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Significance of vitamin C in human health and disease

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Abstract

Most plants and animals synthesize ascorbic acid for their own requirement. However, apes and humans can not synthesize ascorbic acid due to lack of an enzyme, gulonolactone oxidase. Hence, ascorbic acid has to be supplemented mainly through fruits, vegetables and tablets. The current U.S. Recommended Daily Allowance (RDA) for ascorbic acid ranges between 200 mg/per day for adults. Many health benefits have been attributed to ascorbic acid such as antioxidant, antiatherogenic, anticarcinogenic, immunomodulator and prevention of cold. Vitamin C plays an important role in a number of metabolic functions including the activation of the folic acid, conversion of cholesterol to bile acids and the conversion of the amino acid tryptophan to the neurotransmitter serotonin. It is a good antioxidant that protects body from free radicals damages. Despite intensive researches in the last 50 years, more mechanistic and human *in vivo* studies are needed to understand and elucidate the molecular mechanism, underlying the biological effects of ascorbic acid.

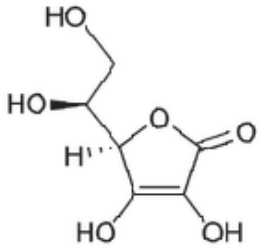
Key words: Vitamin C, Antioxidants, Diseases, Oxidative stress, Health

Introduction

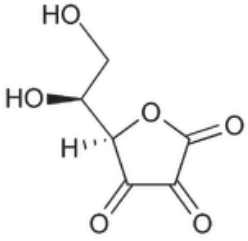
Vitamin C (ascorbic acid) is a six-carbon lactone that is synthesized from glucose in the liver of most mammalian species except humans, some non-human primates and guinea pigs (Nishikimi and Yagi, 1996 and Naidu, 2003). These species do not have the enzyme gulonolactone oxidase, which is essential for synthesis of the ascorbic acid immediate precursor 2-keto-l-gulonolactone (Burns, 1956). Vitamin C is, thus, an essential nutrient for humans and certain other animal species. Vitamin C refers to a number of vitamers that have vitamin C activity in animals, including ascorbic acid and its salts, and some oxidized forms of the molecule like dehydroascorbic acid (Iqbal *et al*., 2004). Ascorbate and ascorbic acid are both naturally present in the body when either of these is introduced into cells, since the forms interconvert according to pH (Naidu, 2003).

Vitamin C *discovery*

In 1747, Scottish naval surgeon James Lind discovered that a nutrient (now known to be vitamin C) in citrus foods prevented scurvy (Lind, 1753). It was rediscovered by Norwegians, A. Hoist and T. Froelich in 1912. Vitamin C was the first vitamin to be artificially synthesized in 1935. A process invented by Dr. Tadeusz Reichstein, of the Swiss Institute of Technology in Zurich.



Ascorbic acid (Reduced form)



Dehydroascorbic acid (oxidized form)

Figure 1: Structure of vitamin C

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Vitamin C (Ascorbic acid) is a water-soluble antioxidant. It is an unstable, easily oxidized acid and can be destroyed by oxygen, alkali and high temperature (Moser and Bendich, 1990). Unlike animals, humans can not synthesize vitamin C, rendering its ingestion from exogenous supplement or diet necessary (Naidu, 2003). It has been proposed that the cause of human inability to synthesize ascorbic acid is the absence of the active enzyme, l-gulonolactone oxidase in the liver (Burns, 1959). Body requires vitamin C for normal physiological functions. It helps in the metabolism of tyrosine, folic acid and tryptophan. It helps to lower blood cholesterol and contributes to the synthesis of the amino acids, carnitine and catecholamine that regulate nervous system (Levine, 1986 and Hulse *et al*., 1978). It is needed for tissue growth and wound healing. It helps in the formation of neurotransmitters and increases the absorption of iron in the gut (Olson, 1999). Being an antioxidant, it protects the body from the harmful effects of free radicals and pollutants (Du *et al*., 2012 and Berger *et al*., 1997).

***Dietary sources of vitamin* C**

Ascorbic acid, the accepted name for vitamin C, is available in reduced form (L-ascorbic acid) and oxidized form (L dehydroascorbic acid). It is found in citrus fruits, green peppers, red peppers, strawberries, tomatoes, broccoli, brussels sprouts, turnip and other leafy vegetables. Fish and milk also contain small amounts of vitamin C (Johnson *et al*., 1998). There is a gradual decline in the amount of vitamin C as foods age (Naidu, 2003).

Metabolism of ascorbate

Ascorbic acid is a white crystalline sugar that naturally occur in chemical forms of L-xylo-ascorbic acid and D-xylo-ascorbate. L-xylo- ascorbate is without vitamin activity. It is reversibly oxidized to L-dehydroascorbic acid upon exposure to copper, heat or mildly alkaline conditions. Both L- ascorbic acid and L-dehydroascorbic acid are physiologically active forms of vitamin C (Thurnham, 2000). Further oxidation of L-dehydroascorbic acid to 2, 3-diketo-L-gulonic acid and oxalate is irreversible (Thurnham, 2000).

The principal pathway of oxidation and turnover of ascorbic acid is believed to involve the removal of two electrons in succession and to yield first the ascorbate free radical (AFR) and then dehydroascorbate (Bates, 1981). Two molecules of AFR may react together to form one molecule of ascorbate and one of dehydroascorbate. Alternatively, AFR may be reduced by a microsomal NADH-dependant enzyme, mono-dehydro-L-ascorbate oxidoreductase to ascorbate (Rizvi *et al*., 2006, 2009).

***Physiological role of vitamin* C**

Vitamin C helps in the metabolism of tyrosine, folic acid and tryptophan. It also helps in the metabolism of cholesterol, increasing its elimination and, thereby, assisting lower blood cholesterol (Rath, 1993).

Vitamin C contributes to the synthesis of the amino acid carnitine and the catecholamines that regulate the nervous system. It also helps the body to absorb iron and to break down histamine, the inflammatory component of many allergic reactions (Gaby and Singh, 1991).

Absorption of iron, especially the non-heme variety found in plants and drinking water is enhanced by Vitamin C. It has been shown to facilitate iron absorption by its ability to reduce ferric iron to the ferrous form (Sayers *et al*., 1973). Ordinarily absorption of iron is quite poor, putting us at risk of iron deficiency anemia. One milligram of ascorbic acid is approximately equivalent in enhancing power to 1 g of cooked MFP (iron present in meat, fish and poultry) or 1.3 g of raw MFP (Monsen, 1978). It is also necessary for the conversion of tryptophan to 5-hydroxy tryptophan and the neurotransmitter serotonin and the formation of the neurotransmitter, nor epinephrine from dopamine.

One important function of vitamin C is in the formation and maintenance of collagen, the basis of connective tissues, which is found in skin, ligaments, cartilages, vertebral discs, joint linings, capillary walls and the bones and teeth (Gaby and Singh, 1991). Collagen requires vitamin C to achieve the best configuration and prevent from becoming weak and susceptible to damage (Gaby and Singh, 1991).

As an antioxidant, vitamin C's primary role is to neutralize free radicals (Frei *et al*., 1989). Since ascorbic acid is water soluble, it can work both inside and outside the cells to combat free radical damages. Free radicals seek out an electron pair to regain their stability. Vitamin C is an excellent source of electrons, therefore, it "can donate electrons to free radicals such as hydroxyl and superoxide radicals and quench their reactivity" (Bendich, 1990).

Vitamin C protects the DNA of the cells from the damage caused by free radicals and mutagens (Du *et al*., 2012). It prevents harmful genetic alterations within cells and protects lymphocytes from mutations to the chromosomes (Gaby and Singh, 1991).

Vitamin C prevents free radical damage in the lungs and may even help to protect the central nervous system from such damage (Eerhard *et al*., 1989). In a study of guinea pigs, pretreatment of ascorbic acid effectively diminished the acute lung damage, caused by the introduction of super oxide anion free oxygen radicals to the trachea (Becher and Winsel, 1989).

Vitamin C has been proposed by some to have pharma-cological benefits in preventing cancer, infections, and the

common cold (Padayatty *et al*., 2003). However, these benefits have yet to be reported in the scientific literature. The role of vitamin C in preventing cancer is controversial, but has been studied for cancers of the oral cavity, uterus, esophagus, bladder, and pancreas (Naidu, 2003). The research is at best equivocal and more studies are needed to further address the role of vitamin C in preventing cancer.

Elderly people who take vitamin C and vitamin E supplements have a 50% lower risk of dying prematurely from disease than do people who do not supplement (Losonczy, 1996). A Californian study has concluded that people who consume more than 750 mg/d of vitamin C reduce their risk of dying prematurely by 60% (Enstrom, 1992).

Vitamin* C*, immunity and infections

Infection means the entrance, growth and multiplication of a microorganism (pathogen) in the body of a host, resulting in the establishment of a disease process. An infectious disease represents a combat between two living forces - the organism invading and the organism invaded. The invader may be bacterium, fungus, virus or reckittsia and in human pathology, the human body is invaded. Infections initiate bidirectional interactions with the defense mechanisms of the host, both immunological and nonspecific and also interact with the nutritional status of the host.

Vitamin C can enhance the body's resistance to an assortment of diseases, including infectious disorders. It strengthens and protects the immune system by stimulating the activity of antibodies and immune system cells such as phagocytes and neutrophills (Eerhard *et al*., 1989).

Vitamin C helps the immune system to fight viruses (Anderson and Lukey, 1987). It acts as an antiviral agent (Gerber, 1975), elevating body's interferon level. Even taken in small amounts, it appears to reduce the duration and severity of illnesses (Hemila, 1992).

***Recommended Daily Allowance (*RDA*) of vitamin* C**

The current RDA of 60 mg/d is clearly far too low and the proposed new RDA of 200 mg/d while perhaps adequate for healthy, young males, would seem to be quite inadequate for older people and certainly too low for sick people. As a matter of fact, a scientific advisory panel to the U.S. Government sponsored alliance for ageing research recently recommended that all healthy adults increase their vitamin C intake to 250-1000 mg/d (Voelker, 1994). An adequate intake of vitamin C is perhaps the best and most cost effective health insurance available today.

***Deficiency of vitamin* C**

Deficiency of vitamin C can cause anemia, scurvy, infections, bleeding gums, muscle degeneration, poor wound healing, atherosclerotic plaques and capillary hemorrhageing. Neurotic disturbances consisting of hypochondriasis, hysteria and depression followed by decreased psychomotor performances have been reported in ascorbic acid deficiency (Kinsman and Hood, 1971). Vitamin C deficiency is often associated with gingivitis (Bruno, 2002).

Vitamin* C *toxicity

The saturable kinetics of vitamin C makes toxicity more likely when multiple large doses (~1gram) are consumed throughout a day versus one single dose. Toxicity normally does not occur since vitamin C is water-soluble and is regularly excreted by the body. Excess ascorbic acid excreted in the urine gives a false-positive test for sugar (Brandt *et al*., 1977). High levels of vitamin C interfere with copper absorption (Finley and Cerklewski, 1983). Vitamin C should be avoided by those who suffer from kidney stones, as it can convert to oxalate (Piesse, 1985). As a precaution, people who are prone to kidney stones may want to avoid large doses (10 times the DRI or greater) of the vitamin. People who lack the control to regulate iron uptake should also avoid large doses of the vitamin. As stated earlier, vitamin C enhances iron absorption which, can lead to toxicity of iron in some people (Food and Nutrition Board, 2000). Furthermore, excess ascorbate in the urine and feces can falsify lab tests such as glucose in the urine and fecal occult blood test. However, some research suggests that vitamin C only undergoes this transformation in urine after the urine has left the body (Wandzilak *et al*., 1994).

Conclusion

Ascorbic acid is one of the important and essential vitamins for human health. It is needed for many physiological functions in human biology. Fresh fruits, vegetables and also synthetic tablets supplement the ascorbic acid requirement of the body. Based on available biochemical, clinical and epidemiological studies, the current RDA for ascorbic acid is suggested to be 200 mg/day to achieve cellular saturation and optimum risk reduction of heart diseases, stroke and cancer in healthy individuals. In view of its antioxidant property, ascorbic acid and its derivatives are widely used as preservatives in food industry. Many health benefits have been attributed to ascorbic acid namely antioxidant, anti-atherogenic and anti-carcinogenic activity. The relation between ascorbic acid and cancer is still a debatable as the molecular mechanism underlying anti-carcinogenic activity of ascorbic acid is not clearly elucidated. However, more

mechanistic and human *in vivo* studies are warranted to establish the beneficial claims on ascorbic acid.

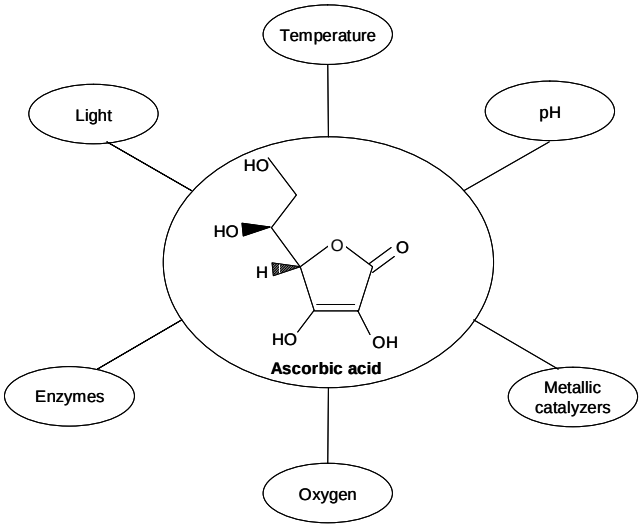

Figure 2: Factors affecting the degradation kinetics of vitamin C

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