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Review Article

Review of Omega-3 Fatty Acid Dietary Supplementation in Cutaneous Inflammatory Disorders

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Relevance

Dietary supplements are commonly used by patients to enhance skin health and for the treatment of cutaneous disorders. Currently, the Food and Drug Administration (FDA) is not authorized to approve the efficacy or safety of dietary supplements prior to public marketing. Therefore, evidence-based medicine is needed for dermatologists to better counsel patients regarding the efficacy and safety of dietary supplements for chronic conditions, such as acne vulgaris, psoriasis, atopic dermatitis, and rosacea.

Objective

To provide an up to date review of the effects of oral supplementation of Omega-3 Fatty Acids (O3FA) such as docosahexanoic acid (DHA) and eicosapentaneoic acid (EPA) on cutaneous inflammatory conditions in the literature. This systematic review examines O3FA's impact on acne vulgaris, psoriasis, atopic dermatitis, and rosacea; ultimately, to determine the efficacy and safety of supplementation.

Methods

A comprehensive electronic search with EPA and DHA for acne vulgaris, psoriasis, atopic dermatitis, and rosacea in PubMed/MEDLINE, Cochrane Central, Embase, and Google Scholar yielded 99 articles. Duplicate, non-English articles, animal studies, and irrelevant articles were excluded. These parameters resulted in 79 articles excluded as they did not meet study qualifications. Initially there were 20 articles included but during the writing process, three additional articles were published, bringing the final total to 23 articles in this review.

Results

Dietary supplementation of O3FAs resulted in varying significance in the improvement of acne vulgaris due to limited studies, small sample sizes, and lack of control groups. While the majority of articles included for psoriasis demonstrated improvement in clinical symptoms, most of the studies for atopic dermatitis did not indicate significant enhancement. Lastly, one placebo controlled study showed O3FA supplementation effectively treated dry eye symptoms associated with ocular rosacea.

Conclusion

There are limited studies investigating the efficacy of O3FA oral supplementation in the treatment of acne vulgaris, psoriasis, atopic dermatitis, and rosacea. In all, some evidence supports the beneficial impact of O3FA supplementation for the treatment of psoriasis and atopic dermatitis, while there are minimal results for acne vulgaris and ocular rosacea. Of the small studies included in this review, there are multiple limiting variables which indicate a need for further evaluation.

INTRODUCTION

Oral supplements may be provided to patients to improve skin health and appearance. Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have demonstrated significant therapeutic potential in dermatological conditions through their anti- inflammatory, immunomodulatory, and skin barrier-enhancing properties. These long-chain polyunsaturated fatty acids are metabolized into specialized pro-resolving lipid mediators,

including resolvins, protectins, and maresins, which counteract inflammation by reducing pro-inflammatory cytokines and eicosanoids derived from arachidonic acid.[1-5] Additionally, DHA enhances regulatory T cell (Treg) differentiation and shifts macrophages toward an anti-inflammatory phenotype, thereby mitigating immune dysregulation in chronic skin disorders.[6] Omega-3 fatty acids also contribute to skin barrier integrity by promoting keratinocyte differentiation and upregulating essential structural proteins such as filaggrin and loricrin, which are crucial for epidermal function.[3,5]

Furthermore, EPA-derived 12-hydroxyeicosapentaenoic acid (12-HEPE) has been shown to inhibit neutrophil infiltration by suppressing CXCL1 and CXCL2 expression in keratinocytes via the retinoid X receptor α pathway, reducing local inflammation.[1] Alterations in the lipid mediator profile further enhance the resolution of inflammatory skin conditions by decreasing pro-inflammatory arachidonic acid-derived metabolites while increasing anti-inflammatory lipid mediators.[2,4] These mechanisms underscore the potential of omega-3 fatty acids as a targeted intervention for inflammatory and barrier-related skin diseases, warranting further investigation into their clinical applications. Since distributing companies are not required to receive approval from the Food and Drug Administration (FDA) prior to public marketing, evidence-based guidelines are essential to increase dermatologists understanding of therapeutic dietary options prior to counseling patients.[7] Herein is a review of the literature to examine the use of two common O3FAs, DHA and EPA, for the treatment of acne, atopic dermatitis, rosacea, and psoriasis.

METHODS

A comprehensive electronic search with search terms “fish oil atopic dermatitis,” “fish oil eczema,” “fish oil atopic eczema,” “eczema omega-3 fatty acids,” “rosacea omega 3,” “fish oil psoriasis,” “omega-3 psoriasis,” “fish oil acne,” “fish oil acne vulgaris,” “omega 3 acne” in PubMed/MEDLINE, Cochrane Central, Embase, and Google Scholar. This search resulted in 99 articles stratified by 41 for atopic dermatitis, 39 for rosacea, 13 for psoriasis, and 6 for acne. Duplicate, non-English, abstracts, and non-relevant articles were excluded resulting in the 79 articles being excluded from analysis. Initially, there were 20 articles included but during the writing process, three additional articles were published, bringing the final total to 23 articles. Included in this review are: 5 studies for acne, 10 for psoriasis, 7 for atopic dermatitis, and 1 for rosacea. Analysis included extraction of study type, number of participants, treatment or intervention, efficacy measures, results, limitations, and adverse events.

ACNE

Acne vulgaris is a common inflammatory, cutaneous disease. Current evidence indicates the role inflammation plays in the development of acne, specifically referring to the relationship between the microbiome and skin health.[8]

Guertler et al evaluated EPA and DHA supplementation in patients with mild-to-moderate acne who were enrolled for a period of 16 weeks with 4 study visits (n = 60). The first three study visits were each 6 weeks apart and the fourth visit was 4 weeks after the third visit. Oral supplementation with DHA and EPA between the first visit and second was 3 daily capsules for a total of 600 mg DHA/300 mg EPA. After the second visit patients were recommended to take 4 capsules daily for a total of 800 mg DHA/400 mg EPA. Guertler et al increased the dose of fatty acid supplementation after the second visit as they noted that many patients had a very low baseline of EPA/DHA. Therefore, increasing supplementation put patients in the study’s target range. Acne severity improved over the course of the study based on dermatological objective assessment which took into consideration the absolute number of noninflammatory and inflammatory lesions between visit 1 and visit 4 ($p < 0.001$). The severity of acne comedonica and acne papulopustulosa were assessed further objectively using a 3-point scale of mild, intermediate, and severe. Similarly, appearance of the skin was self-assessed using the same 3-point scale. Patient facial sebum levels were measured using a Sebumeter SM 18. At visit 1, the patients’ facial serums were positively associated with the number of comedones, but there was no significant correlation for inflammatory skin lesions ($p = 0.017$, $r = 0.306$). No adverse effects were reported throughout the study.[9]

A study explored the effects of omega-3 supplementation on the gut microbiota and its ability to treat acne vulgaris in a clinical trial design and animal study design. In the clinical trial design, 46 acne patients and 20 matched healthy controls were randomized to oral isotretinoin with or without omega-3 fatty acids for 12 weeks. The isotretinoin was dosed at 0.5-1.0 mg/kg/d and omega-3 fatty acids were dosed at 2400 mg/d. The effects of the supplementation were evaluated using the Global Acne Grading System (GAGS). After 12 weeks of treatment, the GAGS score in patients with supplementation was lower than the control. However, it is important to note that the GAGS score and percentage of red area and porphyrins (scleryerythrin), which were measured respectively by the VISIA-CR imaging system, were improved by isotretinoin intervention with or without omega-3 fatty acid supplementation. In patients treated with omega-3 and isotretinoin, gut microbiota diversity was found to be increased from baseline compared to healthy controls based on the Shannon index and Simpson diversity index. There was no change in microbiome diversity from baseline by isotretinoin intervention without omega-3 fatty acid supplementation. The diversity type encompasses Lactococcus, Coprococcus, and Eubacterium and the effects of omega-3 supplementation on the abundance of these bacteria. No side effects were listed, but dosage of the isotretinoin was adjusted based on drug side effects.[10]

One study examined patients (n = 5) with mild-to-moderate acne who consistently utilized an O3FA nutrient combination consisting of 1,000 mg of EPA, 200 mg of epigallocatechin-3-gallate (EGCG), 15 mg of zinc gluconate, 200 mcg of selenium, and 200 mcg of chromium within four

capsules daily for at least 2 months. A total comedonal lesion and inflammatory papule count was performed to determine the total number of inflammatory lesions. Patients completed the Arizona Integrative Outcomes Scale to measure changes in their mental, emotional, and social well-being over time. While no significant conclusions can be drawn from the observations due to a small sample size and absence of a placebo group, results showed 4/5 patients had a reduction in the total of inflammatory lesions and an average 24% improvement in the mental, emotional, and social well-being among users of the supplement. No side effects were reported.[11]

A different study investigated healthy males with mild-to-severe acne (n = 13) who consumed 3 capsules of fish oil daily, which consisted of a total of 930 mg of EPA, 720 mg DHA, and 174 mg of DPA for 12 weeks. The results were inconclusive as statistical significance was not obtained for acne severity or total lesion counts. It should be noted this study had a small sample size and did not have a control group. There were no side effects disclosed.[12]

In a randomized, double-blinded controlled trial, daily supplementation with 2 O3FA capsules, which contained 2000 mg of EPA and DHA for 10 weeks (n = 15) showed significant reductions in the inflammation of acne lesions (10.1 ± 3.2 to 5.8 ± 3.4) compared to placebo (n = 15). Moreover, supplementation with this dosage was found to be tolerable and safe, offering a suitable treatment for mild-to-moderate acne vulgaris. Two patients in the treatment group and one in the placebo group experienced mild gastrointestinal discomfort. One patient in the treatment group had temporary diarrhea. All complications resolved spontaneously after a few days without treatment.[13]

Summary: Due to minimal studies investigating the effects of O3FAs, evidence provided by the literature has shown varying results regarding the efficacy of oral supplementation of O3FAs for the treatment of acne vulgaris. The studies mentioned used a dose range of O3FAs from 600 mg DHA/300 mg EPA to a combined 2000 mg DHA/EPA. Side effects were not reported in the majority of the studies. One study mentioned mild gastrointestinal side effects which resolved spontaneously without treatment.

PSORIASIS

Psoriasis is a chronic inflammatory disease characterized by erythematous indurated plaques and silvery scales on the scalp and/or extensor surfaces of the body. The pathogenesis of psoriasis features an immune-mediated response with Th17 and Th22 lymphocytes accumulating within the skin and an increase in inflammatory biomarkers such as IL-6. While numerous treatment options exist for psoriasis, O3FA supplementation may serve as a safer alternative and/or as an effective adjunctive therapy.[14]

Tveit et al designed a randomized, double-blind study to evaluate the efficacy of a dietary supplement containing herring roe oil (compared to coconut oil only) for the treatment of stable, plaque psoriasis. Patients received 10 capsules daily of 292 mg herring roe oil (HRO) which has a ratio of 3:1 DHA:EPA. The total daily dose of EPA and DHA was 2600 mg. Treatment efficacy was determined by the change in mean Psoriasis Area Severity Index (PASI) score. Each group received 5 capsules in the morning and 5 in the evening with their meals for 26 weeks. After 26 weeks, the treatment group (n = 32) showed statistically significant improvement compared to the placebo treatment (n = 32) with a mean PASI score change of -1.1 (p = 0.0451, CI -2.2, -0.025). There was no significant difference in adverse events between the active and placebo groups. Approximately 90% of patients had one or more adverse events and one patient had to withdraw due to gastrointestinal effects. Adverse events related to skin and subcutaneous tissue were equally distributed between the treatment and control groups. Infections and infestations were also equal across groups. Gastrointestinal events reported (47% treatment vs 34% control) were nausea, diarrhea, upper abdominal pain, flatulence, and abdominal discomfort.[15]

In a prospective, open, observational study, patients with mild-to-moderate chronic plaque psoriasis (n = 100) consumed 6 capsules consisting of 300 mg of EPA and DHA in 3 divided doses daily for 3 months. Each capsule contained 300 mg of EPA and DHA and patients took a total of 1800 mg per day. The patients were also advised to apply paraffin to the skin once a day. Antihistamines were prescribed as needed. The placebo group (n = 100) was instructed to use only topical paraffin therapy and antihistamines for 3 months. Results indicated a significant difference in the severity (1.23 ± 0.37, p = 0.009), erythema (0.44 ± 0.11, p = 0.001), and induration of psoriasis lesions (0.33 ± 0.15, p = 0.0256) in the treatment group compared to placebo. Adverse events in the treatment group included 5 cases of fishy odor burps, 1 case of abdominal discomfort, and 1 case of folliculitis; where in the placebo group there were 3 cases of folliculitis and 1 of contact dermatitis.[14]

Gupta et al conducted a study where for 15 weeks, patients with stable psoriasis (n = 9) defined as 10-50% total body surface area (TBSA) received 10 fish oil capsules (Max-EPA) twice daily for a daily total of 3600 mg of EPA and 2400 mg of DHA. The control group was given only olive oil (n = 11). After the first 3 weeks, patients were exposed to twice weekly UVB suberythemal doses of UVB phototherapy for the next 8 weeks, after which only fish or olive oil were given for the last 4 weeks of the study. By the conclusion of the study, the treatment group had a significantly greater decrease of 46% in TBSA of psoriasis (p = 0.0001). The placebo group increased by 32% compared to pre-therapy levels. No adverse effects were reported in either groups.[16]

In a different randomized, double-blinded controlled study, patients with stable plaque psoriasis (n = 10) consumed 10 capsules of Max-EPA– 5400 mg of EPA and 3600 mg DHA– 3 times daily for 9 weeks. When assessing the improvement in the patients' psoriasis, based on size, erythema, and thickness on a 6-point scale (0 being absent and 6 being severe), the results showed no clinically significant benefits between the treatment or placebo group (n = 15). Side effects included fishy taste upon burping experienced by 1 patient in each group, and transient diarrhea at the beginning of the study for patients on fish oil.[17]

Another study examined patients with chronic psoriasis (n = 14) who received 10 fish-oil capsules for a daily total of 1800 mg of Max-EPA daily for 8 weeks. This supplement is estimated to provide approximately 12000 mg EPA daily. In addition, Max-EPA consists mainly of DHA, and palmitic and oleic acids. After the allocated time, patients experienced significantly less itching (-1.3% vs -0.3%), erythema (-1.1% vs -0.2%), and scaling (-0.8% vs -0.1%) in the treatment group compared to the placebo group at week 12 (n = 14). No side effects were reported.[18]

In a double-blind, randomized study, patients with psoriasis (n = 13) consumed 10 capsules of MaxEPA consisting of 1800 mg EPA for 8 weeks. The fatty acid composition is approximately 324 mg (18%) EPA, 216 mg (12%) DHA, 540 mg (30%) total O3FAs and 54 (3%) omega-6 fatty acids (O6FAs). The results indicated no significant change in the clinical manifestations of psoriasis in either the treatment or control group (n = 14). Both the treatment and placebo groups were found to have total clinical psoriasis scores (measuring erythema, infiltration, and desquamation) at 14.4 and 14.3, respectively. In addition, the treatment group displayed a significant increase in the amount of O3FAs in serum phospholipids, while the level of O6FAs was decreased at the end of the trial. No side effects were discussed.[19]

A separate study investigated patients with stable plaque psoriasis (n = 80) who consumed 2 capsules 3 times daily for 8 weeks. Each capsule contained 187 mg EPA and 126 mg DHA for a daily total of 1122 mg EPA and 756 mg DHA. The severity of psoriasis lesions was assessed based on erythema, induration, scaling, and pruritus based on a 4-point scale where 0 was lack of and 4 was severe appearance. Psoriasis Association Scoring Index (PASI) was used to further assess psoriatic lesions. At the end of the study, pruritus, scaling, and induration of the plaques had decreased significantly. Moreover, 7 patients experienced a significant decrease ($p < 0.001$) in PASI scores compared to baseline and 13 patients had more than 75% healing observed based on the change in PASI scores. Pruritus decreased most rapidly followed by scaling and induration while erythema was most persistent. In 14 patients there was a decline in or poor response to the intervention. Two patients in the treatment group reported severe pain and a few patients reported fishy odor after taking the treatment.[1](https://paperpile.com/c/XcMQXg/Hnwx)4

Soyland et al conducted 4 month, double-blind, multicenter trial, where patients with moderate-to-severe psoriasis (n = 62) were given 6000 mg of fish oil a day, containing 5000 mg of EPA and DHA (2550 mg (51%) EPA and 1600 mg (32%) DHA), and the control group was given corn oil. While the fish oil group showed significant increases in serum n-3 fatty acids ($p< 0.001$), a decreased arachidonic acid-to-EPA ratio ($p < 0.001$), and reduced n-6 fatty acids ($p < 0.001$), these biochemical changes did not translate into clinical improvements. In contrast, the corn oil group exhibited a significant increase in DHA ($p < 0.05$) and improvements in desquamation and redness ($p < 0.05$). A subset of patients in this group also showed a reduction in clinical signs in a selected skin area ($p < 0.05$), with improvements correlating with increased EPA and total n-3 fatty acids. Both groups had reduced scaling ($p < 0.01$), and the fish oil group showed less cellular infiltration ($p < 0.01$). But overall, there were no significant differences in psoriasis severity between groups. No side effects were reported.[20]

In a randomized, open trial study, patients received a daily dose of 20 mg of etretinate capsules alone (0.3-0.5 mg/kg/day) or an equivalent dose of etretinate combined with 1800 mg/day of commercially available, highly-purified EPA ethyl ester capsules (n = 20). After 12 weeks of treatment, clinical improvement was obtained in all the patients receiving EPA therapy and 18 patients receiving etretinate monotherapy. None of the patient's symptoms had worsened. Adverse effects were reported in both treatment groups, including 7 patients with ReEPA therapy and 9 patients with etretinate monotherapy. Patients reported gastric symptoms, folliculitis, dry eyes, dry mouth, cheilitis, desquamation of palms as well as increased liver enzymes. The study found no significant differences in the incidence of these adverse events between the two treatment groups. There were also no differences found in side effects.[21]

In a prospective, open, single-centered, controlled observational study, patients with stable mild-to-moderate plaque psoriasis began treatment for two groups. Group A was treated with both tacalcitol and 2 daily capsules of Oravexfor 8 weeks (n = 15). The dosage of EPA and DHA totaled 640 mg daily. Additionally, Group B received monotreatment with tacalcitol for 8 weeks (n = 15). The study was not blinded to either the patient or to the observer as there was no placebo. Groups showed no difference in baseline sex, age, and body mass index. Results showed significant effects in Group A, including improved quality of life, a decrease in the severity of psoriasis, and decreased scalp lesions, pruritus, erythema, and scaling. No side effects are discussed.[22]

Summary: The daily total dose range across ten studies was 640 mg EPA/DHA to 5400 mg EPA/3600 mg DHA, with one study consisting of only 12000 mg EPA supplementation. Three studies indicated no significant change in clinical manifestations of psoriasis with supplementation. One out of the ten studies exposed patients to UVB suberythemal doses of UVB phototherapy which showcased that treatment group has a decrease in TBSA of psoriasis. Etretinate, when combined with O3FA supplementation, demonstrated reduction in psoriasis clinical scores. Talcalcitol when combined with O3FA supplementation demonstrated improved quality of life, decrease in psoriasis severity, and decrease in scalp lesions, pruritus, erythema, and scale. Furthermore, all six studies resulted in the improvement of clinical symptoms, such as severity, TBSA, pruritus, erythema, scaling, scalp lesions, induration, and quality of life.

ATOPIC DERMATITIS

Atopic dermatitis is a chronic, relapsing inflammatory condition. This condition is most prevalent in children but can also impact adults. Common triggers include asthma, weather changes, food allergy, and allergic rhinitis. The

cause of atopic dermatitis has been addressed with two leading theories. The first theory suggests that allergy causes skin barrier breakdown, leading to further allergen infiltration, which ultimately leads to inflammation. The second suggests that the patient had a preexisting impairment in their skin barrier, which leads to immune system dysregulation and reduced function.[23] Atopic dermatitis can have varied presentations, but most common manifestations include erythematous papules that develop scaling, exudate, or xerosis. This paper divides the treatment course into two categories: treating active disease and disease prevention. Common long-term or maintenance treatment includes antihistamines, steroids, immunosuppressive and immunomodulatory agents, and the avoidance of known triggers.[23-25]

Disease Management: In a randomized, double-blind, controlled clinical trial, 21 patients between the ages of 18-40 with eczema received 5400 mg of DHA and 370 mg EPA treatment capsules daily for 8 weeks, while the remaining 23 patients received 4170 mg of caprylic acid and 2840 mg of capric acid control capsules (n = 23) for 8 weeks. Supplementation resulted in a significantly higher proportion of total O3FAs, decreased O6FA/O3FA ratio, and elevated plasma levels of DHA and EPA compared to control. Supplementation with O3FAs led to a significant clinical improvement of severity scoring of atopic dermatitis (SCORAD) compared to baseline scores. DHA average at week 8 was 28.5 (17.6-51.0) compared to baseline average of 37.0 (17.9-48.0); the control group average at week 8 was 33.4 (10.7-56.2) which is a decrease from the baseline average of 35.4 (17.2-63.0). There was no significant difference between treatment and control groups. Furthermore, there was a significant decrease in anti-CD40/interleukin 4 mediated IgE production of peripheral blood mononuclear cells (PBMC) in the treatment group, while PBMCs were activated in both groups. Side effects were not reported.[26]

500 mg of marine fish oil capsules containing 36% EPA and 24% DHA (n = 34) or 2500 mg of placebo with sunflower-seed oil (n = 31) for 4 months. In the placebo group, short-term particulate matter exposure resulted in significantly elevated levels of IL-1a and carbonyl protein (biomarkers of inflammation and oxidative stress-induced protein damage, respectively). This demonstrates supplementation with O3FAs may improve skin inflammation and response to oxidative stress due to fine particulate matter air pollution exposure.[27]

DISEASE PREVENTION

In a randomized placebo control trial by Furuhjelm et al, pregnant women were given either 1600 mg EPA coupled with 1100 mg of DHA or placebo after 25 weeks of gestation and continued for 3.5 months in those breastfeeding. Although there was no significant difference in EPA/DHA preventing any kind of eczema, there was a significant decrease in IgE associated eczema in children within the treatment group. Throughout the course of the study, 6 patients discontinued treatment due to nausea and 3 patients due to abdominal pain.[28]

In a double-blind randomized controlled trial, infants (n = 450) with a high risk of atopic dermatitis were either given a daily supplement with 280 mg DHA and 110 mg EPA (n = 218) or placebo (n = 202) with olive oil beginning from birth until 6 months of age. After 6 months of age, the infants' erythrocytes, plasma, and mother's breast milk were measured for fatty acid levels. The levels for both DHA and EPA were significantly higher and erythrocyte arachidonic acid levels (O6FAs) were significantly lower in the treatment group compared to the placebo. After 12 months, symptoms of eczema, food allergy, asthma, and sensitization were assessed (n = 323). There was no significant difference in the prevention of allergic disease between fatty acid supplementation (n = 156) and placebo group (n = 167). Participants were more likely to withdraw from the fish oil group due to the fishy smell. No other side effects were reported.[29]

In a double-blind, randomized controlled trial, pregnant women at 24 weeks of gestation (n = 695) were given either 2400 mg of O3FAs (55% EPA and 37% DHA) or olive oil (placebo) in four 1000 mg capsules until 1 week post-delivery. Follow-up continued until 3 (n = 136) or 5 years of age (n = 142). The effect of supplementation was strongest in children whose mothers had a dietary intake of <321 mg of EPA and DHA per day prior to the study or mothers with the FADS gene variant, which is associated with decreased levels of EPA and DHA. Among women who received daily supplementation of O3FAs, the risk of persistent wheeze or asthma decreased by ⅓ in children within the first 5 years of life. Infants in the treatment group were associated with a reduced risk of lower respiratory tract infections, but not with eczema or allergic sensitization. No specific side effects were noted, and the safety profiles of the supplement and placebo were similar.[30]

In a randomized, controlled trial, pregnant women <21 weeks gestation with a history of allergic disease were selected to participate in the study (n = 706). Of the 706 women, 368 were supplemented daily with O3FA capsules containing 800 mg DHA and 100 mg EPA until delivery, while the remaining 338 participants were given vegetable oil until delivery. In a 6-year follow up, children were assessed for allergic disease symptoms (eczema, wheeze, or rhinitis) and sensitization to allergens. Results showed no difference between treatment (n = 116) and control (n = 106) groups with allergic disease symptoms, but there was a significant decrease in the sensitization of the dust mite *Dermatophagoides farinae* between groups. There was no significant difference between adverse events in both groups.[31]

In a randomized, controlled trial conducted by Gunaratne et al, infants born prematurely (<33 weeks) were given either high-DHA diet (1% total O3FA) or standard-DHA diet (0.3% total O3FA) from 2-4 days old to 40 weeks via enteral feeds. Parents reported results of eczema from birth to seven years of age did not differ between the high-DHA diet (1% total O3FA) or standard-DHA diet (0.3% total O3FA) in patients born prematurely. No side effects were reported.[32]

Summary: While there may be some indications for O3FA supplementation to improve skin inflammation, studies have shown there is no difference in the prevention of allergic disease. The daily total doses assessed across studies ranged from 100-6000 mg of O3FA supplementation. On the other hand, one trial resulted in a significant decline in the prevalence of eczema and another indicated a difference in clinical improvement compared to baseline, but not in comparison to placebo. Overall, only one study found adverse effects in its treatment group consisting of nausea and abdominal pain, and these effects were only found in 9 patients.

OCULAR ROSACEA

Rosacea is an inflammatory cutaneous disorder that primarily, but not exclusively, affects the skin of the face in papular and/or pustular eruptions, erythema, or telangiectasia. There are four classic subtypes with ocular manifestations being one of the most common in 50-75% of those affected.[33,34] Ocular symptoms also precede cutaneous eruptions or may be the only clinical manifestation in 20% of those with disease.

In a prospective, randomized controlled trial conducted by Bhargava et al, symptomatic patients with dry eyes were randomized to either a treatment or a placebo group, both ingesting 2 capsules twice daily for 6 months. Both capsules within the placebo group contained olive oil, while the intervention group was given 1 capsule containing 180 mg of EPA and 1 containing 120 mg DHA. Efficacy measures include dry eye scores, meibomian gland score, tear film breakup time (TBUT), and the Schirmer test. Dry eye scores were graded using the Dry Eye Scoring System (DESS) questionnaire. Scores of 0 to 6 were mild, 6.1 to 12 were moderate, and 12.1 to 18 indicated severely symptomatic dry eye. The treatment group displayed a statistically significant decrease in scores compared to the placebo group at pre-intervention to 1 month, 3 months, 6 months, and from 3 months to post-intervention. Symptom scores were 9.1 ± 2.4 at baseline, 8.5 ± 1.8 after 1 month, 5.8 ± 1.6 after 3 months, and 3.8 ± 2.4 ($p < 0.001$) after 6 months. There were no significant changes in meibomian gland scores in the O3FA group compared to placebo. The TBUT in the treatment group were not significant at one month but were significant at 3 months, 6 months, and from 3 months to 6 months when compared to the placebo. The Schirmer test demonstrated the same results as the TBUT. Side effects of gastric intolerance to O3FAs resulted in the dropout of eight patients.[34]

Summary: While there is limited published data regarding the efficacy of O3FAs in the treatment of rosacea, symptomatic treatment of ocular manifestations may be alleviated with a combination of 180 mg EPA/ 120 mg DHA twice daily.

DISCUSSION

Dietary supplementation for the management of dermatological conditions is a common topic brought to discussion by patients. Given the variation in treatment for acne, psoriasis, atopic dermatitis, and ocular rosacea, it is important for dermatologists to understand evidence-based integrative treatments to provide safe and effective recommendations.

In general, diet is a significant factor which alters the diversity of the gut microbiome. Omega-3 PUFA supplementation has been shown to modulate gut microbiota composition by increasing beneficial bacteria such as Lactobacillus, Bifidobacterium, and Akkermansia, while reducing potentially pathogenic fungi like Aspergillus and Penicillium.[35] Additionally, omega-3 PUFAs have been linked to a decrease in Faecalibacterium and an increase in Bacteroidetes and butyrate-producing Lachnospiraceae, changes that may help restore microbial balance in inflammatory bowel disease.[36] These alterations are accompanied by an increase in short-chain fatty acids, such as butyric and valeric acid, and an enhanced colonic mucus barrier, suggesting a prebiotic role for omega-3 PUFAs in supporting gut health, immune regulation, the gut-brain axis, and skin health.[35,36] While the ideal relationship between the microbiota and optimal health is still controversial, it is important to consider the effects of dietary supplementation with O3FAs. The analyzed studies paired with the concept of the gut-skin-axis have suggested that O3FAs may alter the gut by reducing the growth of certain bacteria and improving the growth of others.[37] Specifically, one study suggests that alterations in the gut microbiota may trigger a rise in oxidative stress levels, which can lead to intestinal permeability and inflammation that may manifest as cutaneous symptoms of common dermatological disorders.[38]

Inflammatory conditions involve the production of polyunsaturated free fatty acids, which have been shown to help regulate the body's inflammatory responses. The enzyme phospholipase A2 (PLA2) generates polyunsaturated free fatty acids, such as O3FAs and O6FAs. Prostaglandins, thromboxanes, and leukotrienes are derived from O6FAs and exhibit pro-inflammatory effects, while eicosanoids derived from O3FAs, such as EPA and DHA have anti-inflammatory properties.[38]

The results of this review suggest O3FA supplementation may be the most efficacious in symptomatic treatment of psoriasis and might play a role in the clinical improvement of atopic dermatitis. A commonality found between studies on these conditions is an increase in O3FAs and a decrease in O6FAs after dietary supplementation, though there was no consistent association between this ratio and clinical symptom improvement. Given these findings, O3FA supplementation may be considered as an adjunctive therapy for psoriasis, particularly at doses ranging from 1,800 mg to 5,400 mg of combined EPA/DHA but should not replace first-line treatments. In atopic dermatitis, while some studies indicate benefits in inflammatory markers and skin barrier function, clinical results remain mixed, limiting routine recommendations. Evidence for acne vulgaris is insufficient to support O3FAs as a standalone therapy, though their anti-inflammatory properties warrant further investigation. In ocular rosacea, limited data suggest supplementation (720 mg EPA + 480 mg DHA daily) may alleviate dry eye

symptoms. Until more data is available, O3FA supplementation should be approached as a potential adjunctive therapy rather than a primary treatment for dermatologic disorders.

O3FA supplementation across many of the studies found no adverse effects across control and treatment groups. Few studies found O3FA supplementation led to mild gastrointestinal side effects such as nausea, abdominal pain, flatulence, diarrhea. Others found adverse effects including burps with a fishy odor or smell, folliculitis, contact dermatitis, and dry mouth. Freezing fish oil capsules before ingestion can help reduce gastrointestinal side effects, such as fishy aftertaste, belching, and nausea, by delaying their breakdown in the stomach and allowing them to reach the intestines for absorption. This mechanism is similar to the effect observed with enteric-coated fish oil capsules, as demonstrated in the study by Belluzzi et al, which found that delayed release can mitigate GI discomfort in patients with Crohn's disease.[39] While freezing is not explicitly discussed in the available literature, it aligns with established strategies for improving fish oil tolerability. In addition to these side effects, safety concerns regarding bleeding may affect a patient's ability to add omega-3 supplementation to their diet. Nordy et al found that O3FA supplementation, to both low and high saturated fat diets, led to a prolonged skin bleeding time in patients.[40] Javaid et al found that there was a 50% increased relative risk of bleeding events in patients receiving "high-dose purified EPA." The authors note that the absolute increase in bleeding was modest at 0.6% without evidence of serious bleeding such as intracranial or hemorrhagic stroke.[41] In patients with clotting disorders, O3FA may not be appropriate treatment for psoriasis, atopic dermatitis, ocular rosacea, or acne vulgaris.

Limitations to this review include the quantity of studies resulting from the search despite using multiple terms and search engines. Furthermore, there are several limitations to studies included in this review, such as the age range, number of patients, lack of control groups, generalizability, and a lack of control for omega-6 intake. Significant heterogeneity exists among the studies based on variations in study design, dosing regimens, treatment durations and supplementations, and outcome measures. While some studies utilized high doses of EPA and DHA, others focused on lower potent doses or mixed formulations which can affect treatment efficacy and comparison. In addition to variable study designs, study populations, disease severity, and concurrent therapies contribute to heterogeneity. This variability complicates the ability to establish standardized dosing guidelines and recommendations for patient populations who may benefit from O3FA supplementation. Despite these limitations, this review highlights further well-controlled, large-scale investigation is necessary to discern the efficacy of dietary supplementation of O3FAs in the treatment of acne, atopic dermatitis, and ocular rosacea.

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Table 1. Summary of studies and results

Study Reference	Skin Condition	Intervention	Study Design; Sample Size Results	Results
[9]Guertler A, Neu K, Lill D, Clanner-Engelshofen B, French LE, Reinholz M. Exploring the potential of omega-3 fatty acids in acne patients: A prospective intervention study. J Cosmet Dermatol. Published online July 10, 2024. doi:10.1111/jocd.16434	Acne	16 weeks of 600 mg DHA/300 mg EPA and 800 mg DHA/400 mg EPA	Prospective intervention study; 60 Acne severity significantly improved over the course of the study based on dermatological objective assessment ($p < 0.001$)	Acne severity significantly improved over the course of the study based on dermatological objective assessment ($p < 0.001$)
[10]Huang Y, Liu F, Lai J, et al. The adjuvant treatment role of ω-3 fatty acids by regulating gut microbiota positively in the acne vulgaris. J Dermatolog Treat. 2024;35(1):2299107.doi:10.1080/09546634.2023.2299107	Acne	12 weeks of isotretinoin dosed at 0.5-1.0 mg/(kg d) and omega-3 fatty acids dosed at 2400 mg/d	Randomized, clinical trial; 66 (46 treatment, 20 matched healthy controls) Significant increase in gut microbiota in treatment group versus healthy controls	Significant increase in gut microbiota in treatment group versus healthy controls
[11]Rubin MG, Kim K, Logan AC. Acne vulgaris, mental health and omega-3 fatty acids: a report of cases. Lipids Health Dis. 2008;7:36.	Acne	2 months of 1000 mg EPA, 300 mg EGCG, 15 mg zinc gluconate, 200 mcg selenium, 200 mcg chromium	Case report; 5 80% of patients had reduction in total inflammatory lesions and average 24% increase in mental, emotional, and social well-being	80% of patients had reduction in total inflammatory lesions and average 24% increase in mental, emotional, and social well-being
[12]Khayef G, Young J, Burns-Whitmore B, Spalding T. Effects of fish oil supplementation on inflammatory acne. Lipids Health Dis. 2012;11:165.	Acne	12 weeks of 930 mg EPA, 720 mg DHA, 174 mg DPA	Prospective intervention study; 13 Statistical significance was not obtained and the results are inconclusive	Statistical significance was not obtained and the results are inconclusive
[13]Jung JY, Kwon HH, Hong JS, et al. Effect of dietary supplementation with omega-3 fatty acid and gamma-linolenic acid on acne vulgaris: a randomised, double-blind, controlled trial. Acta Derm Venereol. 2014;94(5):521-525.	Acne	10 weeks of supplementation with 2000 mg EPA and DHA or 1000 mg borage oil with 200 mg gamma-linolenic acid	Double-blind, randomized controlled trial; 45 (15 across 3 groups) Significant reductions in inflammation of lesions	Significant reductions in inflammation of lesions
[14]Adil M, Singh PK, Maheshwari K. Clinical evaluation of omega-3 fatty acids in psoriasis. Przegl Dermatol. 2017;3:314-323.	Psoriasis	6 capsules consisting of 300 mg of EPA and DHA in 3 divided doses daily for 3 months	Prospective observational study; 100 Significant difference in the severity, erythema, and induration of lesions	Significant difference in the severity, erythema, and induration of lesions
[15]Tveit KS, Brokstad KA, Berge RK, et al. A Randomized, Double-blind, Placebo-controlled Clinical Study to Investigate the efficacy of Herring Roe Oil for treatment of Psoriasis. Acta Derm Venereol. 2020;100(10):adv00154. Published 2020 May 28. doi:10.2340/00015555-3507	Psoriasis	2920 mg herring roe oil with total daily dose of EPA and DHA 2.6 g	Randomized, double-blind; 64 (32 treatment, 32 placebo) Significant decrease in Psoriasis Area Severity Index score in treatment group versus control group	Significant decrease in Psoriasis Area Severity Index score in treatment group versus control group
[16]Gupta AK, Ellis CN, Tellner DC, Anderson TF, Voorhees JJ. Double-	Psoriasis	10 fish oil capsules (Max-	Double-blind, randomized clinical	Treatment group had a significant decrease

Study Reference	Skin Condition	Intervention	Study Design; Sample Size Results	Results
blind, placebo-controlled study to evaluate the efficacy of fish oil and low-dose UVB in the treatment of psoriasis. Br J Dermatol. 1989;120(6):801-807.		EPA) twice daily which consisted of a daily total of 3.6 g of EPA and 2.4 g of DHA for 15 weeks with UVB suberythemal doses of UVB phototherapy twice weekly for 8 weeks	trial; 20 (9 treatment, 11 placebo) Treatment group had a significant decrease in total body surface area of psoriasis lesions	in total body surface area of psoriasis lesions
[17]Gupta AK, Ellis CN, Goldfarb MT, Hamilton TA, Voorhees JJ. The role of fish oil in psoriasis. A randomized, double-blind, placebo-controlled study to evaluate the effect of fish oil and topical corticosteroid therapy in psoriasis. Int J Dermatol. 1990;29(8):591-595.	Psoriasis	10 capsules of Max-EPA, which consisted of 5.4 g of EPA and 3.6 g DHA, 3 times daily for 9 weeks	Double-blind, randomized clinical trial; 25 (10 treatment, 15 placebo) No clinically significant difference between groups	No clinically significant difference between groups
[18]Bittiner SB, Tucker WF, Cartwright I, Bleehen SS. A double-blind, randomised, placebo-controlled trial of fish oil in psoriasis. Lancet. 1988;1(8582):378-380.	Psoriasis	10 capsules of MaxEPA consisting of 1.8 g EPA for 8 weeks	Randomized, clinical trial; 28 (14 treatment, 14 placebo) Significantly decreased itching, erythema, and scaling in treatment group	Significantly decreased itching, erythema, and scaling in treatment group
[19]Bjørneboe A, Smith AK, Bjørneboe GE, Thune PO, Drevon CA. Effect of dietary supplementation with n-3 fatty acids on clinical manifestations of psoriasis. Br J Dermatol. 1988;118(1):77-83.	Psoriasis	10 capsules of MaxEPA consisting of 1.8 g EPA for 8 weeks	Double-blind, randomized study; 27 (13 treatment, 14 placebo) No significant difference in clinical manifestations of psoriasis between groups	No significant difference in clinical manifestations of psoriasis between groups
[42]Lassus A, Dahlgren AL, Halpern MJ, Santalahti J, Happonen HP. Effects of dietary supplementation with polyunsaturated ethyl ester lipids (Angiosan) in patients with psoriasis and psoriatic arthritis. J Int Med Res. 1990;18(1):68-73.	Psoriasis	2 capsules of 1122 mg EPA/ 756 mg DHA 3 times daily for 8 weeks	Prospective intervention study; 80 Significant decrease in itching, scaling, and induration of psoriasis lesions	Significant decrease in itching, scaling, and induration of psoriasis lesions
[20]Søyland E, Funk J, Rajka G, et al. Effect of dietary supplementation with very-long-chain n-3 fatty acids in patients with psoriasis. N Engl J Med. 1993;328(25):1812-1816.	Psoriasis	6 g of oil per day, containing 5 g of EPA and DHA	Double-blind, randomized clinical trial; 124 (62 treatment, 62 placebo) No significant difference between groups	No significant difference between groups
[21]Danno K, Sugie N. Combination therapy with low-dose etretinate and eicosapentaenoic acid for psoriasis vulgaris. J Dermatol. 1998;25(11):703-705.	Psoriasis	20 mg of etretinate capsules alone (0.3-0.5 mg/kg/ day) or an equivalent dose of etretinate combined with 1800 mg/day of commercially available, highly-	Open, randomized clinical trial; 40 (20 etretinate capsules alone, 20 etretinate + highly-purified EPA ethyl ester capsules) Clinical improvement in all receiving EPA and in 90% of etretinate monotherapy	Clinical improvement in all receiving EPA and in 90% of etretinate monotherapy

Study Reference	Skin Condition	Intervention	Study Design; Sample Size Results	Results
		purified EPA ethly ester capsules (n = 20)		
[22]Balbás GM, Regaña MS, Millet PU. Study on the use of omega-3 fatty acids as a therapeutic supplement in treatment of psoriasis. Clin Cosmet Investig Dermatol. 2011;4:73-77.	Psoriasis	A dosage of EPA and DHA totaled 640 mg daily for 8 weeks	Open, controlled observational study; 30 (15 tacalcitol, 15 tacalcitol + Oravex) Significant decrease in itching, erythema, scaling, and scalp lesions. Significant increase in quality of life	Significant increase in quality of life and significant decrease in itching, erythema, scaling, and scalp lesions from baseline was observed in the two groups, however, it was significantly greater in the tacalcitol + Oravex group.
[26]Koch C, Dölle S, Metzger M, et al. Docosahexaenoic acid (DHA) supplementation in atopic eczema: a randomized, double-blind, controlled trial. Br J Dermatol. 2008;158(4):786-792.	Atopic Dermatitis	5.4 g of DHA and 0.37 g EPA treatment capsules (n = 21) daily or 4.17 g of caprylic acid and 2.84 g of capric acid control capsules (n = 23) for 8 weeks.	Double-blind, randomized clinical trial; 44 (21 treatment (DHA + EPA), 23 control (capric acid)) Significant improvement of atopic dermatitis compared to baseline in DHA + EPA group, but no significant difference between treatment and control group	Significant improvement of atopic dermatitis compared to baseline in DHA + EPA group, but no significant difference between treatment and control group
[28]Furuhjelm C, Warstedt K, Fagerås M, et al. Allergic disease in infants up to 2 years of age in relation to plasma omega-3 fatty acids and maternal fish oil supplementation in pregnancy and lactation. Pediatr Allergy Immunol. 2011;22(5):505-514.	Atopic Dermatitis	1.6 g EPA coupled with 1.1 grams of DHA or placebo after 25 weeks of gestation and continued for 3.5 months in those breastfeeding.	Randomized clinical trial; 145 (70 treatment, 75 soya bean oil) No significant difference in EPA/ DHA preventing any kind of eczema. There was a significant decrease in IgE associated eczema in children within the treatment group	No significant difference in EPA/ DHA preventing any kind of eczema. There was a significant decrease in IgE associated eczema in children within the treatment group
[29]D'Vaz N, Meldrum SJ, Dunstan JA, et al. Postnatal fish oil supplementation in high-risk infants to prevent allergy: randomized controlled trial. Pediatrics. 2012;130(4):674-682.	Atopic Dermatitis	A daily supplement of fish oil containing 280 mg docosahexaenoic acid and 110 mg eicosapentaenoic acid or a control (olive oil), from birth to age 6 months	Randomized controlled trial; 323 (156 treatment, 167 placebo) No significant difference in the prevention of allergic disease between fatty acid supplementation and placebo group	No significant difference in the prevention of allergic disease between fatty acid supplementation and placebo group
[30]Bisgaard H, Stokholm J, Chawes BL, et al. Fish Oil-Derived Fatty Acids in Pregnancy and Wheeze and Asthma in Offspring. N Engl J Med. 2016;375(26):2530-2539.	Atopic Dermatitis	2.4 g of n−3 LCPUFA (fish oil) or placebo (olive oil) per day at 24 weeks of gestation until 1 week after delivery	Double-blind, randomized controlled trial; 695 (Follow-up continued until 3 (n = 136) or 5 years of age (n = 142)) Among women who received daily supplementation of	Among women who received daily supplementation of O3FAs, the risk of persistent wheeze or asthma decreased by ⅓ in children within the first 5 years of life. Infants in the treatment group

Study Reference	Skin Condition	Intervention	Study Design; Sample Size Results	Results
			O3FAs, the risk of persistent wheeze or asthma decreased by ⅓ in children within the first 5 years of life. Infants in the treatment group were associated with a reduced risk of lower respiratory tract infections, but not with eczema or allergic sensitization	were associated with a reduced risk of lower respiratory tract infections, but not with eczema or allergic sensitization
[31]Best KP, Sullivan T, Palmer D, et al. Prenatal Fish Oil Supplementation and Allergy: 6-Year Follow-up of a Randomized Controlled Trial. Pediatrics. 2016;137(6). doi:10.1542/peds.2015-4443	Atopic Dermatitis	~800 mg/day DHA and 100 mg/day EPA (Intervention), or 500 mg vegetable oil capsules from 21 weeks' gestation until delivery	Randomized, controlled trial; 222 (116 treatment, 106 control) No difference between treatment and control groups with allergic disease symptoms, but there was a significant decrease in the sensitization of the dust mite *Dermatophagoides farinae* between groups	No difference between treatment and control groups with allergic disease symptoms, but there was a significant decrease in the sensitization of the dust mite *Dermatophagoides farinae* between groups
[32]Gunaratne AW, Makrides M, Collins CT, et al. Docosahexaenoic acid supplementation of preterm infants and parent-reported symptoms of allergic disease at 7 years corrected age: follow-up of a randomized controlled trial. Am J Clin Nutr. 2019;109(6):1600-1610.	Atopic Dermatitis	High-DHA diet (six 0.5-g capsules of DHA-rich fish oil per day (900 mg of DHA and 195 mg of eicosapentaenoic acid)) (1% total O3FA) or standard-DHA diet (six 0.5 g capsules per day of soy oil) (0.3% total O3FA) from 2-4 days old to 40 weeks via enteral feeds	Randomized, controlled trial; 569 (278 high DHA, 291 standard DHA) No significant difference between treatment and control groups	No significant difference between treatment and control groups
[27]Lin Z, Niu Y, Jiang Y, et al. Protective effects of dietary fish-oil supplementation on skin inflammatory and oxidative stress biomarkers induced by fine particulate air pollution: a pilot randomized, double-blind, placebo-controlled trial. Br J Dermatol. 2021;184(2):261-269.	Atopic Dermatitis	2500 mg of marine fish oil capsules containing 900 mg EPA and 600 mg DHA for 4 months	Double-blind, randomized controlled trial; 65 (34 treatment, 31 placebo) Supplementation with O3FAs may improve skin inflammation and response to oxidative stress due to fine particulate matter air pollution exposure	Supplementation with O3FAs may improve skin inflammation and response to oxidative stress due to fine particulate matter air pollution exposure
[34]Bhargava R, Chandra M, Bansal U, Singh D, Ranjan S, Sharma S. A Randomized Controlled Trial of Omega 3 Fatty Acids in Rosacea Patients with Dry Eye Symptoms. Curr Eye Res.	Rosacea	O3FA group received two capsules, each containing 180 mg of eicosapentaenoic	Randomized controlled trial; 130 (65 treatment, 65 placebo) Statistically significant decrease	Statistically significant decrease in dry eye scores in the O3FA group compared to the placebo group at pre-

Study Reference	Skin Condition	Intervention	Study Design; Sample Size Results	Results
2016;41(10):1274-1280.		acid (EPA) and 120 mg DHA, twice daily for 6 months (720 mg of EPA +480 mgDHA/day). The placebo group received two capsules containing olive oil, twice daily for 6 months.	in dry eye scores in the O3FA group compared to the placebo group at pre-intervention to 1 month, 3 months, 6 months, and from 3 months to post-intervention No significant changes in meibomian gland scores. TBUT and Schirmer test results were not significant at one month, and became significant at 3 months, 6 months, and from 3 months to 6 months	intervention to 1 month, 3 months, 6 months, and from 3 months to post-intervention No significant changes in meibomian gland scores. TBUT and Schirmer test results were not significant at one month, and became significant at 3 months, 6 months, and from 3 months to 6 months

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