Treating Psoriasis with Fish Oil

Biological Adjuvant Therapy Yields Good Test Results

by Dr. phil. nat. Wolfgang Rothe
1. Introduction
Psoriasis is an autosomally dominant hereditary disease. Approximately 1–2% of the population suffers from this inflammatory dermatosis, the etiology of which remains largely unknown. Based on epidemiological findings regarding new therapeutic aspects, statistical surveys show that psoriasis is twenty times more common in Europeans than Eskimos.14,18

This remarkable difference is attributed to the unique Eskimo diet (under their traditional way of life) that includes a high proportion of maritime food (seals, whales, fish).3,10 These foods are characterized by a high content of n-3 fatty acids (EPA and DHA). At the same time, their intake of n-6 fatty acids is quite low. Consequently, the ratio of n-3 to n-6 fatty acids is sharply tilted toward the former. This is then reflected in the composition of the blood and tissue lipids. The elevated n-3/n-6 quotient seems to be typical for populations who eat a lot of fish, such as Eskimos and Japanese fisherfolk.

2. Biochemical Basis
With the aid of the enzyme 5-lipoxygenase, the strongly inflammation-promoting leukotrienes of the so-called “Four Series” (leukotriene B₄, C₅, and D₅) and 15-hydroxyeicosapentaenoic acid (15-HEPE) are formed, of which leukotriene B₅ in particular has only 10% of the inflammatory potential of the “Four Series” leukotrienes. Moreover, LTB₄ and 15-HEPE are considered inhibitors of LTB₄. As a result of this, the concentration of strong-acting LTB₄ is lower when EPA is present than when this competing fatty acid is absent.

It is possible that the ratio of leukotrienes B₄ and B₅ is more significant than the absolute concentrations of the individual components. This would parallel the behavior of the prostaglandins I₂ and I₃, or the thromboxanes A₂ and A₃, whose relationship with each other has a decisive influence on blood clotting and thus on the occurrence of arteriosclerosis.

Psoriasis foci contain abundant polymorphic acinous leukocytes that are responsible for the release inflammation mediators.5,6,19 Since psoriasis is an inflammatory dermatosis, its inflammatory component is in the forefront of pathogenic considerations and therapeutic consequences. In psoriatic foci, the concentration of arachidonic acid, 12-HETE and LTB₄, as substrates or products of the lipoxygenase reaction is sharply elevated.7,11,13 Enzyme preparations from psoriatic tissue exhibit increased synthesis of 12-HETE and LTB₄ from arachidonic acid.11

The activity of glutathion peroxidase in erythrocytes and thrombocytes is also significantly higher than the norm (p < 0.001 or < 0.02). Furthermore, increased formation of malonaldehyde was observed in psoriasis patients (p < 0.001).8

After taking fish oil for two months (approx. 1.9 g EPA and 2.5 g DHA per day), the patients’ malonaldehyde level in both cell types was down (p < 0.001) and the activity of glutathion peroxidase was further elevated (p < 0.001)8. The authors conclude that EPA leads to a competitive reduction in lipoxygenation of arachidonic acid. This explains the positive effects of fish oil in the treatment of psoriasis.

Conversely, intracutaneous injections of products of 5-lipoxygenase (LTB₄, LTC₄, LTD₄ and LTE₄) into normal skin lead to inflammation reactions such as erythema and the infiltration of neutrophilic leukocytes.24 In addition, the local application of LTB₄ on normal skin in concentrations such as those shown to be present in psoriatic foci led to intraepidermal microabscesses that resemble characteristic histological psoriasis.7

Logically, substances that block the cyclooxygenase pathway that competes for the substrate arachidonic acid would have to increase the proportion of the inflammation-promoting mediators formed via the lipoxygenase pathway, and thereby lead to a deterioration of the psoriasis symptoms, insofar as only n-3 fatty acids are supplied. In fact, the course of the disease was aggra-
In human keratocyte cultures with LTB4 concentrations of $10^{-12}$ to $10^{-8}$ M, a 100% increase in DNA synthesis and increased proliferation of these cells was able to be demonstrated. In general, the leukotrienes LTB$_4$, LTC$_4$, and LTD$_4$ proved to be potent mitogens - i.e. they promoted inflammation-conditioned proliferation. In contrast to this, the LTB$_5$ formed from EPA via the lipoxygenase pathway has a more weakly chemotactic effect and is moreover a weaker stimulator of keratocyte proliferation.

It is thus pathophysiologically natural to consider making therapeutic use of a possible suppression of the arachidonic acid content in the membrane phospholipids by supplying EPA in the diet, with the goal of thereby suppressing at least the inflammatory components of psoriasis. Therefore, anti-proliferative substances such as Methotrexat, Anthralin, retinoids and glucocorticosteroids are made use of to suppress, locally and systematically, inflammatory phenomena and cell multiplication.

Irradiation with UV-B light has the same goal, as does combined phototherapies with a sensitizing psoralen and UV-A light (so-called PUVA treatment). However, these forms of therapy are associated with more or less pronounced side-effects. There has thus been no lack of efforts to suppress the formation of the pro-inflammatory 12-HETE and LTB$_4$, which are so abundantly present in psoriatic foci, with lipoxygenase inhibitors.

The systematic application of the substance Benoxaprofen, a non-steroidal anti-inflammatory substance with an inhibitory effect, both on cyclooxygenase and on lipoxygenase, yielded impressive clinical improvements of psoriasis findings. These results support the hypothesis that the mediators (formed via the 5-lipoxygenase pathway) for the inflammatory components of psoriasis have a crucial pathogenic significance.

Although the strong side-effects made it necessary to terminate Benoxaprofen treatments, at the same time, the excellent results with this model substance triggered

<table>
<thead>
<tr>
<th>Author</th>
<th>Case count</th>
<th>Oil dosage (g/day)</th>
<th>EPA dosage (g/day)</th>
<th>DHA dosage (g/day)</th>
<th>Result</th>
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<tr>
<td>Allen, 1985*</td>
<td>8</td>
<td>50</td>
<td>9.0</td>
<td>6.0</td>
<td>+</td>
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<tr>
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<td>13</td>
<td>60-75</td>
<td>10.8-13.5</td>
<td>7.2-9.0</td>
<td>+</td>
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<tr>
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<td>10</td>
<td>25-50</td>
<td>4.5-9.0</td>
<td>6.0</td>
<td>+</td>
</tr>
<tr>
<td>Bittner, 1988**</td>
<td>14</td>
<td>10</td>
<td>1.8</td>
<td>1.2</td>
<td>+</td>
</tr>
<tr>
<td>Bjorneboe, 1988**</td>
<td>15</td>
<td>10</td>
<td>1.8</td>
<td>1.2</td>
<td>-</td>
</tr>
<tr>
<td>Lowe, 1988**</td>
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<td>10</td>
<td>1.8</td>
<td>1.2</td>
<td>-</td>
</tr>
<tr>
<td>Kettler, 1988*</td>
<td>25</td>
<td>18</td>
<td>3.2</td>
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<tr>
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<td>26</td>
<td>30</td>
<td>5.4</td>
<td>3.6</td>
<td>-</td>
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<tr>
<td>Gupta, 1989*</td>
<td>18</td>
<td>20</td>
<td>3.6</td>
<td>2.4</td>
<td>-</td>
</tr>
<tr>
<td>Linzer, 1989**</td>
<td>60</td>
<td>9</td>
<td>1.6</td>
<td>1.0</td>
<td>-</td>
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</tbody>
</table>

* Open study, ** Controlled study, (+) clear improvement in only one case with pustular psoriasis

Table 1: Clinical studies with fish oil in psoriasis cases (overview)
efforts to pursue this therapeutic approach further. Accordingly, the search for substances with lower side-effects, but with the same therapeutic effectiveness was begun. Based on the described epidemiological and experimental findings, it seemed logical to start with the long-chain n-3 fatty acids (EPA and DHA) used in psoriasis treatment; these are present in high-seas fish oils: herring, mackerel, sardines. The synthesis of mediators formed from arachidonic acid was to be reduced by competitive inhibition and at the same time replaced by benign mediators, without having to worry about significant side-effects.

3. Clinical Results
A positive influence was demonstrated for fish oil in patients with various forms of psoriasis\textsuperscript{2,4,12,16,23,32}. 10-20 ml of fish oil (1.1-3.6 g eicosapentaenoic acid) per day turns out to be a sufficient dosage. Overall, improvement of psoriasis symptoms along with reduced formation of LTB\textsubscript{4} in polymorphic acinous leukocytes\textsuperscript{23} was observed. The results of all these studies are summarized in Table 1. The fish oil was observed to have been especially effective in the pustular form of psoriasis (cited in\textsuperscript{25}). In individual cases, astonishing effects were observed even for widespread psoriasis foci.

In an open study involving 8 patients with acute psoriasis who had not responded to conventional therapy, 50 ml of fish oil per day for three months led to a slight improvement of psoriasis symptoms in seven out of eight cases\textsuperscript{2}. Also, a 50\% increase in the EPA/AA ratio in the plasma, a sevenfold increase in the EPA/AA ratio in the thrombocytes and a significant decline in LTB\textsubscript{4} formation (p < 0.013) were noted. Further investigation confirmed proof of LTB\textsubscript{4} and a reduction of LTB\textsubscript{4} in polymorphic acinous leukocytes.

In another open study, 13 patients with psoriasis\textsuperscript{32} received 60 ml of fish oil per day for eight weeks. Eight of the study participants showed clinical improvement of the psoriasis symptomatology. Two patients with psoriatic arthritis also had clear symptomatic improvement. Five patients reported a clear diminution of their pruritus as well. The improvement in psoriasis symptoms correlated significantly with an increase in the EPA/AA quotient in the epidermis (determined from skin biopsies). Generally, the best clinical results were achieved in those patients exhibiting a high incorporation of EPA and DHA into the epidermal lipids - a clear indication of the causal connection between biochemical effects and clinical effectiveness.

In yet another open study, Maurice et al.\textsuperscript{23} noted, in eight out of ten patients with extensive psoriasis (infestation of 5-60\% of body surface), after a six-week treatment with 25-50 g of fish oil per day, only a moderate clinical improvement (decline in erythema and scaling), even though LTB\textsubscript{4} formation in the polymorphic acinous leukocytes of the peripheral blood in vitro had demonstrably gone down. The spread of the foci was barely affected. Two patients with no change in findings showed only small increases in the EPA/arachidonic acid quotient in the plasma lipids, so that their compliance was questionable.

There is evidently a discrepancy between the clinical appearance and the changes in the LTB\textsubscript{4} values in the polymorphic acinous leukocytes in vitro. From this, it was concluded that, on the one hand, there is in vivo probably not a tight correlation between the LTB\textsubscript{4} concentrations in the blood cells and those in the epidermis, and that, on the other hand, LTB\textsubscript{4} is possibly not the only pathogenic factor for the origin of psoriasis foci.

In a random placebo-controlled double-blind study involving 14 patients with chronic stationary psoriasis\textsuperscript{4}, 10 g of fish oil per day was administered for 12 weeks. Standard local therapy was maintained. The 14 psoriasis patients of the placebo group received, over the same time period, 10 capsules filled with olive oil. At four-week intervals, the degree of severity of the following symptoms was determined: itching (patient self-evaluation), erythema, scaling and the area of infested body surface, using a rating scale of 0 to 5. The results are summarized in Table 2.

Of the patients who received fish oil, after 8 and 12 weeks, a significant easing of the itching compared to the initial condition was noted. In the placebo group, however, there was no improvement in the symptomatology. After 8 weeks, there was - compared to the placebo group - a significant easing of the itching (p < 0.05). After 12 weeks, this difference was no longer
In a random double-blind study of 20 patients with chronic stationary psoriasis, the following study design was used: one group of 9 patients received 20 fish-oil capsules, containing 3.6 g of EPA and 24 g of DHA, per day. The control group (11 patients) received 20 olive-oil capsules per day. After 3 weeks, for the next 8 weeks each group additionally received suberythemal UV-B radiation; after an additional 4 weeks, the study was ended. Eight patients of the verum group and ten patients of the placebo group remained at the end of the study.

While there was only a moderate improvement in the first 3 weeks, when only the fish oil was administered, combining it with ultraviolet radiation therapy led to a clear improvement of the disease picture in the verum group (erythema, infiltration, scaling and infested skin area). The difference relative to the placebo group was significant (p < 0.05). Four weeks after the end of the study, the fish-oil group improved even more, while the placebo group got noticeably worse (p < 0.0001). The authors therefore recommend a combination therapy of fish oil and UV-B radiation.

The most comprehensive study to date was carried out by Linker et al. in 20 patients with chronic stationary psoriasis, under the conditions of a dermatological physician’s practice, received 9 g of fish oil or a placebo (olive oil) for 12 weeks. The standard psoriasis therapy was continued unaltered. Gaschromatographic analyses of total lipids

### Table 2: Change in the symptom picture compared to the initial symptomatology (0 to 5 rating scale). Minus sign indicates improvement (summary of 4).

<table>
<thead>
<tr>
<th>Symptom Treatment</th>
<th>After 8 weeks</th>
<th>After 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Verum: n = 14</td>
<td>Placebo: n = 14</td>
</tr>
<tr>
<td></td>
<td>Verum: n = 11</td>
<td>Placebo: n = 13</td>
</tr>
<tr>
<td>Erythema</td>
<td>-1.6*</td>
<td>-1.3</td>
</tr>
<tr>
<td></td>
<td>-0.4</td>
<td>-0.3</td>
</tr>
<tr>
<td>Scaling</td>
<td>-1.1*</td>
<td>-1.1*</td>
</tr>
<tr>
<td></td>
<td>-0.2</td>
<td>-0.2</td>
</tr>
<tr>
<td>Infested area</td>
<td>-3.1</td>
<td>-3.0</td>
</tr>
<tr>
<td></td>
<td>-1.5</td>
<td>+0.2</td>
</tr>
</tbody>
</table>

* p < 0.05

statistically significant; all that could be noted was a tendency to reduction of the symptoms.

The reddening of the plaques was noticeably less after taking fish capsules within the 12 week period. Here, too, there was no change to be noted in the control group. After both 8 and 12 weeks, the difference between the two groups was significant (p < 0.05). Scale formation in the plaques was (not significantly) better in the EPA group; no reduction of scale formation was observed in the control group.

All in all, it could be shown that administering fish oil clearly improves the symptomatology of chronic psoriasis. This treatment is therefore sensible, especially for women of child-bearing age, in order to cut back on the usual treatment strategies or, if possible, to do without them entirely.

An open study of 26 patients with 30 ml of fish oil per day for 4 months resulted in a clear improvement of the psoriasis symptomatology in 58% of the cases and a moderate effect in a further 19%. The evaluation criterion was the area of infested body surface. However, typical psoriasis symptoms such as erythema, scaling and infiltration exhibited no change. The greatest treatment effect only appeared after 4 months. On the other hand, there was a clear increase in the LTB₄/LTB₃ quotients in the neutrophilic leukocytes that preceded the clinical improvement. At higher quotients, there was a (non-significantly) stronger clinical effect.
showed a clear increase of EPA and DHA in the fish oil group as a confirmation of patient compliance. There was a significant improvement of the typical psoriasis symptoms erythema and infiltration. The placebo group also experienced, as expected, some improvement in the symptoms, since - for ethical reasons - the external and internal standard therapy was continued, which of course showed some effect. In the fish oil group, however, the improvement in all symptoms was clearly more pronounced. If one compares the number of cases with severe and mild findings, then fish oil shows a greater reduction in the severe symptoms.

All the authors of clinical studies agreed that the anti-psoriatic effect of n-3 fatty acids was in many cases not enough for a monotherapy. The application of fish-oil therapy should therefore be done in the context of adjuvant therapy, i.e. a combination treatment. The proof of effectiveness of this kind of treatment regime with n-3 fatty acids as adjuvant therapy has been provided by Gupta et al. in combination with UV radiation.

The study by Linker et al. also showed that, in particular, strongly effective preparations with numerous side-effects (e.g. glucocorticoids, retinoids and cytostatics) offer possibilities when combined with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil. It could thus be demonstrated that, for patients with psoriasis, the hyperlipidemias induced by Isotretinoin and Etretinate can be countered with fish oil.

The Cyclosporin-induced reduction in kidney function (5 mg/kg) can also be avoided or ameliorated by administering fish-oil concentrate (corresponding to 6 g of n-3 fatty acids) at the same time. Under Cyclosporin, glomerulur filtration fell by 18%, under Cyclosporin + fish oil by only 9%; under Cyclosporin, the actual plasma flow fell by 11% and remained unchanged under Cyclosporin + fish oil. This has led to concluding a protective influence on the part of fish oil against Cyclosporin’s nephrotoxic effect.

4. Conclusion
Due to the mainly positive findings, most authors recommend the n-3 fatty acids at least as an adjuvant to recognized forms of psoriasis therapy. Fish oil can thus be used as a supplement to the established varieties of psoriasis treatment. In particular, the inflammatory aspect of psoriasis, which is such a major component of the patient’s suffering, is clearly inhibited. Still, complete healing of psoriasis foci is not to be expected in all cases. In view of the periodicity of the disease and the side effects, fish oil treatment recommends itself, especially since no psoriasis-specific diet has yet been developed.

References


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