

(n-3) Fatty Acids and Cancer Therapy

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FROM ABSTRACT

Supplementing the diet of tumor-bearing mice or rats with oils containing n-3 (omega-3) or with purified n-3 fatty acids has slowed the growth of various types of cancers, including lung, colon, mammary, and prostate.

The efficacy of cancer chemotherapy drugs and of radiation therapy has been improved when the diet included n-3 fatty acids.

Some potential mechanisms for the activity of n-3 fatty acids against cancer include modulation of eicosanoid production and inflammation, angiogenesis, proliferation, susceptibility for apoptosis, and estrogen signaling.

In humans, n-3 fatty acids have also been used to suppress cancer-associated cachexia and to improve the quality of life.

In one study, the response to chemotherapy therapy was better in breast cancer patients with higher levels of n-3 fatty acids in adipose tissue (indicating past consumption of n-3 fatty acids) than in patients with lower levels of n-3 fatty acids.

Thus, in combination with standard treatments, supplementing the diet with n-3 fatty acids may be a nontoxic means to improve cancer treatment outcomes and may slow or prevent recurrence of cancer.

Used alone, an n-3 supplement may be a useful alternative therapy for patients who are not candidates for standard toxic cancer therapies.

Abbreviations used:

AA arachidonic acid

COX cyclooxygenase

DHA docosahexaenoic acid

EPA eicosapentaenoic acid

THIS AUTHOR ALSO NOTES:

In animals, researchers have repeatedly shown that the growth of cancers and of human cancer xenografts can be slowed or completely inhibited by incorporation of n-3 fatty acids in the diet [5 references].

There are 2 articles indicating that n-3 fatty acids are beneficial for human cancer therapy.

"The objective of this article is to briefly review the evidence for the effects of n-3 fatty acids on cancer growth or cancer therapy, and to highlight rational mechanisms for those effects."

n-3 fatty acids may be one of the "nontoxic alternative therapies for cancer."
[IMPORTANT]

Humans can synthesize saturated fatty acids and monounsaturated n-9 fatty acids but cannot synthesize either the n-6 or the n-3 double bond. **[IMPORTANT]**

"The n-3 and n-6 fatty acids are essential components in cell membrane phospholipids and as a substrate for various enzymes; thus, fatty acids containing these bonds are essential fatty acids (EFA) and must be obtained in the diet."

The n-6 fatty acids are consumed primarily as linoleic acid from vegetable oils.

Arachidonic acid (AA; 20:4n-6) is also obtained from meats.

The n-3 fatty acid alpha-linolenic acid [18:3n-3], is 8% of soybean oil, 11% of canola oil, 57% of flaxseed oil. It is also found in leafy green vegetables.

The long-chain n-3 fatty acids EPA and DHA are found in fish and fish oils. "The best source of EPA and DHA is from fish or fish oils in the diet."

The production of AA from linoleic acid is suppressed by alpha-linolenic acid, EPA, and DHA.

"Suppression of AA production by n-3 fatty acids also suppresses the production of AA-derived eicosanoids."

The 2-series prostaglandins produced from AA tend to be proinflammatory and cancer proliferative in most tissues.

"Incorporation of n-3 fatty acids has been shown to suppress the production of COX 2 and can reduce the inflammatory response by changing the types of eicosanoids that are produced." Inflammation has been associated with cancer promotion, and reduced inflammation has shown promise as a cancer prevention strategy. **[Very Important]**

Supplementing the diet of animals with oils containing EPA or DHA has slowed the growth of various types of cancers, including lung, colon, mammary, and prostate.

"The n-3 fatty acids have been shown to increase the efficacy of various cancer chemotherapy drugs and of radiation therapy against cancer." **[Important]**

"Another potential benefit of n-3 fatty acid supplementation is the effect of these fats on cachexia." Cachexia is the wasting away of lean muscle mass that is not corrected by increasing energy consumption, such as carbohydrates and protein.

It is likely that suppression of tumor cell growth by n-3 fatty acids is due to the combination of mechanisms rather than to a single mechanism of action.

"If n-3 fatty acids are available, they will be used as a substrate by COX 2. It has been reported that DHA inhibits eicosanoid synthesis from AA, EPA is a better substrate for COX than AA, and EPA competes more successfully than AA for COX activity. The result is that if n-3 fatty acids are included in the diet and are incorporated into cell membranes, then less of the inflammation-producing and growth-promoting prostaglandin E2 will be produced in normal and in tumor tissues." **[Important]**

AA promotes tumor growth by increasing the multiplication of the cells, while n-3 fatty acids inhibit tumor cell multiplication.

The AA-derived products of COX and LOX stimulate cancer cell multiplication, whereas the EPA-derived products of COX and LOX decrease cancer growth.

The n-3 fatty acids can slow growth of cancer cells by direct action and by their activity as second messengers.

The n-3 fatty acids restore functional apoptosis (programmed cell death by cancer cells), which in turn down-regulates COX 2 expression, reducing the production of PGE2. (COX 2 expression also blocks apoptosis, resulting in cells that do not die at the appropriate time).

The n-3 fatty acids induce differentiation of breast cancer cells so they do not multiply, which could stop the growth of tumors.

“As cancers grow, new blood vessels must develop to supply nutrients to the cells and to remove wastes. Inhibition of angiogenesis has been proposed as a strategy to inhibit or to limit tumor growth. The n-3 fatty acids inhibit angiogenesis by multiple mechanisms, including alterations in prostaglandin production.” **[Very Important]**

“Many early breast cancers are estrogen dependent.” Prostaglandin E2, a product of AA, increases the production of estrogen. **[Very Important]** The n-3 fatty acids can decrease the growth of estrogen-dependent breast cancers by decreasing estrogen stimulation of these tumors.

In summary, it is likely that multiple mechanisms contribute to suppression of cancer growth by n-3 fatty acids.

Clinical trials on n-3 fatty acids for cancer patients have used doses as high as 13.1 g of EPA plus DHA per day.

A study has shown that EPA increased appetite and weight gain in patients with cancer-associated wasting. “An effective dose of EPA to reduce cachexia may be between 2 and 4 g/d.”

A study shows that the “level of DHA in breast adipose tissue of patients with complete or partial remission in response to cytotoxic drugs was higher than in patients with no response or progression.”

One can increase DHA in breast tissue by 3 months of consumption of n-3 fatty acids.

The studies cited in this article, “even though scant in number, these reports provide encouraging evidence that n-3 fatty acids may be beneficial for cancer therapy in humans.”

CONCLUSIONS FROM AUTHORS:

- 1) “The n-3 fatty acids should be beneficial for cancer treatment.”
- 2) “The n-3 fatty acids may be beneficial when consumed before chemotherapy.”

KEY POINTS FROM DAN MURPHY

- 1) In humans, n-3 fatty acids have been used to suppress cancer-associated cachexia and to improve the quality of life.
- 2) Supplementing the diet with n-3 fatty acids may be a nontoxic means to improve cancer treatment outcomes and may slow or prevent recurrence of cancer.

- 3) Research has repeatedly shown that the growth of cancers can be slowed or completely inhibited by incorporation of n-3 fatty acids in the diet.
- 4) Humans cannot synthesize either the n-6 or the n-3 fatty acids, and they must be obtained from the diet.
- 5) The n-6 fatty acids are from vegetable oils.
- 6) Arachidonic acid is also obtained from meats.
- 7) The long-chain n-3 fatty acids EPA and DHA are found in fish and fish oils.
- 8) Prostaglandin E2, produced from AA, is proinflammatory and cancer proliferative.
- 9) Alpha-linolenic acid, EPA and DHA inhibit the production of AA from linoleic acid, which also suppresses the production of proinflammatory PGE2.
- 10) Reduced inflammation has shown promise as a cancer preventive strategy.
- 11) Supplementing the diet of animals with oils containing EPA or DHA has slowed the growth of various types of cancers, including lung, colon, mammary, and prostate.
- 12) The n-3 fatty acids have been shown to increase the efficacy of cancer chemotherapy drugs and of radiation therapy against cancer.
- 13) If n-3 fatty acids are included in the diet, less of the inflammation-producing and cancer growth-promoting prostaglandin E2 will be produced in normal and in tumor tissues.
- 14) The n-3 fatty acids inhibit angiogenesis, which reduces cancer growth and spread.
- 15) Prostaglandin E2, a product of AA, increases the production of estrogen, which increases breast cancer.
- 16) Clinical trials of n-3 for cancer patients have used doses as high as 13.1 g of EPA plus DHA per day.
- 17) One can increase DHA in breast tissue by 3 months of consumption of n-3 fatty acids.