

Biological Significance of Ascorbic Acid (Vitamin C) in Human Health – A Review

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Abstract: The recognition of vitamin C (Ascorbic acid) is associated with history of an unrelenting search for the cause of the ancient hemorrhagic disease scurvy. Isolated in 1928, vitamin C is essential for the development and maintenance of connective tissues. It plays an important role in bone formation, wound healing and the maintenance of healthy gums. Vitamin C plays an important role in a number of metabolic functions including the activation of the B vitamin, folic acid, the conversion of cholesterol to bile acids and the conversion of the amino acid, tryptophan, to the neurotransmitter, serotonin. It is an antioxidant that protects body from free radicals' damages. It is used as therapeutic agent in many diseases and disorders. Vitamin C protects the immune system, reduces the severity of allergic reactions and helps fight off infections.

Key words: Ascorbic acid (Vitamin C), biological significance, human health

Introduction

Vitamins are a class of nutrients that are essentially required by the body for its various biochemical and physiological processes. Mostly, the human body does not synthesize them; therefore, they must be supplied by the diet in the required amount. Vitamins are subdivided into fat-soluble and water soluble vitamins. Fat-soluble vitamins are those that are soluble in fat solvents. They are A, D, E and K. Water-soluble vitamins are those, which are soluble in water and include vitamin C and vitamin B series that are usually termed as vitamin B complex.

Vitamin C (Ascorbic Acid) is a water-soluble antioxidant. It was first isolated in 1928, by the Hungarian biochemist and Nobel Prize winner Szent-Gyorgyi. It is an unstable, easily oxidized acid and can be destroyed by oxygen, alkali and high temperature.

Unlike animals humans can not synthesize vitamin C, rendering its ingestion from exogenous supplement or diet necessary. It has been proposed that the cause of human inability to synthesize ascorbic acid is the absence of the active enzyme, L-gulonolactone oxidase from 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. 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. Being an antioxidant, it protects the body from the harmful effects of free radicals and pollutants.

Mega doses of vitamin C is used in the treatment and prevention of large number of disorders like diabetes, cataracts, glaucoma, macular degeneration, atherosclerosis, stroke, heart diseases and cancer.

Deficiency of this vitamin can lead to anemia, scurvy, infections, bleeding gums, muscle degeneration, poor wound healing, atherosclerotic plaques, capillary hemorrhaging and neurotic disturbances. Toxicity normally does not occur.

Infections deplete the body stores of vitamin C, thus making the body immune system weak. For strong immunity, body requires vitamin C. Optimal tissue stores maintain resistance to infections. Vitamin C therapy is beneficial in the treatment of different infections and infectious diseases, for example hepatitis, HIV, H. pylori infection, common cold, flu and influenza etc. This review is an attempt to report the results of research studies done on the biological role of vitamin C, its uses in various disorders and the important role it plays in the treatment and prevention of infections and infectious diseases.

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. There is a gradual decline in the amount of vitamin C as foods age (Platt *et al.*, 1963).

Absorption of vitamin C: In human and guinea pigs, the absorption of vitamin C occurs in the buccal mucosa, stomach and the small intestine. The buccal absorption of vitamin C is mediated by passive diffusion through the membrane of the buccal cavity. While gastrointestinal absorption is through an efficient and an active sodium dependent, energy-requiring and carrier-mediated transport mechanism (Stevenson, 1974). Gabby and Singh (1991) have also explained the absorption of

vitamin C through an active transport system located in the gut and its re-absorption in the kidneys. Since the absorption mechanism in the gut and kidney can reach a saturation point, it is better to take multiple and smaller doses of vitamin C through out the day than one large dose. At higher intakes, the process is saturated; up to 180 mg, there is an average absorption of 70% in both smokers and non-smokers, but absorption decreases from 50 to 16% at intakes over the range of 1.5-12 g (Kubler and Gehler, 1970). About 80-90% ascorbic acid is absorbed in the gastrointestinal tract. The absorbed acid circulates freely in plasma, leukocytes and red blood cells and enters all tissues, with maximum concentrations of 68-86 Fmol/l plasma being achieved with oral intakes of 90-150 mg/day (Olson and Hodges, 1987). The body uses it in two hours and then usually out of the blood within three to four hours. Vitamin C is used up more rapidly under stressful conditions, with the use of alcohol and with smoking. Vitamin C blood levels of smokers are much lower than those of non-smokers given the same intakes. Fever, viral illnesses, antibiotics, pain medicines, petroleum products or carbon monoxide and exposure to heavy metals reduce absorption or increase utilization. Sulfa antibiotics increase elimination of vitamin C from the body by 2 to 3 times (Bill Misner).

The total body pool size of ascorbate is affected by limited intestinal and renal tubular absorption. Body ascorbate reaches a maximum of 20 mg/kg body weight, i.e. with a total pool size of about 1.5 g, when ascorbate intake is increased from 30 to 180 mg/day. Above this level of intake, the excretion in the urine rises rapidly (Kallner *et al.*, 1979).

Metabolism of ascorbate: Ascorbic acid is a white crystalline sugar that naturally occurs 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 on exposure to copper, heat or mildly alkaline conditions. Both L-ascorbic acid and L-dehydroascorbic acid are physiologically active forms of vitamin C. Further oxidation of L-dehydroascorbic acid to 2,3-diketo-L-gulonic acid and oxalate is irreversible (Thurnham, 2000). The sulphation of ascorbate to ascorbate-2-sulphate is a minor pathway with at present, no known clear biological significance for man. It is unlikely to have antiscorbutic properties nor to act as an important sulphating agent *in vivo* (Bates, 1981).

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. 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 (Bates, 1981).

Biological functions 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 our 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 collagens, the basis of connective tissues, which are found in skin, ligaments, cartilages, vertebral discs, joint linings, capillary walls and the bones and teeth. Collagen protein requires vitamin C for "hydroxylation", a process that allows the molecule to achieve the best configuration and prevent collagen from becoming weak and susceptible to damage. Recent evidence indicates that vitamin C increases the level of procollagen messenger RNA (Gaby and Singh, 1991). Collagen subunits are formed within fibroblasts as procollagen, which are excreted into extra cellular spaces. Vitamin C is required to export the procollagen molecules out of the cell. The final structure of the collagen is formed after pieces of the procollagen are enzymatically cleaved (Gaby and Singh, 1991). Collagen and thus vitamin C is needed to give support and shape to the body to help wounds heal and to maintain healthy blood vessels. Vitamin C protects small blood vessels from damage; this may help to prevent excessive menstrual blood loss (Cohen and Rubin, 1960). Specifically ascorbic acid works as a coenzyme to convert proline and lysine to hydroxyproline and hydroxy lysine both important to the collagen structure. It also helps in production of thyroid hormones. Vitamin C supplementation (1000 mg/day) has also been found to significantly decrease the risk of developing pressure sores in surgical patients (Taylor *et al.*, 1974).

Vitamin C is important for collagen formation and strong collagens are necessary for strong bones. Both the densities of bones and level of vitamin C begin to decrease with age. While a number of factors contribute to osteoporosis, studies show that a person's vitamin C status is also related to the maintenance of healthy bones. In fact, vitamin C may directly affect the growth of bone cells, above and beyond its call of duty in forming collagen. Ascorbic acid intake at moderate doses is important and safe for bone maintenance and therefore a factor in mitigating or delaying osteoporosis (Gaby and Singh, 1991).

As an antioxidant, vitamin C's primary role is to neutralize free radicals. 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. 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 (Kronhausen *et al.*, 1989a). 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). Ascorbic acid also has been tested as an antioxidant to inflammatory reaction in mice. High doses given after but not before the injury successfully suppressed edema (Spillert, 1989).

As an antioxidant, vitamin C can rejuvenate vitamin E, making it an indirect contributor to the fight against free radical damage in the lipids. It's not surprising, then, that these two nutrients can be effective partners in reducing the destructive process of lipid per-oxidation. In human and animal studies this reduction took place in subjects with diabetes, cerebral arteriosclerosis or a heart disorder (Karagezian and Gevorkian, 1989; Bobyrev *et al.*, 1989; Berta, 1991). Together vitamin C and vitamin E can help to prevent blood from clotting, a condition that contributes to the risk of stroke (Kronhausen *et al.*, 1989b). The synergistic combination of vitamin C and vitamin E may be further enhanced by the addition of vitamin A. In one study this combination was effective in enhancing the "characteristics of enzymatic and non-enzymatic antioxidant protection of the liver" in mice (Kuvshinnikov, 1989). A classical antioxidant combination is formed when vitamin C is added with vitamin E, beta-carotene and selenium. It has helped to alleviate pancreatitis, or an inflammation of the

pancreas, in one study.

(Reactive Oxygen Species) ROS-induced enhancement in lipid per oxidation plays an important role in the mechanism of gastric damage induced by (aspirin) ASA, vitamin C attenuates the deleterious effect of ASA on ulcer healing due to its antioxidizing activity by mechanism involving preservation of gastric microcirculation and attenuation of lipid per oxidation and cytokine release and coupling of NO to aspirin fails to delay the ulcer healing suggesting that NO might compensate for prostaglandin deficiency induced by nonsteroidal anti-inflammatory drugs (NSAID) (Brzozowski *et al.*, 2001).

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 protects sperm from oxidative damage (Fraga *et al.*, 1991), improves sperm quality in smokers (Dawson *et al.*, 1992) and is effective in treating sperm agglutination, a condition, which causes sperm to stick together (Dawson *et al.*, 1983). One gram of Vitamin C, taken daily, helps to increase fertility in men who have problems with sperm agglutination (Dason *et al.*, 1990). Vitamin C fights off widespread environmental pollutants including CO, hydrocarbons, pesticides and heavy metals by stimulating enzymes in the liver that detoxify the body. In several studies, vitamin C has reduced chromosome abnormalities in workers exposed to pollutants such as coal tar, styrene, methyl methacrylate and halogenated ethers. Vitamin C also protects us by preventing the development of nitrosamines, the cancer-causing chemicals that stem from the nitrates contained in many foods (Gaby and Singh, 1991).

Combine intake of Vitamin E and vitamin C, for at least 10 years help to maintain better cognitive functions in women in their 70's (Grodstein *et al.*, 2003).

Role of vitamin C in the various body disorders: It has been reported that diabetic individual have low levels of vitamin C in the plasma and in the white blood cells (Cunningham *et al.*, 1991), which constitute our immune defense. Large-scale clinical trials are needed to determine whether supplementation with large doses of the vitamin is beneficent or not. Some smaller trials have found that supplementation with 2 g/d lowered fasting glucose levels (a beneficial effect) and reduced capillary fragility in diabetics. Mega doses of vitamin C may, however, be toxic in diabetics with certain kidney disorders (Goldburg, 1993; Will and Tyers, 1996). It is suspected that vitamin C helps the body to reduce glycolysation, which is an abnormal attachment of sugars to proteins. It also lowers accumulation of the

sugar sorbitol (Will and Tyers, 1996), which can damage eyes and kidneys.

Vitamin C lowers blood pressure and cholesterol levels, helps thin the blood and protects it against oxidation and works in close synergism with vitamin E (Rath, 1993; Whitaker, 1985; Trout *et al.*, 1991).

Vitamin C in doses of approximately 1g daily has shown to help protect the body against Low Density Lipoprotein (LDL) cholesterol (Frei, 1991). Atherosclerosis is a major contributor to heart diseases; vitamin C may prevent this plaque formation by inhibiting the oxidative modification of LDLs. LDLs may contribute to the atherosclerotic process by its cytotoxic effects, uptake by the scavenger receptor and influence on monocyte and macrophage motility (Jialal, 1990). Vitamin C also helps prevent atherosclerosis by strengthening the artery walls through its participation in the synthesis of collagen and by preventing the undesirable adhesion of white blood cells to damaged arteries (Rath, 1993; Weber, 1996; Lehr, 1995).

Supplementation with 2 g/day of vitamin C has been found to reduce adhesion of monocytes (white blood cells) to the lining of blood vessels and thereby reduce the risk of atherosclerosis (Weber, 1996; Lehr, 1995; Heitzer, 1996). Vitamin C supplementation (2 g/d) also effectively reverses the vasomotor dysfunction often found in patients with atherosclerosis (Levine, 1996). In addition vitamin C may increase the beneficial High-Density Lipoprotein (HDL) cholesterol (Gaby and Singh, 1991). Some very recent research carried out in Japan has shown that restenosis (reclosing of opened arteries) after angioplasty can be significantly reduced by supplementing with ascorbic acid (500 mg/day) (Tomoda, 1996).

An adequate intake of the vitamin is highly protective against stroke and heart attack (Gale, 1995; Wood House *et al.*, 1994; Sahyoun, 1996). A recent study has shown that people who supplement with more than 700 mg/day of vitamin C have a 62% lower risk of dying from heart disease than do people with a daily intake of 60 mg/day or less (Sahyoun, 1996).

One study has shown that low serum ascorbic acid (SAA) levels are marginally associated with an increased risk of fatal CVD and significantly associated with an increased risk for all-cause mortality. Low SAA levels have also been a risk factor for cancer death in men, but unexpectedly were associated with a decreased risk of cancer death in women. If the association between low SAA levels and all-cause mortality is causal, increasing the consumption of ascorbic acid and thereby SAA levels, can decrease the risk of death among Americans with low ascorbic acid intakes (Joel *et al.*, 2001).

Vitamin C has an antihistamine effect. Persons with low plasma ascorbic acid levels have elevated blood histamine levels and supplementation with ascorbic

acid lowers blood histamine.

Recent studies have shown that vitamin C concentration in the blood from rheumatoid arthritis patients are extremely low and that vitamin C may protect against further damage to inflamed joints (Lunec, 1985; Halliwell, 1987). Vitamin C also increases the urinary excretion of uric acid (Stein, 1976). Vitamin C may provide podiatrists with a supplemental or alternative treatment for patients with rheumatoid arthritis (Davis, 1990). Another study found that the rapid depletion of vitamin C at the site of an inflammation such as a rheumatoid joint may facilitate proteolytic damage (Helliwell, 1987).

Ascorbic Acid has also been helpful for relief of back pain and pain from inflamed vertebral discs. Antioxidants such as vitamin C and vitamin E are an important part of the body's defense against muscle damage from exercise. Strenuous exercise increases the body's production of free radicals, which in turn can cause muscle damage, which manifest as swollen or painful muscles. While exercise increases the body's natural defense against free radicals, athletes who are doing intense training may benefit from the addition of antioxidant supplements to their diets (Dekkers *et al.*, 1996).

Vitamin C acting as an antioxidant is helpful in the treatment of asthma (Ruskin, 1947). In asthma, vitamin C may relieve the bronchospasm caused by noxious stimuli or when this tight-chest feeling is experienced during exercise (Meric *et al.*, 1991). Large doses (1-2 g/d) of vitamin C have been found to reduce asthma symptoms significantly (Hatch *et al.*, 1995).

Cataracts are extremely common and happen with most people as they age (Kahn *et al.*, 1977). They appear more frequently in smokers and those with diabetes. A diet rich in antioxidants (Vitamin E and Vitamin C especially) may help prevent or delay the formation of cataracts, as oxidative damage appears to be a cause of their development (Palmquist *et al.*, 1884). Since oxidative damage is a suspected cause of cataracts, the addition of antioxidants to the diet may help prevent their occurrence. Low antioxidants levels have often been found in patients with cataracts (Jacques and Chylack, 1991). Vitamin C, is the most commonly found antioxidant in the eyes (Taylor *et al.*, 1991). Since levels of vitamin C appear to decrease with age (Taylor, 1993), supplements are recommended and appear to decrease the likelihood of developing cataracts (Jacques *et al.*, 1988).

Vitamin C reduces elevated pressure in the eye due to glaucoma (Ringsdorf and Cheraskin, 1981). It must be taken in large doses - often upto 20 grams daily - and is not a cure; if vitamin C therapy is stopped, glaucoma will continue to develop at its previous pace. As supplementing with vitamin C has been found to significantly lower the risk of cataracts and glaucoma

(Hankinson, 1992), some very recent works has shown that open angle glaucoma can be reversed by supplementing with large doses of vitamin C (Boyd, 1995).

Vitamin C has been shown to improve the effects of retinopathy (Crary and McCarty, 1984; Sinclair *et al.*, 1992). People with high levels of vitamin C, vitamin E and selenium appear to have a 70% lower risk of developing macular degeneration.

Vitamin C is a natural laxative and may help with constipation problem. Bioflavonoids, taken with vitamin C (1200 mg each) has been shown to help relieve hot flashes associated with menopause (Smith, 1964).

It has long been accepted that a diet rich in vitamin C from fruits and vegetables provides protection against cancer (Uddin and Sarfraz, 1995). Numerous studies have shown that an adequate intake of vitamin C is effective in lowering the risk of developing cancers of the breast, cervix, colon, rectum, esophagus, larynx, lung, mouth, prostate and stomach (Levine, 1996; Block, 1992; Frei, 1994; Block, 1991; Jacobs, 1993). Vitamin C intake has been shown to have an inverse relationship with gastric cancer. Recent follow-up studies on high-risk populations suggest that ascorbic acid, the reduced form of vitamin C, protects against gastric cancer, for which *H. pylori* is a significant risk factor (Feiz and Mobarhan, 2002).

Daily supplementation with 500 mg of vitamin C for ten years has been found to cut the risk of developing bladder cancer by 60% (Bruemmer *et al.*, 1996). The spread of breast cancer (metastasis) is now believed to be predominantly due to free radical damage which can be controlled through intake of increased amount of vitamin C (Malins, 1996). Supplementation with 3 g/d of vitamin C has been found to effectively prevent further polyp. Growth in colon cancer and a vitamin C intake of more than 157 mg/d has been found to reduce the risk of developing colon cancer by 50% (Ferraroni, 1994; DeCosse, 1977).

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 reickitsia and in human pathology, the human body is invaded. Infections initiate bi-directional 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 neutrophils (Kronhausen *et al.*, 1989). Vitamin C works by stimulating the immune system and protecting against damage by the free radicals released by the body in its fight against the infection (Sies and Wilhelm, 1995). As a constituent of collagen, vitamin C may contribute to immune defense in an even more fundamental way "skin and the epithelial lining of the body's orifices, both of which contain collagen, serve as first line of defense against foreign invaders (Gaby and Singh, 1991). It also stimulates the production of PGE 1, a prostaglandin, which assists lymphocytes, the defender cells in our immune system.

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

Gaby and Singh (1991) reports that in 1981, in one study, when 1 g of vitamin C was given intravenously to healthy individuals, after one hour, the neutrophil motility and leukocyte transformation in the subjects blood increased significantly. Other studies support that vitamin C enhances the leukocyte functions. It has also been shown to decrease bacteriological activity (Gaby and Singh, 1991). Test-tube studies show that vitamin C stimulates phagocytosis. In addition the nutrient may reduce the suppressor activity of the mononuclear leukocytes, which weakens the overall effectiveness of the immune system (Gaby and Singh, 1991).

In one study of guinea pigs, the antibody to a particular antigen responded faster when the animals received vitamin C. Meanwhile a study of chickens showed that with intake of 330 mg vitamin C, only 19% of the supplemented animals got the infection while 76% of the unsupplemented control subjects were infected, when exposed to *E. coli* challenge infection (Gross and Cherry, 1988).

Further research must be done for more definitive knowledge about its role in the, strengthening of immunity, prevention and treatment of infections.

Two-time Nobel Prize winner, Dr. Linus Pauling was the first to realize vitamin C's crucial importance in the maintenance of a healthy immune system. In 1970, Linus Pauling, proposed that taking 1,000 mg of vitamin C daily would reduce the incidence of colds by 45% for most people, but that some persons might need much larger doses (Pauling, 1970). In 1976, he proposed even higher doses, in his book "Vitamin C, the Common Cold and the Flu" (Pauling, 1976). Pauling himself reportedly took 12,000 mg vitamin C daily and raised it to 40,000 mg when symptoms of a cold appeared (Pauling, 1982). Various studies do not support the hypothesis that mega doses of vitamin C have a prophylactic effect on common cold (Hamila, 1992). However, Vitamin C constantly decreases the duration and severity

of symptoms. No conclusion can be drawn as to the effective dose or duration of treatment. Benefit appeared to have been greater when the background level of intake was lowest. In one study, urinary excretion before supplementation was three hundred mg per day, indicating normal intakes even higher than this. The benefit may be due to the anti-oxidant property of vitamin C. In infection, phagocytic leukocytes become activated and produce oxidizing compounds, which are released from the cell. By reacting with these oxidants, vitamin C may decrease their inflammatory effects (Hamila, 1992). Vitamin C supplementation decreases the duration and severity of common cold infection. However, the magnitude of the benefit has substantially varied, hampering conclusions about the clinical significance of the vitamin. On the average, vitamin C produces greater benefit for children than for adults. The dose of vitamin C may also affect the magnitude of the benefit; there being, on average greater benefit from 2 g/day compared to 1 g/day of the vitamin. Since few trials have examined the effects of therapeutic supplement and their results have been variable, further therapeutic trials are required to examine the role of vitamin C in treatment of cold (Hamila, 1997).

Large doses of Vitamin C have been found to decrease the duration and severity of colds, an effect that may be related to the antihistamine effects found to occur with large doses (2 grams) of Vitamin C. Ascorbic acid intake has physiological effects on susceptibility to common cold infections, although the effect seems quantitatively meaningful only in specific groups of subjects and is not very large (Hemila, 1997).

Long term daily supplementations, with vitamin C in large doses, do not appear to prevent colds. There appears to be a modest benefit in reducing duration of cold symptoms from ingestion of relatively high doses of vitamin C. The relation of dose to therapeutic benefit needs further exploration (Douglas *et al.*, 2001).

Claims that vitamin C can prevent common cold or decrease severity of symptoms or duration is only one side of the picture. There are also some conflicting reports.

Vitamin C does not prevent cold (Shult and Dick, 1990). Another study has found that vitamin C neither prevents nor brings any benefit against cold (Briggs, 1984).

Though vitamin C has been shown in clinical studies to boost immunity (Johnson, 1993). Its role in the treatment and prevention of common cold is very controversial and needs further study.

In laboratories, Vitamin C has been found to inhibit HIV replication (Harakeh, 1990). With its antioxidant and immunity-enhancing abilities, vitamin C is an excellent supplement for HIV patients, as it may help with disease resistance and overall well being (Cathcart, 1984).

Vitamin C, taken at levels of 2 grams daily, may help the body fight against infection via hepatitis-contaminated

blood (Morishige and Murata, 1978). Vitamin E deficiencies are often found in hepatitis patients. High dose supplementation (1200 IU daily) appears to reduce liver damage in adult patients. This is by no means a foolproof preventive measure (Knodell *et al.*, 1981); however, more promising is the use of Vitamin C as a treatment in already-infected patients (Baur and Staub, 1954).

In one large study, 260 patients with viral hepatitis A took 300 mg of vitamin C a day for several weeks. The researchers, who studied immune indicators, such as serum immunoglobulin and neutrophil phagocytosis, concluded that vitamin C "exerts a remarkable immunomodulating action (Vasiliev *et al.*, 1989). Some other studies have also shown the help of vitamin C in reducing risk of hepatitis infection (Knodell *et al.*, 1981). A study of 14 patients with chronic brucellosis found that vitamin C "might partially restore peripheral, monocyte function and help the monocyte-macrophage system to mount an effective immune response against the infection.

Vitamin C appears to help prevent flue infection (Renker *et al.*, 1954). In addition it appears that when taken in high doses, it speeds recovery from influenza (Klenner, 1949).

Four weeks daily high ascorbic acid treatment in H. Pylori infected patients with chronic gastritis resulted in apparent H. Pylori eradication in 30% patients, which was associated with increased gastric concentration of ascorbic acid. The mechanism for this effect is unclear hence further confirmatory studies are indicated.

Vitamin C also increases the acidity of urine, making it an inhospitable host for bacteria. This may decrease the incidence of urinary tract infection (UTI) (Axelrod, 1985).

RDA of vitamin C: Vitamin C is truly a wonder nutrient and there is not doubt that many of the serious degenerative diseases plaguing the civilized world today can be prevented or even reversed through an adequate intake of this essential nutrient. 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 Aging Research recently recommended that all healthy adults increase their vitamin C intake to 250-1000 mg/d (Voelker *et al.*, 1994). A daily intake of 250-1000 mg/d may be adequate for preventive purposes, but far larger quantities are required in halting or reversing cancer and heart diseases. An adequate intake of vitamin C is surely 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 hemorrhaging. 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.

Vitamin C toxicity: 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. 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). However some research suggests that vitamin C only undergoes this transformation in urine after the urine has left the body (Wandzilak and D'Andre, 1994).

References

- Anderson, R. and P.T. Lukey, 1987. A biological role for ascorbate in the selective neutralization of extra cellular phagocyte-derived oxidants. *Annals of the New York Academy of Sciences*, 498: 229-247.
- Axelrod, D.R., 1985. Ascorbic acid and urinary pH. *JAMA*, 254: 1310.
- Bates, C.J., 1981. The function and metabolism of vitamin C in man. In *Vitamin C (Ascorbic Acid)*, 1st ed., Counsell JN and Hornig DH, Eds., Applied Science, London, pp: 1-22.
- Baur, H. and H. Staub, 1954. Treatment of hepatitis with infusions of ascorbic acid: Comparison with other therapies. *JAMA*, 156: 565.
- Becher, G. and K. Winsel, 1989. "Vitamin C Lessens Superoxide Anion(O₂)-Induced Bronchial Constriction," *Z-Erkr-Atmungsorgane*, 173: 100-104.
- Bendich, A., 1990. "Antioxidant micronutrients and immune responses". In: Bendich, A. and Chandra, R.K. (eds.). *Micronutrients and immune functions*. N.Y. Academy of Sciences, N.Y., pp: 175.
- Block, G., 1991. Epidemiologic evidence regarding vitamin C and cancer. *Am. J. Clin. Nutr.*, 54: 1310S-1314S.
- Block, G., 1992. The data support a role for antioxidants in reducing cancer risk. *Nutr. Res.*, 50: 207-213.
- Bobyrev, V.N., I. Sh. Veselskil and L.E. Bobyreva, 1989. Antioxidants in the prevention and treatment of cerebral arteriosclerosis, *Zh. Nevrapatol. Psikhiatr.*, 89: 60-63.
- Boyd, H., 1995. Eye pressure lowering effect of vitamin C. *J. Orthomolecular Med.*, 10: 165-168.
- Briggs, M.H., 1984. Vitamin C and infectious disease: a review of the literature and the results of a randomized, prospective study over 8 years. In *XH Briggs XH*, (Eds). *Recent Vitamin Research*. Boca Raton, FL: CRC Press, pp: 39-82s.
- Bruemmer, B., 1996. Nutrient intake in relation to bladder cancer among middle-aged men and women. *Am. J. Epidemiol.*, 144: 485-495.
- Brzozowski, T., S. Kwiecie & nacute, P.C. Konturek, S.J. Konturek, M. Mitis-Musiol, A. Duda, Biela & nacute, W. Ski and E.G. Hahn, 2001. *Med Sci. Monit*, 7(4):592-599.
- Burns, (1959). *J. J. Am. J. Med.*, 26: 740.
- Cathcart, R.F., 1984. Vitamin C in the treatment of acquired immune deficiency syndrome (AIDS). *Med. Hypotheses*, 14: 423-433.
- Cohen, J.D. and H.W. Rubin, 1960. Functional menorrhagia: treatments with bioflavonoids and vitamin C. *Curr. Ther Res.*, 2 : 539.
- Crary, E.J. and M.F. McCarty, 1984. Potential clinical applications for high-dose nutritional antioxidants. *Med. Hypoth.*, 13: 77-98.
- Cunningham, J.J., S.L. Ellis and K.L. McVeigh, 1991. "Reduced mononuclear leukocyte ascorbic acid content in adults with insulin-dependent diabetes mellitus consuming adequate dietary vitamin C". *Metabolism*, 40: 146-149.
- Dason, E.B., W.A. Harris and W.A. Powell, 1990. Relationship between ascorbic acid and male fertility. In: *Aspects of Some Vitamins, Minerals and Enzymes in Health and Disease*, de. GH Bourne. *World Rev. Nutr. Diet*, 62: 1-26.
- Davis, R.H., 1990. Vitamin C influence on localized adjuvant arthritis. *J. An. Podiatr. Med. Assoc.*, 80: 414-8.
- Dawson, E.B., W.A. Harris, M.C. Teter and L.C. Powell, 1992. Effect of ascorbic acid supplementation on the sperm quality of smokers. *Fertile Sterile*, 58: 1034-1039.
- Dawson, E.B., W.A. Harris and W.J. McGanity, 1983. Effect of ascorbic acid on sperm fertility. *Fed. Proc.*, 42: 531.
- DeCosse, J.J., 1977. Surgical and medical measures in prevention of large bowel cancer. *Cancer*, 40: 2549-2552.
- Dekkers, J.C., L.J. Van Doornen and H.C. Kemper, 1996. The role of antioxidant vitamins and enzymes in the prevention of exercise-induced muscle damage. *Sports Med.*, 21: 213-238.
- Douglas, R.M., E.B. Chalder and Treacy, 2001. Vitamin C for preventing and treating the common cold (Cochrane REview). In: *The Cochrane Library*. Oxford: Update Software.
- Enstrom, E.J., 1992. Vitamin C intake and mortality among a sample of the United States population. *Epidemiology*, 3: 194-202.
- Feiz, H.R. and S. Mobarhan, 2002. *Nutr. Rev.*, 60: 34-6.
- Ferraroni, M., 1994. Selected micronutrient intake and the risk of colorectal cancer. *Br. J. Cancer*, 70: 1150-1155.
- Finley, E.B. and F.L. Cerklewski, 1983. Influence of ascorbic acid supplementation on copper status in young adult men. *Am. J. Clin. Nutr.*, 37: 553-556.

- Fraga, C.G., P.A. Motchnik and M.K. Shigenaga, 1991. Ascorbic acid protects against endogenous oxidative DNA damage in human sperm. *Proc. Natl. Acad. Sci.*, 88: 11003-11006.
- Frei, B., 1991. Ascorbic acid protects lipids in human plasma and Low-Density Lipoprotein against oxidative damage. *Am. J. Clin. Nutr.*, 54: 1113S-1118S.
- Frei, B., 1994. Reactive oxygen species and antioxidant vitamins: mechanisms of action. *Am. J. Med.*, 97: 5S-13S.
- Gaby, S.K. and V.N. Singh, 1991. "Vitamin C," - Vitamin intake and health: A Scientific Review, Gaby, S.K., Bendich, A., Singh, V. and Machlin, L. (eds.). Marcel Dekker, N.Y.
- Gale, R.C., 1995. Vitamin C and risk of death from stroke and coronary heart disease in cohort of elderly people. *Br. Med. J.*, 310: 1563-1566.
- Gerber, W.F., 1975. Effect of ascorbic acid, sodium salicylate and caffeine on the serum interferon level in response to viral infection. *Pharmacology*, 13: 228.
- Goldburg, B., 1993. *Alternative Medicine: The Definitive Guide*. Future Medicine Publishing, Puyallup, WA.
- Grodstein, F., J. Chen and W.C. Willett, 2003. "High-dose antioxidant supplements and cognitive function in community-dwelling women," *Am. J. Clin. Nutr.*, 77: 975-984.
- Gross, W.B. and D.J. Cherry, 1988. Effect of Ascorbic Acid on the Disease Caused by *Escherichia Coli* Challenge Infection," *Avian-Dis.*, 32: 407-409.
- Halliwell, B., 1987. Biologically significant scavenging of the myeloperoxidase-derived oxidant hypochlorous acid by ascorbic acid: Implications for antioxidant protection in the inflamed rheumatoid joint. *FEBS Lett.*, 213: 15-17.
- Hankinson, E.S., 1992. Nutrient intake and cataract extraction in women: A prospective study. *Br. Med. J.*, 305: 35-39.
- Harakeh, S., 1990. Suppression of human immunodeficiency virus replication by ascorbate in chronically and acutely infected cells. *Proc. Natl. Acad. Sci.*, 87: 7245-7249.
- Hatch, E.G., 1995. Asthma, inhaled oxidants and dietary antioxidants. *Am. J. Clin. Nutr.*, 61: 625S-630S.
- Heitzer, T., 1996. Antioxidant vitamin C improves endothelial dysfunction in chronic smokers. *Circulation*, 94: 6-9.
- Hemila, H., 1992. Vitamin C and the common cold. *Br. J. Nutr.*, 67: 3-16.
- Hemila, H., 1997. Vitamin C intake and susceptibility to the common cold. *Br. J. Nutr.*, 77: 59-72.
- Jacobs, M.M., 1993. Diet, nutrition and cancer research: An Overview, *Nutrition Today*, 19-23.
- Jacques, P.F., L.T. Chylack, R.B. McGandy and S.C. Hartz, 1988. Antioxidant status in persons with and without senile cataract. *Arch Ophthalmol*, 106: 337-340.
- Jacques, P.F. and L.T.Jr. Chylack, 1991. Epidemiologic evidence of a role for the antioxidant vitamins and carotenoids in cataract prevention. *Am. J. Clin. Nutr.*, 53: 352S-355S.
- Jialal, I., 1990. Vega, Gloria Lena and Grundy, Scott.M. "Physiologic levels of ascorbate inhibit the oxidative modifications of Low Density Lipoproteins," *Atherosclerosis*, 82: 185.
- Joel, A., Simon, S.H. Esther and A.T. Jeffrey, 2001. Relation of serum ascorbic acid to mortality among US adults. *J. Am. College of Nutr.*, 20(3).
- Johnson, C., 1993. *Am. J. Clin. Nutr.*, 8: 103-105.
- Kahn, H.A., H.M. Leibowitz and J.P. Ganley, 1977. The Framingham Eye Study: I. Outline and major prevalence findings. *Am. J. Epidemiol.*, 106: 17-32.
- Kallner, A.B., D. Hartmann and D.H. Horning, 1979. Steady state turnover and body pool of ascorbic acid in man. *Am. J. Clin. Nutr.*, 32: 530-539.
- Karagezian, K.G. and D.M. Gevorkian, 1989. "Phospholipid-Glycerides, Cross-resistance of erythrocytes, malonic dialdehyde level and alpha-tocopherol levels in the plasma and erythrocytes of rats with Alloxan diabetes before and after combined antioxidant therapy," *Vopr. Med. Khim.*, 35: 27-30.
- Kinsman, R.A. and J. Hood, 1971. Some behavioral effects of ascorbic acid deficiency. *Am. J. Clin. Nutr.*, 24: 455.
- Klenner, F.R., 1949. The treatment of poliomyelitis and other virus diseases with vitamin C. *J. Southern Med. Surg.*, 111: 210-214.
- Knodell, R.G., M.A. Tate, B.F. Akl and J.W. Wilson, 1981. Vitamin C prophylaxis for post-transfusion hepatitis: lack of effect in a controlled trial. *Am. J. Clin. Nutr.*, 34: 20-23.
- Kronhausen, Eerhard and Kronhausen, Phylles with Demopoulos, B. Harry, 1989. *Formula for Life*. William Morrow and Co., New York.
- Kubler, W. and J. Gehler, 1970. On the kinetics of the intestinal absorption of ascorbic acid: a contribution to the calculation of an absorption process that is not proportional to the dose. *Int. J. Vitamin and Nutr. Res.*, 40: 442-453.
- Kuvshinnikov, V.A., 1989. "Use of the antioxidant complex of vitamins A, E and C in murine leukemia," *Gematol. Transvuziol.*, 34: 23-28.
- Lehr, Hans-Anton, 1995. Protection from Oxidized LDL-Induced Leukocyte Adhesion to Microvascular and Macrovascular Endothelium In-Vivo by Vitamin C but not by Vitamin E. *Circulation*, 91: 1525-1532.
- Levine, N.G., 1996. Ascorbic acid reverses endothelial vasomotor dysfunction in patients with coronary artery disease. *Circulation*, 93:1107-1113.
- Levine, M., 1996. Vitamin C pharmacokinetics in healthy volunteers: Evidence for a recommended dietary allowance. *Proceedings of the National Academy of Sciences USA*, 93: 3704-09.
- Losonczy, G.K., 1996. Vitamin E and vitamin C supplement use and risk of all-cause and coronary heart disease mortality in older persons. *Am. J. Clin. Nutr.*, 64: 190-196.

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- Lunec, J.B., 1985. The determination of dehydroascorbic acid and ascorbic acid in the serum and synovial fluid of patients with rheumatoid arthritis. *Free Radical Research Communications*, 1: 31-39.
- Malins, C.D., 1996. Progression of human breast cancers to the metastatic state is linked to hydroxyl radical-induced DNA damage. *Proceedings of the National Academy of Sciences USA*, 93: 2557-2563.
- Monsen, E.R., 1978. Estimation of available dietary iron. *Am. J. Clin. Nutr.*, 31: 134.
- Morishige, F. and A. Murata, 1978. Vitamin C for prophylaxis of viral hepatitis B in transfused patients. *J. Int. Acad. Prev. Med.*, 5: 54.
- Olson, J.A. and R.E. Hodges, 1987. Recommended dietary intakes (RDI) of vitamin C in humans. *Am. J. Clin. Nutr.*, 45: 693-703.
- Palmquist, B., B. Phillipson and P. Barr, 1984. Nuclear cataract and myopia during hyperbaric oxygen therapy. *Br. J. Ophthalmol.*, 68: 113-117.
- Pauling, L., 1970. *Vitamin C and the common cold*. San Francisco: WF Freeman.
- Pauling, L., 1976. *Vitamin C, the common cold and the flu*. San Francisco: WF Freeman.
- Pauling, L., 1982. Speech at Natural Foods Exposition, reported in *Natural Foods Merchandiser*, pp: 65.
- Piesse, J.W., 1985. Nutritional factors in calcium containing kidney stones with particular emphasis on vitamin C. *Int. Clin. Nutr. Rev.*, 5: 110-129.
- Platt, B.S., T.P. Eddy and P.L. Pellett, 1963. *Food in Hospitals*. Anonymous. Nuffield Provincial Hospitals Trust and Oxford University Press, London.
- Rath, M., 1993. *Eradicating heart disease*. Health Now. San Francisco, CA.
- Renker, K. and S. Wegner, 1954. Vitamin C-Prophylaxe in der Volkswertf Stralsund. *Deutsche Gesundheitswesen*, 9: 702-706.
- Ringsdorf, W.M. Jr. and E. Cheraskin, 1981. Ascorbic acid and glaucoma: A Rev. *J. Holistic. Med.*, 3: 167-172.
- Ruskin, S.L., 1947. Sodium ascorbate in the treatment of allergic disturbances. The role of adrenal cortical hormone-sodium-vitamin C. *Am. J. Dig. Dis.*, 14: 302-306.
- Sahyoun, R.N., 1996. Carotenoids, vitamins C and E and mortality in an elderly population. *Am. J. Epidemio.*, 144: 501-511.
- Sayers, M.H., S.R. Lynch and P. Jacobs, 1973. The effects of ascorbic acid supplementation on the absorption of iron in maize, wheat and soya. *Br. J. Haematology*, 24: 209-218.
- Shult, P.A. and E.C. Dick, 1990. *Proceedings of the Inerscience Conference of Antimicrobial Agents and Chemotherapy*, Atlanta.
- Sies, H. and S. Wilhelm, 1995. Vitamins E and C, beta-carotene and other carotenoids as antioxidants. *Am. J. Clin. Nutr.*, 62: 1315S-1321S.
- Sinclair, A.J., A.J. Girling and L. Gray, 1992. An investigation of the relationship between free radical activity and vitamin C metabolism in elderly diabetic subjects with retinopathy. *Gerontology*, 38: 268-274.
- Smith, C.J., 1964. Non-hormonal control of vaso-motor flushing in menopausal patients. *Chicago Med.*
- Spillert, C.R., 1989. "Inhibitory effect of high dose ascorbic acid on inflammatory edema, *Agents-Actions*, 27: 401-402.
- Stein, H.B., 1976. Ascorbic acid-induced uricosuria: a consequence of megavitamin therapy. *Ann. Intern. Med.*, 84: 385-388.
- Stevenson, N.R., 1974. Active transport of L-ascorbic acid in the human ileum. *Gastroenterology*, 67: 952-956.
- Taylor, A., 1993. Cataract: relationship between nutrition and oxidation. *J. Am. Coll. Nutr.*, 12: 138-146.
- Taylor, A., P.F. Jacques and D. Nadler, 1991. Relationship in humans between ascorbic acid consumption and levels of total and reduce ascorbic acid in lens, aqueous humor and plasma. *Curr. Eye. Res.*, 10: 751-759.
- Taylor, T.V., 1974. Ascorbic acid supplementation in the treatment of pressure-sores. *The Lancet*, 544-546.
- Thurnham, D.I., 2000. Water-Soluble Vitamins (Vitamin C and B Vitamins, Thiamin, Riboflavin and Niacin). In "Human Nutrition and Dietetics". Garrow, J.S., W.P.T. James, A. Ralph (Eds.). Churchill. Livingston Publishers, Edinburgh London, 249-257.
- Tomoda, H., 1996. Possible prevention of post-angioplasty restenosis by ascorbic acid. *Am. J. Cardiology*, 78: 1284-1286.
- Trout, D.L., 1991. Vitamin C and cardiovascular risks factors. *Am. J. Clin. Nutr.*, 53: 322S-325S.
- Uddin, S. and A. Sarfraz, 1995. Antioxidants protection against cancer and other human diseases. *Comprehensive Therapy*, 21: 41-45.
- Vasil'ev, V.S., V.I. Komar and N.I. Kisel, 1989. Humoral and cellular indices of nonspecific resistance in viral hepatitis A and ascorbic acid, *Ter-Arkh.*, 11: 119-129.
- Voelker, R., 1994. Recommendations for antioxidants: How much evidence is enough? *J. Am. Med. Assoc.*, 271: 1148-1149.
- Wandzilak, T.R., S.D. D'Andre , P.A. Davis and H.E. Williams, 1994. Effect of high dose vitamin C on urinary oxalate levels. *J. Urol.*, 151: 834-837.
- Weber, C., 1996. Increased adhesiveness of isolated monocytes to endothelium is prevented by vitamin c intake in smokers. *Circulation*, 93: 1488-1492.
- Whitaker, M.J., 1985. *Reversing Heart Disease*. Warner Books, NY.
- Will, J.C. and T. Tyers, 1996. Does diabetes mellitus increase the requirement for vitamin C? *Nutr. Rev.*, 54: 193-202.
- Woodhouse, P.R. and Khaw, Kay-Tee, 1994. Seasonal variations in vitamin C status, infection, fibrinogen and cardiovascular disease - Are they linked? *Age and Aging*, 23: 5.