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INTRODUCTION & STUDY AIMS

The term vitamin E summarizes 4 different forms of tocopherols as well as tocotrienols. Vitamin E in the diet mainly consists of α - and γ -tocopherol and γ -tocopherol is the major form of vitamin E in the diet at least in the US (1). Commonly used vitamin E supplements exclusively contain α -tocopherol. Supplementation of α -tocopherol causes a significant drop in plasma γ -tocopherol concentrations within 48 h (2). This can be explained by a preference of the α -tocopherol binding protein for α -tocopherol (3) and rapid excretion of γ -tocopherol metabolites (4). However, evidence is increasing that γ -tocopherol exerts beneficial effects not shared by α -tocopherol (5,6).

The aim of this study was to investigate the response of plasma concentrations of α -, γ - and δ -tocopherol after a single dose of mixed tocopherols compared to α -tocopherol.

SUBJECTS & METHODS

In a double-blind, placebo-controlled kinetic study 17 healthy volunteers received a single dose of either 735 mg natural RRR- α -tocopherol (n=5) or a similar dose of a natural mixture of 60 % γ -, 24 % δ -, 14 % α - and 2 % β -tocopherol (n=6) or placebo (n=6).

In the vitamin E preparations used tocopherols were formulated into Hydro cell key® (HCK®) granulate based on guar gum, a polysaccharide that forms a hydrocolloid in the gastrointestinal tract (Unisan Ltd., Konstanz, Germany). The vitamin E dose was taken after an overnight fast along with an English breakfast, followed by standardized meals for the next 24 h.

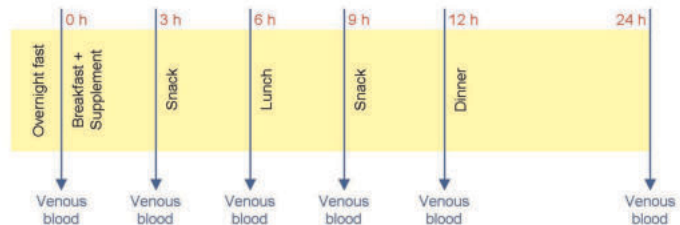
Blood was drawn before and 3, 6, 9, 12, and 24 h after dosing. Plasma α -, γ - and δ -tocopherol concentrations were determined by HPLC (7) and standardized for cholesterol.

RESULTS

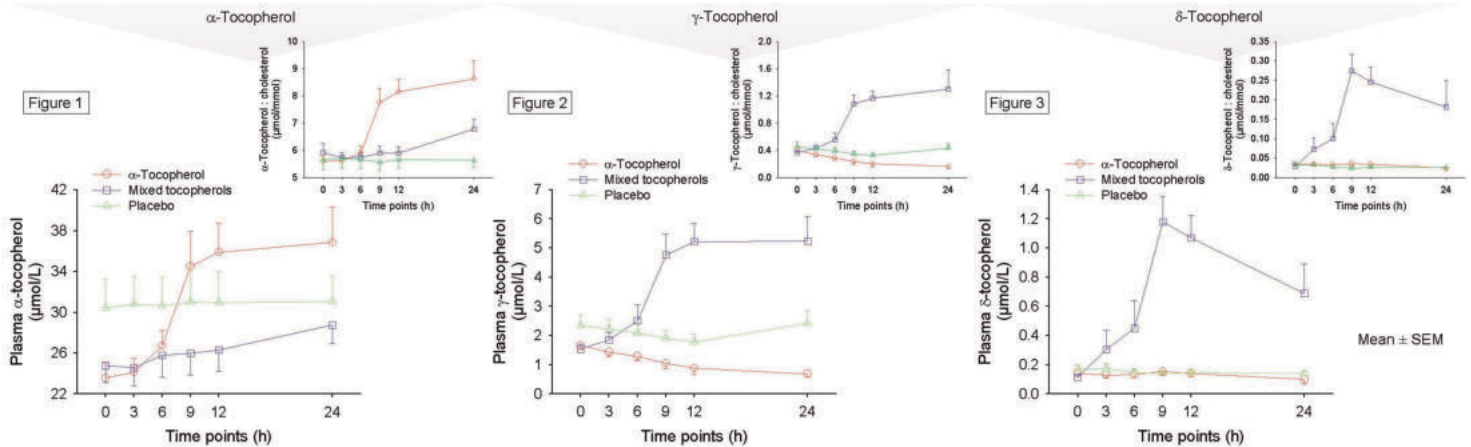
Study Subjects

	Treatment Groups		
	α -Tocopherol	Mixed tocopherols	Placebo
Age (years) (mean \pm SD)	28.2 \pm 5.07	27.2 \pm 3.23	31.3 \pm 7.08
Sex (male / female)	4 / 1	3 / 3	5 / 1
Body mass index (kg/m ²) (mean \pm SD)	22.2 \pm 3.06	21.7 \pm 2.62	22.4 \pm 1.63

Study Design



Vitamin E



SUMMARY

As expected, plasma α -tocopherol concentrations increased 1.7-fold in the α -tocopherol group ($P < 0.001$) and 1.2-fold in the mixed tocopherol group ($P < 0.001$), but did not reach a plateau within 24 h (Fig.1). Ratios of α -tocopherol:cholesterol did not increase significantly in the mixed tocopherol group (Fig. 1, inset).

As expected, there was a significant drop in plasma γ -tocopherol concentrations in the α -tocopherol group ($P < 0.001$) (Fig.2). In contrast, γ -tocopherol concentrations increased 4.3-fold in the mixed tocopherol group ($P < 0.001$), plateaued at 12 h, and did not decrease within 24 h.

A single dose of mixed tocopherols prompted a marked increase in δ -tocopherol concentrations ($P < 0.001$), followed by a significant decrease from 9 h onwards (Fig.3).

CONCLUSIONS

This is the first kinetic study using mixed tocopherols in humans. It provides evidence that, when a slow release preparation is used, not only plasma α -tocopherol but also γ -tocopherol concentrations increase significantly and are maintained up to 24 h after dosing, while δ -tocopherol is rapidly cleared from plasma. Because γ -tocopherol is maintained in the circulation for 24 h, a daily supplement would be suitable for enhancing γ -tocopherol status.

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INTRODUCTION & STUDY AIMS

Nuclear factor kappa B (NF- κ B) is an oxidative stress-responsive transcription factor present in the cytosol as a heterodimer bound to the inhibitory protein, I κ B. After activation, NF- κ B translocates to the nucleus, binds to specific DNA sequences and initiates transcription.

Cigarette smoke is a source of oxidative and nitrosative stress.

The aim of this study was to study the effects of mixed tocopherols versus α -tocopherol on NF- κ B activation in smokers and non-smokers.

SUBJECTS & METHODS

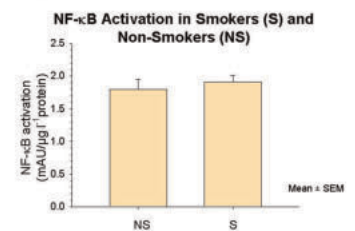
Healthy male smokers (S, n=21) and non-smokers (NS, n=22) took either 294 mg RRR- α -tocopherol or 294, 147, or 73.5 mg mixed tocopherols (60 % γ -, 24 % δ -, 14 % α - and 2 % β -tocopherol, Unisan Ltd., Konstanz, Germany) or placebo for 4 weeks. Tocopherols were determined in plasma before and after supplementation. Mononuclear leukocytes were isolated and activated NF- κ B was determined in the nuclear fraction using an ELISA with an oligonucleotide containing the DNA binding NF- κ B sequence (Active Motif, Carlsbad, CA, USA).

RESULTS

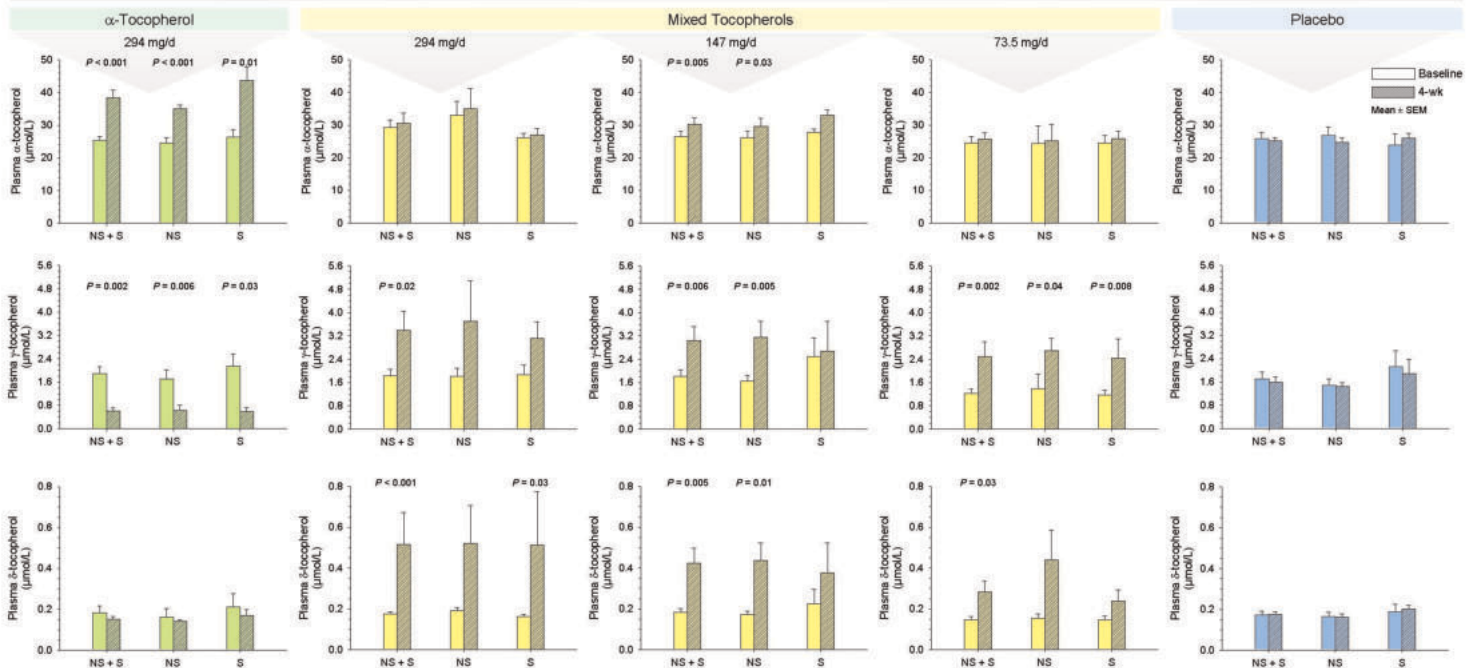
Demographic Data

	Treatment groups				
	α -Tocopherol	Mixed tocopherols			Placebo
	294 mg/d	294 mg/d	147 mg/d	73.5 mg/d	
Number (NS / S)	9 (6 / 3)	11 (5 / 6)	8 (6 / 2)	10 (2 / 8)	5 (3 / 2)
Age (years) (mean \pm SD)	31.6 \pm 6.73	31.5 \pm 7.55	32.9 \pm 5.27	25.0 \pm 4.79	29.7 \pm 6.02
Body mass index (kg/m ²) (mean \pm SD)	23.6 \pm 3.38	25.2 \pm 3.31	25.0 \pm 2.00	23.5 \pm 3.44	23.7 \pm 2.93

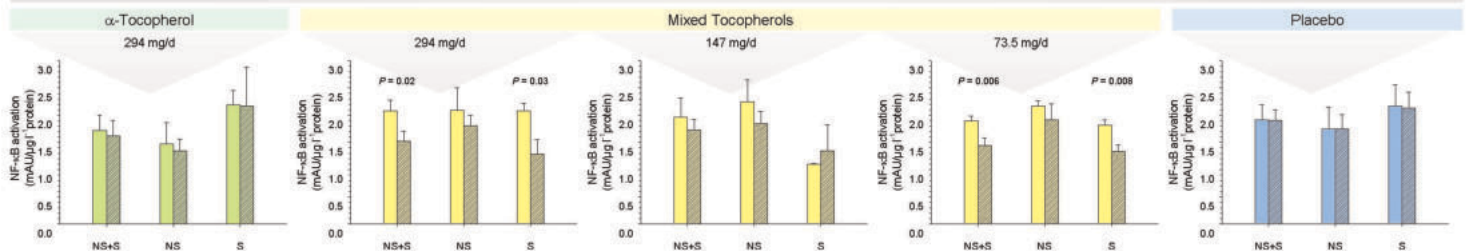
Baseline



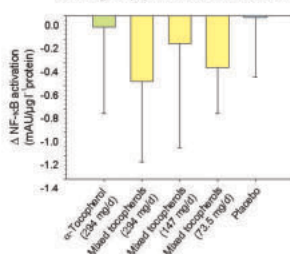
Vitamin E



NF- κ B Activation



Changes (Δ) in NF- κ B Activation



SUMMARY & CONCLUSIONS

- **Response to tocopherols:** In the α -tocopherol group, α -tocopherol increased, while γ -tocopherol decreased and δ -tocopherol did not change. In the mixed tocopherol group, γ - and δ -tocopherol increased, while α -tocopherol increased significantly only in the 147 mg/d group.
- **Effects on NF- κ B activation:** Mixed tocopherols showed a protective effect on NF- κ B activation in leukocytes of healthy male smokers, while such an effect was not observed in non-smokers.
- These data demonstrate for the first time that mixed tocopherols exert a protective effect on NF- κ B activation in smokers.

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