

Sesame Lignans Dramatically Increase Vitamin E Activity



Sesame seeds and its oil have long been considered a health food in Japan and China.^{1,2} Sesame's biological effects, however, have only been identified in the past decade. Sesame lignans are the 1% solid portion of sesame oil and are responsible for all the beneficial effects of sesame.³

Sesame and its lignans have a broad range of applications in human health. This includes increasing the anti-inflammatory index of fish oils,^{4,5} decreasing LDL oxidation,^{6,7} inhibiting lipid peroxidation,⁶⁻⁸ lowering LDL levels in humans,^{9,10} and guarding against DNA mutating toxins.¹¹⁻¹³

The most significant finding about sesame lignans, however, is their unique ability to increase tissue levels of vitamin E (including gamma tocopherol) via several different mechanisms.¹⁴⁻¹⁷ Elevation of gamma tocopherol is of particular importance because gamma tocopherol, but not alpha tocopherol, quenches a particularly dangerous type of free radical (peroxynitrite radical) that plays a major role in

the development of age-related disorders.^{18,19}

The primary purpose for taking vitamin E is to suppress free radicals. Over the past year, four prestigious scientific journals have recognized the unique benefits of gamma tocopherol and have published articles indicating that gamma tocopherol may be the critically important form of supplemental vitamin E.²⁰⁻²³

For the first time, gamma tocopherol has been combined with sesame lignans in a human study that measured tissue oxidative stress and inflammatory levels. The results show that sesame boosts the efficacy of gamma tocopherol by an average of 25% compared to the same amount of gamma tocopherol combined with tocotrienols.^{LEF study}

Increased Gamma Tocopherol Results in Decreased Free Radicals

In a study of Swedish women, supplementing with sesame oil raised gamma tocopherol levels 41.7% without taking any other sources of tocopherols.²⁴

In animal studies, supplementing with gamma tocopherol alone resulted in only small concentrations of gamma tocopherol in the blood and liver of rats. In sharp contrast, feeding of sesame lignans resulted in high concentrations of gamma tocopherol in blood and liver.²⁵ Lipid peroxidation is an important measurement of cell membrane free radical damage. In this study, lipid peroxidation levels were 50% lower in the blood of the sesame+gamma tocopherol group compared to the group fed only gamma tocopherol, while liver peroxidation rates were 30% lower.²⁵

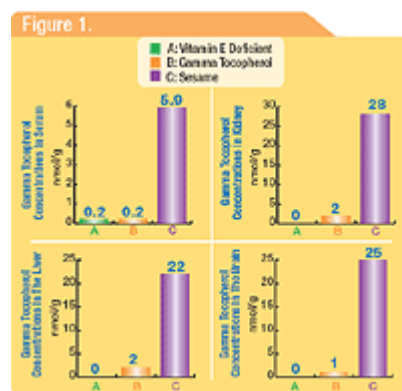
The bar graphs in figure 1 show the differences in gamma tocopherol and levels between the groups of animals fed only gamma tocopherol versus the gamma tocopherol plus sesame lignans-fed group.²⁵

In another study, adding sesame seed to a rat diet increased alpha tocopherol serum levels 40%, and gamma tocopherol levels 800%.²⁶ Sesame lignans have also demonstrated the ability to lower a measure of oxidative cell membrane/DNA damage by 82.8% (thiobarbituric reactive liver levels).⁷

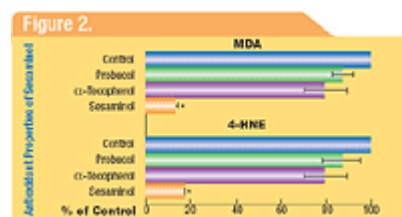
Figure 2 shows the remarkable effects that sesame has on decreasing levels of destructive free radicals.

How Sesame Boosts Vitamin E

In human and animal studies, sesame lignans have been shown to increase tissue and blood levels of alpha and gamma tocopherol.^{25,27} The significance of this is that gamma tocopherol levels are difficult to raise in human tissues and blood. One reason is that the only carrier protein that transports vitamin E from the liver to the tissues (alpha tocopherol carrier protein) is highly selective in transporting alpha tocopherol in almost 2 to 1 ratio to other tocopherols.²⁸ This means relatively little gamma tocopherol ends up in the cell



Enlarge Figure 1. Rats fed a sesame-supplemented diet showed significantly higher concentrations of gamma tocopherol in serum, liver, kidneys, and brain versus those supplemented with gamma tocopherol only or was fed a vitamin E deficient diet.



Enlarge Figure 2. Levels of the major byproducts of lipid peroxidation (4-hydroxy-nonenal (4-HNE) and

membranes, yet what is delivered has a powerful antioxidant effect as demonstrated in studies showing the value of gamma tocopherol over alpha.

malondialdehyde (MDA)) are markedly inhibited in the presence of sesaminol, compared to control, alpha tocopherol, and probucol, a lipid lowering drug.

Human and animal studies show that supplementing with sesame or its lignans produces similar effects in raising all tocopherol levels. In one study, liver, brain, kidney and serum levels of gamma tocopherol in rats were measured after being given gamma tocopherol alone or being given gamma tocopherol and sesame.

The gamma-tocopherol-only fed group increased liver, kidney, brain and blood levels of gamma tocopherol only 3 nmol per gram in tissues and 3 micromoles per liter in blood. When fed sesame and gamma tocopherol together, the rats had gamma tocopherol levels of 25-30 nmol per gram in tissue and 30 nmol per liter in blood, an increase between 833 to 1000% compared to no sesame.²⁶ This study also showed that the urinary excretion of the metabolite of gamma tocopherol (gamma-CEHC) dropped 50% in the sesame-supplemented rats, a factor that helps explain the dramatic increase in tissue and blood levels of in the group fed sesame + gamma tocopherol (see figure 3).

Sesame inhibits the specific enzyme that breaks down tocopherols (tocopherol gamma-hydroxylase, or CYP-3A),^{17,26} which further clarifies how sesame boosts gamma and alpha tocopherol levels in the body.

Life Extension Tests Sesame Lignans in Humans

In response to these remarkable published studies on sesame, Life Extension conducted a clinical trial to see what would happen to people who took supplements containing gamma tocopherol and sesame lignans.

Three markers of oxidative stress and inflammation were measured in the blood of a group of human test subjects to establish a baseline. The group was then divided, with one group given gamma tocopherol plus tocotrienols, while another received the same amount of gamma tocopherol plus sesame lignans.

The three blood markers of oxidative stress and inflammation measured were:

1. Dityrosine
2. Isoprostane
3. PLGF-1

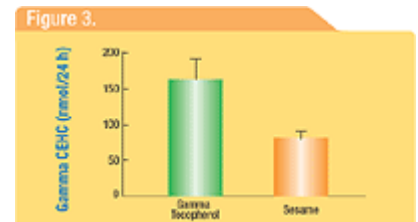
The dityrosine marker measures serum levels of deep tissue protein oxidation caused by the peroxynitrite radical reacting with tyrosine, an amino acid found in all human proteins.²⁹ Tyrosine is the amino acid most readily attacked by peroxynitrite radical. Peroxynitrite is an extremely powerful free radical that has been implicated in a host of disorders. Gamma tocopherol is the only tocopherol that reacts with, or traps, the peroxynitrite radical to any appreciable degree.¹⁸ Compared to the gamma tocopherol-tocotrienol group, those taking gamma tocopherol-sesame showed a 45% reduction in serum dityrosine oxidation levels after two weeks of supplementation.

The isoprostane marker measures the amount of cell membrane damage caused by free radicals.^{30,31} Cell membrane damage, also called lipid peroxidation, is a free radical chain reaction of cell membrane fatty acids. Normally, lipid peroxidation results in free radicals destroying normal molecules before being quenched. Supplementing with vitamin E has been shown to significantly reduce isoprostane generation and reduce aortic lesion areas.³² Compared to the gamma tocopherol-tocotrienol group, those taking gamma tocopherol and sesame showed a 22% reduction in serum isoprostane levels after two weeks of supplementation.

The PLGF-1 marker is an extremely sensitive new test for atherosclerotic risk in humans.³³ PLGF-1 stands for "placental growth factor" because it was originally identified in the placenta.³⁴ For adults, however, high levels of PLGF-1 are indicative of atherosclerotic lesions. PLGF-1 stimulates vascular smooth muscle cell growth, recruits macrophages into atherosclerotic lesions, up-regulates production of tumor-necrosis factor- α and stimulates undesirable angiogenesis.³⁵ In the animal model, inhibition of PLGF-1 suppressed both atherosclerotic plaque growth and arterial wall inflammatory reactions. PLGF-1 may be considered a marker for the presence of unstable arterial wall plaque.³⁶ Compared to the gamma tocopherol-tocotrienol group, those taking gamma tocopherol-sesame showed an 11.5% reduction in serum PLGF-1 levels after two weeks of supplementation.

Since this was a healthy group of people to begin with, whose baseline PLGF-1 was already in the lowest 1% of risk, the 11.5% reduction in the gamma tocopherol-sesame group was impressive. Presumably, those with arterial wall dysfunction, who normally have high PLGF-1 levels, would derive even greater benefit from supplements that lowered this very sensitive inflammatory marker. The same holds true for aging people whose baseline oxidative stress levels are very high compared to this healthy group of test subjects.

Based on these three advanced measurements of free radical and inflammatory damage, gamma tocopherol plus sesame lignans



Enlarge Figure 3. Levels of the major byproducts of lipid peroxidation (4-hydroxy-nonenal (4-HNE) and malondialdehyde (MDA)) are markedly inhibited in the presence of sesaminol, compared to control, alpha tocopherol, and probucol, a lipid lowering drug.

is 25% more effective than the more expensive gamma tocopherol plus tocotrienols.

What is so impressive about these recent findings is that unlike previous studies, it did not compare sesame to a placebo or control group. Instead, this human study compared low cost sesame to the effects of very expensive tocotrienols. The tocotrienols are considered nature's most potent natural antioxidants. Yet sesame was found to work 25% better than the tocotrienols.

This is great news for vitamin consumers, since tocotrienols are costly, whereas the price of standardized sesame lignans is relatively modest.

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