March 27, 2023

Re: Imúne: Curated Blend and Cellular Absorption Technology Clinical Dossier

Here at THREE, we provide curated proactive wellness solutions using our proprietary Cellular Absorption Technology, proven to help you live a life of greater health and purpose.

This dossier contains peer-reviewed clinical studies both on the curated blend and the Cellular Absorption Technologies used in Imúne that validates its ability to do the following:

- Promote health of the innate and adaptive immune system.
- Support the body's healthy immune response.
- Enhance the gut microbiome—as 80% of the immune system is in the gut.

One thing that you can expect from us here at THREE is that we are always in the process of running clinical studies in elucidating new mechanisms of action by which our products work along with discovering additional areas in which our products can promote human health. We have several exciting clinical studies in the pipeline and will announce these when they are completed.

The clinical studies contained herein, and others that will follow, explain why our products provide the powerful health benefits our customers from all around the world experience every time they use a THREE product.

Thank you for joining us on this journey and for trusting us with your proactive wellness needs.

Be well,

Dr. Dan Gubler
Chief Scientific Officer
Three International

Randomized Controlled Trial Phytomedicine. 2021 Oct;91:153668.
doi: 10.1016/j.phymed.2021.153668. Epub 2021 Jul 22.

Effect of processed aloe vera gel on immunogenicity in inactivated quadrivalent influenza vaccine and upper respiratory tract infection in healthy adults: A randomized double-blind placebo-controlled trial

Jeong-Hwan Hwang [1], Mi-Ra Oh [2], Ji-Hyun Hwang [2], Eun-Kyung Choi [2], Su-Jin Jung [2], Eun-Jung Song [3], Erica Españo [3], Richard J Webby [4], Robert G Webster [4], Jeong-Ki Kim [5], Soo-Wan Chae [6]

Affiliations
PMID: 34385093 DOI: 10.1016/j.phymed.2021.153668
Free article

Abstract

Background: Aloe vera is a functional food with various pharmacological functions, including an immune-modulating effect. Until now, A. vera has never been studied as an adjuvant in influenza vaccine, and its effects on upper respiratory tract infection (URI) are unknown.

Purpose: The objective of our study was to investigate the effect of processed A. vera gel (PAG) on immunogenicity of quadrivalent inactivated influenza vaccine and URI in healthy adults.

Study design: A randomized, double-blind, placebo-controlled clinical trial was performed.

Methods: This study was conducted in 100 healthy adults at a single center from September 2017 to May 2018. Subjects were randomly divided into a PAG group (n = 50) and a placebo group (n = 50). The enrolled subjects were instructed to ingest the study drug for 8 weeks. The participants received a single dose of quadrivalent inactivated influenza vaccine after taking the study drug for the first 4 weeks of the study. The primary endpoint was seroprotection rate against at least one viral strain at 4 weeks post-vaccination. Other outcomes were seroprotection rate at 24 weeks post-vaccination, seroconversion rate, geometric mean fold increase (GMFI) at 4 and 24 weeks post-vaccination, seroprotection rate ratio and geometric mean titer ratio (GMTR) at 4 weeks post-vaccination between PAG and placebo groups, and incidence, severity, and duration of URI.

Results: The European Committee for proprietary medicinal products (CPMP) evaluation criteria were met at least one in the PAG and placebo groups for all strains. However, there was no significant difference in the seroprotection rate at 4 weeks post-vaccination against all strains in both PAG and placebo groups. Among secondary endpoints, the GMFI at 4 weeks post-vaccination for the A/H3N2 was significantly higher in the PAG than in placebo group. The GMTR as adjuvant effect was 1.382 (95% CI, 1.014-1.1883). Kaplan-Meier curve analysis showed a reduction in

Methods. 2007 Aug;42(4):388-93. doi: 10.1016/j.ymeth.2007.03.005.

The inner gel component of Aloe vera suppresses bacterial-induced pro-inflammatory cytokines from human immune cells

Fatema Habeeb [1], Graham Stables, Fiona Bradbury, Stephanie Nong, Pamela Cameron, Robin Plevin, Valerie A Ferro

Affiliations

PMID: 17560326 DOI: 10.1016/j.ymeth.2007.03.005

Abstract

The present study was carried out to examine the anti-inflammatory activity of the inner leaf gel component of Aloe barbadensis Miller. A simple in vitro assay was designed to determine the effect of the inner gel on bacterial-induced pro-inflammatory cytokine production, namely TNF-alpha and IL-1 beta, from peripheral blood leukocytes stimulated with Shigella flexneri or LPS. This report describes the suppression of both cytokines with a freeze-dried inner gel powder and a commercial health drink from the same source. Comparison was made with a human monocytic cell-line (THP-1 cells) and a similar trend in responses was demonstrated.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources
Elsevier Science

Medical
MedlinePlus Health Information

Research Materials
NCI CPTC Antibody Characterization Program

Review Medicina (Kaunas). 2007;43(8):597-606.

Effects of beta-glucans on the immune system

Dalia Akramiene [1], Anatolijus Kondrotas, Janina Didziapetriene, Egidijus Kevelaitis

Affiliations
PMID: 17895634
Free article

Abstract

Beta-glucans are naturally occurring polysaccharides. These glucose polymers are constituents of the cell wall of certain pathogenic bacteria and fungi. The healing and immunostimulating properties of mushrooms have been known for thousands of years in the Eastern countries. These mushrooms contain biologically active polysaccharides that mostly belong to group of beta-glucans. These substances increase host immune defense by activating complement system, enhancing macrophages and natural killer cell function. The induction of cellular responses by mushroom and other beta-glucans is likely to involve their specific interaction with several cell surface receptors, as complement receptor 3 (CR3; CD11b/CD18), lactosylceramide, selected scavenger receptors, and dectin-1 (betaGR). beta-Glucans also show anticarcinogenic activity. They can prevent oncogenesis due to the protective effect against potent genotoxic carcinogens. As immunostimulating agent, which acts through the activation of macrophages and NK cell cytotoxicity, beta-glucan can inhibit tumor growth in promotion stage too. Anti-angiogenesis can be one of the pathways through which beta-glucans can reduce tumor proliferation, prevent tumor metastasis. beta-Glucan as adjuvant to cancer chemotherapy and radiotherapy demonstrated the positive role in the restoration of hematopiesis following by bone marrow injury. Immunotherapy using monoclonal antibodies is a novel strategy of cancer treatment. These antibodies activate complement system and opsonize tumor cells with iC3b fragment. In contrast to microorganisms, tumor cells, as well as other host cells, lack beta-glucan as a surface component and cannot trigger complement receptor 3-dependent cellular cytotoxicity and initiate tumor-killing activity. This mechanism could be induced in the presence of beta-glucans.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources

Lithuanian University of Health Sciences

Eur Cytokine Netw. 2001 Apr-Jun;12(2):290-6.

The effect of Sambucol, a black elderberry-based, natural product, on the production of human cytokines: I. Inflammatory cytokines

V Barak [1], T Halperin, I Kalickman

Affiliations
PMID: 11399518

Abstract

Sambucus nigra L. products - Sambucol - are based on a standardized black elderberry extract. They are natural remedies with antiviral properties, especially against different strains of influenza virus. Sambucol was shown to be effective in vitro against 10 strains of influenza virus. In a double-blind, placebo-controlled, randomized study, Sambucol reduced the duration of flu symptoms to 3-4 days. Convalescent phase serum showed a higher antibody level to influenza virus in the Sambucol group, than in the control group. The present study aimed to assess the effect of Sambucol products on the healthy immune system - namely, its effect on cytokine production. The production of inflammatory cytokines was tested using blood - derived monocytes from 12 healthy human donors. Adherent monocytes were separated from PBL and incubated with different Sambucol preparations i.e., Sambucol Elderberry Extract, Sambucol Black Elderberry Syrup, Sambucol Immune System and Sambucol for Kids. Production of inflammatory cytokines (IL-1 beta, TNF-alpha, IL-6, IL-8) was significantly increased, mostly by the Sambucol Black Elderberry Extract (2-45 fold), as compared to LPS, a known monocyte activator (3.6-10.7 fold). The most striking increase was noted in TNF-alpha production (44.9 fold). We conclude from this study that, in addition to its antiviral properties, Sambucol Elderberry Extract and its formulations activate the healthy immune system by increasing inflammatory cytokine production. Sambucol might therefore be beneficial to the immune system activation and in the inflammatory process in healthy individuals or in patients with various diseases. Sambucol could also have an immunoprotective or immunostimulatory effect when administered to cancer or AIDS patients, in conjunction with chemotherapeutic or other treatments. In view of the increasing popularity of botanical supplements, such studies and investigations in vitro, in vivo and in clinical trials need to be developed.

Related information

PubChem Compound (MeSH Keyword)

LinkOut - more resources

BMC Complement Med Ther. 2021 Apr 7;21(1):112. doi: 10.1186/s12906-021-03283-5.

Elderberry for prevention and treatment of viral respiratory illnesses: a systematic review

L Susan Wieland [1], Vanessa Piechotta [2], Termeh Feinberg [3 4 5], Emilie Ludeman [6], Brian Hutton [7 8], Salmaan Kanji [7 9], Dugald Seely [9 10 11], Chantelle Garritty [7]

Affiliations

PMID: 33827515 PMCID: PMC8026097 DOI: 10.1186/s12906-021-03283-5

Free PMC article

Abstract

Background: Elderberry has traditionally been used to prevent and treat respiratory problems. During the COVID-19 pandemic, there has been interest in elderberry supplements to treat or prevent illness, but also concern that elderberry might overstimulate the immune system and increase the risk of 'cytokine storm'. We aimed to determine benefits and harms of elderberry for the prevention and treatment of viral respiratory infections, and to assess the relationship between elderberry supplements and negative health impacts associated with overproduction of pro-inflammatory cytokines.

Methods: We conducted a systematic review and searched six databases, four research registers, and two preprint sites for studies. Two reviewers independently assessed studies for inclusion, extracted data from studies, assessed risk of bias using Cochrane tools, and evaluated certainty of estimates using GRADE. Outcomes included new illnesses and the severity and duration of illness.

Results: We screened 1187 records and included five randomized trials on elderberry for the treatment or prevention of viral respiratory illness. We did not find any studies linking elderberry to clinical inflammatory outcomes. However, we found three studies measuring production of cytokines ex vivo after ingestion of elderberry. Elderberry may not reduce the risk of developing the common cold; it may reduce the duration and severity of colds, but the evidence is uncertain. Elderberry may reduce the duration of influenza but the evidence is uncertain. Compared to oseltamivir, an elderberry-containing product may be associated with a lower risk of influenza complications and adverse events. We did not find evidence on elderberry and clinical outcomes related to inflammation. However, we found evidence that elderberry has some effect on inflammatory markers, although this effect may decline with ongoing supplementation. One small study compared elderberry to diclofenac (a nonsteroidal anti-inflammatory drug) and provided some evidence that elderberry is as effective or less effective than diclofenac in cytokine reduction over time.

Conclusions: Elderberry may be a safe option for treating viral respiratory illness, and there is no

Front Microbiol. 2019 Apr 24;10:867. doi: 10.3389/fmicb.2019.00867. eCollection 2019.

Effect of Quercetin Rich Onion Extracts on Bacterial Quorum Sensing

B X V Quecan [1], J T C Santos [1], M L C Rivera [1], N M A Hassimotto [1], F A Almeida [2], U M Pinto [1]

Affiliations

PMID: 31105665 PMCID: PMC6492534 DOI: 10.3389/fmicb.2019.00867

Free PMC article

Abstract

Quorum sensing (QS) regulates bacterial gene expression and studies suggest quercetin, a flavonol found in onion, as a QS inhibitor. There are no studies showing the anti-QS activity of plants containing quercetin in its native glycosylated forms. This study aimed to evaluate the antimicrobial and anti-QS potential of organic extracts of onion varieties and its representative phenolic compounds quercetin aglycone and quercetin 3-β-D-glucoside in the QS model bacteria *Chromobacterium violaceum* ATCC 12472, *Pseudomonas aeruginosa* PAO1, and *Serratia marcescens* MG1. Three phenolic extracts were obtained: red onion extract in methanol acidified with 2.5% acetic acid (RO-1), white onion extract in methanol (WO-1) and white onion extract in methanol ammonium (WO-2). Quercetin 4-*O*-glucoside and quercetin 3,4-*O*-diglucoside were identified as the predominant compounds in both onion varieties using HPLC-DAD and LC-ESI-MS/MS. However, quercetin aglycone, cyanidin 3-*O*-glucoside and quercetin glycoside were identified only in RO-1. The three extracts showed minimum inhibitory concentration (MIC) values equal to or above 125 μg/ml of dried extract. Violacein production was significantly reduced by RO-1 and quercetin aglycone, but not by quercetin 3-β-D-glucoside. Motility in *P. aeruginosa* PAO1 was inhibited by RO-1, while WO-2 inhibited *S. marcescens* MG1 motility only in high concentration. Quercetin aglycone and quercetin 3-β-D-glucoside were effective at inhibiting motility in *P. aeruginosa* PAO1 and *S. marcescens* MG1. Surprisingly, biofilm formation was not affected by any extracts or the quercetins tested at sub-MIC concentrations. *In silico* studies suggested a better interaction and placement of quercetin aglycone in the structures of the CviR protein of *C. violaceum* ATCC 12472 than the glycosylated compound which corroborates the better inhibitory effect of the former over violacein production. On the other hand, the two quercetins were well placed in the AHLs binding pockets of the LasR protein of *P. aeruginosa* PAO1. Overall onion extracts and quercetin presented antimicrobial activity, and interference on QS regulated production of violacein and swarming motility.

Keywords: antimicrobial activity; glycosylation; onion; phenolic compounds; quorum quenching; quorum sensing.

Randomized Controlled Trial Eur J Drug Metab Pharmacokinet. 2019 Apr;44(2):169-177.
doi: 10.1007/s13318-018-0517-3.

Improved Oral Absorption of Quercetin from Quercetin Phytosome®, a New Delivery System Based on Food Grade Lecithin

Antonella Riva [1], Massimo Ronchi [2], Giovanna Petrangolini [2], Stefania Bosisio [2], Pietro Allegrini [2]

Affiliations

PMID: 30328058 PMCID: PMC6418071 DOI: 10.1007/s13318-018-0517-3
Free PMC article

Abstract

Background and objectives: The importance of quercetin and flavonoids in the diet and as food supplements is well known, and literature studies support their potential use to treat several human diseases. Many beneficial properties have been described for quercetin, so much effort has been directed into overcoming the major drawbacks of this natural compound-its poor solubility and low oral absorption. The aims of this study were to compare a new food-grade lecithin-based formulation of quercetin, Quercetin Phytosome®, to unformulated quercetin in terms of solubility in simulated gastrointestinal fluids and oral absorption in a randomized crossover pharmacokinetic study of healthy volunteers.

Methods: The solubility of the new formulation was determined by in vitro incubation in simulated gastrointestinal fluids, and quercetin was detected by ultra performance liquid chromatography. A single-dose, randomized, six-sequence/three-period crossover clinical trial (3 × 3 × 3 crossover design) with a balanced carryover effect was conducted in healthy volunteers under fasting conditions. Twelve healthy volunteers of both sexes with an age range of 18-50 years were recruited; one dose of quercetin and two different doses of Quercetin Phytosome were administered orally as film-coated tablets. Pharmacokinetic samples were collected at twelve time points (from 0 h to 24 h) after administration, and quercetin levels were measured by HPLC/MS/MS. Data were analyzed using the Phoenix WinNonlin (v.6.4) software package, and the most significant pharmacokinetic parameters were calculated. Statistical analysis involved performing a two-way ANOVA with repeated measures followed by post hoc analysis (Tukey's test).

Results: Significant improvements in both in vitro solubility and oral absorption (in terms of both exposure and maximum concentration achieved) by healthy volunteers in a human clinical study were obtained with the Quercetin Phytosome formulation as compared to unformulated quercetin.

Conclusions: A more soluble formulation of quercetin based on lecithin, Quercetin Phytosome, has recently been developed, and was found to facilitate the attainment of very high plasma levels of

J Appl Microbiol. 2016 Apr;120(4):966-74. doi: 10.1111/jam.13073. Epub 2016 Mar 7.

Quercetin is an effective inhibitor of quorum sensing, biofilm formation and virulence factors in Pseudomonas aeruginosa

J Ouyang [1], F Sun [1], W Feng [1], Y Sun [1], X Qiu [1], L Xiong [1], Y Liu [1], Y Chen [1]

Affiliations
PMID: 26808465 DOI: 10.1111/jam.13073
Free article

Abstract

Aims: The study aimed to perform a systematic investigation of the effects of quercetin on biofilm formation and virulence factors in Pseudomonas aeruginosa.

Methods and results: The Ps. aeruginosa strain PAO1 was selected as the test strain. The results indicated that quercetin did not impact the growth of PAO1 as determined by MIC and growth curve analysis. However, this compound significantly inhibited ($P < 0{\cdot}05$) biofilm formation and production of virulence factors including pyocyanin, protease and elastase at a lower concentration than those for most previously reported plant extracts and substances. Considering the central role of quorum sensing (QS) in the regulation of biofilm and virulence factor, we further detected the transcriptional changes associated with QS and found that the expression levels of lasI, lasR, rhlI and rhlR were significantly reduced ($P < 0{\cdot}05$) by 34, 68, 57 and 50%, respectively, in response to 16 μg ml(-1) quercetin.

Conclusions: This study indicated that quercetin is an effective inhibitor of biofilm formation and virulence factors in Ps. aeruginosa.

Significance and impact of the study: This is the first study to demonstrate that quercetin is an effective inhibitor of QS, biofilm formation and virulence factors in Ps. aeruginosa. Furthermore, quercetin might have potential in fighting biofilm-related infections.

Keywords: Pseudomonas aeruginosa; biofilm; quercetin; quorum sensing; virulence factors.

Related information

PubChem Compound (MeSH Keyword)

Randomized Controlled Trial Int J Sport Nutr Exerc Metab. 2011 Aug;21(4):338-46.
doi: 10.1123/ijsnem.21.4.338.

The acute effect of ingesting a quercetin-based supplement on exercise-induced inflammation and immune changes in runners

Manuela Konrad [1], David C Nieman, Dru A Henson, Krista M Kennerly, Fuxia Jin, Sandra J Wallner-Liebmann

Affiliations
PMID: 21813917 DOI: 10.1123/ijsnem.21.4.338

Abstract

This study tested the acute anti-inflammatory and immune-modulating influence of a quercetin-based supplement consumed by endurance athletes 15 min before an intense 2-hr run. In this randomized, crossover study, 20 runners (11 men, 9 women, age 38.4 ± 2.1 yr) completed two 2-hr treadmill runs at 70% VO(2max) (3 wk apart). Subjects ingested either 4 quercetin-based chews (Q-chew) or placebo chews (PL) 15 min before the runs. The 4 Q-chews provided 1,000 mg quercetin, 120 mg epigallocatechin 3-gallate, 400 mg isoquercetin, 400 mg each eicosapentaenoic acid and docosahexaenoic acid, 1,000 mg vitamin C, and 40 mg niacinamide. Subjects provided blood samples 30 min before, immediately after, and 1 hr postexercise and were analyzed for plasma quercetin, total blood leukocytes (WBC), C-reactive protein (CRP), 9 cytokines (IL-6, TNFα, GM-CSF, IFNγ, IL-1β, IL-2, IL-8, IL-10, and IL-12p70), granulocyte (GR) and monocyte (MO) phagocytosis (PHAG), and oxidative-burst activity (OBA). Plasma quercetin increased from 80.0 ± 26.0 µg/L to 6,337 ± 414 µg/L immediately postexercise and 4,324 ± 310 µg/L 1 hr postexercise after ingestion of Q-chews, compared with no change in PL ($p < .001$). Exercise caused significant increases in, CRP, GM-CSF, IL-10, IL-1β, IL-2, IL-6, IL-8, TNFα, GR-PHAG, and MO-PHAG and decreases in GR-OBA and MO-OBA, but no differences in the pattern of change were measured between Q-chew and PL trials. Acute ingestion of Q-chews 15 min before heavy exertion caused a strong increase in plasma quercetin levels but did not counter postexercise inflammation or immune changes relative to placebo.

Related information

Cited in Books
MedGen
PubChem Compound
PubChem Compound (MeSH Keyword)
PubChem Substance

Review Nutrients. 2018 Sep 1;10(9):1203. doi: 10.3390/nu10091203.

Selenium, Selenoproteins, and Immunity

Joseph C Avery [1], Peter R Hoffmann [2]

Affiliations

PMID: 30200430 PMCID: PMC6163284 DOI: 10.3390/nu10091203

Free PMC article

Abstract

Selenium is an essential micronutrient that plays a crucial role in development and a wide variety of physiological processes including effect immune responses. The immune system relies on adequate dietary selenium intake and this nutrient exerts its biological effects mostly through its incorporation into selenoproteins. The selenoproteome contains 25 members in humans that exhibit a wide variety of functions. The development of high-throughput omic approaches and novel bioinformatics tools has led to new insights regarding the effects of selenium and selenoproteins in human immuno-biology. Equally important are the innovative experimental systems that have emerged to interrogate molecular mechanisms underlying those effects. This review presents a summary of the current understanding of the role of selenium and selenoproteins in regulating immune cell functions and how dysregulation of these processes may lead to inflammation or immune-related diseases.

Keywords: T cell; antibody; cancer; inflammation; macrophage; selenocysteine.

Figures

Figure 1 A summary of selenium and...

Int J Nanomedicine. 2021 Feb 18;16:1345-1360. doi: 10.2147/IJN.S292482. eCollection 2021.

Silver Nanoparticles Attenuate the Antimicrobial Activity of the Innate Immune System by Inhibiting Neutrophil-Mediated Phagocytosis and Reactive Oxygen Species Production

Moran Huang # [1], Kai Ye # [1], Tu Hu # [2], Kexin Liu [3], Mengzhen You [3], Lei Wang [1], Hui Qin [1]

Affiliations

PMID: 33633450 PMCID: PMC7901559 DOI: 10.2147/IJN.S292482

Free PMC article

Abstract

Purpose: Despite the extensive development of antibacterial biomaterials, there are few reports on the effects of materials on the antibacterial ability of the immune system, and in particular of neutrophils. In this study, we observe differences between the in vivo and in vitro anti-infective efficacies of silver nanoparticles (AgNPs). The present study was designed to further explore the mechanism for this inconsistency using ex vivo models and in vitro experiments.

Methods: AgNPs were synthesized using the polyol process and characterized by transmission electron microscopy and X-ray photoelectron spectroscopy. The antibacterial ability of AgNPs and neutrophils was tested by the spread-plate method. The infected air pouch model was prepared to detect the antimicrobial ability of AgNPs in vivo. Furthermore, blood-AgNPs-bacteria co-culture model and reactive oxygen species (ROS) measurement were used to evaluate the effect of AgNPs to neutrophil-mediated phagocytosis and ROS production.

Results: The antibacterial experiments in vitro showed that AgNPs had superior antibacterial properties in cell compatible concentration. While, AgNPs had no significant antibacterial effect in vivo, and pathological section in AgNPs group indicated less neutrophil infiltration in inflammatory site than *S. aureus* group. Furthermore, AgNPs were found to reduce the phagocytosis of neutrophils and inhibit their ability to produce ROS and superoxide during ex vivo and in vitro experiments.

Conclusion: This study selects AgNPs as the representative of inorganic nano-biomaterials and reveals the phenomenon and the mechanism underlying the significant AgNPs-induced inhibition of the antibacterial ability of neutrophils, and may have a certain enlightening effect on the development of biomaterials in the future. In the fabrication of antibacterial biomaterials, however, attention should be paid to both cell and immune system safety to make the antibacterial properties of the biomaterials and innate immune system complement each other and jointly promote the

Review Crit Rev Biochem Mol Biol. 2019 Apr;54(2):184-192.
doi: 10.1080/10409238.2019.1611734. Epub 2019 May 14.

Vitamin A and vitamin D regulate the microbial complexity, barrier function, and the mucosal immune responses to ensure intestinal homeostasis

Margherita T Cantorna [1 2], Lindsay Snyder [1 2], Juhi Arora [1 2]

Affiliations

PMID: 31084433 PMCID: PMC6629036 DOI: 10.1080/10409238.2019.1611734

Free PMC article

Abstract

Diet is an important regulator of the gastrointestinal microbiota. Vitamin A and vitamin D deficiencies result in less diverse, dysbiotic microbial communities and increased susceptibility to infection or injury of the gastrointestinal tract. The vitamin A and vitamin D receptors are nuclear receptors expressed by the host, but not the microbiota. Vitamin A- and vitamin D-mediated regulation of the intestinal epithelium and mucosal immune cells underlies the effects of these nutrients on the microbiota. Vitamin A and vitamin D regulate the expression of tight junction proteins on intestinal epithelial cells that are critical for barrier function in the gut. Other shared functions of vitamin A and vitamin D include the support of innate lymphoid cells that produce IL-22, suppression of IFN-γ and IL-17 by T cells, and induction of regulatory T cells in the mucosal tissues. There are some unique functions of vitamin A and D; for example, vitamin A induces gut homing receptors on T cells, while vitamin D suppresses gut homing receptors on T cells. Together, vitamin A- and vitamin D-mediated regulation of the intestinal epithelium and mucosal immune system shape the microbial communities in the gut to maintain homeostasis.

Keywords: Vitamin A; gastrointestinal tract; microbiota; mucosal immune system; nutrition; vitamin D.

Figures

Review Annu Rev Nutr. 2001;21:167-92. doi: 10.1146/annurev.nutr.21.1.167.

Vitamin A, infection, and immune function

C B Stephensen [1]

Affiliations

PMID: 11375434 DOI: 10.1146/annurev.nutr.21.1.167

Abstract

In populations where vitamin A availability from food is low, infectious diseases can precipitate vitamin A deficiency by decreasing intake, decreasing absorption, and increasing excretion. Infectious diseases that induce the acute-phase response also impair the assessment of vitamin A status by transiently depressing serum retinol concentrations. Vitamin A deficiency impairs innate immunity by impeding normal regeneration of mucosal barriers damaged by infection, and by diminishing the function of neutrophils, macrophages, and natural killer cells. Vitamin A is also required for adaptive immunity and plays a role in the development of T both-helper (Th) cells and B-cells. In particular, vitamin A deficiency diminishes antibody-mediated responses directed by Th2 cells, although some aspects of Th1-mediated immunity are also diminished. These changes in mucosal epithelial regeneration and immune function presumably account for the increased mortality seen in vitamin A-deficient infants, young children, and pregnant women in many areas of the world today.

Related information

LinkOut - more resources

Randomized Controlled Trial J Liposome Res. 2021 Dec;31(4):356-364.
doi: 10.1080/08982104.2020.1820521. Epub 2020 Oct 6.

Evaluation and clinical comparison studies on liposomal and non-liposomal ascorbic acid (vitamin C) and their enhanced bioavailability

Sreerag Gopi [1] [2], Preetha Balakrishnan [1]

Affiliations
PMID: 32901526 DOI: 10.1080/08982104.2020.1820521

Abstract

The aim of this study was to evaluate the oral bioavailability of liposomal vitamin C and non-liposomal vitamin C in healthy, adult, human subjects under fasting conditions through an open label, randomized, single-dose, two-treatment, two-sequence, two-period, two-way crossover, study. The vitamin C loaded liposome was well characterized using transmission electron microscopy (TEM), dynamic light scattering (DLS) and zeta potential measurements for evaluating morphology, particle size and stabilities, respectively. Microscopic image shows the core-type structure that confirms the characteristic pattern of liposome. The encapsulation efficiency (EE%) and the particle size were 65.85 ± 1.84% and below 100 nm, respectively. The results of the clinical studies of liposomal vitamin C by oral delivery to be 1.77 times more bioavailable than non-liposomal vitamin C. The liposomal vitamin C demonstrated higher values of C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ related to non-liposomal vitamin C due to liposomal encapsulation. No adverse events were reported. It could be concluded that liposomal encapsulated ascorbic acid (vitamin C) shows well-organized morphological pattern, uniform particle size and highly efficient, which leads to have enhanced bioavailability.

Keywords: Vitamin C; bioavailability; liposomes; nutraceuticals; pharmacokinetics.

Related information

PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources
Taylor & Francis

Medical
MedlinePlus Health Information

Review Nutrients. 2017 Nov 3;9(11):1211. doi: 10.3390/nu9111211.

Vitamin C and Immune Function

Anitra C Carr [1], Silvia Maggini [2]

Affiliations

PMID: 29099763 PMCID: PMC5707683 DOI: 10.3390/nu9111211

Free PMC article

Abstract

Vitamin C is an essential micronutrient for humans, with pleiotropic functions related to its ability to donate electrons. It is a potent antioxidant and a cofactor for a family of biosynthetic and gene regulatory enzymes. Vitamin C contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system. Vitamin C supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress. Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing. It is also needed for apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis/NETosis and potential tissue damage. The role of vitamin C in lymphocytes is less clear, but it has been shown to enhance differentiation and proliferation of B- and T-cells, likely due to its gene regulating effects. Vitamin C deficiency results in impaired immunity and higher susceptibility to infections. In turn, infections significantly impact on vitamin C levels due to enhanced inflammation and metabolic requirements. Furthermore, supplementation with vitamin C appears to be able to both prevent and treat respiratory and systemic infections. Prophylactic prevention of infection requires dietary vitamin C intakes that provide at least adequate, if not saturating plasma levels (i.e., 100-200 mg/day), which optimize cell and tissue levels. In contrast, treatment of established infections requires significantly higher (gram) doses of the vitamin to compensate for the increased inflammatory response and metabolic demand.

Keywords: ascorbate; ascorbic acid; immune system; immunity; infection; lymphocytes; microbial killing; neutrophil function; vitamin C.

Figures

Review Exp Biol Med (Maywood). 2014 Nov;239(11):1524-30.
doi: 10.1177/1535370214523890. Epub 2014 Mar 25.

Vitamin D, immune regulation, the microbiota, and inflammatory bowel disease

Margherita T Cantorna [1], Kaitlin McDaniel [2], Stephanie Bora [2], Jing Chen [2], Jamaal James [2]

Affiliations

PMID: 24668555 PMCID: PMC4176535 DOI: 10.1177/1535370214523890

Free PMC article

Abstract

The inflammatory bowel diseases are complex diseases caused by environmental, immunological, and genetic factors. Vitamin D status is low in patients with inflammatory bowel diseases, and experimental inflammatory bowel diseases are more severe in vitamin D-deficient or vitamin D receptor knockout animals. Vitamin D is beneficial in inflammatory bowel diseases because it regulates multiple checkpoints and processes essential for homeostasis in the gut. Vitamin D inhibits IFN-γ and IL-17 production while inducing regulatory T cells. In addition, vitamin D regulates epithelial cell integrity, innate immune responses, and the composition of the gut microbiota. Overall, vitamin D regulates multiple pathways that maintain gastrointestinal homeostasis. The data support improving vitamin D status in patients with inflammatory bowel diseases.

Keywords: Vitamin D; inflammatory bowel disease; microbiota.

Figures

Review J Int Med Res. 2012;40(1):28-42. doi: 10.1177/147323001204000104.

A combination of high-dose vitamin C plus zinc for the common cold

S Maggini [1], S Beveridge, M Suter

Affiliations

PMID: 22429343 DOI: 10.1177/147323001204000104

Free article

Abstract

Vitamin C and zinc play important roles in nutrition, immune defence and maintenance of health. Intake of both is often inadequate, even in affluent populations. The common cold continues to place a great burden on society in terms of suffering and economic loss. After an overview of the literature on the effects of the separate administration of either vitamin C or zinc against the common cold, this article presents data from two preliminary, double-blind, randomized, placebo-controlled trials, conducted with a combination of 1000 mg vitamin C plus 10 mg zinc in patients with the common cold. In both studies, a nonsignificant reduction of rhinorrhoea duration (range 9-27%) was seen. In pooled analyses of both studies (n=94), vitamin C plus zinc was significantly more efficient than placebo at reducing rhinorrhoea over 5 days of treatment. Furthermore, symptom relief was quicker and the product was well tolerated. In view of the burden associated with the common cold, supplementation with vitamin C plus zinc may represent an efficacious measure, with a good safety profile, against this infectious viral disease.

Related information

MedGen
PubChem Compound
PubChem Compound (MeSH Keyword)
PubChem Substance

LinkOut - more resources

Full Text Sources

Atypon

Medical

MedlinePlus Health Information

Review Am J Clin Nutr. 1998 Aug;68(2 Suppl):447S-463S. doi: 10.1093/ajcn/68.2.447S.

Zinc and immune function: the biological basis of altered resistance to infection

A H Shankar [1], A S Prasad

Affiliations
PMID: 9701160 DOI: 10.1093/ajcn/68.2.447S

Abstract

Zinc is known to play a central role in the immune system, and zinc-deficient persons experience increased susceptibility to a variety of pathogens. The immunologic mechanisms whereby zinc modulates increased susceptibility to infection have been studied for several decades. It is clear that zinc affects multiple aspects of the immune system, from the barrier of the skin to gene regulation within lymphocytes. Zinc is crucial for normal development and function of cells mediating nonspecific immunity such as neutrophils and natural killer cells. Zinc deficiency also affects development of acquired immunity by preventing both the outgrowth and certain functions of T lymphocytes such as activation, Th1 cytokine production, and B lymphocyte help. Likewise, B lymphocyte development and antibody production, particularly immunoglobulin G, is compromised. The macrophage, a pivotal cell in many immunologic functions, is adversely affected by zinc deficiency, which can dysregulate intracellular killing, cytokine production, and phagocytosis. The effects of zinc on these key immunologic mediators is rooted in the myriad roles for zinc in basic cellular functions such as DNA replication, RNA transcription, cell division, and cell activation. Apoptosis is potentiated by zinc deficiency. Zinc also functions as an antioxidant and can stabilize membranes. This review explores these aspects of zinc biology of the immune system and attempts to provide a biological basis for the altered host resistance to infections observed during zinc deficiency and supplementation.

Related information

Cited in Books
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources
Ovid Technologies, Inc.
Silverchair Information Systems

Other Literature Sources
The Lens - Patent Citations

Medical
ClinicalTrials.gov

Review Age (Dordr). 2013 Jun;35(3):839-60. doi: 10.1007/s11357-011-9377-3.
Epub 2012 Jan 6.

Zinc: dietary intake and impact of supplementation on immune function in elderly

Eugenio Mocchegiani [1], Javier Romeo, Marco Malavolta, Laura Costarelli, Robertina Giacconi, Ligia-Esperanza Diaz, Ascension Marcos

Affiliations

PMID: 22222917 PMCID: PMC3636409 DOI: 10.1007/s11357-011-9377-3
Free PMC article

Abstract

The diet in the elderly does not provide a sufficient level of nutrients needed to maintain an adequate healthy status leading to micronutrient deficiencies and impaired immune response with subsequent development of degenerative diseases. Nutrient "zinc" is a relevant micronutrient involved in maintaining a good integrity of many body homeostatic mechanisms, including immune efficiency, owing to its requirement for the biological activity of many enzymes, proteins and for cellular proliferation and genomic stability. Old people aged 60-65 years and older have zinc intakes below 50% of the recommended daily allowance on a given day. Many causes can be involved: among them, altered intestinal absorption, inadequate mastication, psychosocial factors, drugs interactions, altered subcellular processes (zinc transporters (Zip and ZnT family), metallothioneins, divalent metal transporter-1). Zinc supplementation may remodel the immune alterations in elderly leading to healthy ageing. Several zinc trials have been carried out with contradictory data, perhaps due to incorrect choice of an effective zinc supplementation in old subjects showing subsequent zinc toxic effects on immunity. Old subjects with specific IL-6 polymorphism (GG allele carriers; named C-) are more prone for zinc supplementation than the entire old population, in whom correct dietary habits with foods containing zinc (Mediterranean diet) may be sufficient in restoring zinc deficiency and impaired immune response. We summarise the main causes of low zinc dietary intake in elderly reporting an update on the impact of zinc supplementation upon the immune response also on the basis of individual IL-6 polymorphism.

Figures