Received: 10 August 2020 | Revised: 30 November 2021 | Accepted: 28 December 2021

DOI: 10.1002/ptr.7381

RESEARCH ARTICLE

WILEY

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

Fatemeh Moghtaderi[1,2] | Mojgan Amiri[1,2] | Hamidreza Raeisi-Dehkordi[1,2] | Alireza Zimorovat[1,2] | Matin Mohyadini[3,4] | Amin Salehi-Abargouei[1,2]

[1]Nutrition and Food Security Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[2]Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[3]Student Research Committee, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[4]Department of Medical Laboratory Sciences, School of Para medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Correspondence
Amin Salehi-Abargouei, Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
Email: abargouei@ssu.ac.ir, abargouei@gmail.com

Funding information
Neshatavar food industry company (Datis Corporation, Yazd, Iran); Shahid Sadoughi University of Medical Sciences

Abstract

Limited data exist on the cardiometabolic effects of sesame oil compared with canola oil. In the present study, 77 overweight adults were randomized to replace their regularly consumed oils with canola (CO), sesame (SO), and sesame-canola oils (SCO, 40% SO, and 60% CO) in three 9-week phases. Blood pressure, visceral adiposity index, serum apo-proteins (APOs) and lipid profile, glycemic control markers, kidney markers, liver enzymes, and cardiovascular disease risk scores were assessed at baseline and endline. After adjustment for confounders, SO significantly reduced serum alkaline aminotransferase (ALT) compared to CO ($p \leq 0.05$) in all participants, increased serum urea compared to SCO in males, and decreased serum alkaline phosphatase compared to other oils in males, and improved serum high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) compared to SCO, and eGFR compared with CO in females ($p \leq 0.05$). Canola oil significantly improved serum Apo A1 and APO B/A ratio compared with SO, in males ($p \leq 0.05$). Sesame-canola oil significantly reduced serum urea compared to other oils in all participants ($p \leq 0.05$). Sesame oil and SCO might beneficially affect serum ALT and urea, respectively. Intervention oils might have different cardiometabolic effects in each gender. Further studies are needed to confirm our results (Trial registration code: IRCT2016091312571N6).

KEYWORDS
canola oil, cardiometabolic risk factors, sesame oil

1 | INTRODUCTION

Cardiovascular diseases (CVDs) are the predominant causes of mortality (Mathers & Loncar, 2006) and impose a burden, particularly in low- and middle-income countries (Roth et al., 2017). Cardiometabolic risk (CMR) factors including dyslipidemia, high blood pressure (BP), poor glycemic control, insulin resistance, abdominal obesity, and inflammation are regarded as factors that increase the possibility of CVDs (Eckel, Kahn, Robertson, & Rizza, 2006). Decreased estimated glomerular filtration rate (eGFR) and enhanced probability of chronic kidney disease are also accompanied by the presence of cardiometabolic risk (Lastra, Manrique, & Sowers, 2006; Ruilope, de la Sierra, Segura, & Garcia-Donaire, 2007).

Lifestyle modifications including physical activity and diet are primary steps for elevated CMR treatment (Chatterjee et al., 2012). Recent investigations have revealed that the quality of dietary fat which may be specified by the relative content of saturated fatty acids (SFAs), trans fatty acids, monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs) plays an important role in cardiometabolic health (Howard et al., 2006; Mente, de Koning,

Fatemeh Moghtaderi and Mojgan Amiri contributed equally to this study.

Shannon, & Anand, 2009; Tinker et al., 2008). Some pieces of evidence indicated that monounsaturated fatty acids (MUFAs) intake might improve lipid profile (DiNicolantonio & O'Keefe, 2018), blood pressure (Qian, Korat, Malik, & Hu, 2016; Rasmussen et al., 2006), and insulin resistance (Galgani, Uauy, Aguirre, & Díaz, 2008; Jebb et al., 2010). Moreover, the high intake of polyunsaturated fatty acids (PUFAs) from vegetable oils may favorably affect lipid profile and cardiovascular events (Jakobsen et al., 2009; Mensink, Zock, Kester, & Katan, 2003; Mozaffarian, Micha, & Wallace, 2010). Therefore, MUFAs, as well as PUFAs, may be effective in reducing CVD events, especially when replaced with SFAs (Mozaffarian et al., 2010).

Canola oil (CO), which is regarded as a favorable oil around the world, is comprised of high amounts of mono-unsaturated fatty acids (MUFAs, ~64.4%) and linoleic acid (~20%) while it is low in saturated fatty acids (SFAs, ~7%) (Zambiazi, Przybylski, Zambiazi, & Mendonça, 2007). Besides, favorable amounts of alpha-linolenic acid (ALA) (~8.3%) can be a possible advantage of CO (Zambiazi et al., 2007). Sesame oil (SO), another popular oil consumed especially in Asian countries (Namiki, 2007), is characterized by considerable amounts of vitamin E (~40 mg/100 g oil) (Sankar, Rao, Sambandam, & Pugalendi, 2006), phytosterols, unsaturated fatty acids, and lignans (e.g., sesamin, sesaminol, sesamol, sesamolinol, and sesamolin) (Pathak, Rai, Kumari, & Bhat, 2014; Sukumar, Arimboor, & Arumughan, 2008). It was shown that sesamin, as the most abundant lignan in sesame, has favorable effects on body weight, blood pressure, and lipid profile (Miyawaki et al., 2009; Rogi, Tomimori, Ono, & Kiso, 2011; Yuliana et al., 2011).

Several studies have shown that CO may improve lipid profile (Kruse et al., 2015; Negele et al., 2015; Saedi, Noroozi, Khosrotabar, Mazandarani, & Ghadrdoost, 2017), BP (Baxheinrich, Stratmann, Lee-Barkey, Tschoepe, & Wahrburg, 2012), and glycemic control markers (Nigam et al., 2014), however, the effects on some cardiovascular risk factors was not approved by a recent meta-analysis and it was shown that CO might differently affect CVD risk factors depending on the oil examined for comparison (Amiri, Raeisi-Dehkordi, Sarrafzadegan, Forbes, & Salehi-Abargouei, 2020). Moreover, SO might significantly improve TG (Sankar et al., 2006; Sankar, Ali, Sambandam, & Rao, 2011), HDL-C (Mitra, 2007; Sankar et al., 2011), TC, LDL-C (Mitra, 2007; Sankar et al., 2006), glycemic markers (Mitra, 2007), and blood pressure (Mitra, 2007; Sankar et al., 2006; Sankar, Sambandam, Ramakrishna Rao, & Pugalendi, 2005). Two recent systematic reviews could confirm the beneficial effect of sesame and its fractions only on serum triglyceride and blood pressure; however, a few studies were included and the majority of them were prone to bias (Khalesi, Paukste, Nikbakht, & Khosravi-Boroujeni, 2016; Khosravi-Boroujeni, Nikbakht, Natanelov, & Khalesi, 2017).

Although SO and CO are different in fatty acids content and phytochemicals, we are not aware of any study trying to compare the effect of these two oils on CMR in healthy adults. Therefore, the current study aimed to investigate the effect of replacing ordinary edible oils with CO, SO, and sesame-canola oil (SCO, a novel oil product as the blend of SO and CO) for 9-weeks on lipid profile, CVD risk scores, blood pressure, visceral adiposity index (VAI), glycemic markers, kidney markers, and liver enzymes. In the present study, we hypothesized that the blended oil might have beneficial effects on cardiometabolic markers in comparison with SO and CO alone.

2 | MATERIALS AND METHODS

This study was derived from a large parent triple-blind, randomized, three-way cross-over clinical trial that aimed to compare the effect of CO, SO, and SCO on cardiometabolic risk factors in adults with type 2 diabetes and their spouses. The present analysis was conducted on spouses who had no history of chronic diseases. The precise information about participants' characteristics and the study protocol is published elsewhere (Amiri et al., 2019). The parent study was registered on the 14th of November 2016 at the Iranian Registry of Clinical Trials (IRCT) with the registration code of IRCT2016091312571N6. All participants signed written informed consent before entering the study. The current study was approved by the ethics committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran on the 20th of December 2017 (Ethics code: IR.SSU.SPH.REC.1396.142).

2.1 | Participants

A total of 101 spouses were entered into the parent clinical trial (Amiri et al., 2019). The spouses without a history of T2DM (with fasting blood sugar less than 126 mg/dL) or other chronic diseases such as CVDs, kidney or liver diseases, and cancers were included in the current analysis. Moreover, the exclusion criteria were: being on a special diet or having a specific dietary habit, experiencing pregnancy or chronic diseases including T2DM, CVDs, and cancers during the study period, and not intending to continue the study for any reason.

2.2 | Study design and intervention

The present study aimed to examine the effect of replacing households' regularly consumed oils with three dietary oils [CO, SO, and SCO (40% SO and 60% CO)] on CMR in adults without a history of any chronic diseases. It should be noted that we used the blended oil to check if it has a different beneficial effect on cardiometabolic markers. The detailed fatty acid composition of intervention oils is reported elsewhere (Amiri et al., 2019).

In the first visit, demographic data and medical history were obtained and participants were advised to follow a healthy diet and maintain their regular lifestyle and physical activity during the study period. After that, individuals entered a run-in period (4 weeks). Then, they were randomized to receive the intervention oils in three phases. Indeed, intervention oils were totally replaced with households' regular consumed oils. The intervention phases lasted for 9 weeks which were separated by 4 weeks as washout (sunflower oil was provided in the run-in and washout periods). All intervention oils and the oil provided for run-in and washout periods were freely provided for the study participants by Neshatavar food industry company (Datis Corporation, Yazd, Iran). Intervention oils were delivered to participants

by investigators in bottles with the same appearance which was labeled with three codes by an independent investigator: S, B, and G. Participants and investigators were not aware of codes until after the statistical analysis. Hence, all the participants, personnel, and statisticians were blinded to the treatment oils. Detailed methods used for randomization, allocation concealment, and blinding of participants and personnel are provided elsewhere (Amiri et al., 2019).

2.3 | Dietary intake and physical activity assessments

To estimate each subject's usual energy intake, nutrient composition, and physical activity, participants were carefully trained to fill out 3-day weighed food and physical activity records (2 weekdays and 1 weekend day) at the start, in the middle, and the end of each intervention phase. A digital kitchen scale (model: Electronic kitchen scale, SF-400) was provided for each individual to weight and record ingredients of cooked foods. The daily intake of foods and beverages was converted to grams/day and a computer-based program (Nutritionist IV software, version 3.5.2, Axxya Systems, Redmond, WA) was used for assessing the dietary intake. Physical activity records were converted to metabolic equivalent-min/day using standard methods (Amiri et al., 2019).

2.4 | Anthropometric measurements

Body weight, height, and waist circumference (WC), were assessed at the start, middle, and end of all three phases of the study. All measurements were assessed 3 times in each visit and their mean value was regarded as the final value. A digital calibrated scale (Omron, mode: BF51) was used to measure weight to the nearest 100 g while the participants were with minimum clothes and without shoes. The WC was determined by a non-stretchable measuring tape to the nearest 1 cm. A measuring tape fixed on the wall was used to measure height to the nearest 0.5 cm. The body mass index (BMI) was computed by dividing weight (kg) by height squared (m^2) and the waist to hip ratio (WHR) was calculated by dividing WC by hip circumference (Amiri et al., 2019).

2.5 | Cardiometabolic risk factors measurement

At baseline and endline of each intervention phase, fasting blood samples were collected from each participant. After processing and separating serum from blood samples, they were stored at $-70^{\circ}C$ until analysis. Serum lipid profile measures including triglycerides (TG), total cholesterol (TC), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), apolipoprotein A-I (APO A1), apolipoprotein B (APO B), and lipoprotein (a), and also urea, creatinine, fasting blood sugar (FBS), serum alkaline phosphatase (ALP), gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST), and alanine transaminase (ALT) concentrations were analyzed by an automatic analyzer (Alpha-classic, Iran, model: AT++) using Pars Azmun standard kits. Serum fasting insulin levels were measured by enzyme-linked immunoassay (ELISA) kits (Monobind, Inc., Lake Forest, CA). The intra- and inter-assay %CVs for all measurement kits are indicated in Table S1. In addition, in the beginning, in the middle, and the end of each phase, systolic and diastolic blood pressure were monitored in triplicate after 5 min rest by using a sphygmomanometer (Riester, Germany, model: Diplomat-presameter), and mean values were recorded.

Homeostasis model assessment for insulin resistance (HOMA-IR), for insulin sensitivity (HOMA -%S), and β-cell function (HOMA -% BCF) were calculated by using fasting serum insulin and fasting serum glucose levels using homeostasis model assessment calculator (Willett, 1990). Quantitative insulin sensitivity check index (QUICKI) was estimated using the following equation: (QUICKI = 1/[log (fasting insulin) + log (fasting glucose)]) (Katz et al., 2000). Age, gender, systolic blood pressure (SBP), TC, and HDL-C were also used to calculate cardiovascular disease risk scores by using Framingham Equations (Payne, n.d.; Payne, 2012). Visceral adiposity index (VAI), as an independent risk factor for CVDs, was estimated by using WC, BMI, TG, and HDL-C using formulas separately developed for males and females (Amato et al., 2010). The estimated eGFR was calculated using chronic kidney disease epidemiology collaboration's (CKD EPI) equation (Levey et al., 2009).

2.6 | Treatment compliance

The participants were asked to return all unused intervention oils in each phase. Investigators weighed intervention oil bottles before and after each phase to calculate the approximate amount of consumed oil. Moreover, 3-day weighed food records were evaluated to assess the consumed oils (Amiri et al., 2019).

2.7 | Sample size

A formula suggested for cross-over studies (Chow, Shao, & Wang, 2008): $n = [(z\ 1 - \alpha/2 + z\ 1 - \beta)^2\ s^2]/2\Delta^2$, was used for sample size calculation, considering type one error of 5%, type 2 error of 10% (power of 90%), and 5 mg/dL difference in serum glucose between the intervention periods as key variable based on a study done by Jenkins et al. (Jenkins et al., 2014), at least 34 participants were needed to enter the trial.

2.8 | Statistical analysis

The normal distribution was checked by using the Kolmogorov–Smirnov test. The after-intervention values were compared against before-intervention values by incorporating a general linear model (GLM) repeated measures approach. Change values were compared between intervention phases by using linear mixed models by considering the rolling method and carry-over variables as other fixed factors. Age, sex, baseline BMI, calculated intervention oils consumed

per subject, changes in physical activity level, energy intake in each intervention period, and baseline values were included as covariates in the multivariable-adjusted model. All analyses were replicated based on participants' sex. Statistical analyses were conducted using the statistical package for social sciences (SPSS version 20; IBM Corporation). Variables are reported as mean ± standard error (SE), otherwise indicated. p values less than 0.05 were considered statistically significant.

3 | RESULTS

A total of 77 individuals were eligible to be entered into the current investigation. Three participants were dropped out of the analyses because of the unwillingness to continue. Furthermore, one person was excluded due to a lack of compliance. Of the 73 remaining participants, 5, 1, and 5 participants missed giving blood samples at the beginning or end of SO, SCO, and CO intervention periods, respectively. Therefore, the number of spouses who had complete data for each intervention period were as follows: SO ($n = 68$), CO ($n = 72$), and SCO ($n = 68$) (Figure 1). The baseline characteristics of included participants are provided in Table 1.

The analysis of dietary intakes revealed that the mean intake of MUFAs, PUFAs, SFAs, and vitamin E were significantly different between the three intervention phases ($p < 0.05$). Moreover, analyses indicated that there were no significant differences between the intervention periods regarding energy intake, macronutrients, and physical activity ($p > 0.05$) (Table S2).

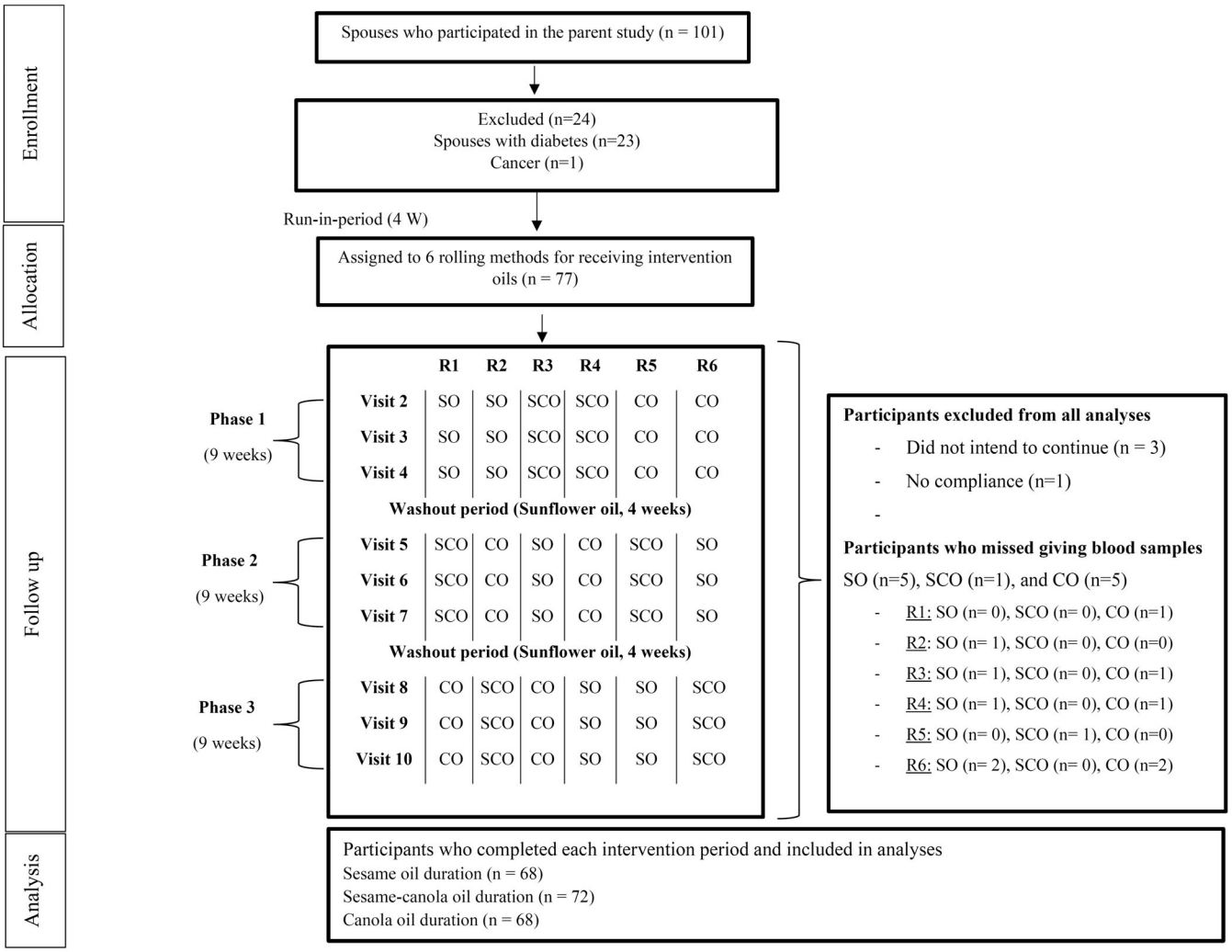

FIGURE 1 Flow of participants throughout the study. Intervention oils were labeled as SO (sesame oil), SCO (sesame-canola oil), and CO (canola oil). A total of 77 participants were allocated to 6 rolling methods (R). Four participants were excluded from all analyses because of unwillingness to continue and lack of compliance. From 73 remaining participants, 5, 1, and 5 participants missed giving blood samples in SO, SCO, and CO periods, respectively [R1: SO ($n = 0$), SCO ($n = 0$), CO ($n = 1$); R2: SO ($n = 1$), SCO ($n = 0$), CO ($n = 0$); R3: SO ($n = 1$), SCO ($n = 0$), CO ($n = 1$); R4: SO ($n = 1$), SCO ($n = 0$), CO ($n = 1$); R5: SO ($n = 0$), SCO ($n = 1$), CO ($n = 0$); R6: SO ($n = 2$), SCO ($n = 0$), CO ($n = 2$)]. Therefore, the number of participants who completed each intervention period and included in the analyses were as follows: SO ($n = 68$), CO ($n = 72$), and SCO ($n = 68$)

TABLE 1 Baseline characteristics of the study participants

Variables	Male ($n = 32$)	Female ($n = 41$)	Total ($n = 73$)
Age (years)	54.09 ± 1.66[a]	42.24 ± 1.08	47.43 ± 1.17
BMI (kg/m^2)	26.99 ± 0.78	29.16 ± 0.72	28.21 ± 0.54
Body fat (percent)	22.95 ± 1.06	41.69 ± 0.85	33.77 ± 1.28
TC (mg/dl)	180.81 ± 5.75	181.75 ± 5.85	181.34 ± 4.11
HDL-C (mg/dl)	38.96 ± 1.73	44.53 ± 1.63	42.09 ± 1.22
LDL-C (mg/dl)	95 ± 3.59	91.78 ± 3.82	93.19 ± 2.65
TG (mg/dl)	136.73 ± 9.31	138.56 ± 10.39	137.76 ± 7.07
Apo B (mg/dl)	100.25 ± 4.32	106.10 ± 6.53	103.54 ± 4.11
Apo A (mg/dl)	148.34 ± 4.68	169.07 ± 4.08	159.41 ± 3.09
Lipoprotein a (mg/dl)	20.84 ± 3.31	28.72 ± 3.59	25.28 ± 2.51
LDL:HDL ratio	2.61 ± 0.16	2.39 ± 0.31	2.49 ± 0.19
TC:HDL ratio	4.97 ± 0.29	4.80 ± 0.71	4.87 ± 0.41
Apo B: Apo A ratio	0.69 ± 0.03	0.63 ± 0.04	0.66 ± 0.02
TG:HDL ratio	4.05 ± 0.49	4.75 ± 1.65	4.44 ± 0.94
Risk of CHD (%)	9.26 ± 1.27	2.23 ± 0.85	5.36 ± 0.84
Risk of MI (%)	4.14 ± 0.85	0.7 ± 0.45	2.23 ± 0.49
Risk of stroke (%)	3.66 ± 2.66	0.21 ± 0.04	1.74 ± 1.18
Risk of CVD (%)	11.63 ± 2.16	2.26 ± 0.63	6.42 ± 1.15
Risk of CHD death (%)	2.13 ± 0.59	0.17 ± 0.14	1.04 ± 0.29
Risk of CVD death (%)	2.82 ± 0.86	0.16 ± 0.09	1.34 ± 0.41
VAI	2.47 ± 0.29	2.77 ± 0.23	2.63 ± 0.18
DBP (mm hg)	7.50 ± 0.17	7.07 ± 0.17	7.26 ± 0.12
SBP (mm hg)	11.82 ± 1.26	9.89 ± 0.26	10.73 ± 0.58
FBS (mg/dl)	89.89 ± 2.44	85.54 ± 1.67	87.45 ± 1.43
Insulin	24.24 ± 2.63	23.83 ± 1.72	24.02 ± 1.52
HOMA -IR	2.99 ± 0.30	2.93 ± 0.19	2.96 ± 0.17
HOMA -S	43.74 ± 4.19	39.55 ± 2.58	41.52 ± 2.39
HOMA -BCF	211.48 ± 18.55	232.44 ± 15.36	222.59 ± 11.91
QUICKI	0.30 ± 0.004	0.30 ± 0.002	0.30 ± 0.002
Creatinine (mg/dl)	1.16 ± 0.02	0.94 ± 0.02	1.04 ± 0.02
Urea	33.81 ± 1.23	27.79 ± 1.19	30.43 ± 0.92
eGFR	72.41 ± 2.38	76.67 ± 1.99	74.80 ± 1.54
ALP	191.96 ± 7.55	176.29 ± 6.49	183.16 ± 4.97
GGT	26.31 ± 1.72	21.73 ± 2.32	23.74 ± 1.52
AST	25.40 ± 1.89	21.48 ± 1.45	23.20 ± 1.17
ALT	23.66 ± 2.38	18.56 ± 2.09	20.80 ± 1.59
Education			
Elementary or lower	15.6%	19.5%	17.8%
High school	56.3%	58.5%	57.5%
College and university	28.1%	22%	24.7%

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; Apo A-1, Apo lipoprotein A-1; Apo B, Apo lipoprotein B; Apo B:Apo A-1, Apo B to Apo A-1 ratio; AST, aspartate aminotransferase; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBS, fasting blood sugar; GGT, gamma-glutamyltransferase; HDL-C, high-density lipoprotein cholesterol; HOMA-%B, homeostasis model assessment for b-cell function; HOMA-IR, homeostasis model assessment for insulin resistance; HOMA-%S, homeostasis model assessment for insulin sensitivity; LDL-C, low-density lipoprotein cholesterol; LDL:HDL, LDL-C to HDL-C ratio; Lp (a), lipoprotein a; MI, myocardial infarction; QUICKI, quantitative insulin sensitivity check indexe; SBP, systolic blood pressure; TC, total cholesterol; TC:HDL, TC to HDL-C ratio; TG:HDL, TG to HDL-C ratio; TG, triglyceride; VAI, visceral adiposity index.

[a]Values are expressed as means ± standard error (SE), otherwise indicated.

3.1 | The effects of intervention oils on cardiometabolic risk factors (CMR)

3.1.1 | Lipid profile, lipoproteins, and cardiovascular disease risk scores

The crude and adjusted after-intervention and change values (mean ± SE) for lipid profile, lipoproteins, CVD risk scores, VAI, and blood pressure are provided in Table 2. The Consumption of SO resulted in a significant improvement in HDL-C and TG ($p < 0.05$), whiles these significant effects disappeared after adjustment for confounders namely participants' age, sex, baseline BMI, oils consumed per subject, changes in physical activity, the energy intake, and baseline values ($p > 0.05$). Moreover, three intervention oils yielded no significant improvement in other lipid profiles, lipoproteins markers, CVD risk scores, VAI, and blood pressure in the whole population after adjustment for confounders ($p > 0.05$).

Sex-stratified analyses showed that serum TC ($p = 0.04$), LDL-C ($p = 0.01$), Apo B ($p = 0.006$), lipoprotein a ($p = 0.03$), and Apo B/A ratio ($p = 0.001$) levels were significantly increased in males after SO consumption. Moreover, CO intake significantly increased serum Apo A-1 levels after adjustment for confounders, in males ($p = 0.008$), whereas other markers were not affected by intervention oils ($p > 0.05$). The between-period comparisons revealed that CO significantly improved serum Apo A-1 and Apo B/A ratio compared to SO in males ($p < 0.05$, Table S3). In females, a significant improvement effect was observed for serum HDL-C ($p = 0.01$) and TG ($p = 0.03$) after SO consumption. Also, the risk of stroke ($p = 0.04$) was significantly increased after SO intervention ($p < 0.05$). The between-period analysis indicated that HDL-C and TG were significantly improved in the SO period compared with the SCO period ($p < 0.05$, Table S4).

3.1.2 | Glycemic control markers

The between- and within-period comparison of glycemic control markers including FBS, Insulin, HOMA-IR, HOMA-S, HOMA–BCF, and QUICKI in the whole population is shown in Table 3. After adjustment for confounders, the SO consumption led to a significant reduction in serum insulin (−4.53 ± 1.51), HOMA-IR (−0.53 ± 0.17), HOMA-BCF (−32.08 ± 7.92); furthermore, insulin sensitivity indicators including HOMA-S (10.32 ± 2.59) and QUICKI (0.009 ± 0.003) were significantly increased after SO intake ($p < 0.05$). Significant improvements in all glycemic markers were seen either in males or females after SO intake except for serum FBS in both gender and HOMA-IR in males (Tables S5 and S6, respectively). Following SCO consumption, a significant improvement was only indicated for HOMA-S in the whole population (Table 3). This oil did not significantly affect glycemic markers in males (Table S5, $p > 0.05$), whereas only FBS was significantly increased in females (Table S6, $p < 0.05$). The analysis also indicated a significant decrease in serum insulin, HOMA-IR, and HOMA-BCF and a significant increase in HOMA-S and QUICKI after CO consumption in the whole population (Table 3, $p < 0.05$). The effect of CO consumption in the male and female is indicated separately in Tables S5 and S6, respectively. No between-period difference in glycemic markers was noticed in the whole population as well as either gender.

3.1.3 | Liver and kidney markers

The crude and adjusted after-intervention and change values for kidney markers (Creatinine, Urea, eGFR) and serum liver enzymes levels (ALP, GGT, AST, ALT) in the whole population are summarized in Table 4. Data for serum ALP is provided for the first phase because a carry-over effect was noticed for this marker. The analysis revealed a significant reduction only in serum ALT after SO consumption ($p = 0.03$). Besides, there was a significant effect on serum Urea levels by SCO intake ($p = 0.02$). Also, the consumption of CO resulted in a significant increase in serum GGT (2.81 ± 1.16) in the whole population (Table 4). The change values for serum urea and ALT levels were significantly different between intervention phases ($p < 0.05$). Indeed, SCO significantly decreased serum Urea in comparison with SO and CO. Also, serum ALT was significantly decreased in SO period compared to CO period.

In males, only SO significantly affected Urea and ALP. The comparison of change values indicated that SO significantly increased serum Urea compared to SCO. Furthermore, serum ALP levels were significantly decreased in the SO period in comparison with SCO and CO in men (Table S7). The analysis indicated that eGFR and Urea were significantly decreased after SO and SCO consumption, respectively in females (Table S8, $p < 0.05$). The between period comparison in females revealed that eGFR was significantly decreased in SO period when compared to CO (Table S8).

4 | DISCUSSION

To the best of our knowledge, the current study is the first investigation that examined substituting regularly consumed oils with SO, CO, and SCO on cardiometabolic risk factors in healthy adults.

After 9 weeks of intervention, there was no difference between intervention oils regarding their effect on cardiovascular risk scores, VAI, blood pressure, and glycemic control markers in the whole population. However, serum HDL-C and TG were significantly improved in the SO period compared with the SCO period, in females. These findings are in line with studies that showed a significant TG- lowering effect of SO (Sankar et al., 2006; Sankar et al., 2011). In a meta-analysis indicating the effect of sesame fractions on lipid profile, it was revealed that SO consumption has a significant reducing effect on serum TG levels (Khalesi et al., 2016). The favorable content of vitamin E, PUFAs, and lignans in sesame might affect TG generation and metabolism (Sankar et al., 2006). Furthermore, animal studies indicated that MUFAs might reduce triglyceride accumulation in the liver (13, 34). Besides, our analysis revealed that CO yielded significant improving effects on Apo A-1 and APO B/A compared to SO, in

TABLE 2 After and change values for lipid profile, CVD scores, VAI, and blood pressure based on the intervention periods

	Sesame oil ($n = 68$)			Sesame-canola oil ($n = 72$)			Canola oil ($n = 68$)				
	After	Change	p^a	After	Change	p^a	After	Change	p^a	p^b	p^c
TC (mg/dl)											
Crude	182.01 ± 3.42[d]	1.69 ± 2.92	0.57	177.21 ± 4.05	−1.42 ± 3.22	0.66	179.95 ± 3.58	−0.98 ± 2.98	0.70	0.39	0.71
Adjusted[e]	182.09 ± 3.58	1.93 ± 3.05	0.50	179.63 ± 4.11	−0.63 ± 3.38	0.87	179.85 ± 3.69	−0.16 ± 2.92	0.81	0.68	0.82
HDL-C (mg/dl)											
Crude	44.36 ± 1.24	2.28 ± 1[a]	0.03	42.51 ± 1.22	−1.61 ± 0.97[b]	0.10	43.38 ± 1.36	1.23 ± 1.25[ab]	0.30	0.17	0.03
Adjusted	44.32 ± 1.28	1.85 ± 1.03	0.09	42.74 ± 1.27	−1.21 ± 0.93	0.23	43.26 ± 1.42	0.64 ± 1.23	0.66	0.28	0.09
LDL-C (mg/dl)											
Crude	93.76 ± 2.22	0.98 ± 1.87	0.62	90.98 ± 2.62	−1.14 ± 2.01	0.57	92.72 ± 2.32	−1.40 ± 1.82	0.41	0.42	0.55
Adjusted	93.90 ± 2.33	0.76 ± 1.95	0.68	92.47 ± 2.68	−0.80 ± 2.12	0.68	92.97 ± 2.42	−0.61 ± 1.75	0.60	0.76	0.79
TG (mg/dl)											
Crude	125.37 ± 7.56	−16.71 ± 7.65	0.03	132.87 ± 6.75	8.88 ± 5.92	0.13	137.41 ± 8.85	2.37 ± 8.51	0.76	0.35	0.06
Adjusted	124.70 ± 7.93	−12.79 ± 7.77	0.09	132.09 ± 7.04	7.58 ± 6.13	0.15	135.32 ± 9.44	5.52 ± 8.59	0.52	0.44	0.16
Apo B (mg/dl)											
Crude	97.24 ± 2.44	−0.82 ± 3.03	0.77	95.84 ± 3.04	−0.80 ± 2.91	0.78	97.31 ± 2.49	−1.33 ± 2.82	0.62	0.81	0.98
Adjusted	97.69 ± 2.57	−0.96 ± 3.19	0.77	97.49 ± 3.12	−0.82 ± 3.10	0.83	97.40 ± 2.61	−0.17 ± 2.81	0.84	0.98	0.97
Apo A-1 (mg/dl)											
Crude	156.96 ± 3.24	−2.24 ± 2.65[ab]	0.39	152.31 ± 3.51	−2.79 ± 2.97[a]	0.36	158.19 ± 3.24	6.41 ± 2.92[b]	0.03	0.26	0.02
Adjusted	156.04 ± 3.31	−2.35 ± 2.79	0.39	152.97 ± 3.70	−1.76 ± 3.08	0.57	157.09 ± 3.24	5.49 ± 2.91	0.08	0.54	0.06
Lp (a) (mg/dl)											
Crude	27.79 ± 3.04	1.64 ± 1.41	0.20	28.04 ± 3.05	1.25 ± 1.59	0.42	26.97 ± 2.99	−0.18 ± 1.50	0.87	0.59	0.71
Adjusted	29.17 ± 3.19	1.74 ± 1.49	0.16	29.23 ± 3.21	1.29 ± 1.70	0.44	28.11 ± 3.15	−0.47 ± 1.56	0.75	0.57	0.63
LDL:HDL ratio											
Crude	2.27 ± 0.12	−0.23 ± 0.20	0.25	2.29 ± 0.10	0.03 ± 0.08	0.63	2.27 ± 0.10	−0.18 ± 0.11	0.13	0.94	0.22
Adjusted	2.28 ± 0.12	−0.20 ± 0.21	0.37	2.32 ± 0.11	0.03 ± 0.08	0.72	2.28 ± 0.10	−0.11 ± 0.10	0.37	0.82	0.43
TC:HDL ratio											
Crude	4.40 ± 0.22	−0.52 ± 0.45	0.25	4.44 ± 0.18	0.08 ± 0.16	0.59	4.36 ± 0.16	−0.36 ± 0.21	0.13	0.84	0.19
Adjusted	4.41 ± 0.24	−0.44 ± 0.47	0.40	4.49 ± 0.19	0.07 ± 0.17	0.66	4.36 ± 0.17	−0.24 ± 0.19	0.34	0.70	0.37
Apo B: Apo A ratio											
Crude	0.64 ± 0.02	0.009 ± 0.02	0.72	0.66 ± 0.03	0.01 ± 0.02	0.50	0.63 ± 0.01	−0.03 ± 0.02	0.09	0.56	0.24
Adjusted	0.64 ± 0.02	0.008 ± 0.02	0.71	0.67 ± 0.03	0.01 ± 0.03	0.59	0.63 ± 0.02	−0.02 ± 0.02	0.21	0.51	0.49
TG:HDL ratio											
Crude	3.37 ± 0.51	−1.48 ± 1.06	0.20	3.57 ± 0.29	0.17 ± 0.35	0.63	3.60 ± 0.33	−0.49 ± 0.46	0.54	0.87	0.33
Adjusted	3.35 ± 0.53	−1.27 ± 1.11	0.35	3.53 ± 0.30	0.12 ± 0.37	0.75	3.54 ± 0.35	−0.33 ± 0.47	0.87	0.91	0.51
Risk of CHD (%)											
Crude	4.53 ± 0.66	−0.79 ± 0.68	0.29	4.42 ± 0.63	0.11 ± 0.30	0.72	4.50 ± 0.62	−0.38 ± 0.44	0.48	0.96	0.48
Adjusted	4.30 ± 0.66	−0.55 ± 0.70	0.55	4.39 ± 0.67	0.16 ± 0.32	0.48	4.35 ± 0.64	−0.20 ± 0.40	0.72	0.97	0.63

(Continues)

TABLE 2 (Continued)

	Sesame oil ($n = 68$)			Sesame-canola oil ($n = 72$)			Canola oil ($n = 68$)				
	After	Change	p^a	After	Change	p^a	After	Change	p^a	p^b	p^c
Risk of MI (%)											
Crude	1.65 ± 0.33	−0.57 ± 0.47	0.27	1.61 ± 0.32	0.09 ± 0.18	0.64	1.62 ± 0.30	−0.18 ± 0.26	0.55	0.98	0.44
Adjusted	1.53 ± 0.32	−0.42 ± 0.48	0.48	1.61 ± 0.33	0.13 ± 0.19	0.38	1.55 ± 0.31	−0.09 ± 0.23	0.76	0.94	0.57
Risk of stroke (%)											
Crude	0.57 ± 0.09	−1.37 ± 1.24	0.27	0.53 ± 0.08	−0.01 ± 0.03	0.76	0.57 ± 0.09	0.01 ± 0.05	0.77	0.63	0.50
Adjusted	0.53 ± 0.09	−1.53 ± 1.30	0.23	0.50 ± 0.08	0.001 ± 0.03	0.89	0.53 ± .09	−0.01 ± 0.04	0.88	0.87	0.50
Risk of CVD (%)											
Crude	5.32 ± 0.79	−1.13 ± 0.95	0.26	5.10 ± 0.75	0.04 ± 0.31	0.91	5.31 ± 0.76	−0.19 ± 0.46	0.73	0.85	0.51
Adjusted	4.99 ± 0.77	−0.99 ± 0.99	0.38	5 ± 0.79	0.15 ± 0.33	0.52	5.05 ± 0.77	−0.14 ± 0.41	0.83	0.98	0.56
Risk of CHD death (%)											
Crude	0.70 ± 0.20	−0.28 ± 0.28	0.35	0.69 ± 0.19	0.08 ± 0.10	0.41	0.69 ± 0.18	−0.07 ± 0.14	0.66	0.99	0.48
Adjusted	0.62 ± 0.20	−0.18 ± 0.28	0.60	0.70 ± 0.20	0.11 ± 0.11	0.21	0.65 ± 0.19	−0.01 ± 0.11	0.96	0.86	0.63
Risk of CVD death (%)											
Crude	0.92 ± 0.30	−0.31 ± 0.38	0.44	0.88 ± 0.25	0.06 ± 0.09	0.51	0.91 ± 0.27	−0.05 ± 0.13	0.71	0.96	0.61
Adjusted	0.84 ± 0.30	−0.23 ± 0.39	0.60	0.88 ± 0.27	0.09 ± 0.10	0.27	0.86 ± 0.29	−0.01 ± 0.11	0.96	0.93	0.70
VAI											
Crude	2.42 ± 0.26	−0.58 ± 0.27	0.34	2.58 ± 0.26	0.22 ± 0.26	0.80	2.45 ± 0.26	−0.34 ± 0.26	0.59	0.86	0.12
Adjusted	2.47 ± 0.27	−0.44 ± 0.27	0.65	2.56 ± 0.27	0.19 ± 0.26	0.98	2.40 ± 0.27	−0.24 ± 0.27	0.94	0.87	0.30
SBP (mm hg)											
Crude	10.35 ± 0.16	−0.50 ± 0.57	0.36	10.12 ± 0.16	−0.19 ± 0.15	0.21	10.36 ± 0.16	0.10 ± 0.15	0.50	0.23	0.30
Adjusted	10.31 ± 0.16	−.058 ± 0.59	0.33	10.12 ± 0.17	−0.12 ± 0.15	0.40	10.32 ± 0.17	0.04 ± 0.15	0.73	0.41	0.49
DBP (mm hg)											
Crude	7.48 ± 0.12	−0.06 ± 0.12	0.64	7.50 ± 0.12	0.01 ± 0.12	0.90	7.52 ± 0.13	0.07 ± 0.12	0.52	0.95	0.74
Adjusted	7.45 ± 0.11	−0.04 ± 0.13	0.66	7.51 ± 0.12	0.09 ± 0.12	0.62	7.48 ± 0.13	0.01 ± 0.12	0.86	0.87	0.74

Note: Values with different superscript are significantly different.

Abbreviations: Apo A-1, Apo lipoprotein A-1; Apo B, Apo lipoprotein B; Apo B:Apo A-1, Apo B to Apo A-1 ratio; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LDL:HDL, LDL-C to HDL-C ratio; Lp (a), lipoprotein a; MI, myocardial infarction; SBP, systolic blood pressure; TC, total cholesterol; TC:HDL, TC to HDL-C ratio; TG, triglyceride; TG:HDL, TG to HDL-C ratio; VAI, visceral adiposity index.

[a]*p* values for within treatment period comparisons using General Linear Model, repeated measures analysis.

[b]*p* values for comparison of after treatment values between the treatment oils using linear mixed effects model.

[c]*p* values for comparison of change values between the treatment oils using linear mixed effects model.

[d]Values are reported as mean ± standard error (SE).

[e]Adjusted for age, sex, baseline BMI, the calculated intervention oils consumed per subject, changes in physical activity level and the energy intake in each intervention period.

TABLE 3 After intervention and change values for glycemic indices based on the intervention periods

	Sesame oil ($n = 68$)			Sesame-canola oil ($n = 72$)			Canola oil ($n = 68$)				
	After	Change	p^a	After	Change	p^a	After	Change	p^a	p^b	p^c
FBS (mg/dl)											
Crude	86.79 ± 1.78[d]	1.26 ± 1.60	0.48	86.71 ± 1.48	2.24 ± 1.26	0.08	88.11 ± 1.69	3.33 ± 1.54	0.03	0.69	0.64
Adjusted[e]	86.52 ± 1.83	1.32 ± 1.68	0.46	85.47 ± 1.41	1.03 ± 1.13	0.24	87.76 ± 1.74	4.32 ± 1.53	0.006	0.38	0.24
Insulin											
Crude	16.02 ± 0.73	−4.62 ± 1.46	0.002	18.01 ± 1.19	−1.60 ± 1.45	0.23	16.64 ± 1.13	−4.14 ± 1.81	0.02	0.38	0.32
Adjusted	16.20 ± 0.76	−4.53 ± 1.51	0.005	17.74 ± 1.26	−1.69 ± 1.53	0.27	16.66 ± 1.20	−3.72 ± 1.85	0.04	0.59	0.39
HOMA -IR											
Crude	2.01 ± 0.09	−0.54 ± 0.17	0.002	2.24 ± 0.13	−0.19 ± 0.16	0.20	2.02 ± 0.13	−0.50 ± 0.20	0.02	0.33	0.31
Adjusted	2.04 ± 0.09	−0.53 ± 0.17	0.005	2.20 ± 0.14	−0.21 ± 0.17	0.22	2.04 ± 0.13	−0.42 ± 0.20	0.04	0.61	0.43
HOMA -S											
Crude	55.95 ± 2.17	10.81 ± 2.52	0.000	53.10 ± 2.50	7.30 ± 2.87	0.01	57.35 ± 2.57	10.06 ± 3.20	0.003	0.29	0.66
Adjusted	55.64 ± 2.26	10.32 ± 2.59	0.000	54.31 ± 2.59	8.06 ± 3.01	0.01	57.49 ± 2.66	9.71 ± 3.29	0.005	0.50	0.85
HOMA -BCF											
Crude	174.84 ± 6.76	−33.65 ± 7.71	0.000	188.48 ± 10.41	−19.24 ± 12.50	0.10	177.48 ± 8.90	−37.54 ± 13.19	0.005	0.47	0.53
Adjusted	176.93 ± 6.86	−32.08 ± 7.92	0.001	190.38 ± 11.03	−15.60 ± 12.86	0.19	177.86 ± 9.29	−39.54 ± 13.62	0.005	0.49	0.42
QUICKI											
Crude	0.32 ± 0.002	0.009 ± 0.003	0.001	0.31 ± 0.002	0.005 ± 0.003	0.07	0.32 ± 0.002	0.008 ± 0.003	0.01	0.44	0.58
Adjusted	0.32 ± 0.002	0.009 ± 0.003	0.003	0.32 ± 0.002	0.006 ± 0.003	0.06	0.32 ± 0.002	0.007 ± 0.003	0.02	0.74	0.78

Abbreviations: FBS, fasting blood sugar; HOMA-%B, homeostasis model assessment for b-cell function; HOMA-IR, homeostasis model assessment for insulin resistance; HOMA-%S, homeostasis model assessment for insulin sensitivity; QUICKI, quantitative insulin sensitivity check index.

[a]*p* values for within treatment period comparisons using General Linear Model, repeated measures analysis.

[b]*p* values for comparison of after treatment values between the treatment oils using linear mixed effects model.

[c]*p* values for comparison of change values between the treatment oils using linear mixed effects model.

[d]Values are reported as mean ± standard error (SE).

[e]Adjusted for age, sex, baseline BMI, the calculated intervention oils consumed per subject, changes in physical activity level and the energy intake in each intervention period.

TABLE 4 After intervention and change values for kidney and liver enzymes based on the intervention periods

	Sesame oil ($n = 68$)			Sesame-canola oil ($n = 72$)			Canola oil ($n = 68$)				
	After	Change	p^a	After	Change	p^a	After	Change	p^a	p^b	p^c
Creatinine											
Crude	1.01 ± 0.02[d]	0.02 ± 0.02	0.28	1 ± 0.01	−0.01 ± 0.02	0.54	0.99 ± 0.02	−0.02 ± 0.02	0.17	0.54	0.24
Adjusted[e]	1.01 ± 0.02	0.01 ± 0.02	0.35	1 ± 0.01	−0.01 ± 0.01	0.58	0.99 ± 0.02	−0.01 ± 0.02	0.40	0.52	0.42
Urea											
Crude	29.86 ± 1.16	0.97 ± 0.90 [a]	0.28	28.57 ± 1.09	−2.22 ± 0.77 [b]	0.006	29.73 ± 1.01	1.32 ± 0.80 [a]	0.10	0.30	0.002
Adjusted	29.77 ± 1.22	1.04 ± 0.94[a]	0.27	28.58 ± 1.15	−1.99 ± 0.81[b]	0.02	29.06 ± 1.04	1.09 ± 0.81[a]	0.15	0.44	0.008
eGFR											
Crude	75.72 ± 1.7	−3.64 ± 1.87	0.10	77.87 ± 1.68	1.45 ± 1.87	0.91	78.26 ± 1.70	1.58 ± 1.87	0.14	0.37	0.11
Adjusted	75.81 ± 1.71	−3.79 ± 1.88	0.10	78.09 ± 1.70	1.61 ± 1.89	0.92	79.17 ± 1.73	1.36 ± 1.87	0.29	0.19	0.10
ALP[f]											
Crude	184.82 ± 9.25	3.34 ± 4.79	0.54	182.57 ± 9.68	2.38 ± 5.02	0.57	184.73 ± 8.70	−0.26 ± 4.51	0.95	0.98	0.85
Adjusted	180.66 ± 9.33	5.26 ± 5.19	0.39	187.67 ± 10	5.70 ± 5.56	0.19	178.70 ± 8.73	−2.04 ± 4.86	0.90	0.78	0.48
GGT											
Crude	21.47 ± 1.11	−3.02 ± 1.56	0.06	22.24 ± 1.40	−0.52 ± 0.79	0.51	25.78 ± 2.49	2.47 ± 1.15	0.04	0.10	0.07
Adjusted	21.19 ± 1.16	−3.08 ± 1.63	0.07	21.83 ± 1.48	−0.61 ± 0.80	0.47	24.10 ± 2.22	2.81 ± 1.16	0.02	0.21	0.056
AST											
Crude	21.95 ± 0.96	−0.35 ± 0.79	0.66	21.54 ± 0.64	−2.09 ± 1.06	0.053	21.43 ± 0.76	−0.95 ± 0.74	0.20	0.85	0.44
Adjusted	21.74 ± 0.99	−0.37 ± 0.83	0.69	21.67 ± 0.68	−1.56 ± 1.10	0.11	21.06 ± 0.75	−0.72 ± 0 .76	0.31	0.71	0.69
ALT											
Crude	18 ± 1.19	−2.17 ± 1.01	0.03	18.17 ± 0.99	−2.68 ± 1.38	0.057	19.93 ± 1.44	1.56 ± 1.31	0.23	0.40	0.06
Adjusted	17.82 ± 1.26	−2.27 ± 1.05[a]	0.03	17.95 ± 1.05	−2.55 ± 1.44[ab]	0.06	19.40 ± 1.48	2.01 ± 1.34 [b]	0.13	0.56	0.03

Note: Values with different superscript are significantly different.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyltransferase.

[a]*p* values for within treatment period comparisons using General Linear Model, repeated measures analysis.

[b]*p* values for comparison of after treatment values between the treatment oils using linear mixed effects model.

[c]*p* values for comparison of change values between the treatment oils using linear mixed effects model.

[d]Values are reported as mean ± standard error (SE).

[e]Adjusted for age, sex, baseline BMI, the calculated intervention oils consumed per subject, changes in physical activity level and the energy intake in each intervention period.

[f]The value is reported for the first phase because carry over effect was seen.

males. Although, it is reported that MUFAs beneficially affect Apo A-1, but no significant effect of CO on this marker was indicated (Negele et al., 2015). It should be noted that some genetic polymorphisms might interact with dietary oils in their effect on cardiometabolic markers (Ramezani-Jolfaie et al., 2020a; Ramezani-Jolfaie et al., 2020b).

Conflicting results were found in males and females in our study; it should be considered that there are some polymorphisms in different genders which are responsible for opposing effects of interventions on lipid profile markers, especially Apo A-1 and HDL-C (Cendoroglo et al., 2005). Furthermore, the conflicting results may be due to hormonal differences between men and women and the moderating effects of female hormones such as progesterone and androgen on lipid metabolism (Wang, Magkos, & Mittendorfer, 2011). Differences in insulin function between men and women might also explain differences in blood lipid metabolism (Magkos, Wang, & Mittendorfer, 2010).

Although no between-period effect was observed, within-period analyses indicated that the intervention oils namely SO and CO had significant favorable effects on insulin resistance and insulin sensitivity. This may support the beneficial effects of PUFAs and MUFAs on glycemic control (Imamura et al., 2016). Our previous study on the effects of CO, SO, and SCO on glycemic control and liver functions enzymes in patients with type 2 diabetes also revealed that SO consumption might improve glycemic control markers compared to CO, in males (Raeisi-Dehkordi et al., 2020). In support of our finding, Vessby et al. indicated that the consumption of an isocaloric MUFAs-rich diet compared to an isocaloric diet rich in saturated fats for 3 months, might significantly improve insulin sensitivity in the healthy individuals (Vessby et al., 2001). A meta-analysis also reported that the substitution of SFAs with PUFAs improved insulin resistance and insulin secretion; whiles, substation of MUFAs had less favorable effects on HOMA-IR and HbA1c (Imamura et al., 2016). This might because of their effect on membrane fluidity (Harayama & Shimizu, 2020; Kröger et al., 2015). Also, MUFAs consumption may decrease serum triglyceride and insulin resistance due to their stimulating effect on fatty acid oxidation by activation of peroxisome proliferator-activated receptor alpha (Soriguer et al., 2006). Besides, MUFAs may affect the affinity of insulin receptors and fluidity of cellular membranes, causing the improvement of insulin resistance (Lovejoy, 2002; Vessby, 2000). Several studies indicated that dietary MUFAs have improving effects on glucagon-like-peptide1 (GLP-1) secretion (Thomsen, Storm, Holst, & Hermansen, 2003). This peptide is an intestinal hormone that exerts favorable effects in stimulating glucose-dependent insulin secretion and regulation of glycemia (García-Flores, Zueco, Álvarez, & Blázquez, 2001). Also, sesamin as a lignan in sesame oil beneficially affects insulin sensitivity through increasing the number of low-affinity insulin receptors (Hong et al., 2013). Furthermore, it has an improving effect on insulin secretion by protecting pancreatic β-cells against oxidative stress (Kong et al., 2015) and has a promoting effect on the expression of insulin receptor-associated proteins genes (Mengxi et al., 2019). In a study conducted by DiNicolantonio et al. it was found that a diet high in MUFAs favorably affects insulin resistance in comparison with a diet high in long-chain SFAs (DiNicolantonio & O'Keefe, 2017). In contrast, in a cross-over clinical trial done in individuals with hyperlipidemia, it was revealed that both rapeseed oil-based diet and dairy fat-based diet significantly decreased FBS; however, none of the mentioned diets affected serum insulin levels (Iggman et al., 2011). In another study which was conducted by Kratz et al., it was shown that olive oil, rapeseed oil, and sunflower oil had no significant effect on HbA1c, serum glucose, and insulin levels after 4 weeks in healthy participants (Kratz et al., 2002).

Our analyses indicated that SCO differently affected serum urea change compared to the other intervention oils, in the whole population. Also, serum ALT change was significantly different between SO and CO periods. In males, SO significantly increased serum Urea compared to SCO. Furthermore, serum ALP levels were significantly decreased in the SO period compared with other oils, in men. Besides, eGFR was significantly decreased in the SO period when compared to CO, in females. A few studies have examined the effect of dietary oils on liver and kidney function tests. In our previous investigation in adults with type 2 diabetes, we found that SO intake might significantly improve serum GGT compared with CO, in females (Raeisi-Dehkordi et al., 2020). In a study conducted by Nigam et al, no significant differences in serum AST and ALT were observed after olive oil, CO, and a widely consumed oil (soybean/safflower oil) intake (Nigam et al., 2014). Furthermore, it was reported that omega-3 polyunsaturated fatty acids might not affect urine albumin and eGFR, in adults with diabetes (Miller 3rd et al., 2013). As data regarding the effect of dietary oils on liver enzymes and kidney markers are still limited, future investigations are needed to confirm our results and to shed light on the possible mechanisms.

The strength of the current study was that participants acted as their own controls due to using a cross-over design, which minimizes the inter-individual variations and confounding variables. Moreover, the substitution of regularly consumed oils with intervention oils might lead to more generalizable and practical results. It should also be noted that we could not estimate the exact amount of intervention oils used by individuals, due to the substitution. However, we tried to estimate the oil consumption by using weighed dietary food records and weighting the given and returned bottles. Moreover, although the mean intake of MUFAs, PUFAs, and SFAs were significantly different between the three intervention phases, it might not be large enough to see clinical effects. However, compared to other studies, the sample size and duration of the present study was sufficient enough to find significant effects. It should be note that the chance of finding significant effects might be lower in this study because participants were healthy adults. It is noteworthy that in the current study, three healthy oils namely SO, CO, and SCO were compared and using other dietary oils like sunflower, palm, or hydrogenated oils might provide more statistically noticeable differences between the intervention oils. We found that the SCO could significantly improve some metabolic markers compared to SO and CO. Therefore, it seems that the blend might improve the beneficial effects of pure oils while it does not adversely affect cardiometabolic markers. This might be because of synergy between ingredients of the two oils (polyphenols, fatty acids, and vitamin E). As this is a novel combination, current results should be interpreted with caution and more investigations are needed to

find the possible explanations and underlying mechanisms for the observed effects. The fatty composition of the three intervention oils was assessed and reported elsewhere (Amiri et al., 2019); however, the chemicals with antioxidant properties were not assessed. Having access to such data would help to interpret the mechanisms for the observed effects.

In conclusion, the present study revealed that intervention oils were not different in their effect on lipid profiles, CVD risk scores, VAI, and blood pressure. In all participants, SCO significantly reduced serum urea compared to other oils and serum ALT levels were significantly decreased in the SO period compared to the CO period. Based on the gender-specific analyses, SO improved serum HDL-C and TG levels compared to SCO, in females. Also, Apo A-1 and Apo B/A change were significantly different between SO and CO, in males. Furthermore, serum ALP levels were significantly decreased in the SO period compared with other periods, in men. Besides, eGFR levels were significantly decreased in the SO period when compared to CO, in females. Conducting future investigations on the effect of SO and CO on liver function and kidney tests and also investigating the gender-specific effects of dietary oils on CMR are highly recommended.

ACKNOWLEDGEMENTS

We thank all the participants for their voluntary and enthusiastic involvement in the study. Also, we are thankful from Shahid Sadoughi University of Medical Sciences (http://www.ssu.ac.ir) and Neshatavar food industry company (Datis Corporation; http://www.neshatavar.com/?l=EN) for their joint funding of this study. Datis Corporation also provided all of the treatment oils consumed during the study including canola, sesame, sesame-canola and sunflower oils. Datis Corporation had no role in the design and conduct of this manuscript; collection, management, analysis, and interpretation of the data; and preparation of this manuscript. We thank the research council of Nutrition and Food Security Research Center and diabetes research center of Shahid Sadoughi University of Medical Sciences, Yazd, Iran, for their scientific support and close cooperation, respectively.

CONFLICT OF INTEREST

The study was jointly funded by Shahid Sadoughi University of Medical sciences and Datis Corporation. The investigators declared that they did not have a direct financial relationship with Datis Corporation and Shahid Sadoughi University of Medical Sciences received the funds and delivered them to the investigators. Datis Corporation did not take any part in the conception, design, the execution of the study protocol, and the reporting of the study results. The corporation did not have any other relationship with the investigators. The authors declare that they have no other potential personal or financial conflicts of interest. The principal investigator (ASA) declares that he has full access to the data and samples provided by this project.

AUTHORS CONTRIBUTIONS

The authors' contributions were as follows: Amin Salehi-Abargouei and Mojgan Amiri designed the study protocol. Mojgan Amiri and Fatemeh Moghtaderi carried out the recruitment of the study participants and had role in data collection. The laboratory analyses were conducted by Hamidreza Raeisi-Dehkordi and Alireza Zimorovat. The data entry was performed by Fatemeh Moghtaderi, Mojgan Amiri, Hamidreza Raeisi-Dehkordi, Alireza Zimorovat, and Matin Mohyadini. Amin Salehi-Abargouei carried out statistical analyses. Fatemeh Moghtaderi provided the first draft of the manuscript. All authors read and approved the final draft of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Amin Salehi-Abargouei https://orcid.org/0000-0002-7580-6717

REFERENCES

Amato, M. C., Giordano, C., Galia, M., Criscimanna, A., Vitabile, S., Midiri, M., & Galluzzo, A. (2010). Visceral adiposity index: a reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care*, *33*(4), 920–922. https://doi.org/10.2337/dc09-1825

Amiri, M., Ghaneian, M. T., Zare-Sakhvidi, M. J., Rahmanian, M., Nadjarzadeh, A., Moghtaderi, F., Raeisi-Dehkordi, H., Zimorovat, A., Jafari, F., Zavar-Reza, J., Jahan-Mihan, A., Aghaei-Meybodi, M. R., & Salehi-Abargouei, A. (2019). 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), 168–178. https://doi.org/10.22122/arya.v15i4.1940

Amiri, M., Raeisi-Dehkordi, H., Sarrafzadegan, N., Forbes, S. C., & Salehi-Abargouei, A. (2020). 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. https://doi.org/10.1016/j.numecd.2020.06.007

Baxheinrich, A., Stratmann, B., Lee-Barkey, Y. H., Tschoepe, D., & Wahrburg, U. (2012). Effects of a rapeseed oil-enriched hypoenergetic diet with a high content of alpha-linolenic acid on body weight and cardiovascular risk profile in patients with the metabolic syndrome. *British Journal of Nutrition*, *108*(4), 682–691. https://doi.org/10.1017/s0007114512002875

Cendoroglo, M. S., Lahoz, C., Martinez, T. L., Ordovas, J. M., Lamon-Fava, S., Cupples, L. A., Wilson, P. W., & Schaefer, E. J. (2005). Association of apo A-IV 360 (Gln --> his) polymorphism with plasma lipids and lipoproteins: The Framingham offspring Study. *Atherosclerosis*, *179*(1), 169–175. https://doi.org/10.1016/j.atherosclerosis.2004.09.020

Chatterjee, A., Harris, S. B., Leiter, L. A., Fitchett, D. H., Teoh, H., & Bhattacharyya, O. K. (2012). Managing cardiometabolic risk in primary care: Summary of the 2011 consensus statement. *Canadian Family Physician*, *58*(4), 389–393.

Chow, S.-C., Shao, J., & Wang, H. (2008). *Sample size calculations in clinical research* (2nd ed.). Boca Raton: Chapman & Hall/CRC.

DiNicolantonio, J. J., & O'Keefe, J. H. (2018). Effects of dietary fats on blood lipids: a review of direct comparison trials. *Open Heart*, *5*(2), e000871. https://doi.org/10.1136/openhrt-2018-000871

DiNicolantonio, J. J., & O'Keefe, J. H. (2017). Good fats versus bad fats: a comparison of fatty acids in the promotion of insulin resistance, inflammation, and obesity. *Missouri Medicine*, *114*(4), 303–307.

Eckel, R. H., Kahn, R., Robertson, R. M., & Rizza, R. A. (2006). Preventing cardiovascular disease and diabetes: a call to action from the American Diabetes Association and the American Heart Association. *Circulation*, *113*(25), 2943–2946. https://doi.org/10.2337/dc06-9911

Galgani, J. E., Uauy, R. D., Aguirre, C. A., & Díaz, E. O. (2008). Effect of the dietary fat quality on insulin sensitivity. *British Journal of Nutrition*, *100*(3), 471–479. https://doi.org/10.1017/S0007114508894408

García-Flores, M., Zueco, J. A., Álvarez, E., & Blázquez, E. (2001). Expression of glucagon-like peptide-1 (GLP-1) receptor and the effect of GLP-1-(7–36) amide on insulin release by pancreatic islets during rat ontogenic development. *European Journal of Biochemistry*, *268*(3), 514–520.

Harayama, T., & Shimizu, T. (2020). Roles of polyunsaturated fatty acids, from mediators to membranes. *Journal of Lipid Research*, *jlr. R120000800*, 1150–1160.

Hong, L., Yi, W., Liangliang, C., Juncheng, H., Qin, W., & Xiaoxiang, Z. (2013). Hypoglycaemic and hypolipidaemic activities of sesamin from sesame meal and its ability to ameliorate insulin resistance in KK-ay mice. *Journal of the Science of Food and Agriculture*, *93*(8), 1833–1838.

Howard, B. V., Van Horn, L., Hsia, J., Manson, J. E., Stefanick, M. L., Wassertheil-Smoller, S., Kuller, L. H., LaCroix, A. Z., Langer, R. D., Lasser, N. L., Lewis, C. E., Limacher, M. C., Margolis, K. L., Mysiw, W. J., Ockene, J. K., Parker, L. M., Perri, M. G., Phillips, L., Prentice, R. L., … Morley Kotchen, J. (2006). Low-fat dietary pattern and risk of cardiovascular disease: The Women's Health initiative randomized controlled dietary modification trial. *JAMA*, *295*(6), 655–666. https://doi.org/10.1001/jama.295.6.655

Iggman, D., Gustafsson, I. B., Berglund, L., Vessby, B., Marckmann, P., & Risérus, U. (2011). Replacing dairy fat with rapeseed oil causes rapid improvement of hyperlipidaemia: a randomized controlled study. *Journal of Internal Medicine*, *270*(4), 356–364. https://doi.org/10.1111/j.1365-2796.2011.02383.x

Imamura, F., Micha, R., Wu, J. H., de Oliveira Otto, M. C., Otite, F. O., Abioye, A. I., & Mozaffarian, D. (2016). 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. https://doi.org/10.1371/journal.pmed.1002087

Jakobsen, M. U., O'Reilly, E. J., Heitmann, B. L., Pereira, M. A., Bälter, K., Fraser, G. E., Goldbourt, U., Hallmans, G., Knekt, P., Liu, S., Pietinen, P., Spiegelman, D., Stevens, J., Virtamo, J., Willett, W. C., & Ascherio, A. (2009). Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. *The American Journal of Clinical Nutrition*, *89*(5), 1425–1432. https://doi.org/10.3945/ajcn.2008.27124

Jebb, S. A., Lovegrove, J. A., Griffin, B. A., Frost, G. S., Moore, C. S., Chatfield, M. D., Bluck, L. J., Williams, C. M., & Sanders, T. A. (2010). Effect of changing the amount and type of fat and carbohydrate on insulin sensitivity and cardiovascular risk: The RISCK (Reading, Imperial, Surrey, Cambridge, and kings) trial. *The American Journal of Clinical Nutrition*, *92*(4), 748–758. https://doi.org/10.3945/ajcn.2009.29096

Jenkins, D. J., Kendall, C. W., Vuksan, V., Faulkner, D., Augustin, L. S., Mitchell, S., Ireland, C., Srichaikul, K., Mirrahimi, A., Chiavaroli, L., Mejia, S. B., Nishi, S., Sahye-Pudaruth, S., Patel, D., Bashyam, B., Vidgen, E., de Souza, R. J., Sievenpiper, J. L., Coveney, J., … Leiter, L. A. (2014). Effect of lowering the glycemic load with canola oil on glycemic control and cardiovascular risk factors: a randomized controlled trial. *Diabetes Care*, *37*(7), 1806–1814. https://doi.org/10.2337/dc13-2990

Katz, A., Nambi, S. S., Mather, K., Baron, A. D., Follmann, D. A., Sullivan, G., & Quon, M. J. (2000). Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *The Journal of Clinical Endocrinology & Metabolism*, *85*(7), 2402–2410. https://doi.org/10.1210/jcem.85.7.6661

Khalesi, S., Paukste, E., Nikbakht, E., & Khosravi-Boroujeni, H. (2016). Sesame fractions and lipid profiles: a systematic review and meta-analysis of controlled trials. *British Journal of Nutrition*, *115*(5), 764–773. https://doi.org/10.1017/S0007114515005012

Khosravi-Boroujeni, H., Nikbakht, E., Natanelov, E., & Khalesi, S. (2017). Can sesame consumption improve blood pressure? A systematic review and meta-analysis of controlled trials. *Journal of the Science of Food and Agriculture*, *97*(10), 3087–3094. https://doi.org/10.1002/jsfa.8361

Kong, X., Wang, G.-D., Ma, M.-Z., Deng, R.-Y., Guo, L.-Q., Zhang, J.-X., Yang, J.-R., & Su, Q. (2015). Sesamin ameliorates advanced glycation end products-induced pancreatic β-cell dysfunction and apoptosis. *Nutrients*, *7*(6), 4689–4704. https://doi.org/10.3390/nu7064689

Kratz, M., von Eckardstein, A., Fobker, M., Buyken, A., Posny, N., Schulte, H., Assmann, G., & Wahrburg, U. (2002). The impact of dietary fat composition on serum leptin concentrations in healthy nonobese men and women. *The Journal of Clinical Endocrinology & Metabolism*, *87*(11), 5008–5014. https://doi.org/10.1210/jc.2002-020496

Kröger, J., Jacobs, S., Jansen, E. H., Fritsche, A., Boeing, H., & Schulze, M. B. (2015). Erythrocyte membrane fatty acid fluidity and risk of type 2 diabetes in the EPIC-Potsdam study. *Diabetologia*, *58*(2), 282–289. https://doi.org/10.1007/s00125-014-3421-7

Kruse, M., von Loeffelholz, C., Hoffmann, D., Pohlmann, A., Seltmann, A. C., Osterhoff, M., Hornemann, S., Pivovarova, O., Rohn, S., Jahreis, G., & Pfeiffer, A. F. (2015). Dietary rapeseed/canola-oil supplementation reduces serum lipids and liver enzymes and alters postprandial inflammatory responses in adipose tissue compared to olive-oil supplementation in obese men. *Molecular Nutrition & Food Research*, *59*(3), 507–519. https://doi.org/10.1002/mnfr.201400446

Lastra, G., Manrique, C., & Sowers, J. R. (2006). Obesity, cardiometabolic syndrome, and chronic kidney disease: The weight of the evidence. *Advances in Chronic Kidney Disease*, *13*(4), 365–373. https://doi.org/10.1053/j.ackd.2006.07.011

Levey, A. S., Stevens, L. A., Schmid, C. H., Zhang, Y. L., Castro, A. F., Feldman, H. I., Kusek, J. W., Eggers, P., Van Lente, F., Greene, T., & Coresh, J. (2009). A new equation to estimate glomerular filtration rate. *Annals of Internal Medicine*, *150*(9), 604–612. https://doi.org/10.7326/0003-4819-150-9-200905050-00006

Lovejoy, J. C. (2002). The influence of dietary fat on insulin resistance. *Current Diabetes Reports*, *2*(5), 435–440. https://doi.org/10.1007/s11892-002-0098-y

Magkos, F., Wang, X., & Mittendorfer, B. (2010). Metabolic actions of insulin in men and women. *Nutrition*, *26*(7–8), 686–693. https://doi.org/10.1016/j.nut.2009.10.013

Mathers, C. D., & Loncar, D. (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Medicine*, *3*(11), e442. https://doi.org/10.1371/journal.pmed.0030442

Mengxi, W., Mo, L., Renjie, Z., Jing, W., Dongya, C., & Hong, L. (2019). Ameliorating effect of sesamin on insulin resistance of hepatic L02 cells induced by high glucose/high insulin. *Pakistan Journal of Pharmaceutical Sciences*, *32*(6), 2733–2739.

Mensink, R. P., Zock, P. L., Kester, A. D., & Katan, M. B. (2003). Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *American Journal of Clinical Nutrition*, *77*(5), 1146–1155. https://doi.org/10.1093/ajcn/77.5.1146

Mente, A., de Koning, L., Shannon, H. S., & Anand, S. S. (2009). A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. *Archives of Internal Medicine*, *169*(7), 659–669. https://doi.org/10.1001/archinternmed.2009.38

Miller, E. R., 3rd, Juraschek, S. P., Anderson, C. A., Guallar, E., Henoch-Ryugo, K., Charleston, J., Turban, S., Bennett, M. R., & Appel, L. J. (2013). The effects of n-3 long-chain polyunsaturated fatty acid supplementation on biomarkers of kidney injury in adults with diabetes: Results of the GO-FISH trial. *Diabetes Care*, *36*(6), 1462–1469. https://doi.org/10.2337/dc12-1940

Mitra, A. (2007). Study on the benefits of sesame oil over coconut oil in patients of insulin resistance syndrome, notably type 2 diabetes and dyslipidaemia. *Journal of Human Ecology*, *22*(1), 61–66. https://doi.org/10.1080/09709274.2007.11906001

Miyawaki, T., Aono, H., Toyoda-Ono, Y., Maeda, H., Kiso, Y., & Moriyama, K. (2009). Antihypertensive effects of sesamin in humans.

Journal of Nutritional Science and Vitaminology, *55*(1), 87–91. https://doi.org/10.3177/jnsv.55.87

Mozaffarian, D., Micha, R., & Wallace, S. (2010). 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. https://doi.org/10.1371/journal.pmed.1000252

Namiki, M. (2007). Nutraceutical functions of sesame: a review. *Critical Reviews in Food Science and Nutrition*, *47*(7), 651–673. https://doi.org/10.1080/10408390600919114

Negele, L., Schneider, B., Ristl, R., Stulnig, T. M., Willfort-Ehringer, A., Helk, O., & Widhalm, K. (2015). Effect of a low-fat diet enriched either with rapeseed oil or sunflower oil on plasma lipoproteins in children and adolescents with familial hypercholesterolaemia. Results of a pilot study. *European Journal of Clinical Nutrition*, *69*(3), 337–343. https://doi.org/10.1038/ejcn.2014.234

Nigam, P., Bhatt, S., Misra, A., Chadha, D. S., Vaidya, M., Dasgupta, J., & Pasha, Q. M. (2014). Effect of a 6-month intervention with cooking oils containing a high concentration of monounsaturated fatty acids (olive and canola oils) compared with control oil in male Asian Indians with nonalcoholic fatty liver disease. *Diabetes Technology & Therapeutics*, *16*(4), 255–261. https://doi.org/10.1089/dia.2013.0178

Pathak, N., Rai, A. K., Kumari, R., & Bhat, K. V. (2014). Value addition in sesame: A perspective on bioactive components for enhancing utility and profitability. *Pharmacognosy Reviews*, *8*(16), 147–155. https://doi.org/10.4103/0973-7847.134249

Payne, R. Cardiovascular Risk Calculator v1.2, Edinburgh: Framingham CVD, ASSIGN, BNF, and Framingham CHD Edinburgh: University of Edinburgh (updated May 10, 2010; cited May 9, 2012).

Payne, R. A. (2012). Cardiovascular risk. *British Journal of Clinical Pharmacology*, *74*(3), 396–410. https://doi.org/10.1111/j.1365-2125.2012.04219.x

Qian, F., Korat, A. A., Malik, V., & Hu, F. B. (2016). Metabolic effects of monounsaturated fatty acid–enriched diets compared with carbohydrate or polyunsaturated fatty acid–enriched diets in patients with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Care*, *39*(8), 1448–1457. https://doi.org/10.2337/dc16-0513

Raeisi-Dehkordi, H., Amiri, M., Zimorovat, A., Moghtaderi, F., Zarei, S., Forbes, S. C., & Salehi-Abargouei, A. (2020). 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. https://doi.org/10.1002/dmrr.3399

Ramezani-Jolfaie, N., Aghaei, S., Farashahi Yazd, E., Moradi, A., Mozaffari-Khosravi, H., Amiri, M., Raeisi-Dehkordi, H., Moghtaderi, F., Zimorovat, A., Yasini Ardakani, S. A., & Salehi-Abargouei, A. (2020a). The combined effects of cholesteryl ester transfer protein (CETP) TaqIB gene polymorphism and canola, sesame and sesame-canola oils consumption on metabolic response in patients with diabetes and healthy people. *Journal of Cardiovascular and Thoracic Research*, *12*(3), 185–194.

Ramezani-Jolfaie, N., Aghaei, S., Farashahi Yazd, E., Moradi, A., Mozaffari-Khosravi, H., Zimorovat, A., Raeisi-Dehkordi, H., Moghtaderi, F., Amiri, M., Yasini Ardakani, S. A., & Salehi-Abargouei, A. (2020b). 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.

Rogi, T., Tomimori, N., Ono, Y., & Kiso, Y. (2011). The mechanism underlying the synergetic hypocholesterolemic effect of sesamin and alpha-tocopherol in rats fed a high-cholesterol diet. *Journal of Pharmacological Sciences*, *115*(3), 408–416. https://doi.org/10.1254/jphs.10287fp

Roth, G. A., Johnson, C., Abajobir, A., Abd-Allah, F., Abera, S. F., Abyu, G., Ahmed, M., Aksut, B., Alam, T., Alam, K., Alla, F., Alvis-Guzman, N., Amrock, S., Ansari, H., Ärnlöv, J., Asayesh, H., Atey, T. M., Avila-Burgos, L., Awasthi, A., … Naghavi, M. (2017). Global, regional, and National Burden of cardiovascular diseases for 10 causes, 1990 to 2015. *Journal of the American College of Cardiology*, *70*(1), 1–25. https://doi.org/10.1016/j.jacc.2017.04.052

Ruilope, L. M., de la Sierra, A., Segura, J., & Garcia-Donaire, J. A. (2007). The meaning of cardiometabolic risk in hypertensive patients. *US Endocrinology*, (1), 60–63. https://doi.org/10.17925/use.2007.00.1.60

Rasmussen, B. M., Vessby, B., Uusitupa, M., Berglund, L., Pedersen, E., Riccardi, G., Rivellese, A. A., Tapsell, L., & Hermansen, K. (2006). Effects of dietary saturated, monounsaturated, and n− 3 fatty acids on blood pressure in healthy subjects. *The American Journal of Clinical Nutrition*, *83*(2), 221–226. https://doi.org/10.1093/ajcn/83.2.221

Saedi, S., Noroozi, M., Khosrotabar, N., Mazandarani, S., & Ghadrdoost, B. (2017). How canola and sunflower oils affect lipid profile and anthropometric parameters of participants with dyslipidemia. *Medical Journal of the Islamic Republic of Iran*, *31*, 5–28. https://doi.org/10.18869/mjiri.31.5

Sankar, D., Ali, A., Sambandam, G., & Rao, R. (2011). Sesame oil exhibits synergistic effect with anti-diabetic medication in patients with type 2 diabetes mellitus. *Clinical Nutrition*, *30*(3), 351–358. https://doi.org/10.1016/j.clnu.2010.11.005

Sankar, D., Rao, M. R., Sambandam, G., & Pugalendi, K. V. (2006). A pilot study of open label sesame oil in hypertensive diabetics. *Journal of Medicinal Food*, *9*(3), 408–412. https://doi.org/10.1089/jmf.2006.9.408

Sankar, D., Sambandam, G., Ramakrishna Rao, M., & Pugalendi, K. V. (2005). Modulation of blood pressure, lipid profiles and redox status in hypertensive patients taking different edible oils. *Clinica Chimica Acta*, *355*(1–2), 97–104. https://doi.org/10.1016/j.cccn.2004.12.009

Soriguer, F., Morcillo, S., Cardona, F., Rojo-Martínez, G., de la Cruz Almaráz, M., de la Soledad Ruiz de Adana, M., Olveira, G., Tinahones, F., & Esteva, I. (2006). Pro12Ala polymorphism of the PPARG2 gene is associated with type 2 diabetes mellitus and peripheral insulin sensitivity in a population with a high intake of oleic acid. *The Journal of Nutrition*, *136*(9), 2325–2330. https://doi.org/10.1093/jn/136.9.2325

Sukumar, D., Arimboor, R., & Arumughan, C. (2008). HPTLC fingerprinting and quantification of lignans as markers in sesame oil and its polyherbal formulations. *Journal of Pharmaceutical and Biomedical Analysis*, *47*(4–5), 795–801. https://doi.org/10.1016/j.jpba.2008.03.018

Thomsen, C., Storm, H., Holst, J. J., & Hermansen, K. (2003). Differential effects of saturated and monounsaturated fats on postprandial lipemia and glucagon-like peptide 1 responses in patients with type 2 diabetes. *The American Journal of Clinical Nutrition*, *77*(3), 605–611.

Tinker, L. F., Bonds, D. E., Margolis, K. L., Manson, J. E., Howard, B. V., Larson, J., Perri, M. G., Beresford, S. A., Robinson, J. G., Rodríguez, B., Safford, M. M., Wenger, N. K., Stevens, V. J., Parker, L. M., & Women's Health, I. (2008). Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: The Women's Health initiative randomized controlled dietary modification trial. *Archives of Internal Medicine*, *168*(14), 1500–1511. https://doi.org/10.1001/archinte.168.14.1500

Vessby, B. (2000). Dietary fat and insulin action in humans. *British Journal of Nutrition*, *83 Suppl 1(S1)*, S91–S96. https://doi.org/10.1017/s000711450000101x

Vessby, B., Uusitupa, M., Hermansen, K., Riccardi, G., Rivellese, A. A., Tapsell, L. C., Nalsen, C., Berglund, L., Louheranta, A., Rasmussen, B. M., Calvert, G. D., Maffetone, A., Pedersen, E., Gustafsson, I. B., & Storlien, L. H. (2001). Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU Study. *Diabetologia*, *44*(3), 312–319. https://doi.org/10.1007/s001250051620

Wang, X., Magkos, F., & Mittendorfer, B. (2011). Sex differences in lipid and lipoprotein metabolism: it's not just about sex hormones. *The Journal of Clinical Endocrinology & Metabolism*, *96*(4), 885–893. https://doi.org/10.1210/jc.2010-2061

Willett, W. (1990). *Nutritional epidemiology*. New York: Oxford University Press.

Yuliana, N. D., Iqbal, M., Jahangir, M., Wijaya, C. H., Korthout, H., Kottenhage, M., Kim, H. K., & Verpoorte, R. (2011). Screening of selected Asian spices for anti obesity-related bioactivities. *Food Chemistry*, *126*(4), 1724–1729. https://doi.org/10.1016/j.foodchem.2010.12.066

Zambiazi, R. C., Przybylski, R., Zambiazi, M. W., & Mendonça, C. B. (2007). Fatty acid composition of vegetable oils and fats. *Boletim Do Centro de Pesquisa de Processamento de Alimentos*, *25*(1). https://doi.org/10.5380/cep.v25i1.8399

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Moghtaderi, F., Amiri, M., Raeisi-Dehkordi, H., Zimorovat, A., Mohyadini, M., & Salehi-Abargouei, A. (2022). 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. https://doi.org/10.1002/ptr.7381