

## **MANNOSIO**

J Urol. 1984 May;131(5):906-10.

### **Mannose-sensitive adherence of Escherichia coli to epithelial cells from women with recurrent urinary tract infections.**

Schaeffer AJ, Chmiel JS, Duncan JL, Falkowski WS.

#### **Abstract**

The effect of D-mannose on adherence of 73 Escherichia coli strains to vaginal and buccal epithelial cells from women with recurrent urinary tract infections, and on agglutination of human and guinea pig erythrocytes was tested. Urinary, vaginal or anal isolates from women with such infections were used. Of the strains 66 (90 per cent) demonstrated adherence to epithelial cells. D-mannose inhibited completely the adherence of 25 strains (42 per cent) that adhered to vaginal cells and inhibited an additional 11 strains (18 per cent) by at least 50 per cent. Similar results were obtained with buccal cells. The inhibitory effect of D-mannose was similar regardless of the origin of the strains. Hemagglutination frequently was inhibited by D-mannose but no consistent association between hemagglutination, and epithelial cell adherence and the effect of D-mannose was observed. The results suggest that mannose-sensitive as well as mannose-resistant adhesins frequently mediate Escherichia coli adherence to vaginal epithelial cells, and may contribute to vaginal colonization and cystitis.

World J Urol. 2014 Feb;32(1):79-84. doi: 10.1007/s00345-013-1091-6. Epub 2013 Apr 30.

**D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial.**

Kranjčec B, Papeš D, Altarac S.

**Abstract**

*PURPOSE:*

To test whether D-mannose powder is effective for recurrent urinary tract infection (UTI) prevention.

*MATERIALS AND METHODS:*

After initial antibiotic treatment of acute cystitis, 308 women with history of recurrent UTI and no other significant comorbidities were randomly allocated to three groups. The first group (n = 103) received prophylaxis with 2 g of D-mannose powder in 200 ml of water daily for 6 months, the second (n = 103) received 50 mg Nitrofurantoin daily, and the third (n = 102) did not receive prophylaxis.

*RESULTS:*

Overall 98 patients (31.8%) had recurrent UTI: 15 (14.6) in the D-mannose group, 21 (20.4) in Nitrofurantoin group, and 62 (60.8) in no prophylaxis group, with the rate significantly higher in no prophylaxis group compared to active groups ( $P < 0.001$ ). Patients in D-mannose group and Nitrofurantoin group had a significantly lower risk of recurrent UTI episode during prophylactic therapy compared to patients in no prophylaxis group (RR 0.239 and 0.335,  $P < 0.0001$ ). In active groups, 17.9% of patients reported side effects but they were mild and did not require stopping the prophylaxis. Patients in D-mannose group had a significantly lower risk of side effects compared to patients in Nitrofurantoin group (RR 0.276,  $P < 0.0001$ ), but the clinical importance of this finding is low because Nitrofurantoin was well tolerated.

*CONCLUSIONS:*

In our study, D-mannose powder had significantly reduced the risk of recurrent UTI which was no different than in Nitrofurantoin group. More studies will be needed to validate the results of this study, but initial findings show that D-mannose may be useful for UTI prevention.

## CRANBERRY

Arch Intern Med. 2012 Jul 9;172(13):988-96. doi: 10.1001/archinternmed.2012.3004.

### **Cranberry-containing products for prevention of urinary tract infections in susceptible populations: a systematic review and meta-analysis of randomized controlled trials.**

Wang CH, Fang CC, Chen NC, Liu SS, Yu PH, Wu TY, Chen WT, Lee CC, Chen SC.

#### Abstract

##### *BACKGROUND:*

Urinary tract infection (UTI) is one of the most commonly acquired bacterial infections. Cranberry-containing products have long been used as a folk remedy to prevent UTIs. The aims of this study were to evaluate cranberry-containing products for the prevention of UTI and to examine the factors influencing their effectiveness.

##### *METHODS:*

MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were systemically searched from inception to November 2011 for randomized controlled trials that compared prevention of UTIs in users of cranberry-containing products vs placebo or nonplacebo controls. There were no restrictions for language, population, or publication year.

##### *RESULTS:*

Thirteen trials, including 1616 subjects, were identified for qualitative synthesis from 414 potentially relevant references; 10 of these trials, including a total of 1494 subjects, were further analyzed in quantitative synthesis. The random-effects pooled risk ratio (RR) for cranberry users vs nonusers was 0.62 (95% CI, 0.49-0.80), with a moderate degree of heterogeneity ( $I(2) = 43\%$ ) after the exclusion of 1 outlier study. On subgroup analysis, cranberry-containing products seemed to be more effective in several subgroups, including women with recurrent UTIs (RR, 0.53; 95% CI, 0.33-0.83) ( $I(2) = 0\%$ ), female populations (RR, 0.49; 95% CI, 0.34-0.73) ( $I(2) = 34\%$ ), children (RR, 0.33; 95% CI, 0.16-0.69) ( $I(2) = 0\%$ ), cranberry juice drinkers (RR, 0.47; 95% CI, 0.30-0.72) ( $I(2) = 2\%$ ), and subjects using cranberry-containing products more than twice daily (RR, 0.58; 95% CI, 0.40-0.84) ( $I(2) = 18\%$ ).

##### *CONCLUSIONS:*

Our findings indicate that cranberry-containing products are associated with protective effect against UTIs. However, this result should be interpreted in the context of substantial heterogeneity across trials.

Antiviral Res. 2016 Aug;132:154-64. doi: 10.1016/j.antiviral.2016.06.006. Epub 2016 Jun 16.

**Inhibition of herpes simplex type 1 and type 2 infections by Oximacro(®), a cranberry extract with a high content of A-type proanthocyanidins (PACs-A).**

Terlizzi ME, Occhipinti A, Luganini A, Maffei ME, Gribaudo G.

**Abstract**

In the absence of efficient preventive vaccines, topical microbicides offer an attractive alternative in the prevention of Herpes simplex type 1 (HSV-1) and type 2 (HSV-2) infections. Because of their recognized anti-adhesive activity against bacterial pathogens, cranberry (*Vaccinium macrocarpon* Ait.) extracts may represent a natural source of new antiviral microbicides. However, few studies have addressed the applications of cranberry extract as a direct-acting antiviral agent. Here, we report on the ability of the novel cranberry extract Oximacro(®) and its purified A-type proanthocyanidins (PACs-A), to inhibit HSV-1 and HSV-2 replication *in vitro*. Analysis of the mode of action revealed that Oximacro(®) prevents adsorption of HSV-1 and HSV-2 to target cells. Further mechanistic studies confirmed that Oximacro(®) and its PACs-A target the viral envelope glycoproteins gD and gB, thus resulting in the loss of infectivity of HSV particles. Moreover, Oximacro(®) completely retained its anti-HSV activity even at acidic pHs (3.0 and 4.0) and in the presence of 10% human serum proteins; conditions that mimic the physiological properties of the vagina - a potential therapeutic location for Oximacro(®). Taken together, these findings indicate Oximacro(®) as an attractive candidate for the development of novel microbicides of natural origin for the prevention of HSV infections.

J Urol. 2007 Jun;177(6):2357-60.

**Cranberry products inhibit adherence of p-fimbriated Escherichia coli to primary cultured bladder and vaginal epithelial cells.**

Gupta K, Chou MY, Howell A, Wobbe C, Grady R, Stapleton AE.

AbstractL2

**PURPOSE:**

Cranberry proanthocyanidins have been identified as possible inhibitors of Escherichia coli adherence to uroepithelial cells. However, little is known about the dose range of this effect. Furthermore, it has not been studied directly in the urogenital system. To address these issues we tested the effect of a cranberry powder and proanthocyanidin extract on adherence of a P-fimbriated uropathogenic E. coli isolate to 2 new urogenital model systems, namely primary cultured bladder epithelial cells and vaginal epithelial cells.

**MATERIALS AND METHODS:**

E. coli IA2 was pre-incubated with a commercially available cranberry powder (9 mg proanthocyanidin per gm) or with increasing concentrations of proanthocyanidin extract. Adherence of E. coli IA2 to primary cultured bladder epithelial cells or vaginal epithelial cells was measured before and after exposure to these products.

**RESULTS:**

Cranberry powder decreased mean adherence of E. coli IA2 to vaginal epithelial cells from 18.6 to 1.8 bacteria per cell ( $p < 0.001$ ). Mean adherence of E. coli to primary cultured bladder epithelial cells was decreased by exposure to 50 mug/ml proanthocyanidin extract from 6.9 to 1.6 bacteria per cell ( $p < 0.001$ ). Inhibition of adherence of E. coli by proanthocyanidin extract occurred in linear, dose dependent fashion over a proanthocyanidin concentration range of 75 to 5 mug/ml.

**CONCLUSIONS:**

Cranberry products can inhibit E. coli adherence to biologically relevant model systems of primary cultured bladder and vaginal epithelial cells. This effect occurs in a dose dependent relationship. These findings provide further mechanistic evidence and biological plausibility for the role of cranberry products for preventing urinary tract infection.

J Obstet Gynaecol Can. 2010 Nov;32(11):1082-101.

**Recurrent urinary tract infection.**

Epp A, Larochelle A, Lovatsis D, Walter JE, Easton W, Farrell SA, Girouard L, Gupta C, Harvey MA, Robert M, Ross S, Schachter J, Schulz JA, Wilkie D, Ehman W, Domb S, Gagnon A, Hughes O, Konkin J, Lynch J, Marshall C, Society of Obstetricians and Gynaecologists of Canada.

**Abstract**

**OBJECTIVE:**

to provide an update of the definition, epidemiology, clinical presentation, investigation, treatment, and prevention of recurrent urinary tract infections in women.

**OPTIONS:**

continuous antibiotic prophylaxis, post-coital antibiotic prophylaxis, and acute self-treatment are all efficient alternatives to prevent recurrent urinary tract infection. Vaginal estrogen and cranberry juice can also be effective prophylaxis alternatives.

**EVIDENCE:**

a search of PubMed and The Cochrane Library for articles published in English identified the most relevant literature. Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies. There were no date restrictions.

**VALUES:**

this update is the consensus of the Sub-Committee on Urogynaecology of the Society of Obstetricians and Gynaecologists of Canada. Recommendations were made according to the guidelines developed by the Canadian Task Force on Preventive Health Care (Table 1).

**OPTIONS:**

recurrent urinary tract infections need careful investigation and can be efficiently treated and prevented. Different prophylaxis options can be selected according to each patient's characteristics.

J Am Geriatr Soc. 2014 Jan;62(1):103-10.

**Effectiveness of cranberry capsules to prevent urinary tract infections in vulnerable older persons: a double-blind randomized placebo-controlled trial in long-term care facilities.**

Caljouw MA, van den Hout WB, Putter H, Achterberg WP, Cools HJ, Gussekloo J.

**Abstract**

**OBJECTIVES:**

To determine whether cranberry capsules prevent urinary tract infection (UTI) in long-term care facility (LTCF) residents.

**DESIGN:**

Double-blind randomized placebo-controlled multicenter trial.

**SETTING:**

Long-term care facilities (LTCFs).

**PARTICIPANTS:**

LTCF residents (N = 928; 703 women, median age 84).

**MEASUREMENTS:**

Cranberry and placebo capsules were taken twice daily for 12 months. Participants were stratified according to UTI risk (risk factors included long-term catheterization, diabetes mellitus,  $\geq 1$  UTI in preceding year). Main outcomes were incidence of UTI according to a clinical definition and a strict definition.

**RESULTS:**

In participants with high UTI risk at baseline (n = 516), the incidence of clinically defined UTI was lower with cranberry capsules than with placebo (62.8 vs 84.8 per 100 person-years at risk, P = .04); the treatment effect was 0.74 (95% confidence interval (CI) = 0.57-0.97). For the strict definition, the treatment effect was 1.02 (95% CI = 0.68-1.55). No difference in UTI incidence between cranberry and placebo was found in participants with low UTI risk (n = 412).

**CONCLUSION:**

In LTCF residents with high UTI risk at baseline, taking cranberry capsules twice daily reduces the incidence of clinically defined UTI, although it does not reduce the incidence of strictly defined UTI. No difference in incidence of UTI was found in residents with low UTI risk.

Adv. Nutr. 2013

## **Cranberries and Their Bioactive Constituents in Human Health**

Jeffrey B. Blumberg, Terri A. Camesano, Aedin Cassidy, Penny Kris-Etherton, Amy Howell, Claudine Manach, Luisa M. Ostertag, Helmut Sies, Ann Skulas-Ray, and Joseph A. Vita

### **Abstract**

Recent observational and clinical studies have raised interest in the potential health effects of cranberry consumption, an association that appears to be due to the phytochemical content of this fruit. The profile of cranberry bioactives is distinct from that of other berry fruit, being rich in A-type proanthocyanidins (PACs) in contrast to the B-type PACs present in most other fruit. Basic research has suggested a number of potential mechanisms of action of cranberry bioactives, although further molecular studies are necessary. Human studies on the health effects of cranberry products have focused principally on urinary tract and cardiovascular health, with some attention also directed to oral health and gastrointestinal epithelia. Evidence suggesting that cranberries may decrease the recurrence of urinary tract infections is important because a nutritional approach to this condition could lower the use of antibiotic treatment and the consequent development of resistance to these drugs. There is encouraging, but limited, evidence of a cardioprotective effect of cranberries mediated via actions on antioxidant capacity and lipoprotein profiles. The mixed outcomes from clinical studies with cranberry products could result from interventions testing a variety of products, often uncharacterized in their composition of bioactives, using different doses and regimens, as well as the absence of a biomarker for compliance to the protocol. Daily consumption of a variety of fruit is necessary to achieve a healthy dietary pattern, meet recommendations for micronutrient intake, and promote the intake of a diversity of phytochemicals. Berry fruit, including cranberries, represent a rich source of phenolic bioactives that may contribute to human health.



**Inhibition of *Escherichia coli* CFT073 *fliC* expression and motility by cranberry materials.**

Hidalgo G, Chan M, Tufenkji N.

**Abstract**

In humans, uropathogenic *Escherichia coli* (UPEC) is the most common etiological agent of uncomplicated urinary tract infections (UTIs). Cranberry extracts have been linked to the prevention of UTIs for over a century; however, a mechanistic understanding of the way in which cranberry derivatives prevent bacterial infection is still lacking. In this study, we used a *fliC*-lux reporter as well as quantitative reverse transcription-PCR to demonstrate that when UPEC strain CFT073 was grown or exposed to dehydrated, crushed cranberries or to purified cranberry-derived proanthocyanidins (cPACs), expression of the flagellin gene (*fliC*) was inhibited. In agreement with these results, transmission electron microscopy imaging of bacteria grown in the presence of cranberry materials revealed fewer flagella than those in bacteria grown under control conditions. Furthermore, we showed that swimming and swarming motilities were hindered when bacteria were grown in the presence of the cranberry compounds. Because flagellum-mediated motility has been suggested to enable UPEC to disseminate to the upper urinary tract, we propose that inhibition of flagellum-mediated motility might be a key mechanism by which cPACs prevent UTIs. This is the first report to show that cranberry compounds inhibit UPEC motility via downregulation of the *fliC* gene. Further studies are required to establish whether these inhibitors play a role *in vivo*.

## **ESTRATTO DEI SEMI DI POMPELMO (GRAPEFRUIT SEED EXTRACT)**

universityhealthnews.com

### **7 Grapefruit Seed Extract Uses, Plus Dangers to Watch Out For**

Grapefruit seed extract uses are numerous due to its action as a highly concentrated, natural general antimicrobial and antioxidant. Grapefruit seed extract benefits include killing all kinds of infectious microbes—bacterial, viral, and fungal—at least in test tube and animal studies.

#### **What's in grapefruit seed extract?**

The main compounds in grapefruit seeds thought to be responsible for its ability to kill infectious agents are chemical compounds (polyphenols) known as limonoids and naringenin.

These intensely powerful compounds act as antimicrobials and antioxidants, not only killing dangerous microbes but protecting the body's tissues against the excessive production of reactive oxygen species which occurs when these pathogens infect the tissues.

Grapefruit seed extract comes in a number of different delivery forms, concentrations, and dosages. Liquids and/or capsules can be used whether the infection is on the skin; in the ears, nose, or mouth; or in the gastrointestinal tract. Grapefruit seed extract is also used as a preservative and antimicrobial in natural personal care products as well as by the food industry for food preservation.

#### **Warnings about grapefruit seed extract**

Grapefruit juice and possibly other grapefruit products, including grapefruit seed extract, are known to interact with certain drugs and may lead to serious adverse reactions. Grapefruit inhibits certain enzyme systems within the body most often involved in drug metabolism. This increases blood concentrations of the drugs concerned, creating a risk of overdose and dose-dependent adverse effects. Grapefruit seed extract can sometimes cause skin irritation when used topically. The liquid grapefruit seed concentrates should always be diluted; never use full strength and avoid contact with eyes or other sensitive areas.

Also, in a report published in 2012, investigators from the Austin, Texas-based American Botanical Council found that many grapefruit seed extract products on the market today contain synthetic chemicals that aren't listed on their labels. They report that any antimicrobial activities in grapefruit seed extract products is likely due to these synthetic additives, and not the grapefruit seed extract itself. Since the actual amount of these unlisted chemicals could vary widely and are unapproved compounds for internal use, some natural health practitioners recommend not taking GSE products internally. If you're considering the use of grapefruit seed extract in treatment of a chronic condition, make sure to consult your physician.

#### **How to take grapefruit seed extract internally to fight infections**

Grapefruit seed extract concentrated liquid and capsules should not be taken by children except under a doctor's supervision. Adults can mix 10 drops of the liquid concentrate into a glass of water or juice (5 oz. or more) and drink, 1-3 times daily, with or without meals. Note that grapefruit seed extract is extremely bitter. To avoid the bitter taste, adults may also take one to two 250 mg capsules one to two times daily with or without meals.

Grapefruit seed extract can deplete normal flora (healthy “good” bacteria) in the gut when taken long-term. If you plan to take GSE for 3 days or more, it’s important to consume a probiotic supplement two hours before taking your GSE dose.

Grapefruit seed extract benefits include killing candida and treating digestive symptoms

Grapefruit seed extract is perhaps best known for its ability to treat digestive disturbances and kill pathogens, especially fungal pathogens like *Candida albicans*, in the gastrointestinal tract. One preliminary human trial investigated the effectiveness of grapefruit seed extract in people with symptoms of irritable bowel syndrome (IBS) and eczema. Subjects received either 2 drops of a 0.5% liquid concentrate of grapefruit seed extract twice a day or 150 mg of encapsulated grapefruit seed extract (ParaMicrocidin®) three times a day.

After a month, all of the subjects taking capsules experienced significant improvements in constipation, flatulence, and abdominal discomfort, as well as night rest, while 20% of the subjects taking the liquid experienced significant improvements in their IBS symptoms. There were no side effects. The fact that these patients’ digestive symptoms improved with grapefruit seed extract suggests that they actually had an infection in the gastrointestinal tract that was causing their symptoms rather than IBS. And in fact, the researchers tested the extract against different intestinal pathogens and found it was most effective against *Candida* species, a type of fungal infection, and some types of parasites.

J Altern Complement Med. 2002 Jun;8(3):333-40.

**The effectiveness of processed grapefruit-seed extract as an antibacterial agent: II. Mechanism of action and in vitro toxicity.**

Heggors JP, Cottingham J, Gusman J, Reagor L, McCoy L, Carino E, Cox R, Zhao JG.

Abstract

**OBJECTIVES:**

Recent testimonials report grapefruit-seed extract, or GSE (Citricidal) to be effective against more than 800 bacterial and viral strains, 100 strains of fungus, and a large number of single and multicelled parasites. This study investigated GSE for antibacterial activity at varying time intervals and concentration levels and tissue toxicity at varying concentrations in an effort to determine if a concentration existed that was both microbicidal and nontoxic and in what period of time.

**DESIGN:**

Gram-negative and gram-positive isolates were introduced into graduated dilutions of GSE (twofold concentrations ranging from 1:1, through 1:512) for determination of bacterial activity. In vitro assays with human skin fibroblast cells were also performed at the same dilutions to determine toxicity.

**RESULTS:**

These tests indicated that from the 1:1 through the 1:128 concentrations, GSE remained toxic as well as bactericidal. However, test results indicated that at the 1:512 dilution, GSE remained bactericidal, but completely nontoxic.

**CONCLUSIONS:**

The initial data shows GSE to have antimicrobial properties against a wide range of gram-negative and gram-positive organisms at dilutions found to be safe. With the aid of scanning transmission electron microscopy (STEM), the mechanism of GSE's antibacterial activity was revealed. It was evident that GSE disrupts the bacterial membrane and liberates the cytoplasmic contents within 15 minutes after contact even at more dilute concentrations.

## **BACILLUS COAGULANS**

Indian J Microbiol. 2012 Sep;52(3):396-9. doi: 10.1007/s12088-011-0233-z. Epub 2011 Sep 23.

### **Clinical Study of Bacillus coagulans Unique IS-2 (ATCC PTA-11748) in the Treatment of Patients with Bacterial Vaginosis.**

Ratna Sudha M, Yelikar KA, Deshpande S.

#### **Abstract**

Bacterial vaginosis (BV) is the most prevalent vaginal infection worldwide and is characterized by reduction of native lactobacilli. Antimicrobial therapy used to cure the disease is often found to be ineffective. We postulate that *Bacillus coagulans* Unique IS-2 (Unique Biotech Limited, India) might provide an appendage to antimicrobial treatment and improve curing rate. In the present study 40 Indian women diagnosed with BV by the presence of symptoms including white discharge, pH greater than 4.7, burning micturation, itching, soreness and redness at vulva. The subjects were divided in 2 groups probiotic (n = 20) and control (n = 20) based on age (control group,  $33 \pm 3$  years and probiotic group,  $32.5 \pm 3$  years), history of previous vaginosis (control group, 75% or 15/20 and probiotic group, 75% or 15/20) and severity of current vaginosis infection (burning micturation and itching, 35% in each group). Probiotic group subjects were assigned to receive a dose of antibiotic therapy [Ofloxacin-Ornidazole with strength of 200-500 mg per capsule/day for 5 days along with vaginal peccaries (co-kimaxazol) for 3 days] simultaneously with two probiotic capsules (10<sup>9</sup> CFUs of *Bacillus coagulans* Unique IS-2 per capsule). The control group received only antibiotic therapy. At the end of the treatment the 80% of probiotic group subjects showed significant positive response as revealed by reduction of vaginosis symptoms compared to the control group which exhibited reduction in 45% subjects only. Thus, the results of present study indicate that strain *Bacillus coagulans* Unique IS-2 can provide benefits to women being treated with antibiotics to cure an infectious condition.

Altern Med Rev. 2012 Mar;17(1):76-81.  
**Bacillus coagulans: Monograph.**  
Jurenka JS.

### **Vaginitis**

Vaginal administration of a commercial formulation of *B. coagulans* tablets called Myconip<sup>®</sup> was given to 44 women with non-specific vaginitis twice daily for 14 days. Total CFUs per tablet was not specified. Subjects with *Trichomonas* or *Candida* vaginitis were excluded from the study. Complete relief of pruritis and discharge was reported by 91 percent of subjects. These results were thought to be due to a beneficial change in vaginal acidity via lactic acid production by *B. coagulans*. Postmenopausal subjects had a slower response to therapy but eventually had complete relief as well.<sup>29</sup>

## VITAMINA C

Mini Rev Med Chem. 2014 May;14(5):444-52.

### **Ascorbic acid: its role in immune system and chronic inflammation diseases.**

Sorice A, Guerriero E, Capone F, Colonna G, Castello G, Costantini S.

#### Abstract

Ascorbic acid (AA), also known as vitamin C, was initially identified as the factor preventing the scurvy disease, and became very popular for its antioxidant properties. It is an important co-substrate of a large class of enzymes, and regulates gene expression by interacting with important transcription factors. AA is important in all stressful conditions that are linked to inflammatory processes and involve immunity. It has been known for decades that the persistence of an inflammatory stimulus is responsible for the onset of many diseases. AA is essential to stimulate the immune system by increasing the strength and protection of the organism. Therefore, its immunostimulant, anti-inflammatory, antiviral and antibacterial roles are well known, we have summarized its main functions in different types of diseases related to the immune system and chronic inflammation. We can conclude that AA, due to its effects and diversity of regulated pathways, is suitable for use in various fields of medicine including immunology, toxicology, radiobiology and others. AA is not preferable to be used as an isolated mode of treatment, but it can be co-applied as an adjuvant to regulate immunity, gene expression and other important physiological processes. However, we propose that future studies will take into consideration the research of new combinations of antioxidant natural substances and drugs.

Indian J Clin Biochem. 2013 Oct;28(4):314-28. doi: 10.1007/s12291-013-0375-3. Epub 2013 Sep 1.

**Vitamin C in disease prevention and cure: an overview.**

Chambial S, Dwivedi S, Shukla KK, John PJ, Sharma P.

**Abstract**

The recognition of vitamin C is associated with a history of an unrelenting search for the cause of the ancient haemorrhagic disease scurvy. Isolated in 1928, vitamin C is essential for the development and maintenance of connective tissues. It plays an important role in bone formation, wound healing and the maintenance of healthy gums. Vitamin C plays an important role in a number of metabolic functions including the activation of the B vitamin, folic acid, the conversion of cholesterol to bile acids and the conversion of the amino acid, tryptophan, to the neurotransmitter, serotonin. It is an antioxidant that protects body from free radical damage. It is used as therapeutic agent in many diseases and disorders. Vitamin C protects the immune system, reduces the severity of allergic reactions and helps to fight off infections. However the significance and beneficial effect of vitamin C in respect to human disease such as cancer, atherosclerosis, diabetes, neurodegenerative disease and metal toxicity however remains equivocal. Thus further continuous uninterrupted efforts may open new vistas to understand its significance in disease management.



## ZINCO

J Immunol Res. 2016;2016:6762343. Epub 2016 Oct 31.

### **Roles of Zinc Signaling in the Immune System.**

Hojyo S, Fukada T.

#### Abstract

Zinc (Zn) is an essential micronutrient for basic cell activities such as cell growth, differentiation, and survival. Zn deficiency depresses both innate and adaptive immune responses. However, the precise physiological mechanisms of the Zn-mediated regulation of the immune system have been largely unclear. Zn homeostasis is tightly controlled by the coordinated activity of Zn transporters and metallothioneins, which regulate the transport, distribution, and storage of Zn. There is growing evidence that Zn behaves like a signaling molecule, facilitating the transduction of a variety of signaling cascades in response to extracellular stimuli. In this review, we highlight the emerging functional roles of Zn and Zn transporters in immunity, focusing on how crosstalk between Zn and immune-related signaling guides the normal development and function of immune cells.

Arch Biochem Biophys. 2016 Dec 1;611:58-65. doi: 10.1016/j.abb.2016.03.022. Epub 2016 Mar 26.

**Zinc and immunity: An essential interrelation.**

Maares M, Haase H.

**Abstract**

The significance of the essential trace element zinc for immune function has been known for several decades. Zinc deficiency affects immune cells, resulting in altered host defense, increased risk of inflammation, and even death. The micronutrient zinc is important for maintenance and development of immune cells of both the innate and adaptive immune system. A disrupted zinc homeostasis affects these cells, leading to impaired formation, activation, and maturation of lymphocytes, disturbed intercellular communication via cytokines, and weakened innate host defense via phagocytosis and oxidative burst. This review outlines the connection between zinc and immunity by giving a survey on the major roles of zinc in immune cell function, and their potential consequences in vivo.

## SELENIO

The Lancet, Volume 356, Issue 9225, 15 July 2000, Pages 233–241

### **The importance of selenium to human health**

Margaret P Rayman, DPhil

#### *Summary*

The essential trace mineral, selenium, is of fundamental importance to human health. As a constituent of selenoproteins, selenium has structural and enzymic roles, in the latter context being best-known as an antioxidant and catalyst for the production of active thyroid hormone. Selenium is needed for the proper functioning of the immune system, and appears to be a key nutrient in counteracting the development of virulence and inhibiting HIV progression to AIDS. It is required for sperm motility and may reduce the risk of miscarriage. Deficiency has been linked to adverse mood states. Findings have been equivocal in linking selenium to cardiovascular disease risk although other conditions involving oxidative stress and inflammation have shown benefits of a higher selenium status. An elevated selenium intake may be associated with reduced cancer risk. Large clinical trials are now planned to confirm or refute this hypothesis. In the context of these health effects, low or diminishing selenium status in some parts of the world, notably in some European countries, is giving cause for concern.

Canadian Journal of Dietetic Practice and Research, 2005, 66(2): 98-102, 10.3148/66.2.2005.98

### **The Relevance of Selenium to Immunity, Cancer, and Infectious/Inflammatory Diseases**

Milly Ryan-Harshman PhD, RD, Walid Aldoori MB, BCh, MPA, ScD

#### **Abstract**

Selenium is an essential trace element involved in several key metabolic activities via selenoproteins, enzymes that are essential to protect against oxidative damage and to regulate immune function. Selenium also may have other health benefits unrelated to its enzymatic functions. It may provide important health benefits to people whose oxidative stress loads are high, such as those with inflammatory or infectious diseases like rheumatoid arthritis or human immunodeficiency virus/acquired immunodeficiency syndrome, or who are at high risk for cancers, particularly prostate cancer. Some studies have generated compelling evidence that selenium is beneficial, either alone or in conjunction with other micronutrients. Additional data from large clinical trials that provide the highest level of evidence will be key to determining the benefits accrued at various selenium intake levels. When the strength of the evidence becomes sufficient, clinical health professionals will need to use dietary and clinical assessment methods to ensure that people at increased risk for cancer or inflammatory and infectious diseases can be appropriately advised about selenium intake.