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Review

Vitamin E supplementation and lifespan in model organisms

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ABSTRACT

We have conducted a comprehensive literature review regarding the effect of vitamin E on lifespan in model organisms including single-cell organisms, rotifers, *Caenorhabditis elegans*, *Drosophila melanogaster* and laboratory rodents. We searched Pubmed and ISI Web of knowledge for studies up to 2011 using the terms "tocopherols", "tocotrienols", "lifespan" and "longevity" in the above mentioned model organisms. Twenty-four studies were included in the final analysis. While some studies suggest an increase in lifespan due to vitamin E, other studies did not observe any vitamin E-mediated changes in lifespan in model organisms. Furthermore there are several studies reporting a decrease in lifespan in response to vitamin E supplementation. Different outcomes between studies may be partly related to species-specific differences, differences in vitamin E concentrations and the vitamin E congeners administered. The findings of our literature review suggest that there is no consistent beneficial effect of vitamin E on lifespan in model organisms which is consistent with reports in human intervention studies.

1. Introduction

The term vitamin E is used to describe a group of eight lipid soluble substances with a chromanol ring and a saturated (tocopherols) or unsaturated (tocotrienols) carbon side chain (see Fig. 1). Depending on the methyl groups found at the chromanol groups these compounds are referred to as α-, β-, γ- or δ-tocopherols and tocotrienols (Kamal-Eldin and Appelqvist, 1996). As a free radical scavenger and lipophilic molecule, vitamin E may protect the membranes from oxidative damage by reacting with fatty acid peroxides via electron transfer (Traber and Atkinson, 2007). Additionally, vitamin E may regulate gene expression (Azzi, 2007; Rimbach et al., 2002, 2010). Over the last few decades a possible influence of vitamin E on longevity has been studied in animals and humans. However, it remains unclear whether this group of antioxidants can prolong or, on the contrary, decrease lifespan. In this review, we summarize the studies on vitamin E supplementation and lifespan in model organisms of increasing biological complexity, thereby addressing the question if and to what extent vitamin E increases the lifespan of single cell organisms and rotifers, nematodes, flies, mice and rats.

2. Vitamin E supplementation in different model organisms

2.1. Single-celled organisms and rotifers

The effect of vitamin E on single-cell organisms and rotifers was examined in five studies (Enesco and Verdone-Smith, 1980; Lam et al., 2010; Minogue and Thomas, 2004; Sawada and Enesco, 1984; Thomas and Nyberg, 1988). Of these studies, four reported an increase in lifespan with vitamin E and one, on *Saccharomyces cerevisiae* (Lam et al., 2010), showed a reduction in lifespan. These findings are summarized in Table 1.

2.1.1. Rotifer Philodina

The first study to investigate the influence of vitamin E on the lifespan of rotifers was conducted by Enesco and Verdone-Smith in (1980) on the rotifer *Philodina*. In this study, DL-α-tocopherol at a concentration of 0.05 μl/ml (solubilized in Tween 80) was added to the medium in which the rotifers were grown. The rotifers were transferred to new medium every 24 h and checked for vitality. Vitamin E treatment significantly increased mean lifespan compared to both the solvent control and the non-solvent control (by 1.9 days (10.2%) and 1.7 days (9.2%) respectively), whilst maximum lifespan was unaffected. Furthermore, the average number of

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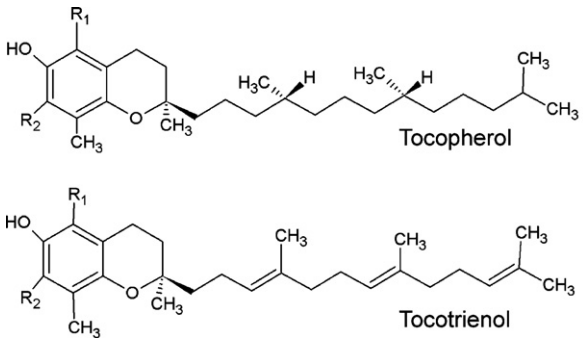

	R_1	R_2
α-	CH_3	CH_3
β-	CH_3	H
γ-	H	CH_3
δ-	H	H

Fig. 1. Chemical structures of tocopherols and tocotrienols.

Table 1
Vitamin E lifespan studies on single-cell organisms and rotifers in chronological order.

Species	*n*	Form of vitamin E	Dose	Initiation of treatment	Mean lifespan	Maximum lifespan	Study
Rotifer philodina	96	DL-α-Tocopherol	0.05 μg/ml	After birth	+1.9 days (10.2%)	No effect	Enesco and Verdone-Smith (1980)
Asplanchna brightwelli	24	DL-α-Tocopherol	25 μg/ml	0–3 h prior to birth	+1.1 day (+17%)	–	Sawada and Enesco (1984)
Paramecium tetraurelia	64 lines	DL-α-Tocopherol	25 μg/ml 25 μg/ml	Day 0 Day 9	+8.5 days (n.s.) +18.3 days	+23 days (n.s.) +80 fissions (n.s.) –	Thomas and Nyberg (1988)
Paramecium tetraurelia	96	α-Tocopherol	10 μg/ml 100 μg/ml 1000 μg/ml 10,000 μg/ml	Day 0 Day 0 Day 0 Day 0	−7.5 days (n.s.) +30 days (n.s.) +115 days +216.5 days	– – – –	Minogue and Thomas (2004)
Saccharomyces cerevisiae	90–110 per plate	α-Tocopherol	20, 50, 80, 120, 150 μM	–	–	–	Lam et al. (2010)

–, data is not available; n.s., not significant.

offspring per rotifer was significantly increased by 10% compared to both control groups.

2.1.2. *Asplanchna brightwelli*

Sawada and Enesco examined the effect of vitamin E on another rotifer, *Asplanchna brightwelli*. DL-α-Tocopherol solubilized in Tween-80 was used at concentrations ranging between 5 and 100 μg/ml. They demonstrated that 25 μg/ml of DL-α-tocopherol extended mean lifespan (±S.E.M.) of the rotifers from 5.5 days (±0.13) to 6.4 days (±0.17) compared to the control, whilst lower concentrations had little effect. Interestingly, the highest concentration used, 100 μg/ml, caused a reduction in lifespan. Based on these initial results, they used α-tocopherol at a concentration of 25 μg/ml in subsequent experiments aimed at elucidating the exact timing of the effects. They solubilized 25 μg/ml α-tocopherol in either Tween-80 or ethanol and found that the increase in mean lifespan was similar with both solvents. By separating the rotifers into pre-reproductive, reproductive and post-reproductive periods, they found that lifespan was only significantly increased during the pre-reproductive period. The number of offspring was unaffected in this experiment (Sawada and Enesco, 1984).

2.1.3. *Paramecium tetraurelia*

In 1988, Thomas and Nyberg were the first to investigate the effects of vitamin E on the lifespan of a single-celled organism, *Paramecium tetraurelia*. The effect of 25 μg/ml DL-α-tocopherol was examined in eight different genotypes, of which only one (that with the shortest mean lifespan) showed a significant increase in mean lifespan, measured in days and fissions. The supplemented subgroups demonstrated a bulk increase in maximum lifespan by 17.6% and in mean lifespan by 14.1% compared with controls (supplementation 58.5 ± 16.6 vs. control 50.5 ± 10.6). Subsequent experiments investigated the impact of switching the organisms from control to vitamin E (25 μg/ml) media early in life at days 0, 1, 9, 17 or 25. Only those subgroups transferred at day 9 showed a significant increase in mean lifespan in days and fissions. Those that were transferred to α-tocopherol-containing media after 9 days of clonal lifespan showed only minor, inconsistent effects on lifespan extension.

Table 2
Maximum clonal lifespan in days and fissions of *P. tetraurelia* supplemented with different amounts of α-tocopherol.

	Control	25 μg/ml	100 μg/ml	1000 μg/ml
Maximum clonal lifespan in fissions	237	260	271	330
Maximum clonal lifespan in days	66	68	74	141

Differences are not statistically significant ($p > 0.05$) (modified from Thomas and Nyberg, 1988)

This study also evaluated the effects of higher concentrations of α-tocopherol (100 and 1000 μg/ml) on maximum clonal lifespan. An increase in the maximum lifespan was observed with increasing doses of α-tocopherol, yet these data were non-significant. Table 2 summarizes the results of this experiment.

Interestingly, however, when comparing controls to organisms given 25 μg/ml of α-tocopherol and organisms given 100 μg/ml