Possibility of Clinical Application of Vitamin E to Cataract Prevention

Yoshiji Ohta*

Department of Chemistry, School of Medicine, Fujita Health University, Toyoake 470–1192, Japan

Received 30 October, 2003; Accepted 10 November, 2003

Summary  It has been implicated that oxidative stress is involved in the development of aged-related and diabetic cataracts in humans and also in cataract development in a variety of in vivo experimental cataract models. Therefore, this article will review the possibility of the clinical application of vitamin E to cataract prevention, based on data concerning the level of vitamin E in normal and cataractous lenses of humans and experimental animals, the relationship between dietary vitamin E intake and the risk of cataracts, the effect of vitamin E supplementation on cataract development in humans, and the effect of oral or parenteral vitamin E treatment or topical vitamin E instillation on cataract development in a variety of in vivo experimental cataract models. These data reported so far may allow us to think of a possibility that vitamin E is clinically applied to cataract development.

Key Words: cataract (humans and experimental animals), oxidative stress, vitamin E, cataract prevention

Introduction

Cataract is the major cause of blindness worldwide. About 40% of the estimated 42 million blind people worldwide are blind from cataract [1]. In Japan, the percentage of people possessing cataracts including early age-related cataracts or senile cataracts is 29–32% in the fortieth year of age, 24–54% in the fiftieth year of age, 43–83% in the sixtieth year of age, 60–97% in the seventieth year of age, and 98–100% in the eightieth year or more of age [2]. Although there are several cataract risk factors in humans, diabetes is one of the major cataract risk factors [2, 3]. In people of middle or advanced age, the frequency of cataract formation is higher in diabetics than in non-diabetics and is raised with an increase in age [4, 5].

Cataract treatment in humans is now conducted by surgical operation, i.e., cataract surgery, and then intraocular lenses are inserted into the cataract surgery-operated eyes to recover visual acuity. However, an ideal treatment of cataracts is carried out without surgical operation. Namely, cataracts are treated by administration of anticataract agents. Although the development of anticataract agents has been attempted in several countries, there is nothing definitively effective in the treatment of human cataracts at present. Much attention has been paid to the involvement of oxidative stress in cataract development in humans and experimental animals. The relationship between vitamin E and cataracts has been studied in humans and experimental animals. In this review, therefore, I will describe the relationship between cataracts and oxidative stress, the level of vitamin E in normal and cataractous lenses of humans and experimental animals, the relationship between dietary vitamin E intake and the risk of cataracts, the effect of vitamin E supplementation on
cataракт development in humans, and the effect of oral or parenteral vitamin E treatment or topical vitamin E instillation on cataract development in a variety of in vivo experimental cataract models, and will discuss whether there is a possibility that vitamin E is clinically applied to cataract prevention.

**Relationship between Cataracts and Oxidative Stress**

Oxidative stress is a state of the imbalance between antioxidant defense systems and oxidative insult, which is most likely resulted from decreased levels of antioxidants or increased oxidative insult or both. There are several reports showing that the level of lipid peroxides, which are produced in the peroxidation of membrane lipids via reactive oxygen species such as superoxide radical, hydroxyl radical, hydrogen peroxide, and singlet oxygen, is higher in cataractous lenses than in clear lenses in humans [6–10] and that the level of lens lipid peroxide is further increased in diabetic patients with cataracts [7, 8, 10]. It is known that the concentration of hydrogen peroxide in aqueous and vitreous humors surrounding the lens is higher in people with cataracts than in people without cataracts [7, 11]. It is also known that cataract patients who have high concentrations of hydrogen peroxide in the aqueous humor possesses high concentrations of hydrogen peroxide in the lens and that there is a significant correlation between aqueous humor and lens hydrogen peroxide concentrations in the cataract patients [11]. It has been reported that hydroxyl radical attack on lens proteins may play a role in the development of age-related nuclear cataracts [12, 13].

The antioxidant defense system in lenses is composed of antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx), glutathione reductase (GR) and antioxidants, such as reduced glutathione (GSH), vitamin C or ascorbic acid, and vitamin E [14, 15]. It has been reported that lens SOD, catalase, GPx, and GR activities and GSH levels are lower in cataractous patients than in normal individuals [7, 9, 10, 16–20] and the extents of reduction of lens SOD and GR activities and GSH levels in cataractous patients are relative to the severity of cataracts [17, 19, 20].

The relationship between cataracts and oxidative stress has been examined in a variety of in vivo experimental cataract models. An increase in lens lipid peroxide levels and/or decreases in lens SOD, catalase and GPx activities and GSH and ascorbic acid levels with cataract development have been reported in rabbits administered with a catalase inhibitor 3-aminotriazole [21, 22], rats with streptozotocin (STZ)-induced diabetes [23, 24], rats fed a diet high in galactose [25, 26], rats treated with selenite [27], diabetic WBN/Kob rats [28, 29], and Emory mice, a suitable model for age-related human cataracts [30, 31]. Kubo et al. [32] have shown that hydroxyl radical formation occurs in accordance with accumulation of galactitol, a polyol, converted from galactose via the polyol pathway in the cataractous lens of galactose-fed rats, and have suggested that hydroxyl radical may play an important role in the early stage of galactose cataract process. Thus, it has been implicated that oxidative stress contributes to cataract development in various cataract models of experimental animals as well as in humans.

**Distribution of Vitamin E in Ocular Lenses**

Vitamin E is well known to exert an antioxidant action by breaking the chain-reaction of lipid peroxidation and scavenging reactive oxygen species and a membrane-stabilizing action [33, 34]. As to the distribution of vitamin E in ocular lenses, Bessembs et al. [35] have reported that, in normal human lenses, the content of α-tocopherol is slightly higher in the nucleus than the cortex and that, in nuclear-cataractous human lenses, the content of α-tocopherol is rather higher in the nucleus than in the cortex. Yeum et al. [36] have also shown in cataractous human lenses that α-tocopherol levels are higher in the epithelial/cortical layer than in the nuclear layer. Thus, the distribution of vitamin E in human lenses seems to be altered in response to cataract development. Hirai et al. [37] have shown that the level of α-tocopherol in the lens fractions of rabbits is as follows: capsule/epithelium>nucleus>anterior cortex>posterior cortex. Nagata et al. [38] have shown that the highest level of α-tocopherol in 1-month-old rat lenses is in the nuclear region followed by the deeper anterior cortex, the shallow anterior cortex, the shallow posterior cortex, and the equatorial region and that the distribution pattern of α-tocopherol is similar in 4- and 12-month-old rat lenses and the level of α-tocopherol in the lens fractions of 4- and 12-month-old rats is as follows: nucleus>deeper posterior cortex>deeper anterior cortex>shallow posterior cortex>shallow anterior cortex>equator. This finding indicates that the distribution of vitamin E
in ocular lenses is altered with aging.

**Relationship between Dietary Vitamin E Intake and Cataracts in Humans and Experimental Animals**

There are several papers on the relationship between vitamin E and cataracts in humans. Leske et al. [39] showed a reduced risk of cortical and mixed-type of opacities among persons with high dietary vitamin E intakes in the Lens Opacities Case-Control Study; in the follow-up study, however, the same authors could not confirm the association between the reduced risk of cortical opacities and higher dietary vitamin E intake but suggested the relation of higher dietary vitamin E intake and higher plasma vitamin E levels to a reduced risk of nuclear opacity progression [40]. Vitale et al. [41] reported that higher levels of plasma \( \alpha \)-tocopherol were associated with a reduced risk of nuclear opacity and that middle levels of plasma \( \alpha \)-tocopherol were associated with a reduced risk of cortical opacity, although no association was observed for high levels of plasma \( \alpha \)-tocopherol. In the Beaver Dam Eye Study, Lyle et al. [42] indicated the possibility that nuclear cataracts may be linked inversely to vitamin E status. However, no significant associations between higher vitamin E intake and less severe nuclear or cortical opacities were found by Jacques and Chylack [43], Mares-Perlman et al. [44], Gale et al. [45], and Taylor et al. [46]. Cai et al. [47] showed in vitamin E deficient rats that vitamin E deficiency caused posterior subcapsular cortical degeneration and/or vacuolization at the equatorial region with a increase in lipid peroxide levels and a decrease in SOD activity in the lenses. Recently, Kojima et al. [48] have shown in a rat model of prednisolone-induced cataract that vitamin E deficiency is a subliminal cataractogenesis risk factor.

**Lens Vitamin E Levels in Cataractous Human Lenses**

In 1983, Dillon et al. [49] reported that when the content of \( \alpha \)-tocopherol in normal human lenses (60–80 years of age) was compared to that in similar aged cataractous human lenses, the cataractous lenses contained 10% lower \( \alpha \)-tocopherol than the normal lenses, although the difference in that level between the normal and cataractous lenses was not statistically significant. Later, Bessemns et al. [35] reported that when \( \alpha \)-tocopherol contents in the cortex and nucleus of nuclear-cataractous human lenses (55–81 years of age) were compared to those of normal human lenses (50–86 years of age), there was no difference in the nucleus content of \( \alpha \)-tocopherol between the cataractous and normal lenses but the cortex content of the vitamin E was significantly higher in the cataractous lenses than in the normal lenses. Yeum et al. [36] have shown in American people with and without cataracts that the concentration of \( \alpha \)-tocopherol is higher in cataractous lenses (76–81 year of age) than in normal lenses (53–60 years of age), while the concentration of \( \gamma \)-tocopherol is lower in the cataractous lenses than in the normal lenses. Leiria et al. [50] have shown that membranes isolated from the lenses of patients with age-related and diabetic cataracts contain two to three-fold higher vitamin E than membranes isolated from normal human lenses, although the cataractous lens membranes contained higher lipid peroxide than the normal lens membranes. Thus, lens vitamin E levels are variable in cataractous human lenses.

**Lens Vitamin E Levels in Cataractous Lenses of Experimental Animals**

In 1986, Hirai et al. [51] reported that although vitamin E was present in the lens of 6-week-old rats, its analogues except for \( \alpha \)-tocopherol were not detected in these lenses and that, in 6-week-old rats with STZ-induced diabetes, lens \( \alpha \)-tocopherol content began to decrease after observation of overt diabetes but before the formation of vacuoles at the equatorial region of the lens and the decrease in that content was gradually enhanced with cataract development. At the same time, the same authors showed that although a transient increase in lens lipid peroxide content occurred before cataract formation, there was no increase in that content during cataract development [51]. In the same year, Hirai et al. [52] showed in another report that, in weanling rats given a diet containing 38% galactose ad libitum, lens \( \alpha \)-tocopherol content began to decrease before the formation of vacuoles at the equatorial region of the lenses, i.e., at 2-day of feeding, and the decreased \( \alpha \)-tocopherol content was maintained at a similar level during cataract development, i.e., at 5- and 7-day of feeding, although increased lipid peroxide and decreased GSH contents were observed in the lens before cataract formation and during cataract development. Ogino et al. [53] showed in adult rabbits...
with 3-aminitriazole administration that lens vitamin E content decreased with lens vitamin C depletion at the onset of cataract formation. Mitton and Trevithick [54] showed in adult rats with STZ-induced diabetes that there was no change in α-tocopherol content in the lens at 2 and 4 weeks after diabetes induction, although decreases in GSH and total ascorbic acid contents were observed in the lens at 1 week after diabetes induction. It is known that the feature and the development of galactose cataracts are different depending on the age of rats used and the content of galactose in diet [55–57]. Namely, the lens of mature rats (6 weeks old or more) fed a diet low in galactose has opacities at the anterior and posterior subcapsular regions of the cortex like in the case of human diabetic cataracts, while the lens of immature rats (less than 6 weeks old) fed a diet high in the sugar has vacuoles at the equatorial region initially and then opacities developing toward the anterior and posterior subcapsular regions of the cortex. It is also known that the speed of cataract development is faster in immature rats fed a diet high in galactose than in mature rats fed a diet low in the sugar [55–57]. Therefore, we examined changes in lens α-tocopherol levels with galactose cataract development in young (5-week-old), mature (12-week-old), and aged (12-month-old) rats given a 25% galactose diet at a fixed dose (15 g/day per animal) [26, 58]. As a result, it was found that 5-week-, 12-week-, and 12-month-old rats given a 25% galactose diet showed different changes in lens α-tocopherol levels with galactose cataract development. Namely, in 5-week-old rats given a 25% galactose diet over a 45-day period, lens α-tocopherol content did not change at 12-day of feeding at which time no vacuole formation occurred at the equatorial region of the lens, but that content was reduced at 18 days of feeding at which time vacuoles appeared at a part of the equatorial region, and the reduced α-tocopherol content was increased over the level of control rats at 45-day of feeding at which time cortical cataracts were observed in the lens. In 12-week-old rats given a 25% galactose diet over a 15-week period, lens α-tocopherol content remained reduced before the formation of vacuoles in the equatorial region of the lens, i.e., at 2-week of feeding, and during cortical cataract development, i.e., at 7- and 15-week of feeding. In 12-month-old rats given a 25% galactose diet over an 8-month period, lens α-tocopherol content did not change before cataract formation, i.e., at 4-month of feeding, but increased at a stage of early cataracts (suture accentuation) appearing in the central of the lens, i.e., at 6-month of feeding, and the increased α-tocopherol content was returned to the level of control rats at a stage of progressed cataracts reaching the nuclear region of the lens, i.e., at 8-month of feeding. Thus, lens vitamin E levels are variable in cataractous lenses of experimental animals.

Effect of Vitamin E Supplementation on Cataract Development in Humans

Teikari et al. [59] reported that when middle aged, Finish smoking men (50–69 years old) were orally supplied with α-tocopherol (50 mg/day) for 5 to 8 years, this vitamin E supplementation did not influence the prevalence and severity of nuclear, cortical, subcapsular cataracts. In the Vitamin E and Cataract Prevention Study, Nadalin et al. [60] showed that when Australian women and men (55–80 years old) were orally supplied with vitamin E (500 IU/day), there was a significant association between prior vitamin E supplementation and the absence of cortical opacity, after adjusting for age, while there was no apparent protective role of prior vitamin E supplementation in terms of nuclear opacity and nuclear color regardless of the level, regularity or duration of vitamin E intake. Olmedilla et al. [61] have shown in elderly Spanish women with age-related cataracts that when improvement of visual function is compared between subjects supplied with and without α-tocopherol (100 mg/day) for 24 months, this vitamin E supplementation has no beneficial effect on the visual performance. However, Seth and Khur [62] have shown in a random trial of 50 patients (50 years or above) with unilateral/bilateral idiopathic immature age-related cataracts requiring surgery at least one eye that when cataractous patients are orally supplied with vitamin E (100 mg twice day) for 30 days, the size of lens opacity in cortical cataractous patients, but not nuclear cataractous patients, receiving vitamin E supplementation is significantly decreased as compared with placebo patients. The same authors have also shown in the random trial that this vitamin E supplementation causes an increase in lens GSH levels in patients with cortical cataracts and an increase in lens vitamin E levels and a decrease in lens lipid peroxide levels in patients with cortical or nuclear cataracts [62]. Thus, the evaluation of vitamin E supplementation in cataract prevention in humans is not always consistent among studies.
reported so far.

Effect of Vitamin E Treatment on Cataract Development in Experimental Animals

In 1950, Charalampous and Hegsted [63] reported that feeding of not only a high fat diet but also a fat-free diet containing a high amount of vitamin E retarded cataract formation in rats with alloxan-induced diabetes. Later than 1970, the preventive or retarding effect of oral or parenteral vitamin E treatment on cataract development has been studied extensively in a variety of in vivo experimental cataract models [64–76]. Effectiveness of oral or parenteral vitamin E treatment in cataract prevention has been confirmed in a variety of in vivo experimental cataract models, as shown in Table 1.

An ideal treatment of cataractous patients with vitamin E is the topical instillation of vitamin E as an ophthalmic solution to the eyes of the patients because topical vitamin E instillation is not troublesome for cataractous patients if the prepared vitamin E ophthalmic solution has a low viscosity and is not stimulative and because topical vitamin E instillation makes it possible to deliver administered vitamin E to ocular lenses in higher concentrations compared to systemic vitamin E administration. Kojima et al. [77] evaluated the efficacy of a 5% vitamin E ophthalmic solution in its topical and systemic administration (twice a day) using a new rat steroid–cataract model developed by them and found that topical administration of the vitamin E ophthalmic solution showed a significant inhibition of cataract development in the rat steroid–cataract model, although the vitamin E ophthalmic solution showed a slightly weaker inhibitory effect in topical administration than in systemic administration. Nagata et al. [78] reported that when a 1% vitamin E acetate solution, which was prepared by emulsifying vitamin E acetate with polysorbate 80, a detergent, was instilled to both eyes of rats with a single oral naphthalene administration 5 times a day everyday for 9 weeks and the effect of the instilled vitamin E acetate on cataract development was evaluated during the instillation period, this vitamin E acetate instillation retarded the progression rather than the formation of naphthalene-induced cataracts. In addition, Nagata et al. [79] measured the concentrations of deuterium (D3)-labeled α-tocopherol acetate and D3-labeled α-tocopherol derived from D3-labeled α-tocopherol acetate in the aqueous humor and lens of rats after instilling a 1% D3-labeled α-tocopherol acetate solution prepared with polysorbate 80 into the cul-de-sac of both eyes of the rats at a dose of 5 μL/eye 5 times a day for successive 1 and 3 weeks. As a result, α-tocopherol acetate was found to be penetrated into the aqueous humor and lens of rats by instillation of the emulsified α-tocopherol acetate solution to their eyes. However, the possibility cannot be excluded that detergents such as polysorbate 80 to emulsify vitamin E are harmful to eye tissues.

Hattori et al. [80] prepared vitamin E-containing liposomes, in which tritium-labeled α-tocopherol is present as a tracer, with dipalmitoylphosphatidylcholine (DPPC), dioleoylphosphatidylcholine (DOPC), or palmitoleoylphosphatidylcholine (POPC) in small unilamellar vesicles and examined the transport of vitamin E into the lens of mice at 30 min after

Vol. 35, No. 1, 2004
instilling each prepared vitamin E-containing liposome suspension to both eyes six times at intervals of 30 min. The highest transport of vitamin E into the lens after topical instillation of vitamin E-containing liposomes was found in DOPC liposomes followed by DPPC liposomes and POPC liposomes. The same authors showed in rabbits with topical instillation of vitamin E-containing liposomes prepared with DOPC to their eyes that vitamin E instilled in a liposomal form was transported into the lens via the aqueous humor and cornea. Furthermore, Hat- tori et al. [81] reported that opacification in isolated rat lenses incubated in medium containing a high concentration of glucose was retarded with prevention of vitamin E depletion and increased lipid peroxidation by treatment with vitamin E-containing liposomes prepared with DPPC. Kaneda et al. [82] also reported that topical instillation of vitamin E-containing liposomes prepared with DPPC to both eyes of rats fed a 50% galactose diet three times a day retarded the progression rather than the formation of sugar cataracts.

We observed that when vitamin E-containing liposomes were prepared with DPPC and DOPC in various ratios (w/w) and α-tocopherol and then the transport of vitamin E in the prepared vitamin E-containing liposomes into isolated rat lenses was examined under osmotic stress induced by a high concentration of glucose, the highest increase in vitamin E in the lens subjected to osmotic stress was found in vitamin E-containing liposomes prepared at the ratio of 7:3 for DPPC and DOPC (unpublished data). Furthermore, it was found that vitamin E-containing liposomes prepared with DPPC and DOPC at the ratio of 7:3 (w/w) delayed opacification in isolated rat lenses treated with xylose [83], methylprednisolone [84] or diethylmaleate [85]. Therefore, we prepared vitamin E-containing liposomes or vitamin E-free liposomes with DPPC and DOPC at the ratio of 3:7 (w/w) and R,R,R-α-tocopherol as an ophthalmic solution as shown in Fig. 1 and examined whether the prepared vitamin E-containing liposome suspension exerts a therapeutic effect on sugar cataracts in 5-week-, 12-week-, and 12-month-old rats fed a 25% galactose diet at a fixed dose (15 g/day per animal) by its topical instillation to their both eyes at a dose of 10 µl/eye (three times a day) [86, 87]. As shown in Table 2, daily instillation of vitamin E-containing liposomes, but not vitamin E-free liposomes, to both eyes of 5- and 12-week-old rats fed a 25% galactose diet for 4 and 9 weeks, respectively, which was started at a stage of early cataracts, i.e., vacuole formation at the equatorial region of the lens, was found to retard the progression of cortical cataracts appearing after vacuole formation significantly. As shown in Table 3, daily instillation of vitamin E-containing liposomes, but not vitamin E-free liposomes, to both eyes of 12-month-old rats fed a 25% galactose diet for 2 months, which was started at a stage of early cata-

---

**Table 1. Outline of the preparation of vitamin E-containing or vitamin E-free liposomes used an ophthalmic solution.**

<table>
<thead>
<tr>
<th>Vitamin E-containing liposomes</th>
<th>Vitamin E-free liposomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.3 M R, R, R-α-tocopherol</td>
<td>10 µl</td>
</tr>
<tr>
<td>Dissolution with 1 ml of chloroform</td>
<td>—</td>
</tr>
<tr>
<td>Evaporation in vacuum overnight</td>
<td>—</td>
</tr>
<tr>
<td>Hydration by repeated vortex mixing under nitrogen gas atmosphere</td>
<td>—</td>
</tr>
<tr>
<td>Liposomes (small unilamellar vesicles)</td>
<td>—</td>
</tr>
</tbody>
</table>

*HBSS, Hanks’ balanced salt solution (pH 7.2)*
Table 2. Effect of vitamin E-containing liposome instillation on cataract progression in 5-week- and 12-week-old rats fed a 25% galactose diet.

<table>
<thead>
<tr>
<th>Treatment period and group</th>
<th>Lens opacity incidence (%)</th>
<th>0</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-week-old rats(b)</td>
<td>0 week of instillation</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>4 weeks of instillation</td>
<td>0</td>
<td>15</td>
<td>30</td>
<td>35</td>
<td>20</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>+ Liposome (– vitamin E)</td>
<td>0</td>
<td>20</td>
<td>35</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>+ Liposome (+ vitamin E)</td>
<td>0</td>
<td>50</td>
<td>30</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>12-week-old rats(c)</td>
<td>0 week of instillation</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>9 weeks of instillation</td>
<td>0</td>
<td>0</td>
<td>30</td>
<td>45</td>
<td>25</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>+ Liposome (– vitamin E)</td>
<td>0</td>
<td>0</td>
<td>50</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>+ Liposome (+ vitamin E)</td>
<td>0</td>
<td>25</td>
<td>45</td>
<td>30</td>
<td>0</td>
</tr>
</tbody>
</table>

* Lens opacity incidence was evaluated based on the following severity gradation: grade 0, no opacity; grade I, vacuoles present at a part of the cortical equator; grade II, vacuoles present at all parts of the cortical equator; grade III, vacuoles and their confluent spreading from the cortical equator toward the center of the cortex; grade IV, large, interconnected opacities covering the whole cortex. The number of 5-week-old rats used is 10–11. The number of 12-week-old rats used is 11–12. * Significantly different from the corresponding galactose-fed group at \(p<0.05\).

Table 3. Effect of vitamin E-containing liposome instillation on cataract progression in 12-month-old rats fed a 25% galactose diet.

<table>
<thead>
<tr>
<th>Treatment period and group</th>
<th>Lens opacity incidence (%)</th>
<th>0</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 week of instillation</td>
<td>Galactose-fed group</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>2 months of instillation</td>
<td>0</td>
<td>0</td>
<td>70</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>+ Liposome (– vitamin E)</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>70</td>
<td>10</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>+ Liposome (+ vitamin E)</td>
<td>0</td>
<td>15</td>
<td>30</td>
<td>50</td>
<td>0</td>
</tr>
</tbody>
</table>

* Lens opacity incidence in each group (10 animals) was evaluated based on the following severity gradation: grade 0, no opacity; grade I, suture accentuation at the central region; grade II, cortical opacities present in the peripheral region; grade III, cortical opacities covering the entire region which tented to become dense in the posterior subcapsular region rather than in the anterior subcapsular region; grade IV, nuclear opacities in addition to cortical opacities covering the entire region. * Significantly different from the galactose-fed group at \(p<0.05\).

Table 4. Effect of vitamin E-containing liposome instillation on lens \(\alpha\)-tocopherol levels in 5-week-, 12-week-, and 12-month-old rats fed a 25% galactose diet.

<table>
<thead>
<tr>
<th>Treatment period and group</th>
<th>Lens (\alpha)-tocopherol (mg/lens)</th>
<th>0 week of instillation</th>
<th>9 weeks of instillation</th>
<th>4 weeks of instillation</th>
<th>0 week of instillation</th>
<th>9 weeks of instillation</th>
<th>4 weeks of instillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-week-old rats(b)</td>
<td>Control group</td>
<td>10.15±0.78(a)</td>
<td>7.22±0.60(a)</td>
<td>8.13±0.71(a)</td>
<td>10.15±0.78(a)</td>
<td>7.22±0.60(a)</td>
<td>8.13±0.71(a)</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>17.03±1.38(a)</td>
<td>17.34±2.38(a)</td>
<td>17.34±2.38(a)</td>
<td>17.03±1.38(a)</td>
<td>17.34±2.38(a)</td>
<td>17.34±2.38(a)</td>
<td></td>
</tr>
<tr>
<td>+ Liposome (– vitamin E)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td></td>
</tr>
<tr>
<td>+ Liposome (+ vitamin E)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td>13.88±0.95(a)</td>
<td></td>
</tr>
<tr>
<td>12-week-old rats(d)</td>
<td>Control group</td>
<td>13.63±2.88</td>
<td>13.01±2.73</td>
<td>12.63±2.88</td>
<td>13.63±2.88</td>
<td>13.01±2.73</td>
<td>12.63±2.88</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>13.63±1.15</td>
<td>13.63±1.15</td>
<td>13.63±1.15</td>
<td>13.63±1.15</td>
<td>13.63±1.15</td>
<td>13.63±1.15</td>
<td></td>
</tr>
<tr>
<td>+ Liposome (– vitamin E)</td>
<td>11.13±1.45(a)</td>
<td>11.13±1.45(a)</td>
<td>11.13±1.45(a)</td>
<td>11.13±1.45(a)</td>
<td>11.13±1.45(a)</td>
<td>11.13±1.45(a)</td>
<td></td>
</tr>
<tr>
<td>+ Liposome (+ vitamin E)</td>
<td>19.13±2.63(a)</td>
<td>19.13±2.63(a)</td>
<td>19.13±2.63(a)</td>
<td>19.13±2.63(a)</td>
<td>19.13±2.63(a)</td>
<td>19.13±2.63(a)</td>
<td></td>
</tr>
<tr>
<td>12-month-old rats(e)</td>
<td>Control group</td>
<td>13.52±2.65</td>
<td>13.52±2.65</td>
<td>13.52±2.65</td>
<td>13.52±2.65</td>
<td>13.52±2.65</td>
<td>13.52±2.65</td>
</tr>
<tr>
<td>Galactose-fed group</td>
<td>7.22±1.76(a)</td>
<td>7.22±1.76(a)</td>
<td>7.22±1.76(a)</td>
<td>7.22±1.76(a)</td>
<td>7.22±1.76(a)</td>
<td>7.22±1.76(a)</td>
<td></td>
</tr>
<tr>
<td>+ Liposome (– vitamin E)</td>
<td>13.72±1.15(a)</td>
<td>13.72±1.15(a)</td>
<td>13.72±1.15(a)</td>
<td>13.72±1.15(a)</td>
<td>13.72±1.15(a)</td>
<td>13.72±1.15(a)</td>
<td></td>
</tr>
<tr>
<td>+ Liposome (+ vitamin E)</td>
<td>18.83±2.62(a)</td>
<td>18.83±2.62(a)</td>
<td>18.83±2.62(a)</td>
<td>18.83±2.62(a)</td>
<td>18.83±2.62(a)</td>
<td>18.83±2.62(a)</td>
<td></td>
</tr>
</tbody>
</table>

* Values are means±S.D. * The number of animals used is 8. * The number of animals used is 8. * The number of animals used is 10. * Significantly different from the corresponding control group at \(p<0.05\). * Significantly different from the corresponding galactose-fed group at \(p<0.05\).
content by galactose feeding was significantly attenuated by instillation of vitamin E-containing liposomes, but not vitamin E-free liposomes (Table 4). In 12-month-old rats fed a 25% galactose diet alone, although lens α-tocopherol content significantly increased at the onset of instillation and did not change at the end of instillation, the lens vitamin E content in the galactose-fed rats was significantly increased by instillation of vitamin E-containing liposomes, but not vitamin E-free liposomes (Table 4). In addition, it was found that although the lenses of 5-week-, 12-week-, and 12-month-old rats fed a 25% galactose diet alone had increased lipid peroxide, galactitol, and water contents and decreased GSH content at the onset and end of instillation, the increased lipid peroxide content and the decreased GSH content in the lenses of these galactose-fed rats were significantly attenuated by instillation of vitamin E-containing liposomes. Thus, daily instillation of vitamin E-containing liposomes to galactose-fed rats was found to be able to retard sugar cataract progression possibly through the antioxidant action of vitamin E present in the instilled vitamin E-containing liposomes regardless of the speed of cataract progression, the pattern of cataract progression, and the change in lens vitamin E levels during cataract progression. These findings suggest that topical instillation of vitamin E in a liposomal form may be effective in retarding cataract progression in humans with galactosemia or diabetes.

Conclusions

It has been implicated that oxidative stress is involved in the development of aged-related and diabetic cataracts in humans and also in cataract development in a variety of in vivo experimental cataract models. Lens vitamin E levels are variable in cataractous lenses of humans and experimental animals. In humans, the relationship between dietary vitamin E intake and the risk of cataract and the effect of vitamin E supplementation on cataract development have not been concluded yet. However, many studies on the effect of oral or parenteral vitamin E treatment on cataract development in a variety of in vivo experimental cataract models indicate that oral or parenteral vitamin E treatment prevents or retards cataract development. In addition, topical instillation of a vitamin E ophthalmic solution in an emulsion form or in a liposomal form has been shown to retard cataract development in some in vivo cataract models. Therefore, there seems to be a possibility that vitamin E is clinically applied to cataract development.

References


Vitamin E and Cataract Prevention


Ross, W.M., Creighton, M.O., and Trevithick, J.R.: Radiation cataractogenesis induced by neutron or...
gamma irradiation in the rat lens is reduced by vitamin E. *Scanning Micros.*, 4, 641–650, 1990.


