



Vitamin C

Common Indications

- Antiaging
- Antioxidant
- Asthma
- Bone Mineral Density
- Cancer prevention & treatment
- Endothelial Function
- Immunostimulant
- Iron-Deficiency Anemia
- Brain/Nerve Function
- Primary/Secondary Deficiency
- Prevention of Sunburn
- Wound Healing

General Comments

Vitamin C is an essential water-soluble nutrient for humans that is required in our diet on a daily basis. This is due to the fact that humans lack the enzyme L-gulonolactone oxidase, which is required for the conversion of glucose to vitamin C.¹ It was first isolated by Albert Szent-Gyorgyi in 1928 from pork adrenal glands and called hexuronic acid. In 1933, its chemical structure was established. It was successfully synthesized, and the name was changed to ascorbic acid. Vitamin C exists in nature in both its reduced form, L-ascorbic acid, and in its oxidized form, L-dehydroascorbic acid. L-ascorbic acid is the most active form. However, in the body they convert back and forth to each other in a reversible equilibrium. This vitamin can be found in a host of foods such as in vegetables and fruits. Up to 100% of a foods vitamin C content can be lost or destroyed in the process of cooking since this vitamin is especially sensitive to cutting, bruising, light, heat, oxygen, and alkali.² Buffered vitamin C refers to the sodium, calcium, magnesium, and potassium ascorbate salts. These forms of vitamin C are less acidic and may be less likely to cause gastric irritation when taken in higher doses.

Benefits & Mechanism of Action

Most of vitamin C's functions are owed to its electron donor capability. This ability also means that this vitamin is a reducing agent and an antioxidant. It is involved in a multitude of biochemical processes such as energy release from fatty acids, metabolism of cholesterol, reduction of nitrosamine formation in the stomach, formation of thyroid hormone, carnitine biosynthesis, modulation of iron and copper absorption, corticosteroid biosynthesis, protection of folic acid

reductase which converts folic acid to folinic acid, collagen biosynthesis, tyrosine biosynthesis and catabolism, and neurotransmitter biosynthesis.

Antiaging

Vitamin C is a well-known potential antiaging agent due to its antioxidant effect and major role in collagen production.³⁻⁶ A 3-month study randomized double-blind vehicle-controlled study was conducted to determine the efficacy of topical vitamin C in photo-damaged skin. Clinical assessment showed significant improvement in many features, including fine wrinkles, tactile roughness, laxity and tone.⁶

Antioxidant

Vitamin C is one of the most effective aqueous antioxidants in plasma, interstitial fluids and soluble phases of cells. It scavenges free radical oxygen and nitrogen species such as superoxide, hydroxyl, peroxy, and nitroxide radicals and non-radical reactive species such as singlet oxygen, peroxy, and hypochlorite.^{7,8} It also increases and regenerates vitamin E and maintaining glutathione in reduced forms.⁹

Asthma

Vitamin C is the major antioxidant present in the extracellular fluid lining of the lung, where it protects against both endogenous free radicals (produced by the inflammation of the lungs) and environmental free radicals. Theoretically, it may be of benefit in reducing symptoms of inflammatory airway conditions such as asthma and exercise-induced bronchoconstriction. Despite its theoretical basis for its use, it is still controversial since most studies either have conflicting data or insufficient evidence.¹⁰

Bone Mineral Density

Studies have shown that there is a positive identification between bone mineral density and the intake of vitamin C.^{11,12} Low vitamin C intake have been associated with lower bone mineral densities especially in the femoral neck and total hip.¹¹ In one study, in which 13,080 adults were enrolled, fracture risk decreased by 49% in postmenopausal women without a history of smoking or estrogen use who also had high serum vitamin C levels.¹³

Brain/Nerve Function

Vitamin C is a cofactor required for the biosynthesis of noradrenaline from dopamine and in the hydroxylation of tryptophan to produce serotonin. It also acts as a modulator of glutaminergic, cholinergic, and GABA-ergic transmission. Also, it works in the maturation of neural structures and acts as a neuroprotective agent.^{7,14,15}

Cancer prevention & treatment / Pro-Oxidant

Several research panels and committees have independently concluded that high fruit and vegetable intake decreases the risk of many types of cancer. Vitamin C is present in high quantities in these foods, so it would lead us to believe that increased intake of vitamin C is associated with a reduction in cancer risk.¹⁶ In most studies, they have shown that higher intakes of vitamin C are associated with decreased incidence of cancers of the mouth, throat, vocal cords, esophagus, stomach, pancreas, colon, rectum, and lung.^{7, 17-20} While supplementation (500mg daily) did not reduce the incidence of developing breast cancer over 9.4 years, there was a decrease in total mortality and breast cancer specific mortality.^{21,22} Vitamin C has a profound pro-oxidant effect in cancer cells when given in high doses and causes cell death.¹⁶ Whether vitamin C acts as an antioxidant or pro-oxidant depends on 3 factors: The redox potential of the cellular environment, the presence/absence of oxidized metal ions, and the local concentrations of vitamin C.¹⁶

Endothelial Function

A double-blind, placebo-controlled study demonstrated that chronic vitamin C supplementation (500mg/day) in type 2 diabetes significantly lowered arterial blood pressure and improved arterial stiffness compared with a placebo.²³ After one-month treatment, SBP fell from 142.1 to 132.3mmHg and DBP fell from 83.9 to 79.5mmHg whereas placebo had no effect. The mechanism of action appears to involve multiple pathways such as reduced LDL oxidation, enhanced endothelial NO synthase activity, NO bioavailability, and reduced insulin resistance.

Immunostimulant

Vitamin C modulates T-Cell gene expression, specifically affecting genes involved with signaling, carbohydrate metabolism, apoptosis, transcription and immune function. It can also stimulate the production of interferons, the proteins that protect cells against viral attack and stimulate the synthesis of humoral thymus factor and antibodies of the immunoglobulin G (IgG) and IgM classes.²⁴ In high doses, it is a potent immunomodulator and is preferentially cytotoxic to neoplastic cells. The antioxidant effects of vitamin C also play a role here since when neutrophils are activated during infection, they release free radicals however neutrophils themselves are susceptible to free radical damage. Vitamin C offers auto-oxidation protection to help further perpetuate immune function.²⁵

Iron-Deficiency Anemia

Vitamin C is a potent enhancer of iron absorption. It does this by forming soluble complexes and may be used with iron supplements and/or a nutritious diet.

Prevention of Sunburn

One controlled study found that oral vitamin C (2000mg/day) in combination with vitamin E (1000IU/day) had a protective effect against sunburn after 8 days' treatment in human subjects.²⁶

Primary/Secondary Deficiency

Primary deficiencies are not likely to happen however the most likely reasons why someone may exhibit primary deficiencies are alcoholics, poverty, famine, young children fed exclusively cow's milk for a long period of time, or institutionalized or isolated elderly.^{27,28} Secondary deficiencies are most commonly caused by smoking, pregnancy, lactation, thyrotoxicosis, acute and chronic inflammatory diseases, burns, infections, and diabetes.^{2,7,8,29} Vitamin C, whether received from diets or supplements are more than able to resolve deficiencies. Please refer to the Dosing Guide later in the monograph to find appropriate daily intakes.

Wound healing

Vitamin C is important for effective wound healing, as deficiency contributes to fragile granulation of tissues and therefore impairs the wound-healing process.³⁰ In vitro studies with skin graft samples, vitamin C extends cellular viability, promotes formation of an epidermal barrier and promotes engraftment.³¹

Dosing Guide					
Australian and New Zealand RDI:	Infants: <ul style="list-style-type: none"> 0-6 months: 25mg 7-12 months: 30mg 	Children: <ul style="list-style-type: none"> 1-8 years: 35mg 9-18 years: 40mg 	Adults: <ul style="list-style-type: none"> >19 years old: 45mg 	Pregnancy: <ul style="list-style-type: none"> <19 years old: 55mg >19 years old: 60mg 	Lactation: <ul style="list-style-type: none"> <19 years old: 80mg >19 years old: 85mg
Appropriate Clinical Doses:	Asthma: <ul style="list-style-type: none"> 500-2000mg before exercise 	Cancer: <ul style="list-style-type: none"> 10-100g/day IV 	CVD Prevention: <ul style="list-style-type: none"> Up to 1000mg/day 	Bone Mineral Density: <ul style="list-style-type: none"> 750mg/day 	Sunburn Protection: <ul style="list-style-type: none"> 2000mg/day Vitamin E: 1000IU/Day

Signs & Symptoms Of Deficiency:

The disease that occurs when a person is deficient in Vitamin C is called scurvy. In this disease, a patient can experience a multitude of symptoms that are detrimental to living an unproblematic and fulfilling life. These symptoms include:

Minor/Moderate:	Weakness/ Fatigue	Swollen Gums	Poor Wound Healing	Poor Appetite and Weight Loss	Emotional Changes (Depression/Irritability)	Bruising	Arthralgia/ Myalgia
Severe:	Fever	Dry Skin and Mucosal Membranes	Increased Infection Risk	Anemia	Hemorrhage	Convulsions/ Shock	Death

Cautions & Side Effects:

- Loose Stools/Diarrhea; at high doses

Drug Interactions:

- Aluminum-based antacids
 - Vitamin C increases the amount of aluminum absorbed, take caution and separate doses by at least 2 hours
- Aspirin
 - Aspirin may interfere with both the absorption and cellular uptake of Vitamin C. Increased Vitamin C supplementation may be required with long-term therapy.³²
- Corticosteroids
 - Corticosteroids may increase the daily requirement of Vitamin C if long-term treatment with corticosteroids is taken.^{33,34}
- Cyanocobalamin (Vit. B12)
 - Vitamin C can reduce the amount of cyanocobalamin absorbed, separate doses by at least 2 hours
- Iron
 - Vitamin C increases the amount of Iron absorbed, potential causing anemia
- Cisplatin, Cyclophosphamide, Doxorubicin, Etoposide, Fluorouracil, Tamoxifen, Vincristine
 - Vitamin C enhances the antitumor effects, drug effects, and lowered some drug side effect in vitro and in vivo.³⁵⁻³⁹

Drugs That Deplete Vitamin C:

Aspirin	Loop Diuretics	Indomethacin
Corticosteroids	Oral Contraceptives	Tetracyclines

Food Sources:

Blackcurrants	Sweet green and red peppers	Hot red peppers	Green chili peppers
Oranges	Strawberries	Watermelon	Papaya
Cantaloupe	Mango	Cabbage	Cauliflower
Broccoli	Tomatoes	Guava	Thyme

Lab Tests:

Supplemental vitamin C can alter the results of a fair number of laboratory tests. It is not accurate to say that it artificially alters or interferes with accurate measurement but rather that it causes beneficial changes in the following lab values:

Carbamazepine	Lactate Dehydrogenase	Serum Aspartate Transaminase	Serum Bicarbonate	Serum Cholesterol
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Serum Creatinine	Serum Creatine Kinase	Serum A1C	Serum Phosphate	Serum Triglycerides
Serum Urea Nitrogen	Stool Guaiac	Theophylline	Urine 17-hydroxy Corticosteroids	Urine 17-ketosteroids
Urine Amphetamine	Urine and Serum Bilirubin	Urine and Serum Glucose	Urine and Serum Uric Acid	Urine Barbiturate
Urine Beta-Hydroxybutyrate	Urine Iodide	Urine Oxalate	Urine Paracetamol	Urine Protein

References:

General Comments

1. Braunwald E et al (ed). Harrison's principles of internal medicine. New York: McGraw Hill, 2003.
2. Wahlqvist M (ed). Food and nutrition, 2nd edn. Sydney: Allen & Unwin, 2002.

Antiaging

3. Humbert PG et al. Topical ascorbic acid on photoaged skin: Clinical, topographical and ultrastructural evaluation: double-blind study vs placebo. *Exp Dermatol* 12.3 (2003): 237-244.
4. Park HJ, et al. Vitamin C attenuates ERK signaling to inhibit the regulation of collagen production by LL-37 in human dermal fibroblasts. *Exp Dermatol* 2009;19:e258e64
5. Taniguchi M, et al. Anti-oxidative and antiaging activities of 2-O-a-glucopyranosil-L-ascorbic acid on human dermal fibroblasts. *Eur J Pharmacol* 2012;674:126e31
6. Traikovitch SS. Use of topical ascorbic acid and its effect on photodamaged skin topography. *Arch Otolaryngol Head Neck Surg* 1999;125:1091e8

Antioxidant

7. FAO/WHO (Food and Agriculture Organization/World Health Organization). Report of a Joint FAO/WHO Expert Consultation, Bangkok, Thailand. FAO/WHO: Rome, 2002.
8. Hendler SS, Rorvik D (eds). PDR for nutritional supplements. Montvale, NJ: Medical Economics, 2001.
9. Vatassery GT. In vitro oxidation of alpha-tocopherol (vitamin E) in human platelets upon incubation with unsaturated fatty acids, diamide and superoxide. *Biochem Biophys Acta* 926.2 (1987): 160-169

Asthma

10. Milan SJ, et al. Vitamin C for asthma and exercise-induced bronchoconstriction. *Cochrane Database of Systematic Reviews* 2013, Issue 10. Art. No.: CD010391

Bone Mineral Density

11. Hall SL, Greendale GA. The relation of dietary vitamin C intake to bone mineral density: results from the PEPI study. *Calcif Tissue Int* 63.3 (1998): 183-189
12. Leveille SG, et al. Dietary vitamin C and bone mineral density in postmenopausal women in Washington State, USA. *J Epidemiol Commun Health* 1997;51:479-85
13. Simon JA, Hudes ES. Relation of ascorbic acid to bone mineral density and self-reported fractures among US adults. *Am J Epidemiol* 154.5 (2001): 427-433

Brain/Nerve Function

14. Bornstein SR et al. Impaired adrenal catecholamine system function in transgenic mice with deficiency of the ascorbic acid transporter (SVCT2). *FASEB J* 17 (2003): 1928-1930
15. Harrison FE, May JM. Vitamin C function in the brain: vital role of the ascorbate transporter SVCT2. *Free Rad Bio Med* 46.6 (2009): 719-730

Cancer prevention & treatment / Pro-Oxidant

16. Li Y, Schellhorn HE. New Developments and Novel Therapeutic Perspectives for Vitamin C. *J Nutr* 137.10 (2007): 2171-2184.
17. Cohen M, Bhagavan HN. Ascorbic acid and gastrointestinal cancer. *J Am Coll Nutr* 14.6 (1995): 565-578
18. Jenab M et al. Plasma and dietary vitamin C levels and risk of gastric cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST). *Carcinogenesis* 27.11 (2006): 2250-2257
19. Negri E et al. Selected micronutrients and oral and pharyngeal cancer. *Int J Cancer* 86.1 (2000): 122-127.
20. You WC et al. Gastric dysplasia and gastric cancer: *Helicobacter pylori*, serum vitamin C, and other risk factors. *J Natl Cancer Inst* 92.19 (2000): 1607-1612.
21. Lin J, et al. Vitamins C and E and beta carotene supplementation and cancer risk: a randomized controlled trial. *J Natl Cancer Inst* 2009;101:14-23
22. Harris HR, et al. Vitamin C and survival among women with breast cancer: a meta analysis. *Eur J Cancer*. 2014 May;50(7):1223-31

Endothelial Function

23. Mullan BA et al. Ascorbic acid reduces blood pressure and arterial stiffness in type 2 diabetes. *Hypertension* 40.6 (2002): 804-809

Immunostimulant

24. Combs Jr, G. F. 2012, "Chapter 9 – Vitamin C," In Combs GF (ed.) *The Vitamins*, Fourth Edition. San Diego: Academic Press, pp. 233-259
25. Muggli, R. 1998, "Vitamin C and the Immune System," In: Delves PJ (ed.) *Encyclopedia of Immunology*, Second Edition. Oxford: Elsevier, pp. 2491-2494

Prevention of Sunburn

26. Eberlein-Konig B et al. Protective effect against sunburn of combined systemic ascorbic acid (vitamin C) and d-alpha-tocopherol (vitamin E). *J Am Acad Dermatol* 38.1 (1998): 45-48

Primary/Secondary Deficiency

27. Pimentel L. Scurvy: Historical review and current diagnostic approach. *Am J Emerg Med* 21.4 (2003): 328-332
28. Richardson RI et al. Will an orange a day keep the doctor away? *Postgrad Med J* 78.919 (2002): 292-294
29. Beers MH, Berkow R (eds). *The Merck manual of diagnosis and therapy*, 17th edn. Whitehouse, NJ: Merck, 2003

Wound healing

30. Russell L. The importance of patients' nutritional status in wound healing. *Br J Nurs* 10.6 (Suppl) (2001): S42-44, S49
31. Boyce ST et al. Vitamin C regulates keratinocyte viability, epidermal barrier, and basement membrane in vitro, and reduces wound contraction after grafting of cultured skin substitutes. *J Invest Dermatol* 118.4 (2002): 565-572

Drug Interactions

32. Basu TK. Vitamin C-aspirin interactions. *Int J Vitam Nutr Res Suppl* 23 (1982): 83-90
33. Chowdhury AR, Kapil N. Interaction of dexamethasone and DHEA on testicular ascorbic acid and cholesterol in prepubertal rat. *Arch Andriol* 12.1 (1984): 65-67; as cited in Pelton R et al. *Drug-induced nutrient depletion handbook 1999-2000*. Hudson, OH: Lexi-Comp, 2000
34. Levine MA, Pollard HB. Hydrocortisone inhibition of ascorbic acid transport by Chromaffin cells. *FEBS Lett* 158.1 (1983): 13408; as cited in Pelton R et al. *Drug-induced nutrient depletion handbook 1999-2000*. Hudson, OH: Lexi-Comp, 2000
35. Abdel-Latif MM et al. Vitamin C enhances chemosensitization of esophageal cancer cells in vitro. *J Chemother* 17 (2005): 539-549
36. Reddy VG et al. Vitamin C augments chemotherapeutic response of cervical carcinoma HeLa cells by stabilizing P53. *Biochem Biophys Res Commun* 282 (2001): 409-415
37. Sarna S, Bhola RK. Chemo-immunotherapeutical studies on Dalton's lymphoma in mice using cisplatin and ascorbic acid: synergistic antitumor effect in vivo and in vitro. *Arch Immunol Ther Exp (Warsz)* 41 (1993): 327-333
38. Lamson DW, Brignall MS. Antioxidants and cancer therapy II: quick reference guide. *Altern Med Rev* 5 (2000): 152-163
39. Nagy B et al. Chemosensitizing effect of Vitamin C in combination with 5-fluorouracil in vitro. *In Vivo* 17 (2003): 289-292