

Therapeutic Effects of Vitamins and Nutritional Supplements on Sinusitis: A Narrative Review

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ABSTRACT: Sinusitis, one of the most prevalent and undertreated disorders, is a term used to describe inflammation of the paranasal sinuses caused by either infectious or non-infectious sources. Bacterial, viral, or fungal infections can all cause sinusitis. Sinusitis is classified into 3 types: acute, subacute, and chronic. Acute sinusitis lasts for less than 1 month, subacute sinusitis lasts from 1 to 3 months, and chronic sinusitis persists for over 3 months. This condition affects a significant portion of the population, imposing a substantial burden on the healthcare system. Antibiotics are the gold standard of bacterial sinusitis treatment. However, due to the rise of antimicrobial resistance, especially in immunocompromised patients, it is necessary to investigate potential adjunctive therapies. Based on the literature, vitamins (eg, vitamin D) have anti-oxidant, anti-inflammatory, and immune-modulatory properties and may effectively treat sinusitis and reduce mucous membrane inflammation. Besides vitamins, many other supplements like quercetin, sinupret, and echinacea have immunomodulatory effects and have shown promising results in sinusitis treatment. In this review, we look at the therapeutic role, safety, and efficacy of vitamins and nutritional supplements in sinusitis treatment.

KEYWORDS: Sinusitis, upper respiratory tract, vitamins, nutritional supplements, zinc supplements, sinupret

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Introduction

Sinusitis is the inflammation of the paranasal sinuses and nasal mucosa that leads to nasal discharge, impairment of the sense of smell, and facial pain.¹ Sinusitis accounts for many general physician visits and prescriptions of antibiotics worldwide.² The prevalence of sinusitis varies from 1% to 12%,³ and despite its ubiquity and negative effect on quality of life, its etiology is not well-understood.⁴ However, recent research suggests that many factors, such as infectious agents, structural abnormalities (nasal polyps), inflammatory and allergic processes, and dysfunctions in the host immune system, contribute to this condition.⁴ The main treatment goals include eliminating the underlying infection and reducing inflammation. The primary treatment for sinusitis includes antibiotics, nasal corticosteroids, decongestants, and surgery for refractory cases.^{5,6} These current treatments have issues, such as the

emergence of antibiotic-resistant bacteria due to excessive antibiotic prescription and surgery complications, especially in children.⁶ Because of these problems, new treatments for sinusitis are needed.⁶

Vitamin supplementation is suggested as an adjunctive therapy for inflammatory conditions, including sinusitis. Recent evidence confirms the anti-inflammatory role of certain vitamins, such as vitamin D or E.⁷⁻⁹ Besides its beneficial impact on bone health and its role in calcium and phosphate metabolism, vitamin D has an immunological and anti-inflammatory role and affects macrophages, T-cells, and dendritic cells.⁷ Numerous studies have been conducted on ways to reduce or eliminate the symptoms of neurological and behavioral problems brought on by alterations in vitamin and other nutrient levels, including omega-3 and iron supplements.¹⁰ Evidence has shown that patients with sinusitis have lower



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vitamin D levels, and vitamin D supplementation alleviates their symptoms.^{7,11} Vitamin E is a potent antioxidant that regulates reactive oxygen species formation and modulates cell-mediated and humoral immune responses.¹² The goal of this review is to highlight the possible therapeutic effects of vitamins and other supplements on sinusitis.

Vitamin A

Vitamin A, also known as retinol, is a fat-soluble vitamin found in various foods such as meat,¹³ fish,¹⁴ and vegetables (provitamin A in form of certain carotenoids).¹⁵ Its presence is crucial for the efficient functioning of organs such as the lungs, kidneys, and heart.⁹

In a study by Unal et al,¹⁶ no significant differences were found between the study group and the control group in terms of the impact of vitamin A on sinus inflammation. However, in a study conducted by Dhanawat,¹⁷ it was reported that there was a significant effect on improving general health and reducing sinus inflammation in individuals with sinusitis when vitamin A was used in conjunction with vitamin E and vitamin C. Linday et al⁶ used multivitamin-mineral and flavored cod liver oil with selenium for children with sinusitis. A suggestion was made that the use of this product can prevent sinusitis in children or at least reduce its severity.⁶

Vitamin C

Vitamin C, also known as ascorbic acid, is a water-soluble vitamin that plays a crucial role in immune system regulation and the prevention of viral infections. Tomatoes, potatoes, citrus fruits such as limes, lemons, and oranges,^{18,19} broccoli,^{20,21} and kiwi^{22,23} are some of the known sources containing a high amount of this compound. Vitamin C content in fruit is related to some variables such as fruit color, size, and firmness^{19,24}; cultivar^{24,25}; technological treatment^{21,23}; and harvest date.²⁶ Researchers reported that vitamin C suppresses the secretion of inflammatory mediators.^{27,28}

The effectiveness of mucociliary clearance and hydration of the mucosal surface depends on epithelial ion transport. Cystic fibrosis transmembrane conductance regulator (CFTR) would be considered a chloride and bicarbonate channel. Vitamin C plays an important role in maintaining the normal level of airway surface liquid, thus improving the effectiveness of mucociliary clearance. Furthermore, researchers have observed that vitamin C can biologically affect CFTR-mediated chloride secretion.²⁹⁻³¹

Considering the possible role of CFTR in chronic rhinosinusitis (CRS), Cho et al³¹ experienced the effect of L-ascorbate on a distinct type of sinonasal tissues that comprised sinus mucosa from CRS, nasal mucosa from CRS, normal sinus mucosa, and normal nasal mucosa. They declared that the administration of L-ascorbate improves chloride secretion. The reduced function of CFTR-mediated chloride secretion might play a role in the progression of CRS, leading researchers

to conclude that vitamin C could have a therapeutic effect by enhancing mucociliary clearance. In another ex vivo study, Zhang et al³² assessed nasal mucus derived from 12 patients. They showed that the combination of *scutellaria baicalensis*, *eleutherococcus senticosus*, and vitamin C might suppress Th-1, Th-2, and Th-17 involved in chronic paranasal disease. Given that these cells play an essential role in the acute inflammation of CRS, suppressing them might be effective.

Unal et al¹⁶ studied serum levels of antioxidant vitamins in 24 children who suffered from CRS. This case-control study showed that the group of patients had lower levels of vitamin C and vitamin Prabhakar Reddy et al³³ assessed serum levels of vitamin C in CRS. The study results showed that the patient group had a lower level of vitamin C than the control group. Besides, the study reported that vitamin C decreased inflammation and allergic responses.

Vitamin D

Vitamin D is known for its effects on calcium metabolism. However, recent studies suggest that this molecule plays an important role in the immune system. So it may have a role in host immunity against CRS.³⁴ Konstantinidis et al,³⁵ in an experiment on the human sinonasal epithelium of patients with eosinophilic CRS, suggest that vitamin D supplementation in eosinophilic CRS patients is effective for innate immunity regulation. Mulligan et al³⁶ examined the impact of vitamin D deficiencies on inflammation in a mouse model of CRS involving *aspergillus fumigatus*. They found out that a low level of vitamin D in the diet selectively intensifies immunological alterations related to CRS with *aspergillus fumigatus*. Mostafa Bel et al,⁷ in 74 participants, determined the level of vitamin D in patients with allergic fungal sinusitis (AFRS) and CRS and found that the level of vitamin D in patients with CRS with nasal polyps and AFRS is incredibly lower than that in those with CRS without nasal polyps and healthy controls. Many other studies have confirmed that the levels of vitamin D are lower in patients with CRS with nasal polyps.³⁷⁻⁴² Sansoni et al⁴³ conducted a clinical trial of 14 CRS patients with polyps and 31 CRS patients without polyps, as well as 12 control patients with noninflammatory pathology. Their blood was assayed for vitamin D and their sinonasal mucus for RANTES and basic fibroblast growth factor (bFGF). Only in CRS patients with polyps a negative correlation was observed between vitamin D status and RANTES and bFGF. They found that vitamin D might be crucial in regulating RANTES and basic fibroblast growth factor expression in CRS. The research by Wang et al⁴⁴ used cultivated fibroblasts from 3 patients' nasal polyps. RANTES and eotaxin were produced in vitro by the cells after being activated with IL-1. Vitamin D derivatives calcitriol and tacalcitrol, which were also given to cultures, blocked this effect.

Tomaszewska et al⁴⁵ measured levels of vitamin D in serum and the expression of vitamin D receptors in 52 patients with

CRS without nasal polyps and 55 patients with CRS with nasal polyps and then showed that vitamin D and the expression of its receptors may be associated with CRS. Bavi et al,⁴⁶ in another study with 166 patients with CRS with nasal polyps and 172 healthy subjects, noticed a considerable decrease in vitamin D levels in Iranian CRS patients with nasal polyps, which shows a positive relevance to disease intensity. Boeva et al,⁴⁷ in a study with 50 patients and 14 subjects comprising the control group, revealed higher levels of vitamin D in the blood serum of the control subjects compared to the patients with chronic polypous rhinosinusitis. Moreover, the patients of the latter group more frequently exhibited the variant of the LCT CT-13910 gene polymorphism, suggesting latent hypolactasia. In contrast, the subjects comprising the control group more frequently had the variant of the LCT CT-13910 gene polymorphism indicative of the normal tolerance of lactose. Duğu et al,⁴⁸ in a study with 6 CRS patients and 21 non-smoking controls, showed that both chitotriosidase and vitamin D could be considered non-invasive biomarkers whose utility in the follow-up of CRS-associated inflammation requires further investigation. Patients with polyps exhibited lower vitamin D values than those without polyps, while patients with microbial biofilms had higher mean values of chitotriosidase and a lower mean value of vitamin D than their counterparts. This finding may reveal the importance of microbial biofilms as an aggravating factor in disease pathogenesis. Hashemian et al,⁴⁹ in a study with 40 CRS patients with nasal polyps, demonstrated vitamin D supplementation's efficacy in reducing the recurrence of polyposis after functional endoscopic sinus surgery in patients with CRS with nasal polyps. Kalińczak-Górna et al,¹¹ in a study of 40 patients suffering from chronic sinusitis, discovered a relationship between a decrease in inflammation and increased vitamin D levels and reduced mental and physical symptoms of chronic inflammation. Konstantinidis et al³⁵ showed that both CRS and CF patients have vitamin D deficiency and nasal polyps. The lower the serum vitamin D level, the more severe the mucosal disease was observed. Lee et al⁵⁰ indicated that low serum vitamin D levels may not significantly correlate with an elevated CRS frequency in Korean adults. However, CRS patients had higher serum vitamin D levels than the control group. In a meta-analysis by Li et al,⁵¹ low vitamin D levels in patients with CRS were observed, suggesting that vitamin D supplements can benefit individuals. Therefore, because of the heterogeneity of the studies, better-designed futuristic RCTs should be performed to further evaluate these findings for the common population in the future. Moreover, Baruah et al,⁵² in a study with 200 CRS patients with vitamin D deficiency and 100 patients that were given oral vitamin D supplements, found that 100 patients on placebo did not have vitamin D deficiency, and there were practically no differences in outcomes for both groups of patients.

Vitamin E

Vitamin E is one of the lipid-soluble vitamins, which comprises 4 isoforms of tocopherol and 4 isoforms of tocotrienol.⁵³ This vitamin can be found in many sources, some of which are: fruits, peanut oil, corn oil,⁵⁴ extra virgin olive oil, pomace olive oil, soybean oil, palm oil,⁵⁵ apricot seed oil, hemp seed oil, flaxseed oil, and sunflower oil.⁵⁶ Vitamin E, as an antioxidant, plays a role in cell membranes and blocks the propagation of free radical reactions.⁵⁷ Vitamin E isomers are well-known for their gene-regulation effects and anti-inflammatory properties.⁵⁸ Unal et al,¹⁶ in a study on 24 children aged 7 to 12 years with CRS and 20 healthy controls, measured serum levels of copper, magnesium, antioxidant vitamins, and zinc. They found that the serum level of vitamin E is lower in CRS patients. However, Westerveld et al⁵⁹ measured antioxidant levels in a mucosal biopsy of the uncinate process of the ethmoid bone in patients with CRS and healthy controls. There was no difference in levels of vitamin E between the 2 groups.

Other Nutritional Supplements

Echinacea

Echinacea is a dietary supplement for the common cold and other infections; the idea is that it could stimulate the immune system to act more effectively against infections.⁶⁰ Echinacea, prepared from the root of *echinacea purpurea*, is sometimes also derived from *echinacea pallida* and *echinacea angustifolia*.⁶¹

Ogal et al⁶⁰ and Vimalanathan et al⁶¹ showed that using echinacea in children from 3 to 12 years old can be helpful for the prevention of RTI and secondary complications such as sinusitis, bronchitis, and pneumonia. The outcome indicated significant differences between the study and control groups in the intensity of sinusitis in the studied patients.

N-acetylcysteine

N-acetyl cysteine is a tolerable and safe dietary supplement.⁶² It is the precursor to L-cysteine, an amino acid that is used to form glutathione molecules.⁶³ N-acetyl cysteine is the antidote to acetaminophen toxicity and a mucolytic agent.⁶⁴ Furthermore, it protects endothelial and mucus cells from free radicals by its sulfhydryl group and increases glutathione levels.⁶³ Evidence has shown that N-acetyl cysteine inhibits bacterial aggregate formation (biofilms), which are involved in many infections, such as bacterial sinusitis.⁶⁵

Several studies have shown the positive impacts of N-acetyl cysteine on sinusitis treatment due to its antioxidant and antimicrobial effects.^{63,65,66} Bezshapochniy et al⁶³ examined the positive effect of N-acetyl cysteine on treating viral sinusitis. They combined 6% N-acetyl cysteine with 3% normal saline and added it to the usual sinusitis treatment

(topical corticosteroids). In this study, 56 participants (29 patients in the experimental group and 27 patients in the control group) received classical sinusitis treatment with either 3% normal saline or 3% normal saline plus 6% N-acetyl cysteine. In this research, the combination of N-acetyl cysteine and normal saline improved patients' symptoms with viral sinusitis. Another study investigated the role of N-acetyl cysteine in bacterial biofilms and its possible benefits in treating bacterial sinusitis. Blasi et al⁶⁵ reviewed both in vitro and clinical studies. They showed that N-acetyl cysteine inhibits the formation of biofilms and may have some therapeutic effect on sinusitis.

Sinupret

Sinupret is a well-known herbal medicine with evidence-based efficacy for several respiratory disorders, such as sinusitis or acute and chronic bronchitis.^{67,68} *Primula veris*, *verbena officinalis*, *sambucus nigra*, *gentiana lutea*, and *rumex acetosa* are among the plants used to make Sinupret.⁶⁹ Since 1934, this herbal preparation has been used to repair and maintain the physiological activity of the mucosa in the paranasal sinuses in both liquid and sugar-coated tablet form.^{69,70} Antibacterial, antiviral, secretolytic, mucolytic, and immunological activities are all found in sinupret extract.^{67,69,71,72} It reduces cyclo-oxygenase-rhino2 expression and prostaglandin E-2 synthesis, resulting in strong anti-inflammatory effects when taken orally.⁷³ Sinupret's general safety has been thoroughly documented.⁶⁹ In some related studies, Zhang et al⁶⁸ observed that sinupret raises airway surface liquid depth, enhances ciliary beat frequency, and promotes transepithelial chloride secretion, which is expected to improve mucociliary clearance. Sinupret, according to their findings, could be employed as a new therapeutic strategy for common respiratory disorders, including sinusitis.

Quercetin

Quercetin (3,3',4',5,7-pentahydroxyflavone) is a kind of flavonoid compound. It is derived from phenylalanine and produced through the phenylpropanoid pathway. Quercetin can be found in a variety of sources, including different kinds of berries,⁷⁴ tomatoes,⁷⁵ vegetables, fruits, nuts, and beverages,⁷⁶ onions,⁷⁷ apples, capers, grapes, and tea,⁷⁸ shallots,⁷⁹ and honey.^{80,81} Researchers studied whether it might have a role in improving mental and physical function and reducing infection risk.⁸²

Since medical plants have lower prices and fewer side effects, they are more popular.⁸³ Some studies have mentioned

that some plants decrease inflammatory factors and have an inhibitory effect on a transcription factor that enhances the secretion of mediators.⁸² Studies have found that quercetin inhibits lipid peroxidation, platelet aggregation, and capillary permeability.⁸⁴ Additionally, a new review published in 2020 by Jafarinia et al⁸⁵ showed some anti-inflammatory effects of quercetin. Zhang et al⁸⁶ investigated the effect of quercetin on chloride secretion and ciliary beat frequency. Their results indicated that quercetin can increase chloride secretion and ciliary beat frequency.

Zinc supplements

Zinc is necessary for cells to develop and function properly by mediating nonspecific immunity, including neutrophils and natural killer cells.⁸⁷ The availability and importance of zinc in diseases and its essential presence in biological fluids should not be ignored.⁸⁸

A study by Mohammadhossein et al,⁸⁹ which used 50 patients with nasal polyposis, suggested that there is no significant difference in sinusitis, but there are signs showing zinc may be useful in the prevention of sinusitis. However, with that being said, in the study by Akbari Dilmaghani et al⁹⁰ it is reported that the treatment group had mild superiority in general health improvement but not in symptoms. Add-on therapy with zinc sulfate supplementation showed no remarkable improvement in patients suffering from CRS and nasal polyposis.

Conclusion

Multiple therapies are required to treat sinusitis patients, including nutritional interventions. In this review, we discussed the possible therapeutic effects of vitamins and a wide range of nutrition on sinusitis. We indicated their pathogenic role in sinusitis. As shown in Table 1 and Figure 1, vitamin C, vitamin D, echinacea, N-acetyl cysteine, sinupret, and quercetin have shown promise in the treatment of sinusitis based on growing positive evidence. The effects of vitamins and nutritional supplements on sinusitis need further evaluation due to a lack of sufficient evidence. Clinicians are encouraged to consider these useful supplements in sinusitis management whenever possible. By complementing these add-on therapies, additional antimicrobial resistance is avoided, and the final treatment outcome might be improved. However, studies on the efficacy of many of these supplements are insufficient, and more research, especially clinical trials with large study samples, is required to assess their effectiveness and potential side effects.

Table 1. Therapeutic effects of vitamins and other nutritional supplements on sinusitis.

AUTHOR	TYPE OF STUDY	INTERVENTION OR MEASURED COMPOUND	PARTICIPANTS	OUTCOME
Ünal et al ⁹¹	Animal study	Vitamin A	20 animals	There was no difference between the study and control groups' sinus inflammation changes.
Fang et al ⁹²	Within-subject control study	Vitamin A	30 patients	Antrostomy stenosis prevention, mucociliary promotion, and adhesion reduction are achieved by topical vitamin A.
Güven et al ⁹³	Prospective controlled animal trial	Vitamin A	20 New Zealand hybrid rabbits	There is no significant statistical difference between the control and study groups.
Unal et al ¹⁶	Case-control	Vitamin A, vitamin E, vitamin C, zinc, and copper	24 patients between 7 and 12y	In the patients' group, the levels of vitamin E, vitamin C, copper (Cu), and zinc (Zn) were found to be significantly lower compared to the control group. However, no significant difference was observed in the levels of vitamin A and magnesium (Mg) between the 2 groups.
Tomiki ⁹⁴	Case-control	Vitamin A and vitamin D	265 school children	Vitamin A was ineffective in the treatment but useful in preventing CRS in children.
Dhanawati ¹⁷	Clinical trial	Prabhakar Reddy et al	53 patients with allergic rhinitis	Vitamins A, E, and C's role (antioxidant, anti-inflammatory) in the treatment of allergic rhinitis was significant.
Prabhakar Reddy et al ⁹³	Case-control	Vitamin C	40 cases and 40 controls	A lower vitamin C level in the cases was observed.
Ogal et al ⁶⁰	Randomized clinical trial	Vitamin C and Echinacea	94 Children (intervention group) and 93 children (control group)	Echinacea prevents RTI better than vitamin C.
Zhang et al ⁹²	In vitro	Combination of Vitamin C with <i>Scutellaria baicalensis</i> And <i>Eleutherococcus senticosus</i>	Nasal mucosal tissue of 12 patients	Suppression of Th-1, Th-2, and Th-17.
Baruah et al ⁵²	Cross-sectional	Vitamin D	100 CRS patients were given oral Vitamin D, and 100 CRS patients were treated with placebo	At baseline, the pretreatment TNSS exhibited an average score of 11.92. Following a duration of 3 mo, the scores experienced a notable reduction with an average decrease of 10.65 points, demonstrating a statistically significant difference.
Bavi et al ⁴⁶	Cross-sectional	Vitamin D	166 CRS patients with nasal polyps and 172 healthy subjects	Decreased vitamin D levels in Iranian patients with CRS with nasal polyps, with an association to disease intensity
Boeva et al ⁴⁷	Cross-sectional	Vitamin D	50 patients with sinusitis and 14 healthy subjects	Higher levels of vitamin D in the control subjects compared to patients with chronic polypous rhinosinusitis.
Duju et al ⁴⁸	Cross-sectional	Vitamin D	6 CRS patients and 21 non-smoking controls	Reducing inflammation increases vitamin D levels.

(Continued)

Table 1. (Continued)

AUTHOR	TYPE OF STUDY	INTERVENTION OR MEASURED COMPOUND	PARTICIPANTS	OUTCOME
Elbistanli et al ⁹⁵	Prospective case-control	Measured Vitamin D	Group 1 consisted of fifteen pediatric patients with ARS-induced preseptal cellulitis complication, Group 2 consisted of fifteen ARS patients without complication, and Group 3 consisted of fifteen healthy volunteers. At the first admission of research participants, serum vitamin D levels (nmol/l) were assessed in addition to regular blood testing.	There was a statistically significant difference according to the existence of ARS (Group-1 and Group 2) and absence of ARS (Group-3) based on categorization in which vitamin D levels were compared with normal values (p 0.05). Between Group 1 and Group 3, a statistically significant difference was also discovered.
Faghieh Habibi et al ⁹⁶	Cross-sectional controlled study	Measured Vitamin D	32 CRS patients with nasal polyps, 35 CRS patients without nasal polyps, and 50 healthy controls	The serum level of Vitamin D was considerably lower in CRS patients compared with the other group.
Hashemian et al ⁴⁹	Cross-sectional	Intervention Vitamin D	40 patients with CRS with nasal polyposis	Vitamin D efficiently reduced the recurrence of polyposis after FESS in CRS patients with nasal polyps.
Kalinczak-Górna et al ¹¹	Cross-sectional	Measured Vitamin D	40 CRS patients	Reducing inflammation increases vitamin D levels.
Konstantinidis et al ⁹⁵	Cross-sectional	Measured Vitamin D	27 CF patients with nasal polyps, 31 CF patients without nasal polyps, 32 CRS patients with nasal polyps, 30 patients without nasal polyps, and 32 healthy controls	Vitamin D deficiency with nasal polyps appears similar in those with CRS and CF. The lower the serum vitamin D level, the more severe the mucosal disease.
Mostafa Bel et al ⁷	Case-control	Measured Vitamin D	25 patients with allergic fungal rhinosinusitis, 15 CRS patients with nasal polyps, 15 CRS patients without nasal polyps, and 19 healthy controls	Vitamin D levels in CRS patients with nasal polyps and AFRS were meaningfully lower than those in CRS patients without nasal polyps.
Schlösser et al ³⁷	Case-control	Measured Vitamin D	Blood and sinus tissue	CRS Patients with nasal polyps and AFRS patients both have decreased sinonasal vitamin D.
Shanaki et al ⁴⁰	Case-control	Measured Vitamin D	45 CRS patients with nasal polyps and 45 controls	CRS patients with nasal polyps have lower levels of vitamin D in their serum compared to controls.
Zand et al ⁴¹	Case-control	Measured Vitamin D	93 CRS patients with nasal polyps	An association between vitamin D levels and disease intensities in CRS patients with nasal polyps.
Tomaszewska et al ⁴⁵	Case-control	Measured Vitamin D	52 CRS patients without nasal polyps, 55 CRS patients with nasal polyps, and 59 controls	Vitamin D and its receptor expression may be associated with CRS.
Thakur and Potluri ⁴²	Case-control	Measured Vitamin D	30 CRS patients without nasal polyps, 30 CRS patients with nasal polyps, and 31 controls	Vitamin D was a predictive factor for the Occurrence of CRS.
Ma et al ⁹⁷	Clinical trial	Measured Vitamin D	Human sinonasal epithelium of fifteen patients with eosinophilic CRS and healthy controls	Topical vitamin D in CRS patients was beneficial for the innate immune system.
Mulligan et al ⁹⁸	Clinical trial	Intervention Vitamin D	Female mice (8wk old)	Loss of vitamin D in the diet intensified immunological changes related to <i>Aspergillus fumigatus</i> -CRS.
Sansoni et al ⁴³	Clinical trial	Measured Vitamin D	57 patients in groups of CRS with and without nasal polyposis	Vitamin D may have a role in the regulation of the immune system.
Westerveld ⁵⁹	Cross-sectional	Measured Vitamin E	Mucosa samples of 9 patients with CRS and 10 healthy persons	There was no difference in levels of vitamin E between patients and the healthy group.

(Continued)

Table 1. (Continued)

AUTHOR	TYPE OF STUDY	INTERVENTION OR MEASURED COMPOUND	PARTICIPANTS	OUTCOME
Ishrefova et al ⁹⁸	Cohort	Echinacea	A number of children in the time 2008 to 2014	Using Echinacea lowers the rate of complications of RTI such as sinusitis, bronchitis, and adenoiditis.
Popov et al ⁶⁶	Clinical trial	N-acetyl cysteine	48 patients in the intervention group and 50 patients in the control group	N-acetyl cysteine alleviated the symptoms, decreased relapses, and increased the efficacy of surgery among the study group.
Bezshapochnyi et al ⁶³	Clinical trial	N-acetyl cysteine	29 patients in the intervention group and 27 patients in the control group	Saline and N-acetyl cysteine solutions alleviated the symptoms.
Perić et al ⁶⁹	Randomized comparative study	Sinupret	20 CRS patients without nasal polyps and 20 patients who used fluticasone spray	Sinupret may be a safe and effective alternative to intranasal corticosteroids for the treatment of CRS patients without nasal polyps.
Sen'kevich et al ¹⁰⁰	Randomized prospective comparative clinical study	Sinupret	107 children aged 4 to 5y with ARS	The use of Sinupret in the treatment of children with acute rhinosinusitis (ARS) caused by a viral etiology is associated with a more pronounced favorable outcome.
Vishnyakov and Sinkov ¹⁰¹	Cohort	Sinupret	25 patients and 25 control group	Overall satisfaction with the treatment was higher in the herbal medication group compared to the antibiotic drug control group.
Popovych et al ¹⁰²	Randomized comparative study	Sinupret	292 children aged 6 to 11 y with ARS	Sinupret was beneficial for ARS in both adults and children.
Passali et al ⁶⁹	Prospective open-label Study	Sinupret	30 patients with ARS were treated with sinupret, and 30 patients used fluticasone	Symptoms improved significantly in all of the patients using sinupret.
Neubauer and März ⁷⁰	Clinical trial	Sinupret	160 patients with acute bacterial sinusitis	Sinupret improved sinusitis symptoms.
Palm et al ⁶⁷	Clinical trial	Sinupret	929 patients with CRS	Sinupret extract was found to be effective in treating CRS patients.
Jund et al ¹⁰³	Clinical trial	Sinupret	589 patients with acute viral rhinosinusitis	Sinupret is an effective and safe herbal drug for viral sinusitis therapy.
Mohammadhossein et al ⁸⁹	Case-control	Zinc supplements	50 participants with nasal polyposis and 50 participants as the control group	The serum level of zinc was low in patients suffering from nasal polyposis.
Akbari Dilmaghani et al ⁹⁰	Randomized clinical trial	Zinc supplements	44 participants	Using zinc supplements offers several advantages for improving general health.

Abbreviation: AFRS, allergic fungal rhinosinusitis; ARS, acute rhinosinusitis; CF, cystic fibrosis; Cl, chloride; CRS, chronic rhinosinusitis; FESS, functional endoscopic sinus surgery; RTI, respiratory tract infection; TNSS, total nasal symptom score.

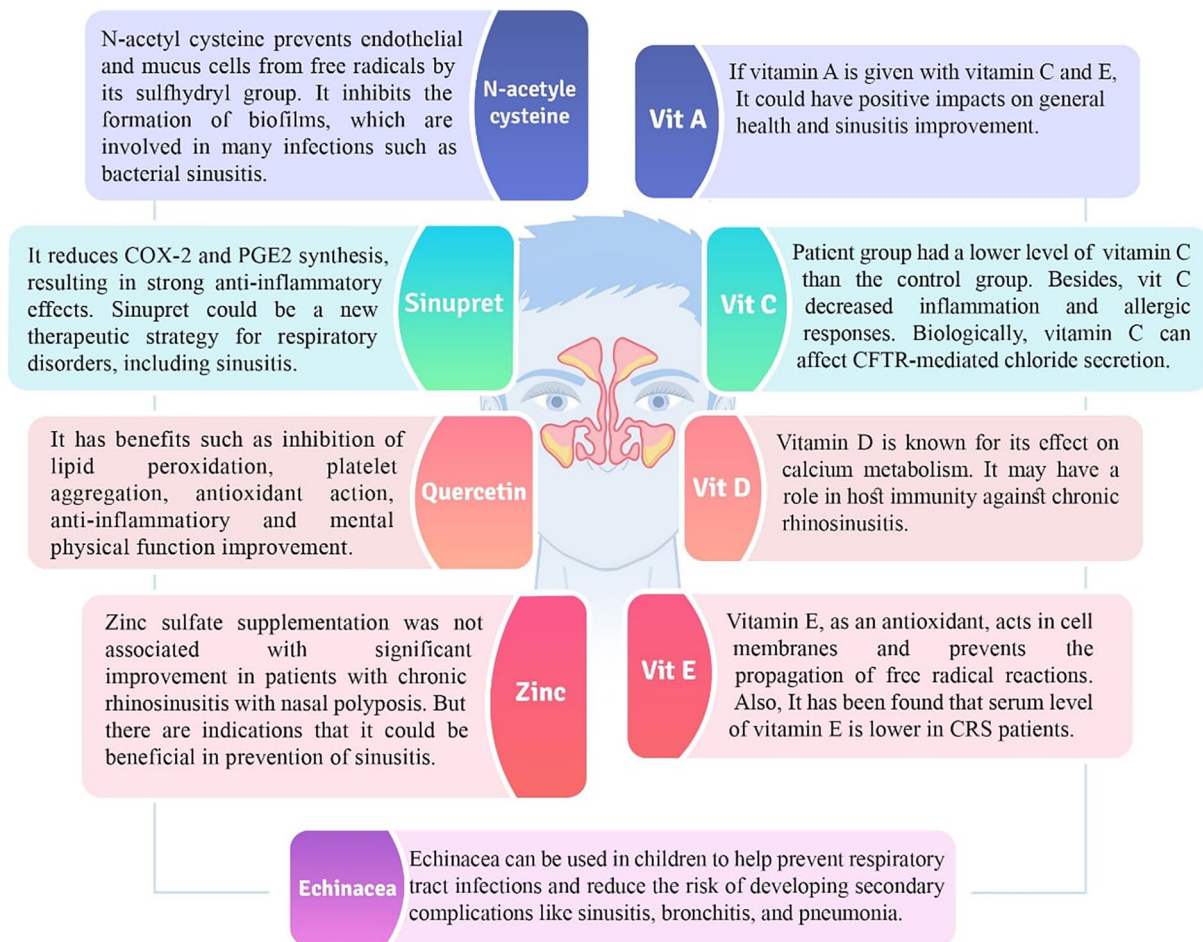


Figure 1. A review of therapeutic effects of vitamins and various nutrition on sinusitis. Vitamins and nutritional supplements can reduce sinusitis symptoms.

Author Contributions

Conceived and designed the analysis: Mohammad Ghaheri, Narjes Sadat Farizani Gohari and Dorsa Abolhasani. Collected data: Sadaf Parvin, Mohammad Mahdi Ghodrati and Shekoufeh Mohammadpour. Contributed data or analysis tools: Erfan Kazemi, Fatemeh Mohammadyari and Armin Alinezhad. Performed the analysis: Farhad Nikzad, Shahin Sabbaghi and Sara Saeedpour. Designed the study: Mohadeseh Poudineh, Sepehr Olangian-Tehrani and Farbod Heydarasadi. Wrote the paper: Mohadeseh Poudineh, Farhad Nikzad, Sadaf Parvin, Mohammad Ghaheri, Shahin Sabbaghi, Erfan Kazemi, Mohammad Mahdi Ghodrati, Fatemeh Mohammadyari, Sara Saeedpour, Shekoufeh Mohammadpour, Narjes Sadat Farizani Gohari, Farbod Heydarasadi, Dorsa Abolhasani, Sepehr Olangian-Tehrani and Armin Alinezhad. All authors reviewed the results and approved the final version of the manuscript.

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