention periods and FADS1 rs174556 genotypes (n = 94). All data are presented as mean ± standard error. ApoA-1, apolipoprotein A-I ; ApoB, apolipoprotein B; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase, BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; GGT, gamma-glutamyltransferase; HDL-C, High-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; LDL-C, Low-density lipoprotein cholesterol; Lp(a), lipoprotein a; QUICKI, quantitative insulin sensitivity check index; SBP, Systolic blood pressure; TC, total cholesterol; TG, Triglyceride; WC, waist circumference *P*1, Interperiod comparison of change values between the treatment oils durations using linear mixed models, adjusted for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake *P*2, Interperiod comparison of change values across the genotypes using linear mixed models, adjusted for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake *P*3, interaction between FADS1 rs174556 variant and treatment oils on the outcomes using linear mixed models, adjusted for age, gender, baseline BMI, amount of consumed oils, change levels of physical activity and change in energy intake

and HDL levels after canola oil consumption. It suggested that PUFAs may affect Apo-A1 levels by regulating the expression of the Apo-A1 gene and its variants[51].

The strengths of the current study are: It is the first study to investigate the effect of vegetable oils (sesame, canola and sesame-canola) on glycemic indices and lipid profile across genotypes of FADS1 gene rs174556 variant in people with type 2 diabetes. Second, it is a three-blind crossover RCT. Third; the intervention had an optimal duration. However, this study also had some limitations, such as the nature of the study design, which replaced the usual oils consumed by the participants with sesame, sesame-canola and canola oils, it could not be determined the exact amount of oils consumed by each participant. The observation of statistically significant interactions was reduced, because the metabolic responses to dietary changes involved in multiple genes. The used oils had low SFAs. If one of them had higher SFAs, more direct and interactive effects might have been observed. However, this would not have been ethical.

Conclusion

The rs174556 variant may cause different metabolic responses in diabetic patients who consumed vegetable oils. Diabetic people with the T allele had a better metabolic effect after consuming sesame oil. Further studies should examine the combined effect of multiple FADS1 gene variants and related genes and edible oil intake for more conclusive results.

Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Received: 13 July 2024; Accepted: 29 October 2024
Published online: 11 November 2024

References

1. Alwashmi, M. F., Mugford, G., Abu-Ashour, W. & Nuccio, M. A digital diabetes prevention program (transform) for adults with prediabetes: Secondary analysis. *JMIR Diabetes.* **4**(3), e13904 (2019).
2. Mokhtari, Z., Gheshlagh, R. G. & Kurdi, A. Health-related quality of life in Iranian patients with type 2 diabetes: An updated meta-analysis. *Diabetes Metab. Syndr.* **13**(1), 402–407 (2019).
3. Carolino, I. D. R., Molena-Fernandes, C. A., Tasca, R. S., Marcon, S. S. & Cuman, R. K. N. Risk factors in patients with type 2 diabetes mellitus. *Rev. Lat. Am. Enfermagem* **16**, 238–244 (2008).
4. Yuan, S. & Larsson, S. C. An atlas on risk factors for type 2 diabetes: a wide-angled Mendelian randomisation study. *Diabetologia* **63**, 2359–2371 (2020).
5. Khazrai, Y., Defeudis, G. & Pozzilli, P. Effect of diet on type 2 diabetes mellitus: A review. *Diabetes Metab. Res. Rev.* **30**(S1), 24–33 (2014).
6. Goodpaster, B. H. et al. Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial. *JAMA.* **304**(16), 1795–1802 (2010).
7. Rees K, Dyakova M, Ward K, Thorogood M, Brunner E. Dietary advice for reducing cardiovascular risk. Cochrane Database of Systematic Reviews. 3, 2128 (2013)
8. Schwab, U. et al. Effect of the amount and type of dietary fat on cardiometabolic risk factors and risk of developing type 2 diabetes, cardiovascular diseases, and cancer: A systematic review. *Food & Nutrition Research.* **58**(1), 25145 (2014).
9. Kim, S. R., Jeon, S. Y. & Lee, S.-M. The association of cardiovascular risk factors with saturated fatty acids and fatty acid desaturase indices in erythrocyte in middle-aged Korean adults. *Lipids in Health and Disease.* **14**(1), 1–10 (2015).
10. Imamura, F. et al. Effects of saturated fat, polyunsaturated fat, monounsaturated fat, and carbohydrate on glucose-insulin homeostasis: a systematic review and meta-analysis of randomised controlled feeding trials. *PLoS Medicine.* **13**(7), e1002087 (2016).
11. Szostak-Wegierek D, Klosiewicz-Latoszek L, Szostak WB, Cybulska B. The role of dietary fats for preventing cardiovascular disease A review. Roczniki Państwowego Zakładu Higieny. 2013;64(4), 263
12. Riccardi, G., Giacco, R. & Rivellese, A. A. Dietary fat, insulin sensitivity and the metabolic syndrome. *Clinical Nutrition.* **23**(4), 447–456 (2004).
13. Mozaffarian, D., Micha, R. & Wallace, S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. *PLoS Medicine.* **7**(3), e1000252 (2010).
14. Kris-Etherton, P. M. Monounsaturated fatty acids and risk of cardiovascular disease. *Circulation.* **100**(11), 1253–1258 (1999).
15. Zambiazi RC, Przybylski R, Zambiazi MW, Mendonca CB. Fatty acid composition of vegetable oils and fats. Boletim do Centro de Pesquisa de Processamento de Alimentos **25**(1) (2007).
16. Sankar, D., Rao, M. R., Sambandam, G. & Pugalendi, K. A pilot study of open label sesame oil in hypertensive diabetics. *Journal of Medicinal Food.* **9**(3), 408–412 (2006).
17. Amiri, M. et al. The effects of sesame, canola, and sesame–canola oils on cardiometabolic markers in patients with type 2 diabetes: a triple-blind three-way randomized crossover clinical trial. *European Journal of Nutrition.* **61**(7), 3499–3516 (2022).
18. Tindall, A. M. et al. Replacing saturated fat with walnuts or vegetable oils improves central blood pressure and serum lipids in adults at risk for cardiovascular disease: a randomized controlled-feeding trial. *Journal of the American Heart Association.* **8**(9), e011512 (2019).
19. Khalesi, S., Paukste, E., Nikbakht, E. & Khosravi-Boroujeni, H. Sesame fractions and lipid profiles: A systematic review and meta-analysis of controlled trials. *British Journal of Nutrition.* **115**(5), 764–773 (2016).
20. Raeisi-Dehkordi, H., Mohammadi, M., Moghtaderi, F. & Salehi-Abargouei, A. Do sesame seed and its products affect body weight and composition? A systematic review and meta-analysis of controlled clinical trials. *Journal of Functional Foods.* **49**, 324–332 (2018).
21. Lin, L. et al. Evidence of health benefits of canola oil. *Nutrition Reviews.* **71**(6), 370–385 (2013).
22. Ordovas, J. M. Genetic interactions with diet influence the risk of cardiovascular disease. *The American Journal of Clinical Nutrition.* **83**(2), 443S-S446 (2006).
23. Corella, D. et al. CLOCK gene variation is associated with incidence of type-2 diabetes and cardiovascular diseases in type-2 diabetic subjects: Dietary modulation in the PREDIMED randomized trial. *Cardiovascular Diabetology.* **15**, 1–12 (2016).
24. Marquardt, A., Stöhr, H., White, K. & Weber, B. H. cDNA cloning, genomic structure, and chromosomal localization of three members of the human fatty acid desaturase family. *Genomics.* **66**(2), 175–183 (2000).

25. Park, W. J., Kothapalli, K. S., Lawrence, P., Tyburczy, C. & Brenna, J. T. An alternate pathway to long-chain polyunsaturates: the FADS2 gene product Δ8-desaturates 20: 2n–6 and 20: 3n–3. *Journal of Lipid Research.* **50**(6), 1195–1202 (2009).
26. Hellstrand, S. et al. Genetic variation in FADS1 has little effect on the association between dietary PUFA intake and cardiovascular disease. *The Journal of Nutrition.* **144**(9), 1356–1363 (2014).
27. Muzsik, A., Bajerska, J., Jeleń, H. H., Gaca, A. & Chmurzynska, A. Associations between fatty acid intake and status, desaturase activities, and FADS gene polymorphism in centrally obese postmenopausal Polish women. *Nutrients.* **10**(8), 1068 (2018).
28. Gonzalez-Casanova, I. et al. Maternal single nucleotide polymorphisms in the fatty acid desaturase 1 and 2 coding regions modify the impact of prenatal supplementation with DHA on birth weight. *The American Journal of Clinical Nutrition.* **103**(4), 1171–1178 (2016).
29. Song Z, Cao H, Qin L, Jiang Y. A case-control study between gene polymorphisms of polyunsaturated fatty acid metabolic rate-limiting enzymes and acute coronary syndrome in Chinese Han population. BioMed Research International. 2013;2013, 928178
30. Norris, J. M. et al. Erythrocyte membrane docosapentaenoic acid levels are associated with islet autoimmunity: The Diabetes Autoimmunity Study in the Young. *Diabetologia.* **57**, 295–304 (2014).
31. Moltó-Puigmartí, C. et al. Genetic variation in FADS genes and plasma cholesterol levels in 2-year-old infants: KOALA Birth Cohort Study. *PLoS ONE.* **8**(5), e61671 (2013).
32. Amiri, M. et al. The effect of canola oil compared with sesame and sesame-canola oil on cardio-metabolic biomarkers in patients with type 2 diabetes: Design and research protocol of a randomized, triple-blind, three-way, crossover clinical trial. *ARYA Atherosclerosis.* **15**(4), 168 (2019).
33. Chow S-C, Shao J, Wang H, Lokhnygina Y. Sample size calculations in clinical research: CRC Press; 2017.
34. Wallace, T. M., Levy, J. C. & Matthews, D. R. Use and abuse of HOMA modeling. *Diabetes Care.* **27**(6), 1487–1495 (2004).
35. Amiri, M., Raeisi-Dehkordi, H., Sarrafzadegan, N., Forbes, S. C. & Salehi-Abargouei, A. The effects of Canola oil on cardiovascular risk factors: A systematic review and meta-analysis with dose-response analysis of controlled clinical trials. *Nutrition, Metabolism and Cardiovascular Diseases.* **30**(12), 2133–2145 (2020).
36. Aslam, F., Iqbal, S., Nasir, M. & Anjum, A. A. White sesame seed oil mitigates blood glucose level, reduces oxidative stress, and improves biomarkers of hepatic and renal function in participants with type 2 diabetes mellitus. *Journal of the American College of Nutrition.* **38**(3), 235–246 (2019).
37. Sohouli, M. H., Haghshenas, N., Hernández-Ruiz, Á. & Shidfar, F. Consumption of sesame seeds and sesame products has favorable effects on blood glucose levels but not on insulin resistance: A systematic review and meta-analysis of controlled clinical trials. *Phytotherapy Research.* **36**(3), 1126–1134 (2022).
38. Raeisi-Dehkordi, H. et al. Canola oil compared with sesame and sesame-canola oil on glycaemic control and liver function in patients with type 2 diabetes: A three-way randomized triple-blind cross-over trial. *Diabetes/Metabolism Research and Reviews.* **37**(5), e3399 (2021).
39. Namayandeh, S. M., Kaseb, F. & Lesan, S. Olive and sesame oil effect on lipid profile in hypercholesterolemic patients, which better?. *International Journal of Preventive Medicine.* **4**(9), 1059 (2013).
40. Hirose, N. et al. Inhibition of cholesterol absorption and synthesis in rats by sesamin. *Journal of Lipid Research.* **32**(4), 629–638 (1991).
41. Liang, Y. T. et al. Cholesterol-lowering activity of sesamin is associated with down-regulation on genes of sterol transporters involved in cholesterol absorption. *Journal of Agricultural and Food Chemistry.* **63**(11), 2963–2969 (2015).
42. Khamlaoui, W. et al. Association between genetic variants in FADS1-FADS2 and ELOVL2 and obesity, lipid traits, and fatty acids in Tunisian population. *Clinical and Applied Thrombosis/Hemostasis.* **26**, 1076029620915286 (2020).
43. Huang, M.-C. et al. FADS gene polymorphisms, fatty acid desaturase activities, and HDL-C in type 2 diabetes. *International Journal of Environmental Research and Public Health.* **14**(6), 572 (2017).
44. Kathiresan, S. et al. Common variants at 30 loci contribute to polygenic dyslipidemia. *Nature Genetics.* **41**(1), 56–65 (2009).
45. Chen, C., Yu, X. & Shao, S. Effects of omega-3 fatty acid supplementation on glucose control and lipid levels in type 2 diabetes: A meta-analysis. *PLoS ONE.* **10**(10), e0139565 (2015).
46. Gieger C, Geistlinger L, Altmaier E, Hrabé de Angelis M, Kronenberg F, Meitinger T, et al. Genetics meets metabolomics: a genome-wide association study of metabolite profiles in human serum. PLoS genetics. 2008;4(11): 282.
47. Rye, K.-A., Bursill, C. A., Lambert, G., Tabet, F. & Barter, P. J. The metabolism and anti-atherogenic properties of HDL. *Journal of Lipid Research.* **50**, S195–S200 (2009).
48. Haldar, S. et al. Two blends of refined rice bran, flaxseed, and sesame seed oils affect the blood lipid profile of chinese adults with borderline hypercholesterolemia to a similar extent as refined olive oil. *The Journal of Nutrition.* **150**(12), 3141–3151 (2020).
49. Moghtaderi, F. et al. The effect of sesame, canola, and sesame-canola oils on cardiometabolic risk factors in overweight adults: A three-way randomized triple-blind crossover clinical trial. *Phytotherapy Research.* **36**(2), 1043–1057 (2022).
50. Ghobadi, S., Hassanzadeh-Rostami, Z., Mohammadian, F., Zare, M. & Faghih, S. Effects of canola oil consumption on lipid profile: A systematic review and meta-analysis of randomized controlled clinical trials. *Journal of the American College of Nutrition.* **38**(2), 185–196 (2019).
51. Ramezani-Jolfaie, N. et al. Association of rs670 variant of APOA-1 gene with cardiometabolic markers after consuming sesame, canola and sesame-canola oils in adults with and without type 2 diabetes mellitus. *Clinical Nutrition ESPEN.* **38**, 129–137 (2020).

Acknowledgements

The authors acknowledge all participants of the study and Diabetes Research Center of Shahid Sadoughi University of Medical Sciences, Yazd, Iran. The authors also thank Shahid Sadoughi University of Medical Sciences and Neshatavar food Industry Company for supporting this study.

Author contributions

A.SA, HR.R, F.M, A.Z and M.A designed and conducted the study. Z.F and SH.A conducted experiments in the laboratory. SS.KH and F. M performed statistical analyzes in one of the work protocols. Z.F and A.AV wrote draft of manuscript. SS.KH and A.SA critically revised the manuscript. The final version of the manuscript was approved by all authors.

Funding

The present study was jointly funded by Shahid Sadoughi University of Medical Sciences (http://www.ssu.ac.ir: grant number: 5799) and Neshatavar food industry company (Datis Corporation, http://www.neshatavar.com/?l=EN: grant number: 6462).

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Correspondence and requests for materials should be addressed to S.S.K.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.