

APPLICAZIONI NUTRACEUTICHE E A BASE DI ESTRATTI VEGETALI PER LA CORRETTA FISIOLOGIA DEL SISTEMA IMMUNITARIO

Dott. Giovanni Corbioli

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Domenica 25 Febbraio 2024

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PARTE 1

Supporti quotidiani. Vitamine e Minerali.

PARTE 2

Rimedi dal Mondo Vegetale.

PARTE 3

Strategie per il recupero fisico.

PARTE 4

Supporti per specifiche condizioni e altri nutrienti.



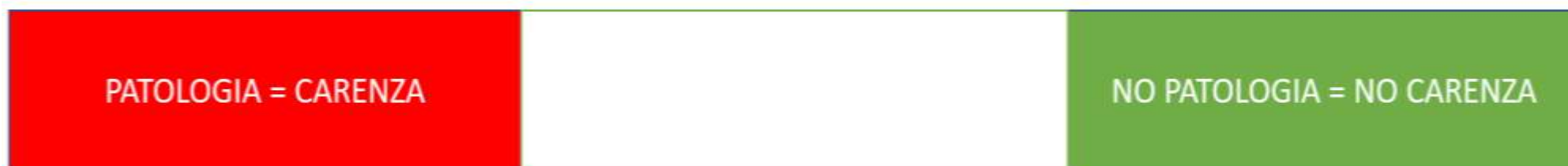


PARTE 1

Supporti quotidiani. Vitamine e Minerali.

Le microcarenze croniche

In passato:



Ora:



Valori non così bassi da evidenziare una patologia, ma abbastanza bassi da portare a possibili alterazioni alla fisiologia dell'organismo (metabolismo, funzione immunitaria, funzione ormonale...)

"Un'adeguata assunzione di
vitamine della longevità
è in grado di prolungare le
aspettative per una vita sana"

Bruce Ames (PhD), autore dell'articolo pubblicato ad ottobre del 2018 "*Prolonging healthy aging: Longevity vitamins and proteins*" (*Prolungamento dell'invecchiamento sano: vitamine e proteine della longevità*), scritto in seguito a decenni di ricerche nel suo laboratorio presso il CHORI (Children's Hospital Oakland Research Institute) in collaborazione con l'università della California San Francisco (UCSF).

Bruce Ames



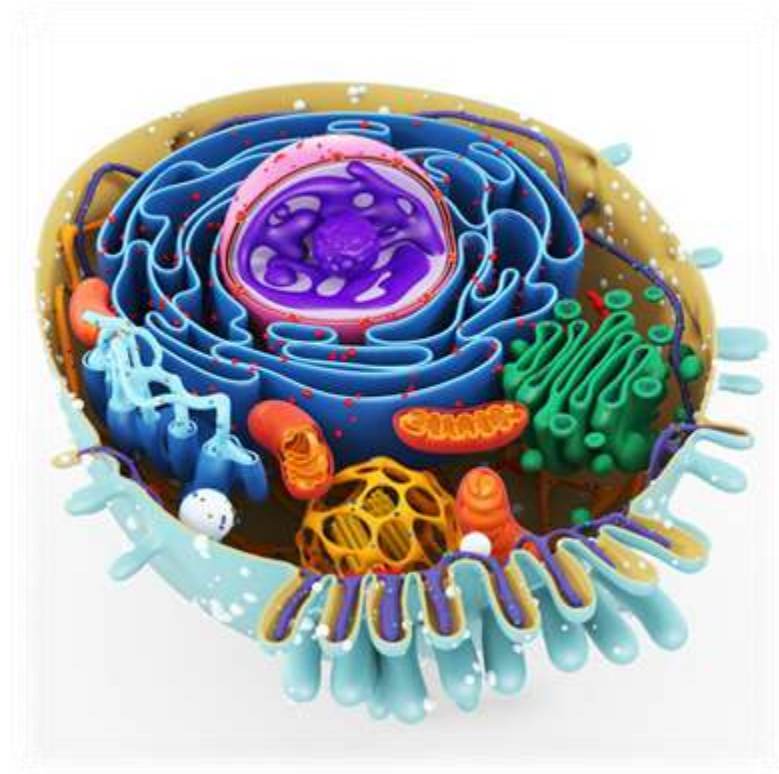
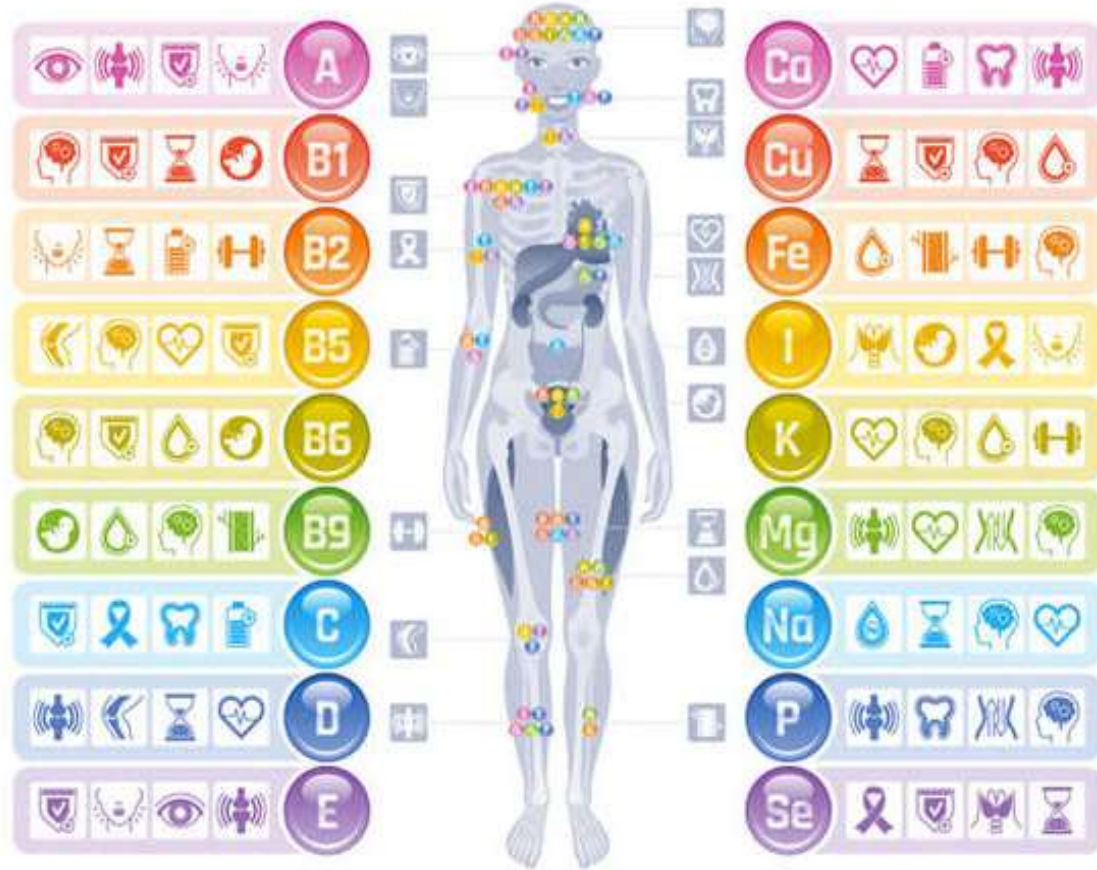
Ames in 2003

Born	Bruce Nathan Ames December 16, 1928 (age 95) ^[1] New York City, U.S
Nationality	American
Alma mater	California Institute of Technology , Cornell University
Known for	Ames test

Vitamine

Benefici

Minerali



Review > Nutrition. 2017 Apr;36:60-66. doi: 10.1016/j.nut.2016.06.003. Epub 2016 Jun 16.

Multivitamin/mineral supplements: Rationale and safety

Hans K Biesalski ¹, Jana Tinz ²

Affiliations + expand

PMID: 28336109 DOI: 10.1016/j.nut.2016.06.003

Abstract

Multivitamin/mineral supplements (MVMs) are widely used in many populations. MVMs, together with iron and folic acid, are recommended for pregnant women to improve birth outcome and to reduce low-birthweight and rates of miscarriage. However, MVM use is common in the general population as well. The aim of the present review was to evaluate the safety of long-term use of these supplements. To examine the safety of MVM use, we performed a literature search for randomized controlled studies involving supplementation with a combination of at least nine vitamins and three minerals at a maximum concentration of 100% of the Recommended Dietary Allowance. We found nine studies evaluating the use and efficacy of MVMs in pregnant women and healthy adults and six studies in the elderly where adverse effects were explicitly addressed. Only minor adverse events (e.g., unspecific gastrointestinal symptoms) were reported in all studies. In particular, there were no significant differences between treatment and placebo groups. MVM use within the range of the Dietary Reference Intake will not result in excess intake, even when including the effect of food and fortified food, and does not increase mortality. Taken together, these findings indicate that MVMs can be safe for long-term use (>10 y).

Vitamina C e Sistema Immunitario



Review

Vitamin C and Immune Function

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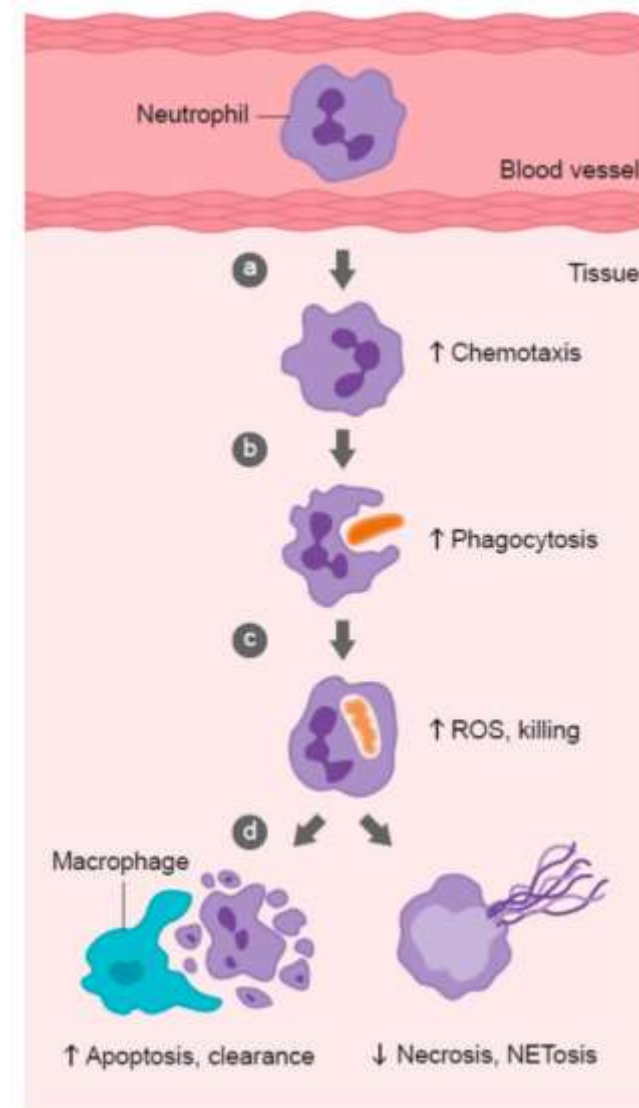


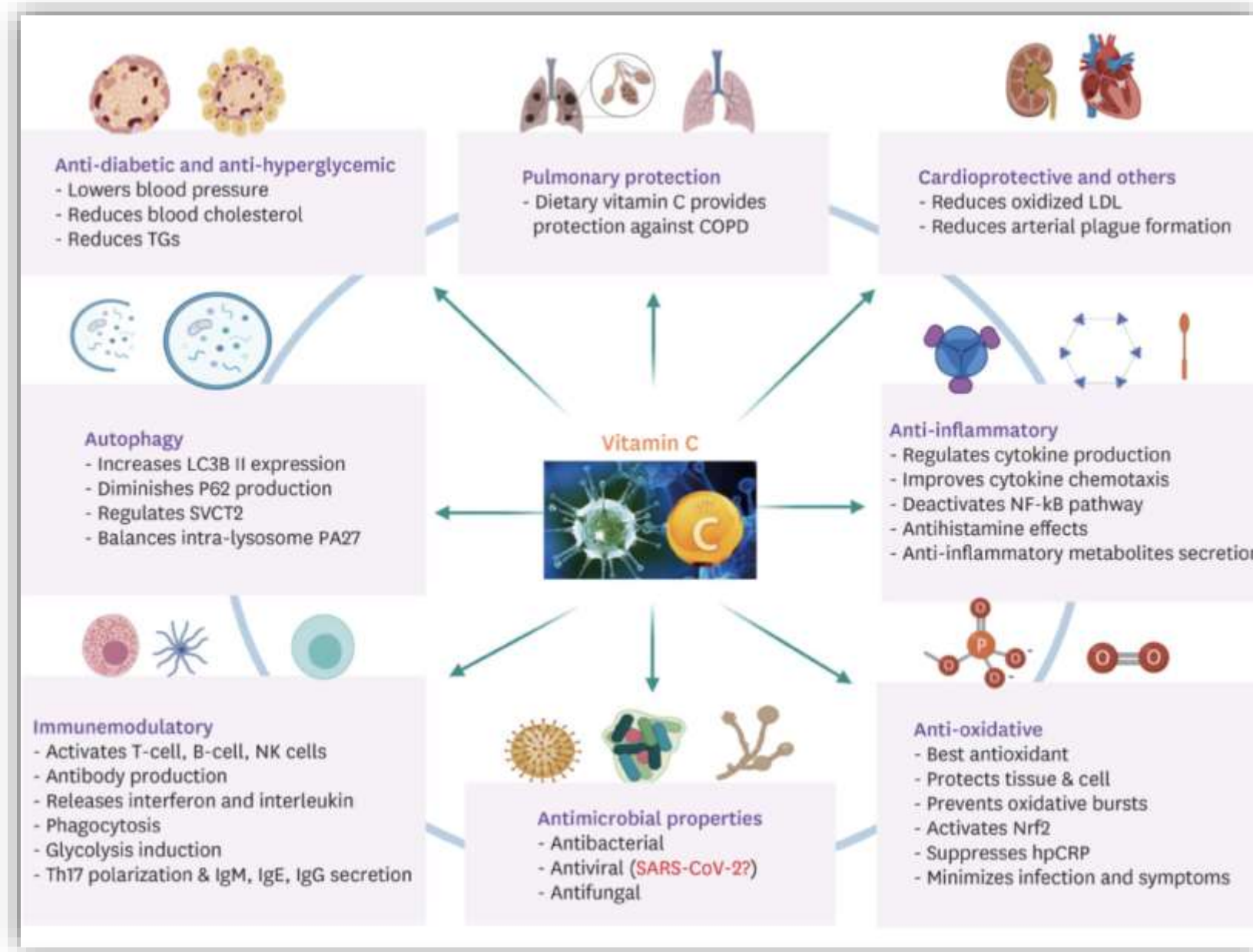
Abstract: Vitamin C is an essential micronutrient for humans, with pleiotropic functions related to its ability to donate electrons. It is a potent antioxidant and a cofactor for a family of biosynthetic and gene regulatory enzymes. Vitamin C contributes to immune defense by supporting various cellular 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.

I principali meccanismi d'azione della vitamina C

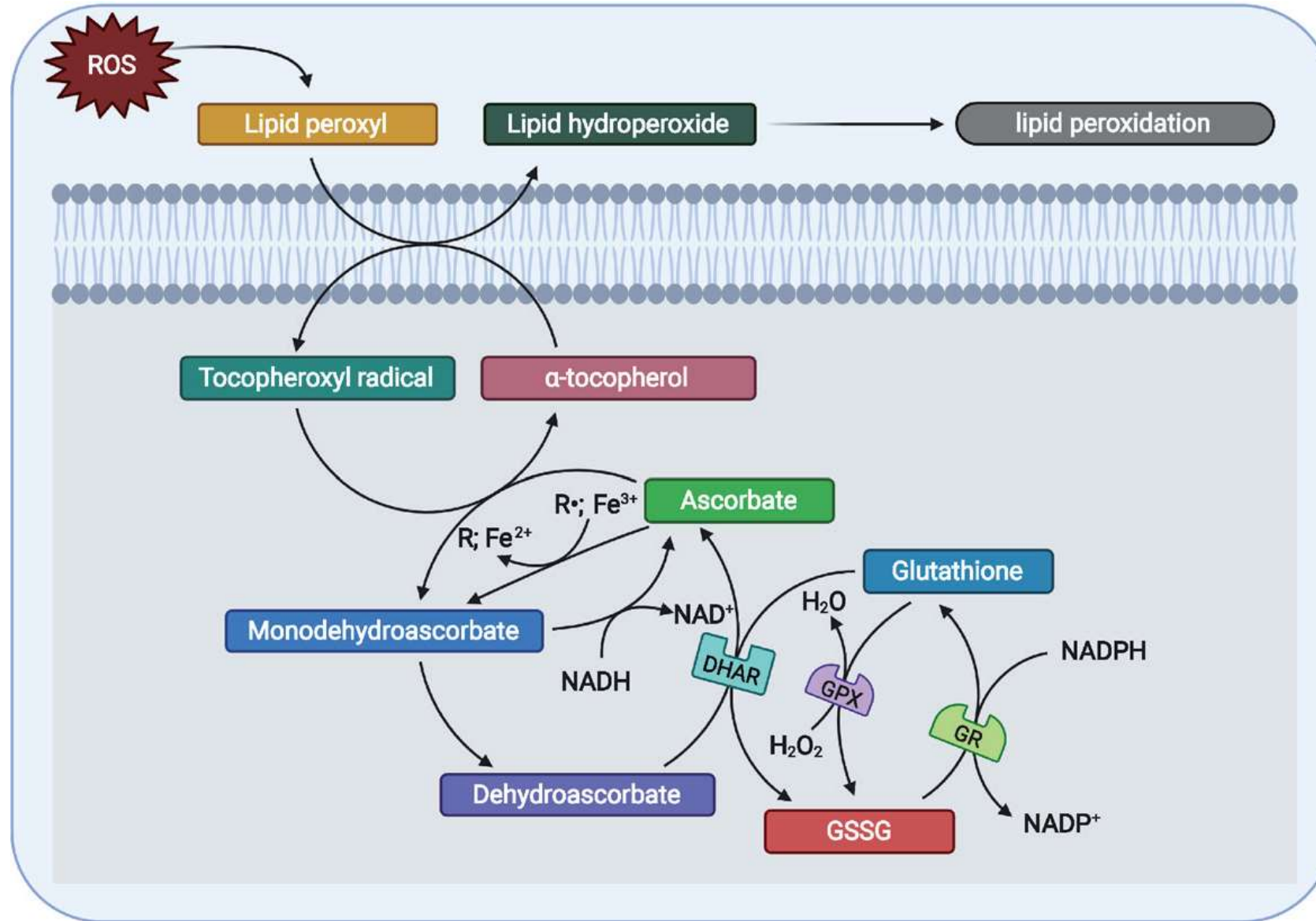
Il supporto della vitamina C al sistema immunitario si esplica in numerosi siti e con vari meccanismi:

- **Barriera cutanea** → Aumenta la sintesi e la stabilizzazione del collagene (integrità di barriera); funzione antiossidante diretta e protezione dai ROS; Riduce i tempi di guarigione da ferite
- **Fagociti** → Aumenta la motilità delle cellule fagocitiche; migliora il riconoscimento dei patogeni e quindi la fagocitosi e l'eliminazione; riduce la necrosi cellulare e aumenta l'apoptosi e la clearance del sito di infezione
- **Linfociti B e T** → Aumenta la differenziazione e la proliferazione; aumenta il numero di anticorpi circolanti
- **Mediatori infiammatori** → Modula la produzione di citochine; riduce i livelli di istamina





Farjana M, et al. Repositioning Vitamin C as a Promising Option to Alleviate Complications associated with COVID-19. Infect Chemother. 2020



Cenni di cinetica

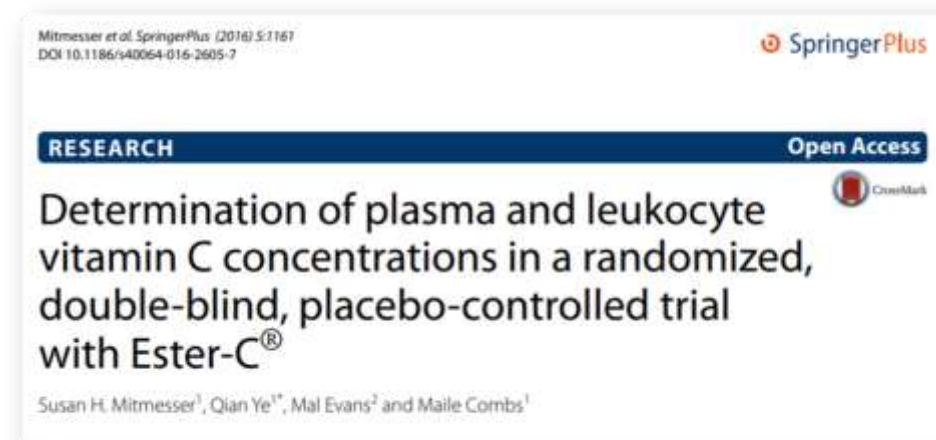
- La vitamina C (acido ascorbico) è una **vitamina idrosolubile**
- Raggiunge il picco plasmatico dopo circa 4 ore
- Quando vengono assunti da 1 a 3 g/die la principale via di escrezione è renale
- Viene completamente eliminata dall'organismo in 8-12 ore, a seconda delle caratteristiche dell'individuo
- E quindi è per questo che possono tornare utili formulazioni innovative...



THE BETTER VITAMIN C

Formula unica di vitamina C, contenente L-ascorbato di calcio e i suoi metaboliti (acido L-treonico, acido L-lixonico e acido L-xilonico)

Forma a pH neutro, **cl clinicamente studiata**, e in cui è dimostrato un significativo **aumento della permanenza della vitamina C nei leucociti, fino a 24 ore.**



Studio randomizzato, in doppio cieco, su 40 partecipanti:

- Gruppo placebo
- Gruppo controllo Acido ascorbico 1000 mg
- Gruppo Ester-C® 1000 mg

Misurazione dei livelli di vitamina C dopo 2, 4, 8 e 24 ore dall'assunzione.

Significativo aumento della permanenza della vitamina C nei leucociti

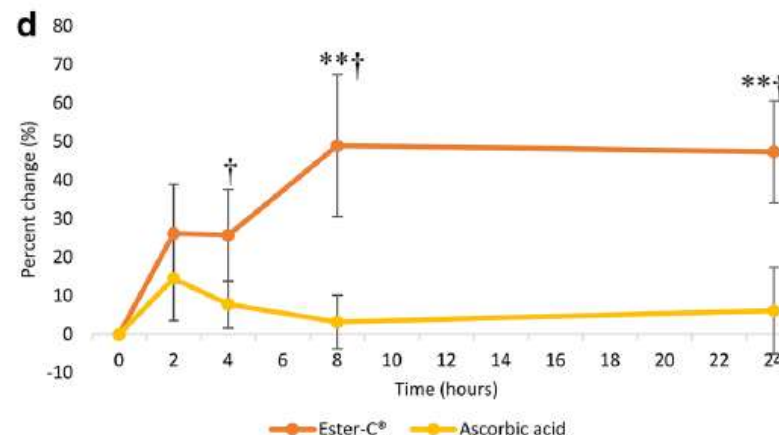
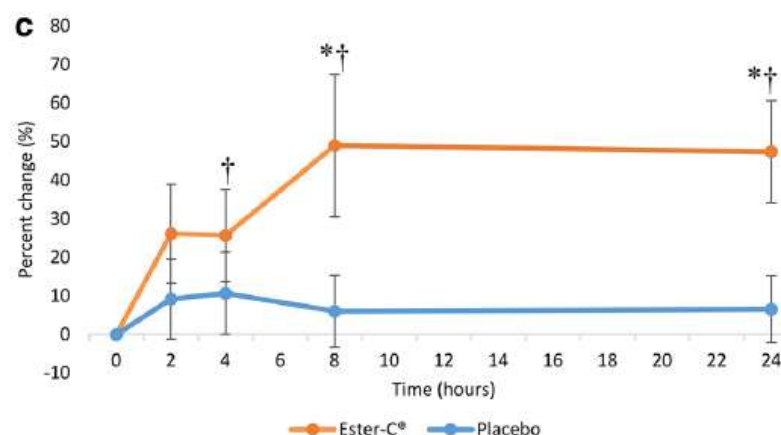


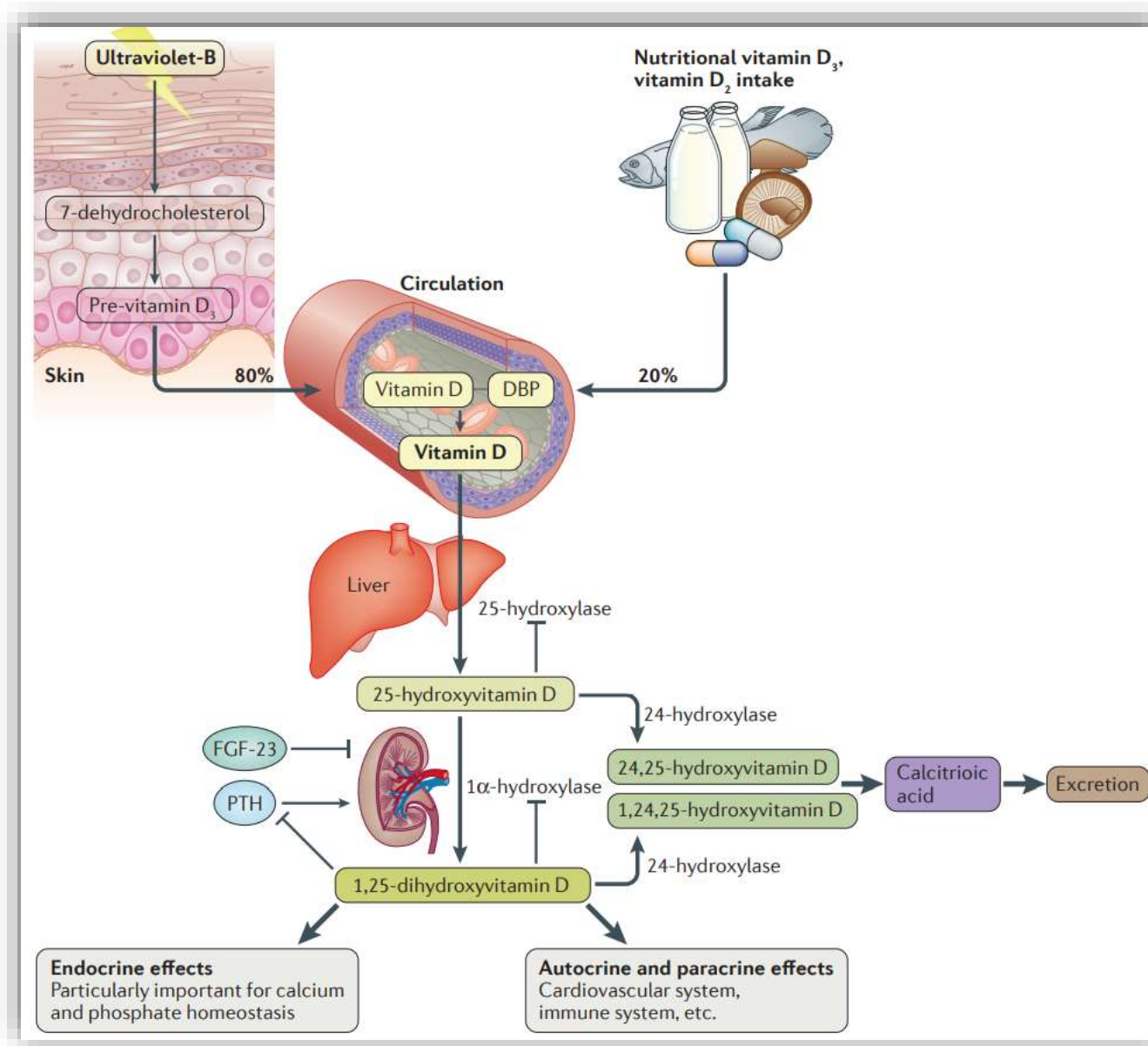
Fig. 5 Mean vitamin C concentration and percent changes in leukocytes over a 24-h period: **a** concentration change, Ester-C® versus placebo; **b** concentration change, Ester-C® versus ascorbic acid; **c** percent change, Ester-C® versus placebo; **d** percent change, Ester-C® versus ascorbic acid. Data are mean $\pm$ standard error. Significant differences are indicated: * $P < 0.05$, Ester-C® versus placebo percent change ($P = 0.042$ at 8 h, $P = 0.036$ at 24 h); ** $P < 0.05$, Ester-C® versus ascorbic acid percent change ($P = 0.028$ at 8 h, $P = 0.034$ at 24 h); $^{\dagger}P < 0.05$, Ester-C® within-group differences (concentration change $P = 0.036$ at 24 h; percent change $P = 0.040$, $P = 0.013$, and $P = 0.001$ at 4, 8, and 24 h, respectively)

Miglioramento della funzionalità dei leucociti, che possono utilizzare la vitamina C fino a 24 ore per il mantenimento delle normali difese immunitarie

Vitamina D

Gli effetti sulla salute sono molteplici:

- ✓ Assorbimento di **calcio** e **fosforo**
- ✓ Mantenimento di **ossa** e **denti normali**
- ✓ Normale **funzionalità del sistema immunitario**
- ✓ Normale **funzionalità muscolare**



Pilz, S., Verheyen, N., Grübler, M. R., Tomaschitz, A., & März, W. (2016). Vitamin D and cardiovascular disease prevention. **Nature Reviews Cardiology**.

Esposizione al sole



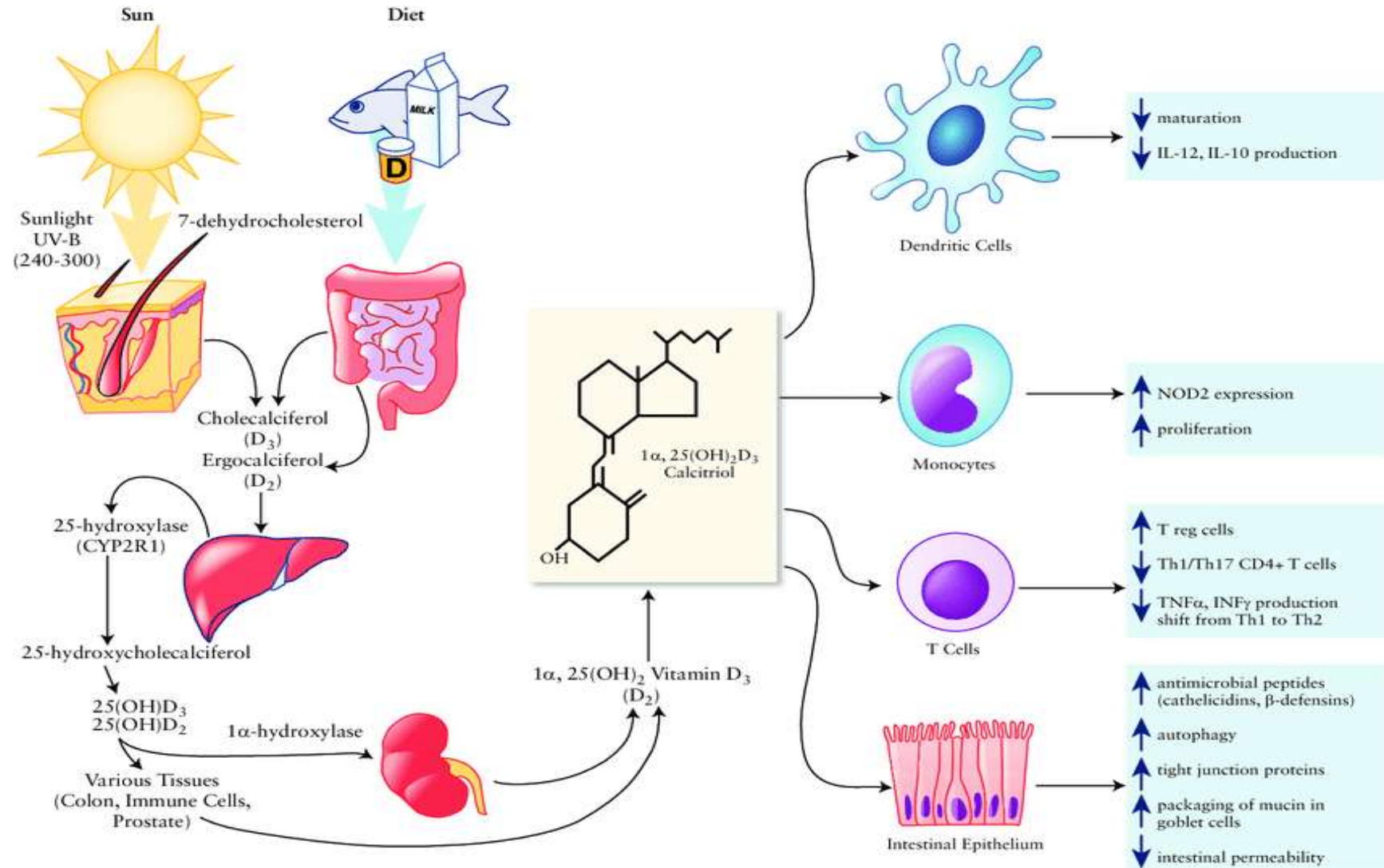
L'esposizione solare necessaria per garantire livelli adeguati di vitamina D varia a seconda di:

- Latitudine
- Stagione
- Ora del giorno in cui ci espone
- Uso di creme protettive (SPF 15 riduce del 99% la produzione di vitamina D)

In generale, per una corretta produzione di vitamina D **bisognerebbe esporsi per 15-20 minuti al giorno, per almeno 4 giorni alla settimana**, scoprendo braccia, viso e gambe.

Piotrowska A, Wierzbicka J, Żmijewski MA. Vitamin D in the skin physiology and pathology. Acta Biochim Pol. 2016

Vitamina D e sistema immunitario



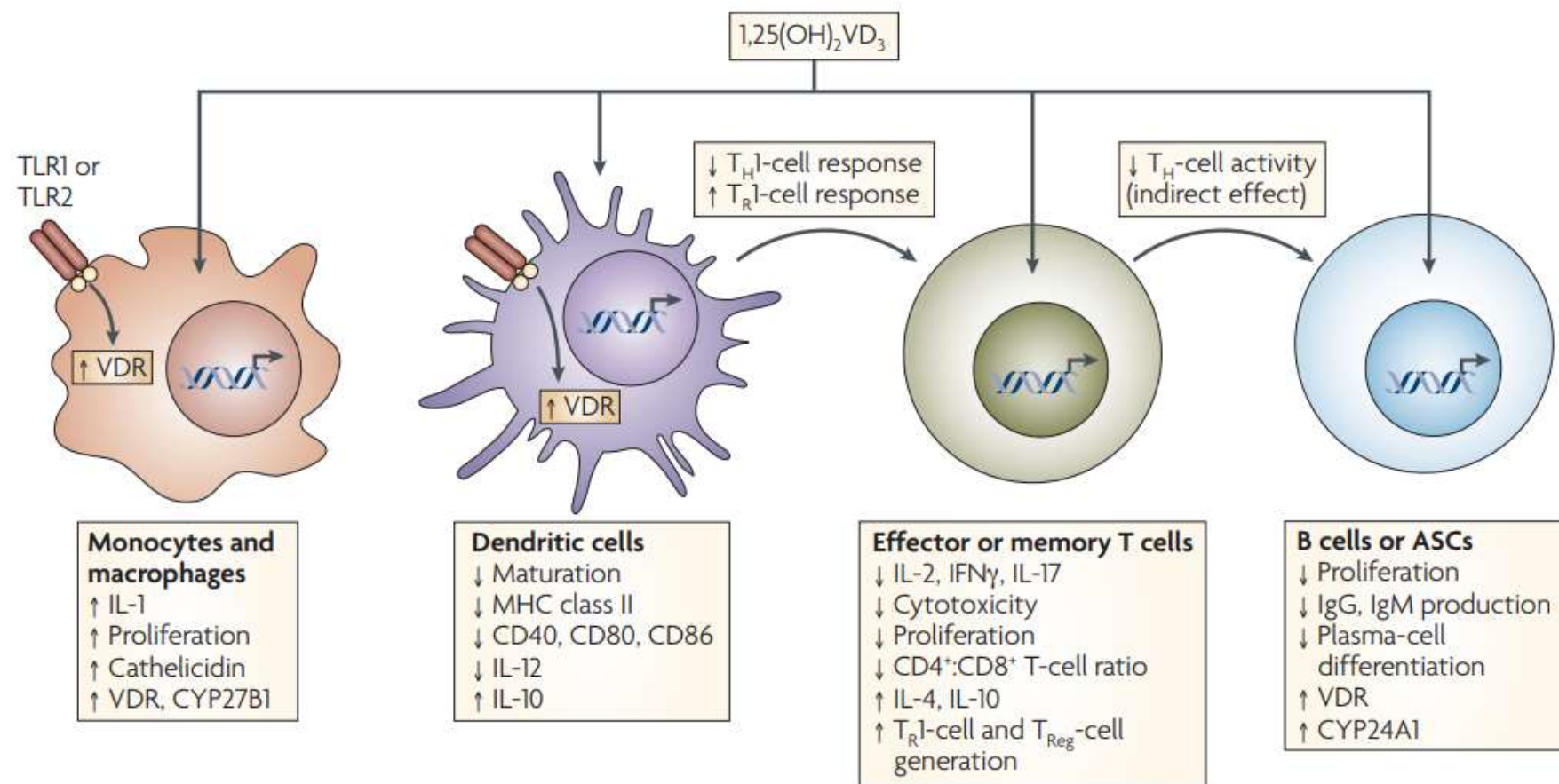
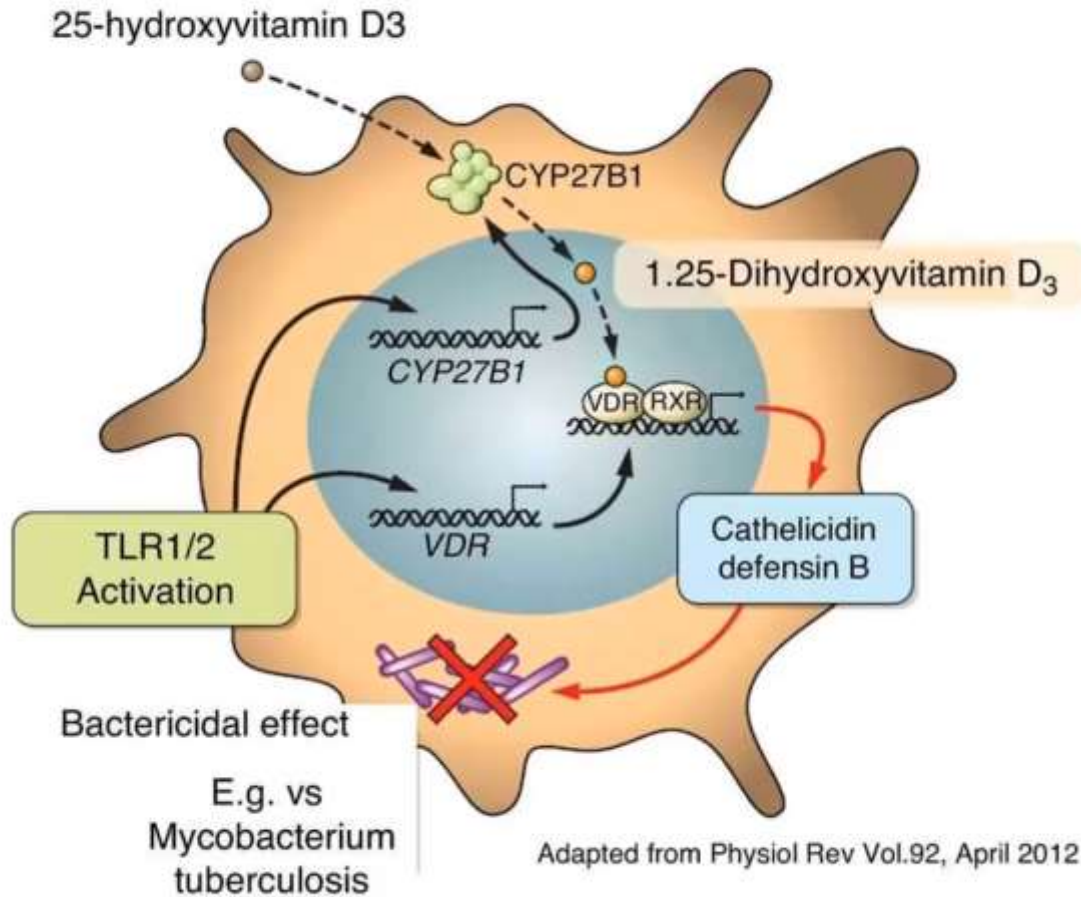


Figure 2 | **Mechanisms of vitamin D immunomodulation.** Systemic or locally produced $1,25(\text{OH})_2\text{VD}_3$ exerts its effects on several immune-cell types, including macrophages, dendritic cells (DCs), T and B cells. Macrophages and DCs

Mora JR, Iwata M, von Andrian UH. (2008) Vitamin effects on the immune system: vitamins A and D take centre stage. *Nature Review Immunology*.

Vitamin D stimulates the production of cathelicidins and defensin B.



A livello delle cellule epiteliali di bronchi e polmoni, la **vitamina D** è in grado di indurre l'espressione di **Catelicidina** e **Defensina B**, peptidi ad attività antibatterica ed antivirale

Endocrinol Diabetes Nutr. 2017;64:162-73

Livelli di Vitamina D3 e integrazione consigliata



Livelli plasmatici	Condizione
Meno di 30 ng/ml	Deficienza
30-40 ng/ml	Livelli adeguati
40-60 ng/ml	Livelli ottimali

IMMUNODEFICIENZA

Quantità consigliata: 2000 U.I./die

SCARSA IMMUNOOMEOSTASI

Quantità consigliata: 1000 - 2000 U.I./die

IMMUNOOMEOSTASI

Quantità consigliata: 400 - 1000 U.I./die

Ormai è confermato da numerosi studi che l'**assunzione quotidiana** di Vitamina D3 sia **più efficace rispetto al bolo** mensile

OPEN ACCESS Freely available online

PLOS ONE

Vitamin D and Respiratory Tract Infections: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Background: Low levels of 25-OH vitamin D are associated with respiratory tract infection (RTI). However, results from randomized controlled trials are inconclusive. Therefore, we performed a systematic review and meta-analysis to assess the preventive effect of vitamin D supplementation on RTI.

Methods: Randomized, controlled trials of vitamin D for prevention of RTI were used for the analysis. The risks of within-trial and publication bias were assessed. Odds ratios of RTI were pooled using a random-effects model. Heterogeneity was assessed using Cochran's Q and I². Meta-regressions and subgroup analyses were used to assess the influence of various factors on trial outcome. The pre-defined review protocol was registered at the PROSPERO international prospective register of systematic reviews, registration number CRD42013003530.

Findings: Of 1137 citations retrieved, 11 placebo-controlled studies of 5660 patients were included in the meta-analysis. Overall, vitamin D showed a protective effect against RTI (OR, 0.64; 95% CI, 0.49 to 0.84). There was significant heterogeneity among studies (Cochran's Q $p < 0.0001$, I² = 72%). The protective effect was larger in studies using once-daily dosing compared to bolus doses (OR = 0.51 vs OR = 0.86, $p = 0.01$). There was some evidence that results may have been influenced by publication bias.

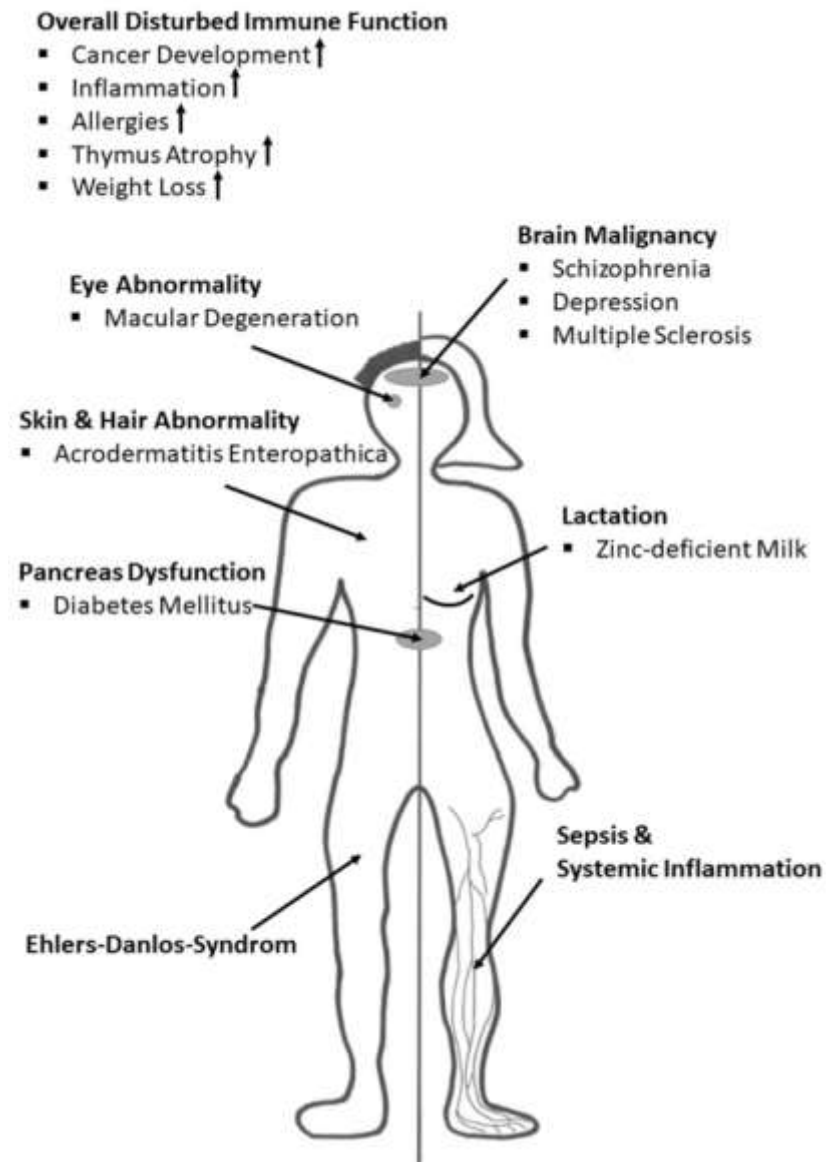
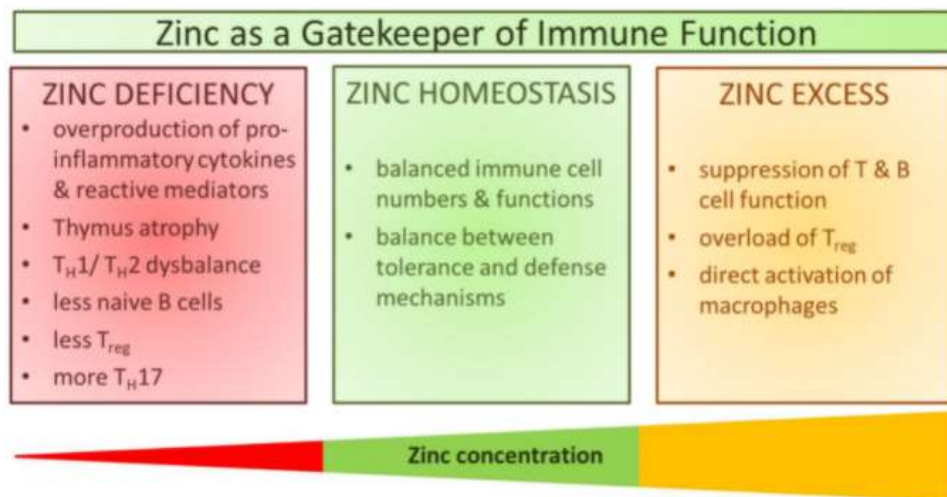
Interpretation: Results indicate that vitamin D has a protective effect against RTI, and dosing once-daily seems most effective. Due to heterogeneity of included studies and possible publication bias in the field, these results should be interpreted with caution.

ZINCO



- Lo zinco è un componente essenziale di **numerosi enzimi** per i quali svolge un ruolo strutturale, di regolazione e catalitico.
- Viene assorbito a livello dell'intestino prossimale circa il 10-40% dello zinco presente negli alimenti.
- La **quota effettivamente assorbita** dipende da:
 - ✓ Competizione con altri microelementi
 - ✓ Agenti chelanti
 - ✓ Concentrazione di metallotionina (cellule della mucosa)
 - ✓ **Alimenti**: le maggiori fonti alimentari di zinco sono alimenti di origine animale (carni, uova, pesce, latte e derivati) e in misura minore i cereali.

Zinco e difese immunitarie



Zinco e difese immunitarie

Lo zinco è necessario per lo sviluppo dei linfociti T, che attaccano i virus e i batteri patogeni aiutandoci a combattere le infezioni. Degli studi viene dimostrato che in soggetti sani con bassi livelli di zinco, una **integrazione di zinco stimola l'innalzamento del numero dei linfociti T e riduce la gravità e la durata delle infezioni.**

> Am J Trop Med Hyg. 2020 Jul;103(1):86-99. doi: 10.4269/ajtmh.19-0718. Epub 2020 Apr 23.

Zinc Supplementation Reduces Common Cold Duration among Healthy Adults: A Systematic Review of Randomized Controlled Trials with Micronutrients Supplementation

Min Xian Wang¹, Shwe Sin Win¹, Junxiong Pang¹

Affiliations + expand

PMID: 32342851 PMID: [PMC7356429](#) DOI: [10.4269/ajtmh.19-0718](#)

[Free PMC article](#)

A 2011 systematic review of 15 clinical trials of oral zinc, involving more than 1,300 people, concluded that zinc helps to reduce the length and severity of the common cold in healthy people when taken within 24 hours after symptoms start. The review also concluded that zinc, taken at low doses for at least 5 months, reduced the number of colds in children.

Wang MX, Win SS, Pang J. Zinc Supplementation Reduces Common Cold Duration among Healthy Adults: A Systematic Review of Randomized Controlled Trials with Micronutrients Supplementation. *Am J Trop Med Hyg.* 2020

Zinc and immunity: An essential interrelation

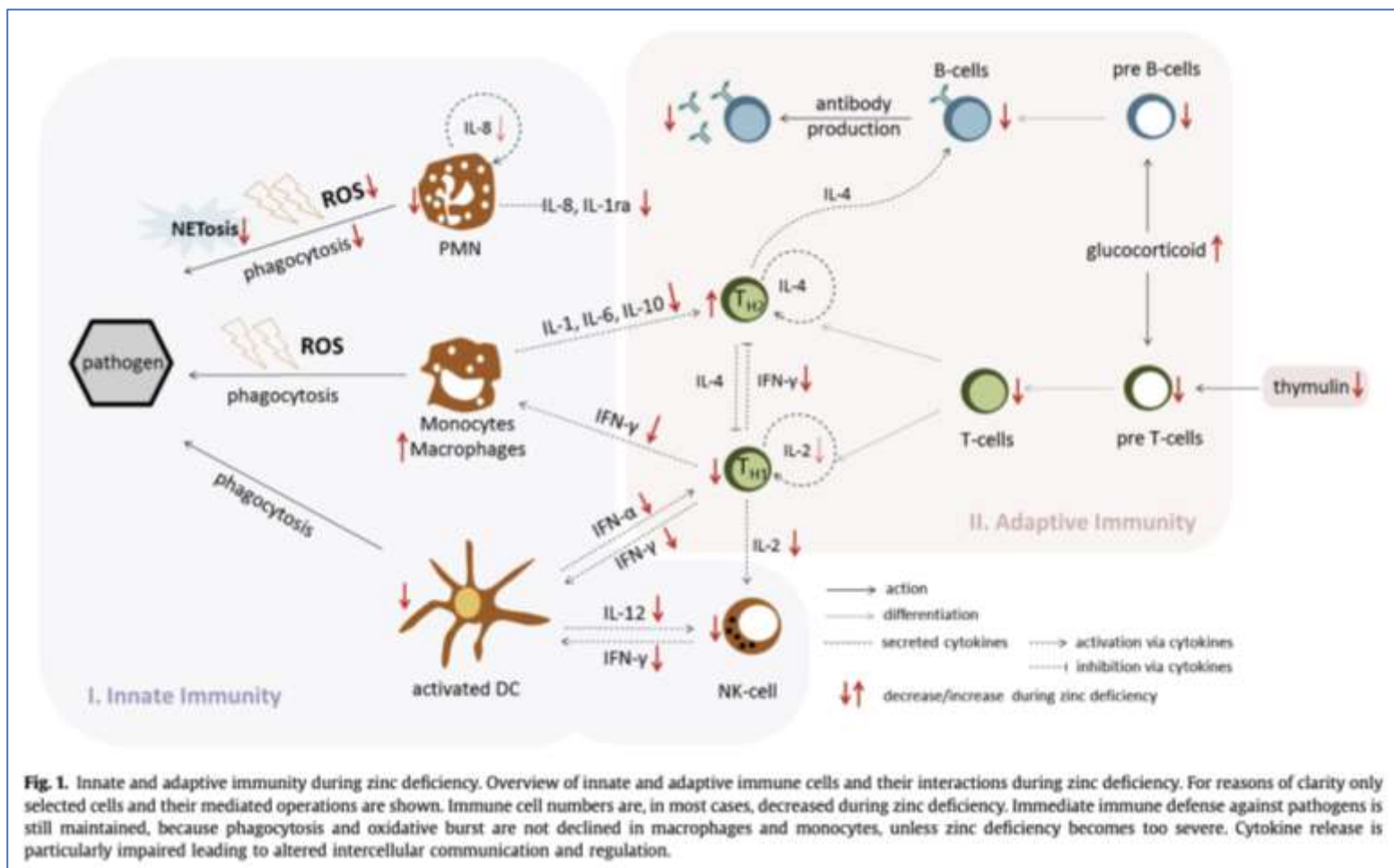
Maria Maares, Hajo Haase*

Department of Food Chemistry and Toxicology, Berlin Institute of Technology, Gustav-Meyer-Allee 25, D-13355 Berlin, Germany



Archives of Biochemistry and Biophysics

Volume 611, 1 December 2016, Pages 58-65



4. Conclusion

The role of zinc in the immune system has been investigated in depth. As discussed above, altered zinc homeostasis critically influences innate and adaptive immunity, and therefore host defense and the immune response in general.

Zinc supplementation can reverse the negative effects of zinc deficiency, including impaired immune cell development, compromised T-cell-mediated immune response, decreased oxidative burst and many more. The potential benefits of zinc supplementation go from anti-inflammatory and immunomodulatory effects, to prevention of allergies and autoimmunity, or even suppression of allogenic reactions. A more detailed understanding of the molecular effects of zinc and their controlled manipulation might prove to be a useful future tool for targeted modulation of the immune system with very limited side effects.

Zinco e gusto



Review

Japan's Practical Guidelines for Zinc Deficiency with a Particular Focus on Taste Disorders, Inflammatory Bowel Disease, and Liver Cirrhosis

Hiroko Kodama ^{1,*}, Makoto Tanaka ², Yuji Naito ³ , Kazuhiro Katayama ⁴ and Mitsuhiro Moriyama ⁵

Received: 13 March 2020; Accepted: 8 April 2020; Published: 22 April 2020

Taste areas on the human tongue



3. Zinc Deficiency and Taste Disorders

Taste sensation allows one to sense important information related to survival. In other words, it allows one to judge whether something is edible or not. This sensation is detected by receptors that categorize taste into the following: sweet, salty, sour, bitter, and umami.

3.1. Taste Perception System

A water-soluble chemical substance that presents a taste in food is received by taste receptors on taste cells of taste buds in the mucous membrane of the tongue and pharynx, and is projected to the gustatory area of the cerebral cortex via taste nerves. There are roughly 7000 taste buds (peripheral receptors of taste) in the oral cavity, pharynx, and larynx, with a particularly high concentration in the lingual papillae on the tongue surface. The five basic tastes are sensed by different taste receptors on taste cells.

The type of taste nerve varies by location inside the oral cavity. Taste information is transmitted from the left and right chorda tympani nerve, large pyramidal nerve, glossopharyngeal nerve, and vagus nerve to the cerebral cortex's gustatory area via the medullary solitary nucleus and thalamus.

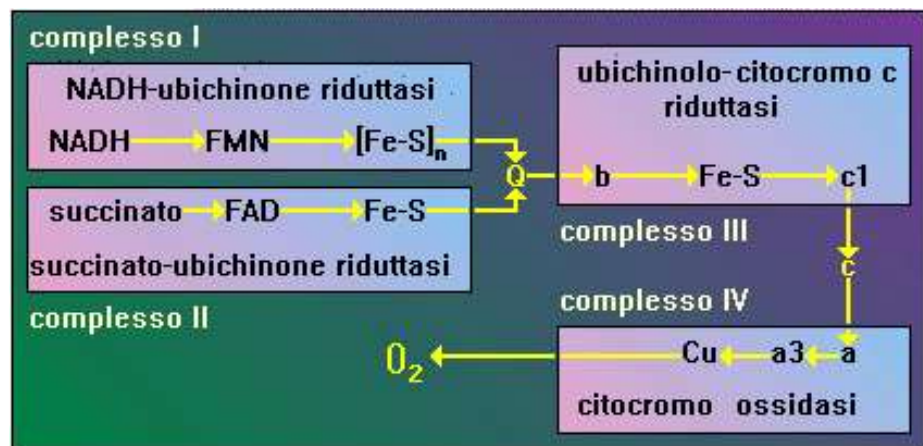
3.2. Effects of Zinc Deficiency on Taste Function in Rats

Rats fed a zinc-deficient diet begin to drink bitter water, which would typically be avoided, in addition to normal water. This suggests that they suffer from a taste disorder, a common symptom of zinc deficiency [34].

3.5. Nutritional Guidance

Nutritional guidance is also effective for treating taste disorders. The standard amount of zinc intake recommended by the Ministry of Health, Labor and Welfare in Japan is 10 mg per day for men and 8 mg per day for women. The actual intake amount, however, is below the recommended standard, at 8.9 mg per day for men and 7.3 mg per day for women. Indeed, half of the Japanese population is at risk of zinc deficiency taste disorder. Therefore, at our facility, we show patients a list of foods that are either rich in zinc, promote zinc absorption, or inhibit zinc absorption, and encourage them to be more aware of their daily eating habits.

RAME



- Il rame è un micronutriente presente in vari distretti e implicato soprattutto nelle **reazioni di ossido-riduzione**.
- Viene infatti utilizzato come cofattore/coenzima da parte del **Complesso IV** (catena di trasporto degli elettroni a livello mitocondriale) e della **Superossido Dismutasi**
- Tra i **cibi** più ricchi di rame ricordiamo: frattaglie, molluschi, crostacei, alcuni semi e legumi (pinoli, noci, fagioli, semi di girasole)

Rame e Zinco

Review > J Biol Chem. 2015 Jul 31;290(31):18954-61. doi: 10.1074/jbc.R115.647099.

Epub 2015 Jun 8.

The Role of Copper and Zinc Toxicity in Innate Immune Defense against Bacterial Pathogens

Karrera Y Djoko¹, Cheryl-lynn Y Ong¹, Mark J Walker¹, Alastair G McEwan²

Affiliations + expand

PMID: 26055706 PMCID: PMC4521016 DOI: 10.1074/jbc.R115.647099

Free PMC article

Abstract

Zinc (Zn) and copper (Cu) are essential for optimal innate immune function, and nutritional deficiency in either metal leads to increased susceptibility to bacterial infection. Recently, the decreased survival of bacterial pathogens with impaired Cu and/or Zn detoxification systems in phagocytes and animal models of infection has been reported. Consequently, a model has emerged in which the host utilizes Cu and/or Zn intoxication to reduce the intracellular survival of pathogens. This review describes and assesses the potential role for Cu and Zn intoxication in innate immune function and their direct bactericidal function.



Mechanisms of Ageing and Development

Volume 151, November 2015, Pages 93-100



Review

Serum copper to zinc ratio: Relationship with aging and health status

Marco Malavolta^{1,2}, Francesco Piacenza, Andrea Basso, Robertina Giacconi, Laura Costarelli, Eugenio Mocchegiani

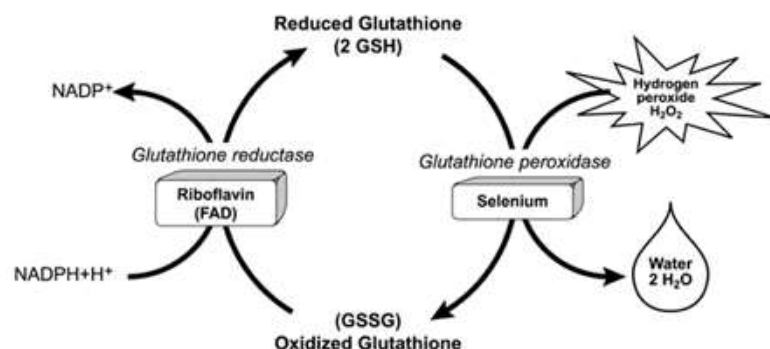
Rapporto ottimale

Zn : Cu
10:1

SELENIO

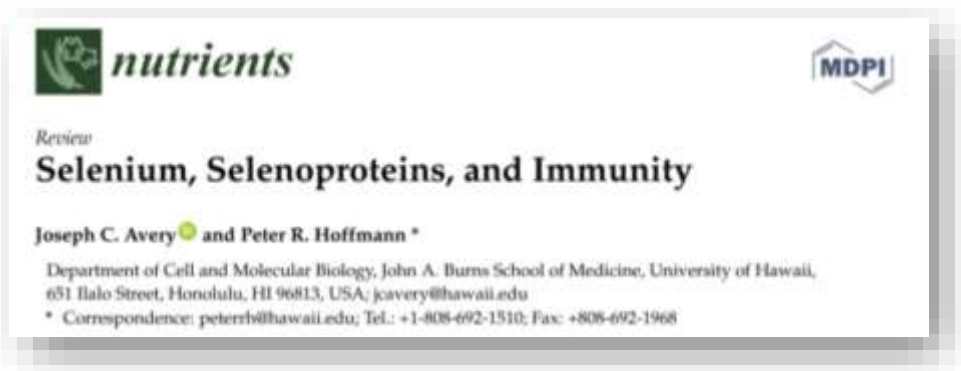


- Si trova principalmente negli alimenti sotto forma di **selenio-metionina** e **selenio-cisteina**.
- La maggior **fonte alimentare** è costituita dalle frattaglie e dai pesci; seguono le carni, i cereali e i prodotti lattiero caseari. Il contenuto in frutta e verdura invece, è basso e variabile, dipendendo dal tipo di terreno di coltivazione. In Italia il frumento e i suoi derivati costituiscono la fonte principale. Il grano duro apporta maggiori quantità di selenio rispetto al grano tenero; quindi la pasta è una fonte di selenio migliore del pane, solitamente preparato a partire da farina di grano tenero.
- È il principale coenzima della **glutathione-perossidasi**, enzima che limita l'ossidazione dell'**emoglobina**. Ha quindi una un'**attività antiossidante**.
- È inoltre implicato come cofattore delle **deiodinasi**, enzimi chiave nella produzione degli ormoni tiroidei



- Nell'organismo, il selenio si ritrova in numerose proteine vitali denominate **selenoproteine**.
- Ad oggi sono state identificate 25 selenioproteine tra cui
 1. Le **perossidasi**, che possiedono importanti proprietà anti-infiammatorie e proteggono le membrane cellulari dai danni causati dai radicali liberi
 2. Le **deiodinasi**, coinvolte nella produzione dell'ormone tiroideo attivo
 3. Le proteine coinvolte nella *replicazione* e nella *riparazione* del DNA.
- Scarsi livelli di assunzione di selenio con la dieta può diminuire la produzione di selenoproteine, che a loro volta possono **influenzare i meccanismi di riparazione del DNA** (specie a seguito di danni ossidativi), **indebolire le risposte immunitarie e anti-infiammatorie** e ridurre la protezione generale verso malattie.

Selenio e difese immunitarie



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 immunobiology. 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.

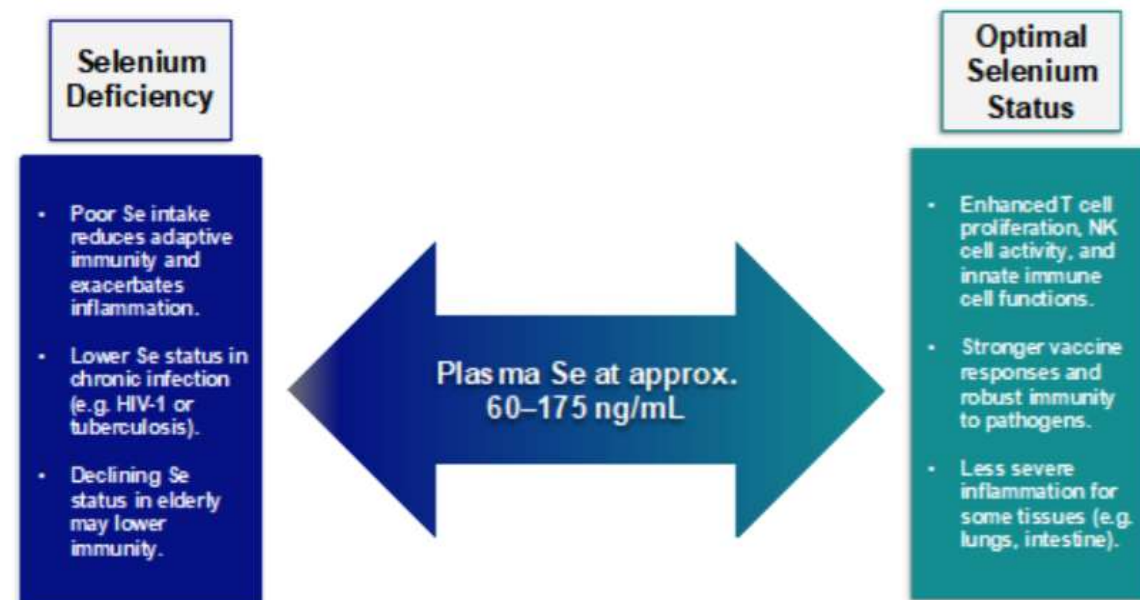


Figure 1. A summary of selenium and immune responses.



who 

Micronutrients, such as vitamins D and C and zinc, are critical for a well-functioning immune system and play a vital role in promoting health and nutritional well-being.

Protocollo Nutraceutico a base di Vitamine e Minerali



Remind **FOUNDATIONAL HEALTH**
Polinutriente + Omega-3 + Probiotici

Cosa?	Quanto e quando?	Per quanto tempo?
Vitamina C	500 – 1000 mg/die, dopo colazione	Foundational Health, specialmente da settembre a marzo
Vitamina D3	Modulabile in funzione dei livelli plasmatici. Fino a 50 mcg/die = 2000 U.I./die. Dopo un pasto che contiene dei grassi (colazione o cena)	Foundational Health, specialmente da settembre a marzo
Zinco	<i>Bambini e adolescenti:</i> fino a 7,5 mg/die <i>Adulti e anziani:</i> fino a 15 mg/die Dopo un pasto (colazione o cena)	Cicli di integrazione di 2-3 mesi, specialmente da settembre a marzo