Current Developments in Nutrition 10 (2026) 107635

American Society for Nutrition
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Current Developments in Nutrition CDN

journal homepage: https://cdn.nutrition.org/

Nutritional biochemistry and physiologic mechanisms

Foods Fortified with Soybean or Palm Oil Show No Effect on Inflammation or Oxidized Low-Density Lipoprotein in Adults with Overweight or Obesity: a Secondary Analysis of a Randomized Placebo-Controlled Crossover Trial

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A B S T R A C T

Background: Popular and social media outlets have recent posts claiming that vegetable and seed oils high in linoleic acid (LA) cause inflammation and oxidative stress. However, substantial evidence in the scientific literature shows LA biomarkers are associated with lower risks for type 2 diabetes, cardiovascular disease, and systemic inflammation.
Objectives: The primary aim of this study is to evaluate the impact of dietary fortification with soybean oil (high in LA) compared with palm oil on markers of systemic inflammation and oxidized low-density lipoprotein (oxLDL) in healthy overweight adult participants.
Methods: This double-masked crossover clinical trial consisted of 2 diet periods where adults with overweight or obesity were randomly assigned to receive 3 study foods delivering 30 g oil/d of either soybean or palm oil for 4-wk periods. During a 2-wk wash-out period, participants refrained from consuming study foods. Erythrocyte and plasma fatty acid composition, blood biomarkers of systemic inflammation and oxLDL, desaturase indices, and body weights were measured at each study visit.
Results: After 4 wk of consuming 30 g/d of soybean or palm oil snacks, most inflammatory markers and oxLDL remained unchanged. However, interleukin-6 showed a trend toward reduction in the soybean oil group ($P = 0.09$). Fatty acid analysis revealed that C20:4n–6 (arachidonic acid) significantly decreased in erythrocytes after soybean oil intake ($P = 0.0234$), suggesting altered n–6 fatty acid metabolism through δ-6 and δ-5 desaturases. There were no lingering treatment effects during the 2-week washout period between diet periods 1 and 2.
Conclusions: Incorporating study foods containing 30 g oil/d of soybean or palm oil had no significant impact on inflammatory markers, suggesting that higher LA intake is not proinflammatory as is stated in popular media outlets. In addition, a two week washout period may be sufficient for dietary oil interventions in crossover study designs.
This trial was registered at clinicaltrials.gov as NCT04975763.

Keywords: linoleic acid, soybean oil, inflammation, omega-6 fatty acids, seed oils, oxidized LDL, IL-6, arachidonic acid

Abbreviations: AA, arachidonic acid; ALA, α-linolenic acid; CRP, C-reactive protein; D5D, δ-5 desaturase; D6D, δ-6-desaturase; DBS, dried blood spots; LA, linoleic acid; LBP, LPS-binding protein; oxLDL, oxidized LDL; PBMC, peripheral blood mononuclear cells; RBC, red blood cells; SCD1, stearoyl-CoA desaturase-1; sCD14, soluble CD14.

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https://doi.org/10.1016/j.cdnut.2025.107635
Received 2 September 2025; Received in revised form 19 December 2025; Accepted 30 December 2025; Available online 7 January 2026
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Introduction

Linoleic acid [LA; 18:2n–6], an essential fatty acid, is primarily obtained from plant oils (such as sunflower, safflower, soybean, and corn) and nuts, and is recommended for health in most dietary guidelines [1,2]. LA plays essential roles in maintaining skin barrier integrity, regulating inflammation, supporting cardiometabolic health, and potentially influencing brain function [3]. LA intake is inversely associated with coronary artery disease risk: higher dietary LA intake is related to reduced heart disease [2,4]. In addition, LA intake promotes insulin sensitivity and reduces the risk of hypertension [2]. Currently, the United States Adequate Intakes (AIs) for LA in adults are set at 11 to 12 g/d for females and 14 to 17 g/d for males, which corresponds to ~6% of daily energy intake [5]. However, many oils that were once high in LA have been replaced with oleic acid-rich alternatives, indicating that LA intake in the United States may be gradually declining [6]. Therefore, incorporating LA through sources like snack foods may be necessary to help maintain AI.

The metabolism of LA is well characterized and highly controlled through enzymatic regulation. LA is converted to γ-LA (GLA) by δ-6 desaturase (D6D), then elongated to dihomo-GLA, and subsequently converted to arachidonic acid (AA) by δ-5 desaturase (D5D) [7]. AA serves as a precursor for various proinflammatory and anti-inflammatory and thrombogenic metabolites, including prostaglandins, thromboxanes, leukotrienes, and lipoxins, which act as signaling molecules to initiate and resolve the inflammatory process by modulating the production of cytokines such as IL-6 [8,9]. Although AA plays a central role in inflammation, the conversion rate of LA to AA in plasma is extremely low, estimated at only ~0.2% [10]. Nevertheless, it is often claimed, without evidence, LA is directly converted into AA and thereby promotes inflammation [11]. Moreover, omega (ω)-6 fatty acids, particularly LA, have been hypothesized to play a role in initiating the formation of oxidized LDL (oxLDL) [12]. Therefore, some edible vegetable and seed oils rich in LA have recently come under public scrutiny, largely due to unsubstantiated claims circulating in print, televised, and social media regarding purported negative health effects. However, inflammation and oxidative stress have not been shown to increase with higher LA intake in clinical trials [13,14]. The primary objective of this study was to evaluate whether delivering 30 g/d of LA-rich soybean oil through snack foods influences biomarkers of inflammation and oxLDL. On the basis of prior randomized controlled trials [13,15], we hypothesized that LA-enriched snacks using 30 g soybean oil/d would not promote inflammation.

Methods

Experimental design

This is a secondary study leveraging samples and data from our previous pilot study [16], which was a double-masked, randomized, placebo-controlled crossover trial involving 10 adult participants. The study protocol was approved by the Ohio State University Institutional Review Board (IRB #2021H0232) and registered on clinicaltrials.gov (NCT04975763). Each participant was assigned to the 2 groups in random order in blocks of 2 or 4 using a randomization scheme that was generated by a person outside of the study team. Participants were provided with study foods delivering 30 g/d of either soybean oil or palm oil. Palm oil was selected as a comparator because it is rich in SFA and MUFA and contains relatively little PUFA, in contrast to the PUFA-rich profile of soybean oil [17,18]. This distinction allows us to differentiate the effects of PUFA from those of saturated and monounsaturated fats. In addition, the mixed fatty acid profile of palm oil aligns with that of the typical United States adult diet [19]. Study visits were conducted at the beginning and end of each diet period. At the first study visit of each diet period, participants received their assigned study foods and then returned any uneaten portions at the ensuing visit. The detailed adherence results are reported in the primary manuscript [16]. A registered dietitian nutritionist met with participants at the study visit preceding each diet period to strategize how study foods could be incorporated into their habitual daily intake as parts of meals or snacks composed of similar foods. The goal of working with the dietitian was to minimize or prevent weight gain during the diet periods.

After completing a 2-wk run-in period, each diet period consisted of 4 wk interrupted by a 2-wk wash-out period. Blood samples were collected at each visit to analyze dried blood spots (DBS), peripheral blood mononuclear cells (PBMC), plasma, and red blood cells (RBC) fatty acid profile. In addition, the primary markers of this study were systemic inflammatory markers, including soluble CD14 (sCD14), IL-6, C-reactive protein (CRP), LPS-binding protein (LBP), and oxLDL, which were measured from these blood samples. Additional assessments, such as anthropometric measurements, were measured in every visit. Figure 1 illustrates the study design flowchart; Figure 2 presents the participant recruitment flowchart.

Participant characteristics

Eligible participants included males and females with overweight or obesity, and a BMI ranging from 25 to 55 kg/m^2 between ages 25 and 80 y. All participants were nonsmokers and were screened by self-report to exclude individuals with a current or history of cardiovascular or renal disease, diabetes, and some hepatic and autoimmune diseases and current gastrointestinal diseases, cancer diagnosis, and food allergies, or those who were pregnant or lactating. Participants were instructed to abstain from the use of weight-loss supplements, medications contraindicated with the study foods (such as weight-loss drugs like Orlistat and Alli that may affect fat absorption), supplements high in LA, and the consumption of alcohol or recreational drugs throughout the study period. The study included 10 participants (4 males and 6 females), with a mean age of 47.0 ± 17.3 y and a mean BMI of 33.4 ± 4.5 kg/m^2. Detailed participant characteristics are provided in the primary manuscript [16].

Study foods consumption and dietary intake

Dietary intake was assessed using 24-h recalls via the ASA24 tool, and physical activity via ACT24 and dietary recalls with daily intake >1000 kcal were included in the analysis. Study foods were prepared at 2 locations: a classroom kitchen in The Ohio State University campus and the Original Goodie Shop bakery. Participants selected from a variety of food items based on personal preference, including garlic spread, brownies, chocolate cookies, spice cookies, quick bread muffins, and yeast

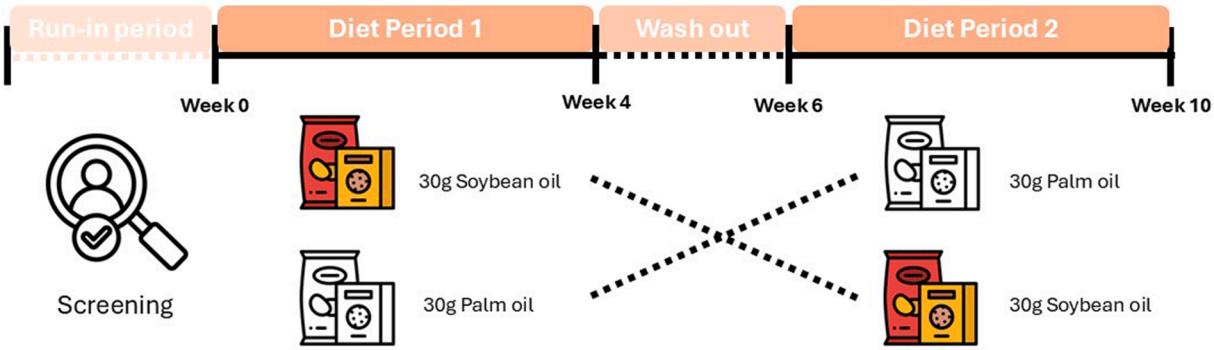

FIGURE 1. Study design flowchart.

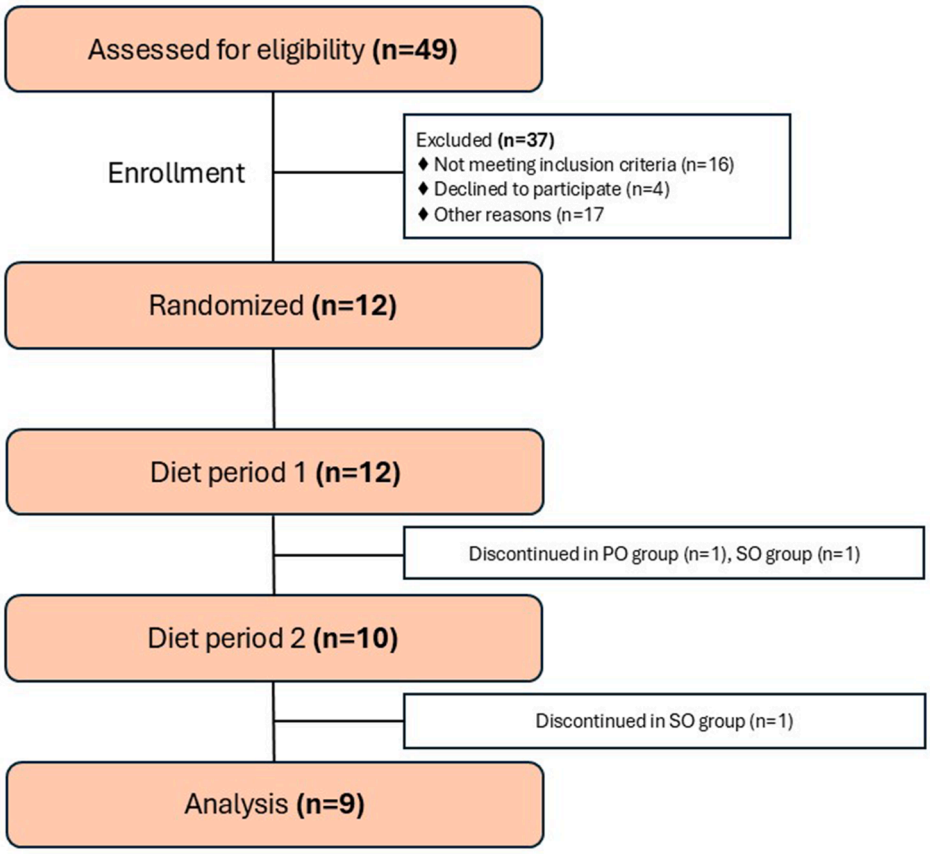

FIGURE 2. Participant recruitment flowchart. SO, soybean oil; PO, palm oil.

bread rolls. Each serving of test foods contained 10 g of either soybean or palm oil, so that consuming 3 servings/d amounted to a total daily intake of 30 g of the designated oil. The fortification goals for each diet period are shown in Table 1, which indicates that participants were provided 30 g/d of soybean oil, consisting of 16 g of additional LA, an amount comparable to that used in previous studies demonstrating significant biological effects [17,18,20]. The 4-wk duration was chosen to align with previous clinical trials that replenished dietary oils at 4-wk intervals [13,21]. The objective of the primary study was to evaluate acceptability and adherence to consuming 3 study foods daily, and this timeframe supported that aim while matching the planned replenishment schedule for future longer studies [16]. The nutrient composition of oil and study foods was calculated using the Nutrition Data System for Research software, version 2020, developed by the Nutrition Coordinating Center at the University of Minnesota, Minneapolis, MN. Detailed nutrient composition of the study foods is provided in the primary research paper [16].

Fatty acid profiling and desaturase activity estimation

Procedures for analyzing fatty acids in DBS [22,23], erythrocytes [24], plasma [25,26], and PBMC [25] were conducted as previously described. All samples were analyzed using gas chromatography equipped with a 30-m Omegawax 320 fused

TABLE 1
Fatty acid fortification goals for each diet period

Fatty acid	Palm oil diet group	Soybean oil diet group
Palmitic acid[1] (C16:0)	13.8	3
Stearic acid[1] (C18:0)	1.5	1.5
Oleic acid[1] (C18:1n–9)	11.7	7.2
Linoleic acid[1] (C18:2n–6)	3	16.2
α-Linolenic acid[1] (C18:3n–3)	0	2.1

Fatty acid analysis was performed using Nutrition Data System for Research software version 2020, Nutrition Coordinating Center, University of Minnesota.
[1] g/day.

silica capillary column (Supelco) and flame ionization detector with conditions as previously described [26,27]. Fatty acid methyl ester retention times were compared against reference standards obtained from Matreya, LLC, and Nu-Check Prep Inc. Desaturase enzyme activities were inferred by calculating the ratios of specific fatty acid products to their precursors in DBS, erythrocytes, plasma, and PBMC. Specifically, stearoyl-CoA desaturase-1 (SCD1) activity was estimated using the ratios C16:1n–7/C16:0 and C18:1n–9/C18:0, referred to as SCD16 and SCD18, respectively. D6D indices were assessed using the ratio C18:3n–6/C18:2n–6, whereas D5D indices were estimated using the ratio C20:4n–6/C20:3n–6 [28], as described in previous research [29].

Blood sample analysis

Serum IL-6 and CRP and plasma LBP were analyzed using the MesoScale Diagnostics MSD kit. Plasma sCD14 and oxLDL were measured with ELISA kits (R&D Systems Inc. and Mercodia).

Statistics

Statistical analysis was performed using STATA Versions 18 (StataCorp LLC). Mixed-effects linear regression with participant-level random intercepts was used to assess the lingering effects of the intervention across multiple biomarkers, accounting for repeated measures and interaction terms. Within-participant changes in fatty acids and biochemical markers within each diet period were compared with 0 using the Wilcoxon Signed Rank Test. Within-participant differences in changes between diet periods were also tested using the Wilcoxon Signed Rank Test.

Results

Lingering effect

The study employed a crossover design, and potential carryover effects were evaluated using mixed-effects linear regression. Results showed that all parameters were nonsignificant, indicating no evidence of a crossover effect.

Impact of palm and soybean oil snacks on markers of inflammation and oxLDL concentrations

Table 2 illustrates the changes in the primary outcomes, which include inflammatory markers and ox-LDL over the course of the diet period for both the palm oil and the soybean oil groups. Among the markers assessed, IL-6 showed a trend for a decrease in the soybean oil group ($P = 0.09$). In contrast, IL-6 concentrations in the palm oil group remained relatively stable throughout the diet period. Other inflammatory markers, including CRP, sCD14, LBP, and oxLDL, did not exhibit significant changes in either group. In summary, most inflammatory markers remained relatively stable during the intervention, whereas the soybean oil group demonstrated a trend of reduction in IL-6 concentrations.

TABLE 2
Markers of inflammation and oxLDL concentrations

Biomarkers	Group	Week 0 mean (SD)	Week 4 mean (SD)	*P* value	Between group
IL-6[1] (pg/mL)	Palm oil	1.73 ± 0.70	1.46 ± 0.49	0.3125	0.2500
	Soybean oil	1.60 ± 0.66	1.43 ± 0.58	0.0938	
CRP[1] (mg/mL)	Palm oil	1.33 ± 1.16	2.76 ± 3.79	0.6406	1.0000
	Soybean oil	2.33 ± 2.77	1.54 ± 2.65	0.2188	
sCD14[1] (μg/mL)	Palm oil	1.44 ± 0.27	1.50 ± 0.35	0.6250	0.2969
	Soybean oil	1.41 ± 0.28	1.49 ± 0.29	0.5781	
LBP[1] (pg/mL)	Palm oil	4.54 ±1.78	3.97 ± 2.22	0.9219	0.6875
	Soybean oil	3.52 ± 2.35	3.35 ± 2.66	1.0000	
oxLDL[1] (U/L)	Palm oil	61.43 ± 14.11	60.20 ± 10.22	0.6406	0.3750
	Soybean oil	57.75 ± 12.85	57.64 ± 15.64	0.2969	

Abbreviations: CRP, C-reactive protein; sCD14, soluble CD14; LBP, LPS-binding protein; oxLDL, oxidized LDL; PO, palm oil group; SO, soybean oil group.
[1] Planned sample sizes were PO ($n = 10$) and SO ($n = 9$); however, due to limited blood availability, actual sample sizes varied: IL-6 and CRP (PO: $n = 8$, SO: $n = 6$), sCD14 and LBP (PO: $n = 10$, SO: $n = 7$), oxLDL (PO: $n = 8$, SO: $n = 7$).

Impact of palm and soybean oil snacks on n–6 and n–3 fatty acids

Concentrations of LA and LA-derived n–6 fatty acids in plasma and RBC are presented in Table 3; data from DBS and PBMC are shown in Supplementary Tables 1 and 2. Overall, other than LA, n–6 fatty acids concentrations remained unchanged in the palm oil or the soybean oil groups. However, in RBC, a trend toward increased concentrations of C22:5n–6 was observed in the soybean oil group ($P = 0.0547$). In addition, AA concentrations in RBC significantly decreased in the soybean oil group ($P = 0.0234$). These findings suggest that although most LA-derived n–6 fatty acids are unaffected by palm or soybean oil consumption, AA decreased in response to soybean oil intake in erythrocytes.

Concentrations of α-linolenic acid (ALA) and ALA-derived n–3 fatty acid in plasma and RBC are presented in Table 3, whereas data from DBS and PBMC are shown in Supplementary Tables 1 and 2. Overall, other than ALA, most n–3 fatty acid concentrations remained stable in either palm oil or the soybean oil group. A significant decrease in C22:6n–3 (DHA) was observed in RBC in the soybean oil group ($P = 0.0078$),

TABLE 3
Fatty acid profile and desaturase indices of plasma and red blood cells

	Fatty acid	Group	Week 0 Mean (SD)	Week 4 Mean (SD)	*P* value	Between group
SFA in plasma	C16:0	Palm oil	20.97 ± 1.16	22.44 ± 1.28	0.0039	0.0273
		Soybean oil	21.01 ± 0.75	20.85 ± 0.83	0.4258	
	C18:0	Palm oil	1.43 ± 0.42	1.28 ± 0.47	0.6953	1.0000
		Soybean oil	7.07 ± 0.77	7.01 ± 0.42	0.7344	
MUFA in plasma	C16:1n–7	Palm oil	1.51 ± 0.55	1.48 ± 0.43	0.6953	0.4258
		Soybean oil	6.86 ± 0.54	6.99 ± 1.20	0.3594	
	C18:1n–9	Palm oil	18.22 ± 2.14	18.56 ± 1.76	0.4316	0.0391
		Soybean oil	18.38 ±2.78	16.70 ± 2.41	0.1289	
LA-derived PUFA in plasma	C18:2n–6	Palm oil	33.62 ± 3.97	32.02 ± 3.70	0.0371	0.0117
		Soybean oil	33.40 ± 3.72	35.75 ± 3.70	0.0742	
	C18:3n–6	Palm oil	0.47 ± 0.17	0.47 ± 0.19	1.0000	0.9102
		Soybean oil	0.42 ± 0.13	0.45 ± 0.21	0.7344	
	C20:3n–6	Palm oil	1.41 ± 0.34	1.47 ± 0.41	0.9219	0.7344
		Soybean oil	1.36 ± 0.28	1.35 ± 0.24	0.5703	
	C20:4n–6	Palm oil	8.13 ± 1.32	7.87 ± 1.72	0.4316	0.4961
		Soybean oil	7.97 ± 1.79	7.93 ± 1.89	1.0000	
	C22:4n–6	Palm oil	0.22 ± 0.07	0.20 ± 0.07	0.5566	0.2031
		Soybean oil	0.21 ± 0.06	0.22 ± 0.06	0.3008	
	C22:5n–6	Palm oil	0.19 ± 0.07	0.20 ± 0.09	0.6953	0.6523
		Soybean oil	0.19 ± 0.09	0.18 ± 0.06	0.7344	
ALA-derived PUFA in plasma	C18:3n–3	Palm oil	0.61 ± 0.20	0.53 ± 0.17	0.2324	0.4961
		Soybean oil	0.75 ± 0.32	0.76 ± 0.22	0.7344	
	C20:5n–3	Palm oil	0.44 ± 0.17	0.48 ± 0.24	0.8457	0.8203
		Soybean oil	0.37 ± 0.08	0.42 ± 0.23	0.7344	
	C22:5n–3	Palm oil	0.36 ± 0.07	0.37 ± 0.10	0.6953	0.5703
		Soybean oil	0.34 ± 0.06	0.39 ± 0.08	0.3008	
	C22:6n–3	Palm oil	1.26 ± 0.25	1.33 ± 0.37	0.3750	0.4961
		Soybean oil	1.24 ± 0.17	1.23 ± 0.25	0.7344	
Desaturase indices in plasma	SCD16	Palm oil	0.07 ± 0.02	0.07 ± 0.02	0.4316	0.4961
		Soybean oil	0.07 ± 0.02	0.06 ± 0.02	0.4258	
	SCD18	Palm oil	2.78 ± 0.55	2.68 ± 0.24	1.0000	0.1641
		Soybean oil	2.61 ± 0.51	2.38 ± 0.30	0.0547	
	D5D	Palm oil	0.02 ± 0.01	0.02 ± 0.01	0.3223	0.3594
		Soybean oil	0.013 ± 0.005	0.01 ± 0.01	1.0000	
	D6D	Palm oil	5.97 ± 1.78	5.74 ± 1.93	0.8457	0.8203
		Soybean oil	6.20 ± 1.81	6.12 ± 2.08	0.6523	
SFA in RBC	C16:0	Palm oil	24.62 ± 1.16	24.97 ± 1.15	0.3750	0.8438
		Soybean[1] oil	24.00 ± 1.01	24.56 ± 1.02	0.0547	
	C18:0	Palm oil	0.31 ± 0.12	0.31 ± 0.11	0.0195	0.0156
		Soybean[1] oil	19.52 ± 0.59	19.86 ± 0.87	0.1953	
MUFA in RBC	C16:1n–7	Palm oil	0.32 ± 0.12	0.33 ± 0.09	0.4316	0.9453
		Soybean[1] oil	20.35 ± 0.74	19.70 ± 0.66	0.7422	
	C18:1n–9	Palm oil	12.97 ± 0.77	13.22 ± 0.68	0.0840	0.0078
		Soybean[1] oil	13.12 ± 0.73	12.53 ± 0.54	0.0078	
LA-derived PUFA in RBC	C18:2n–6	Palm oil	12.76 ± 1.71	12.98 ± 1.85	0.7695	0.0781
		Soybean[1] oil	13.68 ± 1.80	14.77 ± 2.11	0.0547	
	C20:3n–6	Palm oil	1.43 ± 0.28	1.48 ± 0.35	0.5566	0.6406
		Soybean[1] oil	1.50 ± 0.30	1.48 ± 0.30	0.7422	
	C20:4n–6	Palm oil	15.38 ± 1.27	15.22 ± 0.99	0.8457	0.1484
		Soybean[1] oil	15.65 ± 1.31	14.82 ± 1.23	0.0234	
	C22:4n–6	Palm oil	4.15 ± 0.77	4.07 ± 0.77	0.4922	0.1484
		Soybean[1] oil	4.08 ± 0.72	3.87 ± 0.68	0.1484	
	C22:5n–6	Palm oil	0.57 ± 0.19	0.58 ± 0.17	0.6250	0.3125
		Soybean[1] oil	0.57 ± 0.23	0.58 ± 0.15	0.8438	
ALA-derived PUFA in RBC	C18:3n–3	Palm oil	0.17 ± 0.08	0.17 ± 0.06	1.0000	0.5469
		Soybean[1] oil	0.21 ± 0.08	0.24 ± 0.07	0.5469	
	C20:5n–3	Palm oil	0.29 ± 0.18	0.36 ± 0.23	0.6250	0.1484
		Soybean[1] oil	0.34 ± 0.12	0.31 ± 0.12	0.1953	
	C22:5n–3	Palm oil	2.19 ± 0.49	2.23 ± 0.29	0.3750	1.0000
		Soybean[1] oil	2.09 ± 0.32	2.13 ± 0.36	0.9453	
	C22:6n–3	Palm oil	3.07 ± 0.58	3.08 ± 0.60	0.6250	0.0234
		Soybean[1] oil	3.33 ± 0.62	3.02 ± 0.55	0.0078	
Desaturase indices in RBC	SCD16	Palm oil	0.013 ± 0.005	0.013 ± 0.004	0.3750	0.9453
		Soybean[1] oil	0.013 ± 0.005	0.013 ± 0.004	0.9453	
	SCD18	Palm oil	0.65 ± 0.06	0.67 ± 0.04	0.0195	0.0078

(*continued on next page*)

TABLE 3 (*continued*)

	Fatty acid	Group	Week 0 Mean (SD)	Week 4 Mean (SD)	*P* value	Between group
		Soybean[1] oil	0.67 ± 0.05	0.64 ± 0.03	0.0156	
	D5D	Palm oil	11.09 ± 2.59	10.85 ± 2.71	0.2754	0.9453
		Soybean[1] oil	10.96 ± 2.78	10.55 ± 2.72	0.3125	

Fatty acid values are expressed as percentages of total fatty acids.
C16:1n–7 (palmitoleic acid); C18:0 (stearic acid); C18:3n–6 (γ-linolenic acid, GLA); C20:3n–6 (dihomo-γ-linolenic acid, DGLA); C20:4n–6 (arachidonic acid, AA); C22:4n–6 (adrenic acid); C22:5n–6 (DHA n–6); C20:3n–6 (dihomo-γ-linolenic acid, DGLA); C20:4n–6 (arachidonic acid, AA); C22:4n–6 (adrenic acid); C22:5n–6 (DHA n–6); C20:5n–3 (EPA); C22:5n–3 (DHA n–3); C22:6n–3 (DHA); RBC, red blood cells; SCD1, stearoyl-CoA desaturase-1; SCD16 = C16:1n–7/C16:0, SCD18 = C18:1n–9/C18:0, D5D (δ-5 desaturase) = C18:3n–6/C18:2n–6, D6D (δ-6-desaturase) = C20:4n–6/C20:3n–6. Details of C16:0 (palmitic acid), C18:1 n9 (oleic acid), C18:2n–6 (linoleic acid, LA), and C18:3n–3 (α-LA, ALA) are provided in our primary manuscript [16]. C18:3n–6 (γ-linolenic acid, GLA) in RBC is below the detectable range. D6D activity could not be presented in RBC due to the undetectable concentrations of GLA.

[1] $n = 8$, 1 subject is unable to get enough blood to isolate RBC.

accompanied by a significant between-group difference ($P = 0.0234$). These findings suggest that although the majority of n–3 fatty acid profiles are unaffected by these diet periods, DHA concentrations in RBC are negatively affected by soybean oil intake.

Effect of palm and soybean oil snacks on SCD16, SCD18, D6D, and D5D indices in plasma and RBC

Concentrations of C16:1n–7 (palmitoleic acid) and C18:0 (stearic acid) are shown in Table 3. The only significant change observed was decreased C18:0 in the palm oil group ($P = 0.0195$) with a significant difference between groups ($P = 0.0156$). Fatty acid desaturation indices: SCD16, SCD18, D6D, and D5D for plasma and RBC are in Table 3; indices for DBS and PBMC are presented in Supplementary Tables 1 and 2. There are no significant differences in D5D and D6D in any samples in either group. A decrease in SCD18 was observed in the soybean oil group across DBS ($P = 0.0195$), plasma ($P = 0.0547$), and RBC ($P = 0.0156$). In addition, SCD18 significantly increased in the palm oil group in RBC ($P = 0.0195$), with a significant difference between groups ($P = 0.0078$). Our findings show that soybean oil and palm oil intake differentially affect desaturase activity, with significant changes in SCD18 but no effect on D5D or D6D.

Discussion

The primary outcomes of this study were differences between dietary oils for changes in systemic inflammatory markers and oxLDL concentrations; none showed a change in response to 30 g of soybean oil or palm oil consumption. IL-6 and CRP are commonly used as markers of systemic inflammation because they are strongly associated with inflammatory processes and chronic disease [30]. In addition, both LBP and sCD14 are acute-phase inflammatory proteins whose blood concentrations are positively associated with BMI and markers of insulin resistance [31–35]. OxLDL, a modified form of LDL, is commonly used as a surrogate marker of systemic oxidative stress and vascular inflammation in clinical trials [36]. Elevated IL-6, CRP, LBP, and sCD14 are widely recognized as proinflammatory markers linked to cardiometabolic risk and subclinical vascular changes [34,37]. Findings from this study are consistent with our previous supplementation study, where supplementation with 6.9 g LA/d for 16 wk did not affect oxLDL or CRP concentrations [13]. Furthermore, a systematic review of randomized controlled trials found no evidence that dietary LA increases inflammatory marker concentrations [38]. These findings indicate that LA intake, at a dose of ~16 g LA/d, does not increase inflammation as theoretically expected and may decrease risk of cardiovascular disease (CVD), type 2 diabetes, and other cardiometabolic conditions [39,40].

We observed a trend toward reduced IL-6 concentrations after the soybean oil diet period in our current study, consistent with our previous observational findings where erythrocyte LA concentrations were inversely associated with serum IL-6 [27]. In another prior study, we observed a reduction in CRP in the LA-rich safflower oil group in females with type 2 diabetes [15]. In a large population-based cross-sectional study, serum concentrations of n–6 PUFA were not linked to increased systemic inflammation in males; instead, LA was strongly associated with lower concentrations of CRP [14]. In agreement, previous research has shown that individuals with the lowest plasma n–6 PUFA concentrations had the highest concentrations of proinflammatory markers, including TNF-α, IL-6, and CRP, and the lowest concentrations of anti-inflammatory markers (transforming growth factor-beta, TGF-β) [41]. The observed reduction in IL-6, alongside the unchanged CRP concentrations after soybean oil intake, may be explained by the role of IL-6 as an upstream inflammatory cytokine that drives CRP production. As such, IL-6 may respond more rapidly to dietary interventions, whereas downstream markers like CRP may require exposure that is longer than the 4-wk diet period here [42]. In contrast, sCD14 and LBP reflect microbial translocation and chronic low-grade inflammation, which typically respond more slowly and may require extended or targeted interventions to improve [43]. Collectively, these findings reinforce the evidence that LA supplementation does not promote systemic inflammation or LDL oxidation but may in fact, reduce markers of inflammation and oxidation.

Whether LA consumption promotes inflammation and oxidative stress has long been debated in the popular press and in scientific circles [44]. Although some studies suggest that LA may enhance inflammatory responses or oxidative stress, many of these findings are based on in vitro models in cell cultures using excessively high concentrations of LA, ranging from 75 to

600 μM, which may not be achievable as a circulating LA concentration in human [45,46]. Although in vitro studies offer mechanistic insights, they lack the systemic complexity of whole organisms, limiting the applicability of their results to practical dietary settings. In addition, AA is often mischaracterized as proinflammatory [47]. Although AA can be converted into proinflammatory mediators such as leukotrienes, prostaglandins, and thromboxanes, AA also serves as a precursor to anti-inflammatory compounds like lipoxins (e.g., LXA4), which are essential for resolving inflammation [47]. This highlights a dual role of AA in both initiating and resolving inflammatory responses.

Fatty acid composition

We measured the impact of soybean compared with palm oils on fatty acid profiles of plasma, RBC, PBMC, and DBS because each blood fraction provides complementary insights into dietary fatty acid effects on biomarkers. Each blood fraction may offer practical alternatives to tissue sampling, which is not feasible in clinical trials. These blood compartments may serve as accessible indicators of dietary fatty acid intake and may reflect organ fatty acid composition [48]. Plasma reflects short-term intake due to rapid turnover [49], whereas RBC membranes may serve as long-term markers of fat quality intake given 120-d lifespan of erythrocyte [48]. PBMC, with a turnover of 3 to 10 d, offer functional relevance by linking lipid remodeling to immune and cardiometabolic processes [25]. Although RBC and PBMC may be better indicators of chronic fat quality intake, a drawback of RBC and PBMC is the requirement for laboratory processing with immediate storage of samples in −80 freezers [50]. The DBS provides an integrated measure of short- and long-term changes and practical advantages for large-scale studies [50] and can be collected by the participants without assistance from remote locations. After 4 wk of palm oil or soybean oil snack consumption at 30 g oil/d, most n–6 and n–3 fatty acid profiles in DBS, PBMC, plasma, and RBC remain unchanged. However, soybean oil snack intake was associated with reductions in AA and DHA concentrations in erythrocytes, suggesting a potential impact on fatty acid profile in RBC. Although it is often claimed that higher dietary LA intake elevates AA concentrations, our findings support previous studies that do not show dietary LA increases plasma AA [10,51,52]. A systematic review found that increasing dietary LA does not raise plasma AA concentrations in adults, with most studies reporting only minimal and statistically insignificant changes [51]. With higher dietary intake of LA, plasma AA concentrations remained unchanged or were inversely associated with LA [52], suggesting that increased LA does not promote AA synthesis in healthy adults and that factors beyond n–6 fatty acid intake play a significant role in regulating plasma AA concentrations. In a study using stable isotope [^{13}C], increasing dietary intake of LA does not significantly raise concentrations of LA or AA in plasma, as the conversion of LA to AA is extremely low, ∼0.2% [10]. Collectively, these findings support our results, where 16 g LA/d does not increase, and may even reduce, AA concentrations in erythrocytes.

Interestingly, we observed a trend toward increased C22:5n–6 concentrations in DBS in the soybean oil group (P = 0.0547). Although the biological significance of this finding is unclear, and no prior studies have reported similar results, it may reflect alterations in elongation or desaturation pathways in response to increased dietary LA. Given that this trend did not reach statistical significance and was not observed in RBC, further research is needed to confirm and elucidate the underlying mechanisms.

We observed a significant decrease in DHA concentrations in RBC in the soybean oil group. Although the underlying mechanism remains unclear, 1 previous study reported that higher RBC LA concentrations are inversely associated with concentrations of AA, EPA, and DHA in Canadian pregnant females; in this prior study, the authors speculated that the lower AA, EPA, and DHA were due to competition for incorporation into membrane lipids [53]. DHA can be elongated into tetracosahexaenoic acid (THA; 24:6n–3), a C24 fatty acid that may serve additional physiological functions [54]. Unfortunately, we did not measure THA in our study. Given our findings, further research is needed to better understand the mechanisms underlying the reduction of DHA in RBC after soybean oil consumption.

Desaturase indices

Several studies have shown that desaturase indices derived from blood-based fatty acid profiles, such as those in plasma and RBC, can serve as reliable surrogate markers of hepatic enzyme activity, making them useful in clinical research settings [55–57]. SCD16 and SCD18 are rate-limiting lipogenic enzymes anchored in the endoplasmic reticulum membrane, both contributing to the synthesis of MUFA [58]. Specifically, the SCD16 ratio reflects the conversion of C16:0 (palmitic acid) to C16:1n–7 (palmitoleic acid), whereas the SCD18 ratio reflects the conversion of C18:0 (stearic acid) to C18:1n–9 (oleic acid) [28]. In our study, a decrease in SCD18 activity was observed in the soybean oil group across DBS, plasma, and RBC samples. In a previous study, rats fed a purified diet supplemented with corn oil, which contained ∼60% LA by weight of its fatty acids and was adjusted to maintain 410 to 415 kcal/100g, showed reduced hepatic SCD activity, likely due to downregulation of SCD gene expression [59]. Conversely, SCD18 activity was significantly increased in the palm oil group in RBC, with a notable difference between groups. This finding aligns with previous research reporting that palm oil consumption enhances SCD activity in rats, particularly in the phospholipid and free fatty acid fractions of liver tissue, an effect potentially driven by oleic acid derived from palm oil [60]. Supporting this, we also observed a significant reduction in C18:0 concentrations in the palm oil group, which is consistent with elevated SCD18 activity, as a decrease in the substrate (C18:0) corresponds with an increased desaturase index. Overall, our findings suggest that dietary fatty acid composition can modulate SCD activity, with different oils exerting distinct effects on desaturase indices across lipid fractions.

In addition to SCDs, D6D, and D5D are involved in the biosynthesis of PUFA [29]. D6D is the rate-limiting enzyme for essential PUFA conversion, along with D5D, as the main determinants of PUFA concentrations [61]. PUFA ratios are commonly used to estimate desaturase activities in human studies because enzymes reside and are primarily active in the liver [62,63]. There has been speculation that a diet high in n–6 fatty acids may lead to elevated desaturase activity, thereby increasing the bioavailability of AA and promoting the synthesis

of AA-derived proinflammatory eicosanoids [64]. However, our study failed to show significant changes in D5D or D6D in either the soybean oil or the palm oil groups. To the best of our knowledge, this is the first human clinical trial to directly compare the effects of soybean oil compared with palm oil intake on D5D and D6D indices. Others have reported a negative correlation between dietary LA intake and the expression of D5D mRNA and D6D mRNA in PBMC [65]. In addition, mechanistic evidence indicates that PUFA-derived products regulate D5D and D6D expression through transcriptional feedback mechanisms [66]. Our findings suggest that increased LA intake does not enhance the activity of these rate-limiting enzymes to promote AA production, as previously theorized.

Limitations

This study offers valuable insights; however, there are a few limitations. The health status of participants was based on self-reported medical history without confirmation through serum biochemistry or blood pressure measurements. CRP values were within normal ranges, suggesting that the participants with overweight or obesity in this cohort were generally healthy. A notable constraint is our limited analyses of downstream LA and ALA-derived fatty acid, which may hinder a comprehensive understanding of the metabolic pathways involved. We focused on several commonly observed fatty acids that are players in cellular and physiological processes associated with purported inflammation associated with vegetable oils (e.g., "seed oils" in popular press). This investigation was designed as a pilot study to inform and guide future research directions and, therefore, has a small sample size; thus, it is inappropriate to generalize our findings to a broader adult population. Even with these limitations, we believe these findings substantiate a plethora of evidence that dietary intake of n–6 PUFAs does not increase systemic inflammation in healthy overweight adults. In addition, this study sets a foundational framework for evaluating the potential health benefits of LA-fortified snacks in larger cohort studies.

In summary, consumption of snack foods containing either soybean oil or palm oil at 30 g/d for 4 wk did not significantly alter most biomarkers of essential fatty acid metabolism or systemic inflammation. Soybean oil intake notably reduced erythrocyte AA concentrations and demonstrated a trend toward lower circulating IL-6 concentrations. These results suggest that dietary soybean oil does not increase proinflammatory biomarkers and may support favorable shifts in fatty acid metabolism, countering widespread social media claims that ω-6 fatty acids are inherently proinflammatory.

Acknowledgments

We extend our gratitude to Stephan Zarich for his critical evaluation of the data and manuscript.

Author contributions

The authors' responsibilities were as follows – RMC, MAB: designed research; RMC, EC, AA: conducted research; C-TY, RMC, AN: analyzed data; MAB: had primary responsibility for final content; and all authors: wrote the paper, read and approved the final manuscript.

Declaration of generative AI and AI-assisted technologies in the writing process

No generative AI or AI-assisted technologies were used in the preparation or writing of this manuscript.

Conflict of interest

MAB serves on the board of trustees for the American Society for Nutrition Foundation and has received travel reimbursement from the United Soybean Board for a scientific session. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This research was funded by the United Soybean Board (2411-108-0101), Soy Nutrition Institute Global, the Ohio Agriculture 335 Research and Development Center, and the National Center for Advancing Translational Sciences, Grant 336 UM1TR004548. Soybean oil was donated by Cargill, Incorporated. The sponsors had no role in the design or conduct of the study, the data analysis, or the decision to publish.

Data availability

Data described in the manuscript, code book, and analytic code will be made available upon request, pending application and approval.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cdnut.2025.107635.

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