MAGIC OF VITAMIN C

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Introduction

Vitamin C is an odourless, water-soluble antioxidant vitamin. Humans and some other primates cannot synthesise Vitamin C in their body as they lack enzyme (L-gulonolactone oxidase) which converts glucose into Vitamin C in the liver of certain animals (Burns, 1959). Most plants and animals can synthesise this vitamin. Human body procures this vitamin mainly from fresh fruits and vegetables and also from animal products. There are many health benefits of Vitamin C. It plays a vital role in normal functioning of the body. It helps in the formation of collagen, lowers blood cholesterol, regulates nervous system, formation of neurotransmitters and increases iron absorption in gut. Even a high dose of Vitamin C can help in preventing certain chronic diseases like heart disease, cancer, atherosclerosis, diabetes, cataracts and muscular degeneration. Vitamin C or Ascorbic Acid is a powerful antioxidant because it can form a stable free radical by donating hydrogen atom and protects body from harmful free radical pollutants (e.g., superoxide, nitric oxide and hydroxyl radicals) and other reactive species (e.g., hydrogen peroxide, peroxynitrite and hypochlorous acid) (Iqbal, Khan and Khan, 2004).

History

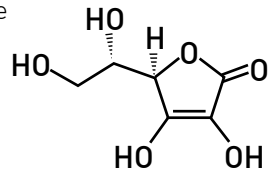
Importance of Vitamin C was noticed during 17th century when the sailors or sea voyagers developed a disease named scurvy when they were in the sea. Some crew members died as the severity of disease increased. It was noticed that fresh fruits and vegetables were lacking in their diet. In the book, *Surgeon's Mate*, written by a ship's surgeon to East India Company, Richard Woodall recommended that citrus juice can be a preventive cure for scurvy. In May 1747, James Lind, a ship's surgeon in British Royal Navy, did a controlled experiment in which he provided citrus or lemon juice to a group of some crew members in addition to normal diet while the other group continued with the normal diet only. Comparing the two groups, he noticed that lemon juice had a positive effect on prevention of the disease.

Chemical Structure of Vitamin C

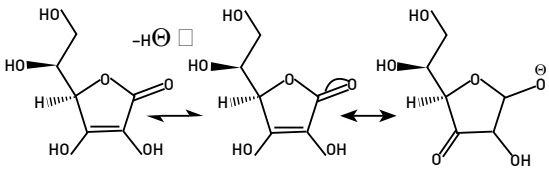
Chemical or molecular formula of Vitamin C is $C_6H_8O_6$ and molecular mass 176.14 grams per mole. Vitamin C naturally exists as L-enantiomer of ascorbate. IUPAC name of Vitamin C is (5*R*)-[(1*S*)-1, 2-dihydroxyethyl]-3,

4-dihydroxyfuran-2(5*H*)-one. Vitamin C is also known as L-ascorbic acid, 3-oxo-L-gulofurenolactone (enol form) and antisorbutic vitamin because of its anti-scurvy properties (Naidu, 2003).

Ascorbic acid is quite acidic in nature as compared to other hydroxl groups because it can donate H^+ ion and form two resonating structures which stablise its deprotonated conjugate base. It reacts with reactive oxygen species quite easily and acts as a powerful reducing agent in certain biochemical reactions.

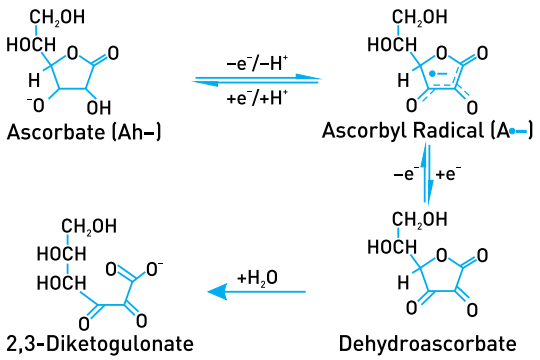


Structure of Vitamin C



Resonance Structures of Ascorbic Acid

The oxidation product of ascorbate is ascorbyl radical and DHA (Dehydro-ascorbic acid), the two electron oxidation products. Both readily reduce back to ascorbic acid but DHA can be hydrolysed irreversibly to 2,3-diketogulonic acid.



Structure of Ascorbic Acid

Discovery

A Polish-American scientist Casmir Funk conducted research in deficiency diseases in early 20th century. In 1912, he formulated the concept of vitamins, those were present in food and were essential to health. From 1928 to 1932, the Hungarian research team of Joesph L. Svirbely and Albert Szent-Györgyi and independently the American Charles Glen King did their research and isolated Vitamin C. In 1937, the Nobel Prize was awarded to Sir Waltor Norman Haworth for mass production of Vitamin C artificially (Svirbely and Szent-Györgyi, 1932; King and Waugh, 1932). In 1959, American J.J. Burns showed that mammalian livers produce the active enzyme L-gulonolactone oxidase which synthesises ascorbic acid, due to which mammals are susceptible to scurvy (Burns, 1959).

Sources of Vitamin C

Ascorbic acid or ascorbate is mainly found in fresh citrus fruits like lemon and orange and green vegetables. Some other fruits include mango, cherry, kiwi fruit, strawberry, honeydew, melon, cantaloupe, tangelo, watermelon and papaya. Vegetables which contain Vitamin C are broccoli, brussels, cabbage, peas, red and green peppers, cauliflower, sprouts, potato and tomato. Most animals can synthesise Vitamin C from glucose in liver. Milk and fish also contain some amount of Vitamin C (Platt, Eddy and Pellet, 1963). Additional supplementation of synthetic ascorbic acid which can be taken along with food is available in the form of tablets, chewable tablets, capsules, crystalline powder and also in liquid form. These should be taken under physician's supervision.

Sensitivity of Vitamin C

Vitamin C is sensitive to heat, light, air and water. It may be lost from food during processing/ cooking, packaging and storage of food because of its reducing property. This loss of ascorbic acid depends upon the extent of its exposure towards heat, oxygen, water and pH. The amount of Vitamin C can also decrease with age of fruit/ vegetable (Platt et al., 1963).

Dietry Reference Intake (DRI) of Vitamin C

Dietry recommendations of Vitamin C for different age-groups based on data given by National Health and Nutrition Examination Survey (NHANES III) are as follows:

RDA (Recommended Daily Allowance) for infants:

0–6 months : 40mg (227µmol)/day of Vitamin C [AI = Adequate Intake]

6–12 months : 50mg (256µmol)/day of Vitamin C [AI = Adequate Intake]

RDA for children:

1–3 years : 15mg (85µmol)/day of Vitamin C

4–8 years : 25mg (142µmol)/day of Vitamin C

9–13 years : 45mg (256µmol)/day of Vitamin C

RDA for adolescents:

Girls 14–18 years: 65mg (370µmol)/day of Vitamin C

Boys 14–18 years: 75mg (426µmol)/day of Vitamin C

RDA for adults:

Women over 19 years: 75mg (426µmol)/day of Vitamin C

Men over 19 years: 90mg (511µmol)/day of Vitamin C

RDA for pregnant and lactating women:

Pregnant women over 18 years: 85mg (483µmol)/day of Vitamin C

Lactating women over 18 years: 120mg (682µmol)/day of Vitamin C

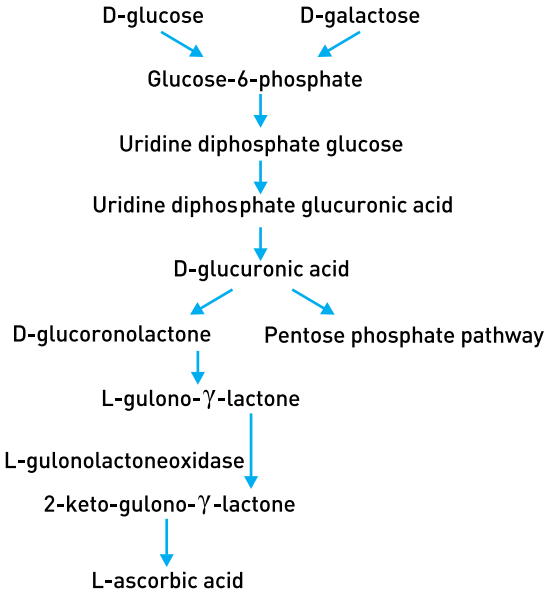
Recommended daily allowance (RDA) is replaced by dietry reference intake (DRI) in 2000 (FAO/WHO, 2000; NRC, 1989).

People who smoke may need an additional amount of 35mg of Vitamin C which is around 50 per cent extra of the regular intake; this is because smoking depletes it more readily. Vitamin C is rapidly used up by body in stressful conditions. In case of alcohol users, during fever, viral illness, exposure to petroleum products and heavy metals, the utilisation of Vitamin C increases. During exercise, Vitamin C is utilised more rapidly than during normal physical tasks (Weber, Bendich and Sclralch, 1996).

Metabolism of Vitamin C

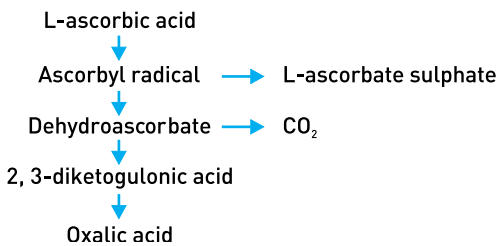
Biosynthesis of Vitamin C occurs in the liver of vertebrates from D-glucose and D-galactose. In the Vitamin C metabolic pathway, semidehydroascorbate is a major product which is reconverted into ascorbate in the cytosol by cytochrome b.

Ascorbic acid is absorbed in buccal mucosa, stomach and small intestine. Gastrointestinal absorption of ascorbic acid occurs through a sodium dependent active transport process that is saturable and dose dependent (Rumsey and Levine, 1998; Stevenson, 1974).



Biosynthesis of L-ascorbic acid in animals

At lower ascorbate concentrations, active transport predominates while at higher concentration, simple diffusion occurs (Gaby and Singh, 1991). When 100mg/day is consumed, its 80–90 per cent is absorbed by the body while the efficiency of absorption declines when the intake is increased up to 500mg/day. The major metabolite of ascorbic acid in humans are DHA, 2,3-ketogulonic acid and oxalic acid. Excess of ascorbic acid is eliminated through urine when consumed in high dose.



Catabolism of ascorbic acid

It is generally non-toxic but in excess dose can cause gastrointestinal disturbances which can be cured by reducing its consumption (Rumsey and Levine, 1998).

Functions of Vitamin C

Vitamin C is truly a wonder nutrient because it helps in regulating normal body functions, and also some serious degenerative diseases can be prevented or reversed by the adequate intake of this nutrient.

Physiological Functioning of Vitamin C

Ascorbic acid is an antioxidant and can reduce oxygen species in a variety of biochemical reactions acting as co-factor in the reactions (Buettner, 1993). Ascorbic acid is electron donor to eight human enzymes which participate in carnitine biosynthesis, amino-acid biosynthesis, collagen hydroxylation, biosynthesis of catecholamines, norepinephrine and epinephrine and amidation of peptide hormones. Carnitine and catecholamines hormones contribute in regulating the nervous system. Ascorbic acid also acts as a co-factor in biosynthesis of neuropeptides (Levine,1996). It regulates iron absorption, storage and transportation; and also helps the body to absorb the iron component of many allergic reactions. Vitamin C helps in metabolism of tyrosine, folic acid and tryptophan. It helps in cholesterol elimination from body hence reducing blood cholesterol levels (Gaby and Singh, 1991).

Ascorbic acid plays a vital role in influencing collagen gene expression, cellular procollagen secretion and biosynthesis of other connective tissue components, including elastin, fibronectin, proteoglycans, bone matrix and elastin associated fibrillin. It helps in maintenance of

collagen and blood vessel integrity. Ascorbic acid functions as inactivator of substrates such as endogenous hormones or xenobiotics (i.e., other chemical compounds such as drugs, pesticide, or carcinogens that are foreign to humans) (Tsao, 1997). Vitamin C itself acts as an antioxidant and also regenerates other antioxidants. Low levels of Vitamin C in body can cause decreased performance in athletes (Dekkers, Van Doornen and Kemper, 1996). For an exercising individual, 100mg to 500mg is sufficient and should be taken in small quantities and at multiple intervals. If it is taken in adequate amount, it may be beneficial to the performance of athletes (Tsao, 1997).

Vitamin C can have some epigenetic role in control of gene expression. There is some evolutionary significance due to which humans and some primates lost their capability of synthesising Vitamin C (Poliseno et al., 2010] The genetics bases behind the losses in the ability to synthesise Vitamin C is due to mutations in the L-gluono-α-lactone oxidase (GLO) gene which codes for the enzyme responsible for catalysing the last step of Vitamin C biosynthesis (Drouin, Godin and Page, 2011). Mutation in this particular gene is likely due to the fact that losing it only affects Vitamin C production, whereas the GLO gene mutation in fish, anthropoid primates and guinea pigs is irreversible; some of the GLO pseudo genes found in bat species have been shown to be reactivated during evolution. The same phenomenon is thought to have occurred in some Passeriformes bird species. Interestingly, these GLO gene losses and reactivations are unrelated to the diet of the species involved. This suggests that losing the ability to make Vitamin C is a neutral trait (Poliseno et al., 2010).

Clinical Importance

Deficiency of Vitamin C can cause scurvy in which deterioration of elastic tissue occurs as it plays an important role in connective tissue synthesis (Ronchetti, Quaglino and Bergamini, 1996). Several symptoms of ascorbic acid deficiency have been recognised including follicular hyperkeratosis, swollen and inflamed gums, loosening of teeth, dryness of the mouth and eyes, loss of hair and dry itchy skin. Depression and hysteria may also occur as psychological symptoms. It can be prevented by adequate consumption of fresh fruits and vegetables (FAO/WHO, 2002).

In common cold, Vitamin C reduces the risk of getting a cold and also helps reduce the duration of the cold (Dougals, Chalder and Treacy, 2001). Due to its antioxidant activity, risk of high blood pressure may also decrease with the adequate amount of Vitamin C in diet. Overall risk of heart attack can also be reduced and it may slow down the progression of atherosclerosis as it helps in maintaining HDL (high density lipoprotein) and helps the body against LDL (low density lipoprotein); and keeps arteries flexible (Levine, 1996). In Alzheimer's disease, Vitamin C shows positive results as it may dissolve some toxic protein aggregates which are found in the brain of patient. Vitamin C is also associated with the lower rates of cancer and also osteoporosis (Gaby and Singh, 1991). Its antioxidant property is helpful in asthma (Ruskin, 1947). It may protect against rheumatoid arthritis and may stop damage to inflamed joints (Lunec, 1985). It is also helpful in decreasing blood sugar levels, improvement of vision, boosting of immune system, reducing the effect of sun exposure and healing of burns and wounds (Iqbal et al., 2004).

Conclusion

Vitamin C or ascorbic acid is a non-toxic acid which acts as an antioxidant in the human body and helps in regulating and maintaining vital roles in the body. It can not be produced by body and can not be stored in large quantities in the body so it has to be procured from fresh fruits and vegetables. It can be beneficial in certain diseases such as atherosclerosis, tuberculosis, muscular degeneration, diabetes, cataracts and Alzhiemer's disease. It also prevents and lowers the rate of occurrence of heart diseases and cancer. It is helpful in the overall improvement of immunity of body. Vitamin C has some epigenetic role in control of gene expression. There is some evolutionary significance due to which humans and other primates have lost their capability of synthesising Vitamin C.

References

Buettner, G.R. 1993. The Pecking Order of Free Radicals and Antioxidants: Lipid Peroxidation, alpha-Tocopherol, and Ascorbate. *Arch Biochem Biophys*. Vol. 300, pp. 535–43.

Burns, J. J. 1959. Biosynthesis of L-ascorbic Acid; Basic Defect in Scurvy. *The American Journal of Medicine*. Vol. 26, p. 740.

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*. Vol. 21, pp. 213–38.

Dougals, R.M., E.B. Chalder and Treacy. 2001. Vitamin C for Preventing and Treating the Common Cold. Cochrane Review In: the Cochrane Library. Oxford: updated software.

Drouin, G., J.R. Godin and B. Page. 2011. The Genetics of Vitamin C Loss in Vertebrates. *Current Genomic*. Vol. 12, pp. 371–78.

FAO/WHO. 2002. Vitamin C. In, Human Vitamin and Mineral Required. Report of a Joint FAO/WHO Expert Consultation. FAO, Rome, pp. 73–86.

Gaby, S.K. and V.N. Singh. 1991. 'Vitamin C'. In S.K. Gaby, A. Bendich, V.N. Singh and L.J. Machkin (Eds), *Vitamin Intake and Health: A Scientific Review* (pp. 103–61). Marcel Dekker, New York.

Iqbal, K., A. Khan and M.M.A. Khan. 2004. Biological Significance of Ascorbic Acid (Vitamin C). *Human Health-A Review*. Vol. 3, No. 3, pp. 5–13.

King, C.G. and W.A. Waugh. 1932. Isolation and Identification of Vitamin C. *Biochemical Journal*. Vol. 97, pp. 325–31.

Levine, N.G. 1996. Ascorbic Acid Reverses Endothelial Vasomotor Dysfunction in Patients with Coronary Artery Disease. *Circulation*. Vol. 93, pp. 1107–1113.

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*. Vol. 1, pp. 31–39.

Naidu, K.A. 2003. Vitamin C in Human Health and Disease is still a Mystery? An Overview. *Nutrition Journal*. 2:7. doi:10.1186/1475-2891-2-7

NRC (National Research Council). 1989. *Recommended Dietry Allowance, 10th edition*. National Academy Press, Washington DC.

Platt, B.S., T.P. Eddy and P.L. Pellet. 1963. *Food in Hospitals*. Anonymous. Nuffield Provincial Hospitals Trust and Oxford University Press, London.

Poliseno, L. et al. 2010. A Coding-independent Function of Gene and Pseudogene mRNAs Regulates Tumour Biology. *Nature*. Vol. 465, pp. 1033–1038. doi:10.1038/nature 09144

Ronchetti, I.P., D Jr Quaglino and G. Bergamini. 1996. Ascorbic Acid and Connective Tissue. *Subcell Biochem*. Vol. 25, pp. 249–64.

Rumsey, S.C. and M. Levine. 1998. Absorption, Transport, and Disposition of Ascorbic Acid in Humans. *The Journal of Nutritional Biochemistry*. Vol. 9, pp. 116–30.

Ruskin, S.L. 1947. Sodium Ascorbate in the Treatment of Allergic Disturbances. The Role of Adrenal Cortical Hormone -Sodium- Vitamin C. *Am. J. Dig*. Vol. 14, pp. 302–306.

Stevenson, N.R. 1974. Active Transport of L-ascorbic Acid in Human Ileum. *Gastroenterology*. Vol. 67, pp. 952–56.

Svirbely, J.L. and A. Szent-Györgyi. 1932. The Chemical Nature of Vitamin C. *Biochemical Journal*. pp. 26865–870.

Tsao, CS. 1997. An Overview of Ascorbic Acid Chemistry and Biochemistry. In L. Packer and J. Fuchs (Eds), *Vitamin C in Health and Disease* (pp. 25–58). Marcel Dekker, New York.

Weber. P., A. Bendich and Sclralch. 1996. Ascorbic Acid and Human Health — A Review of Recent Data Relevant to Human Requirements. *Int J Vit Nutr Res*. Vol. 66, pp. 19–30.