Nutraceutici e immuno-modulazione

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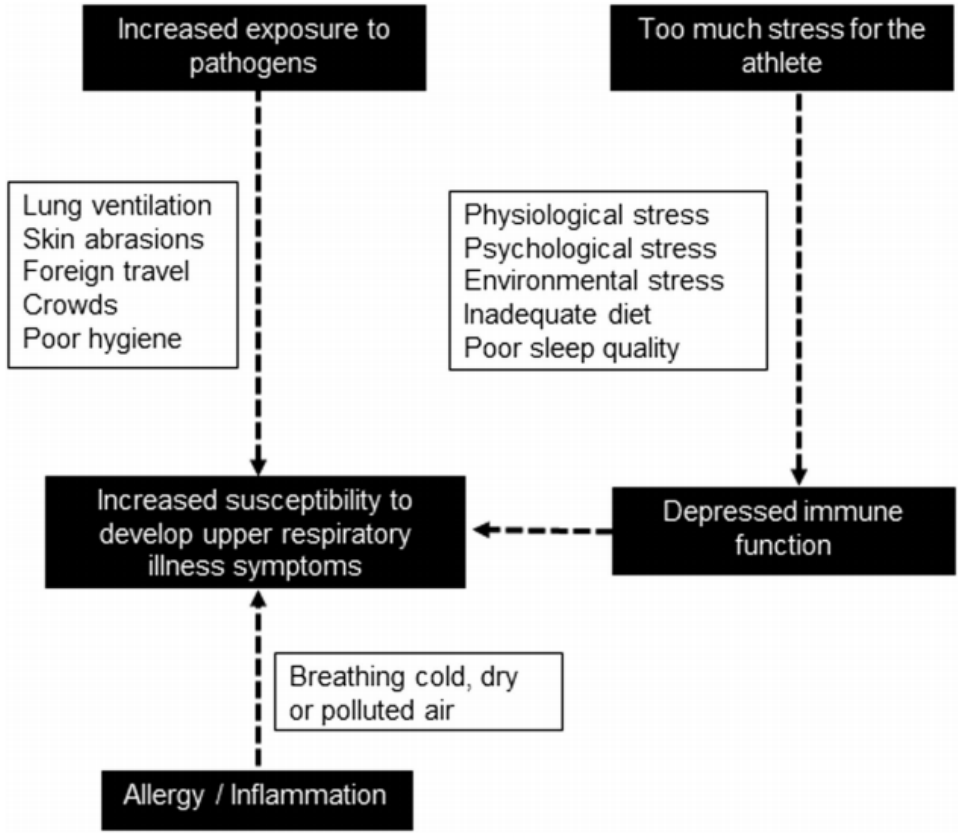


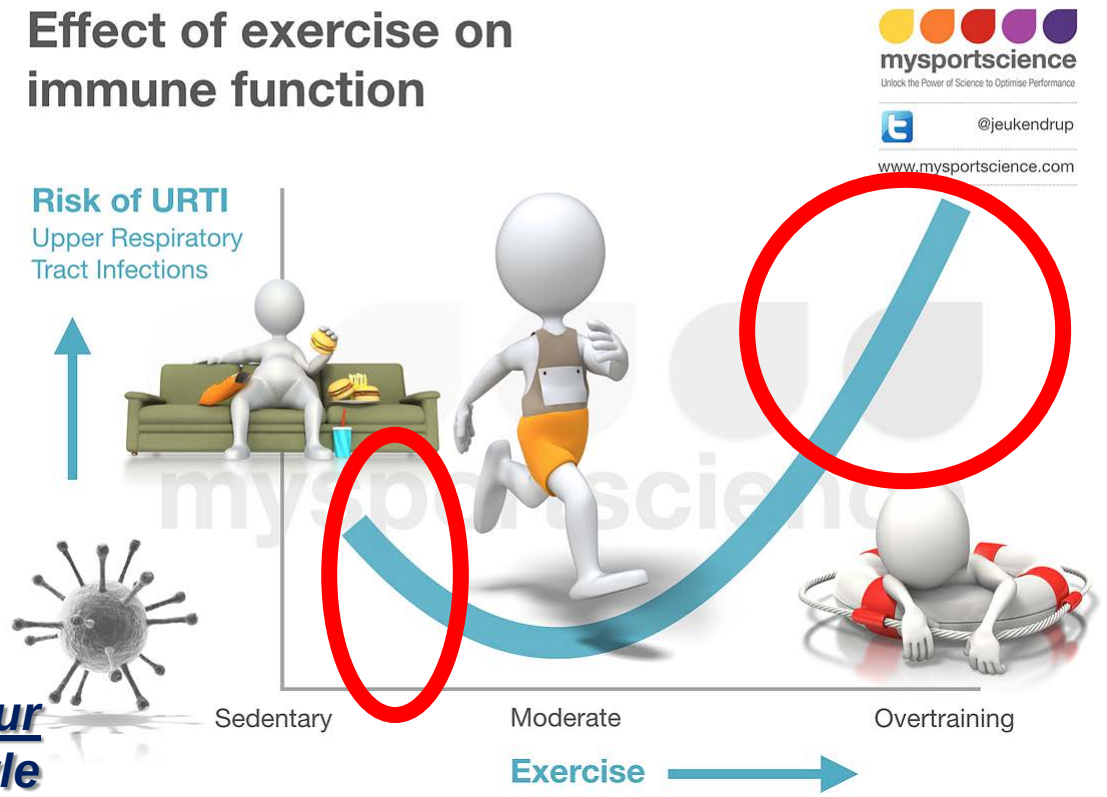
Effects of exercise on immune function and risk of infection

September 26, 2016 | Michael Gleeson

Nutrients. 2012 Sep; 4(9): 1187–1212.
Published online 2012 Sep 4. doi: 10.3390/nu4091187
PMCID: PMC3475230
PMID: 23112908

Exercise-Induced Immunodepression in Endurance Athletes and Nutritional Intervention with Carbohydrate, Protein and Fat—What Is Possible, What Is Not?

Wolfgang Gunzer, Manuela Konrad,* and Elisabeth Pail



Moderate levels of regular exercise seem to reduce our susceptibility to illness compared with an inactive lifestyle but long hard bouts of exercise and periods of intensified training put athletes at increased risk of colds and flu.

Asker Jeukendrup

Nutrition supplement and evidence rating	*Proposed mechanism of action*	*Evidence of efficacy*
β-glucans ●●○○○	Polysaccharides derived from the cell walls of yeast, fungi and oats that stimulate innate immunity	Effective in mice inoculated with influenza virus but mixed results from human studies for immune modulation and URS incidence
Bovine colostrums ●●●○○	First milk of the cow that contains antibodies, growth factors and cytokines. Claimed to boost mucosal immunity and increase resistance to infection	Several studies in athletes that indicate some immune boosting effects and reduced URS incidence and duration
Carbohydrate ●●●○○	Maintains blood glucose during exercise, lowers stress hormone and anti-inflammatory cytokine responses, and thus counters immune dysfunction	Ingestion of carbohydrate (30–60 g h^{-1}) attenuates stress hormone and some (but not all) immune pertubations during exercise but only very limited evidence that this modifies infection risk in human athletes
Echinacea ●○○○○	Herbal extract that is a popular supplement among athletes. Claimed to boost immunity via stimulatory effects on macrophages and there is some *in vitro* evidence for this	Early human studies indicated possible beneficial effects but more recent, larger scale and better controlled studies indicate no effect of *Echinacea* on infection incidence or cold symptom severity
Glutamine ●○○○○	Nonessential amino acid that is a precursor in the synthesis of nucleic acids and important for rapidly dividing cells. Also an important fuel for immune cells. Plasma concentration of glutamine falls during prolonged exercise	Supplementation before and after exercise does not alter immune perturbations despite maintenance of plasma glutamine
Kaloba ●○○○○	Herbal medicine that has been shown to boost some aspects of immunity *in vitro* via stimulatory effects on macrophages	Evidence from human studies for reduction in severity and duration of symptoms of sinusitis and common cold but used as a treatment rather than as a preventative
N-3 polyunsaturated fatty acids ○○○○○	Exert anti-inflammatory effects post exercise	No evidence in exercising humans
Probiotics ●●●○○	Probiotics are live microorganisms, which when administered orally for several weeks, can increase the numbers of beneficial bacteria in the gut. This has been associated with a range of potential benefits to gut health, as well as modulation of immune function	Human studies show improvements in some aspects of acquired immunity and reduced incidence of URS and gastrointestinal problems
Quercetin ●●●○○	A plant flavonoid; *in vitro* studies show strong anti-inflammatory, anti-oxidative and anti-pathogenic effects. Animal data indicate increase in mitochondrial biogenesis and endurance performance	Human studies show some reduction in URS incidence during short periods of intensified training and mild stimulation of mitochondrial biogenesis and endurance performance in untrained subjects
Quercetin with epigallocatechin gallate ●●●○○	Flavonoid mixture promotes anti-inflammatory and anti-oxidative effects, and immune function improvement, above that of quercetin alone	Human study showed strong anti-inflammatory effect, with modest anti-oxidative effect and improvement in innate immunity but no data on URS incidence
Vitamin C ●●○○○	An essential water-soluble antioxidant vitamin that quenches reactive oxygen species and augments immunity. Reduces interleukin-6 and cortisol responses to exercise in humans	Relatively small effects on cortisol compared with carbohydrate; immune measures no different from placebo. Some evidence of efficacy in reducing URS incidence after ultramarathon events
Vitamin D ●●●●○	Fat-soluble vitamin that is mostly produced via the action of sunlight in the skin. Induces production of antimicrobial proteins, enhances natural killer cell cytolytic activity, increases the generation of reactive oxygen species in phagocytic cells, augments macrophage interleukin-1β secretion and upregulates the expression of CD14, the lipopolysaccharide receptor	Low vitamin D status is associated with low saliva immunoglobulin A secretion, low pro-inflammatory cytokine production by antigen-stimulated mononuclear cells and increased respiratory infection risk with longer lasting illness symptoms. Oral vitamin D3 supplements of around 4000 IU per day can reduce URS incidence
Vitamin E ●○○○○	An essential fat-soluble antioxidant vitamin that quenches exercise-induced reactive oxygen species and augments immunity. Good evidence for some immune boosting effects in the frail elderly	No evidence of similar benefit for younger healthy humans or athletes
Zinc ●○○○○	Zinc deficiency results in impaired immunity and zinc deficiency is not uncommon in athletes. An essential mineral that is claimed to reduce incidence and duration of colds	No evidence for reduced infection incidence with zinc supplementation in adult humans. Some (but not all) human studies suggest a reduction in duration of cold symptoms if zinc gluconate lozenges are administered within 24 h of cold symptom onset. Unlikely to be of any real benefit to athletes unless they are zinc deficient

The scientific evidence is indicated with ●●●●● meaning very strong evidence and ○○○○○ meaning limited to no evidence.

Nutraceutica e immunomodulazione nello sportivo: quali evidenze ?

Immunology and Cell Biology (2016) 94, 117–123

Adattogeni

EMEA Definition
(Doc. Ref. EMEA/HMPC/102655/2007)

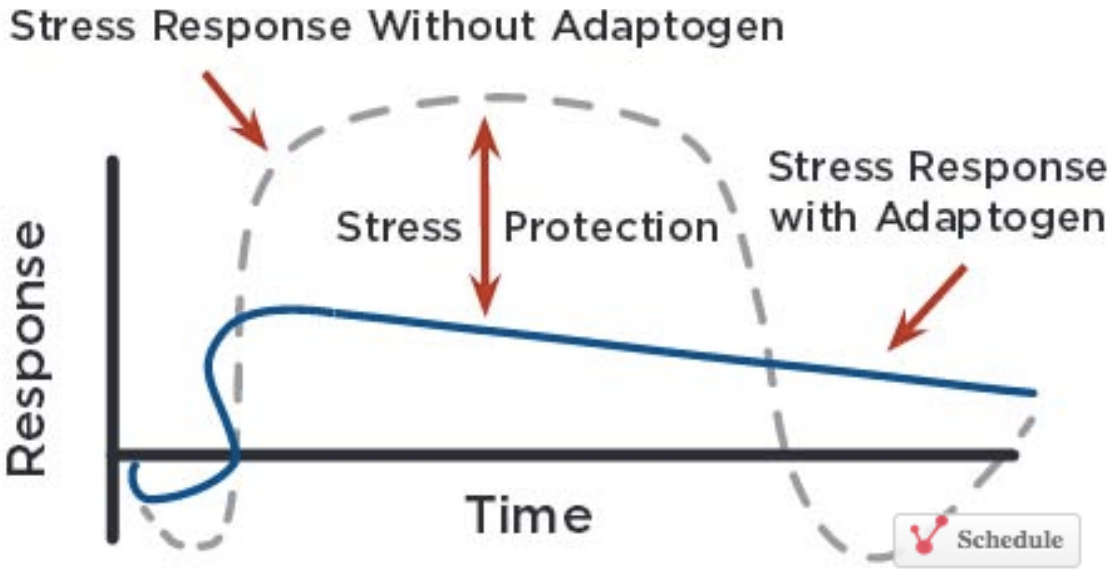
- Gli **adattogeni** costituiscono una classe di **“regolatori metabolici”** in grado di **migliorare la capacità dell’organismo all’adattamento**, in seguito a stimoli provenienti dall’ambiente circostante
- Gli adattogeni presentano una **tossicità minima** per l’organismo
- Gli adattogeni hanno un **effetto ‘‘normalizzante’’** che previene o antagonizza i disturbi causati dagli agenti responsabili dello stress
- Gli adattogeni tendono ad essere **non specifici nelle loro proprietà farmacologiche** e agiscono **aumentando la resistenza dell'organismo** ad un ampio spettro di fattori avversi biologici, chimici e fisici;
- **L'effetto di un adattogeno è tanto pronunciato quanto più profondi sono i cambiamenti patologici nell'organismo**

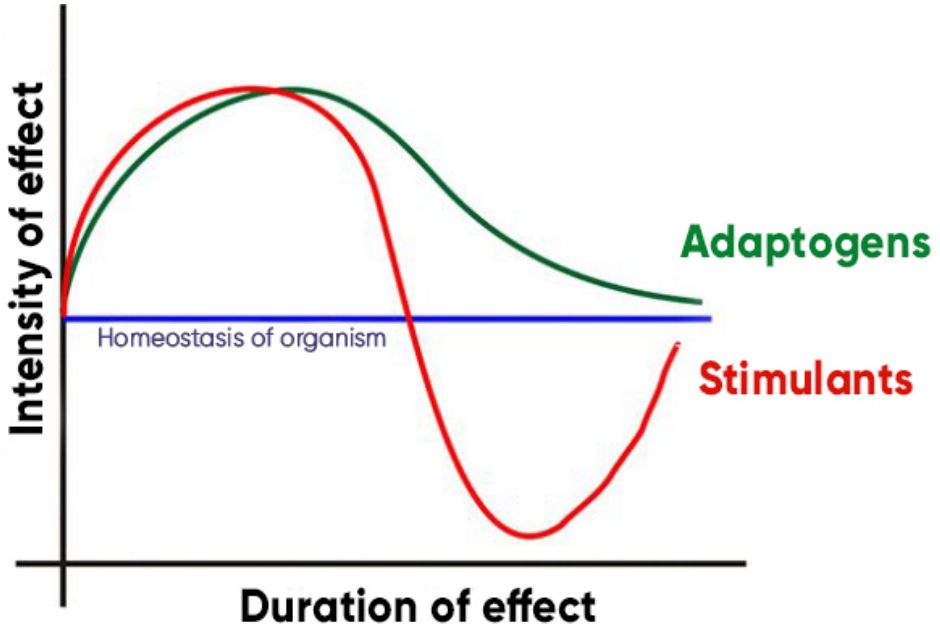
Per evitare confusione…

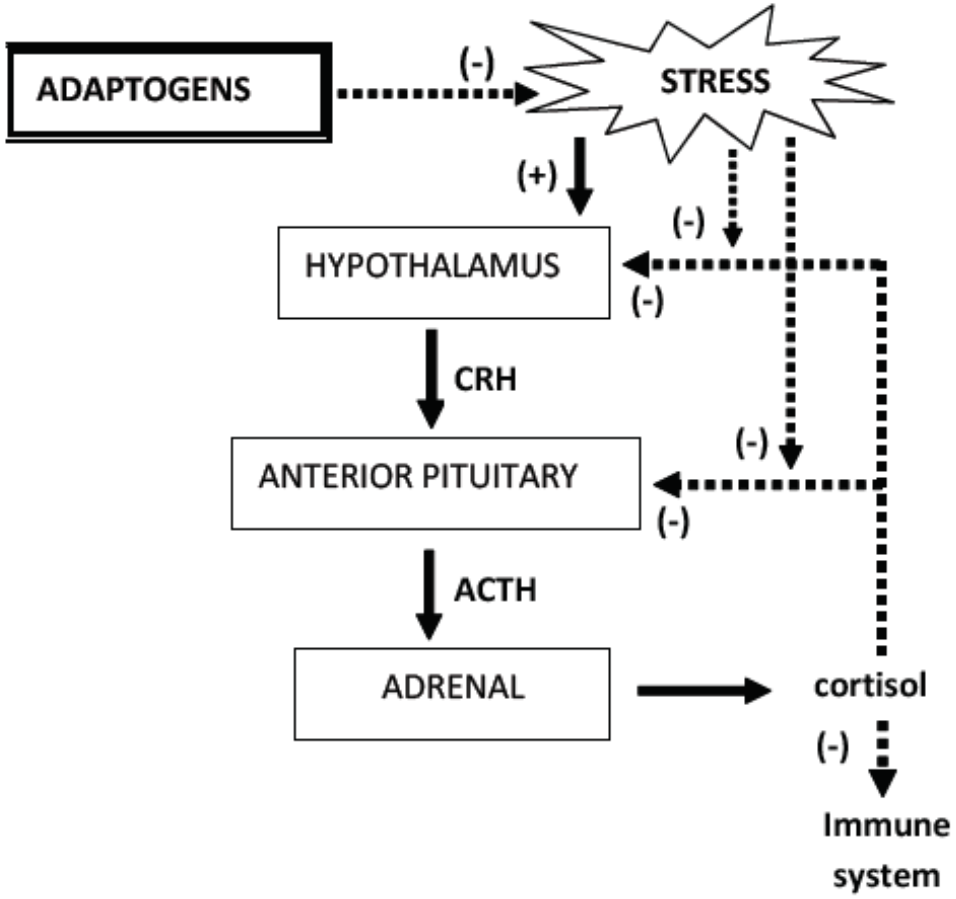
...è necessario differenziare il termine "adattogeno" dalle erbe medicinali con azione…:
- **TONICA**: sono sostanze che *attenuano le condizioni di debolezza* o la mancanza di tono all'interno dell'intero organismo o in particolari organi. Il termine è tipico per la medicina tradizionale, dove i tonici sono usati in condizioni di "astenia". L'effetto tonico può essere caratterizzato da dosi multiple che aumentano il benessere generale e la capacità lavorativa.
- **STIMOLANTE**: sostanze che causano un *aumento temporaneo della capacità di lavoro*, che è *seguito da un periodo di riduzione della capacità lavorativa*. L'effetto stimolante può essere caratterizzato da una singola dose che aumenta la capacità lavorativa. Il termine è usato nella medicina moderna e nella medicina tradizionale.

In contrasto con gli stimolanti, gli **ADATTOGENI** sono noti per causare un *aumento della capacità di lavoro che non è seguita da una diminuzione*

Come lavora un adattogeno… Forse…







Rev. bras. farmacogn. vol.21 no.4 Curitiba July/Aug. 2011

Echinacea: un adattogeno complesso…

Polisaccaridi (echinacina)
Glicoproteine
Acido caffeico e derivati (cinarina)
Acido cicorico
Echinacoside
Lattoni sesquiterpenici
Alcaloidi pirrolizidinici (tussilagine e isotussilagine)
Chetoni
Alcammidi (echinaceina)
Olii volatili (polieni)
Ecc. ecc. ecc.

Possibili meccanismi d'azione immunomodulanti:

- **Attivazione della fagocitosi**
- **Stimolazione dei fibroblasti**
- **Valorizzazione dell'attività respiratoria**
- **Riduzione dei fenomeni infiammatori**

Numerosissimi attivi con attività immunostimolante documentata prevalentemente da studi pre-clinici ed *in vitro*.
Grandissima variabilità di risultati in relazione ai dosaggi somministrati, la durata dei trattamenti, le tipologie di estratti utilizzati, i soggetti trattati, le tipologie di infezioni trattate, la tipologia di sport, ecc. ecc.

Echinacea ed infezioni ricorrenti del tratto respiratorio superiore

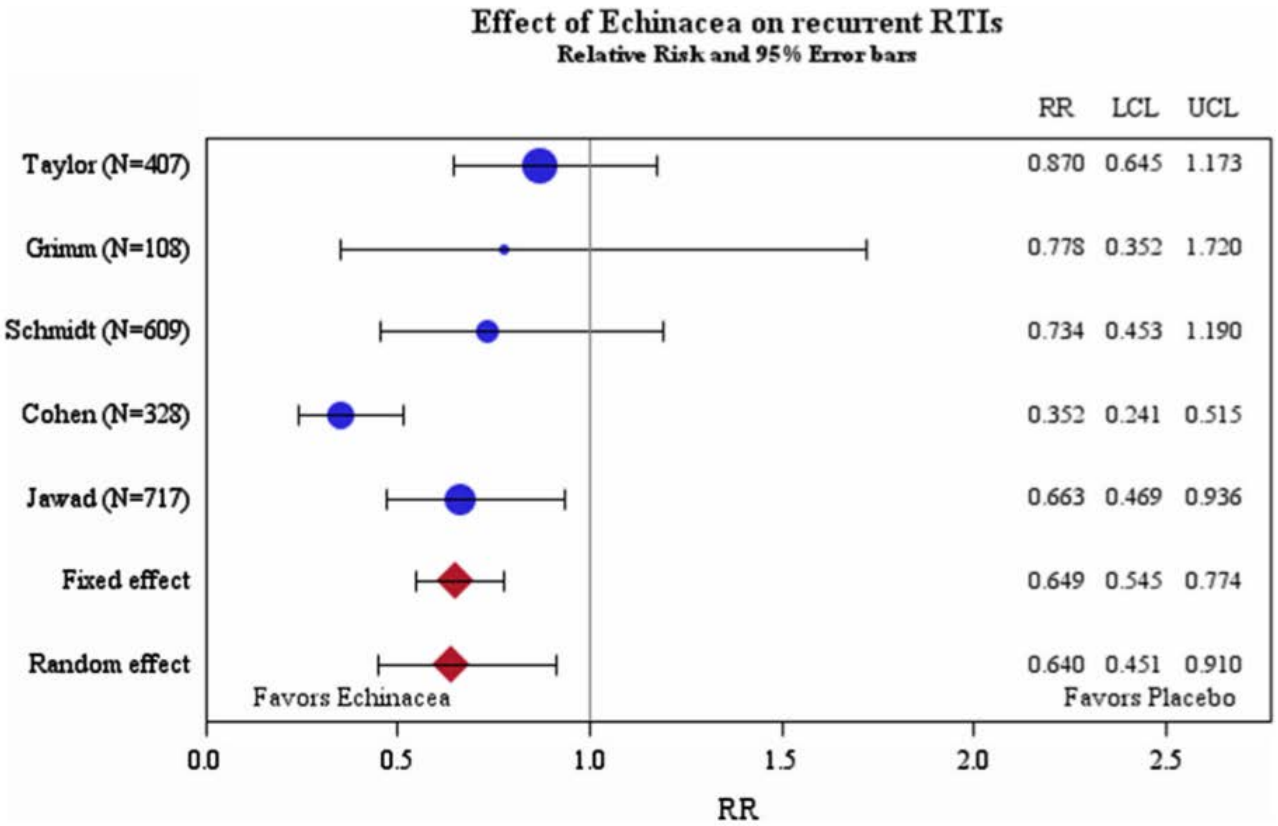


Table 3 Cumulated number of complications including conjunctivitis, sinusitis, otitis media/externa, tonsillitis, pharyngitis, bronchitis, and pneumonia

Complication	Echinacea (N = 569)	Placebo (N = 584)	Relative risk (95% confidence interval) P value
Conjunctivitis	2	3	0.684 (0.114–4.110) $P = 0.676$
Sinusitis	4	5	0.821 (0.219–3.073) $P = 0.768$
Otitis media/ externa	31	74	0.430 (0.278–0.664) $P < 0.0001$
Tonsillitis/ pharyngitis	37	61	0.623 (0.407–0.952) $P = 0.021$
Bronchitis	10	17	0.604 (0.274–1.330) $P = 0.201$
Pneumonia	13	38	0.351 (0.185–0.666) $P < 0.0001$
Total	97	198	0.503 (0.384–0.658) $P < 0.0001$

Conclusion: **Echinacea presents an effective option for the longer term management of recurrent RTIs and related complications**. **Differences in efficacy** may exist, possibly **explained by differences in preparation methods**. People with presumed lower immune function and a consequently high susceptibility might benefit most. In parallel with the reduced risk for infections, complications like pneumonia, otitis, or tonsillitis are prevented, as well as the associated need for antibiotic therapy. Finally, the good safety profile allows for long-term prevention with echinacea.

Adv Ther. 2015 Mar;32(3):187-200.

Echinacea e raffreddore comune

Lancet Infect Dis. 2007 Jul;7(7):473-80.

Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis.

Shah SA[1], Sander S, White CM, Rinaldi M, Coleman CI.

Abstract

Echinacea is one of the most commonly used herbal products, but controversy exists about its benefit in the prevention and treatment of the common cold. Thus, we did a meta-analysis evaluating the effect of echinacea on the incidence and duration of the common cold. 14 unique studies were included in the meta-analysis. Incidence of the common cold was reported as an odds ratio (OR) with 95% CI, and duration of the common cold was reported as the weighted mean difference (WMD) with 95% CI. Weighted averages and mean differences were calculated by a random-effects model (DerSimonian-Laird methodology). Heterogeneity was assessed by the Q statistic and review of L'Abbé plots, and publication bias was assessed through the Egger weighted regression statistic and visual inspection of funnel plots. Echinacea decreased the odds of developing the common cold by 58% (OR 0.42; 95% CI 0.25-0.71; Q statistic p<0.001) and the duration of a cold by 1.4 days (WMD -1.44, -2.24 to -0.64; p=0.01). Similarly, significant reductions were maintained in subgroup analyses limited to Echinaguard/Echinacin use, concomitant supplement use, method of cold exposure, Jadad scores less than 3, or use of a fixed-effects model. Published evidence supports echinacea's benefit in decreasing the incidence and duration of the common cold.

Riduzione dell'incidenza e della durata del raffreddore comune

N.B.

- **Estratti etanolici >> efficacia** rispetto agli altri
- **Dosaggi >0.5 g** (fino a 3 g/die): l'aumento dei dosaggi durante gli episodi acuti migliora ulteriormente la potenza degli effetti terapeutici
- **Durata degli studi >4 settimane** (<3 mesi): compliance fondamentale
- **Efficacia superiore negli individui** con maggiore sensibilità, stress, o uno **stato di debolezza immunitaria**
- **Buona efficacia** nelle **infezioni virologiche ricorrenti**

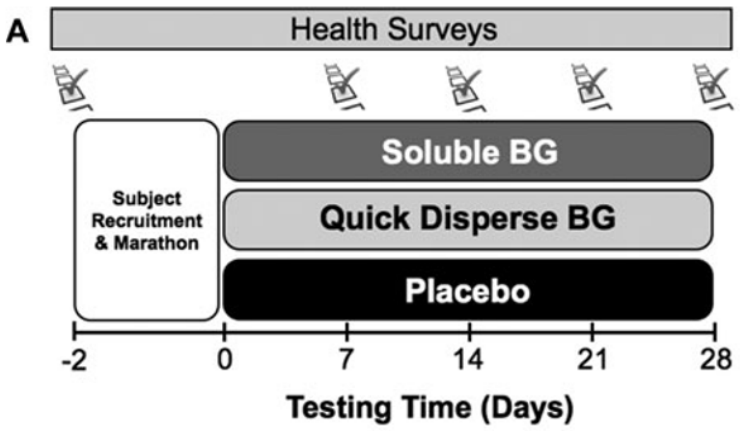
Beta-glucani

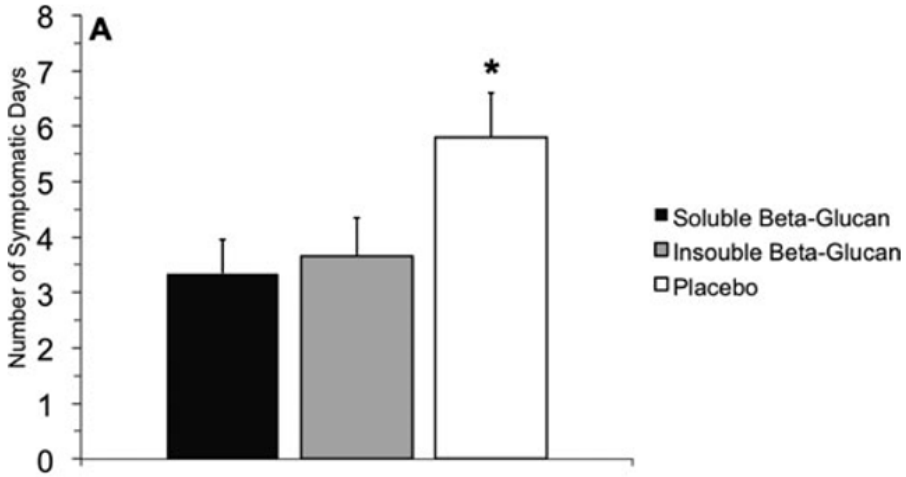
J Diet Suppl. 2013 Sep;10(3):171-83. doi: 10.3109/19390211.2013.820248. Epub 2013 Aug 9.

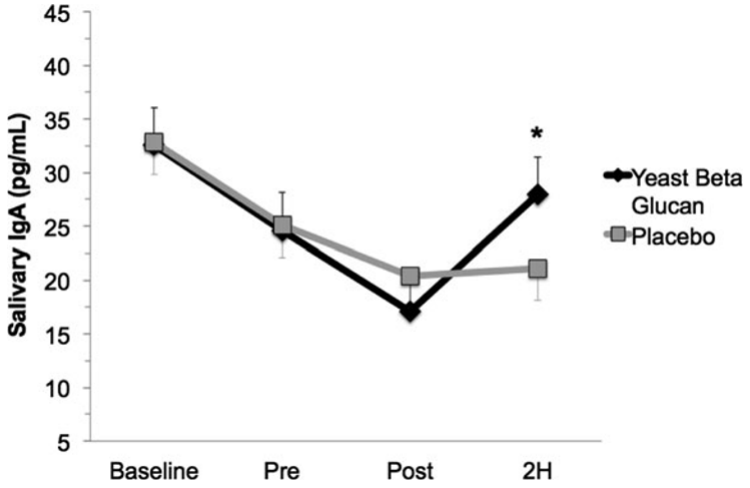
Baker's yeast beta glucan supplementation increases salivary IgA and decreases cold/flu symptomatic days after intense exercise.

McFarlin BK[1], Carpenter KC, Davidson T, McFarlin MA.

Premessa: danneggiamenti temporanei delle mucose orali sono comuni nelle 24 ore dopo un'intensa sessione di allenamento (maratona), con conseguente **aumento del rischio di sviluppare un'infezione del tratto respiratorio superiore** (URTI). Diversi RCTs hanno dimostrato che le **IgA salivari si riducono dopo un'intensa sessione di esercizio** e che la **riduzione delle IgA salivari è associata ad un aumento del numero di giorni sintomatici di URTI post-esercizio.**







Conclusioni: la supplementazione con B-glucano post-maratona, riduce significativamente (-50%) il rischio di URTI oltre a migliorare le concentrazioni di IgA salivari.

Br J Nutr. 2013 Feb 14;109(3):478-86. doi: 10.1017/S0007114512001407. Epub 2012 May 10.

Baker's yeast β-glucan supplementation increases monocytes and cytokines post-exercise: implications for infection risk?

Carpenter KC[1], Breslin WL[1], Davidson T[1], Adams A[1], McFarlin BK[1].

It appears that 10 d of **supplementation with BG increased the potential of blood leucocytes for the production of IL-2, IL-4, IL-5 and IFN-γ**. The key findings of the present study demonstrate that **BG may have potential to alter immunity following a strenuous exercise session.**

Appl Physiol Nutr Metab. 2010 Dec;35(6):755-62. doi: 10.1139/H10-070.

Effect of Pleuran (β-glucan from Pleurotus ostreatus) supplementation on cellular immune response after intensive exercise in elite athletes.

Bobovčák M[1], Kuniaková R, Gabriž J, Majtán J.

These results indicate that insoluble **β-glucan supplementation from P. ostreatus may play a role in modulating exercise-induced changes in NKCA in intensively training athletes.**

J Sports Sci Med. 2009 Dec 1;8(4):509-15. eCollection 2009.

Effect of BETA 1, 3/1, 6 GLUCAN on Upper Respiratory Tract Infection Symptoms and Mood State in Marathon Athletes.

Talbott S[1], Talbott J.

BETA-GLUCAN may prevent URTI symptoms, and **improve overall health and mood following a competitive marathon**. Key points**: Beta-Glucan supplementation maintains immune function in endurance athletes**. **Beta-Glucan supplementation reduces post-exercise URTIs in marathon runners**. **Maintenance of post-exercise immune function is associated with improved mood state, including reduced fatigue and increased vigor in athletes**.

Reishi (*Ganoderma lucidum*)

- **Study design**: RCT
- **Subjects**: 40 football players on "living high-training low»
- **Treatment**: Ganoderma lucidum for 6 weeks days
- **Result:** Significant improvement in CD4+/CD8 ratio

Br J Sports Med. 2008;42(10):819-22.

Omega-3

Oxid Med Cell Longev. 2016;2016:8950384. Epub 2016 Sep 6.

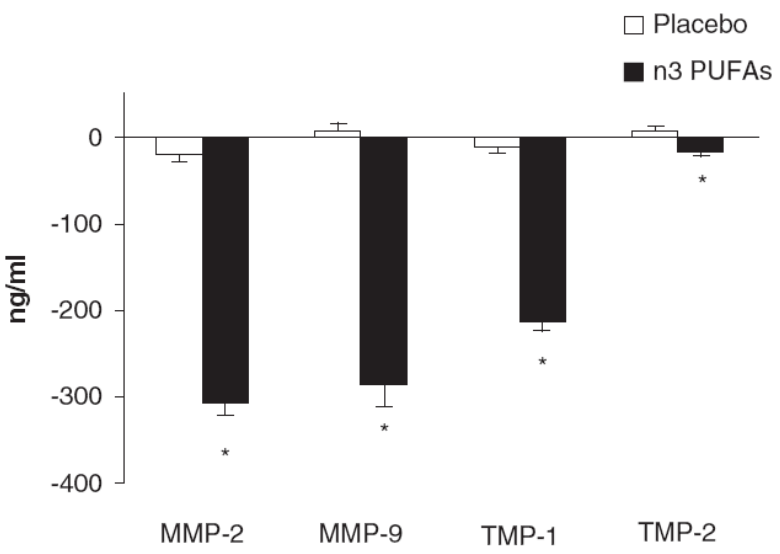
Training Enhances Immune Cells Mitochondrial Biosynthesis, Fission, Fusion, and Their Antioxidant Capabilities Synergistically with Dietary Docosahexaenoic Supplementation.

Busquets-Cortés C[1], Capó X[1], Martorell M[2], Tur JA[3], Sureda A[3], Pons A[3].

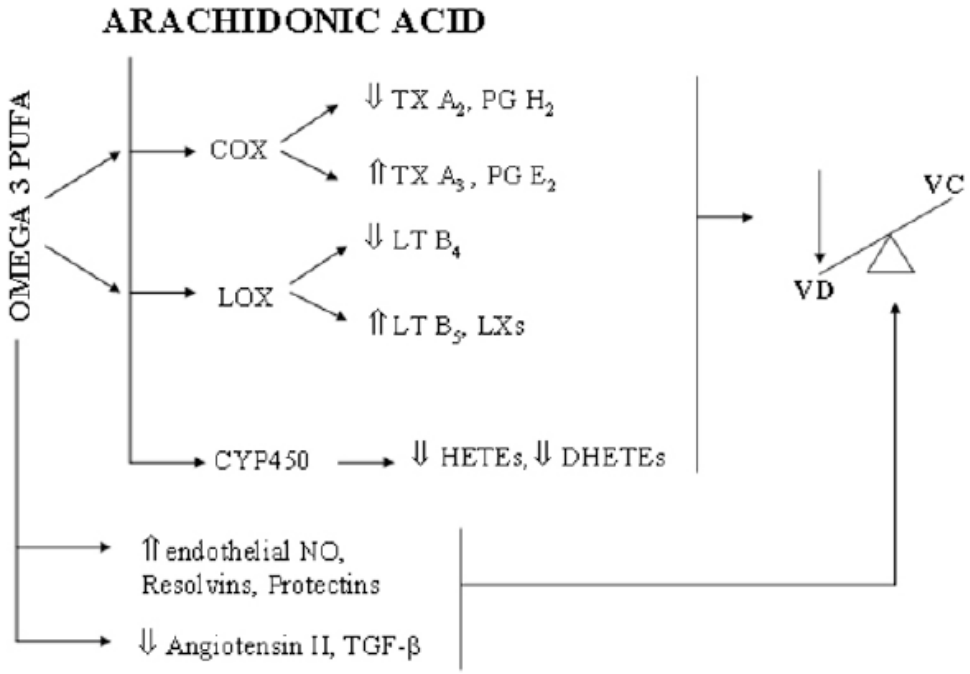
Int J Sport Nutr Exerc Metab. 2009 Oct;19(5):536-46.

n-3 polyunsaturated fatty acids do not alter immune and inflammation measures in endurance athletes.

Nieman DC[1], Henson DA, McAnulty SR, Jin F, Maxwell KR.



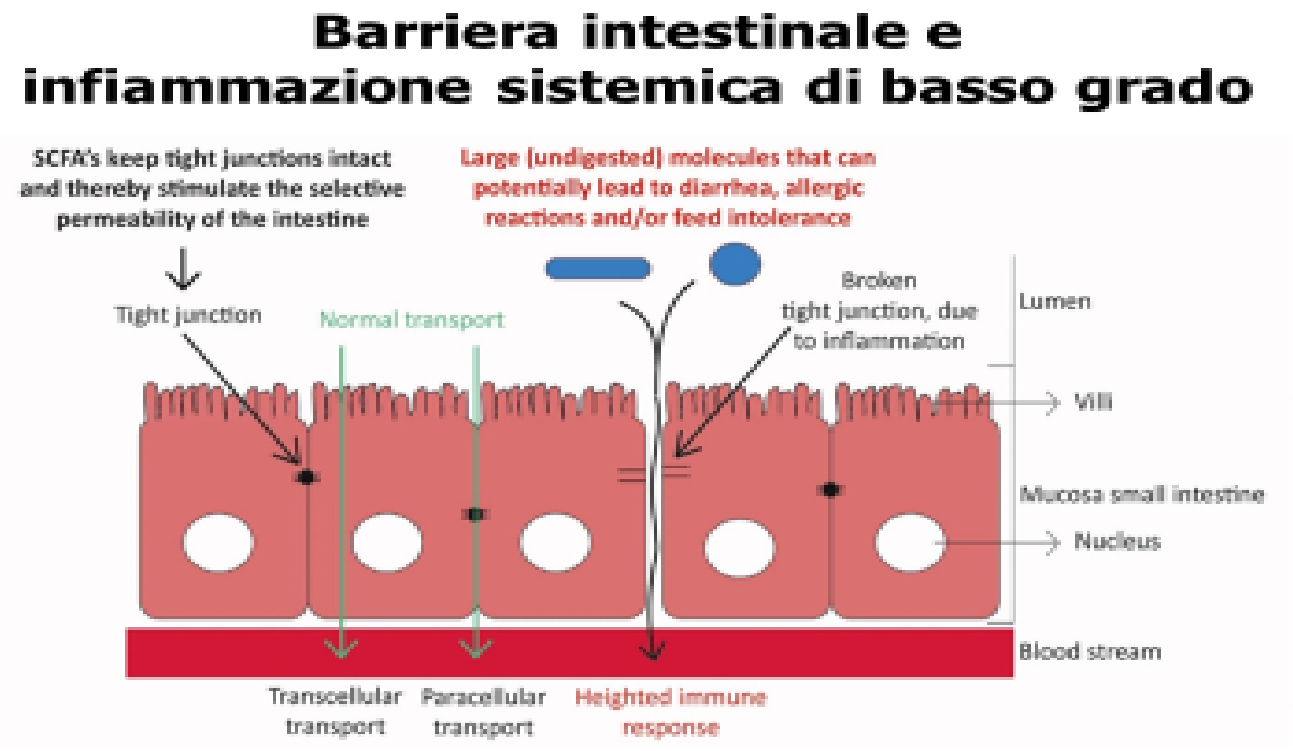
Derosa et al. Exp Opin Pharmacother 2009;10(8):1239-47



Cicero et al. Curr Vasc Pharmacol 2009; 7(3): 330-37

- **Poche evidenze e dati contrastanti su effetti degli omega 3 sul sistema immunitario nello sportivo**
- **Buone evidenze sulla riduzione dei processi di "inflammaging" ed in prevenzione cardiovascolare (primaria e secondaria)**

Disbiosi intestinale, infiammazione e… disfunzioni immunitarie



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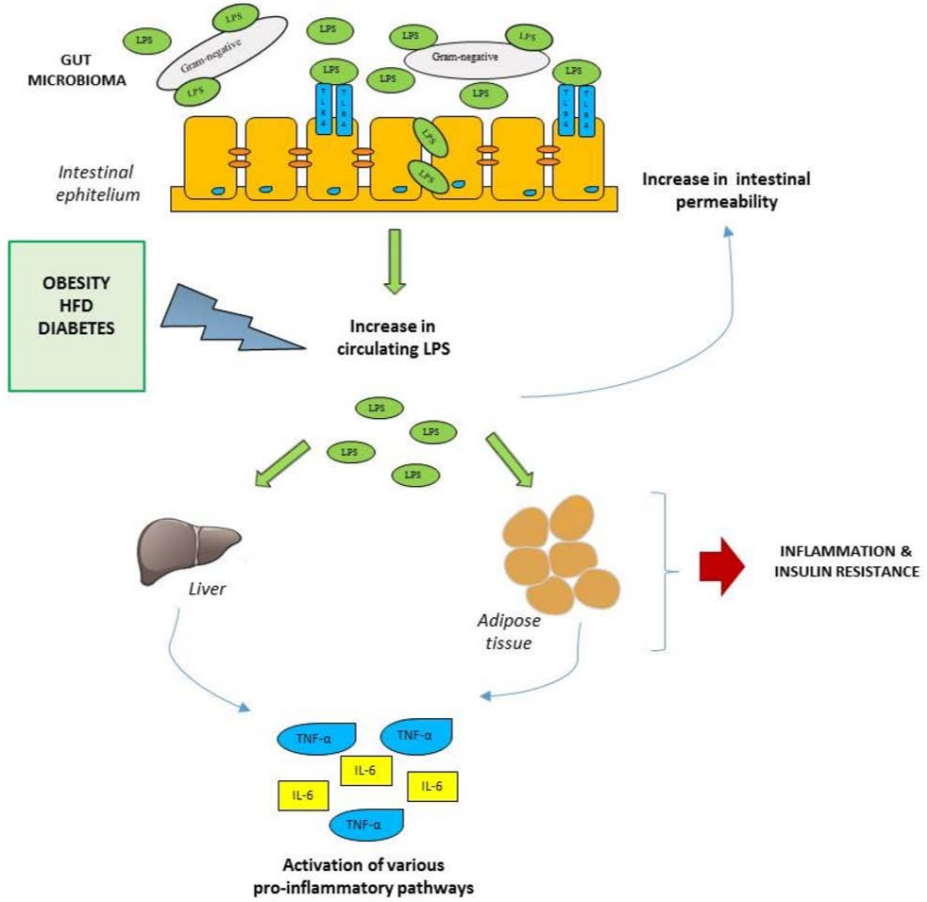
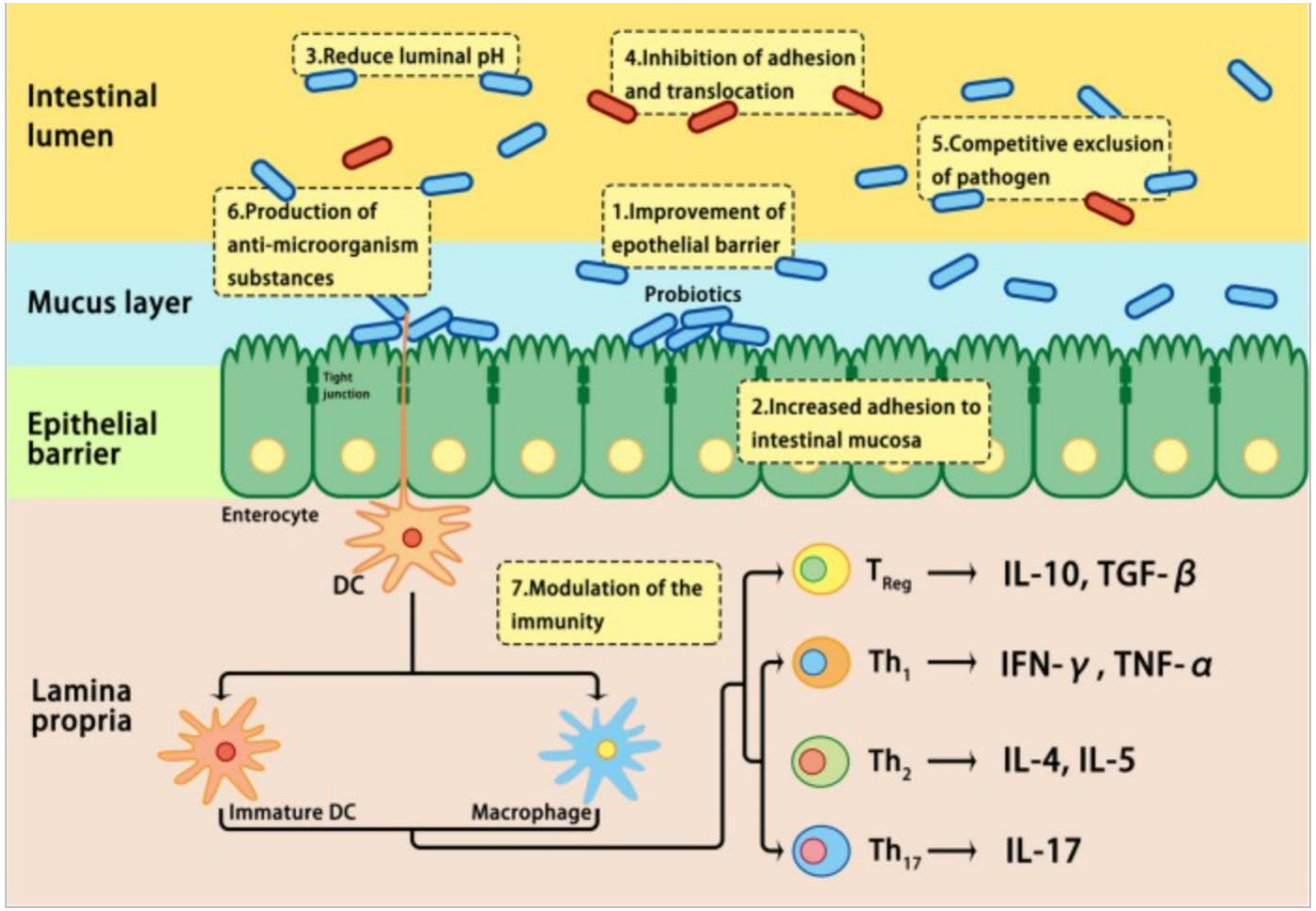


Yuji Nagatomo et al. Journal of Cardiac Failure Vol. 21 No. 12 2015



Disbiosi intestinale, infiammazione e… disfunzioni immunitarie

1) **Miglioramento della funzionalità della barriera intestinale**
2) **Aumentata adesione degli eubiotici alla mucosa intestinale**
3) **Riduzione pH intestinale**
4) **Inibizione dell'adesione e traslocazione batterica (antagonismo diretto)**
5) **Esclusione**: i probiotici possono alterare il microambiente per impedire agli agenti patogeni di accedere ai recettori appropriati, per limitare l'attaccamento, l'ingresso o la traslocazione del patogeno o per migliorare la funzione di barriera.
6) **Produzione di metaboliti anti-microbici**
7) **Modulazione diretta ed indiretta dell'immunità innata** (70% delle cellule immunitarie sono localizzate a livello intestinale (GALT))

Front Immunol. 2017; 8: 942.

Appl Physiol Nutr Metab. 2016 Jul;41(7):782-9. doi: 10.1139/apnm-2015-0541. Epub 2016 Mar 17.

Lactobacillus helveticus Lafti L10 supplementation reduces respiratory infection duration in a cohort of elite athletes: a randomized, double-blind, placebo-controlled trial.

Michalickova D[1], Minic R[2], Dikic N[3], Andjelkovic M[3], Kostic-Vucicevic M[3], Stojmenovic T[3], Nikolic I[3], Djordjevic B[1].

Eur J Appl Physiol. 2016 Aug;116(8):1555-63. doi: 10.1007/s00421-016-3415-x. Epub 2016 Jun 13.

Effects of Lactobacillus casei Shirota ingestion on common cold infection and herpes virus antibodies in endurance athletes: a placebo-controlled, randomized trial.

Gleeson M[1], Bishop NC[2], Struszczak L[2].

J Sci Med Sport. 2014 Jul;17(4):356-60. doi: 10.1016/j.jsams.2013.08.004. Epub 2013 Aug 30.

Probiotic supplementation reduces the duration and incidence of infections but not severity in elite rugby union players.

Haywood BA[1], Black KE[2], Baker D[3], McGarvey J[3], Healey P[3], Brown RC[1].

Eur J Sport Sci. 2015;15(1):63-72. doi: 10.1080/17461391.2014.971879. Epub 2014 Oct 23.

Probiotics supplementation for athletes - clinical and physiological effects.

Pyne DB[1], West NP, Cox AJ, Cripps AW.

Br J Sports Med. 2010 Mar;44(4):222-6. doi: 10.1136/bjsm.2007.044628. Epub 2008 Feb 13.

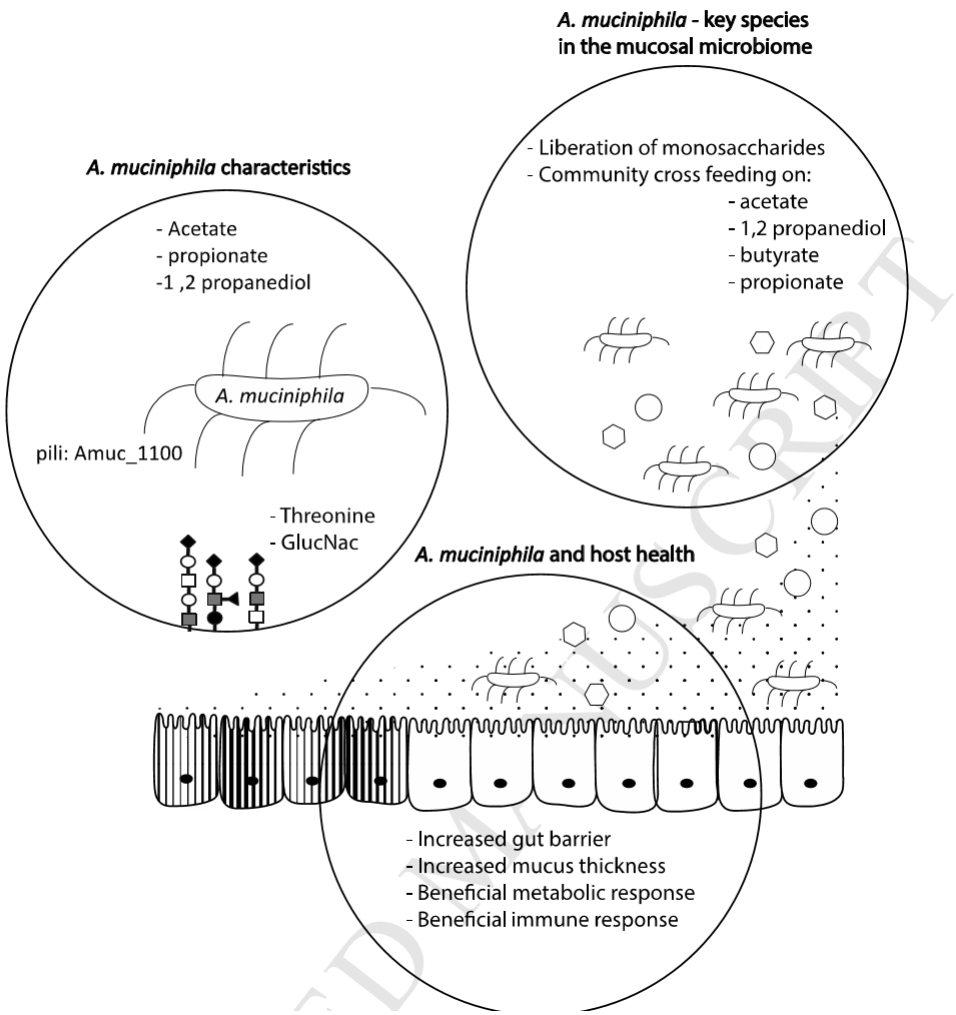
Oral administration of the probiotic Lactobacillus fermentum VRI-003 and mucosal immunity in endurance athletes.

Cox AJ[1], Pyne DB, Saunders PU, Fricker PA.

Best Pract Res Clin Gastroenterol. 2017 Dec;31(6):637-642. doi: 10.1016/j.bpg.2017.10.001. Epub 2017 Oct 13.

Action and function of Akkermansia muciniphila in microbiome ecology, health and disease.

Ottman N[1], Geerlings SY[2], Aalvink S[2], de Vos WM[3], Belzer C[4].



A. *A. Muciniphila:* ***0,4-1%*** del totale del microbiota fecale a partire dall'inizio della vita

B. Abbondantemente **presente nello strato della mucosa del colon**

C. Livelli bassi di *A. muciniphila* nell'intestino sono correlati a numerose patologie, tra cui le malattie infiammatorie intestinali (IBD), **obesità e diabete**.

D. Ulteriori studi meccanicistici hanno evidenziato il **ruolo chiave antinfiammatorio** di *A. muciniphila* nell'intestino

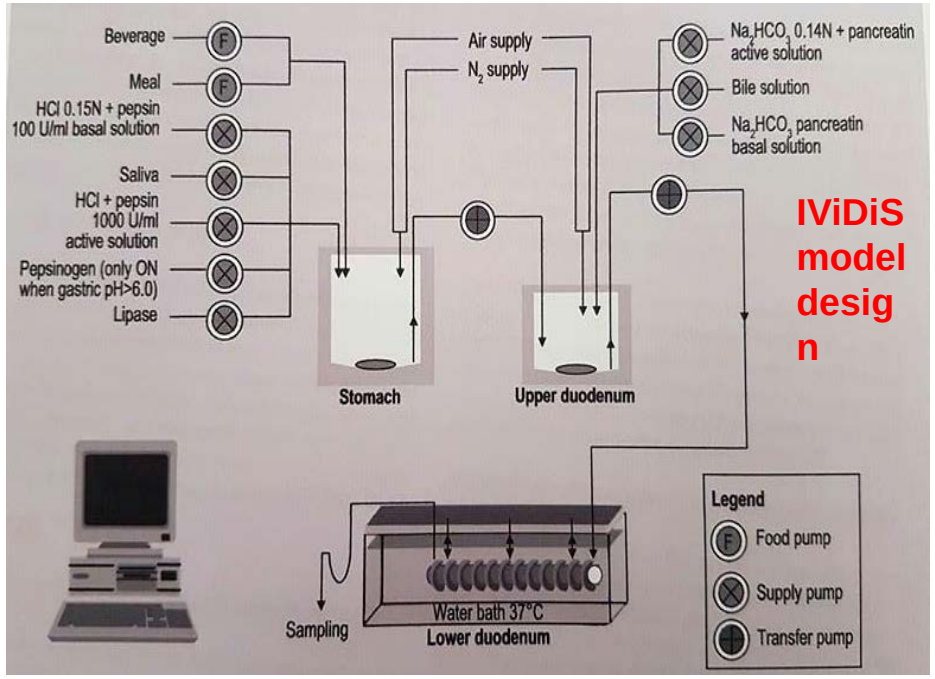
E. Meccanismi chiave:

- Colonizzazione muco intestinale e **produzione di SCFAs**
- Produzione di una singola proteina, chiamata **Amuc_1100** con un potenziale ruolo migliorativo di alcune componenti della sindrome metabolica
- **Degradazione di parte delle proteine della mucina** (N-acetilglucosamina) e liberazione di substrati zuccherini fonte metabolica per altri commensali (*Faecalibacterium prausnitzii*, *Eubacterium rectale*, *Roseburia intestinalis),* soprattutto produttori di butirrato
- **Azione immunomodulatoria**

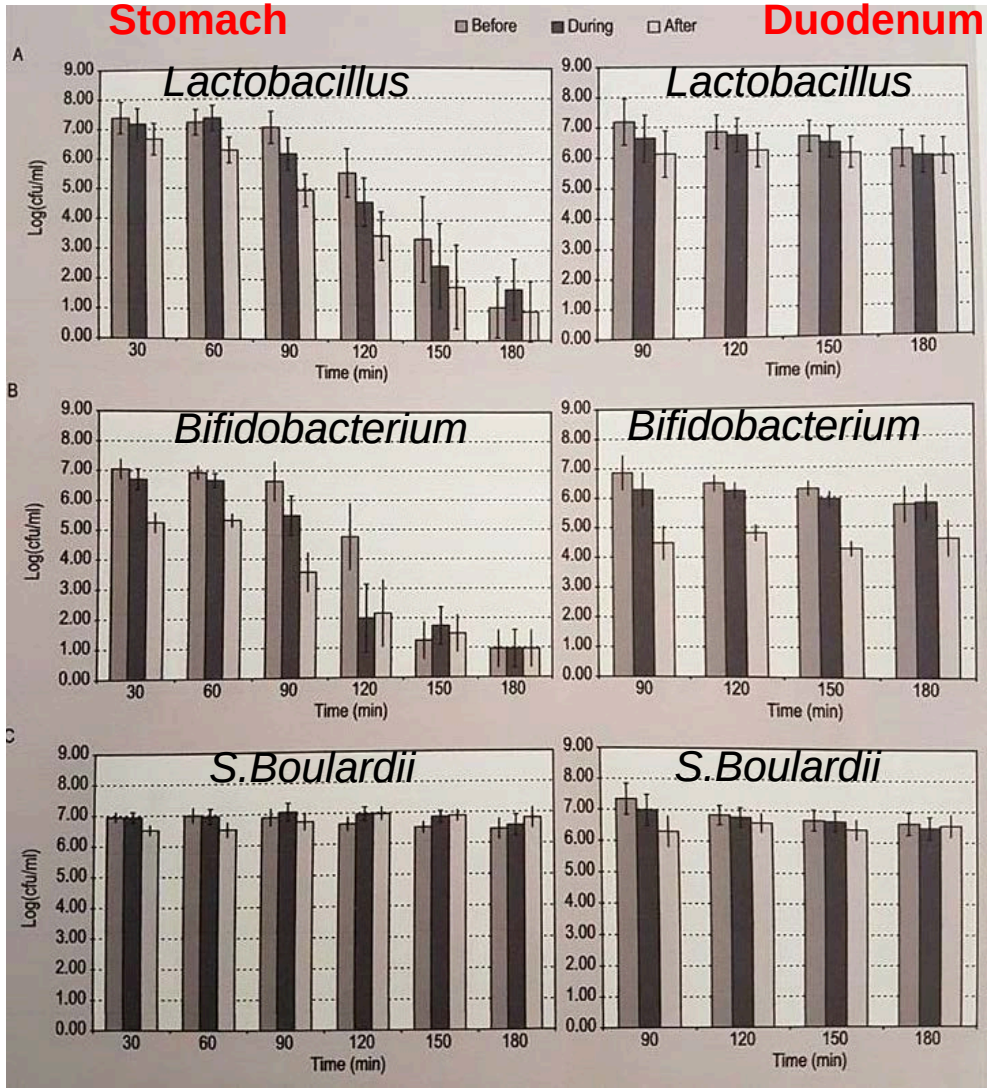
In breve… Probiotici sì o no?

- Alcuni **ceppi probiotici** (Lattobacilli, Bifidi e Saccaromiceti) posso avere un **ruolo importante nell'attività di immunomodulazione** sia nel sedentario che nello sportivo.
- Nello **sportivo** la **supplementazione con probiotici** può avere un razionale nel **ripristino dell'eubiosi intestinale**, nella **riduzione dello stato infiammatorio**, e potenzialmente nella **prevenzione e/o trattamento di alcune tipologie di infezioni** (soprattutto batteriche) soprattutto quelle relative al tratto respiratorio superiore.
- Alcune evidenze preliminari (Curr Sports Med Rep. 2007 Jul;6(4):269-73.) ed altri RCTs in corso, hanno evidenziato possibili **correlazioni fra disbiosi intestinale** e **fatica/recupero post-attività fisica.**
- **Alcuni ceppi probiotici sono dotati di attività pleiotropiche in prevenzione cardiovascolare (miglioramento della colesterolemia, pressione, BMI, acido urico, hsCRP) ed in particolare nei soggetti che praticano sport, hanno mostrato di migliorare la forza muscolare e la risposta agli stimoli infiammatori indotti dall'esercizio fisico (**Appl Physiol Nutr Metab. 2017)
- **Non tutti i probiotici sono uguali**: attenzione alle **forme di dosaggio** (latte e yogurt vs capsule e compresse), **ceppi di probiotici** (Lattobacilli, Bifidi e Saccaromiceti vs altri), **dosaggi** (>3.5 UFC/die di vitali), **associazioni**, **durata del trattamento** (>30 giorni).
- **Probiotic strains as the element of nutritional profile in physical activity – new trend or better sports results?** (Smarkusz J et al, 2017)**: Probiotic strains properly applied may have a positive influence on the athletes' bodies, but still randomized controlled trials are required to prove this thesis.**

Somministrazione di probiotici: in fase Fed o Fasted?



IViDiS model design



Considerations:

- ***Lactobacillus* and *Bifidobacterium*: > survival if administrated before (30 min.) or during meals. 60 min. after meals there's a significant drop of [L. and B.]**
- ***S.Boulardii*: no great differences**

Tompkins et al. Beneficial Microbes. 2011

Adv Nutr. 2016 May 16;7(3):488-97. doi: 10.3945/an.115.010538. Print 2016 May.

Effect of Flavonoids on Upper Respiratory Tract Infections and Immune Function: A Systematic Review and Meta-Analysis.

Somerville VS[1], Braakhuis AJ[2], Hopkins WG[3].

Abstract

Go to:

Previous research on animals indicates flavonoid compounds have immunomodulatory properties; however, human research remains inconclusive. The aim of this systematic review was to assess the efficacy of dietary flavonoids on upper respiratory tract infections (URTIs) and immune function in healthy adults. A created search strategy was run against Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE and EMBASE classic, CINAHL, and AMED. The returned studies were initially screened, and 2 reviewers independently assessed the remaining studies for eligibility against prespecified criteria. Fourteen studies, of 387 initially identified, were included in this review, and the primary outcome measure was the effect of flavonoids on URTI incidence, duration, and severity. Of the included studies, flavonoid supplementation ranged from 0.2 to 1.2 g/d. Overall, flavonoid supplementation decreased URTI incidence by 33% (95% CI: 31%, 36%) compared with control, with no apparent adverse effects. Sick-day count was decreased by 40% with flavonoid supplementation, although unclear. Differences in bio-immune markers (e.g., interleukin-6, tumor necrosis factor-α, interferon-γ, neutrophils) were trivial between the intervention and control groups during the intervention and after exercise when a postintervention exercise bout was included. These findings suggest that flavonoids are a viable supplement to decrease URTI incidence in an otherwise healthy population.

Quercetina

Med Sci Sports Exerc. 2007 Sep;39(9):1561-9.

Quercetin reduces illness but not immune perturbations after intensive exercise.

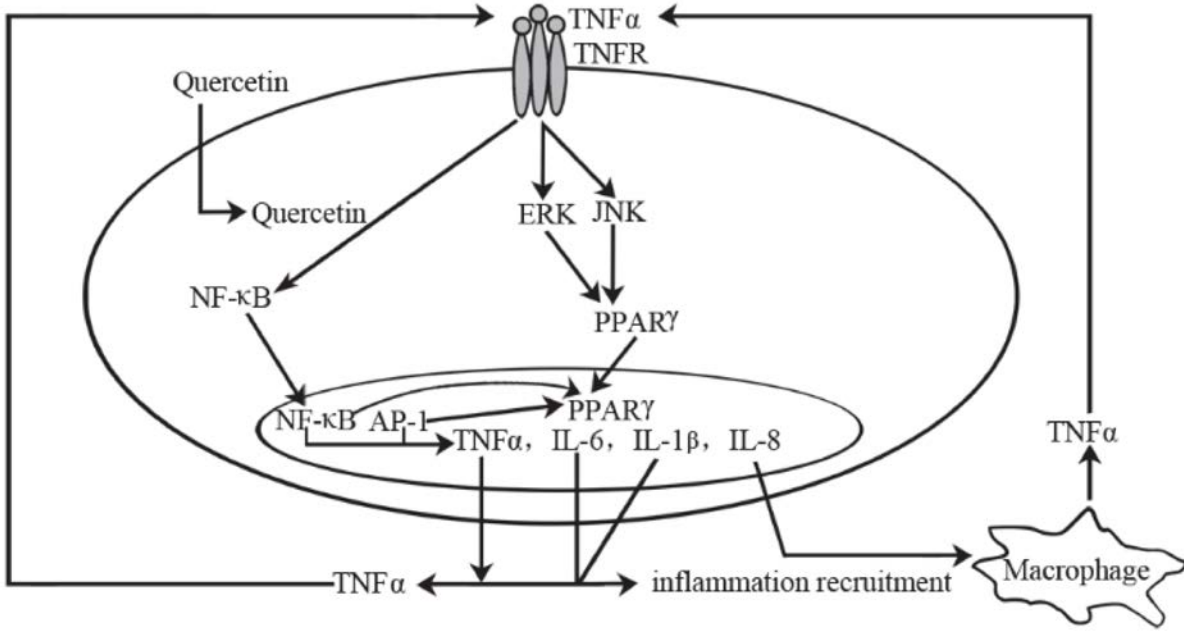
Nieman DC[1], Henson DA, Gross SJ, Jenkins DP, Davis JM, Murphy EA, Carmichael MD, Dumke CL, Utter AC, McAnulty SR, McAnulty LS, Mayer EP.

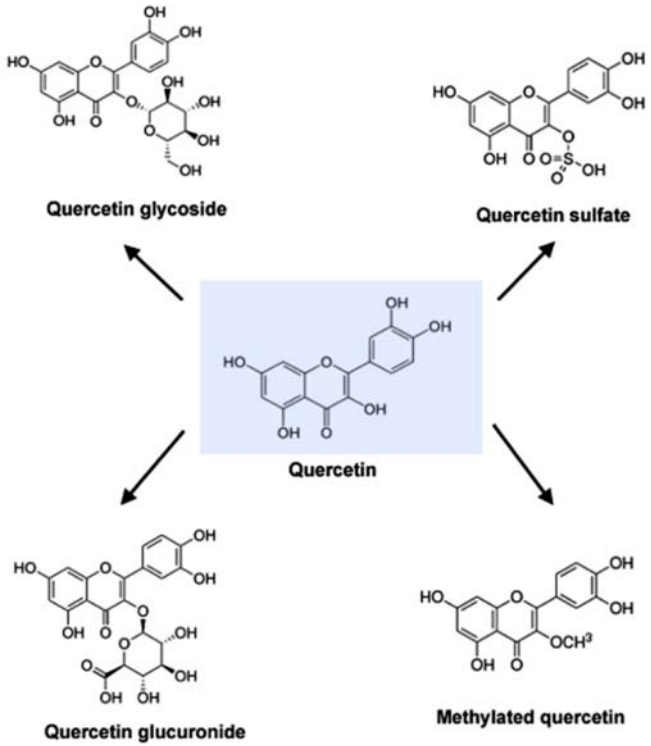
Int J Sport Nutr Exerc Metab. 2011 Aug;21(4):338-46.

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

Konrad M[1], Nieman DC, Henson DA, Kennerly KM, Jin F, Wallner-Liebmann SJ.

The first investigation on the pharmacokinetics of quercetin in humans suggested **very poor oral bioavailability** after a single oral dose **(~2%)**. The estimated absorption of **quercetin glucoside**, the naturally occurring form of quercetin, ranges from 3% to 17% in healthy individuals receiving 100 mg. The relatively low bioavailability of quercetin may be attributed to its **low absorption, extensive metabolism and/or rapid elimination**.





Nutrients **2016**, *8*(3), 167; doi:10.3390/nu8030167

Quercetina: la bionutraceutica

Human	Subjects	Effect	Mechanism	Reference
50 and 100 mg/person	Elderly Human subject	Anti-inflammatory properties	Inhibition of proteasome (nitric oxide, C-reactive protein, γ-glutamyltransferase) activity	[71]
500 and 1000 mg/day	Human subject	Reduction of upper respiratory tract infection and total sick days; Improvement in 12-min treadmill time trial performance	No effect	[72]
1000 mg/day	Human in treadmill		No effect	[76]
500 and 1000 mg/day	Human subject	No effect on innate immune function or inflammation, illness rates	No effect	[73]
1000 mg/day	Human cyclist		No effect	[74]
1000 mg/day	Human runner		No effect	[75]
1000 mg/day	Human cyclist		No effect	[77]

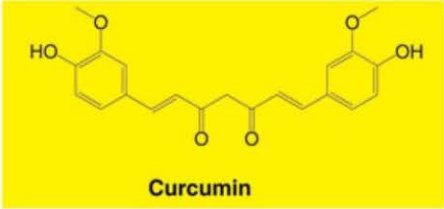
Il successo di un trattamento farmacologico non dipende soltanto dalla scelta del principio attivo e dalla dose somministrata ma anche da una sua corretta formulazione dal punto di vista tecnico e biofarmaceutico.

Nutrients **2016**, *8*(3), 167; doi:10.3390/nu8030167

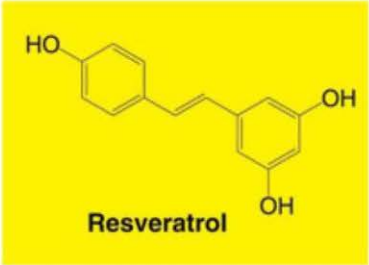
Non tutti i polifenoli sono uguali

Low bioavailability

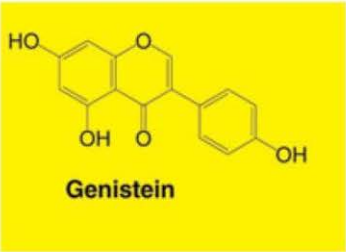
Turmeric
(*Curcuma ionga*)



Grape
(*Vitis vinifera*)

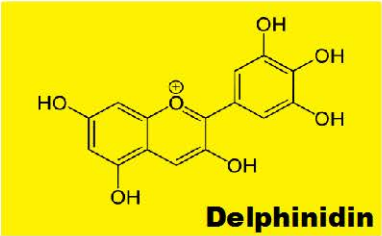


Soybean
(*Glycine max*)

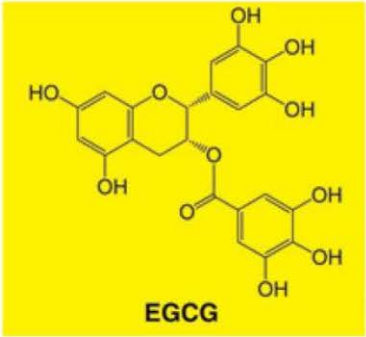


Better bioavailability

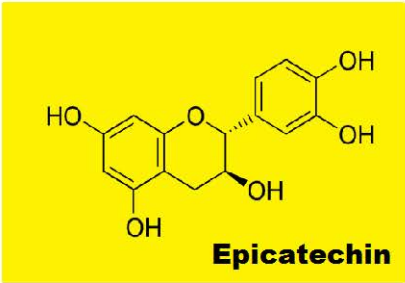
Blueberry



Green Tea
(*Camellia sinensis*)



Cocoa
(*Theobroma cacao*)



Colostro bovino

Med Sport Sci. 2012;59:62-9. doi: 10.1159/000341966. Epub 2012 Oct 15.

Bovine colostrum and immune function after exercise.

Davison G[1].

Author information

Abstract

Strenuous and/or prolonged exercise causes transient perturbations in immune function. It is well accepted that this is one mechanism contributing to the higher occurrence of infection (e.g. upper respiratory tract infection (URTI)) in athletes, especially endurance athletes. URTI or upper respiratory tract (URT) symptoms can negatively affect training and competition performance but athletes must train intensively to be successful. Therefore, interventions that can legitimately enhance immune function and reduce URTI risk can be of benefit to athletes. Bovine colostrum supplementation has been investigated as a possible nutritional countermeasure to enhance (or maintain) immune function, and reduce URTI risk, following strenuous or prolonged exercise and during intensive training periods. There is convincing evidence that daily supplementation with bovine colostrum, for a number of weeks (and preliminary evidence for acute effects after a single dose), can maintain intestinal barrier integrity, immune function and reduce the chances of suffering URTI or URT symptoms in athletes or those undertaking heavy training. The mechanisms are not fully understood at present but there is preliminary evidence suggesting that the effects on immune function are attributable, at least in part, to small bioactive components that survive digestion and are biologically available after consumption, but further work is required. In summary, the balance of existing evidence does support the notion that bovine colostrum is beneficial for certain groups of athletes, such as those involved in strenuous training (e.g. endurance athletes), in terms of immunity and resistance to infection.

29 ottobre 2017

Serie A, perché così tanti infortuni? Il ruolo della forza e della Vitamina D

I rischi della carenza di Vitamina D in uno sportivo

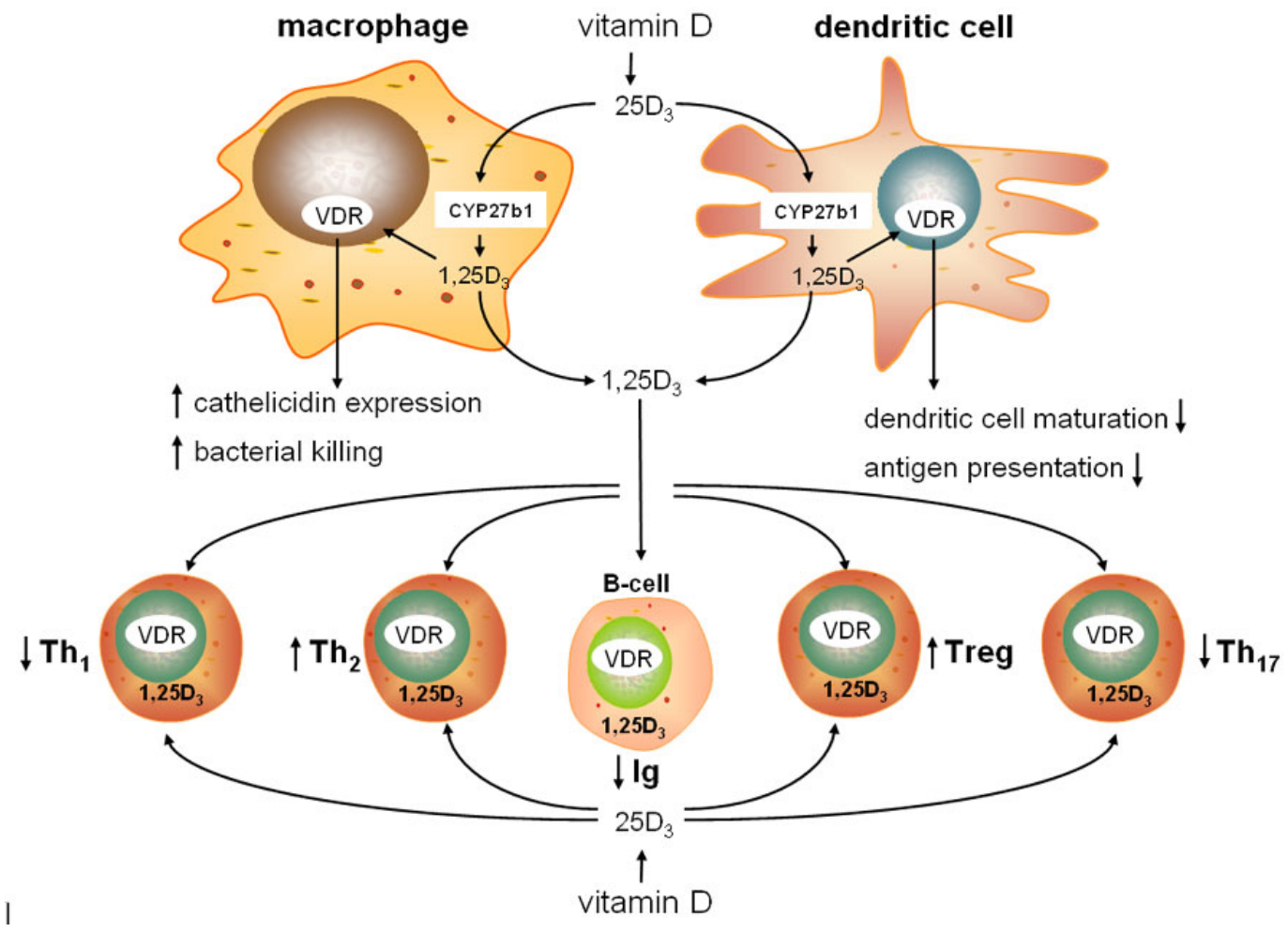
"C'è un legame forte e scientificamente dimostrato tra i livelli di vitamina D nel sangue e le prestazioni dei calciatori professionisti – dice Claudio Tozzi". Quali? "Una carenza di vitamina D fa rima con performance ridotte e soprattutto maggior rischio di infortuni. Questo perché buoni livelli di questo ormone si traducono in un miglior assorbimento del calcio a livello osseo e muscolare, con risultati evidenti sulla coordinazione motoria e muscolare. Sulla forza e la capacità di recupero". Non solo, importante è sottolineare come nei vari mesi dell'anno ci sia un andamento variabile e marcato dei livelli di vitamina D nel sangue dei calciatori (in particolare d'inverno, quando l'esposizione al sole diminuisce): "I valori minimi scendono tra gennaio e febbraio. A certificarlo è un recente studio pubblicato sulla rivista Chronobiology International condotto da ricercatori dell'IRCCS Istituto Ortopedico Galeazzi di Milano, che ha focalizzato le attenzioni su un campione di 167 calciatori del Bari, Lanciano e Pescara, sottoposti a vari prelievi sanguigni nell'arco degli anni 2013 e 2014. E nonostante i partecipanti dello studio fossero giovani sportivi sani, il dato ha evidenziato che 55 dei 167 calciatori presi in esame – il 32,9% – presentava carenze lievi di vitamina D almeno in una fase dell'anno, mentre 15 di essi – il 9% – mostrava un deficit più marcato di questo ormone. In pratica un calciatore su tre ne è carente".

Ecco nel dettaglio come questa Vitamina possa migliorare la salute del giocatore: "Feci un lavoro alla Juventus nel 2010 - spiega Fabrizio Angelini -, dove andammo a vedere il decremento del livello della vitamina D dei giocatori durante la stagione, situazione che era già stata segnalata in letteratura. Ma nel 2010 anche in clinica non si parlava molto di questa vitamina. In generale la si prescriveva in dosi minimali nei casi di osteoporosi. Era una vitamina legata all'osso. In realtà la D è un ormone che ha un'azione precisa nel nucleo cellulare. Ha diversi organi bersaglio ed è una sostanza ad azione precisa. Nei casi clinici c'è una pandemia di deficit di Vitamina D e viene associata a tante malattie, da quelle muscolari a quelle metaboliche. Anche se non è detto che poi risolvano le patologie semplicemente con la sua integrazione. Ma se siamo Vitamina D carenti, allora dobbiamo integrarla. Nello sport la Vitamina D ha importanza a vari livelli: sull'osso per esempio. Il picco di massa ossea è correlata alla performance sportiva. Ha importanza sul muscolo, sia sulla forza che la potenza. Ci sono dei lavori che la correlano al consumo massimo di ossigeno, il V02MAX, la capacità aerobica massima del muscolo, ovvero il massimo volume di ossigeno consumato per minuto. E' molto importante nel sistema immunitario. Io stesso la utilizzo nell'approccio delle malattie autoimmuni tiroidee. Sembra in grado di diminuire le infezioni delle alte vie respiratorie nei maratoneti per esempio. Dopo una corsa di endurance nelle 48/72 ore successive c'è un aumento delle tracheite e delle infezioni, in quanto queste corse producono deficit immunitari".

Nutrients. 2017 Jun 24;9(7). pii: E651. doi: 10.3390/nu9070651.

Vitamin D and Infectious Diseases: Simple Bystander or Contributing Factor?

Gois PHF[1,2], Ferreira D[3], Olenski S[4], Seguro AC[5].



http://ortho.ucla.edu/images/Research/Vitamin_D_Fig4lg.jpg

Evidenze:

- **Trilioni** di recettori della vitamina D nel nostro organismo (molti di essi localizzati nelle cellule immunitarie)
- **Bassi livelli plasmatici di vitamina D** negli atleti sono associati a **bassi livelli di IgA** salivari che a loro volta sono associati ad una maggiore incidenza di RTIs
- **Ruolo chiave nella produzione di citochine antinfiammatorie** (IL-10) e nell'inibizione di citochine infiammatorie (IL-17, -21)
- Riduzione del rilascio dalle cellule dendritiche e dai monociti di IL-1, -6, -8, -12, TNF-alfa.
- Aumento del **rilascio di defensine**, catelicidine, della chemotassi e della risposta antimicrobica di natura innata
- Modulazione dell'**attività delle cellule NK**
- Aumento produzione di **specie ROS** all'interno delle cellule fagocitarie

Vitamina D e sistema immunitario: grandi possibilità per la ricerca…

Exerc Immunol Rev. 2013;19:86-101.

Influence of vitamin D status on respiratory infection incidence and immune function during 4 months of winter training in endurance sport athletes.

He CS[1], Handzlik M, Fraser WD, Muhamad A, Preston H, Richardson A, Gleeson M.

Open Access J Sports Med. 2012 Apr 27;3:35-42. doi: 10.2147/OAJSM.S31022. eCollection 2012.

Vitamin D status and biomarkers of inflammation in runners.

Willis KS[1], Smith DT, Broughton KS, Larson-Meyer DE.

Clin Exp Rheumatol. 2017 Nov 14. [Epub ahead of print]

Vitamin D and systemic lupus erythematous: a review of immunological and clinical aspects.

Dall'Ara F[1], Cutolo M[2], Andreoli L[1], Tincani A[3], Paolino S[2].

Adv Exp Med Biol. 2017;996:169-183. doi: 10.1007/978-3-319-56017-5_14.

Asthma and Allergy "Epidemic" and the Role of Vitamin D Deficiency.

Douros K[1], Boutopoulou B[2], Fouzas S[3], Loukou I[4].

Adv Exp Med Biol. 2017;996:155-168. doi: 10.1007/978-3-319-56017-5_13.

Role of Vitamin D in Rheumatoid Arthritis.

Bellan M[1,2], Sainaghi PP[3], Pirisi M[4,3].

Medicine (Baltimore). 2017 Jun;96(23):e7024. doi: 10.1097/MD.0000000000007024.

Vitamin D supplementation and disease activity in patients with immune-mediated rheumatic diseases: A systematic review and meta-analysis.

Franco AS[1], Freitas TQ, Bernardo WM, Pereira RMR.

nutrients

MDPI

Review

Vitamin C and Immune Function

Anitra C. Carr [1,*] and Silvia Maggini [2]

Table 1. Role of vitamin C in immune defense.

Immune System	Function of Vitamin C	Refs.
Epithelial barriers	Enhances collagen synthesis and stabilization	[30–35]
	Protects against ROS-induced damage [1]	[36–40]
	Enhances keratinocyte differentiation and lipid synthesis	[41–45]
	Enhances fibroblast proliferation and migration	[46,47]
	Shortens time to wound healing in patients	[48,49]
Phagocytes (neutrophils, macrophages)	Acts as an antioxidant/electron donor	[50–53]
	Enhances motility/chemotaxis	[54–63]
	Enhances phagocytosis and ROS generation	[64–71]
	Enhances microbial killing	[54,55,57,58,70,72]
	Facilitates apoptosis and clearance	[71,73,74]
	Decreases necrosis/NETosis	[73,75]
B- and T-lymphocytes	Enhances differentiation and proliferation	[62,63,76–82]
	Enhances antibody levels	[78,83–85]
Inflammatory mediators	Modulates cytokine production	[75,77,86–94]
	Decreases histamine levels	[56,61,95–101]

[1] ROS, reactive oxygen species; NET, neutrophil extracellular trap. Note that many of these studies comprised marginal or deficient vitamin C status at baseline. Supplementation in situations of adequate vitamin C status may not have comparable effects.

Vitamina C e sport…

Int J Sports Physiol Perform. 2008 Dec;3(4):516-30.

Vitamin C supplementation and salivary immune function following exercise-heat stress.

Carrillo AE[1], Murphy RJ, Cheung SS.

Cochrane Database Syst Rev. 2013 Jan 31;(1):CD000980. doi: 10.1002/14651858.CD000980.pub4.

Vitamin C for preventing and treating the common cold.

Hemilä H[1], Chalker E.

Eur J Clin Nutr. 2007 Apr;61(4):443-60. Epub 2006 Nov 29.

Nutritional modulation of exercise-induced immunodepression in athletes: a systematic review and meta-analysis.

Moreira A[1], Kekkonen RA, Delgado L, Fonseca J, Korpela R, Haahtela T.

Clin J Sport Med. 2010 Jan;20(1):39-46. doi: 10.1097/JSM.0b013e3181cb4086.

Upper respiratory tract infection symptoms in ultramarathon runners not related to immunoglobulin status.

Peters EM[1], Shaik J, Kleinveldt N.

Eur J Appl Physiol. 2003 Mar;89(1):100-7. Epub 2003 Jan 21.

Influence of vitamin C supplementation on oxidative and salivary IgA changes following an ultramarathon.

Palmer FM[1], Nieman DC, Henson DA, McAnulty SR, McAnulty L, Swick NS, Utter AC, Vinci DM, Morrow JD.

- **Miglioramento dell'immunodepressione linfocitaria indotta dall'overtraining**
- **Riduzione dell'incidenza, della durata e della severità di URTI**
- **Attenuazione dell'aumento dei livelli plasmatici di citochine proinfiammatorie (dosaggi >1 g/die)**

Current recommendations for immuno-nutrition support in athletes include:

- Ingest **adequate amounts of micronutrients** (Zn, Vit A, Fe, Vit B6, Vit B12, Vit E)
- Take a daily oral **vitamin D3** supplement of 1000 IU
- Take a daily **probiotic supplement** containing at least 3 billion of live bacteria
- Include a variety of **fruit and vegetables** as part of the normal diet (at least on 5 days per week); this can be supplemented with plant polyphenol supplements or beverages (for example, green tea and non-alcoholic beer) or concentrated fruit/vegetable extracts
- Consider taking a daily **10–20 g bovine colostrum powder supplement**
- Consider taking **zinc supplement** in the days leading up to an important competition in case cold symptoms should begin at that important time

Gleeson M. Immunology (2016)

In addition…

To minimise the chances of developing immunodepression:

- **Avoid very prolonged training sessions**, overtraining and chronic fatigue
- **Keep other life stresses to a minimum**
- **Get adequate sleep quantity** (at least 7 h) **and quality**
- **Avoid rapid weight loss**
- **Avoid consumption of large quantities of alcohol**

Gleeson M. Immunology (2016)

Riassumendo

- **Esiste un potenziale razionale per l'immunomodulazione "nutraceutica" sia nello sportivo agonista sia nello sportivo amatoriale**
- **Principi attivi potenzialmente efficaci sono i beta-glucani, le vitamine D e C, alcune piante adattogene, alcuni ceppi probiotici ed i polifenoli anche se…**
- **Pochi RCTs a disposizione, piccole popolazioni campionarie, grande eterogeneità di risultati (tipologia di sport, età, sesso, livello di agonismo, tipologia di nutraceutico… ecc.)**

ATTENZIONE AI DOSAGGI, TITOLAZIONI, STANDARDIZZAZIONI E FORME FARMACEUTICHE !

- **Grande necessità di nuovi RCTs su popolazioni selettive di sportivi**