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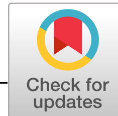

RESEARCH ARTICLE

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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

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Abstract

Background: This study aimed to compare the effects of sesame (SO), canola (CO), and sesame-canola (SCO: a blend) oils on glycaemic control markers and liver function enzymes in adults with type 2 diabetes.

Methods: In this randomized, triple-blind, three-way, cross-over clinical trial, participants replaced their usual oil with the intervention oils for 9 weeks. Serum fasting blood sugar, fasting serum insulin (FSI), insulin resistance (HOMA2-IR), beta-cell function (HOMA2-%B), insulin sensitivity (HOMA2-%S), quantitative insulin sensitivity check index (QUICKI), as well as serum liver function enzymes were measured at baseline and end of intervention periods.

Results: Ninety-two participants completed all treatment periods. After adjusting for confounders, all treatment oils resulted in significant improvements in FSI and HOMA2-%S ($p < 0.05$). SO and SCO led to favourable changes in HOMA2-IR and QUICKI ($p < 0.05$). Following CO and SCO, there was a significant decrease in HOMA2-%B ($p < 0.05$). The sex-stratified analysis revealed that FSI and HOMA2-IR were decreased after SO compared to CO in males ($p = 0.024$). Serum gamma-glutamyltransferase (GGT) was significantly lower following SO compared to CO in females ($p = 0.02$), however, the difference in change values was not significant ($p = 0.058$).

Conclusions: SO consumption appears to improve glycaemic control markers in males and serum GGT in females compared with CO in patients with type 2 diabetes (registration code: IRCT2016091312571N6).

KEYWORDS
canola oil, glycaemic control, liver function enzymes, rapeseed oil, sesame oil, type 2 diabetes mellitus

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1 | INTRODUCTION

The prevalence of type 2 diabetes mellitus (T2DM) is increasing worldwide, leading to a large economic burden.[1] Globally, individuals diagnosed with T2DM are projected to increase to 366 million by 2030.[2] T2DM is correlated to a variety of metabolic disorders ranging from dyslipidaemia, hyperglycaemia, and insulin resistance to cardiovascular and liver disease.[3,4] T2DM and glycaemic control are associated with abnormal liver enzymes, non-alcoholic fatty liver disease, cirrhosis, and hepatocellular carcinoma that all increase the risk of hepatic complications.[5] The associations between elevated liver function enzymes and development of T2DM have been previously addressed.[6,7]

Lifestyle modification, such as dietary interventions, is a frontline strategy for glucose control in T2DM.[8,9] A large clinical trial ($N = 3234$ non-diabetic participants) revealed that lifestyle interventions were more effective than metformin in reducing the risk of diabetes.[10] Current dietary guidelines promote a diet low in saturated fat and sugar.[11,12] A recent systematic review and meta-analysis found that replacing saturated fatty acids (SFAs) or carbohydrates with an isocaloric quantity of plant-derived polyunsaturated fatty acids (PUFAs) significantly improved fasting insulin and HOMA-IR in non-diabetic patients.[13] In contrast, a meta-analysis including 83 randomized controlled trials examining omega-3, omega-6, or total PUFAs supplementation had little or no effect on diabetes prognosis or measures of glucose control; with only alpha-linolenic acid (ALA) increased fasting insulin levels (~7%).[14]

Canola oil (CO) is among the most widely consumed vegetable oils and contains low amounts of SFAs (~7%), moderate amounts of PUFAs (~28%) and ALA (~8.3%), and high amounts of monounsaturated fatty acids (MUFAs, ~64%).[15] CO's fatty acids profile along with an unsaturated to SFA ratio of 15:1[16] makes CO an ideal dietary strategy to enhance glucose control. Presently, there are a large number of clinical trials that have investigated the effects of CO-based diets on lipid profiles and body composition[17,18]; however, only a few studies have examined glucose metabolism, insulin sensitivity, and liver enzymes concurrently.[19,20] Södergren et al. reported that a CO-based diet decreases fasting plasma glucose, but not insulin levels in comparison with an SFA-based diet.[21] Iggman et al. replaced dairy fat with CO for 3 weeks in hypercholesterolemia patients. CO replacement did not significantly alter insulin sensitivity or fasting glucose concentrations.[22] Sesame oil (SO) is another vegetable oil that is widely used in Asian countries.[23] SO contains high amounts of lignans (i.e., sesamin, sesamol, episesamin, and sesamolin) that may impact several physiological responses, due to their antioxidant and hypoglycaemic properties.[24,25] SO is also considered a 'good' source of MUFAs (40%) and PUFAs (43%) as well as vitamin E.[26] A limited number of studies have evaluated SO in conjunction with anti-diabetic agents or in combination with other edible oils on glycaemic control,[27,28] with a lack of evidence of SO on liver function. The objective of the present study was to compare the effects of replacing edible oils rich in MUFAs and PUFAs, including SO, CO, and a blend of sesame and canola oil (SCO) on glycaemic control and serum liver enzymes in patients with T2DM in a three-way randomized cross-over clinical trial. In addition, sex-based differences are well established in certain areas of research such as cardiovascular disease,[29] however, data regarding the effects of dietary oils in males and females are limited. Thus, we aimed to further explore the impact of CO, SO, and SCO in both sexes.

2 | METHODS

The present study was derived from a large three-way cross-over clinical trial primarily aimed to compare the effects of canola, sesame, and SCOs on fasting blood glucose and lipid profiles in adults with T2DM and their spouses. The participants' characteristics, as well as detailed methodology, are published elsewhere.[30] All individuals provided written informed consent before enrolment. The trial was registered in the Iranian Registry of Clinical Trials (IRCT; registration ID: IRCT2016091312571N6). The present study was approved by the ethics committee of Shahid Sadoughi University of Medical Sciences with a reference number of IR.SSU.SPH.REC.1396.156.

2.1 | Participants

Participants were recruited from the Diabetes Research Center located at the Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Participants meeting the following criteria: (i) males and females between 18 and 60 years of age, (ii) diagnosed with T2DM at least 6 months and at most 10 years prior to the start of the study, (iii) an HbA1c ≤ 8%, (iv) treated with oral antidiabetic agents, (v) not prescribed insulin, and (vi) or a dose of lipid-lowering medications that had not been changed within the last 3 months, were invited. Participants with a history of any other chronic disease(s) including cardiovascular diseases such as coronary artery disease, stroke, congestive heart disease, and coronary artery bypass grafting, kidney or liver diseases (serum aspartate aminotransferase [AST] and serum alanine aminotransferase [ALT] three times greater than normal values), or cancer, were excluded. Participants that altered their dietary habits or followed a special diet, went on insulin therapy, became pregnant, or were diagnosed with a chronic disease during the study were removed.[30] Once participants were enrolled demographic data and education level were recorded.

2.2 | Study design

This study used a randomized, triple-blind, cross-over clinical trial. Statistical package for social sciences (SPSS) was used to randomly assign the participants (51 males and 51 females; eligible participants) into six rolling sequences (stratified by sex) to receive the treatment oils.[30] The sequences were kept in sealed envelopes and were later allocated to participants. The treatment oils were provided in similar-shaped containers which were labelled with three

codes (S, B, and G). All oils underwent purification and odour removal to blind the participants. The fatty acid profiles of the three treatment oils are provided in Table S1. The participants, study co-ordinators, technicians, and statisticians were blinded to the treatments. The specific methods used for randomization, allocation concealment, and blinding are detailed in the published study protocol.[30]

The total daily energy requirement was calculated using standard formulas.[31] A dietary recommendation was designed based on the American Diabetic Association recommendations; 30%–32% of total energy intake from fats, 50%–52% from carbohydrates, and 16%–18% from proteins was individually prescribed.[32] Participants then entered a 4-week run-in period in which sunflower oil was provided for participants. Following the 4-week run-in, the edible oils used at home were replaced by either CO, SO, and SCO (with 40% SO and 60% CO). The treatment periods were 9 weeks in length and were separated by 4-week wash-out periods (sunflower oil was provided during the wash-out periods). Sunflower oil is one of the most consumed dietary oils in Iran since this dietary oil is produced widely and is affordable. Sunflower oil is also well-known among Iranian families and is used as the main cooking oil.[33] The treatment oils were provided for the participants and their families to assist with adherence.[30]

2.3 | Dietary intake measurement

To measure total dietary energy intake, as well as macro- and micronutrient composition, weighted food records (including 2 weekdays and 1 weekend day) were obtained at the start, middle, and end of the intervention periods and analysed using Nutritionist IV software (version 3.5.2, Axxya Systems) that was modified for Iranian foods. Participants were instructed on how to complete the food records correctly by a nutritionist. The total daily intake of all foods and nutrients were calculated and converted to grams/day.[34]

2.4 | Physical activity assessment

Physical activity was assessed at the start, middle, and end of the intervention periods using a 3-day self-report record (2 weekdays and 1 weekend day). In total, physical activity was recorded nine times for each participant (three time points and three conditions). The participants were asked to maintain their normal physical activity patterns throughout the study. Physical activity data were converted to metabolic equivalents•min per day (Met•min/day), using a compendium of physical activities.[35]

2.5 | Anthropometric measurements

Height was measured to the nearest 0.1 cm using a measuring tape fixed to a wall. Body mass was measured, while participants were wearing light clothing without shoes, to the nearest 0.1 kg, by a digitally calibrated scale (Omron, mode: BF51). Body mass index (BMI) was computed by dividing body mass (kg) by height in metres squared (m^2).

2.6 | Blood markers assessment

Blood samples were collected at baseline and following each intervention period. All samples were collected in the early morning after an overnight fast. Detailed blood sampling information has been described previously.[30] Briefly, commercial kits were used to measure fasting blood sugar (FBS), serum alkaline phosphatase (ALP), gamma-glutamyltransferase (GGT), AST, and ALT concentrations (Pars Azmun). The intra- and inter-assay coefficients of variation (CVs) were 1.50% and 0.90%, 1.16% and 1.10%, 1.42% and 0.90%, 2.36% and 2.15%, and 3.28% and 1.86%, respectively. Fasting serum insulin (FSI) was measured using enzyme-linked immunoassays kits (Monobind, Inc.). The intra- and inter-assay CVs for serum insulin were 3.1% and 5.9%, respectively. HOMA-2 indices (updated homoeostasis model assessment) including HOMA2-%S (homoeostasis model assessment for insulin sensitivity), HOMA2-%B (homoeostasis model assessment for b-cell function), and HOMA2-IR (homoeostasis model assessment for insulin resistance) were calculated using the computer model HOMA Calculator version 2.2.[36] The updated version of HOMA accounts for peripheral and hepatic glucose resistance variations and includes renal glucose losses, thus improves accuracy for hyperglycaemic individuals.[36,37] The quantitative insulin sensitivity check index was calculated based on a published formula.[38]

2.7 | Intervention compliance

Considering the design of the current study which was the replacement of the participants' regular oil intake with the intervention oils and regarding that, the intervention oils were provided for the participants and their family, it was hard to assess the exact amount of oils consumed. Accordingly, two methods were used to determine compliance: (i) the returned containers were weighed and the amount of oils consumed were estimated, (ii) the 3-day dietary records were used to assess the amount of oils consumed. The averages of mid- and post-intervention values for dietary intakes were compared between intervention periods to assess compliance.

2.8 | Sample size calculation

The sample size was estimated using the following formula [$n = [(z\ 1-\alpha/2 + z\ 1-\beta)^2 \times s^2]/2\Delta^2$][39] with serum glucose as the primary variable.[40] The type 1 error was set at 5% and type 2 error was set at 10% (power of 90%). A minimum of 34 participants was determined. In the present study, we aimed to have enough power to

conduct sex-specific analyses. We predicted that the attrition rate would be high in the present study; therefore, we targeted to enter 50 males and 50 females. The primary outcomes were glycaemic control indices (FBS, FSI, HOMA-2 indices, and QUICKI) and the secondary outcomes were liver enzymes (ALT, AST, ALP, and GGT).

2.9 | Statistical analyses

The quantified variables are reported as mean ± standard error (SE), unless otherwise indicated. Kolmogorov–Smirnov test was used to confirm normality. The end values were compared against the baseline values using repeated measures analysis of variance. The change values were compared between the intervention phases using linear mixed models considering the rolling method and carry-over variable as fixed factors in the crude (unadjusted) and multivariate-adjusted model. The potential confounders: age, sex, baseline BMI, intervention oils consumed, physical activity, energy intake in each intervention period, and baseline values were included as covariates in the multivariate-adjusted model. The sex-stratified analyses were conducted to explore possible sex-specific effects. In the sensitivity analysis, all analyses were replicated after removing participants who changed the dose or the type of medications used for blood glucose or lipid control. Statistical analyses were conducted using IBM SPSS (version 20; IBM Corporation). $p \leq 0.05$ was considered as statistically significant.

3 | RESULTS

One hundred and two participants were enrolled and randomly assigned. Six participants dropped out or were excluded (moved to another city [$n = 1$], began insulin therapy [$n = 1$], diagnosed with cardiovascular disease [$n = 1$], personal reasons [$n = 3$]). One additional participant was excluded from the statistical analyses because of insufficient compliance based on dietary records. Three participants were excluded from the final analysis in the SO condition due to insufficient visits. In total, 92, 95, and 95 participants completed the SO, SCO, and CO conditions, respectively (Figure 1). Baseline participant characteristics ($n = 46$ males; $n = 49$ females) are provided in Table 1. Serum ALT was significantly higher in males compared to females ($p = 0.008$).

The averages of mid- and post-intervention values for energy intake and macro- and micro-nutrient composition, as well as physical activity for each condition, are shown in Table 2. There were no significant differences between conditions for total energy, carbohydrates, proteins, or fat intake. Significant differences were observed between conditions for dietary intakes of MUFAs and PUFAs ($p < 0.001$ and $p = 0.008$, respectively). Physical activity remained unchanged throughout the duration of the study and was similar between conditions (Table 2).

3.1 | The effect of intervention oils on glycaemic control markers and liver enzymes

Importantly, no significant carry-over effects were observed for any dependent variable. The unadjusted and multi-variate adjusted endpoint and change values are presented in Table 3.

3.1.1 | Sesame oil

SO significantly decreased serum insulin (−6.00 ± 1.72 mIU/ml), HOMA2-IR (−0.72 ± 0.20), and HOMA2-%B (−26.44 ± 7.28) and increased HOMA2-%S (+9.27 ± 2.45) and QUICKI (+0.009 ± 0.003) from baseline ($p < 0.05$). The results remained significant after adjusting for potential confounders, including age, sex, baseline BMI, amount of oils consumed, physical activity, baseline values, and energy intake (Table 3). The sex-stratified analysis revealed significant changes following SO in males for serum insulin, HOMA2-IR, HOMA2-%S, HOMA2-%B, and QUICKI (Table 4, $p < 0.05$). In females, SO significantly changed HOMA2-IR, HOMA2-%S, and QUICKI (Table 5, $p < 0.05$).

3.1.2 | Sesame-canola oil blend

Changes in FSI (−5.03 ± 1.54 mIU/ml), HOMA2-IR (−0.62 ± 0.18), HOMA2-%S (+9.21 ± 2.26) and QUICKI (+0.009 ± 0.003) were significantly different following SCO in both unadjusted and adjusted models ($p < 0.05$, Table 3). These results were replicated in sex-specific analyses for both males and females (Tables 4 and 5). The mean changes in glycaemic control markers based on intervention periods are summarized in Figure 2 for all participants and in Figures S1 and S2 for males and females, respectively.

3.1.3 | Canola oil

In both unadjusted and adjusted models, CO significantly increased serum FBS (+7.72 ± 3.15 mg/dl), and HOMA2-%S (+4.71 ± 2.29), while decreasing FSI (−2.68 ± 1.36 mIU/ml) and HOMA2-%B (−25.01 ± 5.52; $p < 0.05$; Table 3). Males demonstrated significant changes in FBS, HOMA2-%S, and HOMA2-%B following CO intake ($p < 0.05$; Table 4). In females, only HOMA2-%B was reduced in response to CO ($p = 0.005$; Table 5).

3.1.4 | Liver function enzymes

No significant changes were observed for serum levels of enzymes (ALP, GGT, AST, and ALT) between SO, SCO, and CO ($p > 0.05$; Table 3). Stratified sex analysis found that SO intake significantly decreased serum GGT in females ($p = 0.048$; Table 5).

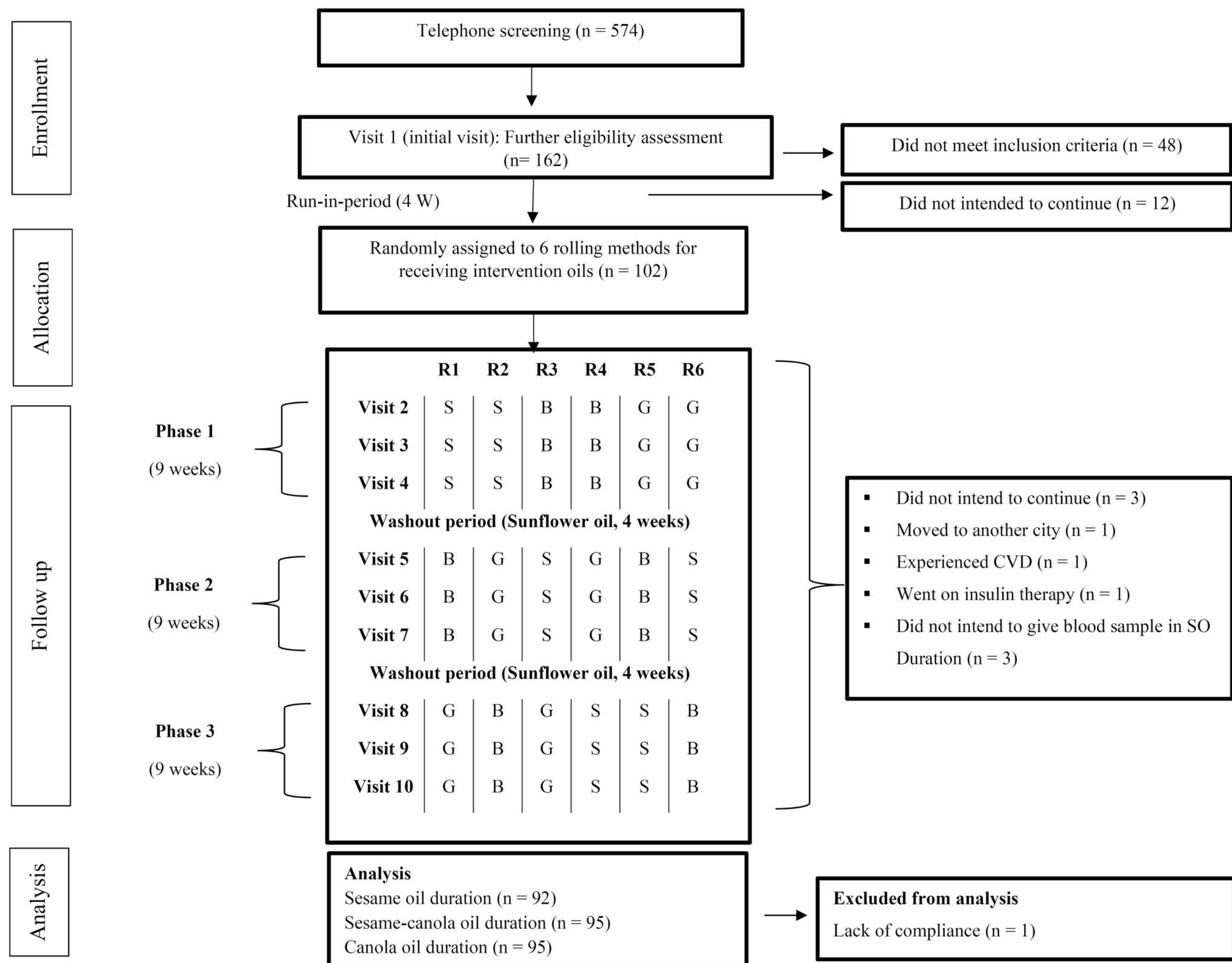

FIGURE 1 Flow chart of the participants' recruitment. Intervention oils were labelled by three codes (S, B, and G). R, rolling method

3.1.5 | Comparisons of CO, SO, and SCO

No significant differences in glycaemic control and serum liver function enzymes were observed between conditions (Table 3). Stratified-sex based analyses adjusted for confounders found that mean FSI and HOMA2-IR were significantly decreased in the SO condition compared with the CO in males (Table 4). FBS was significantly lower after the SCO condition compared with CO in males; however, the difference in change values for FBS was not significant ($p = 0.069$; Table 4). In females, serum GGT was significantly lower in the SO condition compared to CO and the difference in change values in serum GGT was not significant ($p = 0.058$; Table 5).

3.2 | Sensitivity analysis

A total of 12 individuals altered their glucose-lowering medication during the study. Ten participants altered their glycaemic control medication and two patients changed their drug dose (glucose lowering medications were increased within SO intake and were decreased within SCO intake for each patient). After removing these participants from the analyses, the multivariate-adjusted analysis revealed that serum GGT levels were significantly reduced in the SO condition when compared with CO (Table S2). The analyses revealed that the effect of SO compared with CO on FSI and HOMA2-IR in males became non-significant ($p > 0.05$, Table S3). All other analyses remained unchanged.

4 | DISCUSSION

The purpose of the present study was to compare the effects of SO, CO, or a blend (SCO) on glycaemic control markers and serum liver function enzymes in patients with T2DM. Following 9-weeks of supplementation, SO intake favourably changed FSI and insulin resistance, despite no effect on FBS. Similar results were observed following SCO consumption, except for HOMA2-%B which was not changed. Serum FBS was increased after CO; however, changes from baseline for FSI, HOMA2-%S, and HOMA2-%B were favourable. Furthermore, serum liver function enzymes were similarly unaltered

TABLE 1 Subject characteristics at baseline

Variables	Male ($n = 46$)	Female ($n = 49$)	Total ($n = 95$)	p-value
Age (years)	49.73 ± 1.02[a]	48.65 ± 0.96	49.17 ± 0.70	0.442
BMI (kg/m^2)	28.52 ± 0.54	29.32 ± 0.56	28.93 ± 0.39	0.311
Diabetes duration (years)	4.56 ± 0.45	4.56 ± 0.42	4.56 ± 0.3	0.998
PA (MET-min/day)	2201.56 ± 26.64	2151.37 ± 14.32	2174.82 ± 14.65	0.345
FBS (mg/dl)	114.57 ± 4.29	116.46 ± 3.77	115.55 ± 2.83	0.741
FSI (mIU/ml)	31.52 ± 3.59	25.86 ± 2.43	28.47 ± 2.12	0.186
HOMA2-IR	3.93 ± 0.41	3.37 ± 0.29	3.63 ± 0.25	0.265
HOMA2-%S	35.34 ± 3.05	38.12 ± 2.38	36.84 ± 1.90	0.470
HOMA2-%B	177.23 ± 24.51	149.89 ± 12.32	162.48 ± 13.10	0.301
QUICKI	0.29 ± 0.003	0.29 ± 0.003	0.29 ± 0.002	0.370
ALP (U/L)	178.56 ± 6.26	192.37 ± 7.20	185.68 ± 4.82	0.154
GGT (U/L)	32.01 ± 2.35	26.32 ± 1.72	29.08 ± 1.46	0.055
AST (U/L)	25.43 ± 1.41	22.13 ± 1.97	23.73 ± 1.23	0.183
ALT (U/L)	30.84 ± 1.84	21.97 ± 2.69	26.26 ± 1.70	0.008
Education				
Elementary or lower	10.5%	22.1%	32.6%	0.89
High school	26.3%	21.1%	47.4%	-
College and university	11.6%	8.4%	20%	-

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; FBS, fasting blood sugar; FSI, fasting serum insulin; GGT, gamma-glutamyltransferase; HOMA2-%B, homoeostasis model assessment for b-cell function; HOMA2-%S, homoeostasis model assessment for insulin sensitivity; HOMA2-IR, homoeostasis model assessment for insulin resistance; MET-min/day, metabolic equivalent-min/day; PA, physical activity; QUICKI, quantitative insulin sensitivity check index.

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

TABLE 2 The average of mid- and post-intervention of calculated daily intake of energy and nutrients as well as the physical activity level in each intervention phase[a]

Variables	SO	SCO	CO	p-value[b]
Energy (Kcal)	1764.42 ± 37.61[c]	1805.77 ± 37.65	1768.20 ± 37.70	0.298
PA (MET-min/day)	2182.69 ± 26.56	2144.98 ± 26.58	2182.88 ± 26.70	0.190
Carbohydrate (gr)	259.41 ± 6.65	268.58 ± 6.65	260.98 ± 6.65	0.198
Protein (gr)	69.02 ± 1.64	69.78 ± 1.64	68.88 ± 1.64	0.804
Fat (gr)	54.08 ± 1.46	53.88 ± 1.46	53.64 ± 1.45	0.956
SAT (gr)	15.80 ± 0.46	15.56 ± 0.46	15.34 ± 0.46	0.641
MUFA (gr)	16.85 ± 0.53[a]	18.30 ± 0.53[b]	19.10 ± 0.52[c]	<0.001
PUFA (gr)	12.62 ± 0.53[a]	11.03 ± 0.52[b,c]	11.32 ± 0.52[b,c]	0.008

Abbreviations: CO, canola oil; MET-min/day, metabolic equivalent-min/day; MUFAs, monounsaturated fatty acids; PA, physical activity; PUFAs, polyunsaturated fatty acids; SATs, saturated fatty acids; SCO, sesame-canola oil; SO, sesame oil.

[a]All data are represented as mean ± standard error (SE).

[b]p-value for the comparison between treatment periods. The analysis was done using linear mixed models. Values with different superscripts are significantly different $p < 0.05$.

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

regardless of dietary oil consumed. Stratified-sex analyses revealed a significant difference for end point values for FBS between SCO and CO in males. Between treatment comparisons showed a significant difference between SO and CO on FSI and HOMA2-IR change in males. In females, serum GGT levels were significantly lower after SO compared to CO consumption period.

TABLE 3 After intervention and change values for glycaemic indices and serum enzymes mainly produced by liver based on the treatment periods in all participants

	Sesame oil (n = 92)			Sesame-canola oil (n = 95)			Canola oil (n = 95)				
Variables	After	Change	P^a	After	Change	P^a	After	Change	P^a	P^b	P^c
FBS (mg/dl)											
Crude	117.06 ± 2.72[d]	2.85 ± 2.23	0.208	116.28 ± 2.60	−1.76 ± 3.16	0.578	122.40 ± 3.46	7.43 ± 3.01	0.016	0.176	0.092
Adjusted[e]	116.04 ± 2.42	1.59 ± 2.11	0.454	116.85 ± 2.74	−2.53 ± 3.26	0.423	122.64 ± 3.52	7.72 ± 3.15	0.013	0.158	0.060
FSI (mIU/ml)											
Crude	17.48 ± 0.88	−5.68 ± 1.62	0.001	16.33 ± 0.63	−5.59 ± 1.52	<0.001	17.33 ± 0.74	−2.78 ± 1.28	0.031	0.364	0.241
Adjusted	17.01 ± 0.87	−6.00 ± 1.72	0.001	16.10 ± 0.63	−5.03 ± 1.54	<0.001	17.25 ± 0.74	−2.68 ± 1.36	0.048	0.397	0.274
HOMA2-IR											
Crude	2.32 ± 0.11	−0.70 ± 0.19	0.001	2.19 ± 0.08	−0.68 ± 0.18	<0.001	2.35 ± 0.10	−0.27 ± 0.16	0.107	0.314	0.147
Adjusted	2.28 ± 0.11	−0.72 ± 0.20	0.001	2.16 ± 0.08	−0.62 ± 0.18	<0.001	2.34 ± 0.10	−0.25 ± 0.17	0.150	0.295	0.179
HOMA2-%S											
Crude	50.82 ± 2.11	9.13 ± 2.33	<0.001	51.48 ± 1.67	9.31 ± 2.19	<0.001	49.24 ± 1.69	4.95 ± 2.21	0.025	0.560	0.304
Adjusted	51.39 ± 2.20	9.27 ± 2.45	<0.001	51.98 ± 1.73	9.21 ± 2.26	<0.001	49.21 ± 1.72	4.71 ± 2.29	0.042	0.423	0.275
HOMA2-%B											
Crude	109.93 ± 5.10	−27.29 ± 6.96	<0.001	112.68 ± 6.76	−24.62 ± 10.93	0.027	105.87 ± 5.06	−24.17 ± 5.30	<0.001	0.511	0.932
Adjusted	108.62 ± 5.03	−26.44 ± 7.28	<0.001	111.17 ± 7.06	−20.09 ± 11.28	0.068	104.82 ± 4.97	−25.01 ± 5.52	<0.001	0.558	0.888
QUICKI											
Crude	0.30 ± 0.002	0.008 ± 0.002	0.001	0.31 ± 0.002	0.009 ± 0.003	<0.001	0.30 ± 0.002	0.003 ± 0.002	0.254	0.294	0.145
Adjusted	0.30 ± 0.002	0.009 ± 0.003	0.001	0.31 ± 0.002	0.009 ± 0.003	<0.001	0.30 ± 0.002	0.002 ± 0.003	0.327	0.233	0.114
ALP (U/L)											
Crude	179.04 ± 5.00	−0.60 ± 2.60	0.325	178.69 ± 4.78	−3.40 ± 3.17	0.833	183.98 ± 4.89	2.62 ± 2.18	0.871	0.120	0.285
Adjusted	177.22 ± 5.14	−1.20 ± 2.60	0.640	177.87 ± 5.03	−2.90 ± 3.20	0.325	182.90 ± 5.00	3.20 ± 2.20	0.147	0.087	0.239
GGT (U/L)											
Crude	28.64 ± 1.95	−0.73 ± 1.08	0.297	29.35 ± 1.93	1.23 ± 1.22	0.232	29.96 ± 1.88	1.65 ± 0.76	0.218	0.453	0.168
Adjusted	29.01 ± 2.05	−0.81 ± 1.14	0.206	29.42 ± 2.00	1.03 ± 1.25	0.224	30.46 ± 1.97	1.76 ± 0.80	0.202	0.417	0.139
AST (U/L)											
Crude	22.17 ± 0.90	0.21 ± 0.80	0.232	21.89 ± 0.76	−1.36 ± 0.84	0.964	23.25 ± 0.89	−0.69 ± 0.89	0.325	0.266	0.430
Adjusted	22.18 ± 0.93	0.76 ± 0.73	0.318	21.66 ± 0.76	−1.49 ± 0.87	0.098	23.10 ± 0.92	−0.54 ± 0.93	0.536	0.300	0.139

(Continues)

TABLE 3 (Continued)

Variables	Sesame oil ($n = 92$)			Sesame-canola oil ($n = 95$)			Canola oil ($n = 95$)				
	After	Change	P^a	After	Change	P^a	After	Change	P^a	P^b	P^c
ALT (U/L)											
Crude	23.80 ± 1.23	0.05 ± 1.01	0.152	23.92 ± 1.28	−1.50 ± 0.98	0.688	26.26 ± 1.30	−0.01 ± 1.31	0.393	0.083	0.467
Adjusted	24.02 ± 1.29	0.38 ± 1.04	0.725	23.96 ± 1.32	−1.75 ± 1.00	0.088	26.56 ± 1.36	0.18 ± 1.37	0.952	0.079	0.237

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FBS, fasting blood sugar; FSI, fasting serum insulin; GGT, gamma-glutamyltransferase; HOMA2-%B, homoeostasis model assessment for b-cell function; HOMA2-%S, homoeostasis model assessment for insulin sensitivity; HOMA2-IR, homoeostasis model assessment for insulin resistance; QUICKI, quantitative insulin sensitivity check index.

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

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

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

[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, baseline values, and the energy intake in each intervention period.

The role of different dietary approaches on the management of T2DM has received significant attention[9]; however, no study has compared the health benefits of dietary CO and SO either in healthy participants or those with metabolic diseases. Moreover, the number of studies concerning the effects of CO on glycaemic indices as well as serum liver function enzymes are limited. In a parallel study, Baxheinrich et al. examined patients with metabolic syndrome that ingested rapeseed and olive oil for 6 months. After the intervention, FBS decreased in the olive oil group while remaining unchanged in the rapeseed oil group. Serum insulin levels were significantly decreased in both groups.[41] A cross-over clinical trial in healthy participants that were randomized to either rapeseed oil-based diet or a dairy fat-based diet provided contrasting results. After 3 weeks, FBS decreased following both treatments, while serum insulin remained unchanged.[22] Another clinical trial investigating the effects of a MUFA-rich diet (rapeseed oil-based diet) or a PUFA-rich diet (sunflower oil-based diet), in participants with hyperlipidaemia, found small but favourable effects of both interventions on serum FBS, but not insulin concentrations.[42] Kratz et al. compared the effects of olive oil, rapeseed oil, and sunflower oil in healthy individuals for 4 weeks and found HbA1c, serum glucose, and insulin levels were unaltered.[43] Nigam et al. ($N = 93$) examined males with non-alcoholic fatty liver disease that were given olive oil, CO, and a commonly used oil as control (soybean/safflower oil) for 6 months; compared with the control, CO and olive oil led to a significant decrease in FSI, HOMA-IR, and HOMA-B levels despite no significant changes in serum AST and ALT.[20]

Presently, there is a lack of randomized clinical trials (RCTs) comparing SO with other edible oils on glycaemic control as well as liver function enzymes. In a parallel RCT on patients with T2DM, the effects of SO and glibenclamide alone and in combination were assessed. A significant decrease was found in FBS and HbA1c in all conditions, with the combination group showing the greatest hypoglycaemic responses.[27] Three-hundred individuals with T2DM receiving a SO blend (comprising 20% SO and 80% rice bran oil) ($n = 100$), glibenclamide ($n = 100$), or the combination of SO blend and glibenclamide ($n = 100$); all improved fasting and postprandial blood glucose as well as HbA1c after 8 weeks.[28] These studies examining FBS are in contrast with our observations. Importantly, previous studies concerning SO lacked methodological rigour; due to a lack of blinding of participants and researchers, no assessment of physical activity, failure to report medication changes, and did not assess dietary intake.

To the best of our knowledge, no single study has examined sex-based differences with SO, while there have been limited studies with CO. Liu et al.[44] found a larger android fat mass reduction in males following CO and canola oleic oil in comparison to a blend of flaxseed and safflower oil. Kratz et al. randomly assigned ($N = 48$ males and females) participants to olive oil ($n = 17$), rapeseed oil ($n = 13$), and sunflower oil ($n = 18$) and found similar increases in plasma apo A-IV in both sexes.[45] Previous research has also shown sex-related differences in lipid profiles following various oils-based diets.[46,47] Importantly, the present

TABLE 4 After intervention and change values for glycaemic indices and serum enzymes mainly produced by liver based on the treatment periods in the male participants

	Sesame oil (n = 46)			Sesame-canola oil (n = 46)			Canola oil (n = 46)				
Variables	After	Change	P^a	After	Change	P^a	After	Change	P^a	P^b	P^c
FBS (mg/dl)											
Crude	117.95 ± 4.16[d]	5.39 ± 3.23	0.103	115.11 ± 3.41	−3.74 ± 5.48	0.499	126.76 ± 5.74	10.14 ± 4.78	0.040	0.087	0.130
Adjusted[e]	117.18 ± 3.66[b,c]	2.82 ± 2.90	0.434	116.53 ± 3.75	−6.09 ± 5.81	0.227	130.29 ± 5.98[c]	11.79 ± 5.18	0.031	0.046	0.069
FSI (mIU/ml)											
Crude	16.61 ± 1.24	−8.59 ± 1.97	<0.001	16.79 ± 1.00	−5.96 ± 2.70	0.033	17.08 ± 1.30	−2.05 ± 1.60	0.197	0.935	0.037
Adjusted	15.35 ± 1.13	−9.69 ± 2.15	<0.001	16.32 ± 1.03	−4.71 ± 2.84[b,c]	0.004	16.82 ± 1.33	−1.76 ± 1.79[c]	0.201	0.539	0.024
HOMA2-IR											
Crude	2.23 ± 0.16	−1.04 ± 0.24	<0.001	2.25 ± 0.13	−0.72 ± 0.31	0.028	2.33 ± 0.18	−0.10 ± 0.22	0.620	0.833	0.021
Adjusted	2.07 ± 0.15	−1.20 ± 0.26	<0.001	2.19 ± 0.13	−0.60 ± 0.33[b,c]	0.002	2.32 ± 0.18	−0.05 ± 0.25[c]	0.701	0.404	0.012
HOMA2-%S											
Crude	53.54 ± 3.43	13.32 ± 3.23	<0.001	50.28 ± 2.40	7.33 ± 3.49	0.042	51.23 ± 2.79	6.94 ± 3.05	0.028	0.688	0.330
Adjusted	55.79 ± 3.70	14.62 ± 3.58	<0.001	51.10 ± 2.62	6.94 ± 3.83	0.038	51.31 ± 2.92	6.51 ± 3.28	0.026	0.514	0.235
HOMA2-%B											
Crude	104.71 ± 7.50	−37.92 ± 8.02	<0.001	110.17 ± 6.89	−33.22 ± 19.79	0.101	98.80 ± 6.70	−24.85 ± 7.33	0.002	0.338	0.468
Adjusted	98.11 ± 6.73	−36.35 ± 8.86	0.001	106.22 ± 7.10	−21.75 ± 21.32	0.137	91.81 ± 5.92	−26.48 ± 7.75	0.002	0.136	0.666
QUICKI											
Crude	0.31 ± 0.003	0.012 ± 0.003	0.001	0.30 ± 0.003	0.008 ± 0.004	0.058	0.30 ± 0.003	0.003 ± 0.003	0.319	0.721	0.254
Adjusted	0.31 ± 0.003	0.014 ± 0.003	0.001	0.30 ± 0.003	0.008 ± 0.004	0.015	0.30 ± 0.003	0.003 ± 0.003	0.277	0.355	0.132
ALP (U/L)											
Crude	173.80 ± 6.19	4.65 ± 3.71	0.218	167.90 ± 6.15	−9.24 ± 5.40	0.095	173.43 ± 5.74	−1.99 ± 2.92	0.500	0.530	0.069
Adjusted	168.19 ± 6.43	2.81 ± 3.80	0.608	165.48 ± 6.77	−7.49 ± 5.89	0.118	169.77 ± 5.97	−0.95 ± 2.91	0.745	0.753	0.204
GGT (U/L)											
Crude	33.77 ± 3.25	1.28 ± 1.76	0.471	31.80 ± 2.50	−0.40 ± 1.55	0.796	32.48 ± 2.83	1.30 ± 0.95	0.179	0.555	0.668
Adjusted	35.59 ± 3.52	1.40 ± 1.92	0.496	32.04 ± 2.69	−1.16 ± 1.59	0.435	34.10 ± 3.07	1.66 ± 1.00	0.103	0.199	0.384
AST (U/L)											
Crude	24.34 ± 1.17	−0.32 ± 1.17	0.785	24.28 ± 1.00	−0.55 ± 1.07	0.611	24.50 ± 1.06	−1.31 ± 0.96	0.179	0.979	0.787
Adjusted	24.40 ± 1.20	1.09 ± 0.93	0.285	23.66 ± 1.01	−0.80 ± 1.14	0.428	24.05 ± 1.11	−0.94 ± 1.04	0.296	0.720	0.253

(Continues)

TABLE 4 (Continued)

Variables	Sesame oil ($n = 46$)			Sesame-canola oil ($n = 46$)			Canola oil ($n = 46$)				
	After	Change	P^a	After	Change	P^a	After	Change	P^a	P^b	P^c
ALT (U/L)											
Crude	29.49 ± 1.86	−0.10 ± 1.78	0.955	29.76 ± 1.98	−1.67 ± 1.59	0.300	31.10 ± 1.74	−0.85 ± 1.53	0.581	0.667	0.793
Adjusted	30.67 ± 2.00	0.84 ± 1.90	0.837	29.96 ± 2.21	−2.40 ± 1.70	0.142	32.16 ± 1.89	−0.47 ± 1.67	0.727	0.539	0.367

Note: Values with different superscripts are significantly different $p < 0.05$.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FBS, fasting blood sugar; FSI, fasting serum insulin; GGT, gamma-glutamyltransferase; HOMA2-%B, homoeostasis model assessment for b-cell function; HOMA2-%S, homoeostasis model assessment for insulin sensitivity; HOMA2-IR, homoeostasis model assessment for insulin resistance; QUICKI, quantitative insulin sensitivity check index.

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

[b]p-values for comparison of after treatment values between the treatment oils using linear mixed models.

[c]p-values for comparison of change values between the treatment oils using linear mixed models.

[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, baseline values, and the energy intake in each intervention period.

study is the first to provide sex-specific responses for multiple glycaemic markers and liver enzymes following SO, CO, and SCO intake. Currently, sex differences and potential mechanisms in response to SO and CO on metabolic markers are unclear. As such, sex-based research as well as studies to investigate possible sex-related polymorphisms pertaining to glycaemic control and liver enzymes are warranted. Sex-specific studies may improve patient care and any sex-based differences are important to highlight in clinical recommendations and appropriately applied for diabetic males and females independently.[48] In the present study, in males SO led to greater reductions in FSI and HOMA2-IR compared with CO. In addition, SO and SCO had more favourable effects on glycaemic markers compared to CO. Serum GGT decreased following SO compared with CO only in females. These differences may be associated with the fatty acid profiles, CO contains a greater amount of MUFAs (more than 60%) in comparison to SO (41%) and SCO (53%). While, the PUFA content of the CO, SCO, and SO in our study were approximately 28%, 35%, and 43% of total fatty acid compositions, respectively.[30] Furthermore, the source of PUFAs differed between SO and CO; since linoleic acid comprises almost all PUFAs in SO compared to CO that contains a higher amount of ALA.[30] In support of our findings, a meta-analysis of controlled feeding trials suggested that different dietary fats including SFAs, MUFAs, and PUFAs may have diverse effects on glucose-insulin homoeostasis. Substitution of SFAs with PUFAs led to a favourable outcome on glycaemia, insulin resistance and insulin secretion capacity; whereas less favourable improvements on HbA1c and HOMA-IR were observed for dietary MUFAs substitution.[49] PUFAs may interfere with the toxicity of tissues free fatty acids[50] and increase membrane fluidity, which may enhance insulin sensitivity and subsequently decrease the risk of T2DM.[51,52] These effects have been attributed to linoleic acid (an omega-6 fatty acid), rather than ALA, which has been suggested in previous meta-analyses.[53,54] A meta-analysis of observational studies found that both dietary and circulating biomarker levels of ALA were not associated with a lower risk of diabetes.[53] In contrast, a recent pooled analysis on 39,740 adults from 20 prospective cohort studies suggested that biomarker levels of linoleic acid are inversely associated with the risk of T2DM.[54]

Along with dietary PUFAs, canola, sesame, and SCOs contain MUFAs which may augment the effects of PUFAs on fasting insulin and insulin sensitivity. Although the precise mechanisms linking dietary MUFA to insulin resistance remains to be elucidated, potentially, MUFAs can improve adipocytokine profiles due to their impact on mRNA expression of genes involved in lipid metabolism as well as inflammation and alterations in fatty acid composition.[55] Chronic inflammation of hypertrophic adipocytes interferes with insulin signalling and induces insulin resistance.[56] In contrast, an increase in macrophage infiltration has been associated with adipose tissue inflammation.[57] In addition, considering macrophages are likely the major source of resistin,[58] as such MUFAs ingestion that suppresses the expression of genes encoding macrophage markers and white adipose tissue inflammation decreases the secretion of

TABLE 5 After intervention and change values for glycaemic indices and serum enzymes mainly produced by liver based on the treatment periods in the female participants

	Sesame oil ($n = 46$)			Sesame-canola oil ($n = 49$)			Canola oil ($n = 49$)				
Variables	After	Change	P^a	After	Change	P^a	After	Change	P^a	P^b	P^c
FBS (mg/dl)											
Crude	115.58 ± 3.35[d]	−0.31 ± 3.13	0.923	117.29 ± 4.05	0.29 ± 3.58	0.936	119.80 ± 3.98	5.90 ± 3.86	0.134	0.515	0.368
Adjusted[e]	114.39 ± 3.32	−0.82 ± 3.21	0.687	117.77 ± 4.14	0.81 ± 3.65	0.759	118.65 ± 3.97	5.48 ± 3.96	0.166	0.474	0.425
FSI (mIU/ml)											
Crude	18.00 ± 1.23	−4.03 ± 2.12	0.064	15.80 ± 0.82	−5.00 ± 1.52	0.002	17.53 ± 0.85	−3.51 ± 2.05	0.094	0.161	0.832
Adjusted	17.91 ± 1.29	−4.62 ± 2.22	0.056	15.83 ± 0.84	−4.45 ± 1.49	0.008	17.49 ± 0.87	−3.55 ± 2.10	0.086	0.209	0.923
HOMA2-IR											
Crude	2.34 ± 0.16	−0.56 ± 0.24	0.027	2.12 ± 0.10	−0.63 ± 0.19	0.003	2.37 ± 0.11	−0.40 ± 0.26	0.126	0.175	0.796
Adjusted	2.39 ± 0.16	−0.54 ± 0.25	0.042	2.13 ± 0.11	−0.55 ± 0.19	0.001	2.36 ± 0.11	−0.41 ± 0.26	0.240	0.200	0.903
HOMA2-%S											
Crude	49.02 ± 2.50	6.39 ± 2.88	0.032	52.73 ± 2.44	11.17 ± 2.76	<0.001	47.40 ± 2.15	4.04 ± 3.26	0.231	0.161	0.235
Adjusted	48.75 ± 2.58	6.17 ± 2.97	0.042	52.80 ± 2.51	10.57 ± 2.79	0.001	47.61 ± 2.20	4.16 ± 3.35	0.240	0.183	0.183
HOMA2-%B											
Crude	114.51 ± 7.30	−19.31 ± 10.23	0.065	113.67 ± 11.85	−16.05 ± 11.16	0.158	110.73 ± 7.35	−24.85 ± 8.05	0.004	0.870	0.735
Adjusted	116.35 ± 7.40	−19.70 ± 10.57	0.097	112.51 ± 12.14	−15.62 ± 11.47	0.172	112.20 ± 7.45	−25.03 ± 8.27	0.005	0.869	0.727
QUICKI											
Crude	0.30 ± 0.003	0.006 ± 0.003	0.041	0.31 ± 0.002	0.010 ± 0.003	0.001	0.30 ± 0.002	0.003 ± 0.004	0.479	0.167	0.313
Adjusted	0.30 ± 0.003	0.007 ± 0.003	0.044	0.31 ± 0.002	0.009 ± 0.003	0.006	0.30 ± 0.002	0.003 ± 0.004	0.474	0.250	0.434
ALP (U/L)											
Crude	185.25 ± 7.78	−4.63 ± 3.68	0.164	189.83 ± 6.90	2.52 ± 3.62	0.490	194.35 ± 7.64	6.16 ± 3.03	0.048	0.091	0.139
Adjusted	187.48 ± 7.79	−4.04 ± 3.78	0.196	191.10 ± 7.01	1.98 ± 3.69	0.527	195.94 ± 7.73	5.87 ± 3.11	0.078	0.139	0.204
GGT (U/L)											
Crude	24.34 ± 2.13	−2.36 ± 1.31	0.067	27.27 ± 2.94	2.71 ± 1.91	0.162	27.75 ± 2.53	1.82 ± 1.22	0.142	0.023	0.053
Adjusted	24.74 ± 2.17	−2.43 ± 1.35	0.048	27.84 ± 2.98[a]	2.87 ± 1.95[a]	0.178	28.27 ± 2.56[a]	1.80 ± 1.25[a]	0.180	0.020	0.058
AST (U/L)											
Crude	20.16 ± 1.36	0.63 ± 1.16	0.670	19.58 ± 1.06	−2.04 ± 1.29	0.122	21.90 ± 1.42	−0.06 ± 1.51	0.964	0.179	0.363
Adjusted	20.29 ± 1.40	0.68 ± 1.20	0.512	19.70 ± 1.08	−2.09 ± 1.33	0.089	21.95 ± 1.46	−0.14 ± 1.56	0.988	0.218	0.361

(Continues)

TABLE 5 (Continued)

Variables	Sesame oil ($n = 46$)			Sesame-canola oil ($n = 49$)			Canola oil ($n = 49$)				
	After	Change	P^a	After	Change	P^a	After	Change	P^a	P^b	P^c
ALT (U/L)											
Crude	18.48 ± 1.24	0.32 ± 1.08	0.774	18.28 ± 1.15	−1.26 ± 1.25	0.319	21.24 ± 1.60	0.55 ± 2.13	0.797	0.118	0.528
Adjusted	18.50 ± 1.27	0.24 ± 1.11	0.840	18.59 ± 1.15	−1.22 ± 1.29	0.332	21.35 ± 1.64	0.55 ± 2.19	0.727	0.125	0.584

Note: Values with different superscripts are significantly different $p < 0.05$.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FBS, fasting blood sugar; FSI, fasting serum insulin; GGT, gamma-glutamyltransferase; HOMA2-%B, homoeostasis model assessment for b-cell function; HOMA2-%S, homoeostasis model assessment for insulin sensitivity; HOMA2-IR, homoeostasis model assessment for insulin resistance; QUICKI, quantitative insulin sensitivity check index.

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

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

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

[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, baseline values, and the energy intake in each intervention period.

pro-inflammatory adipocytokines and improves insulin sensitivity.[55] Furthermore, MUFAs may interfere with insulin resistance by altering cellular membrane fluidity and insulin receptor affinity.[59,60] MUFAs may also help modulate intracellular lipid storage and insulin sensitivity due to their high oxidation rate compared with other dietary fatty acids.[61] Modifying intramuscular fat deposition following unsaturated fatty acids intake is another possible mechanism for alleviating insulin resistance since SFAs, unlike unsaturated fatty acids, tend to aggregate fat deposition and cause insulin resistance.[62]

The present study has several strengths and limitations. The large sample size with low attrition along with a frequent assessment of dietary intake and physical activity minimized the potential risk of biases. Using a cross-over design, minimized the influence of genetic polymorphisms, limiting between subject variations in diet and responsiveness. Moreover, the external validity and practically of the present study may be superior to controlled feeding trials. There are a number of limitations that should be noted when interpreting our results. There was no inclusion of oils high in SFAs like palm oil and partially hydrogenated oils typically found in western diet (as a control). It is worth mentioning that specific amounts of dietary oils were not prescribed in the current study; as the participants replaced their household dietary oil intakes with the treatment oils. Furthermore, there may be ethical considerations in clinical trials that allow an unhealthy dose of dietary oils such as SFAs for a long period of time (e.g., 9 weeks). All of the three conditions used healthy vegetable oils and reduced the between group difference in glycaemic control markers and liver enzymes. Furthermore, we could not calculate the exact amounts of oil ingested by each participant; however, a 3-day dietary record was used at multiple time points as a surrogate marker of compliance, as well as the returned containers. Future research should use more objective methods of assessing red blood cell content of MUFAs and PUFAs to confirm adherence.[63,64] Using dietary reference intakes (DRIs) to calculate the energy intake is another potential limitation of the current study. However, due to the rigour of the study and cross-over design, in addition to the use of dietary monitoring, the impact of dietary changes (beyond the treatment oils) influencing the results are unlikely.

In conclusion, although some significant improvements over time were seen for some glycaemic control markers and liver function tests, no significant differences were found between the interventions when all participants were included in the analyses. The sex-based analysis found a significant difference in end point values for FBS between SCO and CO in males. According to our findings, end point values for FBS were decreased and increased after SCO and CO intake in males, respectively. Furthermore, in males the between-period analysis revealed that SO intake favourably effects FSI and HOMA2-IR compared with CO. In females, serum GGT was significantly lower after SO consumption compared with CO period. Therefore, designing sex-specific studies concerning the effects of polymorphisms following dietary oil interventions are recommended.

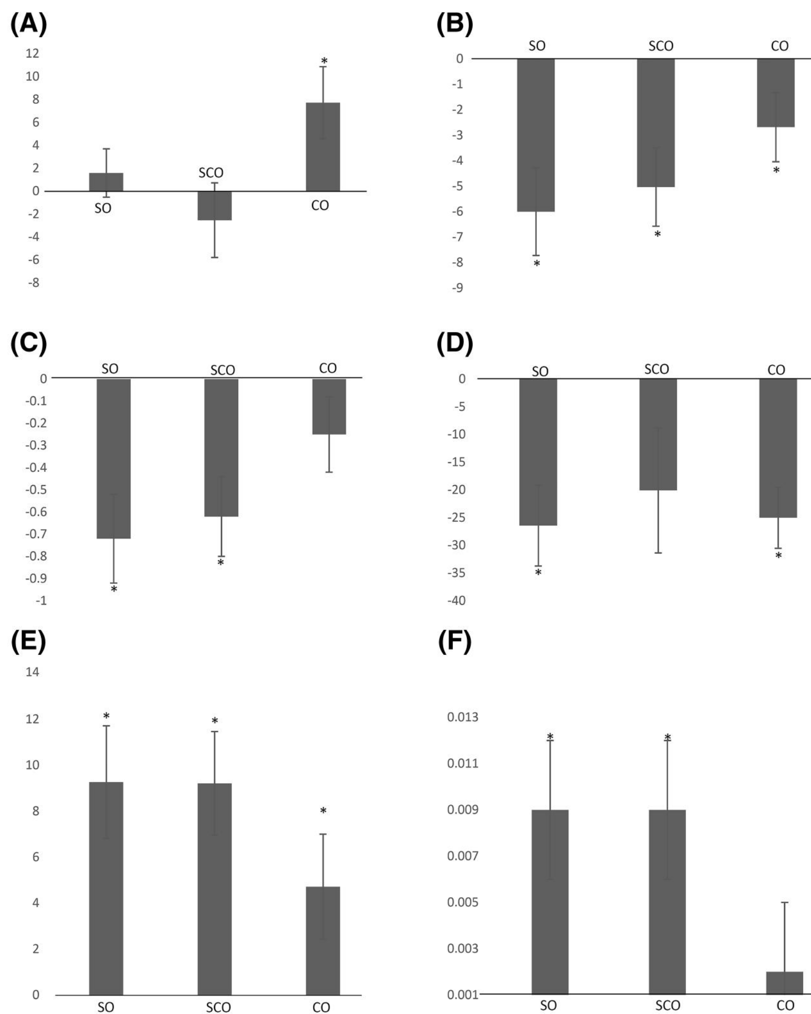

FIGURE 2 Adjusted mean change ± standard error for fasting blood sugar (A), fasting serum insulin (B), homoeostasis model assessment for insulin resistance (C), homoeostasis model assessment for b-cell function (D), homoeostasis model assessment for insulin sensitivity (E), and quantitative insulin sensitivity check index (F) in sesame oil (SO), sesame-canola oil (SCO), and canola oil (CO) intervention periods for total participants. Significant within-period changes ($p < 0.05$) are shown by asterisks

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AUTHOR CONTRIBUTIONS

The principal investigator (Amin Salehi-Abargouei) declares that he has full access to the data and samples provided by this project. Amin Salehi-Abargouei and Mojgan Amiri conceived and designed the study. Mojgan Amiri and Fatemeh Moghtaderi managed the participants' recruitment. Mojgan Amiri and Fatemeh Moghtaderi conducted the data collection. Mojgan Amiri, Hamidreza Raeisi-Dehkordi, Fatemeh Moghtaderi, Alireza Zimorovat performed the data entry. Hamidreza Raeisi-Dehkordi and Sadegh Zarei performed the biochemical analyses. Amin Salehi-Abargouei conducted the statistical analyses. Hamidreza Raeisi-Dehkordi wrote the first draft of the manuscript. Amin Salehi-Abargouei is the guarantor of the submitted work and takes full responsibility for the work as a whole. All authors approved the final draft of the manuscript and agreed to be accountable for all aspects of the work, ensuring its integrity and accuracy.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

All individuals provided written informed consent before enrolment. The trial was registered in the Iranian Registry of Clinical Trials (IRCT; registration ID: IRCT2016091312571N6). The present study was approved by the ethics committee of Shahid Sadoughi University of Medical Sciences with a reference number of IR.SSU.SPH.REC.1396.156.

DATA AVAILABILITY STATEMENT

The data of the present study can be obtained by contacting the corresponding author.

TRIAL REGISTRATION NUMBER

The trial was registered in the Iranian registry of clinical trials (registration code: IRCT2016091312571N6), URL: https://en.irct.ir/trial/12622.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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