Antioxidant Supplement: Is Taking Antioxidant Supplement Vitamin C and Vitamin E Provide Benefits or Drawbacks?

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ABSTRACT

Recently, antioxidant supplements, such as high doses of vitamin C and vitamin E have been widely used by many people. However, some researchers claim that antioxidant supplements do not help to prevent disease. The reliance on antioxidant supplements for preventing disease is a concern to some people. This paper will evaluate the benefits and drawbacks of taking vitamin C and E supplements by looking at the evidence for and against the use of antioxidant supplements, especially vitamin C and vitamin E. The result shows that there are still inconsistent results of using antioxidant supplements as disease prevention. Although much research has found that antioxidant supplements may have a beneficial effect, there still lack a significant outcome for the general population. Since antioxidant supplements are complex mixture of ingredients, a better option would be the intake of vitamin C and E, as a daily antioxidant, is consumed from fruits and vegetables. Taking a higher dose of antioxidant supplementation does not replace the need to eat a healthy diet. Fruits and vegetables are the best source of antioxidants compared with those antioxidant supplements which have too high a dose and may be harmful for people. The information about the benefits of a diet high in fruits and vegetables should be provided.

Key words: *antioxidant, dietary supplement, vitamin C, vitamin E*

INTRODUCTION

Researchers have discovered natural antioxidants in fruits and vegetables which contribute to the prevention of disease that are linked to damage caused by free radicals. Recently, antioxidant supplements, such as high doses of vitamin C and vitamin E have been widely used by many people. However, some researchers claim that antioxidant supplements do not help to prevent disease and also prevent early aging. The reliance on antioxidant supplements for preventing disease is a concern to some people. This paper will evaluate the benefits and drawbacks of taking vitamin C and E supplements.

This paper will first define what an antioxidant is and the mechanism of antioxidant protection on health. This will be followed by a review of antioxidant sources and why people are using antioxidant supplements, and also comparing foods and supplement antioxidants. Finally, this essay will look at the evidence for and against the use of antioxidant supplements, especially vitamin C and vitamin E.

DEFINITION AND ANTIOXIDANT MECHANISM

Haliwell (1996 cited in Carr and Frei, 1999) defined antioxidants as "any substance that, when present at low concentration compared to those of an oxidizable substrate (e.g., proteins, lipids, carbohydrates and nucleic acids), significantly delays or prevent oxidation of that substrate". The definition which cited in Carr and Frei (1999) by Panel on Dietary Antioxidants and Related Compounds of the Food and Nutrition Board is that "a dietary antioxidant is a substance in food that significantly decreases the adverse effect of reactive oxygen species (ROS), reactive nitrogen species, or both on normal physiological function in human". Another definition state that antioxidant is a substance which works against (anti)-oxidation (the process in which oxygen reacts with another chemical) and thereby prevents the harmful effect of oxygen on tissue via radical formation, called free radicals (Simone, 1983).

Free radicals are unstable chemical substances with high energy. Normal enzymes can produce free radicals, which can form more radicals and singlet oxygen (very-high-energy-oxygen). Oxygen reacting with lipids to free its stored energy may also produce hydroperoxides. All of these will cause tissue damage and may lead to the development of cancer. The body does have defenses to protect its self against these, involves the antioxidant protection (Simone, 1983). Free radicals are produced at normal level by everyday bodily functions such as breathing. However, their numbers increase to dangerous levels as a result of smoking, pollution, alcohol and sunbathing (WCRF, 2000).

There are many mechanisms of antioxidant protection in humans and animals. Salganik (2001) points out that since cellular oxidants, called reactive oxygen species are constantly produced in animals and human cells, when it reaches excessive amounts it can induce oxidative damage in cells and encourage some degenerative diseases and aging. Therefore cellular antioxidants provide protection

against the damaging effect of ROS, as they act as ROS scavengers by suppressing in apoptosis and preventing the "apoptotic death of precancerous and cancer cells" (Salganik, 2001).

We know that all life requires oxygen, but sometimes oxygen can produce radicals and high-energy (singlet) oxygen. Because of this, most animals have developed many lines of defense against free radical formation to preserve their very existence and to lessen the chance of abnormal cells (cancer) development (Simone, 1983). Moreover, human life can not avoid free radicals because they live in "an oxygen-rich atmosphere' and radicals, are naturally produced by the respiration process. There are also triggering factors for the production of free radicals such as exposure to X-rays, ozone, tobacco smoke, air pollutants, microbial infections, industrial chemicals and intensive exercise (Melton, 2006).

Many studies show the role of antioxidant nutrients on aging. In aged, antioxidant systems become less effective due to more free radicals production. Aging and age related degenerative diseases might induce changes and that foster a systemic antioxidant/pro-oxidant imbalance, which results in oxidative stress. Many food antioxidant play a positive effect on biological age association with serum dehydroepiandrosterone sulfate (DHEAS) as a biomarker for aging process (Edi, 2000).

There are many mechanisms which prevent or decrease the occurrence of radicals and the formation of hydroperoxide and thereby decrease the amount of the cell membrane damage. The most obvious one is the protective protein coat that lines the surface of the cell membrane. This protective coat prevents oxygen from directly reacting with lipid lipids in membrane, which otherwise would produce many radicals. In this situation the protein coat is called antioxidant, a substance which works against (anti)- oxidation (the process in which oxygen reacts with another chemical) and thereby prevents the harmful effect of oxygen on tissue via radical formation.

A second mechanism involves protective enzymes which float around in all cell membranes. These are another group of antioxidants; they prevent radical formation and also convert existing hydroperoxyl radicals into stable oxygen and hydrogen peroxide. They eliminate the danger of radicals and prevent radical damage to the cell membrane. These protective enzymes are small proteins which swim in the membrane fluid around polyunsaturated fats and hence are in close proximity to them. They include superoxide dismutase, catalase, and selenium-containing glutathione peroxidase (Simone, 1983).

THE SOURCE OF ANTIOXIDANTS AND ITS FUNCTION

Scientists have discovered that antioxidant substances found in vegetables and fruits, and play an important role in preventing serious illness like cancer. In fact, current evidence shows that people who consume diets rich antioxidants have a lower risk of cancer. According to Kim *et al* (2003), diets high in vegetables and fruits and/or a high blood concentration of antioxidant vitamins may protect against cancer of the mouth, thorax, esophagus, lung, stomach, colon and rectum. Each of these antioxidants is found in many types of food, especially fruits and vegetables which are a rich source of antioxidants that can neutralize free radicals by donating electrons. People, whose diets are rich in fruits and vegetables, have a lower incidence of heart disease, diabetes, dementia, stroke and certain types of cancer-the very diseases that are associated with free radical damage (Melton, 2006). In general, food products rich in antioxidant and free radical scavenger are potential candidates to directly counteract carcinogenesis. Food compounds increasing the processes of detoxification and DNA repair, as well as those decreasing the metabolic activation of procarcinogens, also contribute to anticarcinogenesis, acting directly (Szyfer and J. Gawecki, 2006).

The important of food nutrients as source of antioxidant for preventing cancer has well documented. Many nutrient agents in food and their functions especially vitamin C and vitamin E as antioxidants will be discussed below:

a. Vitamin C (Ascorbate)

Vitamin C or ascorbate is water-soluble substance contain 6-carbon lactone synthesized from glucose by many animal. Most mammals synthesize ascorbate (ascorbic acid) in liver, and synthesis occurs in kidney in reptiles and some birds. However, several species are unable to synthesize ascorbate, including human, non human primates, guinea pig, and also some fish. Human and primates lack gulonolactone oxidase, the terminal enzyme in these species has undergone substantial mutation so that no protein is produced. Human and primates must ingest it to survive, and hence ascorbate is a vitamin (Levine *et al*, 2006).

In guinea pigs, ascorbate is absorbed in the ileum and probably in jejunum of the small intestine. This absorption is Na^+-dependent. Bioavailability is a measure of the amount of substance absorbed. The absolute amount of the dose absorbed is its true bioavailability. Because it is water soluble and not protein bound, it is likely that ascorbate distribute easily into the extracellular space. Ascorbate is accumulated by adrenal cortex, adrenal medulla, pituitary, white blood cells, endothelial cells, and many other tissues. Until relatively recently, mechanisms of ascorbate accumulation were unclear. Two major possibilities were identified. One that ascorbate was transported against its concentration gradient. The other possibility was transport of oxidized ascorbate as dehydroascorbate, with subsequent reduction within cells to ascorbate (Levine *et al.*, 2006).

Conventionally, ascorbate has been regarded solely as a highly effective scavenger of free radical (Olinski

et al., 2006). Ascorbate can quench free radicals as well as singlet oxygen. It has been shown to react directly with superoxide and hydroxyl radicals (Edi, 2000). In addition to being an antioxidant, vitamin C is also reducing agent, capable of reducing ferric ions to ferrous ions and hence promoting the reaction that may have important biological consequences.

Ascorbate is found in many fruits and vegetables. Fruits high in vitaminC include kiwi, strawberries, lemons, orange, manggo and papaya. Good vegetable sources are broccoli, red pepper, spinach, tomatoes and asparagus (WCRF, 2000). The Indonesian recommended daily intake for vitamin C for human adult is range 75 mg for women and 90 for man. Recommendation for pregnant women is added by 10 mg, therefore the total intake for pregnant woman is 85 mg daily (Budi Setiawan and Rahayuningsih, 2004).

b. Vitamin E (Tocopherol)

Vitamin E is the collective term for all of structurally related tocopherols and tocotrienols and their derivates that qualitatively exhibit the biological activity of α-tocopherol. Therefore, the term vitamin E is not synonymous with α-tocopherol. Naturally, γ-tocopherol is the major form of vitamin E consumed in the diet, whereas the current dietary intake recommendations consider only α-tocopherol (Parker, 2006).

Vitamin E is present in all cellular membranes, where it is thought to act to protect membrane lipids and perhaps proteins from free radical-induced oxidative damage. The reaction of α-tocopherol with polyunsaturated fatty acid peroxyl radicals to prevent uncontrolled lipids peroxidation is the best understood action of vitamin E. Lipids peroxidation is the most common indicator of free radical production in living systems. Antioxidant activity of tocopherols is experimentally determined by their chemical reactivity with radicals or by their ability to inhibit autoxidation of fats and oils. Each compound acts as antioxidant at different stages and cellular locations. However, vitamin E works in a specific position in the overall antioxidant picture owing to its localization in cell membranes.

Vitamin E is found in the highest levels in vegetables oil (particularly in sunflower oil), nuts (particularly almond and hazelnuts), wheatgerm, soya, avocados. Smaller amount of vitamin E are found in tomatoes, wholegrain product, green vegetables, especially spinach. The Indonesian's recommended daily intake of vitamin E for human adult is 15 mg for. No added intake recommended for pregnant women, but for lactating women is added by 4 mg, therefore the total intake for lactating woman is 19 mg daily (Muhilal and A. Sulaeman, 2004).

DIETARY SUPPLEMENT AND ANTIOXIDANT SUPPLEMENT

What are dietary supplements? Supplements are manufactured versions of those vitamin and minerals that naturally occur in food. They can be 'natural' (extracted from food) or synthetic. Some are licensed as medicines; they and other substances such as ginseng, royal jelly and primrose oil, often claimed as tonic food that have effect on human health (WCRF, 2000). Nowadays, people also relied on an antioxidant supplement. What is antioxidant supplement? Antioxidant supplement is some substance which artificially made by pharmaceutical company. In the US, the greater number of antioxidant supplements contain vitamin C, vitamin E and carotenoids (Rock *et al.*, 2004).

Based on the definition above, we can conclude that dietary supplements and antioxidant supplements are the same materials. Some dietary supplements contain antioxidant compound, they called as antioxidant supplements, and other contain other essential compound which needed by the human body but they have not the antioxidant function. The name that mentioned, actually more likely depend on the reason why do people consume supplements. Are they consume supplement to meet their body daily requirement, or because therapeutic and medical reasons or to prevent diseases.

Not surprisingly, many health conscious people take supplements hoping to keep well. Some take them because they believe that vegetables and fruits aren't fresh enough or maybe they or their children just do not like vegetables and fruits. Other groups of supplements consumers include slimmers; people who leaving little time to eat properly; alcoholic; smokers hoping supplements will make up for their bad habit; and people on an unbalanced diet. Some believe that supplements improve their immune systems and others believe that they can even prevent cancer.

THE CONSUMPTION OF ANTIOXIDANT SUPPLEMENTS

The use of dietary supplements has increased substantially in the past two decades in a number of countries (Ford 2001 cited in McNaughton *et al.*, 2005). There is an estimation that around of half of the population in The US consumed antioxidant supplements. People who regularly consume antioxidant supplements believe that it may prevent disease (Melton, 2006). Food Standard Agency (2002 cited in McNaughton *et al*., 2005) reported that recent dietary surveys in the United Kingdom found that 40% of women and 29% of men aged 19–64 years consumed supplements regularly.

In addition, Earnest, Wood, Church (2003) also indicates that from recent survey evidence in the US only

20% to 30% of the population meets the required dietary guidelines that an individual should consume at least five servings of fruits and vegetables per day. Consequently, this is become a possibility of increasing consumption of antioxidant supplements in population. Furthermore, it has also been argued that the activity of vitamins may decline in the process of food preparation, storage and reheating. Vitamin deficiency, which is related to a higher risk of chronic disease, such as cardiovascular disease and cancer, may be caused by this combination of factors or a single factor (Fairfield and Fletcher 2002 cited in Earneast *et al.*, 2003). However, the decreasing amounts of vitamin in food could be minimized by some method, such as not using high temperature for cooking vegetables or serve vegetables and fruits freshly.

One argument for the wide use of antioxidant supplements is as a result of the people's concern that food alone may not provide enough micronutrients. Moreover, Misner (2006) shows that between 1996 and 2005, 70 diets from an athletes menu or sedentary subjects seeking to improve the quality of micronutrient intake from food choice fell short of the recommended 100% RDA micronutrient level from food alone. However, research which was conducted by Misner did not represent the population, because the small number of the samples.

The American Dietetic Association suggests that additional nutrition from fortification and supplementation may be needed by some people when there is no adequate intake of vitamins and minerals from food or diet (Misner, 2006). It is argued that the daily intake of minerals and vitamins may not be sufficient in some people who have problems with chewing, digesting and absorbing or elderly peoples, consequently they should consider nutritional supplements because their daily intake may not sufficient meet the dietary intake requirement (Balch, 1999).

Most vitamin E supplements contain only α-tocopherol. And their used associated with suppression of plasma levels of other tocopherol (Parker, 2006). However, results of several recent studies suggest that other forms of vitamin E may have beneficial biological effects, perhaps not involving antioxidant activity. Supplementation with γ-tocopherol inhibit protein nitration and ascorbate oxidation in rats with inflammation. Other studies demonstrate that dietary supplementation with γ-tocopherol reduced inflammation by suppressing the synthesis of various proinflammatory substance produced by cells of immune system (Hensley *et al.*, 2004 and Jiang *et al.*, 2001 **in** Parker, 2006). Some have suggested that vitamin E supplements be composed of a mixture of tocopherols similar to that in a typical diet.

FOOD VS SUPPLEMENT ANTIOXIDANT

Despite overwhelming evidence that vegetables and fruits can reduce the risk of cancer, there is no proof of similar benefits when antioxidants are isolated in supplement pill form. The reason is probably that these nutrients work in conjunction with a whole range of other 'bioactive' non nutrient compounds, called phytochemicals which present in the same foods.

Phytochemicals its self may sound futuristic, its meaning is simple: "plant chemical." It is different with vitamin that is a food substance essential for the body health. Phytochemicals in contrast, are substance in plant that may possess health protective effects, even though they are not essential for life. Phytochemicals are complex chemicals that vary from plant. They include hundreds of compound, pigments, and natural antioxidant. Plants contain phytochemicals because these substances are benefits to the plant their self. Singly and together, these compound help plants resist the attack of bacteria and fungi, the ravages of free radical, and high level of ultraviolet light from the sun (Insel *et al.*, 2002). Examples include flavonoids in apple, carotenoids in carrot and other red orange fruits, lycopene in tomatoes, and within these groups there are literally hundreds of different types (WCRF, 2000).

How do phytochemicals work to prevent cancer? Two of the major phytochemical mechanisms of prevention are modification of hormone effect and neutralization of free radicals. A number of phytochemicals, including those from soybeans and from cabbage family, are able to modify estrogen metabolism or block the effect of estrogen on cell growth. Since levels of estrogen and other hormones are in turn closely linked to the development of breast, ovarian, and prostate tumor, it apparent how phytochemicals might inhibit development of such cancer (Insel *et al.*, 2002)

Despite of many evidences reveal the beneficiary of foods to protect against carcinogenic agent, some people believe that antioxidants are just as effective when taken in pill form or other materials as supplement. However, many others, such as dietitians and expert committees, disagree. There is no substitute for food rich in antioxidants such as vegetables and fruits.

Truscott (2000) proof evident that protective effect of combinations of antioxidants more effective than single antioxidant. Combination of antioxidants, such as carotenoids and vitamin C and vitamin E, can help to form the best protection against the very early stages of toxin-induced cell damage and the development of cancer. The most effective combination is believed to be lycopene plus vitamin C. In a trial with non-smokers this combination significantly protected human cells from damage by nitrogen dioxide, a carcinogen from cigarette smoke and exhaust gases.

Some of combinations of antioxidants can be found when we consume vegetables and fruits. Combination of lycopene and vitamin C can be found in tomatoes, meanwhile carrot rich of beta carotene and slight of vitamin C. We can fulfill this requirement by enjoying a diet rich in a variety of vegetables, fruits and other plant-based foods. Indonesian foods yield ample source of vitamin and other antioxidant substance, also

phytocemicals, because many Indonesian foods contain mixture and combination of food stuff rather than single food.

THE BENEFITS AND DRAWBACKS OF ANTIOXIDANT SUPPLEMETS

There is some conflicting evidence regarding some research into antioxidant supplements concerning the effect of the prevention of some degenerative disease. Not all antioxidants will be discussed in this essay, only vitamin C and vitamin E. The Recommended Dietary Allowance (RDA) for vitamin E for men and women is 15 mg/day, whereas the tolerable intake level (UL) for vitamin E is 1000 mg/day (Food and Nutrition Board 1998 cited in Hathcock *et al.*, 2005). Chiney *et al.*, (1997) believe that vitamin E (alpha-tocopherol) at very high doses has the capability of "promoting apoptosis" in cancer cells, which is probably related to a process where free radicals reach an excess, so that it could damage the cell.

The finding of the benefit of vitamin E from observational research in America which involved 39,910 US male health professional 40 to 75 years of age, reports that people with a higher intake of vitamin E supplements have a lower risk of coronary diseases (Rimm *et al.*, 1993). Blot *et al.*, 1993 cited in Salganik 2001, discovered that people who consume a daily intake supplementation with beta-carotene, vitamin E and selenium for more than 5 years had lower gastric and esophageal cancer rate and mortality reduction. However, both of these research studies were observational studies which had limitations, especially confounding factors which related to health effects. A higher intake of vitamin E supplement may not the single factor that reduced the cardiovascular risk. Both of these research studies had not evaluated different lifestyles such as exercise and composition of diet which also play important roles in decreasing cardiovascular risk.

On the other hand, Melton (2006) points out that a high dose of vitamin E supplements can be harmful and increase overall mortality according to a study by the team from The John Hopkins Medical Institution in Baltimore. Supporting this, Seisfried *et al.* (2003) warns that antioxidants supplements are not always safe because an intake of very high levels for antioxidants supplements can bring about toxicity.

Zigler (2002), emphasizes that taking a supplement means that an artificial supplement only supplemented with one particular form of a nutrient. In a real situation, for example there are eight different kinds of vitamin E that have different biological activity. It needs to be considered that consuming one particular form might be blocking the action of others that could also be important to health.

Vitamin C, which is regarded as an antioxidant has also dietary intake recommendation. Recommended Dietary Allowance (RDA) for vitamin C for men is 90 mg/day and for women is 75 mg/day and tolerable upper intake level (UL) is 2000 mg/day (Food and Nutrition Board 1998 cited in Hathcock *et al*, 2005). The Food and Drug Agency (FDA) stated that vitamin C acts as a scavenger of free radicals which shields the cells from damage. According to Carr and Frei (1999), who evaluated some evidence from human studies, "a dietary intake of 90–100 mg/day of vitamin C is associated with reduced risk of cardiovascular disease and cancer.

Another finding, based on research in Japan (Kim *et al.*, 2003) reveals that consuming vitamin C for 5 years at a dose 500 mg has the capability of increasing in serum vitamin C which has clinical and public health implications. In contrast, a study that was carried out by Rimm *et al.* (1993) reports that a high intake of vitamin C was not associated with a lower risk of coronary disease. Furthermore, The United States Preventive Services Task Force (USPTSTF) 2003, concludes that observational studies have generally shown no significant association between the use of vitamin C supplements and the risk of breast, prostate, colon and lung cancer. The vitamin C supplementation effect on cardiovascular disease has also produced inconsistent results from observational cohort studies. Similarly *et al.* (2004) insist that routine use of antioxidant supplements for prevention and treatment of cardiovascular disease is not justified by the existing scientific database and it is supported by The American College of Cardiology/American Heart Association which warns that "there is no basis for recommending that patients take vitamin C or E supplements or other antioxidants for the express purpose of preventing or treating coronary artery disease". Seisfried *et al.* (2003) argues that "antioxidants supplementation may actually cause harm in terms of increased risk of new disease or interference with treatment or existing disease".

Another argument against antioxidant supplementation is that antioxidant supplement is dangerous because the doses are too high and generate free radicals production (Jackson cited in Melton 2006). The best way to meets the daily needs of antioxidants come from fruits and vegetables not those of antioxidant supplementation. Haliwell, cited in Melton report argues that the vitamin in vegetables and fruits which are comprised of fibrous material are more adaptable in highly acidic environments in the gastrointestinal tract (Melton, 2006). Supplements would not be able to overcome this environment and as a result it is digested more rapidly so that it may not perform as well as fresh vegetables and fruits.

CONCLUSION

In conclusion, there are still inconsistent results of using antioxidant supplements as a disease prevention. Although much research has found that antioxidant supplements may have a beneficial effect, there still lack a significant outcome for the general population.

Since antioxidant supplements are complex mixture of ingredients, a better option would be the intake of vitamin C and E, as a daily antioxidant, is consumed from fruits and vegetables. Taking a higher dose of antioxidant supplementation does not replace the need to eat a healthy diet. We believe that fruits and vegetables are the best source of antioxidants compared with those antioxidant supplements which have too high a dose and may be harmful for people. The information about the benefits of a diet high in fruits and vegetables should be provided for people, as well as information on other food and nutrient that should be emphasized or avoided in people's daily diet.

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