Antioxidant Properties of Vitamins C and E:   
A Literature Review

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**Introduction**

Antioxidants have received a great deal of attention in recent years due to their ability to repair cellular damage caused by oxidative stress. Oxidative damage from reactive oxygen species (ROS) contributes to numerous diseases, including cardiovascular disease, diabetes, and cancer.1 The body endogenously forms ROS during physiological processes such as stress, reproduction, aerobic metabolism, infection, injury, and illness. Free radicals also accumulate from exposure to environmental factors like air pollution, cigarette smoke, and UV radiation. These free radicals are strong initiators of lipid peroxidation, which is linked to the pathogenesis of a wide range of diseases and disorders.2 Antioxidants are critical in protecting the body from oxidative stress by neutralizing and removing free radicals.

Antioxidants fulfill several roles in maintaining cellular homeostasis; they donate hydrogen atoms, scavenge free radicals, chelate metal ions,2 and function as chain breakers in the lipid peroxidation cycle.3 Antioxidants are either synthesized endogenously in the body, like glutathione and alpha lipoic acid, or obtained exogenously from the diet, like vitamins C, E, and A. Epidemiologic studies indicate that increased fruit and vegetable intake is associated with decreased risk of heart disease and most cancers.1 The antioxidant content of fruits and vegetables may help mitigate oxidative damage that contributes to these diseases. Two essential antioxidants receiving considerable attention are vitamin C and vitamin E; this review examines the functional properties of these two vitamins.

**Science Behind Vitamin C**

Vitamin C (also referred to as ascorbic acid, *L-*ascorbic acid, or ascorbate) is a water-soluble vitamin. While plants and most animals endogenously synthesize vitamin C, humans lack L-gulonolactone oxidase (GO), the enzyme that catalyzes the final step in the biosynthesis of ascorbate.4 Therefore, humans require ascorbate from dietary sources. Ascorbic acid is highly sensitive to oxidation, particularly in the presence of heat or acid catalysts. As ascorbate reduces a reactant, the ascorbic acid itself is oxidized into dehydroascorbic acid, 5 lowering its overall concentration in the system. This means vitamin C concentration will decrease in food products such as orange juice, and supplements, over time. Ascorbic acid participates in reciprocal oxidation-reduction reactions. While many juice and supplement containers are tightly sealed at the time of production preventing immediate oxidation of vitamin C, degradation begins as soon as the container’s seal is broken and the product is exposed to air.

Vitamin C is required for a great number of reactions in the human body. It improves absorption of nonheme iron when consumed with nonheme iron-containing foods. Ascorbate is also vital to the synthesis of L-carnitine, collagen, and certain neurotransmitters.1 Its role in collagen synthesis is widely studied due to collagen being the most abundant protein in the body, and an essential component in connective tissue. Ascorbate is involved in protein metabolism and regeneration of other antioxidants, including α-tocopherol, or vitamin E.1 Vitamin C serves as an enzyme co-factor in biosynthesis of neurotransmitters, neuropeptide hormones, and many amino acid-derived macromolecules. It also acts as a hydroxylase co-factor in gene transcription regulation.6

As a reducing agent, ascorbate can act as either a pro-oxidant or an antioxidant. Generally, ascorbic acid tends to function as a pro-oxidant at low concentrations, and as an antioxidant at high concentrations.4 According to Mandl et al.,4 ascorbate has the ability to reduce pro-oxidant metals such as copper and iron, which can lead to undesirable effects in the body. Pro-oxidant functionality of ascorbic acid can, however, be useful; pharmacological concentrations of ascorbate have been shown to generate hydrogen peroxide, thereby selectively killing cancer cells, but not normal cells.

In NHANES 2003-2006, 49% of adults surveyed reported supplement use, most commonly a multivitamin-multimineral (33%).7 The NHANES (National Health and Nutrition Examination Survey) 2003-2004 study reported vitamin C intakes for adults below the Estimated Average Requirement (EAR) of 75 mg/day for men and 60 mg/day for women.8 NHANES 2003-2004 also reported an increased risk of deficiency among smokers and low-income persons, while individuals taking a supplement or those with adequate dietary intake were at decreased risk of vitamin C deficiency.

Vitamin C deficiency leads to a condition known as scurvy. Signs and symptoms of scurvy develop after several weeks of intakes below 10 mg/day, and include fatigue, gum inflammation, depression, inhibited collagen synthesis, hyperkeratosis, joint pain, poor wound healing, and corkscrew hairs.1 Vitamin C toxicity is considered low, as excess is excreted in urine, and absorption rates fall as intake increases.1 Symptoms of vitamin C toxicity typically include gastrointestinal upset such as nausea, abdominal cramps, and diarrhea.

Confusion seems common over which form – whole foods, juice, or supplements – offers optimum bioavailability of vitamin C. Food-derived and synthetic ascorbic acid are chemically identical. Seven human studies reviewed by Carr and Vissers6 found comparable bioavailability in plasma and/or urine between synthetic ascorbic acid and that in fruits, vegetables and juices. Carr and Vissers’ own pharmacokinetic study revealed comparable relative bioavailability between whole-fruit-derived vitamin C and its synthetic counterpart. Recent research by Crowe and Murray9 demonstrated that the antioxidant density of whole fruit versus its juice counterpart is variable, most likely due to the density of the whole fruit itself, growing conditions, and processing techniques employed by juice manufacturers. While 100% fruit juice can contribute notable amounts of vitamin C to the diet, it also contributes more calories and sugar without the beneficial fiber and micronutrients of whole produce. Additional phytochemicals, micronutrients, and fiber in fruits and vegetables reaffirm that whole foods are the preferred choice for daily consumption.

**Science Behind Vitamin E**

Vitamin E is naturally found in a variety of foods such as nuts, seeds, vegetable oils, and green vegetables.10 It is a fat-soluble vitamin that naturally occurs in eight chemical forms – four tocopherols and four tocotrienols. Biological activity varies considerably among the eight compounds; α-tocopherol is considered the most biologically active in humans, though it falls second in consumption to γ-tocopherol in the typical American diet.3

Vitamin E serves numerous antioxidant roles in the body. It is involved in immune function, nervous system development, cell signaling, regulation of gene expression, and inhibition of protein kinase C. Vitamin E plays a pivotal role in the inhibition of platelet aggression by stimulating the expression of enzymes responsible for suppressing arachidonic acid metabolism, ultimately dilating blood vessels.10 Additionally, vitamin E functions as a peroxyl radical scavenger,11 ultimately preventing free radical propagation in plasma lipoproteins and in membranes by stopping free radical chain reactions. Following oxidation by the peroxyl radical, vitamin E can then be reduced by vitamin C or other hydrogen donors, resulting in a recycling of vitamin E.

While frank vitamin E deficiency is rare, select groups may be susceptible to moderate vitamin E deficiency, such as very low birth weight infants (<1,500 grams), and individuals with fat malabsorption disorders10 such as Crohn’s disease, Celiac disease, and cystic fibrosis. For conditions such as these, water-soluble forms of vitamin E may be required. Deficiency symptoms include ataxia, retinopathy, skeletal myopathy, peripheral neuropathy, and immune system impairment. Vitamin E toxicity is rare when intake is from food. High doses from supplements can more easily result in toxicity, increasing the risk of bruising, bleeding, and hemorrhagic stroke.10

The 2001-2002 NHANES study found that Americans consume vitamin E levels below the RDA, though cooking fats are unaccounted for.10 Recommended daily intake for adults is 15 mg, or 22.4 IU. Most daily multivitamins contain roughly 30 IU of vitamin E, though vitamin E-only supplements contain 100 to 1,000 IU per pill.12 Approximately 100 IU of naturally-derived vitamin E is equivalent to about 150 IU of synthetically-derived vitamin E. Tolerable upper intake levels for adults are 1,000 mg, or 1,500 IU.

**Highlighting Primary Intervention Research on Vitamin E – Article 1**

As the number of obese children rises, so does the prevalence of pediatric nonalcoholic fatty liver disease (NAFLD). Cho, Kim and Paik conducted a small retrospective study in 2012 to examine the efficacy of supplementing body mass index (BMI) reduction with vitamin E and UDCA in obese pediatric patients diagnosed with nonalcoholic fatty liver disease.13 The objective of the pediatric study was to determine whether or not the combination of weight loss via diet and exercise and pharmacological supplementation with vitamin E and UDCA would effectively improve patients’ clinical profiles.

Study participants included 29 pediatric patients diagnosed with NAFLD via liver biopsy. The patients were selected based on strict inclusion and exclusion criteria determined to effectively test the study hypothesis. The retrospective pilot study included supervision of dietitian-administered diet therapy, exercise guidance according to patients’ obesity index, and experimental drug treatment. Drug treatment involved UDCA (ursodeoxycholic acid, 5-10 mg/day) and vitamin E (800 IU/day). Clinical profiles measured for each patient were extensive, including total bilirubin, ALP, ALT, AST, AST/ALT ratio, and γ-glutamyl transpeptidase. The UDCA/vitamin E treatment and patient BMI served as the independent variables in this study; patients’ clinical profiles served as the dependent variables.

The participants were divided into four groups: one that observed their progress without supplementation or BMI reduction, one that reduced their BMI only, one that adhered to the drug therapy without a reduction in BMI, and one group that participated in drug therapy and BMI reduction. 20 of the study participants received the drug therapy for an average of 11.00±9.40 months. All participants were observed for 16.76±10.05 months. No side effects were reported or observed during the period of study. Upon analyzing the four groups, the group who reduced their BMI and adhered to the drug therapy showed statistically significant improvements in their ALP, bilirubin, γ-GT, AST and ALT levels and their AST/ALT ratio. The group who reduced their BMI but did not engage in drug therapy showed statistically significant improvement in their ALT levels and AST/ALT ratio. No significant improvements were noted in the two remaining groups.

While treatment with UDCA and vitamin E did not independently improve NAFLD, it appears to improve biochemical profiles and symptoms when administered in conjunction with a reduction in BMI. Oxidative stress is a primary factor in NAFLD, as lipid peroxidation stimulates production of cytokines, promoting fibrosis of the liver. Cho, Paik and Kim’s study results correlate with findings from a separate study that showed an improvement in histological profiles and serum ALT of adults treated with 300 IU of vitamin E daily for one year.13 A subsequent study involving a larger number of patients could prove useful in verifying the effectiveness of a combined regimen of BMI reduction and UDCA/vitamin E therapy.

**Highlighting Primary Intervention Research on Vitamin E – Article 2**

Oxidative stress, which results from an abundance of oxygen free radicals that cannot be cleared from the body, is long believed to contribute to the pathogenesis of diabetes mellitus and related complications. Antioxidants like vitamin E are vital in preventing and repairing oxidative stress within the body. In 2012, Jain and Jain conducted a prospective clinical study with two objectives: to examine the role of vitamin E in preventing the development of complications in patients with diabetes mellitus (DM), and to evaluate vitamin E’s role in controlling progression of diabetes complications in study participants.14

The patients recruited for the study were type I and type II diabetics over the age of 45 years, and were selected based on strict inclusion and exclusion criteria determined to effectively test the study hypothesis. Participants were first separated into two groups – the primary prevention group contained 64 type I and 64 type II diabetics diagnosed within the last two years, and the secondary prevention group contained 90 type I and 90 type II diabetics diagnosed 5-7 years prior who were experiencing complications. Each of the two prevention groups were further divided: the type I diabetics in each prevention group were split evenly into the test and control groups – those receiving insulin and vitamin E therapy and those receiving insulin only, respectively. The type II diabetics were split evenly into similar groups consisting of those receiving oral hypoglycemic and vitamin E therapy and those receiving oral glycemic only. This ultimately resulted in 4 test groups and 4 control groups. Insulin and vitamin E served as the independent variables in this study; laboratory values and DM-related complications served as the dependent variables.

Physical and laboratory examinations of the study participants were conducted at the start and again 12, 18, and 24 months into the study. Fasting blood sugar, post prandial blood sugar, full lipid profile, creatinine, urea, and blood pressure were all measured. Detailed patient histories were obtained, and complications like foot ulcers, nephropathy retinopathy, and CVD were regularly evaluated. While changes in laboratory values and DM-related complications were insignificant at 12 and 18 months, significant changes were noted in all test groups at 24 months. Diastolic blood pressure, total cholesterol, and post-prandial blood sugar all improved significantly for all test groups, compared to the control groups at the 24-month mark. Significantly fewer patients experienced cardiovascular complications in the test groups when compared to the control groups at 24 months. Additionally, retinopathy and foot ulcers both improved significantly for the test groups. The study results support the theory that long-term vitamin E supplementation can improve complications associated with both type I and type II diabetes mellitus.

**Lay Audience Summary**

Oxidative damage in the body is caused by free radicals, which are unstable, highly reactive molecules. Free radicals are formed as normal by-products in the body; they also form from environmental factors such as air pollution, cigarette smoke, and UV radiation. Oxidative damage from free radicals contributes to the progression of numerous diseases such as cancer, diabetes, and cardiovascular disease. Antioxidants help repair cellular damage caused by oxidative stress, halting or slowing the disease process, by neutralizing and removing free radicals from the body. Two antioxidants receiving considerable attention for their contribution to improvement of disease states are vitamin C and vitamin E.

Vitamin C is a water-soluble vitamin that is critical to collagen synthesis, protein metabolism and antioxidant regeneration. Vitamin E is a fat-soluble vitamin vital to immune function, nervous system development, regulation of gene expression, and inhibition of platelet aggression. Vitamin E may reduce diabetes-related complications, and may improve the overall health of obese children with Nonalcoholic Fatty Liver Disease. Further research is needed, however, to explore these treatment options.

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