



The Analysis Study of Effect of Dietary Stearidonic Acid on Biomarkers of Lipid Metabolism: A Comprehensive Systematic Review

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ABSTRACT

Introduction: The role of dietary oils rich in specific fatty acids, such as stearidonic acid (SDA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), has been extensively studied for their effects on lipid metabolism and cardiovascular health. This study aims to evaluate the impact of these oils on lipid profiles, fatty acid composition, and metabolic outcomes in various populations. **Methods:** A systematic review was conducted by analyzing randomized controlled trials (RCTs), crossover studies, and experimental designs involving SDA, EPA, and DHA. Parameters assessed included changes in lipid profiles, EPA and DHA levels in erythrocytes, and other metabolic markers. Bias was evaluated across seven domains: temporal precedence, selection/allocation, confounding, administration of interventions, outcome assessment, participant retention, and statistical conclusion validity. **Results:** The studies demonstrated variable but significant increases in EPA levels across dietary oils, with SDA-rich oils showing moderate efficiency compared to EPA. DHA levels remained largely unaffected by SDA supplementation. Improvements in triglyceride levels and LDL cholesterol were observed, though some studies reported reductions in HDL cholesterol. Study quality was generally high, but some biases were noted in participant retention and detailed reporting of outcomes. **Conclusion:** Dietary oils rich in SDA and EPA effectively improve EPA status and influence lipid metabolism. However, their efficacy compared to direct EPA supplementation remains limited. Future studies should address biases and explore long-term clinical benefits.

Keywords: dietary oils, stearidonic acid (SDA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), lipid metabolism

INTRODUCTION

Polyunsaturated fatty acids (PUFAs) are essential components of the human diet and are divided into two major families: omega-3 (n-3) and omega-6 (n-6).^{1,2} The primary distinction between these families lies in the location of the first double bond relative to the terminal (methyl) end of the fatty acid chain—at the third carbon for omega-3 and the sixth for omega-6.^{3,4} Among these, the omega-3 family is widely recognized for its role in promoting human health, with benefits extending beyond basic nutritional requirements. Evidence suggests that higher intakes of omega-3 PUFAs are associated with reduced risks of several chronic conditions, including cardiovascular disease, inflammation, and some cancers. This has led to growing interest in the potential of omega-3 supplementation to enhance physiological outcomes across various population groups.⁵⁻⁸

The omega-3 family includes several fatty acids, notably alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA).

Although ALA serves as the metabolic precursor to EPA and DHA, these derivatives are more biologically active and are the primary contributors to omega-3's health benefits. Unfortunately, the conversion of ALA to EPA and DHA in humans is inefficient, significantly limiting the physiological impact of dietary ALA.⁷⁻¹⁰ As a result, increasing direct consumption of EPA and DHA has become a priority for optimizing health outcomes. However, typical dietary intakes in Western populations, including the United States, remain below recommended levels. Average EPA and DHA consumption ranges from 110 to 500 mg/day, with U.S. intake often at the lower end of this spectrum. Research suggests that achieving higher intake levels could drastically reduce cardiovascular mortality, with studies estimating an 80% reduction in deaths if the omega-3 index is adequately elevated.^{11,12}

To address this, the American Heart Association (AHA) advises consuming two fatty fish meals per week, a recommendation aimed at increasing dietary EPA and DHA.

Yet, several obstacles hinder adherence to these guidelines. These include concerns over the sustainability of fish supplies, potential contaminants (e.g., mercury and polychlorinated biphenyls), limited shelf life due to oxidation, and the taste and smell of fish, which many find unappealing.^{11,12} Additionally, vegetarians and vegans face significant challenges obtaining EPA and DHA, as these fatty acids are predominantly found in marine sources. This reliance on fish-based omega-3s underscores the need for alternative strategies to enhance omega-3 status.¹³⁻¹⁴ One potential solution is stearidonic acid (SDA), a naturally occurring omega-3 fatty acid that can be efficiently converted to EPA within the body. SDA is found in certain plant-based oils, such as those derived from echium, black currant, and genetically modified soybeans. Unlike ALA, SDA bypasses the rate-limiting step in the metabolic pathway, leading to a more efficient increase in EPA levels. This makes SDA an appealing alternative for individuals who cannot or prefer

not to consume fish-based products.^{15,16}

The purpose of this systematic review is to evaluate the effects of dietary stearidonic acid (SDA) on biomarkers of lipid metabolism and to explore its potential as a nutritional intervention for improving lipid profiles. By analyzing existing evidence, the review aims to assess the role of SDA in modulating key lipid biomarkers, such as triglycerides, total cholesterol, and high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol levels. Additionally, it seeks to determine SDA's contribution to enhancing omega-3 fatty acid bioavailability, particularly its ability to increase eicosapentaenoic acid (EPA) levels through metabolic conversion.

A significant focus of this review is to compare the efficacy of SDA with other sources of omega-3 fatty acids, including alpha-linolenic acid (ALA), fish oil-derived EPA, and docosahexaenoic acid (DHA).¹⁷ By doing so, the review aims to clarify whether SDA offers distinct advantages or comparable benefits in

optimizing lipid metabolism. Furthermore, it examines the effects of SDA supplementation in specific populations, such as vegetarians, individuals with metabolic disorders, and those with low omega-3 fatty acid intake, to identify variations in outcomes based on dietary habits and metabolic needs. Through a comprehensive analysis of its effects on lipid metabolism, this review aims to inform future dietary guidelines and public health strategies for reducing cardiovascular and metabolic disease risks.

METHODS

Protocol

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparency and methodological rigor. The protocol was specifically designed to evaluate and synthesize existing evidence on the effects of dietary stearidonic acid (SDA) on biomarkers of lipid metabolism. Adherence to PRISMA guidelines ensures that the findings are

comprehensive, robust, and evidence-based, enabling critical insights into the topic.

Criteria for Eligibility

Studies were included if they met the following criteria:

- **Population:** Human or animal studies examining dietary SDA intake and its effects on lipid metabolism.
- **Intervention:** Inclusion of SDA as a dietary source, either as a standalone intervention or in combination with other omega-3 fatty acids.
- **Outcome:** Reports on biomarkers of lipid metabolism, such as triglycerides, cholesterol levels (total, HDL, LDL), or omega-3 index, and metabolic conversion efficiency to EPA and DHA.
- **Study Type:** Original research, including randomized controlled trials (RCTs), cohort studies, or experimental studies.
- **Publication Date:** Articles published from 2000 onward

to capture recent advancements in the field.

Exclusion criteria included reviews without primary data, editorials, opinion pieces, conference abstracts, and studies without clearly defined outcomes related to lipid biomarkers.

Search Strategy

A comprehensive search strategy was developed using keywords and controlled vocabulary terms specific to SDA and lipid metabolism. Key search terms included “stearidonic acid,” “SDA,” “omega-3 fatty acids,” “lipid metabolism,” “biomarkers,” “triglycerides,” “cholesterol,” and “EPA conversion.” Major electronic databases, including PubMed, Scopus, Web of Science, EMBASE, and the Cochrane Library, were systematically searched.

Data Retrieval

The initial search yielded a broad range of studies. Titles and abstracts were screened to exclude irrelevant articles, followed by a detailed full-text review of the remaining studies to ensure eligibility. Data extraction focused on

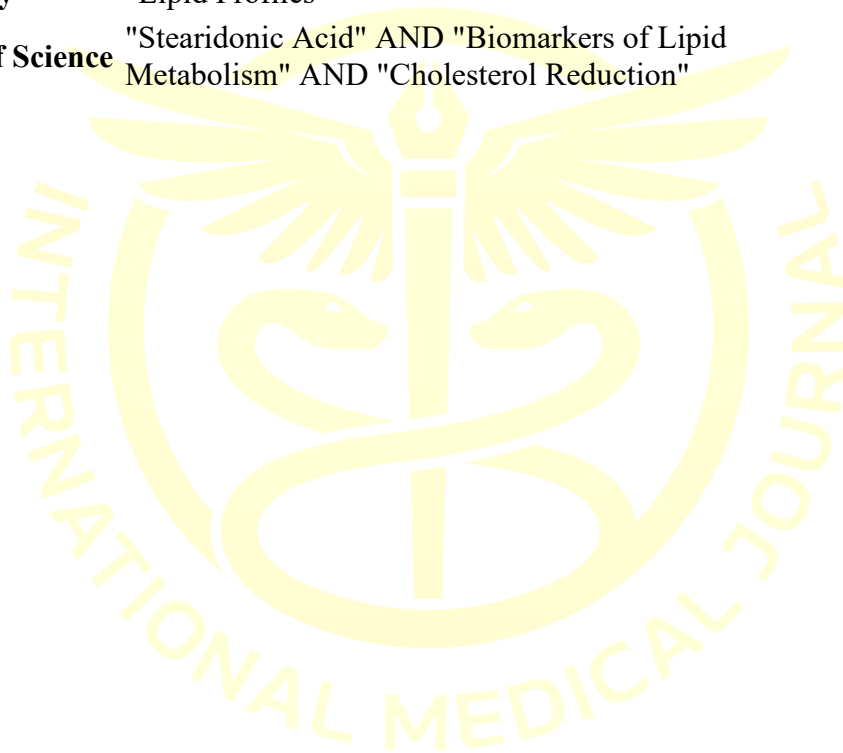
study design, population, intervention details, biomarkers assessed, and key outcomes.

Quality Assessment and Data Synthesis

All included studies underwent a rigorous quality assessment using standardized evaluation tools, focusing on study design, sample size, intervention details, and outcome reporting. The synthesis was narrative, with data summarized in tables to highlight key findings related to the impact of SDA on lipid metabolism. The results were compared across studies to identify trends, gaps, and potential implications for dietary guidelines.

Table 1. Database Search Results

Database	Search Strategy	Hits
PubMed	("Stearidonic Acid" OR "SDA") AND ("Lipid Metabolism" OR "Biomarkers") AND ("Triglycerides" OR "EPA Conversion")	256
ScienceDirect	"Stearidonic Acid" AND "Lipid Biomarkers" AND "Cholesterol" AND "EPA/DHA Conversion Efficiency"	198
Embase	'Stearidonic Acid' OR 'SDA' AND 'Lipid Metabolism' OR 'Triglycerides' AND 'Biomarker Studies'	312
Cochrane Library	"Stearidonic Acid" AND "Omega-3 Fatty Acids" AND "Lipid Profiles"	143
Web of Science	"Stearidonic Acid" AND "Biomarkers of Lipid Metabolism" AND "Cholesterol Reduction"	276



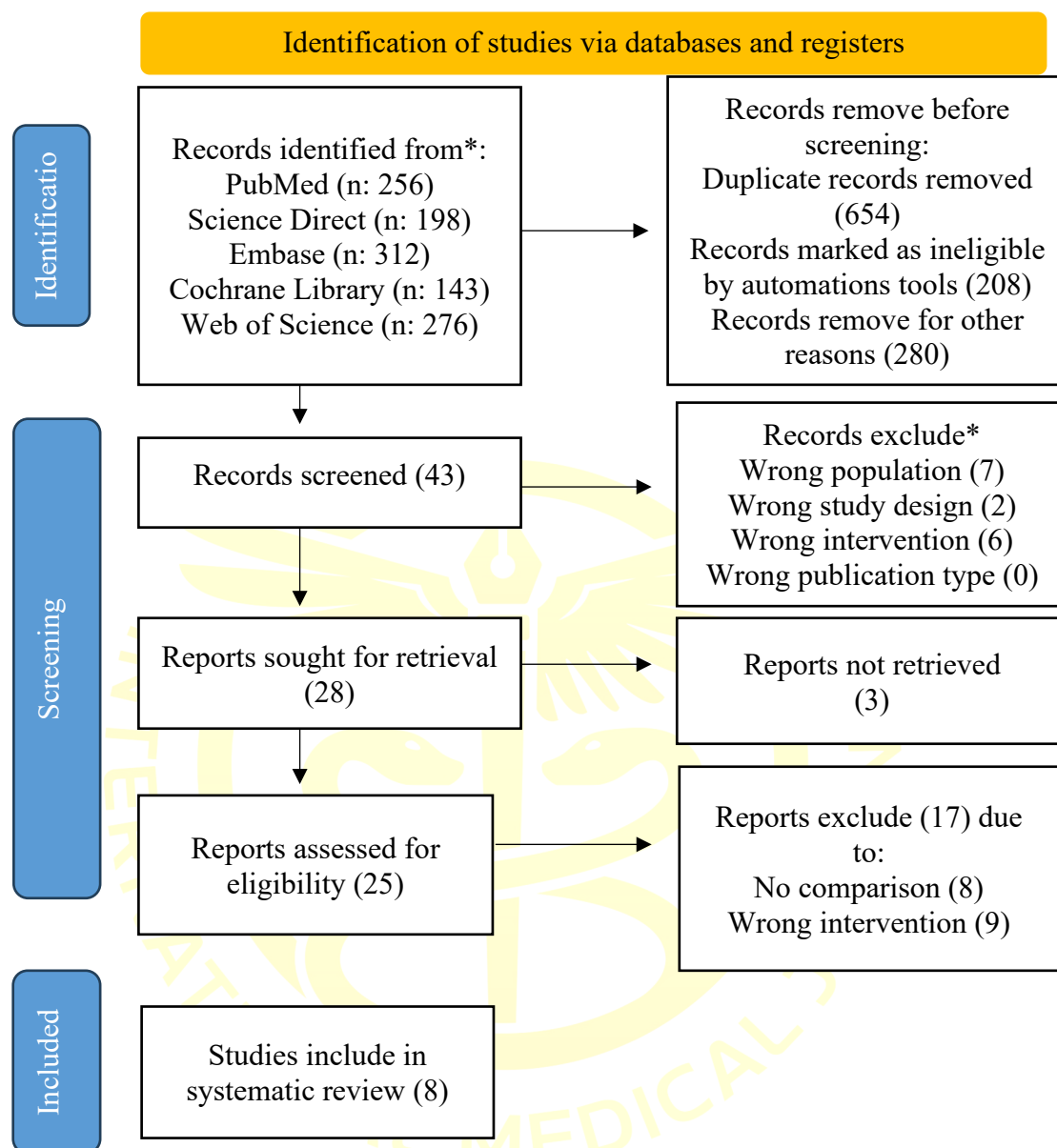


Figure 1. Flowchart of Article Search

RESULT

A systematic search across multiple databases identified a range of studies investigating SDA's effects on lipid metabolism. After a three-level screening process, a subset of studies was selected for inclusion. Detailed findings were synthesized to provide an evidence-based understanding of SDA's role in improving lipid biomarkers and enhancing omega-3 fatty acid profiles.

Table 2. Literature of Review

Author	Origin	Method	Sample	Result
Kuhnt K et al., 2014.¹⁸	Germany	This double-blind, parallel-arm, randomized controlled study started with a 2-wk run-in period.	80 participants.	After the 8-wk EO treatment, increases in the LC n-3 metabolites EPA (168% and 79%) and docosapentaenoic acid [DPA (68% and 39%)] were observed, whereas docosahexaenoic acid (DHA) decreased (25% and 223%) in plasma and peripheral blood mononuclear cells, respectively. Compared with FO, the efficacy of EO to increase EPA and DPA in blood was significantly lower (;25% and ;50%, respectively). A higher body mass index (BMI) was associated with lower relative and net increases in EPA and DPA. Compared with baseline, EO significantly reduced serum cholesterol, LDL cholesterol, oxidized LDL, and triglyceride (TG), but also HDL cholesterol, regardless of age and BMI. In the FO group, only TG decreased.
Pieters et al., 2015.¹⁹	Netherlands	A randomized, double-blind, placebo-controlled crossover trial was conducted.	36 healthy overweight and slightly obese subjects	Serum triacylglycerol and other lipid concentrations were not significantly affected by consumption of Echium oil compared with HOSO. Echium oil significantly increased percentage of EPA in red blood cell (RBC) membranes with $0.14 \pm 0.25\%$ (mean $\pm$ s.d.) compared with HOSO ($P = 0.02$). No significant effects on docosahexaenoic acid in RBC membranes or on the omega-3 index were found.

Seidel U et al., 2024. ²⁰	Germany	In a monocentric, randomized crossover study.	29 healthy male volunteers received three sequential interventions	Oral ahiflower oil intake significantly improved plasma EPA levels (0.2 vs. 0.6% of total fatty acid methyl esters (FAMES)) in humans, whereas DHA levels were unaffected by treatments. EPA-levels in SDA-treated HepG2 cells were 65% higher (5.1 vs. 3.0% of total FAMES) than those in ALA-treated cells. Taurine did not affect fatty acid profiles in human plasma in vivo or in HepG2 cells in vitro. SDA-rich ahiflower oil and isolated SDA led to an increase in EPA-derived oxylipins in humans and in HepG2 cells, respectively.
Miles EA et al., 2004. ²¹	UK	a double-blind randomized controlled trial.	Healthy young males were randomised to consume one of seven oil blends for a period of 12 weeks (9 g oil/day) (n ¼ 8–12 subjects/group).	Significant effects were observed with each lipid fraction. Neither STA nor its derivative 20:4n-3 appeared in any of the lipid fractions studied when STA (up to 1 g/day) was consumed. However, STA (1 g/day), in combination with GLA (0.9 g/day), increased the proportion of EPA in some lipid fractions, suggesting that STA-rich plant oils may offer a novel means of increasing EPA status. Furthermore, this combination tended to increase the dihomo-g-linolenic acid (20:3n-6; DGLA) content of PBMCs, without an increase in arachidonic acid (AA) (20:4n-6) content. EPA consumption increased the EPA content of all lipid fractions studied. Consumption of GLA (2 g/day), in the absence of STA or EPA, increased DGLA content with a tendency to increase AA content in some fractions. This effect was prevented by inclusion of EPA in combination with GLA.
Dittrich M et al., 2015. ²²	Germany	Randomized, double-blind, placebo-controlled, crossover study.	Fifty-nine hypertriglyceridemic subjects (triglycerides > 1.5 mmol/L) were included.	Total cholesterol (TC) and low-density-lipoprotein cholesterol decreased significantly in the LA and ALA groups (LA: P < 0.01, ALA: P < 0.05). No changes in blood lipids were observed in the SDA group. Significant increases in TC and high-density-lipoprotein cholesterol occurred in the DHA group (P < 0.05). In the ALA and SDA groups, the content of eicosapentaenoic acid in erythrocyte lipids

				increased significantly (P < 0.05) after 10 weeks (ALA group: 38 ± 37 %, SDA group: 73 ± 59 %).
William S. et al., 2008. ²³	US	randomized, double-blind, placebo-controlled study.	64 subjects who were screened and gave informed consent, 45 were enrolled and 33 completed the study.	Serum lipids, blood pressure, heart rate, platelet function and safety laboratory tests were measured along with the omega-3 index. A per-protocol analysis was conducted on 33 subjects (11 per group). Compared to baseline, average omega-3 index levels increased 19.5% in the SDA group and 25.4% in the EPA group (p < 0.05 for both, vs. control). DHA did not change in any group. Relative to EPA, SDA increased RBC EPA with about 17% efficiency. No other clinical endpoints were affected by SDA or EPA treatment (vs. control).
Casey JM et al., 2013. ²⁴	US	Experimental study.	Twenty-four male homozygous OZR (fa/fa), and age-matched LZR (+/fa) rats.	After 12 weeks, total adiposity, dyslipidemia, glucose intolerance, and hepatic steatosis were all greater, whereas n3PUFA content in liver, adipose, and muscle was lower in OZR vs. LZR rats. Obese rodents fed modified FISH or SDA diets had lower serum lipids and hepatic fat content vs. CON. The omega-3 index (i.e., ΣEPA + DHA in erythrocyte membrane) was 4.0, 2.4, and 2.0-fold greater in rodents provided FISH, SDA, and FLAX vs. CON diet, irrespective of genotype. Total hepatic n3PUFA and DHA was highest in rats fed FISH, whereas both hepatic and extra-hepatic EPA was higher with FISH and SDA groups.
James et al., 2003. ²⁵	India	Double blind, parallel-group design.	Forty-five healthy subjects, men and postmenopausal women aged 18–65 years old.	Dietary SDA increased EPA and docosapentaenoic acid concentrations but not DHA concentrations in erythrocyte and in plasma phospholipids. The relative effectiveness of the tested dietary fatty acids in increasing tissue EPA was 1:0.3:0.07 for EPA:SDA:ALA.

Table 3. Critical appraisal of Study

Parameters	Kuhnt K et al., 2014	Pieters et al., 2015	Seidel U et al., 2024	Miles EA et al., 2004	Dittrich M et al., 2015	William S et al., 2008	Casey JM et al., 2013	James et al., 2003
1. Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation Was there a control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes.	Yes
3. Bias related to confounding factors Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes. Comparisons made across genotypes	Yes
4. Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Bias related to assessment, detection, and measurement of the outcome Were there multiple measurements of the outcome, both pre and post the	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

intervention/exposure?
Were the outcomes of
participants included
in any comparisons
measured in the same
way?

Yes Yes Yes Yes Yes Yes Yes Yes

Were outcomes
measured in a reliable
way?

Reliable; Reliable; Reliable; Reliability of multiple measurements unclear
consistent consistent consistent consistent consistent
Reliable; Consistent

6. Bias related to participant retention

Was follow-up
complete and, if not,
were differences
between groups in
terms of their follow-
up adequately
described and
analyzed?

Follow-up not detailed Follow-up described Follow-up not detailed Follow-up not described Follow-up adequately described Retention described Follow-up not detailed Follow-up not detailed

7. Statistical conclusion validity

Was appropriate
statistical analysis
used?

Yes Yes Yes Yes Yes Yes Yes Yes

DISCUSSION

The studies reviewed present a diverse set of findings on the impact of stearidonic acid (SDA) and related dietary interventions on lipid metabolism and omega-3 fatty acid profiles. Kuhnt et al. (2014) conducted a double-blind, randomized controlled trial in Germany involving 80 participants. Their study revealed that an 8-week intervention with Echium oil (EO) significantly increased plasma levels of eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA) but decreased docosahexaenoic acid (DHA). Compared to fish oil (FO), EO was less effective at increasing EPA and DPA levels, with a noted association between higher BMI and reduced efficacy. Additionally, EO reduced several lipid parameters, including serum cholesterol, LDL cholesterol, and triglycerides, but also lowered HDL cholesterol.¹⁸

In a similar context, Pieters et al. (2015) conducted a randomized, double-blind, placebo-controlled crossover trial in the Netherlands with 36 overweight and slightly obese

participants. While consumption of Echium oil increased the percentage of EPA in red blood cell (RBC) membranes, it had no significant impact on DHA or overall serum lipid concentrations, including triglycerides.¹⁹ This contrasted with Seidel et al. (2024), whose monocentric, randomized crossover study demonstrated that ahiflower oil, an SDA-rich source, significantly improved plasma EPA levels without affecting DHA. This study also explored the cellular effects, showing increased EPA levels in HepG2 cells treated with SDA compared to alpha-linolenic acid (ALA).²⁰

Miles et al. (2004) conducted a 12-week double-blind, randomized controlled trial in the UK with healthy young males. Their findings highlighted that SDA-rich oils, when combined with gamma-linolenic acid (GLA), enhanced EPA content in certain lipid fractions and increased dihomo-gamma-linolenic acid (DGLA) levels without elevating arachidonic acid (AA). This combination suggested that SDA, particularly in synergy with GLA,

may offer an innovative approach to improving EPA status.²¹

Similarly, Dittrich et al. (2015) explored lipid profile changes in a randomized, double-blind, placebo-controlled crossover study of 59 hypertriglyceridemic subjects. While SDA and ALA increased erythrocyte EPA levels, no significant lipid changes were observed in the SDA group. Conversely, DHA supplementation led to increases in total cholesterol (TC) and HDL cholesterol. This highlights the selective efficacy of SDA in modifying lipid metabolism compared to DHA and ALA.²² William et al. (2008) and James et al. (2003) further emphasized SDA's role in elevating EPA levels. In William et al.'s study, conducted in the US, SDA increased the omega-3 index with approximately 17% efficiency relative to EPA supplementation.²³ However, DHA levels remained unaffected across all groups. James et al., based in India, compared the efficacy of dietary SDA, EPA, and ALA, demonstrating that SDA was moderately effective in raising tissue

EPA levels compared to EPA itself but outperformed ALA.²⁵

Lastly, Casey et al. (2013) used a rodent model to examine dietary SDA's impact on lipid metabolism and hepatic health. Their findings showed that SDA improved serum lipids and reduced hepatic fat content in obese rats while enhancing EPA levels in both hepatic and extra-hepatic tissues. Although DHA was highest in fish oil-fed rodents, the SDA diet was effective in increasing EPA concentrations, supporting its potential role in lipid management. Overall, the studies collectively highlight SDA's ability to enhance EPA levels in various tissues, with limited effects on DHA.²⁴

This systematic review offers valuable insights into the effects of stearidonic acid (SDA) and related dietary interventions on lipid metabolism and omega-3 fatty acid profiles. However, several limitations must be acknowledged. First, the included studies exhibited substantial heterogeneity in their designs, encompassing randomized controlled trials (RCTs), crossover trials, and experimental animal studies. This

diversity in methodologies, intervention durations, and sample sizes makes direct comparisons and meta-analyses challenging. Additionally, the participants in the studies varied significantly in demographics, including age, sex, health status, and baseline lipid profiles, which may limit the generalizability of the findings to broader populations.

The sources and doses of SDA also varied widely across studies, including the use of Echium oil, ahiflower oil, and isolated SDA at differing concentrations. This inconsistency complicates the identification of optimal sources or doses for achieving desired outcomes. Moreover, while the studies primarily focused on biochemical markers, such as plasma EPA levels and lipid profiles, few assessed clinically relevant outcomes, such as cardiovascular health, inflammation reduction, or long-term safety.²⁶ As a result, the findings may have limited applicability in clinical practice. The short duration of most trials, ranging from weeks to a few months, is another limitation, as the long-term

effects of SDA supplementation remain unclear. Furthermore, the geographical and ethnic bias in the included studies, which were predominantly conducted in Western populations, restricts the applicability of results to more diverse populations. Animal studies included in the review, such as those involving rodents, may also have limited generalizability to humans due to physiological differences.

Some studies lacked comprehensive reporting of methodologies, including randomization processes, blinding, and adherence to interventions, potentially introducing bias or reducing the reproducibility of findings. Additionally, limited data were available on potential adverse effects or safety concerns associated with SDA consumption, which are essential for clinical recommendations. Finally, the review may be affected by publication bias, as studies with significant positive results are more likely to be published, potentially leading to an overestimation of SDA's efficacy.

To address these limitations, future research should employ standardized protocols, involve larger and more diverse populations, extend intervention durations, and prioritize the evaluation of clinically relevant outcomes. Such efforts will enhance our understanding of SDA's role in lipid metabolism and its potential health benefits.

CONCLUSION

This systematic review highlights the potential of stearidonic acid (SDA) as a dietary intervention for improving lipid metabolism and increasing the levels of omega-3 fatty acids, particularly eicosapentaenoic acid (EPA), in plasma and erythrocyte membranes. Across the included studies, SDA demonstrated a capacity to elevate EPA concentrations without significantly affecting docosahexaenoic acid (DHA) levels. These findings suggest that SDA may serve as an effective precursor for EPA synthesis, providing an alternative to traditional omega-3 sources like fish oil. Additionally, certain SDA-rich oils, such as ahiflower and Echium oil, showed

promising results in improving specific lipid profiles, including reductions in triglycerides and low-density lipoprotein (LDL) cholesterol, though these effects were not consistently observed across all studies.

However, the review also underscores the variability in SDA's effectiveness, influenced by factors such as dosage, duration of intervention, and individual characteristics like body mass index (BMI). The reviewed studies generally reported favorable biochemical outcomes, but clinically significant impacts, such as long-term cardiovascular benefits or inflammatory modulation, remain underexplored. Moreover, the inclusion of diverse methodologies and populations highlights the need for more standardized research to strengthen the evidence base.

In conclusion, while SDA appears to be a promising nutritional strategy for enhancing EPA levels and potentially improving lipid profiles, further research is required to establish its clinical relevance. Future studies should focus on long-term

trials with larger, more diverse populations, standardized intervention protocols, and evaluations of broader health outcomes. These efforts will be critical to determining the practical applications of SDA as part of dietary interventions aimed at improving lipid metabolism and overall health.

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