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Mixed tocopherols inhibit platelet aggregation in humans: potential mechanisms.

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Source

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Abstract

BACKGROUND:

Epidemiologic studies have shown an inverse correlation between acute coronary events and high intake of dietary vitamin E. Recent clinical studies, however, failed to show any beneficial effects of alpha-tocopherol on cardiovascular events. Absence of tocopherols other than alpha-tocopherol in the clinical studies may account for the conflicting results.

OBJECTIVE:

This study compared the effect of a mixed tocopherol preparation rich in gamma-tocopherol with that of alpha-tocopherol on platelet aggregation in humans and addressed the potential mechanisms of the effect.

DESIGN:

Forty-six subjects were randomly divided into 3 groups: alpha-tocopherol, mixed tocopherols, and control. ADP and phorbol 12-myristate 13-acetate-induced platelet aggregation, nitric oxide (NO) release, activation of endothelial constitutive nitric-oxide synthase (ecNOS; EC 1.14.13.39) and of protein kinase C (PKC), and ecNOS, superoxide dismutase (SOD; EC 1.15.1.1), and PKC protein content in platelets were measured before and after 8 wk of administration of tocopherols.

RESULTS:

ADP-induced platelet aggregation decreased significantly in the mixed tocopherol group but not in the alpha-tocopherol and control groups. NO release, ecNOS activation, and SOD protein content in platelets increased in the tocopherol-treated groups. PKC activation in platelets was markedly decreased in the tocopherol-treated groups. Mixed tocopherols were more potent than alpha-tocopherol alone in modulating NO release and ecNOS activation but not SOD protein content or PKC activation.

CONCLUSIONS:

Mixed tocopherols were more potent in preventing platelet aggregation than was alpha-tocopherol alone. Effects of mixed tocopherols were associated with increased NO release, ecNOS activation, and SOD protein content in platelets, which may contribute to the effect on platelet aggregation.

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Mixed tocopherols have a stronger inhibitory effect on lipid peroxidation than alpha-tocopherol alone.

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Abstract

Intake of vitamin E with food (mixed tocopherols) has been found to counteract the development of atherosclerotic cardiovascular disease, whereas intake of large amounts of pure alpha-tocopherol has shown only a slight or no effect in clinical studies. This study was designed to investigate the effects of alpha-tocopherol alone and a mixed tocopherol preparation (gamma-, delta-, and alpha-tocopherol) on hydrogen peroxide-induced lipid peroxidation in human erythrocytes. Erythrocytes were incubated with different concentrations of alpha-tocopherol or mixed tocopherols and then exposed to hydrogen peroxide. Tocopherol levels and malondialdehyde-thiobarbituric acid-reactive substances were determined by high-performance liquid chromatography and fatty acids by gas chromatography. Incubation of erythrocytes with tocopherols (30-120 microM) increased the tocopherol level in a concentration-dependent manner. The uptake of gamma- and delta-tocopherols was much higher than that of alpha-tocopherol. Hydrogen peroxide strongly increased lipid peroxidation and decreased polyunsaturated fatty acids in erythrocytes. Both alpha-tocopherol and the tocopherol mixture protected the cells from lipid peroxidation, the mixture being much more potent than alpha-tocopherol alone. This study indicates that a mixture of tocopherols has a stronger inhibitory effect on lipid peroxidation induced in human erythrocytes than alpha-tocopherol alone, due to higher uptake of gamma- and delta-tocopherol in the cells.