

Alpha- versus Gamma-tocopherol: What to Supplement ?

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Vitamin E supplements are widely used, either as part of multivitamin preparations or as single vitamin supplements. Supplements are usually exclusively composed of α -tocopherol in contrast to the diet which is rich in γ -tocopherol. Studies both in patients and healthy subjects demonstrated that supplementation with α -tocopherol causes a rapid drop in γ -tocopherol concentrations both in plasma and low-density lipoprotein. This can be explained by the preference of the α -tocopherol transfer protein for α -tocopherol, while γ -tocopherol is preferentially metabolized and excreted. Upon supplementation of mixed tocopherols (MT, composed of α -, β -, γ - and δ -tocopherol) γ -tocopherol increases in buccal mucosal cells at a similar rate as in plasma, while α -tocopherol does so at a lower rate.

There is accumulating evidence of properties of γ -tocopherol that are not shared by α -tocopherol, including anti-inflammatory activity. The only difference in the chemical structure is the unsubstituted 5-position on the chromanol ring of γ -tocopherol, which allows for trapping reactive nitrogen species to form 5-nitro- γ -tocopherol (5-NGT). In smokers, who exhibit increased oxidative and nitrate stress, supplementation with α -tocopherol and subsequently impaired γ -tocopherol status reduces the capacity to detoxify reactive nitrogen species as evidenced by decreased formation of 5-NGT. In smokers, supplementation of MT also decreases activation of nuclear factor kappa B and malondialdehyde formation, while α -tocopherol supplementation does not.

Impairment of γ -tocopherol status due to α -tocopherol supplementation is expected to have a negative impact on different conditions with low-grade inflammation, including obesity, atherosclerosis, and chronic renal failure. This could, at least in part, also explain the fact that supplementation studies with α -tocopherol did not show the expected beneficial effect in contrast to epidemiological evidence of an inverse relation between vitamin E status and risk of cardiovascular disease. Loss of γ -tocopherol from the body might counteract the beneficial effects of α -tocopherol as an antioxidant. Simultaneous supplementation with even small doses of γ -tocopherol is expected to alleviate the negative effects.