

## Omega-3 Fatty Acids and the skin

Multiple studies have identified and confirmed that Omega-3 fatty acids can be beneficial for skin health. Unlike other disease states, there is a great deal of debate over the effectiveness of fish oil on the skin. Subjectively, people who take fish oil for its health benefits do notice improvements in their skin and hair.

Below, in bibliographical form, are abstracts from scientific research papers that have shown the benefits of Omega-3 for skin and certain skin conditions. Links to full text articles are provided when available.

Kim HH, Shin CM, Park CH, Kim KH, Cho KH, Eun HC, Chung JH. **Eicosapentaenoic acid inhibits UV-induced MMP-1 expression in human dermal fibroblasts.** J Lipid Res. 2005 Aug;46(8):1712-20. Epub 2005 Jun 1.

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Ultraviolet (UV) irradiation regulates UV-responsive genes, including matrix metalloproteinases (MMPs). Moreover, UV-induced MMPs cause connective tissue damage and the skin to become wrinkled and aged. Here, we investigated the effect of eicosapentaenoic acid (EPA), a dietary omega-3 fatty acid, on UV-induced MMP-1 expression in human dermal fibroblasts (HDFs). We found that UV radiation increases MMP-1 expression and that this is mediated by p44 and p42 MAP kinase (ERK) and Jun-N-terminal kinase (JNK) activation but not by p38 activation. Pretreatment of HDFs with EPA inhibited UV-induced MMP-1 expression in a dose-dependent manner and also inhibited the UV-induced activation of ERK and JNK by inhibiting ERK kinase (MEK1) and SAPK/ERK kinase 1 (SEK1) activation, respectively. Moreover, inhibition of ERK and JNK by EPA resulted in the decrease of c-Fos expression and c-Jun phosphorylation/expression induced by UV, respectively, which led to the inhibition of UV-induced activator protein-1 DNA binding activity. This inhibitory effect of EPA on MMP-1 was not mediated by an antioxidant effect. We also found that EPA inhibited 12-O-tetradecanoylphorbol-13-acetate- or tumor necrosis factor-alpha-induced MMP-1 expression in HDFs and UV-induced MMP-1 expression in HaCaT cells. In conclusion, our results demonstrate that EPA can inhibit UV-induced MMP-1 expression by inhibiting the MEK1/ERK/c-Fos and SEK1/JNK/c-Jun pathways. **Therefore, EPA is a potential agent for the prevention and treatment of skin aging.**

Sies H, Stahl W. **Nutritional protection against skin damage from sunlight.** *Annu Rev Nutr.* 2004;24:173-200.

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The concept of systemic photoprotection by dietary means is gaining momentum. Skin is continuously exposed to ultraviolet (UV) radiation, the major cause of skin disorders such as sunburn, photodamage, and nonmelanoma skin cancer. Most of the erythemal annual UV dose is encountered under nonvacation conditions, when no sunscreen is applied. In the absence of topically added compounds, skin protection depends solely on endogenous defense. Micronutrients can act as UV absorbers, as antioxidants, or can modulate signaling pathways elicited upon UV exposure. UV-induced erythema is a suitable parameter to assess photoprotection. Dietary protection is provided by carotenoids, tocopherols, ascorbate, flavonoids, or n-3 fatty acids, contributing to maintenance resistance as part of lifelong protection.

Hakim IA, Harris RB, Ritenbaugh C. **Fat intake and risk of squamous cell carcinoma of the skin.** *Nutr Cancer.* 2000;36(2):155-62

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The varied effects of different classes of dietary fatty acids on carcinogenesis suggest that fatty acid composition is an important determining factor in tumor development. In the present study, we investigated the association between dietary n-3 and n-6 fatty acid intake and risk of squamous cell carcinoma of the skin (SCC). Data were taken from a population-based case-control study of skin SCC in Southeastern Arizona. Our data show a consistent tendency for a lower risk of SCC with higher intakes of n-3 fatty acids [p (for trend) = 0.055]. The adjusted odds ratios for increasing levels of n-3 fatty acids were 0.85 [95% confidence interval (CI) = 0.56-1.27] and 0.71 (95% CI = 0.49-1.00) compared with the lower level as the referent. For the ratio of n-3 to n-6 fatty acids, the odds ratios in successively higher levels were 0.88 (95% CI = 0.59-1.32) and 0.74 (95% CI = 0.51-1.05), suggesting a tendency toward decreased risk of SCC with increased intake of diets with high ratio of n-3 to n-6 fatty acid. More studies are clearly needed to elucidate the function of dietary fatty acids so that recommendations can be made to alter the human diet for cancer prevention, particularly in light of the increasing incidence of SCC of the skin.

Ziboh VA, Miller CC, Cho Y. **Metabolism of polyunsaturated fatty acids by skin epidermal enzymes: generation of antiinflammatory and antiproliferative metabolites.** Am J Clin Nutr. 2000 Jan;71(1 Suppl):3618-6S

<http://www.ajcn.org/cgi/reprint/71/1/361S>

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In the skin epidermis, the metabolism of polyunsaturated fatty acids (PUFAs) is highly active. Dietary deficiency of linoleic acid (LA), the major 18-carbon n-6 PUFA in normal epidermis, results in a characteristic scaly skin disorder and excessive epidermal water loss. Because of the inability of normal skin epidermis to desaturate LA to gamma-linolenic acid, it is transformed by epidermal 15-lipoxygenase to mainly 13-hydroxyoctadecadienoic acid, which functionally exerts antiproliferative properties in the tissue. In contrast, compared with LA, arachidonic acid (AA) is a relatively minor 20-carbon n-6 PUFA in the skin and is metabolized via the cyclooxygenase pathway, predominantly to the prostaglandins E(2), F(2)(alpha), and D(2). AA is also metabolized via the 15-lipoxygenase pathway, predominantly to 15-hydroxyeicosatetraenoic acid. At low concentrations, the prostaglandins function to modulate normal skin physiologic processes, whereas at high concentrations they induce inflammatory processes. PUFAs derived from other dietary oils are also transformed mainly into monohydroxy fatty acids. For instance, epidermal 15-lipoxygenase transforms dihomo-gamma-linolenic acid (20:3n-6) to 15-hydroxyeicosatrienoic acid, eicosapentaenoic acid (20:5n-3) to 15-hydroxyeicosapentaenoic acid, and docosahexaenoic acid (22:6n-3) to 17-hydroxydocosahexaenoic acid, respectively. These monohydroxy acids exhibit antiinflammatory properties in vitro. Thus, supplementation of diets with appropriate purified vegetable oils, fish oil, or both may generate local cutaneous antiinflammatory and antiproliferative metabolites which could serve as less toxic in vivo monotherapies or as adjuncts to standard therapeutic regimens for the management of inflammatory skin disorders.

Ziboh VA. **The significance of polyunsaturated fatty acids in cutaneous biology.** Lipids. 1996 Mar;31 Suppl:S249-53.

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The skin epidermis displays a highly active metabolism of polyunsaturated fatty acids (PUFA). Dietary deficiency of linoleic acid (LA) and 18-carbon (n-6) PUFA results in characteristic scaly skin disorder and excessive epidermal water loss. Arachidonic acid, a 20-carbon (n-6) PUFA is metabolized via the cyclooxygenase pathway into predominantly prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) PGF<sub>2</sub> alpha, and PGD<sub>2</sub> and via the lipoxygenase pathway into predominantly 15-hydroxyeicosatetraenoic acid (15-HETE). The prostaglandins modulate normal skin physiological processes at low concentrations and inflammatory reactions at high concentrations. Similarly, the very active epidermal 15-lipoxygenase transforms dihomo-gammalinolenic acid (DGLA) into 15-hydroxy eicosatrienoic acid (15-HETrE), eicosapentaenoic acid (EPA) into 15-hydroxyeicosapentaenoic acid (15-HEPE) and docosahexaenoic acid (DHA) into 17-hydroxydocosahexaenoic acid (17-HDoHE), respectively. These monohydroxy acids exhibit anti-inflammatory properties. In contrast, the 18-carbon (n-6) PUFA is transformed into 13-hydroxy-9,11-octadecadienoic acid (13-HODE), which exerts antiproliferative properties in the tissue. Thus, the supplementation of diets with appropriate purified vegetable oils and/or fish oil may generate local cutaneous anti-inflammatory metabolites which could serve as a less toxic in vivo monotherapy or as adjuncts to standard therapeutic regimens for the management of skin inflammatory disorders.

Grimminger F, Mayser P, Papavassilis C, Thomas M, Schlotzer E, Heuer KU, Fuhrer D, Hinsch KD, Walmrath D, Schill WB, et al. **A double-blind, randomized, placebo-controlled trial of n-3 fatty acid based lipid infusion in acute, extended guttate psoriasis. Rapid improvement of clinical manifestations and changes in neutrophil leukotriene profile.** Clin Investig. 1993 Aug;71(8):634-43.

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Twenty patients hospitalized for acute psoriasis guttata with a minimum 10% of body surface area involvement (range 10-90%) completed a 10-day trial in which they were randomly allocated to receive daily infusions with either an n-3 fatty acid based lipid emulsion [100 ml/day with 2.1 g eicosapentaenoic (EPA) and 21 g docosahexaenoic acid (DHA)] or a conventional n-6 lipid emulsion (EPA + DHA < 0.1 g/100 ml). The severity of disease was evaluated by scoring daily erythema, infiltration, and desquamation and by a subjective scoring of clinical manifestations offered by the patients. Leukotriene (LT) and platelet-activating factor (PAF) generation were investigated in ionophore-stimulated neutrophils obtained on days 0, 1, 3, 5, 10, and 40. Moderate improvement in clinical manifestations was noted in the n-6 group (changes in score systems between 16-25% from baseline within 10 days). In contrast, the severity of disease markedly decreased in all patients of the n-3 group, with improvements in all score systems ranging between 45% and 76% within 10 days ( $P < 0.05$  for each variable). The difference in response to the two regimens was evident within 4-7 days after onset of lipid infusion. A more than ten fold increase in neutrophil EPA-derived 5-lipoxygenase product formation (LTB<sub>5</sub>, its omega-oxidation products, non-enzymatic degradation products of LTA<sub>5</sub> and 5-hydroxyeicosapentaenoic acid) was noted in the n-3 group but not in the n-6 group. Neutrophil PAF generation increased in the n-6 group but decreased in the n-3 group. In conclusion, modulation of eicosanoid metabolism by intravenous n-3 fatty acid supplementation appears to exert a rapid beneficial effect on inflammatory skin lesions in acute guttate psoriasis.

Soyland E, Funk J, Rajka G, Sandberg M, Thune P, Rustad L, Helland S, Middelfart K, Odu S, Falk ES, et al. **Effect of dietary supplementation with very-long-chain n-3 fatty acids in patients with psoriasis.** N Engl J Med. 1993 Jun 24;328(25):1812-6

<http://content.nejm.org/cgi/content/abstract/328/25/1812>

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**BACKGROUND.** In several studies dietary fish oil has been found to have beneficial effect on psoriasis, but the results are contradictory and based mainly on open studies or studies of small numbers of patients. **METHODS.** In a four-month double-blind, multicenter trial, we randomly assigned 145 patients with moderate-to-severe psoriasis to receive in their diet either highly purified ethyl esters of n-3 fatty acids ("fish oil"; 6 g of oil per day, containing 5 g of eicosapentaenoic and docosahexaenoic acid) or an isoenergetic amount of corn oil containing mainly n-6 fatty acids. All the patients were advised to reduce their intake of saturated fatty acids. A 48-hour dietary recall was performed, and the fatty-acid pattern in the serum phospholipids was monitored in a subgroup of patients. **RESULTS.** In the fish-oil group, n-3 fatty acids were increased in serum phospholipids ( $P < 0.001$ ), the ratio of arachidonic acid to eicosapentaenoic acid decreased ( $P < 0.001$ ), and the level of n-6 fatty acids decreased ( $P < 0.001$ ). In the corn-oil group, only docosahexaenoic acid increased significantly ( $P < 0.05$ ). The ratio of polyunsaturated to saturated fatty acids increased in both groups. Plasma concentrations of triacylglycerol decreased from base line in the fish-oil group ( $P < 0.05$ ). The score on the Psoriasis Area and Severity Index, as evaluated by the physicians, did not change significantly during the trial in either group. This was also true of a total subjective score reported by the patients, but a selected area of skin in the corn-oil group showed a significant reduction in the clinical signs ( $P < 0.05$ ). Scaling was reduced from base line in both groups ( $P < 0.01$ ). The fish-oil group had less cellular infiltration ( $P < 0.01$ ), and the corn-oil group had improvement in desquamation and redness ( $P < 0.05$ ). There was no significant difference in clinical manifestations between the groups. Among the patients in the fish-oil group, an increase in the concentration of n-3 fatty acids in serum phospholipids was not accompanied by clinical improvement, whereas in the corn-oil group there was a significant correlation between clinical improvement and an increase in eicosapentaenoic acid and total n-3 fatty acids. **CONCLUSIONS.** Dietary supplementation with very-long-chain n-3 fatty acids was no better than corn-oil supplementation in treating psoriasis. Clinical improvement was not correlated with an increase in the concentration of n-3 fatty acids in serum phospholipids among the patients in the fish-oil group, whereas there was a significant correlation between clinical improvement and an increase in eicosapentaenoic acid and total n-3 fatty acids in the corn-oil group.

Escobar SO, Achenbach R, Iannantuono R, Torem V. **Topical fish oil in psoriasis--a controlled and blind study.** Clin Exp Dermatol. 1992 May;17(3):159-62.

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Omega-3 polyunsaturated fatty acids compete with arachidonic acid as substrates for lipoperoxidases, which transform them into leukotrienes with low biological activity. As this process, in skin, may benefit psoriatic patients, a randomized controlled single blind-study was carried out on a sample of 25 patients. In the study fish oil (FO) was compared with liquid paraffin (LP); both were topically applied and administered daily for 6 h under an occlusive dressing over a 4-week period. Evaluations were performed weekly assessing erythema, scaling, plaque thickness (induration) and itching. The results showed statistically significant improvement in erythema and scaling for both treatments compared to basal values; significant differences between treatments were achieved in scaling but not in erythema. Compared to baseline, FO significantly improved plaque thickness while LP did not. After 4 weeks, FO proved to be significantly better than LP. All patients accepted the treatment despite its unpleasant smell. Irritation and a burning sensation were reported in the FO treated plaque of one patient. This adverse effect reverted after completing the treatment. These findings demonstrate that topical FO shows a better performance than LP under an occlusive dressing.

Kojima T, Terano T, Tanabe E, Okamoto S, Tamura Y, Yoshida S. **Long-term administration of highly purified eicosapentaenoic acid provides improvement of psoriasis.** Dermatologica. 1991;182(4):225-30.

Department of Dermatology, Chiba University School of Medicine, Japan.

Nine patients with chronic stable psoriasis (4 males and 5 females) were entered in this trial. Eicosapentaenoic acid (EPA) ethylester (90% pure) without docosahexaenoic acid (DHA) in gelatin-coated capsules at a daily dose of 3.6 g was administered to 9 patients for 3 months, 7 patients for 6 months and 6 patients for 12 months. The clinical changes of skin lesions of the patients with 12 months of treatment were as follows: marked improvement 1, improvement 3, relative improvement 1, no change 1. A clinical improvement of skin lesions was first observed 2-3 months after EPA treatment. The supplementation of highly purified EPA caused a significant increase in the content of plasma EPA and docosapentaenoic acid without affecting that of arachidonic acid (AA) and DHA. EPA decreased the production of leukotriene B4 (LTB4) and increased the formation of leukotriene B5 (LTB5) and 5-hydroxyeicosapentaenoic acid significantly in A23187-stimulated neutrophils. The LTB5/LTB4 ratio positively correlated with the plasma EPA/AA ratio and was directionally related to the clinical score, although the directional data were not statistically significant. We could not observe any side effects of EPA over 1 year. Although its effects are modest, it is nontoxic and its favorable effect appears to continue for the duration of its usage, indicating that EPA could be beneficial for the long-term treatment of psoriasis.

Wilkinson DI. **Do dietary supplements of fish oils improve psoriasis?** *Cutis*. 1990 Oct;46(4):334-6.

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In theory, a number of skin and systemic diseases with an inflammatory component should be improved by dietary intake of certain polyunsaturated fatty acids, usually of marine origin. The most significant is eicosapentaenoic acid, which may substitute for arachidonic acid in tissue. Inflammation mediators derived from the former compound are much less active biologically, and also can inhibit the chemotactic behavior of leukotrienes derived from arachidonic acid. **A number of studies have appeared describing the effects of such dietary manipulation in patients with psoriasis. Some reports credit fish oil ingestion with moderate improvement of the disease, but problems in the design of these studies have led to criticism of the results.**

Berbis P, Hesse S, Privat Y. **[Essential fatty acids and the skin]** *Allerg Immunol (Paris)*. 1990 Jun;22(6):225-31. [Article in French]

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Metabolism of the essential fatty acids (AGE) in an organism leads to synthesis of eicosanoids, which have various biological properties. Linoleic acid plays an important part in maintenance of epidermal integrity by intervening in the cohesion of the stratum corneum and in prevention of transepidermal water loss. Metabolites of arachidonic acid (mostly those obtained by the lipoxygenase pathway) are important agents in causing many inflammatory skin reactions concurrent with development of skin diseases such as psoriasis and atopic dermatitis. Pharmacological and dietetic control of the metabolism of arachidonic acid is a new and interesting therapeutic concept in the care of skin diseases. **Also, fish oil, which is rich in linoleic acid and poor in arachidonic acid, seems to be useful in basal treatment of psoriasis.** The value of evening primrose oil, which is rich in gamma-linoleic acid, in the treatment of atopic dermatitis is discussed.



Klemeyer-Smith A, Thune PO, Bjorneboe GE. **[New aspects of the treatment of psoriasis]** Tidsskr Nor Laegeforen. 1990 May 30;110(14):1817-9. [Article in Norwegian]

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Psoriasis is an inflammatory condition of the skin which affects about 2% of the population. Several new treatment modalities have been introduced in recent years. This review considers the mode of action of various forms of treatment, side effects and therapeutic results that have been observed. Etretinate is a synthetic vitamin A analogue. It works alone, or even better in combination with psoralen plus ultraviolet light A (PUVA) or ultraviolet light B (UVB). Cyclosporin is still on trial, but seems to be effective in small doses and can be considered as an alternative in cases of psoriasis that are resistant to other therapies. **The interest in dietary measures for psoriasis has been revived after some studies have suggested that dietary supplements of fish oil, a low-fat diet, can improve the condition. Now that n-3-fatty acids are available in capsule form it should be possible to prescribe a diet that is rich enough in fish oils.**

Ziboh VA. **Implications of dietary oils and polyunsaturated fatty acids in the management of cutaneous disorders.** Arch Dermatol. 1989 Feb;125(2):241-5.

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A major proinflammatory metabolite of arachidonic acid, leukotriene B<sub>4</sub>, is known to accumulate in the lesions of psoriasis. Most of this metabolite is biosynthesized by the polymorphonuclear cells that infiltrate into the psoriatic lesions. Epidermal 15-lipoxygenase, on the other hand, metabolizes arachidonic acid into 15-hydroxyeicosatetraenoic acid (15-20:4n-6), presumably serving as a negative feedback to inhibit the local generation of leukotriene B<sub>4</sub>. Eicosapentaenoic acid, a major polyunsaturated fatty acid in fish oil, and gamma-linolenic acid, a poly-unsaturated fatty acid in certain vegetable oils, are both metabolized by epidermal 15-lipoxygenase into 15-hydroxyeicosapentaenoic acid (15-OH-20:5n-3) and 15-hydroxyeicosatriaenoic acid (15-OH-20:3n-3), respectively. Both of these monohydroxy acids are potent in vitro inhibitors of leukotriene B<sub>4</sub> generation. **It seems reasonable, therefore, that adequate dietary supplementation with eicosapentaenoic acid or gamma-linolenic acid may offer a novel and nontoxic approach to suppressing cutaneous inflammatory disorders.**

Kettler AH, Baughn RE, Orengo IF, Black H, Wolf JE Jr. **The effect of dietary fish oil supplementation on psoriasis. Improvement in a patient with pustular psoriasis.** J Am Acad Dermatol. 1988 Jun;18(6):1267-73.

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An open study testing the effects of fish oil supplementation on psoriasis in 26 patients is described. None of the patients with plaque-type psoriasis vulgaris showed clinically significant improvement; however, a patient with generalized pustular psoriasis showed marked improvement with the fish oil supplementation. In this patient, scale leukotriene B4 levels were determined and shown to be significantly decreased after completion of the study, but the leukotriene B4 levels did not correlate with her clinical course. The results of our study are contrasted with those of a recent study that did show beneficial effects of fish oil supplementation on plaque-type psoriasis.

Wolters M. **Diet and psoriasis: experimental data and clinical evidence.** Br J Dermatol. 2005 Oct;153(4):706-14.

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Psoriasis is considered as a T-cell-mediated inflammatory skin disease which is characterized by hyperproliferation and poor differentiation of epidermal keratinocytes. While susceptibility to psoriasis is inherited, the disease is influenced by environmental factors such as infections and stress. Diet has been suggested to play a role in the aetiology and pathogenesis of psoriasis. Fasting periods, low-energy diets and vegetarian diets improved psoriasis symptoms in some studies, and diets rich in n-3 polyunsaturated fatty acids from fish oil also showed beneficial effects. All these diets modify the polyunsaturated fatty acid metabolism and influence the eicosanoid profile, so that inflammatory processes are suppressed. Some patients with psoriasis show an elevated sensitivity to gluten. In patients with IgA and/or IgG antigliadin antibodies the symptoms have been shown to improve on a gluten-free diet. The active form of vitamin D, 1,25-dihydroxyvitamin D(3), exhibits antiproliferative and immunoregulatory effects via the vitamin D receptor, and thus is successfully used in the topical treatment of psoriasis. In this review, dietary factors which play a role in psoriasis are assessed and their potential benefit is evaluated. Furthermore, the risk of drug-nutrient interactions in psoriasis therapy is discussed.

Mayser P, Grimm H, Grimminger F. **n-3 fatty acids in psoriasis.** Br J Nutr. 2002 Jan;87 Suppl 1:S77-82.

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Increased concentrations of free arachidonic acid (AA) and its proinflammatory metabolites have been observed in psoriatic lesions. Replacement of arachidonic acid by alternative precursor polyunsaturated fatty acids (PUFA), especially eicosapentaenoic acid (EPA), which can be metabolized via the same enzymatic pathways as AA, might be a therapeutic option in psoriasis. However the results of studies evaluating the therapeutic benefit of dietary fish oil have been conflicting and not clearly dose-dependent. To overcome the slow kinetics and limited availability of oral supplementation, we have performed three studies to assess the efficacy and safety of an intravenously administered fish oil derived lipid emulsion on different forms of psoriasis. Patients received daily infusions of either an n-3 fatty acid-based lipid emulsion (Omegaven) or a conventional n-6 lipid emulsion (Lipoven) in different time and dose regimens. In addition to an overall assessment of the clinical course of psoriasis, EPA- and AA-derived neutrophil 5-lipoxygenase (LO)--products, thromboxane (TX) B2/B3, PAF and plasma free fatty acids were investigated. Treatment with n-3 fatty acids resulted in a considerably higher response rate than infusion of n-6 lipids. A more than 10-fold increase in neutrophil EPA-derived 5-LO product formation was noted in the n-3 group, accompanied by a rapid increase in plasma-free EPA within the first days. In conclusion, **intravenous n-3-fatty acid administration causes reduction of psoriasis**, which may be related to changes in inflammatory eicosanoid generation. The rapidity of the response to intravenous n-3 lipids exceeds by orders of magnitude the hitherto reported kinetics of improvement of psoriatic lesions upon use of oral supplementation.

Mayser P, Mrowietz U, Arenberger P, Bartak P, Buchvald J, Christophers E, Jablonska S, Salmhofer W, Schill WB, Kramer HJ, Schlotzer E, Mayer K, Seeger W, Grimminger F. **Omega-3 fatty acid-based lipid infusion in patients with chronic plaque psoriasis: results of a double-blind, randomized, placebo-controlled, multicenter trial.** J Am Acad Dermatol. 1998 Apr;38(4):539-47.

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**BACKGROUND:** Profound changes in the metabolism of eicosanoids with increased concentrations of free arachidonic acid (AA) and its proinflammatory metabolites have been observed in psoriatic lesions. Free eicosapentaenoic acid (EPA) may compete with liberated AA and result in an antiinflammatory effect. **OBJECTIVE:** Our purpose was to assess the efficacy and safety of intravenously administered fish-oil-derived lipid emulsion on chronic plaque-type psoriasis. **METHODS:** A double-blind, randomized, parallel group study was performed in eight European centers. Eighty-three patients hospitalized for chronic plaque-type psoriasis with a severity score of at least 15 according to the Psoriasis Area and Severity Index (PASI) participated in a 14-day trial. They were randomly allocated to receive daily infusions with either a omega-3 fatty acid-based lipid emulsion (Omegavenous; 200 ml/day with 4.2 gm of both EPA and docosahexaenoic acid (DHA); 43 patients) or a conventional omega-6-lipid emulsion (Lipovenous; EPA+DHA < 0.1 gm/100 ml; 40 patients). The groups were well matched with respect to demographic data and psoriasis-specific medical history. Efficacy of therapy was evaluated by changes in PASI, in an overall assessment of psoriasis by the investigator, and a self-assessment by the patient. In one center neutrophil 4- versus 5-series leukotriene (LT) generation and platelet 2- versus 3- thromboxane generation were investigated and plasma-free fatty acids were determined. **RESULTS:** The total PASI score decreased by 11.2 +/- 9.8 in the omega-3 group and by 7.5 +/- 8.8 in the omega-6 group (p = 0.048). In addition, the omega-3 group was superior to the omega-6 group with respect to change in severity of psoriasis per body area, change in overall erythema, overall scaling and overall infiltration, as well as change in overall assessment by the investigator and self-assessment by the patient. Response (defined as decrease in total PASI of at least 50% between admission and last value) was seen in 16 of 43 patients (37%) receiving the omega-3 emulsion and 9 of 40 patients (23%) receiving omega-6 fatty acid-based lipid emulsion. No serious side effects were observed. Within the first few days of omega-3 lipid administration, but not in the omega-6 supplemented patients, a manifold increase in plasma-free EPA concentration, neutrophil leukotriene B5 and platelet thromboxane B3 generation occurred. **CONCLUSION:** Intravenous omega-3-fatty acid administration is effective in the treatment of chronic plaque-type psoriasis. This effect may be related to changes in inflammatory eicosanoid generation.

Oliwiecki S, Burton JL. **Evening primrose oil and marine oil in the treatment of psoriasis.** Clin Exp Dermatol. 1994 Mar;19(2):127-9.

Department of Dermatology, Bristol Royal Infirmary, UK.

The effect of dietary supplementation with a combination of n-3 (marine oil) and n-6 (evening primrose oil) essential fatty acids in the treatment of chronic stable plaque psoriasis was observed. Thirty-seven patients in a double-blind parallel trial were studied. There was no significant improvement in clinical severity of psoriasis or change in transepidermal water loss.

Henneicke-von Zepelin HH, Mrowietz U, Farber L, Bruck-Borchers K, Schober C, Huber J, Lutz G, Kohlen R, Christophers E, Welzel D. **Highly purified omega-3-polyunsaturated fatty acids for topical treatment of psoriasis. Results of a double-blind, placebo-controlled multicentre study.** Br J Dermatol. 1993 Dec;129(6):713-7.

Department of Dermatology, University of Kiel, Germany.

We report the results of a multicentre, double-blind, placebo-controlled study of topical therapy with omega-3-polyunsaturated fatty acids (omega-3-PUFA) in 52 patients suffering from moderate plaque-type psoriasis. In each patient, two similar stable psoriatic plaques served as indicator lesions for the study. One indicator lesion was randomly assigned to treatment with topical preparations of highly purified omega-3-PUFA in one of two concentrations (1 or 10%), and the other was treated with placebo. Efficacy assessment was based on changes in local psoriasis severity index, area involved, erythema, desquamation, induration and pruritus. After 8 weeks of treatment, all indicator lesions had improved significantly, compared with baseline. However, **no statistically or clinically relevant differences between the omega-3-PUFA-treated and the placebo-treated lesions were found.** Therapy was well tolerated and, apart from one patient who developed perilesional eczema, no clinically relevant adverse events occurred. In conclusion, topical omega-3-PUFA were not effective in a randomized, placebo-controlled, double-blind setting. Results of non-blind trials should be (re-) considered with caution.

Collier PM, Ursell A, Zaremba K, Payne CM, Staughton RC, Sanders T. **Effect of regular consumption of oily fish compared with white fish on chronic plaque psoriasis.** Eur J Clin Nurt. 1993 Apr;47(4):251-4.

Department of Dermatology, Westminster Hospital, London, UK.

The influence of dietary advice on the severity of chronic plaque psoriasis was studied in 18 patients. Medication was standardized in all patients who were advised to eat 170 g white fish daily for a 4 week run-in period. Then the patients were randomized either to continue with the white fish diet or to substitute 170 g oily fish daily for 6 weeks. At the end of this second period the diets were reversed for a further 6 weeks. The oily fish but not the white fish diet led to a modest clinical improvement (11% and 15%,  $P < 0.01$ ) which was accompanied by a rise in plasma eicosapentaenoic acid (20:5n-3) concentrations. It is concluded that dietary advice to increase the daily intake of oily fish is a useful adjunct in the treatment of psoriasis. The fish that should be recommended include mackerel, sardine, salmon, pilchard, kipper and herring.

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 Oct;29(8):591-5.

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In a randomized, double-blind, placebo-controlled study, patients received 10 fish or olive oil capsules three times daily for the whole study in addition to applying betamethasone dipropionate to their psoriatic plaques for the first 3 weeks. Most patients gradually worsened upon discontinuation of corticosteroids. Using survival analysis methods, no significant difference was found between the fish and olive oil groups. The authors attempt to put the role of fish oil in the therapy of psoriasis into perspective and discuss the efficacy of fish oil when used alone versus in combination therapy.

Gupta AK, Ellis CN, Tellner DC, Anderson TF, Voorhees JJ. **Double-blind, placebo-controlled study to evaluate the efficacy of fish oil and low-dose UVB in the treatment of psoriasis.** Br J Dermatol. 1989 Jun;120(6):801-7.

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Since eicosanoids have been implicated in the pathogenesis of psoriasis, less potent eicosanoid mediators derived from fish oil might improve psoriasis. Using a double-blind, randomized, parallel design, 18 patients with stable, plaque psoriasis received capsules of either fish oil or identical-appearing placebo olive oil for 15 weeks, with concomitant sub-erythral UVB in weeks 3 to 11. At the conclusion of phototherapy, and 4 weeks later, patients in the fish oil group had a greater decrease in the total body surface area of psoriasis and more improvement compared to patients in the olive oil group. **The improvement in the fish oil group was statistically significantly greater for all parameters compared to the change in the olive oil group. The apparent safety and general health-promoting features of fish oil could provide an ideal adjunctive therapy for psoriasis.**

Kragballe K. **Dietary supplementation with a combination of n-3 and n-6 fatty acids (super gamma-oil marine) improves psoriasis.** Acta Derm Venerol. 1989;69(3):265-8.

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Psoriasis may improve during dietary supplementation with fish oil containing n-3 fatty acids including eicosapentaenoic acid. In the present study 17 psoriatic patients were treated with Super Gamma-Oil Marine containing a combination of n-3 and n-6 fatty acids (linoleic acid and gammalinolenic acid). After 4 months, excellent improvement was observed in 2 patients, moderate improvement in 8, mild improvement in 4, and no improvement in 3 patients. **These results may indicate that a combination of n-3 and n-6 fatty acids is useful for the treatment of psoriasis. However, controlled studies including more patients are warranted.**

Isseroff RR. **Fish again for dinner! The role of fish and other dietary oils in the therapy of skin disease.** J Am Acad Dermatol. 1988 Dec;19(6):1073-80.

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Adequate levels of polyunsaturated fatty acids are necessary for the normal functioning of most mammalian cells, both to provide fluidity to the cell membrane lipid bilayer and to function as precursors for the synthesis of the regulatory eicosanoids, prostaglandins, and leukotrienes. The omega-6 class of polyunsaturated fatty acids, such as linoleic and arachidonic acids, are of special importance as precursors for eicosanoid synthesis. The skin is a particularly good organ in which to study the effects of polyunsaturated fatty acids metabolism, inasmuch as either deficiencies of specific PUFA or overproduction of polyunsaturated fatty acids-derived prostaglandin and leukotriene result in specific, clinically recognizable cutaneous diseases. To help understand the pathogenesis of these diseases, polyunsaturated fatty acids metabolism is reviewed here, with emphasis on clinical manifestations of both deficiency syndromes and overproduction of proinflammatory eicosanoids. A rationale is presented for a therapeutic approach to inflammatory disease by dietary manipulation and substitution of omega-6 fatty acids by the unique omega-3 class of polyunsaturated fatty acids found in fish. Evidence for the efficacy of fish oil in the therapy of specific inflammatory diseases is reviewed, as are the caveats regarding its therapeutic use. **Dietary manipulations, specifically fish oil additives, appear to hold promise as therapeutic tools for cutaneous diseases.**



van Gool CJ, Zeegers MP, Thijs C. **Oral essential fatty acid supplementation in atopic dermatitis-a meta-analysis of placebo-controlled trials.** Br J Dermatol. 2004 Apr;150 (4):728-40.

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**BACKGROUND:** Essential fatty acids are components of cell membranes and precursors of immunomodulating factors that may play a role in the inflammatory and immunological pathogenesis of atopic dermatitis. Trials of supplementation with essential fatty acids (EFA) to alleviate atopic dermatitis (AD) have given inconsistent results. **OBJECTIVES:** To summarize and quantify the results of placebo-controlled trials with EFA for AD. **DESIGN:** Publications of clinical trials were searched in a systematic way and the study characteristics assessed independently by three assessors. Trials were selected for inclusion in the meta-analysis when they had included a placebo group and when the outcome measure included the severity of AD. The pooled effect sizes of improvement of the overall severity of AD were calculated by random effects meta-analysis. The dependence of the results on study characteristics was studied using meta-regression analysis. **RESULTS:** We identified 34 publications of controlled trials in AD up to April 2002. Nineteen trials of gamma-linolenic acid (GLA) and five trials of fish oil matched our inclusion criterion of placebo-controlled trial. The effect size of GLA supplementation on the improvement of the overall severity of AD could be calculated from 11 of these trials. The pooled effect size was 0.15 [95% confidence limits (CL) - 0.02, 0.32]. The effect size of fish oil supplementation, calculated from three trials was - 0.01 (95% CL - 0.37, 0.30). For component subscales such as itch, scaling and lichenification, EFA supplementation showed no benefit. The study characteristics showed no detectable influence on the overall result. **CONCLUSIONS:** **Supplementation with EFA has no clinically relevant effect on the severity of AD.**

Trak-Fellermeier MA, Brasche S, Winkler G, Koletzko B, Heinrich J. **Food and fatty acid intake and atopic disease in adults.** Eur Respir J. 2004 Apr;23(4):575-82.

<http://erj.ersjournals.com/cgi/reprint/23/4/575>

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The aim of the study was to assess the relationship between dietary intake of selected foods and fatty acids with atopic disease prevalence in adults. Data from the European Community Respiratory Health Survey in Erfurt, combined with a 3-day weighed records dietary survey, was used. Complete data was available from 469 males and 333 females aged 20-64 yrs. Multiple logistic regression was applied comparing the highest with the lowest quartile of dietary exposures and linear trends were tested stratified by sex. In males, margarine intake and a high ratio of omega-6 to omega-3 fatty acids were positively associated with hay fever. In females, a high intake of total fat, palmitoleic and oleic acids were positively associated with sensitisation. A high total fat, high monounsaturated fatty acid and high oleic acid consumption were positively associated with hay fever. Whilst an excessive intake of fat or imbalance in fat intake, particular of monounsaturated fatty acids, increased the risk for hay fever and allergic sensitisation in females, mostly no significant associations were found for males. **Dietary factors were mostly not related with prevalence rates of bronchial hyperresponsiveness and atopic eczema either in males or in females.**

Berth-Jones J, Graham-Brown RA. **Placebo-controlled trial of essential fatty acid supplementation in atopic dermatitis.** Lancet. 1993 Jun 19;341(8860):1557-60.

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Treatment of atopic dermatitis with essential fatty acids remains controversial. A double-blind, placebo-controlled, parallel-group study was done to investigate the response of patients with atopic dermatitis to essential fatty acid supplements. Patients with atopic dermatitis were randomised to receive evening primrose oil, evening primrose oil and fish oil, or placebo for 16 weeks. Disease activity was monitored by clinical severity scores recorded by the investigator, topical steroid requirement, and symptom scores recorded by subjects. Of 123 subjects recruited, 102 completed the treatment period. No improvement with active treatment was demonstrated. Our study, which avoided the methodological and analytical problems of previous studies, found **no effect of essential fatty acid supplementation in atopic dermatitis.**

Bjorneboe A, Soyland E, Bjorneboe GE, Rajka G, Drevon CA. **Effect of dietary supplementation with eicosapentaenoic acid in the treatment of atopic dermatitis.** Br J Dermatol. 1987 Oct;117(4):463-9.

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The effects of a dietary supplement of n-3 fatty acids in patients with atopic dermatitis were investigated in a 12-week, double-blind study. The experimental group received 10 g of fish oil daily, of which about 1.8 g was eicosapentaenoic acid. This amount of eicosapentaenoic acid can be obtained from a daily intake of fat fish. The controls received an iso-energetic placebo supplement containing olive oil. Compliance was monitored by gas-chromatographic analysis of the fatty acid pattern in serum phospholipids. Results favoured the experimental group with regard to scale (P less than 0.05), itch (P less than 0.05) and overall subjective severity (P less than 0.02) as compared to the controls.

Bjorneboe A, Smith AK, Bjorneboe GE, Thune PO, Drevon CA. **Effect of dietary supplementation with n-3 fatty acids on clinical manifestations of psoriasis.** Br J Dermatol. 1988 Jan;118(1):77-83.

Department of Dermatology, Ulleval University Hospital, Oslo, Norway.

In a double-blind, block randomized study we investigated the effect of dietary supplementation with eicosapentaenoic acid in patients with psoriasis. The experimental group received 10 g of fish oil daily containing approximately 1.8 g eicosapentaenoic acid, while the controls were given an isoenergetic amount of olive oil. We found no significant change in the clinical manifestations of psoriasis in either group after 8 weeks of treatment. In the experimental group, the amount of n-3 fatty acids in serum phospholipids was significantly increased at the end of trial as compared to pre-treatment values, whereas the level of n-6 fatty acids was decreased.