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Randomized Controlled Trial

Effect of different sources of saturated and polyunsaturated fatty acids on postprandial inflammation: A double-blind randomized crossover trial

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SUMMARY

Background and aims: Acute postprandial inflammation is a transient response to food intake and may, if repeatedly exaggerated, contribute to chronic low-grade inflammation associated with cardiometabolic disease. A high-fat meal can trigger an acute inflammatory response in the postprandial state, but the role of dietary fat composition remains unclear. The primary aim of the study was to evaluate the effect of different sources of saturated fatty acids (SFA) and Polyunsaturated fatty acids (PUFA) on the postprandial inflammatory response, and the secondary aim was to identify markers of postprandial inflammation.

Methods: In a double-blind, randomized 4-way crossover trial, 18 healthy adults consumed isocaloric test meals (706 kcal) with 40 g of fat from either butter, coconut oil, flaxseed oil, or corn oil. Postprandial blood samples were collected up to 6 h. Inflammatory proteins were measured using proximity extension assay while glycoprotein acetyls (GlycA) and triacylglycerol (TG) were measured by NMR spectroscopy. Postprandial changes were analyzed with linear mixed models; markers affected by time ($p < 0.05$) were further studied for time × fat source interactions.

Results: Twenty-one (23 %) of 93 proteins changed postprandially, across all meal challenges combined ($p < 0.05$ for time), including GlycA, IL-6, IL-17C, CXCL10, FGF19, and MMP1, indicating a broad but heterogeneous inflammatory response. Significant time × fat source interactions were found for GlycA ($p < 0.001$) and IL-17C ($p = 0.022$). GlycA rose more after PUFA-rich meals (corn, flaxseed) than SFA-rich meals (butter, coconut), while IL-17C was higher after flaxseed oil. Additional pairwise differences were observed but were inconsistent across markers and fat sources. There were no differences in plasma TG concentration between fat sources.

Conclusions: While several markers of inflammation were altered after the high-fat meal, no consistent directional pattern was observed that would favor a specific fat source. PUFA-rich meals elicited slightly stronger inflammatory responses than SFA-rich meals, but overall, fat source had a modest influence. Further research is needed to clarify the clinical relevance and potential implications of the findings.

Clinical trial registry: The study was registered at Clinicaltrials.gov (NCT05674708).

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1. Background

It is well known that chronic low-grade inflammation is linked to the development of numerous non-communicable diseases,

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including obesity, type 2 diabetes, and cardiovascular diseases (CVD) [1]. However, less is known about postprandial inflammation. This phenomenon refers to the acute but transient activation of inflammatory pathways that occur within hours after consumption of a meal high in fat and refined carbohydrates, leading to increases in circulating inflammatory proteins [2,3]. Since, humans spend most of their waking hours in a non-fasted state, meal-induced inflammatory responses may be directly relevant to disease development and progression [4–6]. Postprandial lipemia, characterized by acute elevations in triacylglycerol (TG), is closely linked to fat intake [7] and is in itself associated with an increased risk of CVD [8]. It may also amplify inflammatory processes through several mechanisms, including effects on endothelial function [9] and the translocation of endotoxins across the gut barrier [10,11].

The long-term health implications of postprandial inflammation are still being studied and remain uncertain [12]. It is currently unknown which inflammation markers are affected in the postprandial state and if different food components trigger different responses. Interleukin-6 (IL-6) and glycoprotein acetyls (GlycA), a novel marker of systemic inflammation, have been identified as markers of postprandial inflammation, whereas other markers such as tumor necrosis factor - alpha (TNF-α), c-reactive protein (CRP), and interleukin-8 (IL-8) have demonstrated inconsistent results in previous research [2,4].

Dietary fatty acids have the potential to modulate inflammatory responses and thereby influence the risk of non-communicable disease [13–15]. Variations in fatty acid class and chain length can affect both the magnitude and temporal profile of postprandial lipemia, which in turn may shape the downstream inflammatory response: in particular, saturated fatty acids (SFAs) and polyunsaturated fatty acids (PUFAs) appear to exert distinct effects on postprandial inflammation [1,2,16]. SFAs have been suggested to generate a more pronounced inflammatory response compared to PUFAs [17,18], possibly by facilitating the translocation of lipopolysaccharides into the bloodstream [19]. SFAs chain length could also impact postprandial inflammation, as medium chain SFAs from coconut oil have been shown to be less lipemic than longer chain SFAs from butter or lard [13]. In addition, PUFA classes omega-3 and omega-6 fatty acids have been ascribed different inflammatory properties through their role as precursors to bioactive molecules known as oxylipins. Omega-3 PUFAs generally lead to the formation of anti-inflammatory oxylipins, while omega-6 PUFAs can result in both pro-inflammatory and anti-inflammatory oxylipins [20–22]. This difference highlights the complex and nuanced effects of different fatty acids on inflammation.

Although it is well established that chronic low-grade inflammation contributes to the development of cardiometabolic diseases, the role of dietary fat composition in modulating postprandial inflammation remains underexplored. Previous studies have provided conflicting results regarding the impact of different fatty acids on postprandial inflammatory markers, underscoring the need for controlled dietary interventions to dissect these relationships more clearly [1,18].

The primary aim of the study was to evaluate the effect of different sources of SFA and PUFA on the postprandial inflammatory response and the secondary aim was to identify markers of postprandial inflammation.

2. Methods

A double-blind, randomized, crossover design was chosen to minimize inter-individual variability and enhance statistical power, allowing each participant to serve as their own control, thereby reducing confounding factors. The Postprandial Inflammation fat (PI:fat) trial was conducted at the Department of Internal medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, and at the Department of Nutrition, Institute of basic medical sciences, University of Oslo, Norway, from February 2023 until January 2024. All procedures were conducted according to the Declaration of Helsinki. The study was registered at Clinicaltrials.gov (NCT05674708) and was approved by the Swedish Ethical Review Authority (Dnr 2022-05898-01) and by the Norwegian Regional Committees for Medical and Health Research Ethics (Project nr 603852).

2.1. Study participants

Participants were recruited via social media and posters at both study sites. The study inclusion criteria were 18–50 years old, BMI >18.5 kg/m^2 and willingness to consume the study foods. Exclusion criteria were as follows: diabetes (fasting glucose >7.0 mmol/l), hyperlipidemia (fasting TG > 1.7 mmol/l or use of lipid lowering medication), anemia (Hb < 100 g/l), established CVD, cancer, habitual intake of anti-inflammatory medications, recent weight change (±5% in the last 3 months), pregnancy or lactation, and habitual smoking. Those interested in participating were invited to a screening visit.

At screening, weight was measured in light clothing without shoes, height was measured to the closest cm. Fasting blood and urine samples were collected. Written informed consent was obtained from all participants prior to the study visit.

2.2. Dietary interventions

Participants received four isocaloric meals containing different sources, but similar amounts of fat, protein, and carbohydrate content consumed in a random order on four different days. All meals were consumed in the fasting state, and test days were separated by a four-week washout to account for the menstrual cycle of female participants. Randomization was performed using a random sequence generator (random.org). A researcher not involved in the study blinded the meals, and thus, the study researchers and participants were unaware of which meal contained which fat source. The study design is shown in Fig. 1.

2.3. Test meals

The meals consisted of a brownie containing 40 g of different sources of fat: butter (butter meal), corn oil (corn oil meal), flaxseed oil (flaxseed oil meal), or coconut oil (coconut oil meal). The base recipe for all brownies was identical and included caster sugar (43 g), flour (30 g), egg (39 g), cocoa powder (5 g) and salt (1 g), with the test fat source added as butter (49 g, Arla Foods AB, Sweden) coconut oil (40 g, Flora Food Sweden AB/Upfield Sweden AB, Denmark) corn oil (40 g, ICA Sweden, Belgium), or flaxseed oil (40 g, Zeta/Di Luca & Di Luca, Italy). The selected fat sources represent distinct profiles of SFA (butter, coconut oil) and PUFA (corn oil, flaxseed oil), allowing for a comprehensive analysis of their differential effects on inflammation. Each meal provided 40 g fat originating from the specific fat source used (equivalent to 50% of total energy, estimated on the total energy content of the meal) and in total 46 g fat. This represented a moderate fat load intended to elicit measurable postprandial responses. Flaxseed oil was included because of its high omega-3 fatty acid content while corn oil was included because of its high omega-6 fatty acid content. Butter and coconut oil were included as major sources of SFAs, as coconut oil contains a higher proportion of shorter-chain and

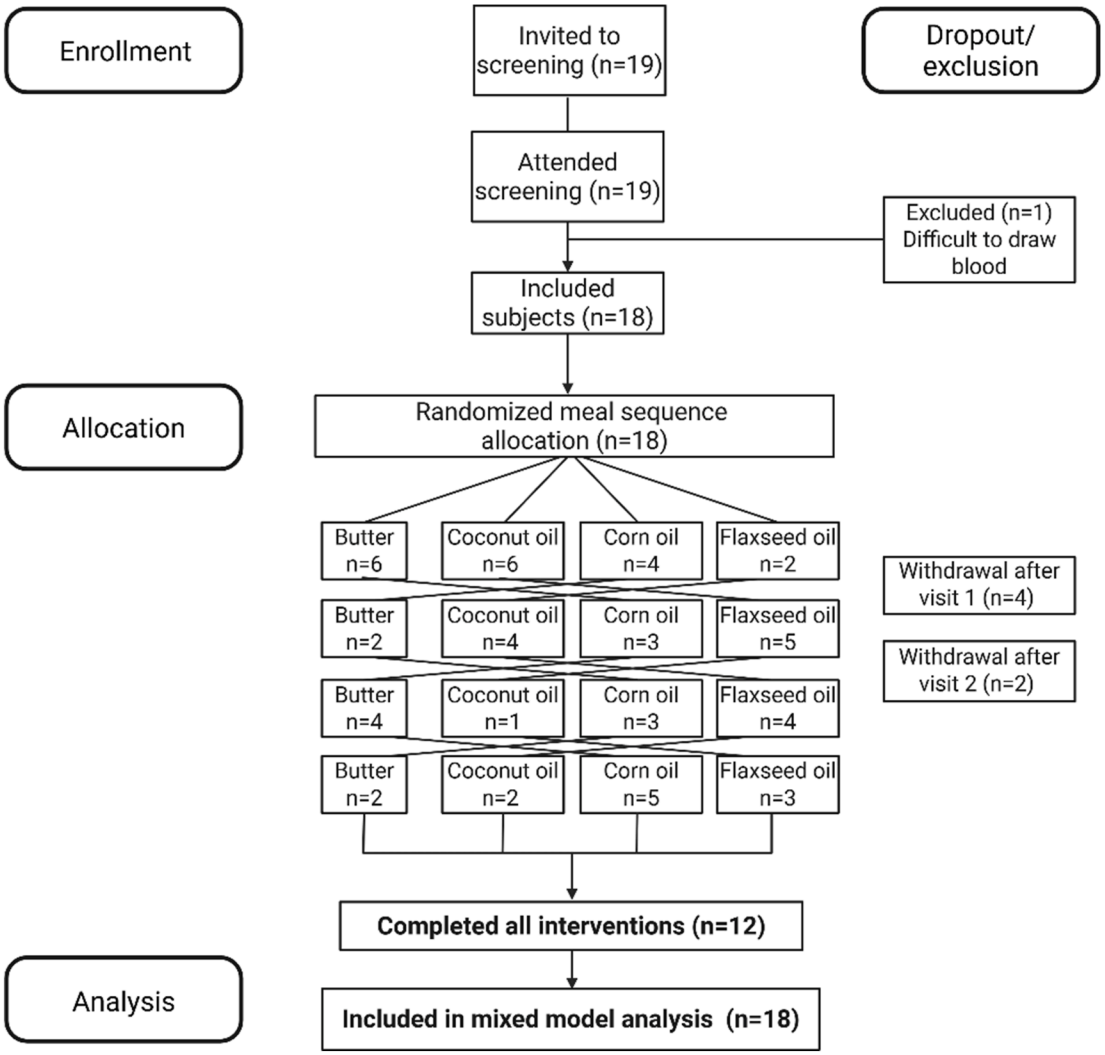

Fig. 1. Flowchart of the study participants. The figure was created with BioRender.com.

medium-chain SFAs and represents a debated source of SFAs with potential neutral or beneficial effects [20–23] while butter contains longer chain SFAs.

All meals were comparable in energy content (~706 kcal) and macronutrient composition (Table 1). The brownies were baked in two batches in Gothenburg and one batch in Oslo. After being baked at 160 °C for approximately 15 min and allowed to cool, the brownies were frozen and stored at −20 °C. On the day of the study, the brownies were reheated at 150 °C for 7–10 min prior to serving.

2.4. Intervention day procedures

Participants were asked to avoid strenuous physical activity, alcohol, and high-fat foods the day before the meal challenge day and to travel to the study center by public transportation or car rather than walking or bicycling.

On each meal challenge day, participants arrived at the study center after an overnight fast (>12 h). Morning or second void samples were collected. After resting for 5 min in a supine position, baseline measurements (0 h) of blood pressure were taken, blood samples were drawn by venipuncture and blood glucose analyzed using capillary blood (Bayer Consumer Care AG, Basel Switzerland). Participants then consumed the test meal together with a glass of water, within 10–15 min, with only water allowed during the remainder of the day at the study center. Blood samples were subsequently collected after 2 h (2 h), 4 h (4 h) and 6 h (6 h) post-consumption.

2.5. Blood sampling and analysis method

At each meal challenge day, approximately 16 ml of venous blood was collected, without use of peripheral venous catheter. Serum samples were collected in 7-ml vacutainer serum separating tubes and were allowed to clot for 30 min at room temperature and then centrifuged at 1500×*g* at 20 °C for 15 min. Plasma samples were collected in 7-ml vacutainer EDTA tubes and were centrifuged within 10 min at 2000×*g* at 4 °C for 15 min. After centrifugation and aliquotation of serum and plasma, all samples were immediately stored in - 20 °C, and at earliest convenience transferred to - 80 °C for storage until analysis.

Ninety-two inflammation-related biomarkers were analyzed in plasma using a multiplex proximity extension assay-based method (Olink® Target 96 inflammation panel, Olink Proteomics AB, analyzed by SciLifeLab, Uppsala, Sweden), as described elsewhere [24]. The final assay data is expressed as a normalized

Table 1
Nutritional content of the meals served during the meal challenges.

	Butter	Coconut oil	Corn oil	Flaxseed oil
Energy, kcal	709	706	706	706
Protein, g	9	9	9	9
Carbohydrate, g	65	65	65	65
Total fat, g	46	46	46	46
Fat from test fat sources, g	40	40	40	40
Total SFA, g	28	39	7	5
Palmitic acid (C16:0), g	13.5	5.0	5.3	2.9
Lauric acid (C12:0), g	1.3	18.5	0	0
MUFA, g	13	4	13	10
Total PUFA, g	2	2	23	28
Alpha-linolenic acid (C18:3 n-3), g	0.2	0	0.4	21.0
Linoleic acid (C18:2n-6), g	1.7	1.5	22.2	6.5
Omega 3, g	0.4	0.1	0.5	21
Omega 6, g	1.8	1.5	22	6.5

Abbreviations: Saturated fatty acids (SFA), Monosaturated fatty acids (MUFA), Polyunsaturated fatty acids (PUFA).

protein expression value (NPX), measured in arbitrary units on a log2-scale, with higher values reflecting higher levels of protein concentrations. NPX values were calculated by Olink's standard data processing pipeline, including normalization to internal controls and inter-plate controls.

Glycoprotein acetyls (GlycA) and plasma TG concentrations were analyzed in serum using 1H nuclear magnetic resonance (NMR) spectroscopy (Nightingale Health. Ltd, Kuopio, Finland). Raw NMR data were processed and analyzed using Nightingale Health's propriety algorithms and GlycA and TG data are presented in mmol/L [25].

2.6. Statistical analysis

All participants that completed at least one test meal was included in the analysis. Descriptive statistics are presented as mean and standard deviations (SDs) unless otherwise noted. Data analyses were conducted in two stages. Postprandial changes in inflammatory biomarkers were first assessed using linear mixed models, with each of the 93 biomarkers analyzed individually. In this initial screening, time point (0 h–6 h) was included as a fixed effect, with baseline values included as covariates, while participant ID and study site were specified as random effects to account for within-participant correlation and between-site variability. Biomarkers showing a significant effect of time ($p < 0.05$) were considered responsive to postprandial changes and were subsequently included in a second round of analysis. For transparency, Holm–Bonferroni-adjusted p-values are also reported. These adjusted p-values were applied to account for multiple comparisons and are presented alongside unadjusted values to support transparent interpretation of the findings (Supplementary Table 1).

In the second step, biomarkers that were considered responsive to postprandial changes, were further analyzed using linear mixed models that included fat source, time, and their interaction as fixed effects, with baseline values included as covariates. Participant ID and site remained as random effects. Sequence was not included as a fixed effect in the statistical model due to the large number of possible unique meal sequences (24 in total) and the limited number of participants per sequence (1–2) (Supplementary Table 2). Including sequence under these conditions would have substantially increased model complexity and risked overfitting. Given the randomized and balanced allocation of treatments across periods, and the long washout period of four weeks, this approach was deemed appropriate [26] and there was no reason to believe that sequence order would have affected the responses. The minimum area under the curve (AUCmin) was calculated for each biomarker to complement the linear mixed model analysis and provide an integrated measure of the total postprandial response. As several biomarkers exhibited values both above and below baseline, AUCmin (defined as the area under the curve relative to each participant lowest observed value) was used to capture the overall magnitude of postprandial change irrespective of direction [27]. Model residuals were visually inspected and found to be in reasonable agreement with model assumptions. No variable transformations were deemed necessary. A sensitivity analysis was conducted to evaluate the robustness of the primary results with a model adjusting for body weight before each meal. All statistical analyses were performed using R software (version 4.4.3, R Foundation for Statistical Computing) within the RStudio environment [28].

Power was originally based on detecting postprandial changes in the primary outcome, IL-6 using measurements at baseline and 4 h. This indicated that 12–14 participants would be required to detect changes corresponding to Cohens' $d = 0.9$ (80% power, alpha = 0.05). After data collection, a decision was taken to analyze samples from all four time points for each meal, and the statistical analysis plan was updated accordingly. Post hoc power calculations showed that, assuming sphericity (Epsilon = 1), approximately 15 participants would be required to detect meal-related differences of the same effect size using repeated measures ANOVA.

2.7. Handling of missing data

About 5% of the values were missing due to failure to draw blood or due to problems with the laboratory analysis. Imputation of missing values was performed using the following approaches: missing values between two time points were imputed using the average of the preceding and following time points for that meal and individual. Missing values at 0 h were imputed using the average 0 h values from the other three meals for that individual. Missing values at 6 h were imputed using the 4 h value and the group average percentage change from 4 h to 6 h for that meal. All analyses were also repeated using the original dataset without any imputed values.

3. Results

3.1. Participants

Nineteen participants were screened. One participant was excluded due to difficulties in drawing blood, leaving 18 participants to enter the study of which all completed the first meal

challenge. Baseline characteristics of all included participants are displayed in Table 2. Mean age of the participants was 30 years, 72% were female and 27% overweight. Concentrations of hemoglobin, blood lipids, and apolipoproteins were within the normal range for all participants. Fourteen participants completed at least two meal challenges, and twelve participants completed all four meal challenges (Fig. 1).

3.2. Systematic screening of markers of postprandial inflammation

Of the 93 inflammation markers investigated, 21 (23%) were affected in the postprandial state ($p < 0.05$ for effect of time) (Fig. 2; Supplementary Table 1 for detailed results and abbreviations). There was no clear pattern in the direction of change for protein expression across different classes of inflammation markers. Among cytokines, IL-6 exhibited a significant time-dependent increase, consistent with an acute inflammatory response, while IL-17C, TNFSF10, and TNFSF11 declined. Chemokines including CCL2, CCL3, and CXCL10 showed progressive decreases, suggesting reduced chemotactic signaling. Hormones and growth factors FGF19 and NTF3 increased over time, whereas FLT3LG and FGF21 decreased. The protein levels of the enzyme MMP1 increased, and MMP10 and PLAU declined. Composite inflammation marker GlycA showed a modest but consistent elevation. After Holm–Bonferroni-adjustment to account for multiple comparisons, five markers remained significant for effect of time (FLT3LG, IL-6, GlycA, FGF23, and CXCL10) (Fig. 2; Supplementary Table 1).

3.3. Impact of fat source on postprandial triglycerides and inflammation

Postprandial TG concentrations (mmol/L) peaked at 2 h reaching 130% of baseline and declined toward baseline by 6 h across all fat sources. Neither the effect of fat source nor the fat × time interaction was significant ($p = 0.891$ and $p = 0.308$, respectively). Consistent with these findings, TG AUCmin over 0–6 h did not differ between fat sources ($p = 0.095$) (Fig. 3).

Among the 21 markers of postprandial inflammation, GlycA and IL17C ($p < 0.001$ and $p = 0.022$ respectively) showed significant interactions between time and fat source. GlycA concentrations increased more over the 6-h period after consumption of both corn oil and flaxseed oil than after consumption of butter and coconut oil (Fig. 4; Supplementary Table 3). After Holm–Bonferroni-adjustment to account for multiple comparisons, only the time x fat source interaction for GlycA remained significant. Pairwise comparisons showed that GlycA concentrations were significantly higher after intake of corn- and flaxseed oil compared to butter and coconut oil (all $p < 0.001$), with no differences observed within SFA or PUFA sources. IL-17C expression was significantly higher after intake of flaxseed oil compared to all other fat sources ($p < 0.05$) (Fig. 5). Among SFA sources, coconut oil significantly lowered FGF19 compared with butter, but increased MMP1. Among PUFA sources, IL-17C was significantly lower after intake of corn oil compared to flaxseed oil. In general, when differences were detected, SFA elicited smaller effects on inflammatory markers compared with PUFA sources (Fig. 5). Significant differences between meals were also observed for AUCmin of GlycA ($p < 0.001$) and urokinase-type plasminogen activator (PLAU) ($p < 0.05$) (Fig. 4).

Sensitivity analyses showed that neither additional adjustment for body weight nor repetition of the analyses using the original dataset without imputed values meaningfully changed the results.

Table 2
Baseline characteristics of the included study participants.

	(n = 18)
Sex, n (%)	
Male	5 (28%)
Female	13 (72%)
Age, y	30 ± 6 [23–50]
Height, cm	169 ± 0.1 [157–183]
Weight, kg	66 ± 10 [51–89]
BMI, kg/m^2	23 ± 3 [19–29]
Hemoglobin (g/l)	130 ± 12 [110–155]
Triglycerides (mmol/l)	0.8 ± 0.3 [0.4–1.1]
Apolipoprotein A (g/l)	1.6 ± 0.2 [1.3–1.9]
Apolipoprotein B (g/l)	0.8 ± 0.1 [0.6–1.0]
Fasting blood glucose (mmol/l)	4.7 ± 0.5 [3.7–5.5]
SBP (mmHg)	110 ± 12 [82–133]
DBP (mmHg)	65 ± 7 [50–70]

Data are presented as means and SDs, min and max values in brackets.
Abbreviations: Body mass index (BMI); Systolic blood pressure (SBP); Diastolic blood pressure (DBP).

4. Discussion

To the best of our knowledge, this is one of the first studies to systematically assess a broad panel of potential postprandial inflammatory biomarkers in response to different dietary fat sources using a controlled, double-blind crossover design. A total of 21 inflammatory markers were found to be altered in the postprandial state, although only limited differences were observed between fat sources. Both PUFA sources - corn oil (predominantly omega-6 linoleic acid) and flaxseed oil (rich in omega-3 α-linolenic acid) - elicited significantly elevated GlycA levels compared to the SFA sources butter (rich in palmitic acid) and coconut oil (rich in lauric acid). Additionally, flaxseed oil led to increased IL-17C concentrations relative to butter, coconut oil, and corn oil. AUCmin for PLAU also differed between fat sources, though no significant pairwise differences were observed. Despite these specific findings, the overall results suggest that the source of dietary fat has a relatively modest impact on postprandial inflammation, with few consistent or robust differences observed between fat sources. Therefore, the results should be interpreted cautiously and considered specific to the fat sources and fatty acids examined. Nonetheless, the findings offer novel insights into the acute inflammatory effects of dietary fat from different sources and contribute to a more nuanced understanding of how fat quality may influence metabolic response.

The fat content originated from the fat source used (40 g) corresponding to approximately 50 E% of the total energy content of the meal. This level was selected to represent a moderate fat load that is realistic for a typical mixed meal in daily life. This dose is also about half of the average daily fat intake among Swedish adults (70–80 g/day) [29]. Previous studies comparing the postprandial inflammatory effects of SFA and PUFA used fat loads from approximately 40 g–95 g per meal or 30–60 E% of total energy [2,30,31], with larger amounts often exceeding habitual intake and primarily intended to induce a pronounced metabolic challenge. The 40 g dose used in the present study therefore reflects a physiologically relevant amount that elicits measurable postprandial responses.

4.1. Findings in relation to previous studies

Our findings suggest that PUFA-rich meals increase some markers of postprandial inflammation more than SFA-rich meals and this partially contrasts with findings in previous studies. Studies by Masson et al. and Rathnayake et al. found that SFA induced a higher response in some markers of inflammation

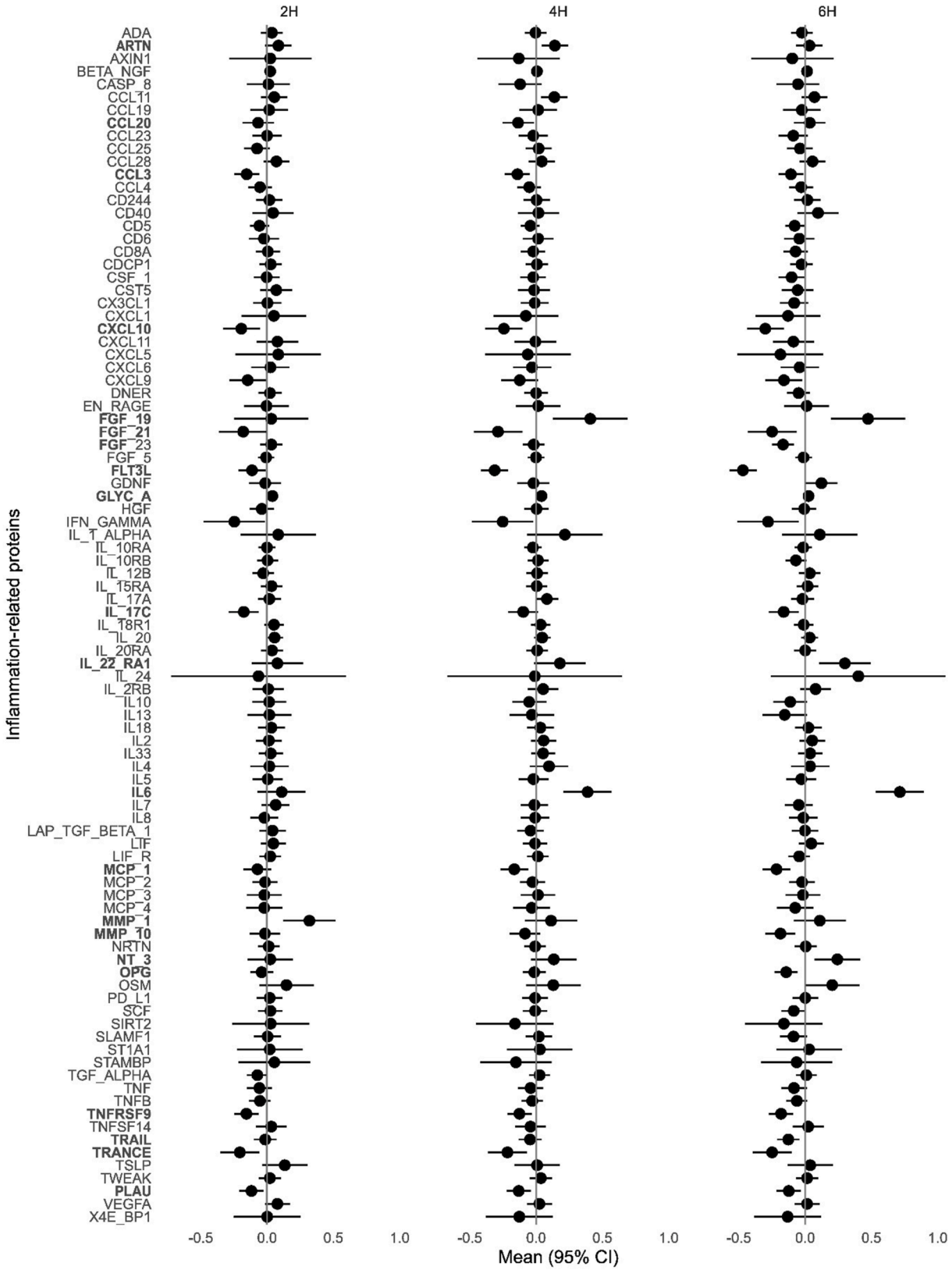

Fig. 2. Changes in concentrations of inflammation-related proteins across time points, measured across all meals in participants (n = 18). Concentrations are expressed as normalized protein expression (NPX) values on a semiquantitative log2 scale, where higher values reflect higher protein concentrations. Glycoprotein acetyls (GlycA) concentrations are presented in mmol/L (Nightingale Health Output). Data were analyzed using a linear mixed model with time point as fixed effect, participant ID and study site as random effects while baseline values included as covariates. Proteins shown in bold are statistically significant. See Supplemental Table 1 for abbreviations.

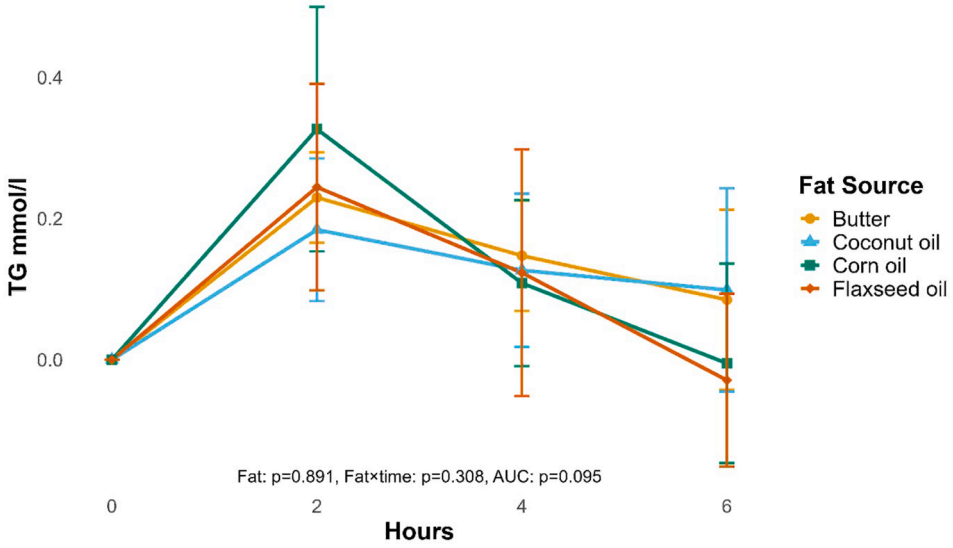

Fig. 3. Postprandial responses in TG concentration after intake of 40 g of fat from four different fat sources. Data are presented as mean ± SD.

compared to PUFA, while Lyte and Esser et al. found no differences in markers of postprandial inflammation comparing different fat sources [18,32–34]. However, a recent randomized controlled trial by Hall et al. reported higher postprandial GlycA concentrations following consumption of PUFA compared to SFA [35], consistent with our results. The relevance of postprandial inflammatory response for long term health outcomes is unclear and may differ between inflammation markers. However, recent findings by Monahan et al. [36] show that higher GlycA response following a test meal was associated with increased risk of type 2 diabetes and this association was independent of fasting GlycA concentrations. Further, both Monahan et al. [36] and findings from the PREDICT study [4] demonstrate that postprandial GlycA response is strongly associated with TG response, indicating that lipid metabolism may mediate the inflammatory response reflected in GlycA. Mechanistically, GlycA is a composite ^{1}H-NMR marker reflecting several circulating acute-phase glycoproteins and their glycosylation, providing an integrated marker of the acute-phase inflammatory response [37]. Different fatty acids may influence upstream postprandial signaling,e.g., via lipid-derived mediators, which could in turn modulate acute-phase glycoprotein production and thereby GlycA. In the present study, postprandial TG responses did not differ between meals suggesting that the impact on GlycA is independent of TG response. In addition, postprandial changes were also observed for IL-17C, while other IL-17 family members remained unchanged. Since IL-17C is primarily described as an epithelial/barrier cytokine acting in an autocrine manner rather than a classical circulating mediator [38], the observed plasma response, most evident after flaxseed oil, may reflect transient barrier associated innate activation during the postprandial period. This finding should be interpreted with caution and confirmed in future studies.

In the broader screening, several biomarkers were effected postprandially, although the direction of response was not uniform, with some markers increasing and others decreasing. In parallel with changes in inflammatory markers, postprandial levels of FLT3LG and FGF23 were lower than fasting levels. FLT2LG is involved in dendritic-cell homeostasis and FGF23 is an osteocyte-hormone central to phosphate regulation and has previously been reported to decrease following a glucose load [39,40], and the observed decrease could thereby be attributed to the carbohydrate component of the test meals. While IL-6 and other inflammatory mediators are clinically important in a range of contexts, the clinical significance of acute postprandial fluctuations in these biomarkers among healthy individuals remains uncertain [4,36].

The relatively modest postprandial inflammatory responses observed in our study may, in part, reflect characteristics of the study population, which was predominantly young (mean age 30 years), female (72%), and with a low prevalence of overweight (27%). These demographic features are generally associated with lower baseline inflammatory activity, which could influence the magnitude of postprandial changes. As such, the findings may not be directly generalizable to older or metabolically compromised populations, where inflammatory responses to dietary challenges may differ. Nevertheless, we observed a clear postprandial inflammatory response in markers such as IL-6 and GlycA, consistent with previous reports in more heterogenous populations, including the PREDICT study [4], suggesting that meal-induced inflammatory response occur even in young, healthy individuals. Additionally, although overall adherence was high, the number of participants completing all four meal challenges ($n = 12$) was limited, which may have reduced the statistical power to detect more subtle or nuanced differences between fat sources, particularly in pairwise comparisons. As such, results from these pairwise comparisons should be considered exploratory, and conclusions should be drawn with caution.

4.2. Strengths and limitations

There are some limitations that should be acknowledged. First, complete blinding of test meals is inherently challenging in dietary intervention trials. Although the test meals were standardized in appearance and composition aside from the fat source, it is possible that certain fats, such as flaxseed oil, which has a distinctive flavor, may have been perceptible to some participants. However, based on participant feedback and the controlled setting in which the meals were consumed, any potential unblinding is likely to have had minimal impact. All meals were consumed under supervision at the study centers to ensure full intake, and both participants and study personnel were blinded to meal allocation, reducing the risk of bias. Second, given the broad biomarker panel

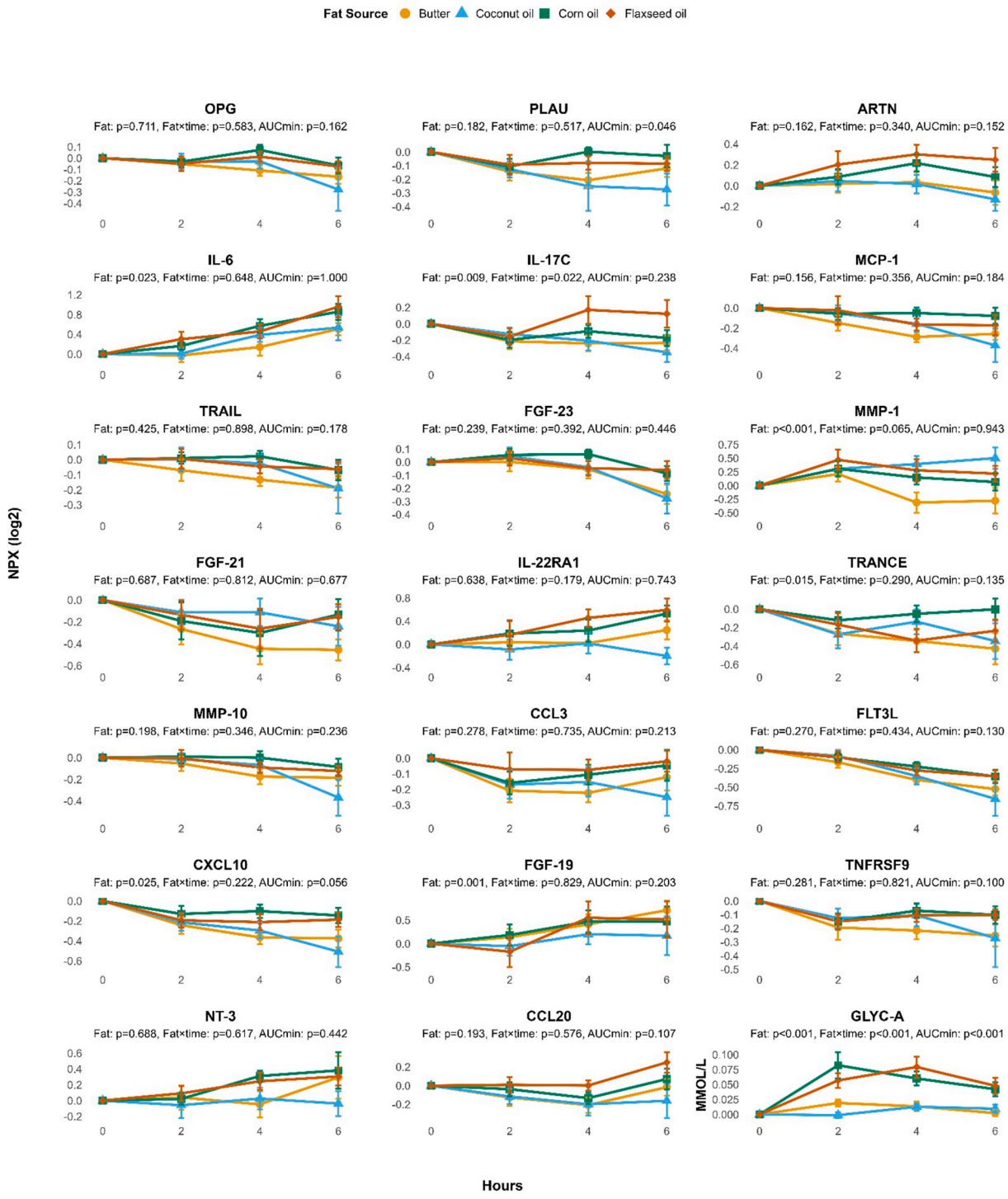

Fig. 4. Postprandial responses in inflammation markers after intake of 40 g of fat from four different fat sources. Data are presented as mean ± SD.

and multiple comparisons, there is an increased risk of type 1 error. However, as the study was designed to detect biologically relevant changes and generate hypotheses for future research, we prioritized minimizing the risk of type II errors (false negatives). For transparency, we have provided both unadjusted and Holm–Bonferroni-adjusted p-values, the latter being an alternative to a standard Bonferroni correction [41]. Lastly, while the targeted number of participants was reached, the number of participants may have been too small to detect significant differences in some inflammation markers.

The study also has several notable strengths, such as the utilization of a double-blind study design. Another methodological strength is the use of a 4-week washout period between test meals, which was implemented to account for the potential influence of the menstrual cycle of female participants. This interval far exceeds the typical resolution time for postprandial inflammatory and metabolic markers,

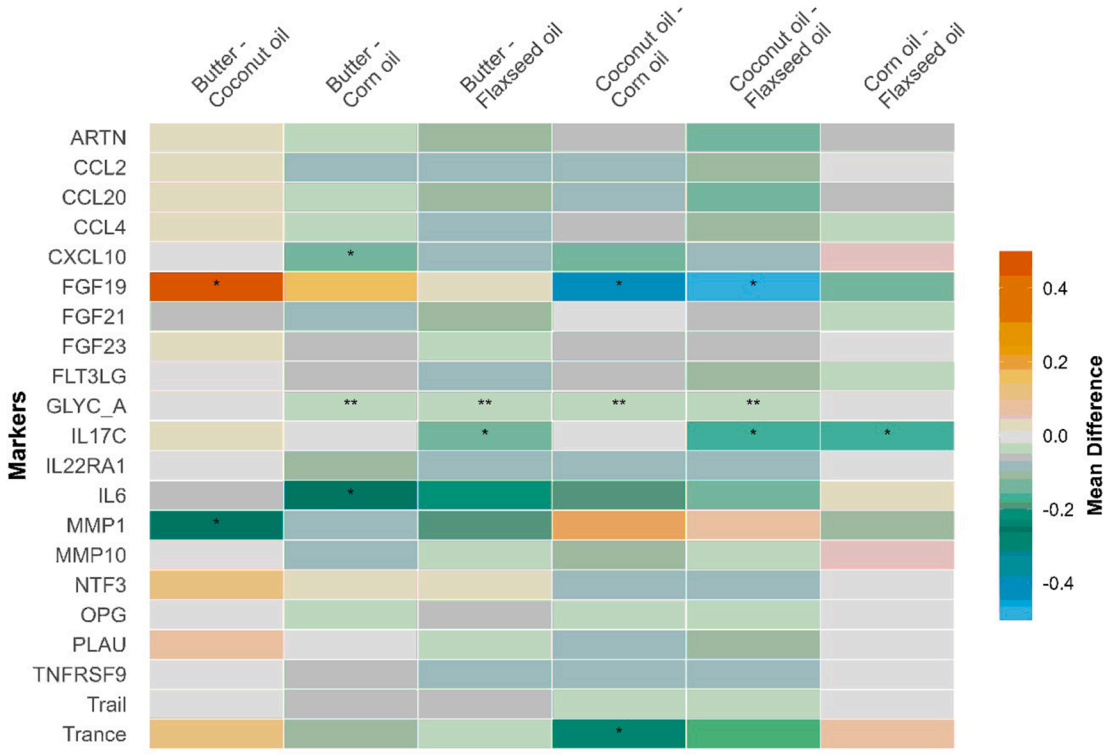

Fig. 5. Pairwise comparisons of responses in the identified markers of postprandial inflammation after intake of 40 g of fat from four different fat sources. Mean differences are reported in NPX (log2) for protein markers and in mmol/l for GlycA. *p-value <0.05, **p-value <0.001.

which generally return to baseline within 24–48 h, as highlighted by Teeman et al. [42]. This conservative approach minimizes the risk of carry-over effects and enhances the internal validity of the crossover design. The randomized meal sequence distribution, (shown in Supplementary Table 2), also reduced potential for systematic bias. Another strength is the supervised consumption of all test meals under controlled conditions, which ensured complete intake and high compliance, thereby reducing variability due to differences in eating behavior. In addition, although the use of AUCmin is unconventional, it was selected to account for biomarkers that exhibited both increases and decreases relative to baseline. This approach allowed the quantification of the overall postprandial variation and provided complementary information to the model-based analysis.

Importantly, this is, to our knowledge, the first study to systematically examine differences in postprandial inflammatory responses across a broad panel of biomarkers following the intake of distinct dietary fat sources. The double-blind, controlled crossover design adds methodological rigor, allowing for a nuanced and unbiased comparison of fat types. This comprehensive and well-controlled approach provides valuable insights into the complexity of postprandial inflammation and the potential role of dietary fat composition. These findings are also relevant in the context of public concerns about seed oils and potential link to inflammation. Despite widespread perceptions that seed oils such as corn- and flaxseed oil may promote inflammation, our results indicate that their acute inflammatory effects are modest and not consistently greater than those of SFA sources.

5. Conclusion

This study provides one of the first systematic evaluations of postprandial inflammatory response using a broad inflammatory biomarker panel, while also comparing the effects of different dietary fat sources within a double-blind, crossover design. The results of this study demonstrate that many inflammation markers are affected in the postprandial state, although no clear direction of change was found across different classes of inflammation markers and fat sources. While PUFA sources tended to induce a slightly greater inflammatory response than SFA for GlycA, the type of fat source appears to only have a minor impact on postprandial inflammation. Future studies are needed to confirm these findings and to elucidate the clinical relevance of postprandial inflammation as a metabolic phenomenon.

Author contributions

NL: Formal analysis, Data curation, Visualization, Project administration, Methodology, Writing – Original Draft, Writing – Review & Editing; HH: Writing – Review & Editing; MM: Writing – Review & Editing; VS: Writing – Review & Editing; RL: Writing – Review & Editing; HL: Writing – Review & Editing; KH: Writing – Review & Editing; SMU: Writing – Review & Editing; LB: Conceptualization, Study design, Funding acquisition, Methodology, Supervision, Project administration, Writing – Review & Editing.

Data sharing statement

Data described in the manuscript, code book, and analytic code will not be made available because of participant privacy concerns and the General Data Protection Regulation.

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

During the preparation of this work NL used OpenAI's ChatGPT-5 to improve readability of the written original text. After using

this tool, NL reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Conflicts of interest

The authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2026.103335.

References

[1] Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, et al. Chronic inflammation in the etiology of disease across the life span. Nat Med 2019;25:1822–32. https://doi.org/10.1038/s41591-019-0675-0.
[2] Emerson SR, Kurti SP, Harms CA, Haub MD, Melgarejo T, Logan C, et al. Magnitude and timing of the postprandial inflammatory response to a high-fat meal in healthy adults: a systematic review. Adv Nutr 2017;8:213–25. https://doi.org/10.3945/an.116.014431.
[3] Dimina L, Mariotti F. The postprandial appearance of features of cardiometabolic risk: acute induction and prevention by nutrients and other dietary substances. Nutrients 2019;11. https://doi.org/10.3390/nu11091963.
[4] Mazidi M, Valdes AM, Ordovas JM, Hall WL, Pujol JC, Wolf J, et al. Meal-induced inflammation: postprandial insights from the personalised REsponses to DIetary composition trial (PREDICT) study in 1000 participants. Am J Clin Nutr 2021;114:1028–38. https://doi.org/10.1093/ajcn/nqab132.
[5] Meessen ECE, Warmbrunn MV, Nieuwdorp M, Soeters MR. Human postprandial nutrient metabolism and low-grade inflammation: a narrative review. Nutrients 2019;11. https://doi.org/10.3390/nu11123000.
[6] Jackson KG, Poppitt SD, Minihane AM. Postprandial lipemia and cardiovascular disease risk: interrelationships between dietary, physiological and genetic determinants. Atherosclerosis 2012;220:22–33. https://doi.org/10.1016/j.atherosclerosis.2011.08.012.
[7] Lopez-Miranda J, Williams C, Lairon D. Dietary, physiological, genetic and pathological influences on postprandial lipid metabolism. Br J Nutr 2007;98:458–73. https://doi.org/10.1017/s000711450774268x.
[8] Borén J, Taskinen M-R, Björnson E, Packard CJ. Metabolism of triglyceride-rich lipoproteins in health and dyslipidaemia. Nat Rev Cardiol 2022;19:577–92. https://doi.org/10.1038/s41569-022-00676-y.
[9] Zhao Y, Liu L, Yang S, Liu G, Pan L, Gu C, et al. Mechanisms of atherosclerosis induced by postprandial lipemia. Front Cardiovasc Med 2021;8:636947. https://doi.org/10.3389/fcvm.2021.636947.
[10] Vors C, Pineau G, Drai J, Meugnier E, Pesenti S, Laville M, et al. Postprandial endotoxemia linked with chylomicrons and lipopolysaccharides handling in obese versus lean men: a lipid dose-effect trial. J Clin Endocrinol Metabol 2015;100:3427–35. https://doi.org/10.1210/jc.2015-2518.
[11] Jawamis A, Al-Domi H, Al Sarayreh N. Effect of dietary fat intake on metabolic endotoxemia: mechanisms and clinical insights. Clin Nutr eSPEN 2025;69:415–20. https://doi.org/10.1016/j.clnesp.2025.07.1124.
[12] Klop B, Proctor SD, Mamo JC, Botham KM, Castro Cabezas M. Understanding postprandial inflammation and its relationship to lifestyle behaviour and metabolic diseases. Int J Vasc Med 2012;2012:947417. https://doi.org/10.1155/2012/947417.
[13] Panth N, Dias CB, Wynne K, Singh H, Garg ML. Medium-chain fatty acids lower postprandial lipemia: a randomized crossover trial. Clin Nutr 2020;39:90–6. https://doi.org/10.1016/j.clnu.2019.02.008.
[14] Pirillo A, Norata GD, Catapano AL. Postprandial lipemia as a cardiometabolic risk factor. Curr Med Res Opin 2014;30:1489–503. https://doi.org/10.1185/03007995.2014.909394.
[15] Furman D, Chang J, Lartigue L, Bolen CR, Haddad F, Gaudilliere B, et al. Expression of specific inflammasome gene modules stratifies older individuals into two extreme clinical and immunological states. Nat Med 2017;23:174–84. https://doi.org/10.1038/nm.4267.
[16] Vazquez-Madrigal C, López S, Grao-Cruces E, Millán-Linares MC, Rodríguez-Martin NM, Martín ME, et al. Dietary fatty acids in postprandial triglyceride-rich lipoproteins modulate human monocyte-derived dendritic cell maturation and activation. Nutrients 2020;12:3139. https://doi.org/10.3390/nu12103139.
[17] Monfort-Pires M, Crisma AR, Bordin S, Ferreira SRG. Greater expression of postprandial inflammatory genes in humans after intervention with saturated when compared to unsaturated fatty acids. Eur J Nutr 2018;57:2887–95. https://doi.org/10.1007/s00394-017-1559-z.
[18] Masson CJ, Mensink RP. Exchanging saturated fatty acids for (n-6) polyunsaturated fatty acids in a mixed meal may decrease postprandial lipemia and markers of inflammation and endothelial activity in overweight men. J Nutr 2011;141:816–21. https://doi.org/10.3945/jn.110.136432.
[19] Guarner F, Malagelada JR. Gut flora in health and disease. Lancet 2003;361:512–9. https://doi.org/10.1016/s0140-6736(03)12489-0.
[20] Harris WS, Mozaffarian D, Rimm E, Kris-Etherton P, Rudel LL, Appel LJ, et al. Omega-6 fatty acids and risk for cardiovascular disease. Circulation 2009;119:902–7. https://doi.org/10.1161/CIRCULATIONAHA.108.191627.
[21] Hussein N, Ah-Sing E, Wilkinson P, Leach C, Griffin BA, Millward DJ. Long-chain conversion of [13C] linoleic acid and α-linolenic acid in response to marked changes in their dietary intake in men. JLR (J Lipid Res) 2005;46:269–80. https://doi.org/10.1194/jlr.M400225-JLR200.
[22] Fritsche KL. Too much linoleic acid promotes inflammation—doesn't it? Prostagl Leukot Essent Fat Acids 2008;79:173–5. https://doi.org/10.1016/j.plefa.2008.09.019.
[23] Innes JK, Calder PC. Omega-6 fatty acids and inflammation. Prostagl Leukot Essent Fat Acids 2018;132:41–8. https://doi.org/10.1016/j.plefa.2018.03.004.
[24] Assarsson E, Lundberg M, Holmquist G, Björkesten J, Bucht Thorsen S, Ekman D, et al. Homogenous 96-Plex PEA immunoassay exhibiting high sensitivity, specificity, and excellent scalability. PLoS One 2014;9:e95192. https://doi.org/10.1371/journal.pone.0095192.
[25] Soininen P, Kangas AJ, Würtz P, Tukiainen T, Tynkkynen T, Laatikainen R, et al. High-throughput serum NMR metabonomics for cost-effective holistic studies on systemic metabolism. Analyst 2009;134:1781–5. https://doi.org/10.1039/B910205A.
[26] Baños H, Susko E, Roger AJ. Is over-parameterization a problem for profile mixture models? Syst Biol 2023;73:53–75. https://doi.org/10.1093/sysbio/syad063.
[27] Brouns F, Bjorck I, Frayn KN, Gibbs AL, Lang V, Slama G, et al. Glycaemic index methodology. Nutr Res Rev 2005;18:145–71. https://doi.org/10.1079/NRR2005100.
[28] Team RCR. A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2025.
[29] Amcoff E, Edberg A, Enghardt Barbieri H, Lindroos A, Nälsén C, Pearson M, et al. Riksmaten–vuxna 2010–11. Livsmedels- och näringsintag bland vuxna i sverige (dietary habits and nutrient intake in Sweden 2010–11. The third national food consumption survey). Uppsala: National Food Agency (Livsmedelsverket); 2012.
[30] Hansson P, Holven KB, Øyri LKL, Brekke HK, Biong AS, Gjevestad GO, et al. Meals with similar fat content from different dairy products induce different postprandial triglyceride responses in healthy adults: a randomized controlled cross-over trial. J Nutr 2019;149:422–31. https://doi.org/10.1093/jn/nxy291.
[31] Kienēs HF, Egert S. A systematic review of the impact of fat quantity and fatty acid composition on postprandial vascular function in healthy adults and patients at risk of cardiovascular disease. Curr Dev Nutr 2023;7:102025. https://doi.org/10.1016/j.cdnut.2023.102025.
[32] Rathnayake KM, Weech M, Jackson KG, Lovegrove JA. Meal fatty acids have differential effects on postprandial blood pressure and biomarkers of endothelial function but not vascular reactivity in postmenopausal women in the randomized controlled dietary intervention and VAScular function (DIVAS)-2 study. J Nutr 2018;148:348–57. https://doi.org/10.1093/jn/nxx042.
[33] Lyte JM, Gabler NK, Hollis JH. Postprandial serum endotoxin in healthy humans is modulated by dietary fat in a randomized, controlled, cross-over study. Lipids Health Dis 2016;15:186. https://doi.org/10.1186/s12944-016-0357-6.
[34] Esser D, van Dijk SJ, Oosterink E, Müller M, Afman LA. A high-fat SFA, MUFA, or n3 PUFA challenge affects the vascular response and initiates an activated state of cellular adherence in lean and obese middle-aged men. J Nutr 2013;143:843–51. https://doi.org/10.3945/jn.113.174540.
[35] Hall WL, Alkoblan A, Gibson PS, D'Annibale M, Coekaerts A, Bauer M, et al. Postprandial lipid and vascular responses following consumption of a commercially-relevant interesterified palmitic acid-rich spread in comparison to functionally-equivalent non-interesterified spread and spreadable butter: a randomised controlled trial in healthy adults. Food Funct 2024;15:2733–50. https://doi.org/10.1039/d3fo05324e.
[36] Monahan RC, Li-Gao R, Noordam R, van der Velde J, Willems van Dijk K, de Koning E, et al. Glycoprotein acetyls response to a mixed meal is associated with increased insulin resistance and risk of type 2 diabetes in a middle-aged population. Clin Nutr e-SPEN 2025;66:523–9. https://doi.org/10.1016/j.clnesp.2025.02.013.

[37] Otvos JD, Shalaurova I, Wolak-Dinsmore J, Connelly MA, Mackey RH, Stein JH, et al. GlycA: a composite nuclear magnetic resonance biomarker of systemic inflammation. Clin Chem 2015;61:714–23. https://doi.org/10.1373/clinchem.2014.232918.

[38] Ramirez-Carrozzi V, Sambandam A, Luis E, Lin Z, Jeet S, Lesch J, et al. IL-17C regulates the innate immune function of epithelial cells in an autocrine manner. Nat Immunol 2011;12:1159–66. https://doi.org/10.1038/ni.2156.

[39] Saito Y, Boddupalli CS, Borsotti C, Manz MG. Dendritic cell homeostasis is maintained by nonhematopoietic and T-cell-produced Flt3-ligand in steady state and during immune responses. Eur J Immunol 2013;43:1651–8. https://doi.org/10.1002/eji.201243163.

[40] Ursem SR, Vervloet MG, Büttler RM, Ackermans MT, Oosterwerff MM, Eekhoff EMV, et al. The interrelation between FGF23 and glucose metabolism in humans. J Diabetes Complicat 2018;32:845–50. https://doi.org/10.1016/j.jdiacomp.2018.06.013.

[41] Holm S. A simple sequentially rejective multiple test procedure. Scand J Stat 1979;6:65–70.

[42] Teeman CS, Kurti SP, Cull BJ, Emerson SR, Haub MD, Rosenkranz SK. Post-prandial lipemic and inflammatory responses to high-fat meals: a review of the roles of acute and chronic exercise. Nutr Metabol 2016;13:80. https://doi.org/10.1186/s12986-016-0142-6.