

## Letter to the Editor

# Studies with vitamin E and $\beta$ -carotene as single agents do not prove lack of benefit

Recent articles in the *British Journal of Nutrition*<sup>1</sup> and elsewhere<sup>2</sup> highlight the paradox that foods rich in vitamin E and  $\beta$ -carotene confer resistance to cancer and heart disease<sup>3–10</sup>, but diets enriched with the single-agent  $\alpha$ -tocopherol (usually DL) or  $\beta$ -carotene do not, and can even be harmful<sup>1,11–16</sup>. Perhaps these substances, present in foods not as single agents but mixed with a large group of similar compounds, are not beneficial in themselves, but act only as markers for other members of their groups that provide the true benefit. This seems unlikely, however. Rather it is likely that the human body, exposed for millennia to mixtures of all eight tocopherols and tocotrienols and all the numerous carotene-like substances, responds properly only to the natural mixtures, and that taking a high dose of any single agent can upset the biochemical balance amongst these components. Furthermore, when DL- $\alpha$ -tocopherol is used, only half of it, the D isomer, is beneficial. Thus, results with natural mixed tocopherols–tocotrienols or carotenes might well be superior to those with single-agent  $\alpha$ -tocopherol or  $\beta$ -carotene. Indeed, some recent human studies report that  $\gamma$ -tocopherol<sup>17–20</sup>,  $\alpha$ -tocotrienol<sup>21</sup>, mixed tocopherols<sup>22</sup> (or  $\alpha$ -carotene)<sup>23</sup> can equal or even surpass  $\alpha$ -tocopherol (or  $\beta$ -carotene) in activity. Moreover,  $\alpha$ -tocopherol is a double-edged sword. In the study by Hercberg *et al.*<sup>1</sup> the potential of  $\alpha$ -tocopherol for prooxidative behaviour and for disrupting the natural balance of antioxidative substances was noted in passing, but had no influence on the study's design, or conclusions that vitamin E does not prevent cancer or CVD. Although it is widely taken to be a (lipid-soluble) antioxidant, this is true only in the presence of an aqueous phase containing vitamin C<sup>24</sup>. Without vitamin C,  $\alpha$ -tocopherol becomes a prooxidant, i.e. it promotes oxidative degradation of LDL<sup>25</sup>, a harmful rather than beneficial process. Apparently, unless they are first quenched by vitamin C, tocopheryl radicals are capable of initiating new oxidative radical chains. Therefore it is essential that all subjects in vitamin E dietary studies be replete with vitamin C at all times, which is rarely done. This problem is obviously magnified when supernormal doses of vitamin E (> about 50 IU/d) are given.

The upshot of these considerations is that there is really no paradox, and that only studies involving complete natural mixtures of vitamin E (ensuring repletion with vitamin C at all times) and  $\beta$ -carotene congeners can determine their efficacy in cancer or heart disease.

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