

Cmmune Plus Chewable Tablets: Effective Supplementation for Cellular Functions of Both the Innate and Adaptive Immunity

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ABSTRACT

Vitamin C, also known as ascorbic acid and ascorbate, is a vitamin found in various foods and sold as a dietary supplement. It is used to prevent and treat scurvy. Vitamin C is an essential nutrient involved in the repair of tissue and the enzymatic production of certain neurotransmitters. It is required for the functioning of several enzymes and is important for immune system function. It also functions as an antioxidant. There is some evidence that regular use of supplements may reduce the duration of the common cold, the aim of the study was to determine the role of vitamin C to boost immunity. Humans cannot synthesize vitamin C, because lack of enzyme l-gulonolactone oxidase. In Cmmune Plus vitamin C, Zinc and Vitamin D3 are essential to boost immunity. Zinc affects multiple aspects of the immune system. Zinc is crucial for normal development and function of cells mediating innate immunity, neutrophils, and NK cells. Macrophages also are affected by zinc deficiency. Phagocytosis, intracellular killing, and cytokine production all are affected by zinc deficiency. Vitamin D has important functions beyond those of calcium and bone homeostasis which include modulation of the innate and adaptive immune responses. The present paper Reviews the Role of Vitamin C in Immunity along with Zinc and Vitamin D3.

Introduction

Vitamin C, also known as ascorbic acid and ascorbate, is a vitamin found in various foods and sold as a dietary supplement. It is used to prevent and treat scurvy. Vitamin C is an essential nutrient involved in the repair of tissue and the enzymatic production of certain neurotransmitters. It is required for the functioning of several enzymes and is important for immune system function. It also functions as an antioxidant. There is some evidence that regular use of supplements may reduce the duration of the common cold, but it does not appear to prevent infection.

It is unclear whether supplementation affects the risk of cancer, cardiovascular disease, or dementia. It may be taken by mouth or by injection. Vitamin C is generally well tolerated. Large doses may cause gastrointestinal discomfort, headache, and trouble sleeping, and flushing of the skin. Normal doses are safe during pregnancy. The United States Institute of Medicine recommends against taking large doses. Vitamin C is an essential vitamin, meaning your body can't produce it. Yet, it has many roles and has been linked to impressive health benefits.

Source of Vitamin C

It's water-soluble and found in many fruits and vegetables, including oranges, strawberries, kiwi fruit, bell peppers, broccoli, kale, and spinach. While it's commonly advised to get your vitamin C intake from foods, many people turn to supplements to meet their needs.

Role of Vitamin C

Role of Vitamin c on Immunity Vitamin C is needed for the growth and repair of tissues in all parts of your body. It is used to: Form an important protein used to make skin, tendons, ligaments, and blood vessels. Heal wounds and form scar tissue.

Role of vitamin C in immune defense	
Immune System	Function of Vitamin C
Epithelial barriers	Enhances collagen synthesis and stabilization.
	Protects against ROS-induced damage.
	Enhances keratinocyte differentiation and lipid synthesis.
	Enhances fibroblast proliferation and migration.
	Shortens time to wound healing in patients.
Phagocytes (neutrophils, macrophages)	Acts as an antioxidant/electron donor.
	Enhances motility/chemoattractants.
	Enhances phagocytosis and ROS generation.
	Enhances microbial killing.
	Facilitates apoptosis and clearance.
	Decreases necrosis/NETosis.
B- and T – Lymphocytes	Enhances keratinocyte differentiation and lipid synthesis.
	Enhances fibroblast proliferation and migration.
	Shortens time to wound healing in patients.
Inflammatory mediators	Modulates cytokine production.
	Decrease histamine levels.

ROS-reactive oxygen species, **NET**-neutrophil extracellular trap.

Benefits of Vitamin C

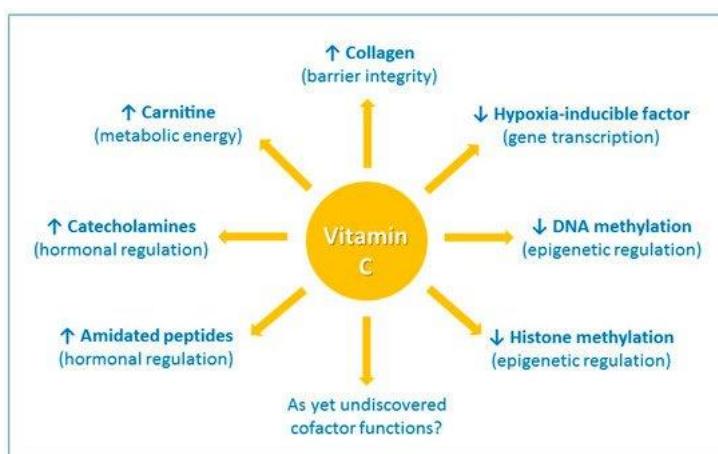


Figure 1: Enzyme cofactor activities of vitamin C

The enzyme cofactor activities of vitamin C. Vitamin C is a cofactor of a family of biosynthetic and gene regulatory monooxygenase and dioxygenase enzymes. These enzymes are involved in the synthesis of

collagen, carnitine, catecholamine hormones, e.g., norepinephrine, and amidated peptide hormones, e.g., vasopressin. These enzymes also hydroxylate transcription factors, e.g., hypoxia-inducible factor 1 α , and methylated DNA and histones, thus playing a role in gene transcription and epigenetic regulation. ↑ indicates an increase and ↓ indicates a decrease. Figure 1 shows the enzyme cofactor activities of vitamin C. Vitamin C is a cofactor of a family of biosynthetic and gene regulatory monooxygenase and dioxygenase enzymes. These enzymes are involved in the synthesis of collagen, carnitine, catecholamine hormones, e.g., norepinephrine, and amidated peptide hormones, e.g., vasopressin. These enzymes also hydroxylate transcription factors, e.g., hypoxia-inducible factor 1 α , and methylated DNA and histones, thus playing a role in gene transcription and epigenetic regulation. ↑ indicates an increase and ↓ indicates a decrease.

(1) Boosts immunity

One of the main reasons people take vitamin C supplements is to boost their immunity, as vitamin C is involved in many parts of the immune system. First, vitamin C helps encourage the production of white blood cells known as lymphocytes and phagocytes, which help protect the body against infection. Second, vitamin C helps these white blood cells function more effectively while protecting them from damage by potentially harmful molecules, such as free radicals. Third, vitamin C is an essential part of the skin's defense system. It's actively transported to the skin, where it can act as an antioxidant and help strengthen the skin's barriers. Studies have also shown that taking vitamin C may shorten wound healing time. For example, people who have pneumonia tend to have lower vitamin C levels, and vitamin C supplements have been shown to shorten the recovery time.

(2) May reduce your risk of chronic disease

Vitamin C is a powerful antioxidant that can strengthen your body's natural defenses. Antioxidants are molecules that boost the immune system. They do so by protecting cells from harmful molecules called free radicals. When free radicals accumulate, they can promote a state known as oxidative stress, which has been linked to many chronic diseases. Studies show that consuming more vitamin C can increase your blood antioxidant levels by up to 30%. This helps the body's natural defenses fight inflammation.

(3) May lower your risk of heart disease

Heart disease is the leading cause of death worldwide. Many factors increase the risk of heart disease, including high blood pressure, high triglyceride or LDL (bad) cholesterol levels, and low levels of HDL (good) cholesterol. Vitamin C may help reduce these risk factors, which may reduce heart disease risk. For example, an analysis of 9 studies with a combined 293,172 participants found that after 10 years, people who took at least 700 mg of vitamin C daily had a 25% lower risk of heart disease than those who did not take a vitamin C supplement.

(4) Helps prevent iron deficiency

Iron is an important nutrient that has a variety of functions in the body. It's essential for making red blood cells and transporting oxygen throughout the body. Vitamin C supplements can help improve the absorption of iron

from the diet. Vitamin C assists in converting iron that is poorly absorbed, such as plant-based sources of iron, into a form that is easier to absorb. This is especially useful for people on a meat-free diet, as meat is a major source of iron. In fact, simply consuming 100 mg of vitamin C may improve iron absorption by 67%. As a result, vitamin C may help reduce the risk of anemia among people prone to iron deficiency.

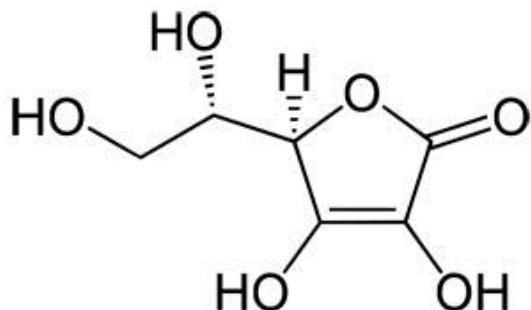
In one study, 65 children with mild iron deficiency anemia were given a vitamin C supplement. Researchers found that the supplement alone helped control their anemia. If you have low iron levels, consuming more vitamin-C-rich foods or taking a vitamin C supplement may help improve your blood iron levels.

(5) Protects your memory and thinking as you age

Dementia is a broad term used to describe symptoms of poor thinking and memory. It affects over 35 million people worldwide and typically occurs among older adults. Studies suggest that oxidative stress and inflammation near the brain, spine, and nerves (altogether known as the central nervous system) can increase the risk of dementia. Vitamin C is a strong antioxidant. Low levels of this vitamin have been linked to an impaired ability to think and remember.

Moreover, several studies have shown that people with dementia may have lower blood levels of vitamin C.

Vitamin C Structure



Pharmacodynamics

Ascorbic Acid (vitamin C) is a water-soluble vitamin indicated for the prevention and treatment of scurvy, as ascorbic acid deficiency results in scurvy. Collagenous structures are primarily affected, and lesions develop in bones and blood vessels. Administration of ascorbic acid completely reverses the symptoms of ascorbic acid deficiency.

Mechanism of Action

In humans, an exogenous source of ascorbic acid is required for collagen formation and tissue repair by acting as a cofactor in the posttranslational formation of 4-hydroxyproline in -Xaa-Pro-Gly- sequences in collagens and other proteins. Ascorbic acid is reversibly oxidized to dehydroascorbic acid in the body. These two forms of the vitamin are believed to be important in oxidation-reduction reactions. The vitamin is involved in tyrosine metabolism, conversion of folic acid to folinic acid, carbohydrate metabolism, synthesis of lipids and proteins, iron metabolism, resistance to infections, and cellular respiration.

- ❖ **Absorption:** 70% to 90%
- ❖ **Protein binding:** 25%
- ❖ **Uses:** Used to treat vitamin C deficiency, scurvy, delayed wound and bone healing, urine acidification, and in general as an antioxidant. It has also been suggested to be an effective antiviral agent.

Aim and Objective

- ❖ **Aim:** The aim of the study was to determine the role of vitamin C to boost immunity.
- ❖ **Objective:** To assess the role of vitamin C to boot immunity.

Literature Review

Anitra C Carr, et al, (2017): Vitamin C is an essential micronutrient for humans, with pleiotropic functions related to its ability to donate electrons. It is a potent antioxidant and a cofactor for a family of biosynthetic and gene regulatory enzymes. Vitamin C contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system. Vitamin C supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress.

Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing. It is also needed for apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis/NETosis and potential tissue damage. The role of vitamin C in lymphocytes is less clear, but it has been shown to enhance differentiation and proliferation of B- and T-cells, likely due to its gene regulating effects. Vitamin C deficiency results in impaired immunity and higher susceptibility to infections. In turn, infections significantly impact on vitamin C levels due to enhanced inflammation and metabolic requirements.

Furthermore, supplementation with vitamin C appears to be able to both prevent and treat respiratory and systemic infections. Prophylactic prevention of infection requires dietary vitamin C intakes that provide at least adequate, if not saturating plasma levels (i.e., 100-200 mg/day), which optimize cell and tissue levels. In contrast, treatment of established infections requires significantly higher (gram) doses of the vitamin to compensate for the increased inflammatory response and metabolic demand.

Harri Hemilä, et al, (2017): In the early literature, vitamin C deficiency was associated with pneumonia. After its identification, a number of studies investigated the effects of vitamin C on diverse infections. A total of 148 animal studies indicated that vitamin C may alleviate or prevent infections caused by bacteria, viruses, and protozoa. The most extensively studied human infection is the common cold. Vitamin C administration does not decrease the average incidence of colds in the general population, yet it halved the number of colds in physically active people. Regularly administered vitamin C has shortened the duration of colds, indicating a biological effect. However, the role of vitamin C in common cold treatment is unclear. Two controlled trials found a statistically significant dose-response, for the duration of common cold symptoms, with up to 6-8 g/day of vitamin C. Thus, the negative findings of some therapeutic common cold studies might be explained

by the low doses of 3-4 g/day of vitamin C. Three controlled trials found that vitamin C prevented pneumonia. Two controlled trials found a treatment benefit of vitamin C for pneumonia patients. One controlled trial reported treatment benefits for tetanus patients. The effects of vitamin C against infections should be investigated further.

H C Gorton, K Jarvis, et al, (1999): An ever increasing demand to evaluate the effect of dietary supplements on specific health conditions by use of a "significant scientific" standard has prompted the publication of this study to study the effect of megadose Vitamin C in preventing and relieving cold and flu symptoms in a test group compared with a control group. Prospective, controlled study of students in a technical training facility. A total of 463 students ranging in age from 18 to 32 years made up the control group. A total of 252 students ranging in age from 18 to 30 years made up the experimental or test group. Investigators tracked the number of reports of cold and flu symptoms among the 1991 test population of the facility compared with the reports of like symptoms among the 1990 control population. Those in the control population reporting symptoms were treated with pain relievers and decongestants, whereas those in the test population reporting symptoms were treated with hourly doses of 1000 mg of Vitamin C for the first 6 hours and then 3 times daily thereafter. Those not reporting symptoms in the test group were also administered 1000-mg doses 3 times daily.

Overall, reported flu and cold symptoms in the test group decreased 85% compared with the control group after the administration of megadose Vitamin C. Vitamin C in megadoses administered before or after the appearance of cold and flu symptoms relieved and prevented the symptoms in the test population compared with the control group.

Discussion

Vitamin C contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system. Vitamin C supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress.

Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing. Vitamin C (ascorbate) is maintained at high levels in most immune cells and can affect many aspects of the immune response. The role of vitamin C in lymphocytes is less clear, but it has been shown to enhance differentiation and proliferation of B- and T-cells, likely due to its gene regulating effects.

Increased needs of Vitamin C due to pollution and smoking, fighting infections, and diseases with oxidative and inflammatory components, e.g., type 2 diabetes, etc. Ensuring adequate intake of vitamin C through the diet or via supplementation, especially in groups such as the elderly or in individuals exposed to risk factors for vitamin C insufficiency, is required for proper immune function and resistance to infections.

In Cmmune Plus vitamin C, Zinc and Vitamin D3 are essential to boost immunity. Zinc affects multiple aspects of the immune system. Zinc is crucial for normal development and function of cells mediating innate immunity, neutrophils, and NK cells.

Macrophages also are affected by zinc deficiency. Phagocytosis, intracellular killing, and cytokine production all are affected by zinc deficiency. Vitamin D has important functions beyond those of calcium and bone homeostasis which include modulation of the innate and adaptive immune responses.

Conclusion

Vitamin-C decrease inflammation, which may help improve your immune function. Vitamin C also keeps your skin healthy by boosting collagen production, helping the skin serve as a functional barrier to keep harmful compounds from entering your body. It promotes the growth and spread of lymphocytes, a type of immune cell that increases your circulating antibodies, proteins that can attack foreign or harmful substances in your blood. High dose vitamin C may be as a treatment for hospitalized people with COVID-19. It may improve lung function in people with COVID-19, but further investigation is required on this subject for assure the results.

Vitamin C Safety Profile

To summarize, it. Vitamin- C is a naturally occurring with multiple desirable effects. With an excellent safety profile, it finds increasing use in photo ageing, hyperpigmentation, tissue inflammation and promotion of tissue healing. When taken at appropriate doses, oral vitamin C supplements are generally considered safe. In some people; oral use of vitamin C can cause kidney stones. Long-term use of oral vitamin C supplements over 2,000 milligrams a day increases the risk of significant side effects.

References

1. Anitra C Carr, Silvia Maggini, Vitamin C and Immune Function, PMID: 29099763, PMCID: PMC5707683, DOI: 10.3390/nu9111211.
2. Harri Hemilä, Vitamin C and Infections, Nutrients. 2017 Apr; 9(4): 339., Published online 2017 Mar 29. doi: 10.3390/nu9040339.
3. Emma Derbyshire, Joanne Delange, COVID-19: is there a role for immunonutrition, particularly in the over 65s, BMJ Nutrition, Prevention & Health. 2020 Apr: bmjnph-2020-000071. Published online 2020 Apr 16.
4. Scott A Read, Stephanie Obeid, The Role of Zinc in Antiviral Immunity, Adv Nutr. 2019 Jul; 10(4): 696–710, Published online 2019 Apr 22.
5. Cynthia Aranow, Vitamin D and the Immune System, J Investig Med. 2011 Aug; 59(6): 881–886, doi: 10.231/JIM.0b013e31821b8755.
6. Ranil Jayawardena, Piumika Sooriyaarachchi, Michail Chourdakis, Chandima Jeewandara, and Priyanga Ranasinghe, Enhancing immunity in viral infections, with special emphasis on COVID-19, Diabetes Metab Syndr. 2020 July-August; 14(4): 367–382.
7. H C Gorton, K Jarvis, The effectiveness of vitamin C in preventing and relieving the symptoms of virus-induced respiratory infections, Clinical Trial J Manipulative Physiol Ther 1999 Oct;22(8):530-3. doi: 10.1016/s0161-4754(99)70005-9.

8. H.Clay Gorton, DC, Kelly Jarvis, DC, The effectiveness of vitamin C in preventing and relieving the symptoms of virus-induced respiratory infections, Volume 22, Issue 8, P530-533, October 01, 1999.
9. Jacob RA, Sotoudeh G. Vitamin C function and status in chronic disease. Nutr Clin Care 2002; 5:66-74.
10. Carr AC, Frei B. Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. Am J Clin Nutr 1999; 69:1086-107.
11. Gershoff SN. Vitamin C (ascorbic acid): new roles, new requirements? Nutr Rev 1993; 51:313-26.
12. Institute of Medicine. Food and Nutrition Board. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids external link disclaimer. Washington, DC: National Academy Press, 2000.
13. Padayatty SJ, Sun H, Wang Y, Riordan HD, Hewitt SM, Katz A, Wesley RA, Levine M. Vitamin C pharmacokinetics: implications for oral and intravenous use. Ann Intern Med 2004; 140:533-7.
14. Bates CJ. Bioavailability of vitamin C. Eur J Clin Nutr 1997; 51 (Suppl 1):S28-33.
15. Mangels AR, Block G, Frey CM, Patterson BH, Taylor PR, Norkus EP, et al. The bioavailability to humans of ascorbic acid from oranges, orange juice and cooked broccoli is similar to that of synthetic ascorbic acid. J Nutr 1993; 123:1054-61.
16. Johnston CS, Luo B. Comparison of the absorption and excretion of three commercially available sources of vitamin C. J Am Diet Assoc 1994; 94: 779-81.
17. Levine M, Conry-Cantilena C, Wang Y, Welch RW, Washko PW, Dhariwal KR, et al. Vitamin C pharmacokinetics in healthy volunteers: evidence for a recommended dietary allowance. Proc Natl Acad Sci U S A 1996; 93: 3704-9.
18. Levine M, Rumsey SC, Daruwala R, Park JB, Wang Y. Criteria and recommendations for vitamin C intake. JAMA 1999; 281: 1415-23.
19. Pumori Saokar Telang, Vitamin C in dermatology, Indian Dermatol Online J. 2013 Apr-Jun; 4(2): 143–146. doi: 10.4103/2229-5178.110593
20. Cynthia Aranow, Vitamin D and the Immune System, J Investig Med. 2011 Aug; 59(6): 881–886, doi: 10.231/JIM.0b013e31821b8755.