Review Article

Vitamin C as a therapeutic healing agent

T. Vinishdharma[1], K. R. Don[2]*

ABSTRACT

Vitamin C is also known as ascorbic acid, L-ascorbic acid, dehydroascorbic acid, and the antiscorbutic vitamin. Chemically, it is called L-xyloascorbic acid and L-threo-hex-2-uronic acid g-lactone. The very highest concentrations of Vitamin C are found in the adrenal and pituitary gland. High levels are also found in liver, leukocytes, brain, kidney, and pancreas. Most of the Vitamin C is found in liver and skeletal muscle due to their relative size to the rest of the body. Ascorbic acid is one of the important water-soluble vitamins. It is essential for collagen, carnitine, and neurotransmitters biosynthesis. Most plants and animals synthesize ascorbic acid for their own requirement. However, humans cannot synthesize ascorbic acid due to lack of an enzyme gulonolactone oxidase. Hence, ascorbic acid has to be supplemented mainly through fruits, vegetables, and tablets. Vitamin C is literally amazing in the wide variety of function it performs in healing the body and maintaining body health. Many health benefits have been attributed to ascorbic acid such as antioxidant, antiatherogenic, anticarcinogenic, immunomodulator, and prevent cold. The best-characterized function is the synthesis of collagen connective tissue protein at the level of hydroxylation of the prolyl and lysyl residues of procollagen. Vitamin C also plays important roles in the synthesis of neurotransmitters, steroid hormones, carnitine, conversion of cholesterol to bile acids, tyrosine degradation, and metal ion metabolism. This vitamin also may enhance iron bioavailability. The role of ascorbic acid as a biological reducing agent may be linked to its prevention of degenerative diseases such as cancer and cardiovascular diseases.

KEY WORDS: Ascorbic acid, Healing agent, Vitamin C

INTRODUCTION

Vitamin is defined as various organic substances that are essential in minute quantities to the nutrition of most animals and some plants, act especially as coenzymes and precursors of coenzymes in the regulation of metabolic processes but do not provide energy or serve as building units, and are present in natural foodstuffs or sometimes produced within the body. Mostly human does not synthesize them; therefore, they must be supplied by diet in the required amount.[2] Vitamin is subdivided into fat-soluble and water-soluble vitamins. Fat-soluble vitamin is vitamins which are soluble in fats.[18] Example of water-soluble vitamins is Vitamins A, D, E, and K. Water-soluble vitamin is those which are soluble in water and include Vitamin C and Vitamin B that usually termed as Vitamin B complex.

Access this article online

Website: jprsolutions.info | ISSN: 0975-7619

Ascorbic acid was first isolated in 1928 by the Hungarian scientist and Nobel Prize winner Szent-Gyorgyi. The Nobel Prize-winning scientist, Dr. Linus Pauling, was among the first to recognize the importance of high-dose Vitamin C supplementation >30 years ago. Since then, scientists have amassed impressive evidence supporting the numerous benefits of high-dose Vitamin C. Vitamin C is also known as ascorbic acid. Ascorbic acid is a water-soluble antioxidant.[4] It is an unstable, easily oxidized acid and can be destroyed by oxygen, alkali, and high temperature.

SOURCES

Ascorbic acid is widely distributed in both plants and animals. Ascorbic acid is available in reduced form (L-ascorbic acid) and oxidized form (L-dehydroascorbic acid). Fruits, vegetables, liver, and kidney are generally the best sources; only small amounts are found in muscle meat. Plants synthesize L-ascorbic acid from carbohydrates.[8] The very

[1]Graduate Student, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, Tamil Nadu, India, [2]Senior Lecturer, Department of Oral and maxillofacial Pathology, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai

***Corresponding author:** K. R. Don, Department of Oral and Maxillofacial Pathology, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Saveetha University, 162, PH Road, Chennai - 600 077, Tamil Nadu, India. Phone: +91-9443215893. E-mail: drkrdon@gmail.com

Received on: 10-08-2018; Revised on: 12-09-2018; Accepted on: 19-10-2018

richest sources are acerola, guavas, red sweet peppers, kale leaves, parsley, collard leaves, turnip greens, green sweet peppers, broccoli, brussels sprouts, and mustard greens. Good sources are all fresh fruits and vegetables (especially green, leafy vegetables).[6]

DAILY REQUIREMENTS

The new average daily intake level that is sufficient to meet the nutritional requirement of ascorbic acid or recommended dietary allowances (RDA) for adults (>19 years) are 90 mg/day for men and 75 mg/day for women. Consumption of 100 mg/day of ascorbic acid is found to be sufficient to saturate the body pools (neutrophils, leukocytes, and other tissues) in healthy individual. As a matter of fact, a scientific advisory recommended that healthy adults increase their Vitamin C intake to 250–1000 mg/d maybe adequate for preventive purpose.[8]

CHEMISTRY OF ASCORBIC ACID

L-ascorbic acid ($C_6H_8O_6$) is the trivial name of Vitamin C. The chemical name is 2-oxo-L-threo-hexono-1,4–lactone-2,3–enediol. L-ascorbic and dehydroascorbic acid are the major dietary forms of Vitamin C. Ascorbyl palmitate is used in commercial antioxidant preparations.[1] All commercial forms of ascorbic acid except ascorbyl palmitate are soluble in water. L-ascorbic acid and its fatty acid esters are used as food additives, antioxidants, browning inhibitors, reducing agents, flavor stabilizers, dough modifiers, and color stabilizers.[20] Ascorbyl palmitate has been used for its greater lipid solubility in antioxidant preparations. In foods, pH influences the stability of ascorbic acid. It exhibits maximal stability between pH 4 and 6. Cooking losses of ascorbic acid depend on the degree of heating, surface area exposed to water, oxygen, pH, and presence of transition metals.[17]

CATABOLISM OF ASCORBIC ACID

Ascorbic acid present in foods is readily available and easily absorbed by active transport in the intestine. Most of it (80–90%) will be absorbed when the intake is up to 100 mg/day, whereas at higher levels of intake (500 mg/day), the efficiency of the absorption of ascorbic acid rapidly declines.[3] Ascorbic acid is sensitive to air, light, heat, and easily destroyed by prolonged storage and over processing of food. Ascorbic acid is a water-soluble compound is easily absorbed, but it is not stored in the body. The average adult has a body pool of 1.2–2.0 g of ascorbic acid that may be maintained with 75 mg/d of ascorbic acid. About 140 mg/d of ascorbic acid will saturate the total body pool of Vitamin C. The average half-life of ascorbic acid in adult human is about 10–20 days, with a turnover of 1 mg/kg body and a body pool

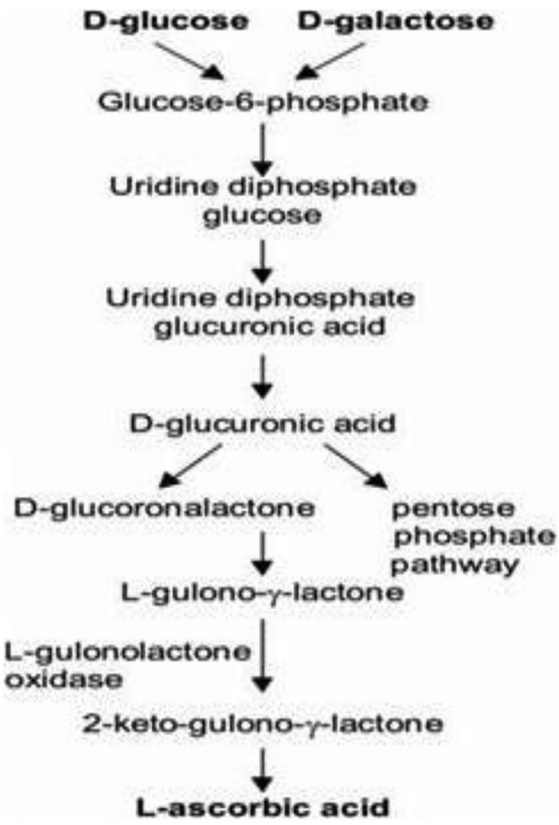

Figure 1: Catabolism of ascorbic acid in animal. Courtesy of Vitamin C in human health and disease, K Akhilender Naidu, Nutrition Journal 2003;2:7

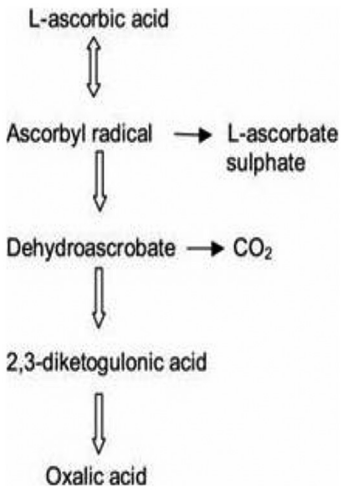

Figure 2: Catabolism of ascorbic acid. Courtesy of Vitamin C in human health and disease, K A Khilender Naidu, Nutrition Journal 2003;2:7

of 22 mg/kg at plasma ascorbate concentration of 50 µmol/L. Hence, ascorbic acid has to regularly supplemented through diet or tablets to maintain ascorbic acid pool in the body.

Ascorbic acid is a white crystalline sugar that naturally occurs chemical forms of L-xyloascorbic acid and D-xyloascorbate. L-xyloascorbic acid is without vitamin activity. It is reversibly oxidized to

L-dehydroascorbic acid on exposure to copper, heat or mildly alkaline condition. Both L-ascorbic acid and L-dehydroascorbic are physiologically active form of Vitamin C.[14]

The major metabolites of ascorbic acid in human are dehydroascorbic acid, 2,3-diketogulonic acid, and oxalic acid.[7] [Figures 1 and 2] The main route of the elimination of ascorbic acid and its metabolites is through urine. It is excreted unchanged when high doses of ascorbic acid are consumed. Ascorbic acid is generally non-toxic, but at high doses (2–6 g/day), it can cause gastrointestinal disturbances or diarrhea.[15] The side effects are generally not serious and can be easily reversed by reducing intake of ascorbic acid. Furthermore, there is no consistent and compelling data on serious health effects of Vitamin C in humans.

BIOLOGICAL FUNCTION

Ascorbic acid, commonly known as Vitamin C, plays significant functions in the human body, though its function at the cellular level is not very clear.[13]

The main role of Vitamin C is in the manufacture of collagen. This protein forms the basis of connective tissue, the most abundant tissue in the body, and acts as a cementing substance between cells. It helps support and protects blood vessels, bones, joints, organs, and muscles, and forms a sizable proportion of skin, tendons, the cornea of the eye, ligaments, cartilage, teeth, and bone. Collagen forms a protective barrier against infection and disease and promotes healing of wounds, fractures, and bruises.

Vitamin C is involved in the manufacture of carnitine, a substance necessary for the production of energy from fatty acids in cells, especially cardiac and skeletal muscle cells.[11] Vitamin C is necessary for the activity of the enzyme system which metabolizes drugs in the body. It is also necessary for iron absorption and plays a role in the conversion of cholesterol to bile acids for excretion.

Vitamin C plays a role in the manufacture of neurotransmitters necessary for proper functioning of the nervous system. It is necessary for the conversion of tryptophan to serotonin and of tyrosine to dopamine and adrenaline.

Vitamin C is a powerful water-soluble antioxidant and plays a vital role in protecting against oxidative damage caused by free radicals.[12] It neutralizes potentially harmful reactions in the blood and the fluid inside and surrounding cells. It also helps protect low-density lipoprotein cholesterol against free radical damage.[31] The antioxidant action helps to protect against cancer, the effects of aging, heart disease, and an array of health problems.[19,29]

This vitamin also helps the liver in the detoxification of toxic substances in the system and the blood in fighting infections.[21] Ascorbic acid is important in the proper function of the immune system. As an antioxidant, it reacts with compounds such as histamines and peroxides to reduce inflammatory symptoms. Its antioxidant property is associated with the reduction of cancer incidences. An interesting observation is that platelets from scorbutic experimental animals tend to lose ascorbic acid into the blood plasma at a higher rate than control groups during the process of aggregation, prior to clot formation.[5] Also sub-optimal plasma ascorbate levels are associated with increased blood histamine levels, both in guinea pigs and in man.[9]

Vitamin C is critical to immune function as it is involved in antibody production and white blood cell function and activity. Other functions include the production of interferon, an antiviral, and anticancer substance. Vitamin C requirements are raised when the immune system is under stress.[25]

Ascorbic acid is known to enhance the availability and absorption of iron from non-heme iron sources. Ascorbic acid supplementation is found to facilitate the dietary absorption of iron. The reduction of iron by ascorbic acid has been suggested to increase dietary absorption of non-heme iron.[27]

As an antioxidant, Vitamin C helps to prevent cataracts - the clouding of the lens of the eye that can lead to blindness in older adults. The lens needs a lot of Vitamin C to counteract all the free radicals that form as a result of sunlight on the eye.[20] Vitamin C is concentrated in the lens. When there is plenty of this Vitamin floating through your system, it is easy for the body to pull it out of your blood and put it into the lens, protecting it from damage.[10]

Vitamin C is important in the synthesis of adrenal hormones and is depleted from the adrenal glands in times of stress.

Asthmatics tend to have higher needs for Vitamin C due to its antioxidant function in the lungs and airways. Doses of 1000–2000 mg per day improve asthmatic symptoms and lessen the body's production of histamine, which contributes to inflammation.

People with diabetes can benefit from extra Vitamin C, too. This nutrient can help regulate blood sugar levels. Since insulin helps Vitamin C, as well as glucose, get into cells, people with diabetes may not have enough Vitamin C inside many of their cells. Just like glucose, Vitamin C cannot do its work if it is not inside of a

cell.[19] Supplementing Vitamin C can force it into body cells, where it can protect against the many complications of diabetes.

As an antioxidant, vitamins 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 radicals damage.[20] 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.[28]

Ascorbic acid and wound healing ascorbic acid play a critical role in wound repair and healing/regeneration process as it stimulates collagen synthesis. Adequate supplies of ascorbic acid are necessary for normal healing process, especially for post-operative patients. It has been suggested that there will be rapid utilization of ascorbic acid for the synthesis of collagen at the site of wound/burns during post-operative period. Hence, administration of 500 mg–1.0 g/day of ascorbic acid is recommended to accelerate the healing process.[25,26]

Vitamin C increases cancer survival. In battling cancer, some patients invariably exhaust all available treatment options such as drugs, surgery, and radiation. Scientists are now investigating nutritional remedies that may benefit such patients. Researchers recently reported that administering high-dose, intravenous Vitamin C to several patients with advanced terminal stage cancer led to unexpectedly long survival times. While further studies are needed, these findings support earlier reports showing that high-dose Vitamin C, administered either orally or intravenously, helped improve symptoms and prolong life in cancer patients.[30]

CONTROVERSY

Vitamin C is an important dietary antioxidant; it significantly decreases the adverse effect of reactive species such as reactive oxygen and nitrogen species that can cause oxidative damage to macromolecules such as lipids, DNA, and proteins which are implicated in chronic diseases including cardiovascular disease, stroke, cancer, neurodegenerative diseases, and cataractogenesis.

Recently, it has been reported that lipid hydroperoxide can react with ascorbic acid to form products that could potentially damage DNA, suggesting that it may form genotoxic metabolites from lipid hydroperoxides implicating that ascorbic acid may enhance mutagenesis and risk of cancer.[22]

TOXICITY

Although too much dietary Vitamin C is unlikely to be harmful, megadoses of Vitamin C supplements may cause diarrhea, nausea, vomiting, heartburn, abdominal bloating and cramps, headache, insomnia, and kidney stones. The upper limit for Vitamin C intake is 2000 mg/day.[23] Up to 10 g/day of Vitamin C are sometimes taken for unproven health benefits such as preventing or shortening the duration of viral infections or slowing or reversing the progression of cancer or atherosclerosis. Such doses may acidify the urine, cause nausea and diarrhea, interfere with the healthy antioxidant-prooxidant balance in the body, and, in patients with thalassemia or hemochromatosis, promote iron overload.

DEFICIENCIES

A lack of Vitamin C leads eventually to scurvy. The symptoms are mainly due to poorly formed collagen and include the breaking open of small blood vessels, the reddening and bleeding of gums, loose teeth, joint pains, dry scaly skin, and blood vessel damage. Other symptoms include general weakness, fluid retention, depression, and anemia. Vitamin C deficiency can also cause slower wound healing, increased susceptibility to infections, male infertility, and increased genetic damage to sperm cells, which may lead to birth defects.[8]

Scurvy and severe Vitamin C deficiency are rare in developing countries, but marginal deficiencies may be relatively common and may play a role in the development of diseases such as cancer and heart disease.[24]

Men, the elderly, smokers, diabetics, those with high blood pressure, and those taking oral estrogen-containing contraceptive users have lowered plasma Vitamin C levels and are at greatest risk of deficiency-related disease.[25]

Vitamin C deficiency has been linked to cardiovascular disease, high blood pressure, cancer, cataracts, the increased effects of diabetes, asthma, and poor lung function and reduced immunity.[15]

Vitamin C deficiency may also play a role in macular degeneration of the eye, arthritis, Parkinson's disease, preeclampsia of pregnancy, the common cold gum disease, low sperm counts, and skin ulcers.

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. It is very clear from the roles of ascorbic acid as enumerated above that ascorbic acid plays significant roles in biological functions. Besides, ascorbic acid

is an essential vitamin that is derived only from exogenous sources and makes its role in human health of significant importance. Based on available biochemical, clinical, and epidemiological studies, the current RDA for ascorbic acid is suggested to be 100–120 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, antiatherogenic, and anticarcinogenic activity. The current evidences also suggest that ascorbic acid protects against atherogenesis by inhibiting LDL oxidation. Thus, though ascorbic acid was discovered in the 17th century, the role of this important vitamin in human health and disease still remains a mystery in view of many beneficial claims and contradictions.

REFERENCES

1. Allard JP, Aghdassi E, Chau J, Tam C, Kovacs CM, Salit IE, *et al.* Effects of Vitamin E and C supplementation on oxidative stress and viral load in HIV-infected subjects. AIDS 1998;12:1653-9.
2. Ashino H, Shimamura M, Nakajima H, Dombou M, Kawanaka S, Oikawa T, *et al.* Novel function of ascorbic acid as an angiostatic factor. Angiogenesis 2003;6:259-69.
3. Boyd HH. Eye pressure lowering effect of Vitamin C. J Orthomol Med 1995;10:165-8.
4. Burns DJ, Rivers JM, Machlin D. Third conference on Vitamin C. Am N Y Acad Sci 1987;258:498-502.
5. Byshevskii A, Solovey GS, Galian SL, Solovey VG, Solovey SV. Effects of Vitamins A, E, C and P on intensity of blood coagulation in experimental animals. Bull Exp Biol Med 1992;114:262-5.
6. Bielski BH. Chemistry of ascorbic acid radicals. In: Seib PA, Tolbert BM, editors. Ascorbic Acid: Chemistry, Metabolism, and Uses. Vol. 200. Washington DC: American Chemical Society; 1982. p. 81-100.
7. Chatterjee IB, Majumder AK, Nandi BK, Subramanian N. Synthesis and some major functions of Vitamin C in animals. Ann N Y Acad Sci 1975;258:24-47.
8. Chatterjee IB. Evolution and the biosynthesis of ascorbic acid. Science 1973;182:1271-2.
9. Clemetson CA. Vaccination, inoculation and ascorbic acid. J Orthomol Med 1999;14:35-8.
10. Clemetson CA. Histamine and ascorbic acid in human blood. J Nutr 1980;110:662-8.
11. Davison G, Gleeson M. Influence of acute Vitamin C and/or carbohydrate ingestion on hormonal, cytokine, and immune responses to prolonged exercise. Int J Sport Nutr Exerc Metab 2005;15:465-79.
12. Furumoto K, Inoue E, Nagao N, Hiyama E, Miwa N. Age-dependent telomere shortening is slowed down by enrichment of intracellular Vitamin C via suppression of oxidative stress. Life Sci 1998;63:935-48.
13. Buettner GR, Schafer FQ. Albert Szent-Györgyi: Vitamin C identification. Biochem J 2006;28:31-3.
14. Calcutt G. The formation of hydrogen peroxide during the autoxidation of ascorbic acid. Experientia 1951;7:26.
15. Hemilä H. Vitamin C supplementation and the common cold-was Linus Pauling right or wrong? Int J Vitam Nutr Res 1997;67:329-35.
16. Hemilä H. Vitamin C and common cold incidence: A review of studies with subjects under heavy physical stress. Int J Sports Med 1996;17:379-83.
17. Haworth WN, Hirst EL. Synthesis of ascorbic acid. J Soc Chem Ind (London) 1933;52:645-7.
18. Graumlich JF, Ludden TM, Conry-Cantilena C, Cantilena LR Jr., Wang Y, Levine M, *et al.* Pharmacokinetic model of ascorbic acid in healthy male volunteers during depletion and repletion. Pharm Res 1997;14:1133-9.
19. Svirbely JL, Szent-Györgyi A. The chemical nature of Vitamin C. Biochem J 1933;27:279-85.
20. Kallner A, Horing D, Hartman D. Kinteics of ascorbic acid in humans. In: Seib PA, Tolbert BM, editors. Ascorbic acid: Chemistry, metabolism and uses. Advances in Chemistry Series No. 200. Washington, DC: American Chemical Society; 1982. p. 385-400.
21. Loguercio C, Cuomo A, Tuccillo C, Gazzerro P, Cioffi M, Molinari AM, *et al.* Liver p53 expression in patients with HCV-related chronic hepatitis. J Viral Hepat 2003;10:266-70.
22. Lind J. A treatise of scurvy. Printed by Sands, Murray and Cochran for Kincaid, A and Donaldson, A. Edinburgh 1753.
23. Moser U, Bendich A. Vitamin C. In: Machlin LJ, editor. Handbook of Vitamins. Ch. 5. New York: Marcel Dekker; 1990.
24. Khan MM, Martell AE. Metal ion and metal chelate catalyzed oxidation of ascorbic acid by molecular oxygen. II. Cupric and ferric chelate catalyzed oxidation. J Am Chem Soc 1967;89:7104-11.
25. Chen Q, Espey MG, Krishna MC, Mitchell JB, Corpe CP, Buettner GR, *et al.* Pharmacologic ascorbic acid concentrations selectively kill cancer cells: Action as a pro-drug to deliver hydrogen peroxide to tissues. Proc Natl Acad Sci U S A 2005;102:13604-9.
26. Sauberlich HE. Bioavailability of vitamins. Prog Food Nutr Sci 1985;9:1-33.
27. Sauberlich HE: Ascorbic acid. In: Present knowledge in Nutrition. Edited by: Brown ML. Nutrition Foundation, Washington DC; 1990.
28. Udenfriend S, Clark CT, Axelrod J, Brodie BB. Ascorbic acid in aromatic hydroxylation. I. A model system for aromatic hydroxylation. J Biol Chem 1954;208:731-9.
29. Steinbrecher UP, Zhang HF, Lougheed M. Role of oxidatively modified LDL in atherosclerosis. Free Radic Biol Med 1990;9:155-68.
30. Yokoo S, Furumoto K, Hiyama E, Miwa N. Slow-down of age-dependent telomere shortening is executed in human skin keratinocytes by hormesis-like-effects of trace hydrogen peroxide or by anti-oxidative effects of pro-vitamin C in common concurrently with reduction of intracellular oxidative stress. J Cell Biochem 2004;93:588-97.
31. Waugh WA, King CG. Isolation and identification of Vitamin C. J Biol Chem 1932;97:325-31.

Source of support: Nil; Conflict of interest: None Declared