International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
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ARTICLE TITLE	OMEGA-3 FATTY ACID INTAKE AND ITS IMPACT ON INFLAMMATORY SKIN DISEASES: A COMPREHENSIVE LITERATURE REVIEW
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5724
RECEIVED	16 February 2026
ACCEPTED	27 May 2026
PUBLISHED	10 June 2026
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OMEGA-3 FATTY ACID INTAKE AND ITS IMPACT ON INFLAMMATORY SKIN DISEASES: A COMPREHENSIVE LITERATURE REVIEW

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ABSTRACT

Background: Inflammatory skin diseases, including atopic dermatitis (AD), psoriasis, and acne vulgaris, are chronic conditions characterized by complex immune dysregulation, compromised skin barrier function, and a significant negative impact on patient quality of life. Recently, increasing scientific attention has been directed toward the immunomodulatory potential of nutritional interventions, particularly omega-3 fatty acids (n-3 FAs), due to their established anti-inflammatory properties. This review synthesizes and critically evaluates current evidence on the impact of n-3 FAs on these conditions, integrating clinical, epidemiological, genetic, and mechanistic perspectives.

Methods: A structured literature review was conducted using multiple electronic databases, including PubMed/MEDLINE, Google Scholar, and Embase, to identify peer-reviewed studies published between 2016 and 2026, of which 25 met the predefined inclusion criteria. Eligible peer-reviewed original studies and systematic reviews assessed the effects of n-3 FAs on dermatological outcomes, focusing on clinical severity scales (e.g., SCORAD, PASI, GAGS), biochemical biomarkers, or genetic causal associations. The gathered evidence was categorized into five thematic domains: clinical efficacy, preventive effects, epidemiological associations, genetic evidence (Mendelian randomization), and mechanistic insights.

Results: Synthesis of the literature suggests that n-3 FA supplementation is generally associated with improvements in disease severity and patient-reported outcomes, most notably in atopic dermatitis and acne vulgaris. However, findings in psoriasis remain heterogeneous, with conflicting reports on clinical efficacy. Epidemiological data indicates a high prevalence of n-3 FA deficiency in acne-prone populations, although a direct causal link in observational settings remains elusive. Genetic research, specifically Mendelian randomization studies, suggests a protective role of n-3 FAs in specific inflammatory phenotypes, while also highlighting complex, context-dependent risks such as susceptibility to solar dermatitis. Mechanistically, n-3 FAs appear to modulate pro-inflammatory cytokine signaling, keratinocyte differentiation pathways, and lipid mediator profiles, providing biological plausibility for their clinical use.

Conclusion: Omega-3 fatty acids represent promising adjunctive therapy in the management of inflammatory skin diseases. Nonetheless, the current evidence is constrained by methodological heterogeneity, small sample sizes, and the frequent use of combination treatments. Further well-designed, standardized clinical trials are required to establish optimal dosing regimens and clarify the independent role of n-3 FAs in dermatological practice.

KEYWORDS

Omega-3 Fatty Acids, Inflammatory Skin Diseases, Atopic Dermatitis, Psoriasis, Acne Vulgaris, Nutritional Dermatology, Polyunsaturated Fatty Acids

CITATION

Marta Krężołek, Julia Dobrowolska, Alicja Palus, Filip Kamyszek, Kornel Pawlak, Marcin Stępiński, Mateusz Balicki, Oliwia Zynek, Paula Kaczmarczyk, Tomasz Arkuszyński. (2026) Omega-3 Fatty Acid Intake and Its Impact on Inflammatory Skin Diseases: A Comprehensive Literature Review. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5724

Introduction

Inflammatory skin diseases represent a diverse and clinically challenging group of chronic conditions characterized by dysregulated immune responses, impaired epidermal barrier integrity, and recurrent symptomatic flares. Highly prevalent disorders such as atopic dermatitis, psoriasis, and acne vulgaris impose a substantial burden on both individual quality of life and global healthcare systems. The pathogenesis of these conditions is inherently multifactorial, involving a sophisticated interplay between genetic susceptibility, environmental triggers, and aberrant immune-mediated signaling pathways.

In recent years, the focus of dermatological research has expanded to include the role of nutrition in modulating chronic inflammation. Omega-3 fatty acids (n-3 FAs), a class of long-chain polyunsaturated fatty acids including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have emerged as potent bioactive lipids with established immunomodulatory properties. These compounds act as regulators of the inflammatory cascade, influencing the production of lipid mediators, inhibiting pro-inflammatory cytokines, and modulating intracellular signaling pathways that govern cutaneous health. Consequently, n-3 FAs are increasingly being investigated not only as nutritional supplements but as therapeutic adjuncts capable of enhancing conventional pharmacological treatments.

Despite this growing interest, the existing body of clinical evidence remains characterized by significant heterogeneity. While some randomized trials report improvements in disease severity and symptom control, others demonstrate limited or inconsistent effects. This variability is likely attributable to differences in study design, patient populations, and non-standardized intervention protocols, which complicate the formulation of definitive clinical recommendations. Furthermore, although experimental and genetic studies, including Mendelian randomization, have begun to elucidate underlying biological mechanisms, a gap persists in translating these insights into consistent clinical outcomes. This comprehensive review aims to address this gap by synthesizing current multi-disciplinary evidence to assess the viability of n-3 FAs in the management of atopic dermatitis, psoriasis, and acne vulgaris.

Aim

The primary objective of this study was to evaluate the impact of omega-3 fatty acid intake on inflammatory skin diseases, with particular emphasis on clinical efficacy, underlying biological mechanisms, and potential preventive effects. This review synthesizes current evidence across clinical, epidemiological, genetic (including Mendelian randomization), and experimental domains to assess the therapeutic role of omega-3 fatty acids in acne vulgaris, psoriasis, and atopic dermatitis. Additionally, it aims to identify key gaps in the existing literature and to clarify how fatty acid modulation may influence disease severity and patient-reported outcomes in dermatological practice.

Materials and Methods

Search Strategy and Data Sources

This structured literature review was conducted to evaluate the impact of omega-3 fatty acids (n-3 FAs) on inflammatory skin diseases using a thematic approach. Relevant studies were identified through a comprehensive search of multiple electronic databases, including PubMed/MEDLINE, Google Scholar, and Embase.

The search was limited to peer-reviewed studies published between 2016 and 2026 to prioritize current research trends and recent clinical advancements. Additionally, manual screening of reference lists from key reviews and meta-analyses was performed to ensure comprehensive coverage.

Search strategies incorporated combinations of controlled vocabulary (MeSH terms) and free-text keywords, including *omega-3 fatty acids, n-3 PUFA, atopic dermatitis, psoriasis, acne vulgaris, cutaneous inflammation, chronic inflammatory diseases,* and *Mendelian randomization*.

Inclusion and Exclusion Criteria

Studies were selected according to predefined criteria to ensure methodological consistency.

Inclusion Criteria:

- Peer-reviewed studies investigating the role of n-3 FAs in the context of acne, psoriasis, or atopic dermatitis.
- Studies reporting measurable outcomes, including clinical severity scales (e.g., SCORAD, PASI, GAGS), biochemical biomarkers, or genetic causal associations.
- High-level evidence, including randomized controlled trials (RCTs), systematic reviews, meta-analyses, and Mendelian randomization studies, supplemented by relevant observational and experimental models.
- Studies involving human participants as well as mechanistic experimental models were included.

Exclusion Criteria:

- Studies focusing on non-inflammatory or purely neoplastic conditions unrelated to n-3 FA pathways.
- Publications lacking full-text availability, methodological transparency, or clearly defined outcome measures.
- Studies focusing exclusively on other fatty acid classes (e.g., n-6 only) without a comparative n-3 FA component.

Data Categorization and Synthesis

A total of 25 studies met the predefined inclusion criteria and were included in the final analysis. The selected literature was systematically categorized into five thematic domains:

- Clinical efficacy (severity and treatment outcomes)
- Preventive effects (prenatal and risk-related factors)
- Epidemiological associations (biomarkers and deficiency patterns)
- Genetic evidence (Mendelian randomization)
- Mechanistic insights (molecular and cellular pathways)

This framework enabled a structured synthesis of findings across different levels of evidence. The heterogeneity in study design, populations, and intervention protocols was qualitatively assessed and considered during data interpretation and formulation of conclusions.

Results

Clinical Efficacy of n-3 FA Supplementation in Inflammatory Skin Diseases

Studies evaluating the clinical efficacy of n-3 fatty acids suggest a generally beneficial impact across a spectrum of inflammatory dermatoses [3, 13, 15, 22]. Most available data indicate that supplementation is associated with measurable improvements in clinical severity scores, most notably SCORAD in atopic dermatitis [22], PASI in psoriasis [3], and lesion counts or GAGS in acne patients [13, 15].

Beyond monotherapy, n-3 FAs appear to function effectively as adjuncts to standard pharmacological interventions, such as isotretinoin [8, 20] or conventional antipsoriatic therapies [3], frequently enhancing overall treatment outcomes and potentially mitigating treatment-related adverse effects [20]. Additionally, improvements in patient-reported outcomes, including quality of life, pruritus intensity, and sleep quality, are commonly reported [13, 22]. These clinical findings are often supported by underlying biological changes, such as modulation of lipid metabolites [8] and alterations in gut microbiota composition [15]. Recurring observation, particularly in acne-focused studies, is the high prevalence of baseline n-3 FA deficiency, which, when corrected, is associated with clinical improvement [13].

However, the evidence remains heterogeneous. While several studies report reductions in psoriasis severity, others demonstrate limited or no benefit, indicating variability in clinical response. Furthermore, as many improvements are observed in the context of combination therapies, isolating the independent effect of n-3 FAs remains challenging [3].

Preventive and Developmental Effects: Prenatal and Risk Modification

Evidence regarding the preventive role of n-3 fatty acids during the prenatal period remains limited and heterogeneous. Current data indicate that maternal n-3 FA supplementation does not significantly reduce the overall incidence of atopic dermatitis in the general pediatric population. However, some studies suggest age-specific benefits, including a reduced risk of IgE-associated eczema in children aged three years or younger [16].

These findings highlight the importance of fatty acid balance rather than absolute n-3 FA levels alone. While no consistent association has been observed between prenatal n-3 FA status and atopic dermatitis risk, higher levels of n-6 fatty acids have been linked to increased susceptibility [10]. Additionally, inconsistent and context-dependent relationships between combined EPA and DHA levels and disease risk have been observed.

The evidence base remains inconsistent. While subgroup analyses from randomized controlled trials indicate potential protective effects in selected populations [16], observational studies often fail to confirm these findings. Moreover, the magnitude of the effect may vary across different study populations, suggesting potential effect modification.

Epidemiological and Biomarker Associations

Observational and epidemiological studies suggest an association between n-3 FA status and the prevalence of inflammatory skin conditions, particularly acne vulgaris and atopic dermatitis [12, 21, 22]. Available data indicate that a substantial proportion of acne patients present with systemic n-3 FA levels below the recommended physiological range. Dietary patterns, specifically the intake of fatty fish and other n-3-rich foods are associated with higher systemic levels and lower disease prevalence, supporting the role of fatty acid status as a potentially modifiable risk factor [12]. Clinical intervention studies demonstrate that n-3 FA supplementation can significantly improve disease severity in pediatric atopic dermatitis, with reductions in symptom scores and topical corticosteroid requirements [22].

However, these observational findings do not establish causality [12]. While population-level associations are consistent and controlled trials show therapeutic benefits [22], they should be interpreted with caution due to potential confounding factors and the need for condition-specific research. Nevertheless, the high prevalence of n-3 FA deficiency in affected populations highlights a plausible link between fatty acid status and disease expression, supporting further investigation within controlled clinical settings [12, 22].

Genetic and Causal Inference: Mendelian Randomization

Genetic research utilizing Mendelian randomization (MR) has provided a new layer of evidence regarding the causal role of n-3 FAs in dermatology. Most MR studies support a protective relationship, indicating that higher genetically predicted levels of n-3 FAs correlate with a significantly reduced risk of atopic [6, 17] and nummular dermatitis [7]. These findings are considered robust due to the minimal evidence of pleiotropy and the high consistency of results across various analytical models [7, 17], strengthening the case for a causal protective link.

However, genetic evidence also introduces important caveats. While n-3 FAs appear protective against chronic inflammatory conditions, some genetic proxies suggest an increased risk of solar dermatitis and certain skin malignancies, such as squamous cell carcinoma, particularly in relation to docosapentaenoic acid (DPA) [6]. Furthermore, the influence of n-3 FAs is heavily mediated by polymorphisms in the FADS1 and FADS2 gene clusters, which regulate fatty acid desaturation [6, 17]. This underscores that the biological impact of n-3 FAs is not universal; rather, it is governed by an individual's unique genetic architecture and specific environmental exposures.

Mechanistic and Experimental Studies: Cellular and Molecular Insights

Mechanistic research provides the biological framework for the clinical observations reported in this review. *In vitro* and animal models demonstrate that n-3 FAs, particularly alpha-linolenic acid and EPA, can inhibit keratinocyte hyperproliferation and promote healthy epidermal differentiation, key processes in the normalization of psoriatic and eczematous skin models [11, 25]. These effects are primarily mediated through the modulation of lipid signaling pathways, including the suppression of pro-inflammatory n-6-derived eicosanoids and the activation of the ERK1/2 signaling cascade [25].

Additionally, n-3 FAs provide significant photoprotective benefits and act as essential components of the cutaneous defense system [5, 14]. Experimental findings indicate that systemic intake can increase the minimal erythema dose (MED) [5], mitigate UVB-induced structural damage [14], and inhibit UV-induced genotoxicity [5]. By modulating cytokine production and strengthening the skin's resistance to environmental damage, n-3 FAs contribute to the maintenance of epidermal barrier integrity and reduce transepidermal water loss (TEWL) [14].

Overview of Findings and Methodological Characteristics

Evidence derived from narrative and systematic reviews indicates that omega-3 fatty acids have been investigated across a broad spectrum of inflammatory skin diseases, with reported effects on acne, psoriasis, and atopic dermatitis [1, 2, 4, 9]. Across these studies, supplementation has been associated with reductions in clinical severity scores and improvements in patient-reported outcomes [4, 9, 23]. Reported biological effects include modulation of inflammatory pathways, alterations in cytokine profiles, and support of tissue repair processes [4, 24]. In addition, both experimental and clinical studies have described potential benefits of topical omega-3 applications, including improved skin barrier function, enhanced wound healing, and reduced inflammatory responses [4, 18].

At the same time, findings across studies remain heterogeneous [2, 4]. Some reports demonstrate beneficial effects, whereas others show inconclusive results or no significant differences when compared with omega-6 fatty acids [2]. In the context of skin cancer, results are inconsistent, with studies reporting both protective effects and lack of clear associations depending on the outcome assessed [19]. Furthermore, studies evaluating combined interventions frequently report greater clinical improvement compared with omega-3 monotherapy [2, 9].

Across the included studies, several methodological characteristics were identified that may influence the reported outcomes [4]. Considerable variability was observed in supplementation protocols, including differences in dosage (ranging from less than 1 g to more than 4 g per day), duration of treatment, and chemical form of omega-3 fatty acids (e.g., triglycerides versus ethyl esters) [18]. Many studies were conducted in relatively small cohorts, potentially limiting statistical power [4]. In addition, omega-3 fatty acids were often administered alongside standard pharmacological therapies, such as isotretinoin or topical corticosteroids.

The evidence base also includes a substantial proportion of mechanistic data derived from in vitro and animal models [4]. Genetic analyses were predominantly conducted in populations of European ancestry. Across studies, variability in study design, intervention strategies, and outcome measures was consistently reported, along with limited data on optimal dosing, formulation, and long-term effects [4,18].

Discussion

The synthesis of evidence in this review suggests that omega-3 fatty acids (n-3 FAs) play a discernible and multifaceted role in the modulation of inflammatory skin diseases [1, 2, 4, 6, 11, 24]. However, the strength and consistency of this effect are highly dependent on the specific clinical context and study methodology [2, 4]. While supplementation is frequently associated with improvements in atopic dermatitis [6, 10, 17, 22] and acne [8, 9, 12, 13, 15, 20], findings in psoriasis remain inconsistent [1-3]. This discrepancy may be attributed to the varying inflammatory pathways unique to each condition or significant differences in the baseline n-3 FA status of study participants [12], which may influence the threshold for therapeutic response [13].

A key observation is the divergence across levels of evidence. Observational data highlight a widespread deficiency in patient populations [12, 13], yet they cannot independently confirm causality. In contrast, Mendelian randomization (MR) provides compelling evidence for a causal protective role in AD [6, 7, 17], while simultaneously cautioning that n-3 FAs may have context-dependent effects, such as increasing sensitivity to solar radiation and potentially influencing skin cancer risk [6, 5, 19]. This suggests that n-3 FAs should not be considered a universal anti-inflammatory intervention, but rather as a precise nutritional tool whose efficacy is governed by an individual's unique genetic architecture and environmental exposures [2].

The biological plausibility provided by mechanistic studies, specifically regarding keratinocyte differentiation and the modulation of lipid mediators via the ERK1/2 pathway [4, 11, 25], supports the clinical improvements observed in adjunctive therapy settings [3, 20, 22]. However, since these results are largely grounded in experimental models [11], their direct translation into standard dermatological practice remains incomplete [4]. The current reliance on small-scale trials [3, 22] and the widespread use of combination therapies [3, 8, 22] represent a significant barrier to the implementation of standardized clinical protocols [4, 18].

Consequently, there remains a need for high-quality, large-scale randomized controlled trials focusing on isolated n-3 FA interventions [1, 2, 4, 23]. Future research must prioritize standardized dosing regimens and the use of high-bioavailability formulations to clarify the individual roles of EPA versus DHA [6, 13, 17, 18]. Determining the optimal therapeutic window and establishing long-term safety profiles will be essential for successfully integrating n-3 FAs into evidence-based dermatological care pathways.

Conclusions

The role of omega-3 fatty acids in inflammatory skin diseases remains a dynamic and clinically relevant area of investigation. Current evidence suggests that n-3 fatty acids may offer benefit as an adjunctive strategy for reducing disease severity and improving quality of life in patients with atopic dermatitis and acne. While the evidence for psoriasis is less definitive, the overall safety profile and mechanistic potential of these fatty acids make them a valuable component of a holistic approach to dermatological care.

However, the inherent heterogeneity of existing literature currently prevents the establishment of definitive dosing guidelines. Future prospective research must prioritize well-powered, standardized trials to identify the patient populations most likely to benefit and to define optimal therapeutic strategies. In conclusion, while n-3 FAs show significant promise as a supportive tool in dermatology, their full integration into standard care pathways requires further rigorous validation through high-quality clinical research.

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All authors have read and agreed with the published version of the manuscript.

Funding Statement: Study did not receive special funding.

Declaration on the Use of AI: In preparing this manuscript, the authors used ChatGPT for the purpose of improving language and readability. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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