OFFICIAL JOURNAL

REVIEW ARTICLE

Oral Health Effect of High Dose Vitamin C in the Treatment of COVID-19 Infection: A Review

Fatin Hazimah Mazlan[1], Kannan Thirumulu Ponnuraj [1,2], and Wan Nazatul Shima Shahidan[1,*]

[1]School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia
[2]Human Genome Centre, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

Abstract

Vitamin C (ascorbic acid, ascorbate) supplementation is believed by many to cure a common cold and flu. They are ubiquitous, and involved in a variety of biological activities include cell oxidation, hydroxylation reactions, and collagen formation. During the new coronavirus outbreak, vitamin C was taken as a preventative or therapeutic drug for coronavirus-19's (COVID-19) critical phase. In patients with severe COVID-19, high dosages of vitamin C have been shown to decrease endothelin-1 and interleukin-6 mediators. Given the fact that vitamin C is both safe and inexpensive, the use of a low to high dose of vitamin C as a preventative measure has grown in popularity. However, according to a previous report, consuming vitamin C on a daily basis causes considerable tooth surface loss. Their findings demonstrate how uncontrolled tooth erosion can have negative consequences for the dental and stomatognathic systems. The usage of vitamin C and its impact on oral health during pandemic COVID-19 infection are discussed in this review. While vitamin C supplementation may have promise as a treatment or preventive agent for COVID-19, it may have a number of detrimental consequences for oral health.

Keywords: Vitamin C; high dose; Oral health; COVID-19

Introduction

Vitamin C, known as ascorbic acid, is a water-soluble vitamin required for sustaining life. It plays a crucial function in human metabolism as well as in the development of a variety of food and pharmaceutical products (National Research Council, 2000). As vitamin C is a water-soluble vitamin, it cannot be stored in the body and is eliminated from the body once it reaches an acceptable level. Chemists frequently use vitamin C to prepare fine compounds, enzymatic reagents, and nanomaterials (Sun et al., 2009). Ascorbate is a reduced form of vitamin C. Dehydroascorbic acid is the oxidised form of ascorbic acid that is biologically active and interconvertible, making it an important antioxidant. Alkali, oxygen, and heat oxidises and destroys vitamin C (Chambial et al., 2013; Schnellbaecher et al., 2019). Almost all plant and animal species can use the uronic acid pathway from glucose and galactose to produce vitamin C. Due to a lack of the enzyme L-gluconolactone oxidase (EC 1.1. 3.8), which is essential for the process, humans and other primates are unable to synthesise vitamin C (Padayatty et al., 2004).

The conversion of bile acids from cholesterol is facilitated by vitamin C. As a result, cholesterol levels in the blood are reduced. Furthermore, it converts ferric to become ferrous, increasing iron absorption in intestine (Du et al., 2012). Vitamin C protects the body from the harmful effects of pollutants, pollution, and free radicals by acting as an antioxidant (Chen et al., 2015). Even though Linus Pauling was the one who investigated the therapeutic benefit of vitamin C in 1970, the findings sparked debate. He also popularised the concept of supplementing with large amounts of vitamin C to cure a variety of ailments (Pauling, 1971). Since then, large dosages of vitamin C have been used to prevent and cure diseases such as cancer, atherosclerosis, cataracts, the common

Received: 17 January 2022**; Accepted revised manuscript:** 29 March 2022 **Published online:** 10 April 2022
***Corresponding author:** Dr. Wan Nazatul Shima Shahidan, School of Dental Sciences, Universiti Sains Malaysia Kota Bharu, 16150, Kelantan, Malaysia
Tel: +6097675806 **Email**: shima@usm.my

cold, glaucoma, diabetes, heart disease, stroke, and macular degeneration (Du et al., 2012).

Coronavirus is a large plus-strand RNA genome genus in the Coronaviridae family. It has capped and polyadenylated ends in its genomic RNA and around 27 to 32 kb in size (Van et al., 2002; Enjuanes et al., 2006; Perlman et al., 2009). Coronaviruses were discovered in mammalian and avian species that are morphologically and chemically similar (Li and Fang, 2015). Coronaviruses have been divided into three classes based on their serological characteristics. The viruses' genomic sequence and host range are used to classify them (Lai and Michael, 2003). Animals such as mice, cats, turkeys, rats, horses, chickens, swine, cattle, dogs, rabbits, and people have been shown to carry these viruses (Decaro et al., 2020).

In the therapy of coronaviruses, vitamin C is a debatable topic. Erroneous information about vitamin C's effectiveness in preventing and treating the common cold, boosting longevity, and several other dubious health claims have led to some people being misled in the past. Several well-known Instagram and Facebook users claim that vitamin C in near-lethal doses was the cure for coronavirus-19 (COVID-19) during the current new coronavirus outbreak (Colunga et al., 2020). However, it has also been reported that vitamin C is unlikely to be beneficial in the treatment of coronavirus (Nicoletta, 2020). More studies into ascorbate pharmacokinetics mechanisms against antivirals have been published, and as evidence from case studies has grown, scientists and clinicians have been more interested in this therapy.

In Shanghai, a panel of COVID-19 clinical treatment experts advised giving COVID-19 patients with moderate or nonspecific symptoms a larger dose of intravenous vitamin C to avert cytokine storms (Rozga et al., 2020). In Chinese hospitals, COVID-19 patients are being treated with vitamin C (Anderson and Paul, 2020). According to records kept by some Chinese doctors, 50 patients with moderate-to-severe COVID-19 were successfully treated for 7 to 10 days with a high dose of 10 g intravenous vitamin C daily for moderate cases and 20 g daily for severe cases with a high dose of 10 g intravenous vitamin C daily for mild cases and 20 g daily for severe cases with a high dose of 10 g intravenous vitamin C daily for severe cases and discovered that the clinical outcome was enhanced as a result (Cheng, 2020).

In hypertensives, taking vitamin C regularly lowers blood pressure. Higher plasma levels are achieved with high-dose intravenous vitamin C. However, there is a lack of evidence on the implications of high blood pressure in acute blood pressure. A daily dose of vitamin C of 90 mg is advised for adults. However, a more significant vitamin C dose is required during acute infection in order to satisfy the higher metabolic demand (Soar and Jagjit, 2020). Abdominal pain, nausea, and diarrhoea can occur if people consume more than 2 g of vitamin C each day (Kim et al., 2020). Oxaluria can be caused by taking up to 10 g of vitamin C daily, which raises the risk of oxalate kidney stones and nephropathy (Nabzdyk et al., 2018). Vitamin C in high doses may have limitations and may be contraindicated in patients with neuropathy; thus, each COVID-19 patient must have a complete assessment before delivering large doses of vitamin C.

Since the human body cannot store vitamin C, it must be obtained from the diet daily in order to be healthy. The exact amount required depends on an individual's overall health, weight, and gender, though it is estimated that a 70 kg of male needs about 60 mg of vitamin C each day (Monsen et al., 2020). Vitamin C is renowned for its low pH, which can cause tooth erosion as described in a case study of excess of vitamin C. In the study, over the course of three years, a patient experienced moderate to severe dental erosion, which was ascribed to the practically daily ingestion of chewable vitamin C tablets. On identification of the source of problem, specific preventative guidance was given, and localised composite resin restorations were used to restore the missing tooth tissue. The patient tolerated the treatment well, and subsequently the vitamin C intake was lowered to a healthy level. This case highlights on the role of physicians in educating patients on potential causes of acid erosion and guiding them towards acceptable levels of use to avoid any negative consequences on their dentition (Bahal et al., 2014). On the other hand, many people are storing up on vitamin C during the COVID-19 pandemic to strengthen their antibodies. While vitamin C supplementation has potential as a COVID-19 therapeutic or preventive agent, the high dose and long-term use of chewable vitamin C pills may be harmful to oral health (Cagetti et al., 2020). If not appropriately controlled, this can have harmful repercussions for both the teeth and the stomatognathic system. As a COVID-19 treatment, high-dose vitamin C therapy provides several advantages, including lower mortality rates and safety in the early stages of the disease. The effect of high-dose vitamin C treatment on dental health, on the other hand, may be a cause for concern.

However, the implications on the use of high dose of vitamin C in relation to COVID-19 and in particular on oral health have not been clearly discussed. Bearing that in mind, the aim of this review is to throw light on the effect of high dose of vitamin C consumption in the prevention and treatment of COVID-19 in general with special emphasis on oral health. It is the responsibility of the physicians to alert patients about the potential cause of acid erosion and guiding them towards acceptable levels of usage to avoid tooth damage. This review, it is hoped will enlighten the readers on the clinical effects of high vitamin C intake on dental health. This highlights the significance of the manufacturer's instructions and the clinician's responsibility in advising patients on the precise therapeutic doses that are safe for oral health. The efficacy of high-dose vitamin C therapy on oral health is re-evaluated in this review, which may help oral healthcare providers overcome dental-related problems in COVID-19 patients (Figure 1).

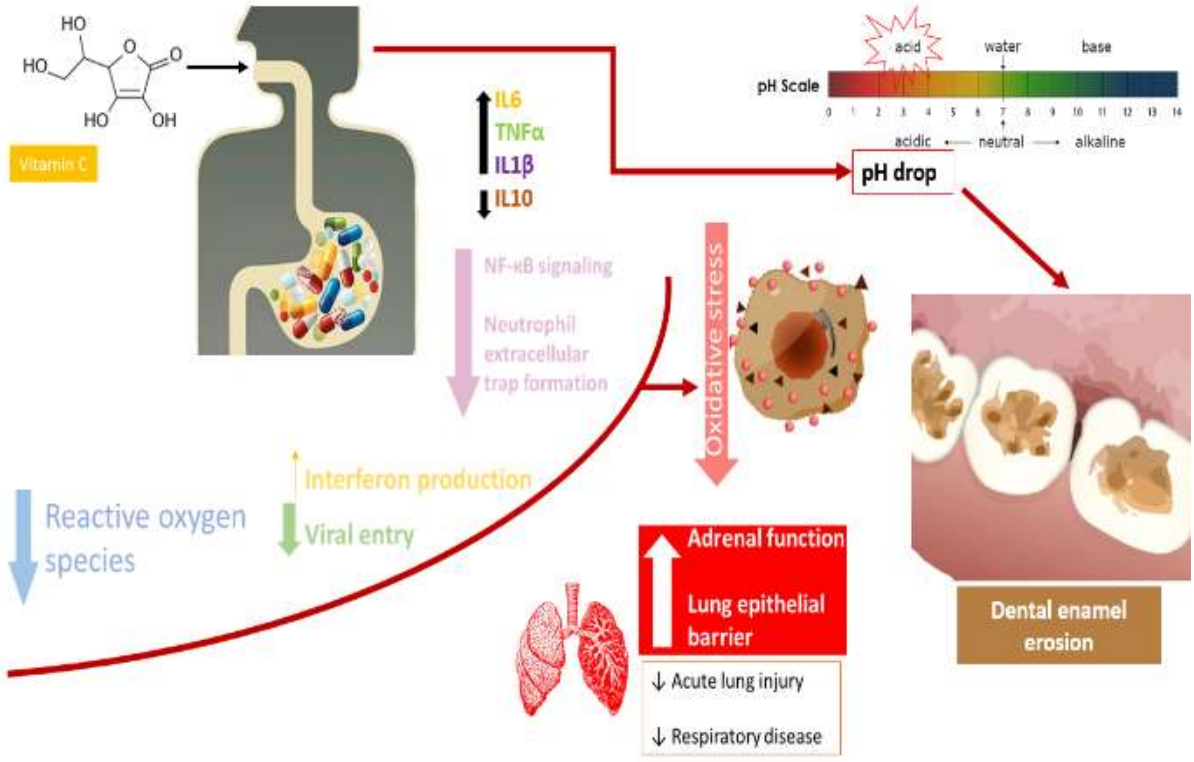

Figure 1: Illustration of the effect of high-dose vitamin C on respiratory system and dentition. Adaptation from the article by Lummis and Daniel, 2019; Cerullo et al., 2020.

COVID-19

Alphacoronavirus (alphaCoV), Deltacoronavirus (deltaCoV), Betacoronavirus (betaCoV), and Gammacoronavirus are the four genera of the Coronaviruses subfamily (gammaCoV). According to genomic characterisation, bats and rodents are the gene sources for betaCoVs and alphaCoVs, while avian species are the gene sources for gammaCoVs and deltaCoVs. Before the current COVID-19 epidemic, there were six different types of human respiratory coronaviruses: HCoV-229E (Alphacoronavirus), HCoV-NL63(Alphacoronavirus), HCoV-OC43 (Betacoronavirus), HKU1 (Betacoronavirus), SARS-CoV (Betacoronavirus), MERS-CoV (Betacoronavirus), S SARS-CoV and MERS-CoV are viruses that cause mild to moderate lower respiratory infections that can progress to severe or even fatal infections (Wu et. al., 2020). Coronaviruses have positive-stranded RNA that, under an electron microscope, appears to have a crown-like form due to the presence of spike glycoproteins on its envelope. Although there has been some debate about this, the SARS-whole-genome CoV-2's resemblance to that of bat coronavirus as a starting point is roughly 96 per cent (Zhang et al., 2020). SARS-CoV-2 appears to spread mostly through microscopic particles or droplets, requiring contact points in the nose, mouth, eyes, or other upper digestive system areas (Brosseau et al., 2020). Furthermore, evidence of SARS-CoV-2 transmission via faecal-oral

transmission has been discovered (Ciceri et al., 2020).

SARS-CoV-2-induced pneumonia reaction mechanisms are commonly known as a cytokine storm. With defective coagulation, the result is significant tissue injury. MicroCLOTS stands for the syndrome of microvascular COVID-19 lung vessels obstructive thromboinflammatory, a phrase introduced by an Italian researcher to describe the underlying lung viral damage associated with pulmonary microvascular thrombosis and inflammatory reaction (Conti et al., 2020). The cytokines involved in the pathogenic cascade of the COVID-19 are tumour necrosis factor-alpha (TNF-), interferon-gamma inducible protein (IP10), monocyte chemoattractant protein 1 (MCP1), and macrophage inflammatory protein 1A (MIP1A). Interleukin 6 (IL-6) is the central figure in this storm, as it is produced primarily by activated leukocytes and affects a wide range of cells and tissues. It is related to cytokine release syndrome (CRS), an acute systemic inflammatory condition characterised by numerous organ dysfunction and fever. SARS-CoV-2 binds to the Toll-Like Receptor (TLR) and forms fibrosis, releasing pro-IL-1, which cleaves into active mature IL-1 and mediates lung inflammation (Dwivedi et al., 2020).

HCoV-229E and HCoV-OC43 were identified as human coronaviruses that caused common colds in the mid-1960s (Wu et al., 2020). SARS-CoV, the most dangerous human coronavirus, was recently found, and it could cause life-threatening pneumonia (Peiris et al., 2003). Because of their ability to inhibit an animal reservoir, it started the epidemic in humans via a zoonotic transmission (Snijder et al., 2003). Coronaviruses can infect and cause various diseases in a wide range of animals. They've only been linked to mild upper respiratory tract infections in humans, such as common colds (Chang et al., 2014). Although research on these enteric viruses is scarce, gastrointestinal coronavirus infection has been associated with diarrhoea in children on rare occasions (Guy et al., 2000).

COVID-19 enters its deadly phase when it produces too many potent pro-inflammatory chemokines and cytokines, causing organ failures (Grasselli et al., 2020). The lung interstitium and bronchioalveolar space are where neutrophils accumulate and migrate. Acute respiratory distress syndrome (ARDS) arises as a result (Marik, 2020).

Oral Health Consequences of COVID-19 Infection

The destruction of the respiratory system and other organs involved in distributing angiotensin-converting enzyme 2 (ACE2) receptors in humans has been connected to the Coronavirus (Zou et al., 2020). Inflammatory reactions will develop when the ACE2 receptor distribution within cells becomes host cells for the virus in related tissues and organs, such as the salivary glands and tongue mucosa (Xu et al., 2020).

Acute COVID-19 infection can have substantial dental health effects. Due to the compromised immune system and susceptible oral mucosa, diseases such as oral fungal infections, recurrent oral herpes simplex virus (HSV-1) infection, unspecific oral ulcerations, dysgeusia (abnormal sense of taste), fixed drug eruptions, ulcerations, xerostomia linked to decreased saliva flow, and gingivitis may manifest in COVID-19 patients (Dziedzic and Varoni, 2020). COVID-19 patients' oral health is being researched as a secondary lesion resulting from systemic health deterioration or COVID-19 treatment.

Role of vitamin C in COVID-19

The pituitary and adrenal glands have three to ten times higher ascorbic acid concentrations than any other organ in humans. Vitamin C is released from the adrenal cortex in response to adrenocorticotropic hormone (ACTH) stimulation, such as viral exposure or physiological stress, resulting in a high level of vitamin C in plasma (Liu et al., 2020). Vitamin C increases cortisol synthesis and glucocorticoids' anti-inflammatory and cytoprotective effects on endothelial cells. Exogenous glucocorticoids have successfully treated COVID-19 (Ni et al., 2020). COVID-19 patients frequently have symptoms of upper respiratory infection such as slight fever, runny nose, sore throat, dry cough, malaise and fatigue, muscle stiffness, and headache. These individuals frequently have symptoms such as loss of taste, loss of smell, vomiting, and diarrhoea (Cheng *et al*., 2020).

Vitamin C has been shown in studies to shorten the length and severity of colds. Patients with COVID-19 who are given vitamin C may have a lower risk of progressing from a moderate infection to a critical stage of the disease (Hiedra et al., 2020). Vitamin C supplementation has also been proven to minimise the time spent in the Intensive Care Unit; the time spent ventilating COVID-19 patients, and the mortality of sepsis patients who require vasopressor therapy (Liu et al., 2020).

Ascorbic acid has demonstrated its involvement in increasing immunity by promoting the T-cell proliferation pathway following infection. These cells can lyse infected targets by producing high quantities of cytokines. In order to limit inflammatory reactions, B cells are also aided in the production of immunoglobulins (Carr et al., 2017). Vitamin C inhibits the apoptotic pathways in T cells, allowing them to continue to proliferate and fight the infection. This mechanism was proposed after researchers noticed an increased immune response in a rhinitis patient who was given vitamin C (Hemilä and Harri, 2017).

Vitamin C's qualities are controversial, as there have been studies on the subject, but the results have been varied. In mild to severe COVID-19 patients, Kumari et al. (2020) showed that vitamin C administration results in a significant decrease in inflammatory markers (IL-6, CRP, PCT, and ESR), indicating that intravenous vitamin C is effective. Furthermore, the therapy has been demonstrated to minimise inflammation in the body and result in pathogen infectivity by increasing immune defence, minimising organ and tissue damage, and improving overall illness outcomes (Hoang et al., 2020). Vitamin C therapy improves clinical symptoms in COVID-19 patients, according to Kumari et al. (2020). However, there is no information on the influence on mortality or the need for mechanical ventilation. Kumari et al. (2020) discovered that COVID-19 patients who received intravenous vitamin C therapy were symptom-free sooner and spent fewer days in the hospital than those who received standard care.

Hiedra et al. (2020) found that patients who received vitamin C intravenously as part of the COVID-19 treatment had a fraction of inspired oxygen (FiO2) of at least 30%. Inflammatory indicators such as ferritin and D-dimer were also compared before and after treatment. The authors observed a significant drop in inflammatory markers such as D-dimer and ferritin after vitamin C administration and a tendency toward lower FiO2 requirements.

In addition, vitamin C is known for its antiviral properties (Farjana et al., 2020). Vitamin C supplementation has been demonstrated to lower the occurrence of common colds caused by a range of viruses (Butcher et al., 2016). The infectious bronchitis virus (IBV) has been identified as a gammacoronavirus that affects the respiratory tract of chickens, and pathological lesions can be reduced with ascorbic acid therapy (Chand et al., 2014). These findings suggest that vitamin C may have antiviral properties against a range of viruses, including SARS-CoV-2, which requires more investigation.

Nonetheless, Colunga et al. (2020) stated that the mechanism of vitamin C's antiviral effects is only partially understood. It is more likely related to vitamin C's immunomodulatory qualities than direct antiviral action. These studies have concluded that vitamin C therapy, compared to coronavirus prevention, is effective in lowering the symptoms of coronavirus disease. It's due to the development of antiviral properties that can be used against viruses other than coronavirus. According to the World Health Organization, micronutrients like vitamin C are essential for a robust immune system and promote health and nutritional well-being (WHO). There is no clear recommendation for using micronutrient vitamin C supplementation as a COVID-19 treatment.

Vitamin C possesses several qualities that make it an effective medicinal agent. Pneumonia patients were given 100 grams of vitamin C each day, and no side effects or symptoms such as diarrhoea were recorded (Levine et al., 1986). Dizziness, nausea, dry mouth, sweating, and lethargy are all possible side effects of extremely high dosages of intravenous vitamin C (Welsh et al., 2013). Pre and during treatment, appropriate hydration with fluids is required to compensate for these effects. In individuals with end-stage renal failure susceptible to oxaluria, vitamin C ingestion might cause renal failure and kidney stones; therefore, intravenous vitamin C should be used with caution (Auer et al., 1998).

Despite this, some renal failure patients' kidney function improved, and no new problems developed, according to reports (Bazzan et al., 2018; Ferraro et al., 2016). Glucose-6-phosphate dehydrogenase (G6PD) deficiency screening is crucial before administering a high dose of intravenous vitamin C. There have been occurrences of haemolytic anaemia in G6PD-deficient patients after receiving 80 g of vitamin C intravenously. Vitamin C at a lower intravenous dose is commonly used to avoid this condition, and therapy of less than 16 g/day in people with G6PD deficiency is unlikely to cause haemolytic anaemia due to the lack of hydrogen peroxide production at these concentrations (Quinn et al., 2017; Ma et al., 2014).

Vitamin C had a synergistic effect on TET2 expression, apoptosis, and tumour cell proliferation in vitro in one randomised controlled trial (RCT) among patients with acute myeloid leukaemia who were given hypomethylating medications (decitabine). They were given a low dose of intravenous vitamin C, which resulted in a

six-month median overall survival (Zhao et al., 2018). The other RCTs for ovarian cancer groups showed that vitamin C combined with standard treatment improved survival. However, the difference in median overall survival was not significant due to the limited number of patients (Ma et al., 2014).

Effect of Vitamin C on Oral Health

Vitamin C is beneficial to the human body on a chemical and structural level. Ascorbic acid's primary purpose is to aid in the formation of collagen fibres by converting proline to hydroxyproline (Moores, 2013). Vitamin C is essential for the conversion of folic acid to the active form of folinic acid *in vivo* and the hydroxylation of lysine into hydroxylysine in collagen. In addition, Vitamin C is important for metabolic activities such as adrenal gland hormone production and lysine oxidation in muscle proteins (Falchetti et al., 2018). Vitamin C has an important role in the microsomal metabolism of drugs and protecting enzymes like p-hydroxyphenylpyruvic acid oxidase (Cerullo et al., 2020).

The first structural organisation levels in the human body are atoms, cells, tissues, organs, and organ systems. Tendonous and fascial tissue, the matrix of calcified tissues (such as bone and teeth), organ capsular/trabecular tissue, and endothelial cells of the entire circulatory system, including capillaries, are a few examples of it (Han et al., 2012). Vitamin C is necessary at the structural tissue level to generate intercellular molecules and collagen fibres, which come from various connective tissues in which collagen is present.

A normal adult man weighing 70 kg has 1500 mg of vitamin C stored in his body. The presence of general scurvy is indicated when the whole-body pool is less than 300 mg while the maximum quantity is around 2 g (Chambial et al., 2013). Scurvy can be caused by taking lesser than 45 mg of vitamin C per day for 60 days and eating a vitamin C-free diet. Avitaminosis is a disorder caused by a deficiency of vitamin C; as a result, the collagen that is generated becomes unstable and unable to function normally (Azari et al., 2015). Scurvy symptoms include pallor, brown patches on the skin, spongy and swollen gums, and bleeding from all mucous membranes. The thighs and legs are the most commonly affected areas. The patient may be depressed and have limited mobility. Scurvy can cause open, suppurating sores, tooth loss, and death in advanced stages (Armelagos et al., 2014).

Scurvy patients will be administered L-ascorbic acid (approximately 1 g/day for adults), which will result in the rapid disappearance of subcutaneous haemorrhages and a nearly complete reversal of symptoms (Smith et al., 2011). Although gingivitis is not caused by a shortage of vitamin C, it appears that local irritants induced the scorbutic patient's gingivitis. Some believe that a relationship between severe gingival disease and scurvy led to the misguided idea that vitamin C deficiency is a major cause of gingivitis and periodontitis (Kothari et al., 2020). Periodontal pockets are not caused by a lack of vitamin C; in reality, the formation of dental pockets requires local aggravating stimuli (Al-Ghutaimel et al., 2014). Smokers who consume a low-vitamin C diet have a higher chance of developing lung disease than those who have higher vitamin C levels in their blood (Srensen et al., 2010).

Avitaminosis C is mostly linked to a problem with the synthesis of collagen. Wound healing problems and capillary rupture are symptoms of this disorder, which is caused by weakness of intrinsic intercellular and a deficiency in connective tissue support for the walls of capillaries (Kakade et al., 2018). The vascular fragility of scorbutic persons causes bleeding, which leads to petechiae and ecchymoses, which a positive Hess test can confirm. Other signs and symptoms include epistaxis, haematuria, subperiosteal bleeding, haemarthrosis, and bleeding into muscles and deeper tissues (Marik and Paul, 2018). Scurvy siderosis is a skin discolouration caused by bleeding and blood breakdown. There will also be onycholysis and haemorrhage under the nails and hyperkeratotic hair follicles with vascular congestion and perifollicular haemorrhages. There will be a general sense of drowsiness and increased susceptibility to illnesses (Sandhu et al., 2012). When exposed to certain medicines, poisons, or stress, more vitamin C is necessary to maintain normal plasma levels and fulfil the changing metabolic needs (Murakami et al., 2018).

Gingival disease symptoms are more noticeable in scurvy patients who have poor oral hygiene. The gingiva tissue is unaffected when the patient is edentulous or has teeth that have not fully erupted, yet sub-epithelial haemorrhages do occur. With gingival lesions (patient with teeth), general scurvy symptoms such as hair follicle prominence due to keratin blockage, ecchymoses, dermal perifollicular, painful legs, lethargy, joint effusions, vasomotor instability, or pitting oedema of the ankles will develop (Halcrow et al., 2014). The interdental papilla, where the border

epithelium disintegrates, is more vulnerable to bleeding in hyperemic gingiva (Azari et al., 2015).

The use of certain antioxidants to prevent free radical-mediated illnesses and the preventive impact of antioxidant supplements in avoiding precancerous lesions has been the subject of recent scientific research (Elnour et al., 2018). In individuals with a range of dental disorders, six weeks of antioxidant vitamin C treatment was found to be effective (Pacier et al., 2015).

Dental erosion is the permanent loss of tooth structure caused by the chemical process of acid dissolving; however, plaque bacteria are not involved in this process (Johansson et al., 2012). There are both intrinsic and external erosion sources that can occur. Acid reflux and vomiting are intrinsic causes of dental erosion; however, extrinsic factors include drinking, eating, or taking medicine (Johansson, 2002; Bhatti *et al*., 2010). Aside from that, careers and lifestyle choices have an impact on tooth wear, and erosion commonly occurs alongside abrasion or attrition. Long-term exposure to demineralizing chemicals like vitamin C can cause considerable tooth deterioration (Levine et al., 2001).

The crucial pH for enamel to disintegrate is around 5.5, and the pH of vitamin C chewable tablets has been reported to be 2.3. (Blacker et al., 2013). Saliva's buffering ability and its pellicle work to offset the acidic challenge's consequences. Nonetheless, the possibility for protection is negligible. Consider that at a pH lower than critical, acid exposure is continuous and persistent. The loss of dental hard tissues will be irreversible in that case (Warreth et al., 2020). Chewable vitamin C tablets with a pH of 4 to 5 can help prevent enamel erosion by mixing sodium ascorbate or another buffering agent in the proper formulation. Supplements like this should not be produced or promoted without a buffering formulation (Ismail et al., 2020).

According to McClenaghan (2020), Vitamin C is not a cure for COVID-19. Nonetheless, it's a fantastic nutritious supplement. It has been proposed that there is a link between supplemental vitamin C and tooth erosion in tablet form. With the recent COVID-19 outbreak, many people seek additional vitamin C, whether prescribed by a doctor or self-administered. Vitamin C tablets have become increasingly popular (Carr, 2020). Regardless, there is no proof that chewing vitamin C tablets causes tooth decay (Bahal, 2014). However, the Journal of the American Dental Association published a case report of a 30-year-old woman who developed deteriorating posterior dentition due to prolonged chewing of vitamin C tablets, which caused teeth sensitivity. Chewing chewable vitamin C lowers saliva pH, allowing calcium to be lost by producing calcium citrate complexes on tooth enamel (Huew, 2010).

Recommendations

COVID-19 is a severe viral disease caused by the new SARS-CoV-2 coronavirus and can be life-threatening in some situations and pose a substantial threat to public safety and global health. Vitamin C boosts immune responses and protects against infections. When high doses of vitamin C are given to critically ill individuals, they show encouraging results. However, excessive vitamin C intake has been linked to poor dental health in COVID-19 patients. Several dose-dependent vitamin C cohort studies are being done worldwide to validate its role as a possible treatment for COVID-19 reduction. Despite, there is dearth of information on the detrimental side effects of large doses of vitamin C on dental health which makes it imperative for the health care professionals to prescribe the optimum doses without side effects. Acids contained in vitamin C is one of the leading causes of enamel degradation and to protect the teeth, saliva regularly neutralizes acid in the mouth. Hence, the outer layer of enamel can erode over time due to chewing vitamin C for a long time of period. Thus, it is suggested to use buffered Vitamin C which combines a highly absorbable form of vitamin C with the buffering minerals magnesium, potassium, and calcium that can enable greater doses of vitamin C intake without causing stomach distress, to support appropriate muscular relaxation and contraction, as well as to avoid enamel erosion.

Acknowledgement

The authors would like to thank the School of Dental Sciences, Universiti Sains Malaysia and those involved directly or indirectly in the review.

Conflict of Interest

The authors declare no conflict of interest.

References

Al-Ghutaimel H, Riba H, Al-Kahtani S, Al-Duhaimi S (2014). Common periodontal diseases of children and adolescents. *International Journal of Dentistry*, **20**(4): 14-20.

Anderson Paul S (2020). Intravenous ascorbic acid (IVAA) for COVID-19: supportive treatment in hospitalized COVID-19 patients: based on use in China and US settings.

Armelagos GJ, Sirak K, Werkema T, Turner BL (2014). Analysis of nutritional disease in prehistory: the search for scurvy in antiquity and today. *International Journal of Paleopathology*, **5**: 9-17.

Auer BL, Auer D, Rodgers AL (1998). Relative hyperoxaluria, crystalluria and haematuria after megadose ingestion of vitamin C. *European Journal of Clinical Investigation*, **28**(9): 695-700.

Azari O, Kheirandish R, Azizi S, Abbasi MF, Chaman SGG, Bidi M (2015). Protective effects of hydrocortisone, vitamin c and e alone or in combination against renal ischemia-reperfusion injury in rat. *Iranian Journal of Pathology*, **10**(4): 272.

Bahal P, Djemal S (2014). Dental erosion from an excess of vitamin C. *Case Reports in*

Dentistry, **14**(4): 48-87

Bazzan AJ, Zabrecky G, Wintering N, Newberg AB, Monti DA (2018). Retrospective evaluation of clinical experience with intravenous ascorbic acid in patients with cancer. *Integrative cancer therapies*, **17**(3): 912-920.

Bhatti ME, Al-Rashdan A, Boota AS, Al-Rashid Z, Al-Ruwaih S (2010). Determination of fluoride levels in soft drinks, fruit juices, and milk consumed by population in Kuwait using an ion-selective electrode. *Kuwait Journal of Science Engineering*, **37**(2A): 75-86.

Brosseau L (2020). Commentary: COVID-19 transmission messages should hinge on science. *Center for Infectious Disease Research and Policy, University of Minnesota*. Available at: http://www. cidrap. umn.edu/newsperspective/2020/03/commentary -covid-19-transmissionmessages-should-hinge- science.

Cagetti MG, Wolf TG, Tennert C, Camoni N, Lingström P, Campus G (2020). The role of vitamins in oral health. A systematic review and meta-analysis. *International Journal of Environmental Research and Public Health*, **17**(3): 938.

Carr AC (2020). A new clinical trial to test high-dose vitamin C in patients with COVID-19. *Critical Care*, **24**(1): 1-2.

Carr AC, Maggini S (2017). Vitamin C and immune function. *Nutrients*, **9**(11): 1211.

Cerullo G, Negro M, Parimbelli M, Pecoraro M, Perna S, Liguori G, Rondanelli M, Cena H, D'Antona G (2020). The long history of vitamin C: from prevention of the common cold to potential aid in the treatment of COVID-19. *Frontiers in immunology,* **11**: 2636.

Chambial S, Dwivedi S, Shukla KK, John PJ, Sharma P (2013). Vitamin c in disease prevention and cure: An Overview. *Indian Journal of Clinical Biochemistry*, **28**(4): 314-328.

Chand N, Naz S, Khan A, Khan S, Khan RU (2014). Performance traits and immune response of broiler chicks treated with zinc and ascorbic acid supplementation during cyclic heat stress. *International Journal of Biometeorology,* **58**(10): 2153-2157.

Chang HH, Chen P, Lin G, Wang C, Liao C, Hsiao Y, Dong J, Sun D (2014). Cell adhesion as a novel approach to determining the cellular binding motif on the severe acute respiratory syndrome coronavirus spike protein. *Journal of Virological Methods*, **201**: 1-6.

Chen YJ, Yuan RM, Liu YJ, Yang HJ, Liang GY, Tian LX (2015). Dietary vitamin c requirement and its effects on tissue antioxidant capacity of juvenile largemouth bass, micropterus salmoides. *Aquaculture*, **435**: 431-436.

Cheng R (2020). Hospital treatment of serious and critical COVID-19 infection with high-dose vitamin C. Cheng Integrative Health Center Blog http://www. drwlc.com/blog/2020/03/18/hospital-treatment-of-serious-and-critical-covid-19-infection-with-high-dose-vitaminc.

Ciceri F, Beretta L, Scandroglio AM, Colombo S, Landoni G, Ruggeri A, Peccatori J (2020). Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis. *Critical Care and Resuscitation*, **22**(2): 95.

Colunga Biancatelli RML, Berrill M, Catravas JD, Marik PE (2020). Quercetin and vitamin C: an experimental, synergistic therapy for the prevention and treatment of SARS-CoV-2 related disease (COVID-19). *Frontiers in Immunology*, **11**(1451).

Colunga B, Luciano RM, Berrill M, Marik PE (2020). The antiviral properties of vitamin C. *Expert Review of Anti-Infective Therapy*, **18**(2): 99-101.

Conti P, Ronconi G, Caraffa A, Gallenga CE, Ross R, Frydas I, Kritas SK (2020). Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. *Journal of Biological Regulator Homeostatic Agents*, **34**(2): 327-331.

Decaro N, Lorusso A (2020). Novel Human Coronavirus (SARS-CoV-2): A Lesson from Animal Coronaviruses. *Veterinary Microbiology,* **244**:108693.

Du J, Cullen JJ, Buettner GR (2012). Ascorbic Acid: Chemistry, Biology and the Treatment of Cancer. *Biochimica et Biophysica Acta (BBA)-Reviews on Cancer*, **1826**(2): 443-457.

Dwivedi, Ramya. Vitamin C and COVID-19: A Review. News-Medical. https://www.newsmedical.net/news/20201023/Vitamin-C-and-COVID-19-A-Review.aspx.

Dziedzic A, Varoni EM (2020). Challenges of oral medicine specialists at the time of COVID-19 pandemic. Oral diseases. Doi: 10.1111/odi.13520.

Elnour AAM, Mirghani MES, Musa KH, Kabbashi NA, Alam MZ (2018). Challenges of extraction techniques of natural antioxidants and their potential application opportunities as anti-cancer agents. *Health Sciences Journal*, ***12***(5): 596.

Enjuanes L, Almazán F, Sola I, Zuñiga S (2006). Biochemical aspects of coronavirus replication and virus-host interaction. *Annual Review of Microbiology*, **60**: 211-230.

Falchetti A, Cosso R (2018). The interaction between vitamin c and bone health: a narrative review. *Expert Review of Precision Medicine and Drug Development*, ***3*(**3): 215-223.

Farjana M, Moni A, Sohag AAM, Hasan A, Hannan MA, Hossain MG, Uddin MJ (2020). Repositioning vitamin C as a promising option to alleviate complications associated with COVID-19." *Infection and Chemotherapy,* **52**(4): 461-477.

Ferraro PM, Gary CC, Giovanni G, Eric NT (2016). Total, dietary, and supplemental vitamin C intake and risk of incident kidney stones. *American Journal of Kidney Diseases,* **67**(3): 400-407.

Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, Bonanomi E, Cabrini L, Carlesso E, Castelli G, Cattaneo S (2020). Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *Journal of the American Medical Association-Internal Medicine*, **180**(10): 1345-1355.

Guy JS, Breslin JJ, Breuhaus B, Vivrette S, Smith LG (2000). Characterization of a coronavirus isolated from a diarrheic foal. *Journal of Clinical Microbiology*, **38**(12): 4523-4526.

Halcrow SE, Harris NJ, Beavan N, Buckley HR (2014). First bioarchaeological evidence of probable scurvy in southeast asia: multifactorial etiologies of vitamin c deficiency in a tropical environment. *International Journal of Paleopathology*, **22**(5): 63-71.

Han R, Liu L, Li J, Du G, Chen J (2012). Functions, applications and production of 2-O-D-glucopyranosyl-L-ascorbic acid. *Applied Microbiology and Biotechnology*, **95**(2): 313-320.

Hemilä H (2017). Vitamin C and infections. *Nutrients*, **9**(4): 339.

Hiedra R, Lo KB, Elbashabsheh M, Gul F, Wright RM, Albano J, Azmaiparashvili Z, Patarroyo AG (2020). The use of IV vitamin C for patients with COVID-19: a case series. *Expert Review of Anti-Infective Therapy,* **18**(12): 1259-1261.

Hoang BX, Shaw DG, Fang W, Han B (2020). A Possible application of high dose vitamin C in the prevention and therapy for coronavirus Infections. *Journal of Global Antimicrobial Resistance,* **23**(1): 256-262.

Huew R (2010). Dental Erosion in Libyan School Children and Its Association with Potential Risk Factors. Doctoral Dissertation, Newcastle University.

Ismail Y, Mauer LJ (2020). Phase transitions of ascorbic acid and sodium ascorbate in a polymer matrix and effects on vitamin degradation. *Journal of Food Process Engineering*, **43**(5): 13-73.

Kakade A, Raut MS, Santosh A, Nagar S, Bansal S, Desai RS (2018). Gingival enlargement caused by vitamin c deficiency (scurvy) in a boy. *Journal of Dentistry for Children*, **85**(1): 40-42.

Kim SB, Yeom JS (2020). Reply: Vitamin C as a possible therapy for COVID-19. *Infection & Chemotherapy*, **52**(2): 224.

Kothari P, Tate A, Adewumi A, Kinlin LM, Ritwik P (2020). The risk for scurvy in children with neurodevelopmental disorders. *Special Care in Dentistry*, **40**(3): 251-259.

Kumari P, Dembra S, Dembra P, Bhawna F, Gul A, Ali B, Sohail H, Kumar B, Memon MK, Rizwan A (2020). The role of vitamin c as adjuvant therapy in COVID-19. *Cureus*, **12**(11): 11-17.

Lai MM (2003). SARS virus: the beginning of the unraveling of a new coronavirus. *Journal of Biomedical Science,* **10**(6): 664-675.

Levine M (1986). New concepts in the biology and biochemistry of ascorbic acid. *New England Journal of Medicine*, **314**(14): 892-902.

Levine M, Wang Y, Padayatty SJ, Morrow J (2001). A new recommended dietary allowance of vitamin C for healthy young women. *Proceedings of the National Academy of Sciences,* **98**(17): 9842-9846.

Li F (2015). Receptor recognition mechanisms of coronaviruses: a decade of structural studies. *Journal of Virology,* **89**(4): 1954-1964.

Liu J, Li S, Liu J, Liang B, Wang X, Wang H, Li W (2020). Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBioMedicine*, **55**:102763.

Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, Xiao W (2020). Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chinese Medical Journal* **133**(5): 1025-1031.

Liugan M, Carr AC (2019). Vitamin C and Neutrophil Function: Findings from Randomized Controlled Trials. *Nutrients*, **11**(9): 2102.

Ma Y, Chapman J, Levine M, Polireddy K, Drisko J, Chen Q (2014). High-dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer and reduced toxicity of chemotherapy. *Science Translational Medicine*, **6**(222): 218-222.

Marik, Paul E (2020). Vitamin C: an essential "stress hormone" during sepsis. *Journal of Thoracic disease,* **12**(1): 84.

Marik, Paul E (2018). Vitamin C for The Treatment of Sepsis: The Scientific Rationale. *Pharmacology & therapeutics*, **189**: 63-70.

McClenaghan J (2020). Nutrition: Vitamin C is not a cure for covid-19, but it's still a good nutritional supplement. The Irish News.

Monsen ER (2000). Dietary reference intakes for the antioxidant nutrients: vitamin c, vitamin e, selenium, and carotenoids. *Journal of the American Dietetic Association,* **100**(6): 637-640.

Moores J (2013). Vitamin C: a wound healing perspective. *British Journal of Community Nursing*, **18**(12): 6-11.

Murakami S, Mealey BL, Mariotti A, Chapple IL (2018). Dental plaque–induced gingival conditions. *Journal of Clinical Periodontology*, **45**(3): 17-27.

Nabzdyk CS, Bittner EA (2018). Vitamin C in the critically ill-indications and controversies. *World journal of critical care medicine*, **7**(5), 52.

Naclerio RM, Proud D, Lichtenstein L. National Research Council (2000). Dietary reference intakes for vitamin C, vitamin E, selenium and carotenoids. *Food and Nutrition Board*, 507-509.

Ni L, Ye F, Cheng ML, Feng Y, Deng YQ, Zhao H, Wei P, Ge J, Gou M, Li X, Sun L, Cao T, Wang P, Zhou C, Zhang R, Liang P, Guo H, Wang X, Qin CF, Chen F, Dong C (2020). Detection of SARS-CoV-2-Specific humoral and cellular immunity in COVID-19 convalescent individuals. *Immunity*, **52**(6): 971-977

Nicoletta L (2020). Why Vitamin C Won't 'Boost' Your Immune System against the Coronavirus. *Livescience.com.*

Padayatty SJ, Sun H, Wang Y, Riordan HD, Hewitt SM, Katz A, Wesley RA, Levine M (2004). Vitamin C pharmacokinetics: implications for oral and intravenous use. *Annals of Internal Medicine,* **140**(7): 533-537.

Pauling L (1971). Vitamin C and common cold. *Journal of the American Medical Association*, **216**(2): 332-332.

Peiris JSM, Chu CM, Cheng VCC, Chan KS, Hung IFN, Poon LLM, Law KI (2003). Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. *The Lancet*, **361**(9371): 1767-1772.

Perlman S, Netland J (2009). Coronaviruses post-SARS: update on replication and pathogenesis. *Nature reviews microbiology,* **7**(6): 439-450.

Quinn J, Gerber B, Fouche R, Kenyon K, Blom Z, Muthukanagaraj P (2017). Effect of high-dose vitamin C infusion in a glucose-6-phosphate dehydrogenase-deficient patient. *Case reports in medicine.* 2014. https://doi.org/10.1155/2017/5202606 .

Rozga M, Cheng FW, Moloney L, Handu D (2020). Effects of micronutrients or conditional amino acids on COVID-19-related outcomes: an evidence analysis center scoping review. *Journal of the Academy of Nutrition and Dietetics.* **121**(7): 1354-1363.

Schnellbaecher A, Binder D, Bellmaine S, Zimmer A (2019). Vitamins in Cell Culture Media: Stability and Stabilization Strategies. *Biotechnology and Bioengineering,* **116**(6): 1537-1555.

Smith A, Di Primio G, Humphrey-Murto S (2011). Scurvy in the developed world. *Canadian Medical Association Journal*, **183**(11): 752-755.

Snijder EJ, Bredenbeek PJ, Dobbe JC, Thiel V, Ziebuhr J, Poon LLM, Guan Y, Rozanov M, Spaan WJM, Gorbalenya AE (2003). Unique and conserved features of genome and proteome of SARS-coronavirus, an early split-off from the coronavirus group 2 lineage. *Journal of Molecular Biology*, **331**(5): 991-1004.

Soar and Jagjit S (2020). A cost-effective Preventative Approach to Potentially Save Lives in

the coronavirus pandemic, jointly using vitamin d, curcumin, and vitamin c, (with Updated Dosage Parameters). April 29. doi:10.35543/osf.io/cq8sa.

Sørensen LT, Toft BG, Rygaard J, Ladelund S, Paddon M, James T, Taylor R, Gottrup F (2010). Effect of smoking, smoking cessation, and nicotine patch on wound dimension, vitamin c, and systemic markers of collagen metabolism. *Surgery,* **148**(5): 982-990.

Sun K, Qiu J, Liu J, Miao Y (2009). Preparation and characterization of gold nanoparticles using ascorbic acid as reducing agent in reverse micelles. *Journal of Materials Science,* **44**(3): 754-758.

Van SM, Josling P (2002). Preventing the Common Cold with a vitamin C Supplement: A Double-Blind, Placebo-controlled Survey. *Advance Therapy,* **19**(3): 15-19.

Warreth A, Abuhijleh E, Almaghribi MA, Mahwal G, Ashawish A (2020). Tooth surface loss: a review of literature. *The Saudi Dental Journal,* **32**(2): 53-60.

Welsh JL, Wagner BA, Erve TJV, Zehr PS, Berg DJ, Halfdanarson TR, Yee NS (2013). Pharmacological ascorbate with gemcitabine for the control of metastatic and node-positive pancreatic cancer (PACMAN): results from a phase I clinical trial. *Cancer Chemotherapy and Pharmacology,* **71**(3): 765-775.

Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, Zhang L (2020). Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Internal Medicine,* **180**(7): 934-943.

Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, Li SB, Wang HY, Zhang S, Gao HN, Sheng JF (2020). Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *British Medical Journal,* ***368***. doi: 10.1136/bmj.m606

Zhang S, Li H, Huang S, You W, Sun H (2020). High-resolution computed tomography features of 17 cases of coronavirus disease 2019 in Sichuan province, China. *European Respiratory Journal,* **55**(4). doi: 10.1183/13993003.00334-2020

Zhao H, Zhu H, Huang J, Zhu Y, Hong M, Zhu H, Zhang J (2018). The synergy of Vitamin C with decitabine activates TET2 in leukemic cells and significantly improves overall survival in elderly patients with acute myeloid leukemia. *Leukemia research,* **66**: 1-7.

Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, Yu J, Kang M, Song Y, Xia J, Guo Q (2020). SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *New England Journal of Medicine,* **382**(12): 1177-1179.