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"An Analytical study of the resistant assignment and Vitamin C"

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Abstract

For humans, vitamin C is a necessary micronutrient having pleiotropic activities associated with its capacity to transfer electrons. It functions as a cofactor for a variety of biosynthetic and gene regulatory enzymes and is a strong antioxidant. By assisting numerous cellular processes of the innate and adaptive immune systems, vitamin C supports immunological defence. Vitamin C helps the skin's epithelial barrier function against pathogens and encourages its ability to scavenge free radicals, which may help it resist environmental oxidative stress. In phagocytic cells like neutrophils, vitamin C builds up and can increase chemotaxis, phagocytosis, the production of reactive oxygen species, and ultimately, the death of microorganisms. Additionally, it is necessary for the apoptosis of neutrophils and the removal of dead neutrophils by macrophages from infection sites, which reduces necrosis/NETosis and potential tissue injury. Though its function in lymphocytes is less apparent, vitamin C has been demonstrated to promote B- and T-cell differentiation and proliferation. This is probably because it possesses gene-regulating properties. Lack of vitamin C lowers immunity and increases susceptibility to illnesses. As a result of increased inflammation and metabolic demands, infections have a considerable negative influence on vitamin C levels. Additionally, vitamin C supplements seem to be helpful to both prevent and treat systemic and respiratory infections. Dietary vitamin C intakes that give at least adequate, if not saturating plasma levels (i.e., 100–200 mg/day), which optimize cell and tissue levels, are necessary for the prophylactic prevention of infection. As a result of the heightened inflammatory response and metabolic requirement, treating established illnesses need much greater (gramme) vitamin doses.

Keyword: *- Humans, numerous, Environmental, Susceptibility, Established.*

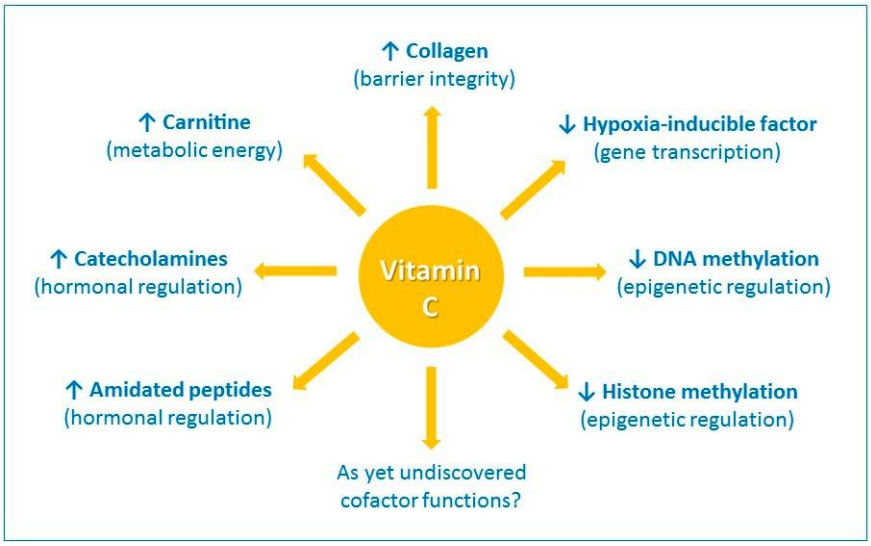
INTRODUCTION

The immune system is a complex network of organs, tissues, cells, proteins, and chemicals that has developed to defend the host from a variety of pathogens, including bacteria, viruses, fungi, parasites, and cancer cells. Epithelial barriers, cellular, and humoral components of either innate (non-specific) or acquired (specific) immunity can be classified as its subsets. These components interact in a variety of intricate ways. Vitamin C has been linked to a number of immune system functions, most notably immune cell activity, for more than 50 years.

Due to the loss of a vital enzyme in the biosynthetic pathway, individuals are unable to manufacture the critical nutrient vitamin C. Scurvy, a potentially lethal condition, is brought on by a severe vitamin C shortage. Collagenous structures are weakened by scurvy, which impairs immunity and causes poor wound healing. Scurvy patients are more vulnerable to potentially deadly illnesses like pneumonia. Due to increased inflammation and metabolic demands, infections can have a considerable influence on vitamin C levels. It was discovered early on that scurvy frequently Scurvy instances have been documented after infectious epidemics in populations and respiratory infections. This is especially clear for people who are already undernourished. The recommended dietary intakes for vitamin C are up to one hundred times greater than those for several other vitamins, despite the fact that the quantity of vitamin C needed to avoid scurvy is only a small amount (i.e., 10 mg/day). In healthy persons, a diet containing 100–200 mg of vitamin C per day offers sufficient to saturate plasma concentrations and ought to satisfy general needs for the reduction of the risk of chronic diseases. Due to the body's limited ability to store the water-soluble vitamin, hypovitaminosis C must be avoided by consuming enough vitamin C on a regular basis. According to epidemiological research, vitamin C deficiency (less than 11 mol/L) and hypovitaminosis C (plasma vitamin C 23 mol/L) are rather common in Western populations.

Is the fourth most common nutritional deficit in the US? Even in nations where there should be an adequate supply of food, vitamin C dietary requirements are not always followed for a number of reasons. Poor dietary practices, life stages and/or lifestyles that limit intakes or increase the need for micronutrients (such as smoking and alcohol or drug abuse), various diseases, exposure to pollutants and smoke (both direct and indirect), and financial factors (poor socioeconomic status and limited access to nutrient-dense foods) are a few of these. Even otherwise "healthy" persons in industrialized nations are susceptible to risk factors connected to lifestyle, such as dieters, people who consume an imbalanced diet, and people who experience prolonged periods of intense physical or mental stress.

Numerous actions of vitamin C may theoretically contribute to its immune-modulating effects. Because of its propensity to donate electrons, it is an extremely powerful antioxidant that shields vital bimolecular (such as proteins, lipids, carbohydrates, and nucleic acids) from oxidants produced both naturally by cells and as a result of exposure to toxins and pollutants (such as cigarette smoke). Additionally, vitamin C functions as a cofactor for the monooxygenase and dioxygenase family of biosynthetic and gene-regulating enzymes. Long known as a cofactor for the Lysol and prolyl hydroxylases necessary for stabilising the tertiary structure of collagen, the vitamin is also a cofactor for the two hydroxylases involved in the biosynthesis of carnitine, a molecule necessary for transporting fatty acids into mitochondria for the production of metabolic energy (Figure 1).



Barrier Integrity and Healing of Wounds

The major role of the skin is to protect the body from viruses and other external disturbances, among its many other vital duties. The dermal layer is made up of fibroblasts that release collagen fibres, the primary component of the dermis, whereas the epidermal layer is highly cellular and predominantly composed of keratinocytes. Vitamin C concentrations in skin are millimolar, with the epidermis containing higher concentrations of the vitamin than the dermis. The two sodium-dependent vitamin C transporter (SVCT) is forms 1 and 2 actively deposit vitamin C into the epidermal and dermal cells, indicating that the vitamin has important roles in the skin. The signs of the vitamin C deficient illness scurvy, which is characterized by bleeding gums, bruising, and sluggish wound healing, provide hints as to the involvement of vitamin C in the skin. The role of vitamin C as a co-factor for the prolyl and lysyl hydroxylase enzymes that maintain the tertiary structure of collagen is assumed to be the cause of these symptoms. Additional studies have demonstrated that vitamin C can boost the expression of the collagen gene in fibroblasts.

The Function of Leukocytes and Vitamin C

Values of vitamin C that are 50–100 times higher than plasma concentrations are obtained by leukocytes such neutrophils and monocytes, which actively accumulate the vitamin against a concentration gradient even while other physiological tissues probably need greater intakes for saturation, these cells acquire maximum amounts of vitamin C at dietary intakes of around 100 mg/day. Vitamin C is accumulated by neutrophils through SVCT2 and is normally present at intracellular concentrations of at least 1 mM. The non-specific uptake of the

oxidized form, dehydroascorbate (DHA), via glucose transporters (GLUT), allows neutrophils to further raise their intracellular concentration of vitamin C after stimulation of their oxidative burst. DHA is then quickly converted inside cells to ascorbate, producing levels of roughly 10 mM. It is thought that the buildup of such high vitamin C concentrations points to significant roles played by these cells.

It is believed that protecting neutrophils from oxidative damage involves accumulating millimolar quantities of vitamin C inside of them, especially after activating their oxidative burst. A powerful water-soluble antioxidant, vitamin C may replenish glutathione and vitamin E, two essential cellular and membrane antioxidants, as well as many reactive oxidants. Vitamin C is lost from neutrophils by phagocytosis or activation with soluble stimulants in an oxidant-dependent manner. A shift in the equilibrium between oxidant production and nuclear factor b (NF-B), a transcription factor that promotes inflammation, is a key player in how antioxidant defenses might affect various signaling pathways [121]. A signaling cascade that results in the ongoing creation of oxidative species and other inflammatory mediators is started when oxidants activate NF-B. Vitamin C has been demonstrated to reduce NF-B activation in neutrophils isolated from septic Gulo knockout mice as well as oxidant production in dendritic cells in vitro. Thiol-containing proteins are frequently essential for the regulation of redox-related cell signaling pathways and can be especially sensitive to redox changes inside cells. T-cells have been shown to modulate thiol-dependent cell signaling and gene expression pathways in a vitamin C-dependent manner.

As a result, vitamin C may influence immune function via altering redox-sensitive cell signaling pathways or by directly defending crucial cell structural components. For instance, neutrophils exposed to oxidants can experience decreased cell motility, which is assumed to be caused by the oxidation of membrane lipids and its subsequent effects on cell membrane fluidity. Improvements in neutrophil motility shown after vitamin C delivery (see below) might theoretically be attributable to oxidant scavenging as well as regeneration of vitamin E because neutrophils have significant quantities of polyunsaturated fatty acids in their plasma membranes. Nuclear Chemo taxis

An initial stage of innate immunity is neutrophil infiltration into contaminated tissues. Marginated neutrophils swarm to the infection site in response to pathogen- or host-derived inflammatory signals, such as N-formylmethionyl-leucyl-phenylalanine (fMLP), interleukin (IL)-8, leukotriene B4, and complement component C5a. Chemotaxis is the name for neutrophil migration in response to chemical stimuli, whereas chemokinesis is the phrase for random migration (Figure 2). More than 30 distinct chemokine and chemoattractant receptors are expressed by neutrophils, enabling them to detect and react quickly to signs of

tissue injury. In contrast to leukocytes obtained from guinea pigs whose diets contained adequate amounts of vitamin C supplements, early studies in scorbutic guinea pigs showed reduced leukocyte chemotactic response (Table 1). These results imply that phagocyte migration to infection sites may be affected by vitamin C deficiency.

Neutrophil chemotactic function is impaired in patients with severe infection. This "paralysis" of neutrophils is thought to be partially caused by elevated amounts of immune-suppressive and anti-inflammatory mediators (such as IL-4 and IL-10) during the compensatory anti-inflammatory response seen after the initial hyper-stimulation of the immune system. However, vitamin C depletion, which is common during acute infection, may possibly play a role. Leukocyte chemotaxis was found to be impaired in patients with recurrent infections, according to studies conducted in the 1980s and 1990s. This impairment might be corrected by supplementing with gramme dosages of vitamin C. Additionally, supplementing newborns with 400 mg/day of vitamin C significantly increased neutrophil chemotaxis in sepsis-suspected neonates.

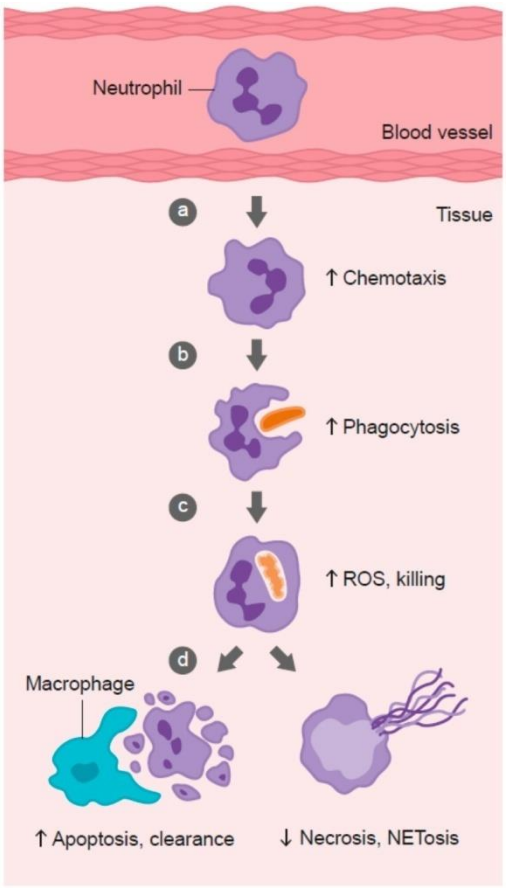


Figure 2 the function of phagocytes in relation to vitamin C According to studies, vitamin C:

It has also been demonstrated that giving healthy volunteers dietary or gramme dosages of vitamin C can improve neutrophil chemotactic activity. According to Johnston et a hypothesis.'s, vitamin C's antihistamine effects are connected with improved chemotaxis. A dietary source of vitamin C (providing 250 mg/day) supplementation led to a 20% increase in neutrophil chemotaxis in people with insufficient vitamin C status (i.e., 50 M). Additionally, supplementing elderly women with 1 g/day of vitamin C and vitamin E improved neutrophil capabilities, such as chemotaxis. Therefore, individuals in the general population may gain from greater vitamin C dietary intake, especially if they have low vitamin C status, which can be more common among the elderly. It should be highlighted that it is yet unclear how much better ex vivo leukocyte chemotaxis correlates with better in vivo immune function. Microbial Killing and Phagocytosis

After moving to the infection site, neutrophils go on to absorb the invasive bacteria (Figure 2). The phagosome is activated and joined by a variety of intracellular granules releasing the phagosome with their arsenal of antimicrobial peptides and proteins [149]. Superoxide is the first of many reactive oxygen species (ROS) that neutrophils produce to destroy infections. It is produced when parts of the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NADPH) oxidase assemble in the phagosomal membrane. Superoxide is changed into hydrogen peroxide by the enzyme superoxide dismutase, which can subsequently be used by the azurophilic granule enzyme myeloperoxidase to produce the oxidant hypochlorous acid. Chloramines are secondary oxidants formed when hypochlorous acid reacts further with amines. The reactivities and specificities of these distinct neutrophil-derived oxidants for biological targets vary, with protein thiol groups being particularly vulnerable.

Vitamin C Deficiency Disorders

The amount of vitamin C in the body can be affected by a variety of environmental and medical factors. Examples that also relate to weakened immunity and increased vulnerability to infection are included in this section. A disruption in the body's oxidant-antioxidant balance, as well as nitrogen dioxide, can lead to oxidative stress. If antioxidant defences are compromised, as may be the case when vitamin C levels are low, oxidative stress can also happen. Particularly in youngsters and the elderly who are at risk of both weakened immunity and vitamin C deficiency, air pollution can harm the fluid that lines the respiratory tract and increase the risk of respiratory disease. Superoxide and peroxyl radicals, hydrogen peroxide, hypochlorous acid, and oxidant air pollutants can all be removed by vitamin C, which is a free-radical scavenger. Various contaminants, heavy metals, pesticides, and xenobiotics can produce oxidants and oxidant-mediated damage to lung cells, which vitamin C's antioxidant qualities can prevent.

In many regions of the world, tobacco smoke is an underappreciated environmental hazard. When compared to non-smokers, smokers and passive smokers have lower levels of vitamin C in their blood and leukocytes. This is partially because they experience more oxidative stress and have lower intake and higher metabolic turnover of vitamin C. Adult smokers' median serum levels of vitamin C are found to be one-third lower than those of non-smokers, and it is advised that smokers take an additional 35 mg of vitamin C daily to ensure there is enough ascorbic acid to repair oxidative damage. Children and teenagers who are exposed to ambient tobacco smoke have reduced vitamin C levels. Vitamin C can defend against protein deterioration and lipid peroxidation, according to research in vitamin C deficient guinea pigs exposed to cigarette smoke. Vitamin C supplementation significantly decreased plasma F2-isoprostane concentrations, a marker of oxidative stress, in non-smokers exposed to ambient tobacco smock. Smoking makes people more vulnerable to bacterial and viral infections, where vitamin C may be involved. For instance, in a population-based investigation, those with the lowest plasma vitamin C concentrations (26mol/L) compared to never smokers had a considerably increased risk of developing obstructive pulmonary disease, a risk that decreased with increasing vitamin C concentration.

Diabetes patients are more likely to contract common infections such the flu, pneumonia, and foot infections, which are linked to higher morbidity and death [220,221]. Obesity is associated with a number of immune-related alterations that support the emergence of type 2 diabetes. One of the main causes of insulin resistance and type 2 diabetes in obese people is persistent low-grade inflammation of the adipose tissue, which is absent in the adipose tissue of lean people. Pro-inflammatory macrophages and T-cells penetrate the adipose tissue, which causes the buildup of pro-inflammatory cytokines such interleukins and TNF- . Studies on type 2 diabetes have shown a decline in plasma vitamin C levels. The high degree of oxidative stress brought on by hyperglycemia is regarded to be a primary factor in type 2 diabetes' increased demand for vitamin C. Plasma vitamin C levels and the risk of diabetes, hemoglobin A1c levels (a measure of glucose tolerance), fasting and postprandial blood glucose, and oxidative stress have been shown to have inverse associations. Vitamin C supplementation may help type 2 diabetics with better glycemic control, according to a meta-analysis of interventional trials.

Vitamin C Infection

The severe vulnerability to infections, especially those of the respiratory system, is a key sign of the vitamin C deficient disease scurvy, with pneumonia being one of its most common consequences and a leading cause of mortality. Plasma vitamin C concentrations are lower in patients with acute respiratory illnesses including pulmonary TB and pneumonia compared to control people. When patients with acute respiratory infections get

vitamin C, their plasma vitamin C levels return to normal and the severity of their respiratory symptoms is reduced. Following intravenous vitamin C therapy, cases of acute lung infections have demonstrated quick clearing of chest X-rays. This neutrophil clearance from sick lungs that is vitamin C-dependent may be a result of increased apoptosis, followed by phagocytosis and clearance of the dead neutrophils by macrophages. Vitamin C administration can increase alveolar fluid clearance, improve bronchoalveolar epithelial barrier function, and attenuate neutrophil sequestration, all of which are crucial components of healthy lung function, according to pre-clinical studies on animals with sepsis-induced lung injury.

According to a meta-analysis, taking vitamin C supplements daily at doses of 200 mg or more is helpful in reducing the severity and length of the common cold as well as its frequency when combined with physical stress. Supplementation of people with poor vitamin C status (i.e., 45 mol/L), reduced the prevalence of the typical cold. Unexpectedly, only a small number of researches have evaluated vitamin C status during the common cold.

Leukocyte vitamin C levels and urinary excretion of the vitamin have both been shown to significantly drop during cold episodes, with levels rising back to normal after the illness. These alterations show that vitamin C is used throughout the infection of the common cold. Vitamin C delivery during an episode of the common cold prevented the fall in leukocyte vitamin C levels, indicating that vitamin C administration may aid in the healing process.

Vitamin C has been found to have positive impacts on recovery from pneumonia. The more severe patients' respiratory symptom scores decreased when vitamin C was administered to older patients with pneumonia who were found to have extremely low vitamin C levels. Other pneumonia patients who received low-dose vitamin C (0.25-0.8 g/day) had a 19% shorter hospital stay than those who received no vitamin C supplementation, while those who received higher doses (0.5-1.6 g/day) had a 36% shorter stay. The normalization of chest X-ray, temperature, and erythrocyte sedimentation rate all showed positive results. It is likely that the low vitamin C levels seen during respiratory infections are both a cause and a symptom of the illness since prophylactic vitamin C therapy also appears to lower the chance of acquiring more severe respiratory infections, such as pneumonia.

CONCLUSIONS

Overall, it appears that the innate and adaptive immune systems' cellular processes are greatly benefited by vitamin C. Despite the fact that vitamin C is a powerful antioxidant that guards the body from both endogenous and exogenous oxidative threats, it is most likely that its position as a cofactor for multiple biosynthetic and gene

regulatory enzymes is crucial to its immune-modulating actions. Vitamin C increases phagocytosis, oxidative production, and microbial death while also encouraging neutrophil migration to the site of infection. It is clear from this that vitamin C is required for the immune system to launch and maintain a sufficient reaction against infections while minimizing harm to the host.

By improving several immune cell functions, vitamin C appears to be able to both prevent and treat respiratory and systemic infections. Dietary vitamin C intakes that give at least adequate, if not saturating plasma levels (i.e., 100–200 mg/day), which optimise cell and tissue levels, are necessary for the prophylactic prevention of infection. In contrast, to make up for the increased metabolic requirement, treating established illnesses calls for substantially greater (gramme) vitamin doses.

According to epidemiological research, hypovitaminosis C is still a problem in Western nations, and vitamin C deficiency is the fourth most frequent dietary deficiency in the country. Reduced intake and limited bodily storage are two causes. Increased demands are brought on by smoking, pollution, combating infections, and illnesses with inflammatory and oxidative components, such as type 2 diabetes, etc. Proper immune function and infection resistance depend on ensuring appropriate intake of vitamin C through food or supplementation, especially in populations like the elderly or those exposed to risk factors for vitamin C insufficiency.

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