

LE Magazine May 2002

REPORT

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Tocotrienols and breast cancer cell growth

We now know that the form of vitamin E used in most commercial preparations (alpha tocopherol acetate) has not been shown to protect against breast cancer in humans. A natural form of vitamin E called alpha tocopheryl succinate, found in more expensive supplements, may provide some protection. In test tube studies, the alpha tocopheryl succinate form of vitamin E has been shown to inhibit breast cancer cell growth. [22-35]

It is the tocotrienols, however, that have demonstrated the most significant potential to not only reduce the incidence of breast cancer, but also to inhibit existing breast cancer cell propagation.

Tocotrienols have been shown to inhibit growth of estrogen receptor positive breast cancer cells by as much as 50% in culture.[36-39] In contrast, many studies have found that alpha tocopherol does not influence proliferation.[36,38-40] Even in studies where alpha tocopherol was shown effective against some breast cancer cell lines, the amount required for 50% growth inhibition was more than 20 times higher than the growth inhibitory concentrations of the tocotrienols.[37]

Comparison of multiple studies indicates that the growth inhibitory effects of alpha tocopherol wears off,[41] whereas limited data suggest that the growth inhibitory effects of the tocotrienols on breast cancer cells is maintained or increases with duration of exposure (in culture).[39,42]

Tamoxifen interferes with breast cancer cell proliferation via several mechanisms, most notably by blocking estrogen receptor sites on the cell membrane surface so that estrogen cannot fuel hyper-proliferation. Tamoxifen is known to induce side effects, but the documented effectiveness of the drug causes many breast cancer patients to use it for two to five years (or longer).

In cell culture, tamoxifen can reduce estrogen receptor positive breast cancer cell proliferation by 50%. When palm-oil derived tocotrienols are added with tamoxifen, the dose of tamoxifen required to induce 50% cell arrest was lowered by 75%.[37]

In estrogen receptor negative cancer cell lines, tamoxifen can inhibit proliferation by 50%, but at much higher concentrations. When tocotrienols are added, the dose of tamoxifen required to inhibit cancer cell proliferation is reduced by as much as 95%![37] When alpha tocopherol is added to these breast cancer cell cultures, it increases the amounts of tamoxifen required to inhibit growth.[37]

These cell culture studies, showing that tocotrienols dramatically potentiate the effects of tamoxifen, indicate the desire to test a combination of tocotrienols and tamoxifen in both estrogen receptor positive and estrogen receptor negative breast cancer patients.

The study showing that alpha tocopherol increases the amount of tamoxifen required to induce cell arrest implies that breast cancer patients using tamoxifen may want to avoid consuming high potencies of alpha tocopherol.

(Note: Life Extension magazine has previously reported that vitamin D3 and melatonin work synergistically with tamoxifen to inhibit breast cancer cell propagation.)

Tocotrienols induce breast cancer cell death

The objective of any cancer therapy is to induce the cancer cells to differentiate in a way that promotes programmed cell death (apoptosis). Several studies indicate that tocotrienols induce breast cancer cell apoptosis.[41-43]



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When different kinds of live breast cancer cells were injected into the mammary tissue of female mice, tocotrienols were found to be growth inhibitory on each breast cancer cell line tested. Although apoptosis could be achieved, the dose of tocotrienol needed to induce 50% apoptosis was 2-4 times higher than the dose of tocotrienol required to induce 50% growth inhibition.[42]

It is interesting to note that the growth inhibition and promotion of apoptosis occur preferentially in the cancerous part of the breast so that healthy cells remain largely unaffected.[42]

Can women obtain enough tocotrienols to reduce breast cancer risk?

For those seeking to use tocotrienols to reduce breast cancer risk, it is essential to quantify the optimal daily dose. In humans not consuming tocotrienol supplements, the average plasma concentration is less than 1 microgram per liter of blood.[45-47] After supplementation with a palm-oil concentrate containing about 78 milligrams of tocotrienols for four weeks, plasma tocotrienol levels increased to 8.14 micrograms per liter of blood (an eight-fold increase).[47]

This plasma concentration of 8.14ug/l of tocotrienol is similar to the amount used to achieve an inhibitory effect on the proliferation of estrogen receptor positive breast cancer cells in vitro by 50%. The amount of tocotrienol to promote apoptosis in vitro by 50% would be approximately 24ug/liter according to this study.[2]

It is interesting to note that the body naturally concentrates tocotrienols into breast adipose tissue. Based on studies done to date, it is likely that breast adipose tissue levels of tocotrienols will be 5 to 10 times greater than plasma.[48-50] This indicates that even lower tocotrienol supplementation might be adequate to saturate breast adipose tissue with the amount of tocotrienols that have inhibited breast cancer cell proliferation and induced apoptosis in culture.

It is encouraging to know that the in vitro tests that document the anti-cancer effects of tamoxifen also show tocotrienols to have similar cell inhibitory properties. Compared to tamoxifen, however, tocotrienols are safe. Human studies have shown that daily doses of up to 240 mg of tocotrienols for 16 months produce no adverse effects.[47,51,52] Further studies will determine whether humans who saturate their breast adipose tissue with tocotrienol from supplements will achieve a reduced incidence of breast cancer. (Please note that it is the palm-oil tocotrienols, and not rice-bran tocotrienols, that have primarily demonstrated these anti-cancer effects.)

Summary of findings

When reviewing all the published evidence, it does not appear that alpha tocopherol vitamin E confers a protective effect against breast cancer. Yet studies show that women who consume foods high in other forms of vitamin E substantially reduce their risk of contracting breast cancer (by as much as 90%).

A cardinal feature of breast tumors are rapidly proliferating cells. Estrogen drugs promote hyper-proliferation and this is one reason why these drugs may quadruple the incidence of breast cancer. [53]

Studies of breast cancer cells in culture indicate that tocotrienols have potent effects in inhibiting proliferation and inducing apoptosis (cancer cell death). These studies show that alpha tocopherol does not have this same benefit.

Alpha tocopherol acetate is the most common supplement form of vitamin E, yet the evidence points to other forms of vitamin E as being responsible for the dramatic reduction in breast cancer incidence observed in large human studies.

We now know that the individual tocopherols and tocotrienols have different biological activities as they relate to their effects on cellular function. Gamma tocopherol, for instance, has demonstrated significant cancer prevention effects compared to alpha tocopherol.

The potential anti-cancer effects of gamma tocopherol and the tocotrienols merits aggressive human clinical research to determine if women who supplement with these unique forms of vitamin E can reduce their risk of contracting breast cancer. Further research

Tocotrienols should be taken with food

For oil-soluble vitamin E to be absorbed, it should be taken with some kind of food. When people take oil-based vitamin E preparations on an empty stomach, very little makes its way into the bloodstream.

It is especially important to take the tocotrienols with some form of oil or fat-containing food. One study showed that when tocotrienols are taken on an empty stomach, absorption was reduced by an average of 64%.44

When taking gamma tocopherol and/or tocotrienol vitamin E supplements, try to take them with a meal or with fatty acid capsules like fish oil (EPA-DHA), GLA, CLA etc.



should be conducted on breast cancer patients to see if the addition of tocotrienols to tamoxifen improves long-term survival rates.

Based on a review of all the published data, we cannot find compelling evidence to indicate that standard (alpha tocopherol) vitamin E supplements reduce breast cancer incidence. While alpha tocopherol has been shown to protect against a wide range of other diseases,[54-70] it would appear that the tocotrienols are the ideal form of vitamin E to specifically reduce breast cancer risk.

For additional information about novel adjuvant ways of preventing and treating breast cancer, refer to the Breast Cancer Treatment Protocol.

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