

# **A meta-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain**

## **Pain**

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### Abbreviations:

- ALA Alpha-linolenic acid  
18 carbon long omega-3 plant fatty acid
- EPA Eicosapentaenoic acid  
20 carbon long omega-3 fish fatty acid
- DHA Docosahexaenoic acid  
22 carbon long omega-3 fish fatty acid
- LA Linoleic acid  
18 carbon long omega-6 plant fatty acid
- AA Arachidonic acid  
20 carbon long omega-6 animal fatty acid

### FROM ABSTRACT

Between 40% and 60% of Americans use complementary and alternative medicine to manage medical conditions, prevent disease, and promote health and well-being.

Omega-3 polyunsaturated fatty acids (n-3 PUFAs) have been used to treat joint pain associated with several inflammatory conditions.

We conducted a meta-analysis of 17 randomized, controlled trials assessing the pain relieving effects of n-3 PUFAs in patients with rheumatoid arthritis or joint pain secondary to inflammatory bowel disease and dysmenorrhea.

Supplementation with n-3 PUFAs for 3–4 months reduces patient reported joint pain intensity, minutes of morning stiffness, number of painful and/or tender joints, and NSAID consumption.

The results suggest that n-3 PUFAs are an attractive adjunctive treatment for joint pain associated with rheumatoid arthritis, inflammatory bowel disease, and dysmenorrhea.

### THESE AUTHORS ALSO NOTE:

33% of those who use complementary medicine cite pain as the primary reason.

Controlled trials demonstrate the efficacy of n-3 PUFAs in reducing joint pain associated with inflammatory conditions, including rheumatoid arthritis (RA), inflammatory bowel disease, and dysmenorrhea.

Nonsteroidal anti-inflammatory drugs are associated with gastrointestinal bleeding and myocardial infarction, and therefore dietary supplementation with long-chain n-3 PUFAs, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), may be an effective adjunct to NSAID therapy.

“The typical North American diet is very low in EPA and DHA and conversion is limited from dietary alpha-linolenic acid, found in vegetable oils, to EPA and DHA.”

Fish oil is a rich source of long-chain n-3 PUFAs EPA and DHA.

“In humans, supplementation with fish oil, or EPA/DHA capsules, increases the incorporation of n-3 PUFAs into phospholipids, conferring anti-inflammatory effects.”

The anti-inflammatory effect of n-3 PUFAs is competition with arachidonic acid for production of inflammatory eicosanoids.

The objective of the present review is to conduct a meta-analysis examining the pain relieving effects of EPA/DHA in patients with RA or joint pain secondary to inflammatory bowel disease or dysmenorrhea.

The therapeutic effects of n-3 PUFAs usually manifest after approximately 3 months, and “taking n-3 PUFA supplementation for 2 months or less would not benefit significantly.” **[Important]**

Seventeen studies were included in this meta-analysis, with a total of 823 patients.

Patients receiving n-3 PUFAs fared better than placebo for morning stiffness.

Patients receiving n-3 PUFAs fared better than placebo for number of painful and/or tender joints.

Patients receiving n-3 PUFAs fared better than placebo for reduced NSAID consumption.

Studies that provided high-dose n-3 PUFAs (i.e., >2.7 g/day of EPA and DHA) showed greater improvements in morning stiffness, and number of painful and/or tender joints compared to low-dose n-3 PUFAs.

## DISCUSSION

"The results of the present meta-analysis support the hypothesis that n-3 PUFA supplementation improves pain outcomes after three months, particularly with respect to patient assessed pain, duration of morning stiffness, number of painful and/or tender joints, and [reduced] NSAID consumption."

"Consideration of treatment time showed that a minimum of three months was required for a therapeutic effect." **[Important]**

A "dose of 2.7 g/day of EPA and DHA is required to achieve anti-inflammatory effects." **[Important]**

"Significant improvements were noted in patient assessed pain and morning stiffness among studies providing high-dose but not low-dose n-3 PUFA supplementation." **[Important]**

"Reducing the intake of n-6 fatty acids (e.g., linoleic acid), which are metabolized to arachidonic acid and inflammatory eicosanoids, would be expected to increase the effectiveness of n-3 PUFA supplements."

Olive oil is a poor choice for a placebo because olive oil itself may have anti-inflammatory properties, thereby lessening the relative effects of EPA/DHA when compared with (olive oil) placebo.

"The main constituent of olive oil, oleic acid, may compete with arachidonic acid for incorporation into phospholipids."

These authors recommend that in future studies use high-dose n-3 PUFAs (at least 2.7 g/day of EPA and DHA) for a minimum duration of 3 months using a non-olive oil placebo control condition.

EPA/DHA supplements may also be useful for other types of chronic inflammatory pain, such as osteoarthritis or chronic back pain.

In chronic neuropathic pain, the production of inflammatory cytokines might potentially be reduced by EPA/DHA.

Alpha-linolenic acid [flax seed oil, etc.] is poorly converted to EPA and DHA.

This meta-analysis indicates that n-3 PUFA supplementation in patients with rheumatoid arthritis or joint pain secondary to inflammatory bowel disease and dysmenorrhea, reduces patient assessed joint pain intensity, morning stiffness, number of painful and/or tender joints, and reduces NSAID consumption.

"Omega-3 PUFA supplementation is an attractive adjunctive treatment for joint pain."

## KEY POINTS FROM DAN MURPHY

- 1) "Between 40% and 60% of Americans use complementary and alternative medicine to manage medical conditions, prevent disease, and promote health and well-being."
- 2) 33% of those who use complementary medicine cite pain as the primary reason.
- 3) "Supplementation with n-3 PUFAs for 3–4 months reduces patient reported joint pain intensity, minutes of morning stiffness, number of painful and/or tender joints, and NSAID consumption."
- 4) Omega-3 PUFAs are an adjunctive treatment for joint pain associated with rheumatoid arthritis, inflammatory bowel disease, and dysmenorrhea.
- 5) Nonsteroidal anti-inflammatory drugs are associated with gastrointestinal bleeding and myocardial infarction.
- 6) "The typical North American diet is very low in EPA and DHA and conversion is limited from dietary alpha-linolenic acid, found in vegetable oils, to EPA and DHA."
- 7) Fish oil is a rich source of long-chain n-3 PUFAs EPA and DHA.
- 8) "In humans, supplementation with fish oil, or EPA/DHA capsules, increases the incorporation of n-3 PUFAs into phospholipids, conferring anti-inflammatory effects."
- 9) The therapeutic effects of n-3 PUFAs usually manifest after approximately 3 months, and "taking n-3 PUFA supplementation for 2 months or less would not benefit significantly." **[Important]**
- 10) Studies that provided high-dose (more than 2.7 g/day of EPA and DHA) n-3 PUFAs showed greater improvements in morning stiffness and number of painful and/or tender joints compared to low-dose n-3 PUFAs.
- 11) "The results of the present meta-analysis support the hypothesis that n-3 PUFA supplementation improves pain outcomes after three months, particularly with respect to patient assessed pain, duration of morning stiffness, number of painful and/or tender joints, and [reduced] NSAID consumption."
- 12) A minimum of three months of supplementation with a dose of 2.7 g/day of EPA and DHA is required to achieve an anti-inflammatory and a therapeutic effect." **[Important]**

13) "Significant improvements were noted in patient assessed pain and morning stiffness among studies providing high-dose but not low-dose n-3 PUFA supplementation." **[Important]**

14) "Reducing the intake of n-6 fatty acids (e.g., linoleic acid), which are metabolized to arachidonic acid and inflammatory eicosanoids, would be expected to increase the effectiveness of n-3 PUFA supplements."

15) EPA/DHA supplements may also be useful for other types of chronic inflammatory pain, such as osteoarthritis or chronic back pain.

16) Alpha-linolenic acid [flax seed oil, etc.] is poorly converted to EPA and DHA.

17) This meta-analysis indicates that n-3 PUFA supplementation in patients with rheumatoid arthritis or joint pain secondary to inflammatory bowel disease and dysmenorrhea, reduces patient assessed joint pain intensity, morning stiffness, number of painful and/or tender joints, and reduces NSAID consumption.