

FluVert

Scientific Substantiation of Product

Summary:

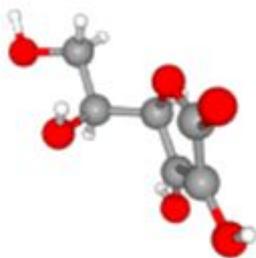
FluVert is a one of a kind unique *Nutraceutical aid in Averting Respiratory Viral Diseases including Corona Virus- Covid 19*

In contrast to other formulations that contain a multitude of elements, mostly at sub therapeutic dosages, Fluvert contains four Evidence based actives at science based dosages. These actives act synergistically to maximise the function of the immune system and in so doing plays a vital role in aiding the prevention of Covid 19 and other Flu Virusses. Fluvert is currently the only product in the world that is formulated in this way.

Fluvert is further unique in that it contains the unique *Effervescent Solvent Enhanced Technology (ESET)* that ensures that the three actives is solubilised effectively and stays in solution for an extended period of time.

For relevant information on the Function, Formulation, and efficacy of the three actives please find below a range of scientific Evidence Based scientific articles published on these subjects.

Vitamin C (Ascorbic acid):



An Update on Current Therapeutic Drugs Treating COVID-19

Renyi Wu¹, Lujing Wang¹, Hsiao-Chen Dina Kuo¹, Ahmad Shannar¹, Rebecca Peter¹, Pochung Jordan Chou¹, Shanyi Li¹, Rasika Hudlikar¹, Xia Liu^{1,2}, Zhigang Liu^{1,3}, George J Poiani^{4,5}, Louis Amorosa⁵, Luigi Brunetti^{4,6}, Ah-Ng Kong¹Free

Abstract

The current pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has presented unprecedented challenges to the healthcare systems in almost every country around the world. Currently, there are no proven effective vaccines or therapeutic agents against the virus. Current clinical management includes infection prevention and control measures and supportive care including supplemental oxygen and mechanical ventilatory support. Evolving research and clinical data regarding the virologic SARS-CoV-2 suggest a potential list of repurposed drugs with appropriate pharmacological effects and therapeutic efficacies in treating COVID-19 patients. In this review, we will update and summarize the most common and plausible drugs for the treatment of COVID-19 patients. These drugs and therapeutic agents include antiviral agents (remdesivir, hydroxychloroquine, chloroquine, lopinavir, umifenovir, favipiravir, and oseltamivir), and supporting agents (**Ascorbic acid**, Azithromycin, Corticosteroids, Nitric oxide, IL-6 antagonists), among others. Vitamin C is an essential nutrient and plays significant roles within the human body. It can neutralize free radicals and assist to prevent or reverse cellular damage as a potent antioxidant agent. It is also involved in some biological processes, many of which are associated with immune health [77]. **Moreover, vitamin C appears to be effective as an antiviral agent, especially against influenza viruses [78]. Many studies showed that vitamin C positively affects the development and maturation of T lymphocytes and NK (natural killer) cells involved in the immune response to viral agents. It also contributes to the inhibition of reactive oxygen species (ROS) production and to the remodulation of the cytokine network typical of systemic inflammatory syndrome were discharged [81]. Moreover, high-dose (1.5 mg/kg body weight) vitamin C has been used for several decades clinically and an NIH panel also documented clearly that this dose regimen is safe and has no major side effects [81, 82].**

Vitamin C Is an Essential Factor on the Anti-viral Immune Responses Through the Production of Interferon- α / β at the Initial Stage of Influenza A Virus (H3N2) Infection

Yejin Kim¹, Hyemin Kim, Seyeon Bae, Jiwon Choi, Sun Young Lim, Naeun Lee, Joo Myung Kong, Young-Il Hwang, Jae Seung Kang, Wang Jae Lee

Abstract

L-ascorbic acid (vitamin C) is one of the well-known anti-viral agents, especially to influenza virus. Since the in vivo anti-viral effect is still controversial, we investigated whether vitamin C could regulate influenza virus infection in vivo by using Gulo (-/-) mice, which cannot synthesize vitamin C like humans. First, we found that vitamin C-insufficient Gulo (-/-) mice expired within 1 week after intranasal inoculation of influenza virus (H3N2/Hongkong). Viral titers in the lung of vitamin C-insufficient Gulo (-/-) mice were definitely increased but production of anti-viral cytokine, interferon (IFN)- α / β , was decreased. On the contrary, the infiltration of inflammatory cells into the lung and production of pro-inflammatory cytokines, tumor necrosis factor (TNF)- α and interleukin (IL)- α / β , were increased in the lung. **Taken together, vitamin C shows in vivo anti-viral immune responses at the early time of infection, especially against influenza virus, through increased production of IFN- α / β .**

Crit Care. 2020; 24: 133.

A new clinical trial to test high-dose vitamin C in patients with COVID-19

Anitra C. Carr[✉]

With the 2019 novel coronavirus (2019-nCoV) outbreak now spreading across the world, people are seeking ways in which to potentially protect themselves from the virus or to alleviate its effects once caught. **One such means that is being touted online and in the media is vitamin C.**

Vitamin C is best known for its antioxidant properties, being able to scavenge damaging reactive oxygen species, thus protecting the body's cells and tissues from oxidative damage and dysfunction. However, the vitamin also

has numerous other important functions within the body, many of which are known to support healthy immune function. During infection, vitamin C levels can become depleted and a person's requirement for vitamin C increases with the severity of the infection [1]. In severe cases, this may require intravenous administration of gram doses in order to achieve high enough levels in the body to compensate for the enhanced turnover of the vitamin.

Res Social Adm Pharm

2020 May 23;S1551-7411(20)30611-2.

Time-trend Analysis of Medicine Sales and Shortages During COVID-19 Outbreak: Data From Community Pharmacies

Sónia Romano¹, Heloísa Galante², Débora Figueira³, Zilda Mendes⁴, António Teixeira Rodrigues⁵

Abstract

Background: COVID-19 is a worldwide public health concern. Disruptions in the drug market are expected and shortages might worsen.

-COVID-19 period. The analyzed drugs were paracetamol, **ascorbic acid**, dapagliflozin plus metformin, rosuvastatin plus ezetimibe, formoterol, and hydroxychloroquine .

Nutrition. 2010 Jan; 26(1): 128–132.

The Effectiveness of Vitamin C in Preventing and Relieving the Symptoms of Virus-Induced Respiratory Infections

H C Gorton, K Jarvis

Abstract

Background: An ever increasing demand to evaluate the effect of dietary supplements on specific health conditions by use of a "significant scientific" standard has prompted the publication of this study.

Objective: To study the effect of megadose Vitamin C in preventing and relieving cold and flu symptoms in a test group compared with a control group.

Design: Prospective, controlled study of students in a technical training facility.

Subjects: A total of 463 students ranging in age from 18 to 32 years made up the control group. A total of 252 students ranging in age from 18 to 30 years made up the experimental or test group.

Method: Investigators tracked the number of reports of cold and flu symptoms among the 1991 test population of the facility compared with the reports of like symptoms among the 1990 control population. Those in the control population reporting symptoms were treated with pain relievers and decongestants, whereas those in the test population reporting symptoms were treated with hourly doses of 1000 mg of Vitamin C for the first 6 hours and then 3 times daily thereafter. Those not reporting symptoms in the test group were also administered 1000-mg doses 3 times daily.

Results: Overall, reported flu and cold symptoms in the test group decreased 85% compared with the control group after the administration of megadose Vitamin C.

Conclusion: Vitamin C in megadoses administered before or after the appearance of cold and flu symptoms relieved and prevented the symptoms in the test population compared with the control group.

Int J Tuberc Lung Dis

Vitamin C and Acute Respiratory Infections

H Hemilä¹, R M Douglas

Abstract

In three trials of subjects under heavy acute physical stress, common cold incidence decreased by on average 50%, and in four trials of British males common cold incidence decreased by on average 30% in the vitamin C groups. The dietary vitamin C intake in the UK is low, and consequently the benefit may be due to the correction of marginal deficiency, rather than high vitamin doses.

Regular vitamin C supplementation (> or =1 g/day) has quite consistently reduced the duration of colds, but the size of the benefit has varied greatly. In the four largest studies the duration of colds was reduced only by 5%. In two of these studies, however, absence from school and work was reduced

by 14-21% per episode, which may have practical importance. Three controlled studies recorded a reduction of at least 80% in the incidence of pneumonia in the vitamin C group, and one randomised trial reported substantial treatment benefit from vitamin C in elderly UK patients hospitalized with pneumonia or bronchitis.

Ascorbic Acid Role in Containment of the World Avian Flu Pandemic

Molecules. 2011 Mar; 16(3): 2032–2052.

John T A Ely¹

Abstract

In this Comment, the ultimate intent is to increase survival of the anticipated global flu pandemic. The apparent failure of "medicine" to provide a completely understood and logically based biochemical prevention and treatment for all influenzas (and many other viral diseases) may be an unavoidable result of the evolving complexity of the H5N1 virus. **However, clinical experience cited in all accounts, including the 2003 to 2006 period, suggest that: (i) ascorbic acid is not being administered to humans infected or at risk for influenza, and (ii) ascorbic acid is (mistakenly) believed to be a vitamin ("vitamin C"). Proper use of ascorbic acid as described here could provide effective containment for the flu pandemic**

Molecules. 2011 Mar; 16(3): 2032–2052.

Antioxidant Therapy as a Potential Approach to Severe Influenza-Associated Complications

Noboru Uchide* and Hiroo Toyoda

Abstract

Ascorbic acid (19, Figure 4) scavenges superoxide anion [78]. **Ascorbic acid inhibited the proliferation of influenza virus in cell cultures [79].** Dehydroascorbic acid, an oxidized form of ascorbic acid without reducing ability, showed much stronger antiviral activity than that of ascorbic acid, indicating that the antiviral activity of ascorbic acid is due to factors other than

antioxidant mechanism [80]. In a controlled trial of 226 patients with influenza A, 114 patients received vitamin C 300 mg/day, and 112 patients served as controls; outcomes measured were development of pneumonia and duration of hospital stay. Pneumonia was reported in two subjects in the treatment group and 10 in the control group, and hospital stays for influenza or related complications averaged nine days in the vitamin C group and 12 days in the control group [81]. **Therefore it has been considered that combined inhalation and oral supplementation of ascorbic acid may prevent influenza virus infection [82].**

Can Fam Physician

2011 Jan;57(1):31-6.

Complementary and Alternative Medicine for Prevention and Treatment of the Common Cold

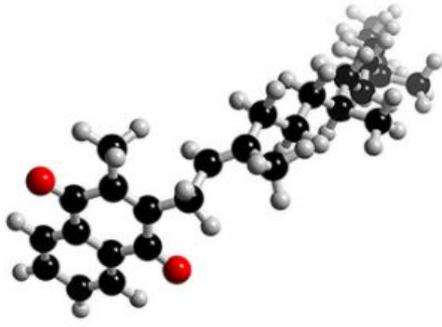
Richard Nahas¹, Agneta Balla

Abstract

Objective: To review the evidence supporting complementary and alternative medicine approaches to treatment and prevention of the common cold in adults.

Main message: **For prevention, vitamin C demonstrated benefit in a large meta-analysis, with possibly increased benefit in patients subjected to cold stress.** Zinc lozenges were effective in 5 of 9 trials, likely owing to dose and formulation issues. **Conclusion:** Vitamin C can be recommended to Canadian patients for prevention of the common cold.

Vitamin D:



Journal.ppat.1008874. eCollection 2020 Sep.2020 Sep 18;16(9):e1008874.

Exploring links between vitamin D deficiency and COVID-19

Mradul Mohan¹, Jerin Jose Cherian², Amit Sharma^{1,3}
Affiliations expand

Abstract

Coronavirus Disease 2019 (COVID-19) pandemic remains a major public health threat in most countries. The causative severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus can lead to acute respiratory distress syndrome and result in mortality in COVID-19 patients. **Vitamin D is an immunomodulator hormone with established effectiveness against various upper respiratory infections. Vitamin D can stall hyper-inflammatory responses and expedite healing process of the affected areas, primarily in the lung tissue. Thus, there are ecological and mechanistic reasons to promote exploration of vitamin D action in COVID-19 patients. As no curative drugs are available currently for COVID-19, we feel that the potential of vitamin D to alter the course of disease severity needs to be investigated.** Clinical studies may be undertaken to address the value of vitamin D supplementation in deficient, high-risk COVID-19 patients.

Maturitas 2020 Oct;140:24-26.

Point of view: Should COVID-19 patients be supplemented with vitamin D?

[Cédric Annweiler¹](#), [Zhijian Cao²](#), [Jean-Marc Sabatier³](#)

Affiliations expand

Abstract

Using Hill's methodology for exploring causality, we aimed to determine in early May 2020 whether evidence supports vitamin D as a biological determinant of COVID-19 outcomes. **Vitamin D is a secosteroid hormone theoretically able to reduce COVID-19 risk through regulation of (i) the renin-angiotensin system, (ii) cellular innate and adaptive immunity, and (iii) physical barriers. Inverse associations were found between 25-hydroxyvitamin D concentrations and COVID-19 incidence and mortality.**

Randomized controlled trials testing vitamin D supplementation in the treatment of COVID-19 are in progress. Positive results in such studies would encourage the use of vitamin D supplements as an adjuvant treatment in COVID-19.

Keywords: Biomarker; COVID-19; Causality; SARS-CoV-2; Treatment; Vitamin

[Mayo Clin Proc.](#) 2020 Aug; 95(8): 1804–1805.

Vitamin D Supplementation During the COVID-19 Pandemic

[Darko Siuka](#), MD

The coronavirus disease 2019 (COVID-19) pandemic has severe short-term and long-term consequences on individuals, health systems, and economies.

Considering the studies on the role of vitamin D in the prevention of acute respiratory infections, supplementation of vitamin D may be reasonable also for the prevention of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and reducing morbidity and mortality in COVID-19 high-risk patients.

Vitamin D deficiency is more common in older age groups, smokers, those who are obese, and in patients with chronic diseases such as diabetes, hypertension, various gastroenterological diseases, and also in African Americans.¹ The high-risk groups that have more complications and higher mortality in COVID-19 coincide with groups that have a high incidence of vitamin D deficiency. We believe that vitamin D deficiency might be one of the important risk factors for COVID-19 complications and higher mortality.

Studies of vitamin D replacement have shown that vitamin D ameliorates innate immunity (the immediate response of macrophages to invading viruses and bacteria in the mucous membranes),² thereby reducing the incidence and severity of acute respiratory infections.³ This effect requires a sufficient serum level of 25(OH)D₃ being crucial for macrophages to activate it into hormone D (calcitriol), which activates genes for the synthesis of antimicrobial factors destroying viruses (such as SARS-CoV-2), fungi, and bacteria.² Also, vitamin D modulates the cellular immune response and, as expected, attenuates the cytokine storm,⁴ the event so fatal in SARS-CoV-2–induced pneumonia. Therefore, we suggest it would be reasonable to supplement vitamin D in subpopulations at risk of vitamin D deficiency and unfavorable COVID-19 outcomes, as well as in individuals already infected with SARS-CoV-2 to achieve optimal 25(OH)D₃ concentrations as quickly as possible.

It is challenging to conduct evidence-based medicine in cases such as the COVID-19 pandemic. To the best of our knowledge, there are no data on the effects of vitamin D in SARS-CoV-2 infection; then again, there are reliable data on the beneficial effects of cholecalciferol in attenuating viral respiratory infections in people with low levels of vitamin D. The European Centre for Disease Prevention and Control makes this argument and encourages health care professionals to take actions that are logical in their own right, based on previously known findings in related fields: “Public health authorities should recognize that extra-scientific factors (e.g. feasibility of implementing scientific advice, time pressure, socio-political factors, institutional factors, economic interests, pressure from neighboring countries etc.) are inherent to the decision-making process. These factors will also influence the implementation of any proposed response measures. **Decisions should therefore always be evidence informed, but they will very rarely be purely evidence based.**”⁵ **In Slovenia, in view of COVID-19 pandemic, medical doctors were urgently advised by leading experts to supplement vitamin D in high-risk and fragile individuals and in COVID-19 patients. With this letter to the editor we address the broader medical community to urgently consider vitamin D supplementation in high-risk patients for adverse COVID-19 outcomes.**

J Transl Med 2020 Aug 26;18(1):322.

The importance of vitamin d metabolism as a potential prophylactic, immunoregulatory and neuroprotective treatment for COVID-19

[Yi Xu](#)^{1,2,3}, [David J Baylink](#)⁴, [Chien-Shing Chen](#)^{5,6}, [Mark E Reeves](#)^{5,6}, [Jeffrey Xiao](#)⁴, [Curtis Lacy](#)⁵, [Eric Lau](#)⁵, [Huynh Cao](#)^{5,6}

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has led to a declaration of a Public Health Emergency of International Concern by the World Health Organization. As of May 18, 2020, there have been more than 4.7 million cases and over 316,000 deaths worldwide. COVID-19 is caused by a highly infectious novel coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), leading to an acute infectious disease with mild-to-severe clinical symptoms such as flu-like symptoms, fever, headache, dry cough, muscle pain, loss of smell and taste, increased shortness of breath, bilateral viral pneumonia, conjunctivitis, acute respiratory distress syndromes, respiratory failure, cytokine release syndrome (CRS), sepsis, etc. While physicians and scientists have yet to discover a treatment, it is imperative that we urgently address 2 questions: how to prevent infection in immunologically naive individuals and how to treat severe symptoms such as CRS, acute respiratory failure, and the loss of somatosensation. Previous studies from the 1918 influenza pandemic have suggested vitamin D's non-classical role in reducing lethal pneumonia and case fatality rates. **Recent clinical trials also reported that vitamin D supplementation can reduce incidence of acute respiratory infection and the severity of respiratory tract diseases in adults and children.** According to our literature search, there are no similar findings of clinical trials that have been published as of July 1st, 2020, in relation to the supplementation of vitamin D in the potential prevention and treatment for COVID-19. In this review, we summarize the potential role of vitamin D extra-renal metabolism in the prevention and treatment of the SARS-CoV-2 infection, helping to bring us slightly closer to fulfilling that goal. We will focus on 3 major topics here: 1. **Vitamin D might aid in preventing SARS-CoV-2 infection:** Vitamin D: Overview of Renal and Extra-renal metabolism and regulation. Vitamin D: Overview of molecular mechanism and multifaceted functions beyond skeletal homeostasis. Vitamin D: Overview of local immunomodulation in human infectious diseases. Anti-viral infection. Anti-malaria and anti-systemic lupus erythematosus (SLE). 2. Vitamin D might act as a strong immunosuppressant inhibiting cytokine release syndrome in COVID-19: Vitamin D: Suppression of key pro-inflammatory pathways including nuclear factor kappa B (NF- κ B), interleukin-6 (IL-6), and tumor necrosis factor (TNF). 3. Vitamin D might prevent loss of neural sensation in COVID-19 by stimulating expression of neurotrophins like Nerve Growth Factor (NGF): Vitamin D: Induction of key neurotrophic factors. .

Keywords: 1,25(OH)2D3; 25(OH)D; COVID-19; Coronavirus; Extra-renal; IL-6; Immunomodulation; Infection; Metabolism; NF-kB; NGF; TNF; Vitamin D.

Nutrients 2020 Apr 2;12(4):988.

Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths

[William B Grant¹](#), [Henry Lahore²](#), [Sharon L McDonnell³](#), [Carole A Baggerly³](#), [Christine B French³](#), [Jennifer L Aliano³](#), [Harjit P Bhattoa⁴](#)

Abstract

The world is in the grip of the COVID-19 pandemic. Public health measures that can reduce the risk of infection and death in addition to quarantines are desperately needed. This article reviews the roles of vitamin D in reducing the risk of respiratory tract infections, knowledge about the epidemiology of influenza and COVID-19, and how vitamin D supplementation might be a useful measure to reduce risk. Through several mechanisms, vitamin D can reduce risk of infections. Those mechanisms include inducing cathelicidins and defensins that can lower viral replication rates and reducing concentrations of pro-inflammatory cytokines that produce the inflammation that injures the lining of the lungs, leading to pneumonia, as well as increasing concentrations of anti-inflammatory cytokines. **Several observational studies and clinical trials reported that vitamin D supplementation reduced the risk of influenza, whereas others did not. Evidence supporting the role of vitamin D in reducing risk of COVID-19 includes that the outbreak occurred in winter, a time when 25-hydroxyvitamin D (25(OH)D) concentrations are lowest; that the number of cases in the Southern Hemisphere near the end of summer are low; that vitamin D deficiency has been found to contribute to acute respiratory distress syndrome; and that case-fatality rates increase with age and with chronic disease comorbidity, both of which are associated with lower 25(OH)D concentration.** To reduce the risk of infection, it is recommended that people at risk of influenza and/or COVID-19 consider taking 10,000 IU/d of vitamin D₃ for a few weeks to rapidly raise 25(OH)D concentrations, followed by 5000 IU/d. The goal should be to raise 25(OH)D concentrations above 40-60 ng/mL (100-150 nmol/L). For treatment of people who become infected with COVID-19, higher vitamin D₃ doses might be useful. Randomized controlled

patients and improving clinical trials outcome through the synergistic action of zinc and chloroquine in patients suffering from the coronavirus disease.

Med Hypotheses

2020 May 6;142:109815.

Does Zinc Supplementation Enhance the Clinical Efficacy of Chloroquine/Hydroxychloroquine to Win Today's Battle Against COVID-19?

R Derwand¹, M Scholz²

Abstract

Currently, drug repurposing is an alternative to novel drug development for the treatment of COVID-19 patients. The antimalarial drug chloroquine (CQ) and its metabolite hydroxychloroquine (HCQ) are currently being tested in several clinical studies as potential candidates to limit SARS-CoV-2-mediated morbidity and mortality. CQ and HCQ (CQ/HCQ) inhibit pH-dependent steps of SARS-CoV-2 replication by increasing pH in intracellular vesicles and interfere with virus particle delivery into host cells. Besides direct antiviral effects, CQ/HCQ specifically target extracellular zinc to intracellular lysosomes where it interferes with RNA-dependent RNA polymerase activity and coronavirus replication. As zinc deficiency frequently occurs in elderly patients and in those with cardiovascular disease, chronic pulmonary disease, or diabetes, **we hypothesize that CQ/HCQ plus zinc supplementation may be more effective in reducing COVID-19 morbidity and mortality than CQ or HCQ in monotherapy.** Therefore, CQ/HCQ in combination with zinc should be considered as additional study arm for COVID-19 clinical trials.

Adv Nutr. 2019 Jul; 10(4): 696–710.

The Role of Zinc in Antiviral Immunity

Scott A Read,^{1,2} Stephanie Obeid,³ Chantelle Ahlenstiel,³ and Golo Ahlenstiel^{1,2}

ABSTRACT

This review focuses on the role of zinc as an essential micronutrient that is required to mount an effective antiviral response. Although zinc possesses

direct antiviral properties (e.g. influenza), it is also critical in generating both innate and acquired (humoral) antiviral responses.

Evid Based Complementary Altern Med

2017 Jan;22(1):166-174.

Prevention and Treatment of Influenza, Influenza-Like Illness, and Common Cold by Herbal, Complementary, and Natural Therapies

Haider Abdul-Lateef Mousa¹

Abstract

There is scientific evidence regarding the effectiveness of several complementary therapies for colds. **Oral zinc may reduce the length and severity of a cold. Taking vitamin C supplements on a regular basis only slightly reduces the length and severity of colds.** It is now accepted that an overwhelming inflammatory response is the cause of human deaths from avian

Int J Mol Med

2020 Apr 14;46(1):17-26.

Zinc and Respiratory Tract Infections: Perspectives for COVID-19 (Review)

Anatoly V Skalny¹, Lothar Rink², Olga P Ajsuvakova³, Michael Aschner¹, Viktor A Gritsenko⁴, Svetlana I Alekseenko⁵, Andrey A Svistunov¹, Demetrios Petrakis⁶, Demetrios A Spandidos⁷, Jan Aaseth¹, Aristidis Tsatsakis¹, Alexey A Tinkov¹

In view of the emerging COVID-19 pandemic caused by SARS-CoV-2 virus, the search for potential protective and therapeutic antiviral strategies is of particular and urgent interest. **Zinc is known to modulate antiviral and antibacterial immunity and regulate inflammatory response. Despite the lack of clinical data, certain indications suggest that modulation of zinc status may be beneficial in COVID-19. In vitro experiments demonstrate that Zn²⁺ possesses antiviral activity through inhibition of SARS-CoV RNA polymerase. This effect may underlie therapeutic efficiency of chloroquine known to act**

as zinc ionophore. Indirect evidence also indicates that Zn²⁺ may decrease the activity of angiotensin-converting enzyme 2 (ACE2), known to be the receptor for SARS-CoV-2. Improved antiviral immunity by zinc may also occur through up-regulation of interferon α production and increasing its antiviral activity. Zinc possesses anti-inflammatory activity by inhibiting NF- κ B signaling and modulation of regulatory T-cell functions that may limit the cytokine storm in COVID-19. Improved Zn status may also reduce the risk of bacterial co-infection by improving mucociliary clearance and barrier function of the respiratory epithelium, as well as direct antibacterial effects against *S. pneumoniae*. Zinc status is also tightly associated with risk factors for severe COVID-19 including ageing, immune deficiency, obesity, diabetes, and atherosclerosis, since these are known risk groups for zinc deficiency. Therefore, Zn may possess protective effect as preventive and adjuvant therapy of COVID-19 through reducing inflammation, improvement of mucociliary clearance, prevention of ventilator-induced lung injury, modulation of antiviral and antibacterial immunity. However, further clinical and experimental studies are required.

Diabetes Metab Syndr

2020 Apr 16;14(4):367-382.

Enhancing Immunity in Viral Infections, With Special Emphasis on COVID-19: A Review

Ranil Jayawardena¹, Piumika Sooriyaarachchi², Michail Chourdakis³, Chandima Jeewandara⁴, Priyanga Ranasinghe⁵

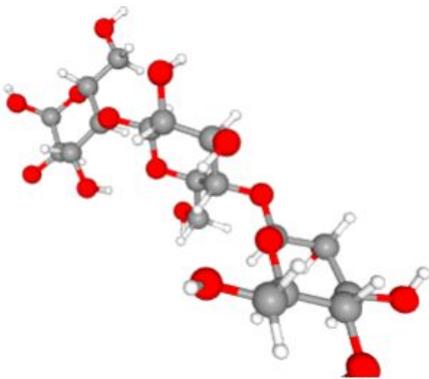
Abstract

Background and aims: Balanced nutrition which can help in maintaining immunity is essential for prevention and management of viral infections. While data regarding nutrition in coronavirus infection (COVID-19) are not available, in this review, we aimed to evaluate evidence from previous clinical trials that studied nutrition-based interventions for viral diseases (with special emphasis on respiratory infections), and summarise our observations.

Methods: A systematic search strategy was employed using keywords to search the literature in 3 key medical databases: PubMed[®], Web of Science[®] and SciVerse Scopus[®]. Studies were considered eligible if they were controlled trials in humans, measuring immunological parameters, on viral and respiratory infections. Clinical trials on vitamins, minerals, nutraceuticals and probiotics were included.

Results: **Among trace elements, selenium and zinc have also shown favourable immune-modulatory effects in viral respiratory infections.** Several nutraceuticals and probiotics may also have some role in enhancing immune functions. Micronutrients may be beneficial in nutritionally depleted elderly population.

Beta 1:3/1:6D Glucan:



J Am Coll Nutr

2012 Aug;31(4):295-300.

Baker's Yeast Beta-Glucan Supplement Reduces Upper Respiratory Symptoms and Improves Mood State in Stressed Women

Shawn M Talbott¹, Julie A Talbott

Affiliations expand

Abstract

Objective: **Several studies have shown a baker's yeast beta-1,3/1,6-d-glucan, extracted from *Saccharomyces cerevisiae*, is effective in reducing the incidence of cold and flu symptoms.**

Results: **Subjects in the Beta Glucan group reported fewer upper respiratory symptoms compared to placebo (10% vs 29%), better overall well-being (global mood state: 99 ± 19 vs 108 ± 23 , $p < 0.05$), and superior mental/physical energy levels (vigor: 19.9 ± 4.7 vs 15.8 ± 6.3 , $p < 0.05$).**

Conclusions: These data show that daily dietary supplementation with Bte Glucan reduces upper respiratory symptoms and improves mood state in stressed subjects, and thus it may be a useful approach for maintaining immune protection against daily stressors.

J Diet Suppl.

2013 Sep 1; 10(3): 171–183.

Baker's Yeast Beta Glucan Supplementation Increases Salivary IgA and Decreases Cold/Flu Symptomatic Days After Intense Exercise

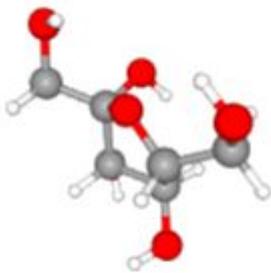
Brian K McFarlin¹, Katie C Carpenter, Tiffany Davidson, Meredith A McFarlin

Abstract

Strenuous exercise, such as running a marathon, is known to suppress mucosal immunity for up to 24 hr, which can increase the risk of developing an upper respiratory tract infection (URTI) and reduced performance capacity (Allgrove JE, Geneen L, Latif S, Gleeson M. Influence of a fed or fasted state on the s-IgA response to prolonged cycling in active men and women. *Int J Sport Nutr Exerc Metab.* 2009;19(3):209-221; Barrett B, Locken K, Maberry R, Schwamman J, Brown R, Bobula J, Stauffacher EA. The Wisconsin Upper Respiratory Symptom Survey (WURSS): a new research instrument for assessing the common cold. *J Fam Pract.* 2002;51(3):265; Carpenter KC, Breslin WL, Davidson T, Adams A, McFarlin BK. Baker's yeast beta glucan supplementation increases monocytes and cytokines post-exercise: implications for infection risk? *Br J Nutr.* 2012;1-9). While many dietary interventions have been used to combat postexercise immune suppression, most have been ineffective. **The key purpose of this study was to determine if baker's yeast β -glucan (BG) could positively affect the immune system of individuals undergoing intense exercise stress using two experiments. In the first (E1; N = 182 men and women), BG was compared to placebo supplementation for the incidence of URTI symptoms for 28 days postmarathon. In the second (E2; N = 60 men and women) changes in salivary immunoglobulin A (IgA) were evaluated after 50-min of strenuous cycling when participants had been supplemented for 10 days with either BG (250 mg/day) or placebo (rice flour).** For E1, subjects reported URTI symptoms using a daily health log. For E2, saliva was collected prior to, immediately, and 2-hr postexercise using a salivette. Data for E1 and E2 were analyzed using separate analyses of variance (ANOVAs) with repeated measures ($p < .05$). **In E1, BG was associated with a 37% reduction in the**

number of cold/flu symptom days postmarathon compared to placebo ($p = .026$). In E2, BG was associated with a 32% increase in salivary IgA ($p = .048$) at 2 hr after exercise compared to placebo. In summary, the present study demonstrates that BG may reduce URTI symptomatic days and improve mucosal immunity (salivary IgA) postexercise

Prebiotics:



Adv Biochem Eng Biotechnol

2008;111:1-66.

Probiotics, Prebiotics, and Synbiotics

Michael de Vrese¹, J Schrezenmeir

Abstract

According to the German definition, probiotics are defined viable microorganisms, sufficient amounts of which reach the intestine in an active state and thus exert positive health effects. Numerous probiotic microorganisms (e.g. *Lactobacillus rhamnosus* GG, *L. reuteri*, bifidobacteria and certain strains of *L. casei* or the *L. acidophilus*-group) are used in probiotic food, particularly fermented milk products, or have been investigated--as well as *Escherichia coli* strain Nissle 1917, certain enterococci (*Enterococcus*

faecium SF68) and the probiotic yeast *Saccharomyces boulardii*--with regard to their medicinal use. Among the numerous purported health benefits attributed to probiotic bacteria, the (transient) modulation of the intestinal microflora of the host and the capacity to interact with the immune system directly or mediated by the autochthonous microflora, are basic mechanisms. They are supported by an increasing number of in vitro and in vivo experiments using conventional and molecular biologic methods. In addition to these, a limited number of randomized, well-controlled human intervention trials have been reported. **Well-established probiotic effects are:** 1. Prevention and/or reduction of duration and complaints of rotavirus-induced or antibiotic-associated diarrhea as well as alleviation of complaints due to lactose intolerance. 2. Reduction of the concentration of cancer-promoting enzymes and/or putrefactive (bacterial) metabolites in the gut. 3. Prevention and alleviation of unspecific and irregular complaints of the gastrointestinal tracts in healthy people. 4. Beneficial effects on microbial aberrancies, inflammation and other complaints in connection with: inflammatory diseases of the gastrointestinal tract, *Helicobacter pylori* infection or bacterial overgrowth. 5. Normalization of passing stool and stool consistency in subjects suffering from obstipation or an irritable colon. 6. Prevention or alleviation of allergies and atopic diseases in infants. 7. **Prevention of respiratory tract infections (common cold, influenza)** and other infectious diseases as well as treatment of urogenital infections. Insufficient or at most preliminary evidence exists with respect to cancer prevention, a so-called hypocholesterolemic effect, improvement of the mouth flora and caries prevention or prevention or therapy of ischemic heart diseases or amelioration of autoimmune diseases (e.g. arthritis). A prebiotic is "a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well being and health", whereas synergistic combinations of pro- and prebiotics are called synbiotics. Today, only bifidogenic, non-digestible oligosaccharides (particularly inulin, its hydrolysis product oligofructose, and (trans)galactooligosaccharides), fulfill all the criteria for prebiotic classification. They are dietary fibers with a well-established positive impact on the intestinal microflora. Other health effects of prebiotics (prevention of diarrhoea or obstipation, modulation of the metabolism of the intestinal flora, cancer prevention, positive effects on lipid metabolism, stimulation of mineral adsorption and immunomodulatory properties) are indirect, i.e. mediated by the intestinal microflora, and therefore less-well proven. In the last years, successful attempts have been reported to make infant formula more breast milk-like by the addition of fructo- and (primarily) galactooligosaccharides.

Effect of Probiotics and Prebiotics on Immune Response to Influenza Vaccination in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

We conducted a meta-analysis to evaluate the effects of probiotics and prebiotics on the immune response to influenza vaccination in adults. We conducted a literature search of Pubmed, Embase, the Cochrane Library, the Cumulative Index to Nursing and Allied Health (CINAHL), Airiti Library, and PerioPath Index to Taiwan Periodical Literature in Taiwan. Databases were searched from inception to July 2017. We used the Cochrane Review risk of bias assessment tool to assess randomized controlled trial (RCT) quality. A total of 20 RCTs comprising 1979 adults were included in our systematic review. Nine RCTs including 623 participants had sufficient data to be pooled in a meta-analysis. **Participants who took probiotics or prebiotics showed significant improvements in the H1N1 strain seroprotection rate (with an odds ratio (OR) of 1.83 and a 95% confidence interval (CI) of 1.19-2.82, $p = 0.006$, $I^2 = 0\%$), the H3N2 strain seroprotection rate (OR = 2.85, 95% CI = 1.59-5.10, $p < 0.001$, $I^2 = 0\%$), and the B strain seroconversion rate (OR = 2.11, 95% CI = 1.38-3.21, $p < 0.001$, $I^2 = 0\%$). This meta-analysis suggested that probiotics and prebiotics are effective in elevating immunogenicity by influencing seroconversion and seroprotection rates in adults inoculated with influenza vaccines.**