menta SYNC™

Optimized Gut-Brain Axis Communication*

amare™ GLOBAL
THE MENTAL WELLNESS COMPANY

TECHNICAL DATA

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menta SYNC™

Optimize communication within and between the Axis "between brains" (the gut-brain-axis) by balancing levels and activity of signaling molecules (cytokines, neurotransmitters, hormones) to optimize interactions between cells of the gut

KEY INGREDIENTS

Beta-Glucan Blend *(Wellmune® Yeast-derived Beta-Glucan & Fucomax™ Seaweed Fucoidan)* - Beta-glucans are polysaccharides (complex sugars) that are found in the cell walls of bacteria, fungi, yeasts, algae, lichens, and plants (such as oats and barley). They act as immune-modulator agents, meaning they trigger a cascade of events that help regulate the immune system, making it more efficient. Specifically, beta glucans stimulate the activity of macrophages, which are versatile immune cells that ingest and demolish invading pathogens and stimulate other immune cells to attack. Macrophages also release cytokines, chemicals that when secreted enable the immune cells to communicate with one another. In addition, beta glucans stimulate lethal white blood cells (lymphocytes and natural killer cells) that bind to tumors or viruses, releasing anti-tumor and anti-viral chemicals.*

Wellmune *(yeast beta-glucan)* - is a natural and unique yeast beta glucan (1-3, 1-6 structure) derived from the cell walls of a highly purified, proprietary baker's yeast (Saccharomyces cerevisiae) that activates key innate immune cells, clinically proven to enhance immune system function, psychological vigor, and overall well-being. One study showed a reduction in the number of upper respiratory tract infections and statistically significant changes and trends in cytokine levels that are part of the body's response to viral encounters and inflammation. Wellmune activates billions of innate immune cells, which are part of both the body's natural defense and systemic communication network, to respond more effectively to stressors and environmental challenges without over stimulating the immune system. It is also shown to Increase energy and improved mental clarity.*

Fucomax *(seaweed fucoidan)* - is produced by extraction from three types of organic brown seaweed: Cladosiphon okamuranus, Laminaria japonica and Undaria pinnatifida. These species of seaweed contain high levels of fucoidan (a sulfated polysaccharide) shown to promote healthy immune system modulation, improved cell-to-cell communication, and superior tissue maintenance. Fucoidan may also directly improve gastric activity and ease a range of GI discomfort, including bloating, heartburn, stomachache and other postprandial symptoms.*

Alpha-Glucan Blend *(High-Polyphenol Purple Mushrooms; Maitake, Shiitake, Agaricus, Chaga)* - Alpha-glucans have demonstrated an ability to enhance a wide range of immune system functions. Grown on purple corn for its high polyphenol content, Amare's alpha-glucan blend combines innovative, patented, certified-organic ingredients that merge purple corn with medicinal mushroom mycelium.*

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Intestinal Intregrity Blend *(Calcium/Magnesium Butyrate & Zinc/Carnosine Complex)*

Calcium/Magnesium Butyrate - a short chain fatty acid that is a potent detoxifier of ammonia and neurotoxins. Butyrate also encourages the growth and resilience of friendly bacteria in the gut. Short-chain fatty acids are produced when dietary fiber is fermented in the colon. It is particularly important for colon health because it is the primary energy source for colonic cells and has anti-carcinogenic as well as anti-inflammatory properties that are important for keeping colon cells healthy.*

Zinc/Carnosine Complex - a complex of the essential mineral Zinc and the amino acid L-Carnosine that helps to relieve occasional gastric discomfort. When zinc is complexed to L-carnosine, it dissociates in the stomach at a slow/controlled rate. This prolonged presence in the stomach allows it to maintain its gastric healing effect over a longer period of time. Zinc/L-carnosine may also help maintain the bacterial balance throughout upper/middle/lower GI tract with a "displacement" effect on certain strains of harmful bacteria. By supporting the bacterial balance in the stomach, it can also help maintain a healthy mucosal tissues that may help to soother irritated gastric linings.*

CLINICAL STUDIES

J Diet Suppl. 2017 Mar 4;14(2):173-185.

Yeast β-Glucan Modulates Inflammation and Waist Circumference in Overweight and Obese Subjects.

Mosikanon K, Arthan D, Kettawan A, Tungtrongchitr R, Prangthip P.

Abstract

Increased inflammation occurs with excessive adiposity and yeast β-glucan modulates immune responses. This study investigated the potential effect of yeast β-glucan on inflammatory cytokines in overweight/obese people. A randomized, double blinded, placebo-controlled, clinical trial design enrolled 44 overweight/obese participants with body mass index ≥23 kg/m2, randomized to two groups receiving β-glucan 477 mg/capsule (n = 22) or placebo (n = 22) orally for six weeks. At weeks one to two, participants received 1 β-glucan or placebo capsule/day and at four weeks two tablets/day. Anthropometric changes, lipid profiles, liver and renal functions, and inflammatory cytokines were measured. β-glucan reduced waist circumference ($p = 0.037$) and blood pressure ($p = 0.006$) compared with controls after six weeks of intervention. No statistical significance between groups was observed for triglyceride, cholesterol, lipid profile, liver and renal function, or energy and nutrient intake compared with controls at week six. β-glucan increased interlukin-10 (IL-10), an anti-inflammatory cytokine, by 23.97% from baseline at week two ($p < 0.001$) and 31.12% at week six ($p < 0.001$) and was significantly increased compared with controls at week two ($p < 0.001$) until week six ($p < 0.001$). β-glucan reduced pro-inflammatory cytokines IL-6 at week six ($p = 0.005$) and tumor necrosis factor-α at week two ($p = 0.037$) compared with controls. Supplementation of yeast β-glucan for six weeks modulated pro-cytokines that accelerate overweight/obese comorbidities and reduced blood pressure as well as waist circumference, the strong risk factors for cardiovascular disease, in overweight/obese subjects. Thus, β-glucan might have the potential to decrease comorbid conditions associated with overweight/ obesity.

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Nutr J. 2014 Apr 28;13:38.

Immune-modulatory effects of dietary Yeast Beta-1,3/1,6-D-glucan.

Stier H, Ebbeskotte V, Gruenwald J.

Abstract

Beta-glucans are a heterogeneous group of natural polysaccharides mostly investigated for their immunological effects. Due to the low systemic availability of oral preparations, it has been thought that only parenterally applied beta-glucans can modulate the immune system. However, several in vivo and in vitro investigations have revealed that orally applied beta-glucans also exert such effects. Various receptor interactions, explaining possible mode of actions, have been detected. The effects mainly depend on the source and structure of the beta-glucans. In the meantime, several human clinical trials with dietary insoluble yeast beta-glucans have been performed. The results confirm the previous findings of in vivo studies. The results of all studies taken together clearly indicate that oral intake of insoluble yeast beta-glucans is safe and has an immune strengthening effect.

Mol Nutr Food Res. 2014 Jan;58(1):183-93.

Effects of orally administered yeast-derived beta-glucans: a review.

Samuelsen AB, Schrezenmeir J, Knutsen SH.

Abstract

Yeast-derived beta-glucans (Y-BG) are considered immunomodulatory compounds suggested to enhance the defense against infections and exert anticarcinogenic effects. Specific preparations have received Generally Recognized as Safe status and acceptance as novel food ingredients by European Food Safety Authority. In human trials, orally administered Y-BG significantly reduced the incidence of upper respiratory tract infections in individuals susceptible to upper respiratory tract infections, whereas significant differences were not seen in healthy individuals. Increased salivary IgA in healthy individuals, increased IL-10 levels in obese subjects, beneficial changes in immunological parameters in allergic patients, and activated monocytes in cancer patients have been reported following Y-BG intake. The studies were conducted with different doses (7.5-1500 mg/day), using different preparations that vary in their primary structure, molecular weight, and solubility. In animal models, oral Y-BG have reduced the incidence of bacterial infections and levels of stress-induced cytokines and enhanced antineoplastic effects of cytotoxic agents. Protective effects toward drug intoxication and ischemia/reperfusion injury have also been reported. In conclusion, additional studies following good clinical practice principles are needed in which well-defined Y-BG preparations are used and immune markers and disease endpoints are assessed. Since optimal dosing may depend on preparation characteristics, dose-response curves might be assessed to find the optimal dose for a specific preparation.

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J Diet Suppl. 2013 Sep;10(3):171-83.

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

McFarlin BK, Carpenter KC, Davidson T, McFarlin MA.

Abstract

Strenuous exercise, such as running a marathon, is known to suppress mucosal immunity for up to 24 hr, which can increase the risk of developing an upper respiratory tract infection (URTI) and reduced performance capacity (Allgrove JE, Geneen L, Latif S, Gleeson M. Influence of a fed or fasted state on the s-IgA response to prolonged cycling in active men and women. Int J Sport Nutr Exerc Metab. 2009;19(3):209-221; Barrett B, Locken K, Maberry R, Schwamman J, Brown R, Bobula J, Stauffacher EA. The Wisconsin Upper Respiratory Symptom Survey (WURSS): a new research instrument for assessing the common cold. J Fam Pract. 2002;51(3):265; Carpenter KC, Breslin WL, Davidson T, Adams A, McFarlin BK. Baker's yeast beta glucan supplementation increases monocytes and cytokines post-exercise: implications for infection risk? Br J Nutr. 2012;1-9). While many dietary interventions have been used to combat postexercise immune suppression, most have been ineffective. The key purpose of this study was to determine if baker's yeast β-glucan (BG) could positively affect the immune system of individuals undergoing intense exercise stress using two experiments. In the first (E1; N = 182 men and women), BG was compared to placebo supplementation for the incidence of URTI symptoms for 28 days postmarathon. In the second (E2; N = 60 men and women) changes in salivary immunoglobulin A (IgA) were evaluated after 50-min of strenuous cycling when participants had been supplemented for 10 days with either BG (250 mg/day) or placebo (rice flour). For E1, subjects reported URTI symptoms using a daily health log. For E2, saliva was collected prior to, immediately, and 2-hr postexercise using a salivette. Data for E1 and E2 were analyzed using separate analyses of variance (ANOVAs) with repeated measures ($p < .05$). In E1, BG was associated with a 37% reduction in the number of cold/flu symptom days postmarathon compared to placebo ($p = .026$). In E2, BG was associated with a 32% increase in salivary IgA ($p = .048$) at 2 hr after exercise compared to placebo. In summary, the present study demonstrates that BG may reduce URTI symptomatic days and improve mucosal immunity (salivary IgA) postexercise.

J Am Coll Nutr. 2012 Aug;31(4):295-300.

Baker's yeast beta-glucan supplement reduces upper respiratory symptoms and improves mood state in stressed women.

Talbott SM, Talbott JA.

Abstract

OBJECTIVE:

Several studies have shown a baker's yeast beta-1,3/1,6-d-glucan, extracted from Saccharomyces cerevisiae, is effective in reducing the incidence of cold and flu symptoms. This study evaluated the effect of a specific beta-glucan supplement (Wellmune) on upper respiratory tract symptoms and psychological well-being in women with moderate levels of psychological stress.

METHODS:

Healthy women (38 ± 12 years old) prescreened for moderate levels of psychological stress, self-administered a placebo (n = 38) or 250 mg of Wellmune (n = 39) daily for 12 weeks. We used the Profile of Mood States (POMS) psychological survey to assess changes in mental/physical energy levels (vigor)

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and overall well-being (global mood state). A quantitative health perception log was used to track upper respiratory symptoms.

RESULTS:

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

CONCLUSIONS:

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

Anticancer Agents Med Chem. 2013 Jun;13(5):709-19.

β-Glucans and their applications in cancer therapy: focus on human studies.

Aleem E.

Abstract

β-glucans belong to a group of polysaccharides located in the cell wall of bacteria, fungi including mushrooms, as well as cereals such as barley and oats. All β-glucans are glucose polymers linked together by a (β 1-3) linear β-glycosidic chain core and they differ by their length and branching structures. They are considered biological response modifiers with immunomodulatory and health beneficial effects including anticancer properties. Few studies using purified β- glucans were performed, but their anticancer potential was demonstrated mainly through studies using extracts from mushrooms, yeast or other sources which contain β-glucan as a key component. Their anticancer effects were demonstrated mainly in in vitro and in vivo experimental systems but fewer studies from human populations are available. β-glucans have been used as adjuvant therapy in clinical trials, mainly in the Far East, with a positive effect on patients' survival and quality of life. The mechanism of action is suggested to be through its stimulation of the immune system. This review focuses on human studies; clinical trials and epidemiological data assessing the efficacy and safety of mushroom-derived β- glucans in cancer treatment and prevention. The potential direct effects of β-glucans on cancer cells are also described.

Anticancer Agents Med Chem. 2013 Jun;13(5):699-708.

The effects of β-glucans on cancer metastasis.

Yoon TJ, Koppula S, Lee KH.

Abstract

Beta-glucans (β-glucans), naturally occurring polysaccharides, are present as constituents of the cell wall of cereal grains, mushrooms, algae, or microbes including bacteria, fungi, and yeast. Since Pillemer et al. first prepared and investigated zymosan in the 1940s and others followed with the investigation of β-glucans in the 1960s and 1970s, researchers have well established the significant role of β-glucans on the immune system relative to cancer treatment, infection immunity, and restoration of damaged bone marrow. However, information on their biological role in anti-metastatic activity remains limited. As an immunomodulating agent, β-glucan acts through the activation of innate immune cells such as macrophages, dendritic cells, granulocytes, and natural killer cells. This activation triggers the responses

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of adaptive immune cells such as CD4(+) or CD8(+) T cells and B cells, resulting in the inhibition of tumor growth and metastasis. Reports have shown that β-glucans exert multiple effects on cancer cells and cancer prevention. However the mechanisms of their actions appear complex due to differences in source, chemical structure, insufficiently defined preparation, and molecular weight, hence the inconsistent and often contradictory results obtained. This review is focused on the potential of β-glucans as anti-metastatic agents and the known mechanisms underlying their biological effects.

Br J Nutr. 2013 Feb 14;109(3):478-86.

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

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

Abstract

Strenuous aerobic exercise is known to weaken the immune system, and while many nutritional supplements have been proposed to boost post-exercise immunity, few are known to be effective. The purpose of the present study was to evaluate whether 10 d of supplementation with a defined source of baker's yeast β-glucan (BG, Wellmune WGP®) could minimise post-exercise immunosuppression. Recreationally active men and women (n 60) completed two 10 d trial conditions using a cross-over design with a 7 d washout period: placebo (rice flour) and baker's yeast BG (250 mg/d of β-1,3/1,6-glucans derived from Saccharomyces cerevisiae) before a bout of cycling (49 ± 6 min) in a hot (38 ± 2°C), humid (45 ± 2 % relative humidity) environment. Blood was collected at baseline (before supplement), pre- (PRE), post- (POST) and 2 h (2H) post-exercise. Total and subset monocyte concentration was measured by four-colour flow cytometry. Plasma cytokine levels and lipopolysaccharide (LPS)-stimulated cytokine production were measured using separate multiplex assays. Total ($CD14^+$) and pro-inflammatory monocyte concentrations ($CD14^+/CD16^+$) were significantly greater at POST and 2H ($P<0{\cdot}05$) with BG supplementation. BG supplementation boosted LPS-stimulated production of IL-2, IL-4, IL-5 and interferon-γ (IFN-γ) at PRE and POST ($P<0{\cdot}05$). Plasma IL-4, IL-5 and IFN-γ concentrations were greater at 2H following BG supplementation. 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.

Nutrition. 2012 Jun;28(6):665-9.

Influence of yeast-derived 1,3/1,6 glucopolysaccharide on circulating cytokines and chemokines with respect to upper respiratory tract infections.

Fuller R, Butt H, Noakes PS, Kenyon J, Yam TS, Calder PC.

Abstract

OBJECTIVE:

Wellmune WGP is a food supplement containing a refined 1,3/1,6 glucopolysaccharide that improves the antimicrobial activity of the innate immune cells by the priming of lectin sites. This study aimed to investigate whether Wellmune decreases the frequency and severity of upper respiratory tract infection (URTI) symptoms over 90 d during the peak URTI season in healthy university students. The

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secondary aims included an assessment of plasma cytokine and chemokine levels.

METHODS:

This was a randomized, double-blinded, placebo-controlled trial lasting 90 d. One hundred healthy individuals (18-65 y old, mean age ~21 y) were randomized to 250 mg of Wellmune once daily or to an identical rice flour-based placebo. Health was recorded daily and two or more reported URTI symptoms for 2 consecutive days triggered a medical assessment and blood collection within 24 h. The URTI symptom severity was monitored. Plasma cytokines and chemokines were measured at day 0, day 90, and during the confirmed URTI.

RESULTS:

Ninety-seven participants completed the trial (Wellmune, n = 48; placebo, n = 49). The Wellmune tended to decrease the total number of days with URTI symptoms (198 d, 4.6%, versus 241 d, 5.5% in the control group, P = 0.06). The ability to "breathe easily" was significantly improved in the Wellmune group; the other severity scores showed no significant difference. Cytokines and chemokines were not different between the groups at study entry or day 90, but monocyte chemotactic protein-1 was lower in the Wellmune group during the URTI.

CONCLUSION:

Wellmune may decrease the duration and severity of URTI. Larger studies are needed to demonstrate this.

Endocr Metab Immune Disord Drug Targets. 2009 Mar;9(1):67-75.

Glucans as biological response modifiers.

Novak M, Vetvicka V.

Abstract

Beta-D-glucans belong to a group of natural, physiologically active compounds, generally called biological response modifiers. Glucans represent highly conserved structural components of cell walls in yeast, fungi, or seaweed. Despite long history of research, the exact mechanisms of glucan action remain unsolved. The present review starts with the history of glucans. Next, the detailed information about the possible glucan sources is followed by a description of the mechanisms of action. Physiological functions of glucan suggest the possible use of glucans not only as non-specific immunomodulator, but also as its possible future use as a drug.

Physiol Behav. 2008 May 23;94(2):276-84.

Dietary modulation of immune function by beta-glucans.

Volman JJ, Ramakers JD, Plat J.

Abstract

The immune response can be modulated by nutrients like beta-glucans, which are glucose polymers that are major structural components of the cell wall of yeast, fungi, and bacteria, but also of cereals like oat and barley. There is a lot of structural variation in the beta-glucans from these different sources, which may influence their physiological functions. In this review the current status concerning possibilities to modulate immune function by beta-glucans is discussed. In vitro as well as in vivo studies in animals and humans show that especially beta-glucans derived from fungi and yeast have immune modulating

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properties. Most frequently evaluated are effects on leukocyte activity, which has been suggested to contribute to the increased resistance against infections observed after beta-glucan interventions. Although most studies supply the beta-glucans parenteral (e.g. intravenous or subcutaneous), also enteral administrated (dietary) beta-glucan influence the immune response. Although more human studies are needed, it is tempting to suggest that dietary beta-glucans may be a useful tool to prime the host immune system and increase resistance against invading pathogens.

Mutat Res. 2008 Mar-Apr;658(3):154-61.

beta-Glucans in promoting health: prevention against mutation and cancer.

Mantovani MS, Bellini MF, Angeli JP, Oliveira RJ, Silva AF, Ribeiro LR.

Abstract

The polysaccharides beta-glucans occur as a principal component of the cellular walls. Some microorganisms, such as yeast and mushrooms, and also cereals such as oats and barley, are of economic interest because they contain large amounts of beta-glucans. These substances stimulate the immune system, modulating humoral and cellular immunity, and thereby have beneficial effect in fighting infections (bacterial, viral, fungal and parasitic). beta-Glucans also exhibit hypocholesterolemic and anticoagulant properties. Recently, they have been demonstrated to be anti-cytotoxic, antimutagenic and anti-tumorogenic, making them promising candidate as pharmacological promoters of health.

Mar Drugs. 2014 Jan 28;12(2):851-70.

Fucoidan as a marine anticancer agent in preclinical development.

Kwak JY1.

Abstract

Fucoidan is a fucose-containing sulfated polysaccharide derived from brown seaweeds, crude extracts of which are commercially available as nutritional supplements. Recent studies have demonstrated antiproliferative, antiangiogenic, and anticancer properties of fucoidan in vitro. Accordingly, the anticancer effects of fucoidan have been shown to vary depending on its structure, while it can target multiple receptors or signaling molecules in various cell types, including tumor cells and immune cells. Low toxicity and the in vitro effects of fucoidan mentioned above make it a suitable agent for cancer prevention or treatment. However, preclinical development of natural marine products requires in vivo examination of purified compounds in animal tumor models. This review discusses the effects of systemic and local administration of fucoidan on tumor growth, angiogenesis, and immune reaction and whether in vivo and in vitro results are likely applicable to the development of fucoidan as a marine anticancer drug.

J Nutr. 2013 Nov;143(11):1794-8.

Supplementation of elderly Japanese men and women with fucoidan from seaweed increases immune responses to seasonal influenza vaccination.

Negishi H, Mori M, Mori H, Yamori Y.

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Abstract

The elderly are known to have an inadequate immune response to influenza vaccine. Mekabu fucoidan (MF), a sulfated polysaccharide extracted from seaweed, was previously shown to have an immunomodulatory effect. We therefore investigated antibody production after influenza vaccination in elderly Japanese men and women with and without oral MF intake. A randomized, placebo-controlled, double-blind study was conducted with 70 volunteers >60 y of age. They were randomly assigned to 1 of 2 groups, consuming either MF (300 mg/d) or placebo for 4 wk, and then given a trivalent seasonal influenza vaccine. Serum was sampled at 5 and 20 wk after vaccination to measure the hemagglutination inhibition titer and natural killer cell activity. The MF group had higher antibody titers against all 3 strains contained in the seasonal influenza virus vaccine than the placebo group. Titers against the B/Brisbane/60/2008 (B) strain increased substantially more in the MF group than in the placebo group over the product consumption period. The immune response against B antigen met the European Union Licensure criteria regarding the geometric mean titer ratio in the MF group (2.4), but not in the placebo group (1.7). In the MF group, natural killer cell activity tended to increase from baseline 9 wk after MF intake (P = 0.08). However, in the placebo group no substantial increase was noted at 9 wk, and the activity decreased substantially from 9 to 24 wk. In the immunocompromised elderly, MF intake increased antibody production after vaccination, possibly preventing influenza epidemics.

Molecules. 2016 Apr 27;21(5).

Polysaccharides from the Marine Environment with Pharmacological, Cosmeceutical and Nutraceutical Potential.

Ruocco N, Costantini S, Guariniello S, Costantini M.

Abstract

Carbohydrates, also called saccharides, are molecules composed of carbon, hydrogen, and oxygen. They are the most abundant biomolecules and essential components of many natural products and have attracted the attention of researchers because of their numerous human health benefits. Among carbohydrates the polysaccharides represent some of the most abundant bioactive substances in marine organisms. In fact, many marine macro- and microorganisms are good resources of carbohydrates with diverse applications due to their biofunctional properties. By acting on cell proliferation and cycle, and by modulating different metabolic pathways, marine polysaccharides (including mainly chitin, chitosan, fucoidan, carrageenan and alginate) also have numerous pharmaceutical activities, such as antioxidative, antibacterial, antiviral, immuno-stimulatory, anticoagulant and anticancer effects. Moreover, these polysaccharides have many general beneficial effects for human health, and have therefore been developed into potential cosmeceuticals and nutraceuticals. In this review we describe current advances in the development of marine polysaccharides for nutraceutical, cosmeceutical and pharmacological applications. Research in this field is opening new doors for harnessing the potential of marine natural products.

Mar Drugs. 2016 Mar 18;14(3).

Looking Beyond the Terrestrial: The Potential of Seaweed Derived Bioactives to Treat Non-Communicable Diseases.

Collins KG, Fitzgerald GF, Stanton C, Ross RP.

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Abstract

Seaweeds are a large and diverse group of marine organisms that are commonly found in the maritime regions of the world. They are an excellent source of biologically active secondary metabolites and have been shown to exhibit a wide range of therapeutic properties, including anti-cancer, anti-oxidant, anti-inflammatory and anti-diabetic activities. Several Asian cultures have a strong tradition of using different varieties of seaweed extensively in cooking as well as in herbal medicines preparations. As such, seaweeds have been used to treat a wide variety of health conditions such as cancer, digestive problems, and renal disorders. Today, increasing numbers of people are adopting a "westernised lifestyle" characterised by low levels of physical exercise and excessive calorific and saturated fat intake. This has led to an increase in numbers of chronic Non-communicable diseases (NCDs) such as cancer, cardiovascular disease, and diabetes mellitus, being reported. Recently, NCDs have replaced communicable infectious diseases as the number one cause of human mortality. Current medical treatments for NCDs rely mainly on drugs that have been obtained from the terrestrial regions of the world, with the oceans and seas remaining largely an untapped reservoir for exploration. This review focuses on the potential of using seaweed derived bioactives including polysaccharides, antioxidants and fatty acids, amongst others, to treat chronic NCDs such as cancer, cardiovascular disease and diabetes mellitus.

Adv Food Nutr Res. 2014;72:195-213.

Anticancer effects of fucoidan.

Senthilkumar K, Kim SK.

Abstract

Recently, there has been an increased interest in the pharmacologically active natural compounds isolated and used for remedies of various kinds of diseases, including cancer. The great deal of interest has been developed to isolate bioactive compounds from marine resources because of their numerous health beneficial effects. Among marine resources, marine algae are valuable sources of structurally diverse bioactive compounds. Fucoidan is a sulfated polysaccharide derived from brown seaweeds and has been used as an ingredient in some dietary supplement products. Fucoidan has various biological activities including antibacterial, antioxidant, anti-inflammatory, anticoagulant, and antitumor activities. So this chapter deals with anticancer effects of fucoidan.

J Med Food. 2014 Jul;17(7):830-2.

Effect of fucoidan administration on insulin secretion and insulin resistance in overweight or obese adults.

Hernández-Corona DM, Martínez-Abundis E, González-Ortiz M.

Abstract

The aim of this article is to evaluate the effect of fucoidan administration on insulin secretion and insulin sensitivity in overweight or obese adults. A randomized, double-blind, placebo-controlled clinical trial was carried out in 25 obese or overweight volunteers. Thirteen patients received an oral dose of 500 mg of fucoidan once daily before breakfast and 12 patients received placebo for 3 months. Before and after the intervention, fasting glucose and 2-h postload, total cholesterol, high-density lipoprotein cholesterol, triglycerides, and insulin levels were measured. Low-density lipoprotein cholesterol (LDL-C) and homeostasis model analysis formulas (HOMA) for β-cell function and insulin resistance were calculated.

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The results showed a significant decrease in diastolic blood pressure (71.7 ± 12.2 vs. 67.8 ± 13.8 mmHg; P<.05) and LDL-C (3.1 ± 0.5 vs. 2.7 ± 0.6 mmol/l; P<.01) with increase in insulin levels (60.6 ± 24.0 vs. 78.6 ± 32.4 pmol/l; P<.05), HOMA β-cell (35.0 ± 20.8 vs. 50.6 ± 18.7; P<.05) and HOMA IR (1.9 ± 1.2 vs. 2.6 ± 1.8; P<.05) were observed after fucoidan administration. We conclude that fucoidan administration during a 3-month period in overweight or obese adults decreased diastolic blood pressure and LDL-C concentrations, increasing insulin secretion and insulin resistance.

Am J Chin Med. 2013;41(1):131-44.

Immunomodulatory activities of medicinal mushroom Grifola frondosa extract and its bioactive constituent.

Wu SJ1, Lu TM, Lai MN, Ng LT.

Abstract

Grifola frondosa (GF), a high value medicinal mushroom in China and Japan, is popularly consumed as traditional medicines and health foods, especially for enhancing immune functions. In this study, our aim was to examine the immunomodulatory activities of GF and its bioactive compound ergosterol peroxide (EPO) in lipopolysaccharide (LPS)-induced human monocytic (THP-1) cells. At low concentrations, EPO but not other extracts showed a full protection against LPS-induced cell toxicity. EPO significantly blocked MyD88 and VCAM-1 expression, and cytokine (IL-1β, IL-6 and TNF-α) production in LPS-stimulated cells. It also effectively inhibited NF-κB activation, which was further confirmed with siRNA treatment. These results conclude that EPO may play an important role in the immunomodulatory activity of GF through inhibiting the production of pro-inflammatory mediators and activation of NF-κB signaling pathway.

J Cancer Res Clin Oncol. 2009 Sep;135(9):1215-21.

A phase I/II trial of a polysaccharide extract from Grifola frondosa (Maitake mushroom) in breast cancer patients: immunological effects.

Deng G, Lin H, Seidman A, Fornier M, D'Andrea G, Wesa K, Yeung S, Cunningham-Rundles S, Vickers AJ, Cassileth B.

Abstract

BACKGROUND:

Cancer patients commonly use dietary supplements to "boost immune function". A polysaccharide extract from Grifola frondosa (Maitake extract) showed immunomodulatory effects in preclinical studies and therefore the potential for clinical use. Whether oral administration in human produces measurable immunologic effects, however, is unknown.

METHODS:

In a phase I/II dose escalation trial, 34 postmenopausal breast cancer patients, free of disease after initial treatment, were enrolled sequentially in five cohorts. Maitake liquid extract was taken orally at 0.1, 0.5, 1.5, 3, or 5 mg/kg twice daily for 3 weeks. Peripheral blood was collected at days -7, 0 (prior to the first dosing), 7, 14, and 21 for ex vivo analyses. The primary endpoints were safety and tolerability.

RESULTS:

No dose-limiting toxicity was encountered. Two patients withdrew prior to completion of the study due to grade I possibly related side effects: nausea and joint swelling in one patient; rash and pruritus in the second. There was a statistically significant association between Maitake and immunologic function (p

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< 0.0005). Increasing doses of Maitake increased some immunologic parameters and depressed others; the dose-response curves for many endpoints were non-monotonic with intermediate doses having either immune enhancing or immune suppressant effects compared with both high and low doses.

CONCLUSIONS:

Oral administration of a polysaccharide extract from Maitake mushroom is associated with both immunologically stimulatory and inhibitory measurable effects in peripheral blood. Cancer patients should be made aware of the fact that botanical agents produce more complex effects than assumed, and may depress as well as enhance immune function.

Ann Transl Med. 2014 Feb;2(2):14.

Immune-enhancing effects of Maitake (Grifola frondosa) and Shiitake (Lentinula edodes) extracts.

Vetvicka V, Vetvickova J.

Abstract

BACKGROUND:

The role of glucan in stimulation of immune reactions has been studied for several decades. In this report, we focused on the effects of orally administered glucan Maitake and Shiitake on immune reactions.

MATERIALS AND METHODS:

We measured phagocytosis, NK cell activity, and secretion of IL-6, IL-12, IFN-γ as well as C-reactive protein (CRP) after 14 days of oral application of tested glucans. For comparison, active hexose correlated compound (AHCC) was used in all reactions.

RESULTS:

We found significant stimulation of defense reaction. In all cases, the most active was the Maitake-Shiitake combination, with Maitake alone being the second strongest, followed by Shiitake on its own and AHCC.

CONCLUSIONS:

Short-term oral application of natural immunomodulating glucans from Maitake and Shiitake mushrooms strongly stimulated both the cellular and humoral branch of immune reactions. These activities were significantly higher than those of AHCC.

J Am Coll Nutr. 2015;34(6):478-87.

Consuming Lentinula edodes (Shiitake) Mushrooms Daily Improves Human Immunity: A Randomized Dietary Intervention in Healthy Young Adults.

Dai X, Stanilka JM, Rowe CA, Esteves EA, Nieves C Jr, Spaiser SJ, Christman MC, Langkamp-Henken B, Percival SS.

Abstract

BACKGROUND:

Mushrooms are widely cited for their medicinal qualities, yet very few human intervention studies have been done using contemporary guidelines.

OBJECTIVE:

The aim of this study was to determine whether consumption of whole, dried Lentinula edodes (shiitake)

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mushrooms could improve human immune function. Primary objectives were to ascertain whether L. edodes consumption would improve γδ-T cell proliferation and activation responses, quantify a dose response, and elicit cytokine secretion patterns. Secondary objectives included determining changes in natural killer T (NK-T) cell proliferation and activation, secretory immunoglobulin A (sIgA) in saliva, and C-reactive protein (CRP) in serum.

DESIGN:

Fifty-two healthy males and females, aged 21-41 years, participated in a 4-week parallel group study, consuming either 5 or 10 g of mushrooms daily. Each subject had blood drawn before and after 4 weeks of daily L. edodes consumption. Saliva and serum were also collected. Peripheral blood mononuclear cells were cultured in autologous serum for 24 hours or 6 days, stained, and examined by flow cytometry.

RESULTS:

Eating L. edodes for 4 weeks resulted in increased ex vivo proliferation of γδ-T (60% more, $p < 0.0001$) and NK-T (2-fold more, $p < 0.0001$) cells. Both cell types also demonstrated a greater ability to express activation receptors, suggesting that consuming mushrooms improved cell effector function. The increase in sIgA implied improved gut immunity. The reduction in CRP suggested lower inflammation. The pattern of cytokines secreted before and after mushroom consumption was significantly different; consumption resulted in increased interleukin (IL)-4, IL-10, tumor necrosis factor (TNF)-α, and IL-1α levels, a decreased macrophage inflammatory protein-1α/chemokine C-C ligand 3 (MIP-1α/CCL3) level, and no change to IL-6, IL-1β, MIP-1β, IL-17 and interferon (IFN)-γ levels.

CONCLUSIONS:

Regular L. edodes consumption resulted in improved immunity, as seen by improved cell proliferation and activation and increased sIgA production. The changes observed in cytokine and serum CRP levels suggest that these improvements occurred under conditions that were less inflammatory than those that existed before consumption.

Nutr Rev. 1996 Nov;54(11 Pt 2):S91-3.

Functional properties of edible mushrooms.

Chang R.

Abstract

Edible mushrooms such as shiitake may have important salutary effects on health or even in treating disease. A mushroom characteristically contains many different bioactive compounds with diverse biological activity, and the content and bioactivity of these compounds depend on how the mushroom is prepared and consumed. It is estimated that approximately 50% of the annual 5 million metric tons of cultivated edible mushrooms contain functional "nutraceutical" or medicinal properties. In order of decreasing cultivated tonnage, Lentinus (shiitake), Pleurotus (oyster), Auricularia (mu-er), Flammulina (enokitake), Tremella (yin-er), Hericium, and Grifola (maitake) mushrooms have various degrees of immunomodulatory, lipid-lowering, antitumor, and other beneficial or therapeutic health effects without any significant toxicity. Although the data for this functional food class are not as strong as those for other functional foods such as cruciferous vegetables, because of their potential usefulness in preventing or treating serious health conditions such as cancer, acquired immune deficiency syndrome (AIDS), and hypercholesterolemia, functional mushrooms deserve further serious investigation. Additionally, there is a need for epidemiological evidence of the role of this functional food class.

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Nat Rev Gastroenterol Hepatol. 2016 Dec;13(12):691-706.

Diet, microorganisms and their metabolites, and colon cancer.

O'Keefe SJ.

Abstract

Colorectal cancer is one of the so-called westernized diseases and the second leading cause of cancer death worldwide. On the basis of global epidemiological and scientific studies, evidence suggests that the risk of colorectal cancer is increased by processed and unprocessed meat consumption but suppressed by fibre, and that food composition affects colonic health and cancer risk via its effects on colonic microbial metabolism. The gut microbiota can ferment complex dietary residues that are resistant to digestion by enteric enzymes. This process provides energy for the microbiota but culminates in the release of short-chain fatty acids including butyrate, which are utilized for the metabolic needs of the colon and the body. Butyrate has a remarkable array of colonic health-promoting and antineoplastic properties: it is the preferred energy source for colonocytes, it maintains mucosal integrity and it suppresses inflammation and carcinogenesis through effects on immunity, gene expression and epigenetic modulation. Protein residues and fat-stimulated bile acids are also metabolized by the microbiota to inflammatory and/or carcinogenic metabolites, which increase the risk of neoplastic progression. This Review will discuss the mechanisms behind these microbial metabolite effects, which could be modified by diet to achieve the objective of preventing colorectal cancer in Western societies.

Pharmacol Ther. 2016 Aug;164:144-51

Benefits of short-chain fatty acids and their receptors in inflammation and carcinogenesis.

Sivaprakasam S, Prasad PD, Singh N.

Abstract

Epidemiological studies have linked increased incidence of inflammatory diseases and intestinal cancers in the developed parts of the world to the consumption of diets poor in dietary fibers and rich in refined carbohydrates. Gut bacteria residing in the intestinal lumen exclusively metabolize dietary fibers. Butyrate, propionate and acetate, which are collectively called short-chain fatty acids (SCFAs), are generated by fermentation of dietary fibers by gut microbiota. Evidences indicate that SCFAs are key players in regulating beneficial effect of dietary fibers and gut microbiota on our health. SCFAs interact with metabolite-sensing G protein-coupled receptors GPR41, GPR43 and GPR109A expressed in gut epithelium and immune cells. These interactions induce mechanisms that play a key role in maintaining homeostasis in gut and other organs. This review summarizes the protective roles of GPR41, GPR43 and GPR109A in dietary fibers-, gut microbiota- and SCFAs-mediated suppression of inflammation and carcinogenesis in gut and other organs.

Neurosci Lett. 2016 Jun 20;625:56-63.

Butyrate, neuroepigenetics and the gut microbiome: Can a high fiber diet improve brain health?

Bourassa MW, Alim I, Bultman SJ, Ratan RR.

Abstract

As interest in the gut microbiome has grown in recent years, attention has turned to the impact of our diet

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on our brain. The benefits of a high fiber diet in the colon have been well documented in epidemiological studies, but its potential impact on the brain has largely been understudied. Here, we will review evidence that butyrate, a short-chain fatty acid (SCFA) produced by bacterial fermentation of fiber in the colon, can improve brain health. Butyrate has been extensively studied as a histone deacetylase (HDAC) inhibitor but also functions as a ligand for a subset of G protein-coupled receptors and as an energy metabolite. These diverse modes of action make it well suited for solving the wide array of imbalances frequently encountered in neurological disorders. In this review, we will integrate evidence from the disparate fields of gastroenterology and neuroscience to hypothesize that the metabolism of a high fiber diet in the gut can alter gene expression in the brain to prevent neurodegeneration and promote regeneration.

Digestion. 2016;93(3):176-81.

Physiological Role of Gut Microbiota for Maintaining Human Health.

Andoh A.

Abstract

BACKGROUND:

The human body is colonized by an extremely complex and abundant aggregation of microbes, collectively referred to as the gut microbiota. Recent studies have focused on the link between these microbes and our health.

SUMMARY:

Diet contributes to shaping the gut microbial structure and influences metabolic functions of the host. Alteration of the microbial structure and function (dysbiosis) is associated with the pathogenesis of various disorders. Fermentation is the process by which anaerobic bacteria (Firmicutes and Bacteroidetes) break down indigestible carbohydrates to short-chain fatty acids (SCFAs; acetate, propionate and butyrate), collaborating with species specialized in oligosaccharide fermentation (e.g. Bifidobacteria). Butyrate and propionate can regulate intestinal physiology and immune function, while acetate acts as a substrate for lipogenesis and gluconeogenesis. The gut microbiota regulates immune homeostasis via the induction of regulatory T cells and Th17 cells. In addition, butyrate has strong anti-inflammatory effects possibly through the inhibition of histone deacetylase activity. Metabolic products generated by the gut microbiota, such as SCFAs, GABA, tryptophan, serotonin and catecholamine, transmit a signal to resident cells in the gut.

Food Funct. 2016 Apr;7(4):1731-40.

Diet, microbiota, and dysbiosis: a 'recipe' for colorectal cancer.

Vipperla K, O'Keefe SJ.

Abstract

The food we consume feeds not only us, but also a vast and diverse community of microbiota within our gastrointestinal tract. In a process of symbiotic co-evolution, the gut microbiota became essential for the maintenance of the health and integrity of our colon. The advent of next-generation DNA sequencing technology and metabolic profiling have, in the recent years, revealed the remarkable complexity of microbial diversity and function, and that the microbiota produce a wide variety of bioactive products that are not only active at the mucosal surface, but also absorbed and circulated throughout the body,

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influencing distant organ health and function. As a result, several microbiota compositional patterns and their associations with both health and disease states have been identified. Importantly, a disturbed microbiota-host relationship, termed dysbiosis, is now recognized to be the root cause for a growing list of diseases, including colorectal cancer (CRC). There is mounting in vitro and in vivo evidence to suggest that diet selects for the microbiota composition and several health promoting and deleterious effects of diet are, in fact, mediated by the microbiota. Recent findings of the feasibility of dietary fiber to boost the colonic microbial synthesis of anti-proliferative and counter carcinogenic metabolites, particularly butyrate, underscores the prerequisite of dietary modification as a key measure to curb the pandemic of CRC in westernized countries. Better understanding of the diet-microbiota interplay and large-scale studies to evaluate the efficacy of dietary modification and gut microbiota modulation in reversing dysbiosis and restoring health could offer novel preventative and/or therapeutic strategies against westernized diseases, which are now considered the chief threat to public health.

Age (Dordr). 2015 Oct;37(5):98.

Improving healthspan via changes in gut microbiota and fermentation.

Keenan MJ, Marco ML, Ingram DK, Martin RJ.

Abstract

Dietary resistant starch impact on intestinal microbiome and improving healthspan is the topic of this review. In the elderly population, dietary fiber intake is lower than recommended. Dietary resistant starch as a source of fiber produces a profound change in gut microbiota and fermentation in animal models of aging. Dietary resistant starch has the potential for improving healthspan in the elderly through multiple mechanisms as follows: (1) enhancing gut microbiota profile and production of short-chain fatty acids, (2) improving gut barrier function, (3) increasing gut peptides that are important in glucose homeostasis and lipid metabolism, and (4) mimicking many of the effects of caloric restriction including upregulation of genes involved in xenobiotic metabolism.

Nat Rev Endocrinol. 2015 Oct;11(10):577-91.

Short-chain fatty acids in control of body weight and insulin sensitivity.

Canfora EE, Jocken JW, Blaak EE.

Abstract

The connection between the gut microbiota and the aetiology of obesity and cardiometabolic disorders is increasingly being recognized by clinicians. Our gut microbiota might affect the cardiometabolic phenotype by fermenting indigestible dietary components and thereby producing short-chain fatty acids (SCFA). These SCFA are not only of importance in gut health and as signalling molecules, but might also enter the systemic circulation and directly affect metabolism or the function of peripheral tissues. In this Review, we discuss the effects of three SCFA (acetate, propionate and butyrate) on energy homeostasis and metabolism, as well as how these SCFA can beneficially modulate adipose tissue, skeletal muscle and liver tissue function. As a result, these SCFA contribute to improved glucose homeostasis and insulin sensitivity. Furthermore, we also summarize the increasing evidence for a potential role of SCFA as metabolic targets to prevent and counteract obesity and its associated disorders in glucose metabolism and insulin resistance. However, most data are derived from animal and in vitro studies, and consequently

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the importance of SCFA and differential SCFA availability in human energy and substrate metabolism remains to be fully established. Well-controlled human intervention studies investigating the role of SCFA on cardiometabolic health are, therefore, eagerly awaited.

Nat Rev Microbiol. 2014 Oct;12(10):661-72.

The gut microbiota, bacterial metabolites and colorectal cancer.

Louis P, Hold GL, Flint HJ.

Abstract

Accumulating evidence suggests that the human intestinal microbiota contributes to the aetiology of colorectal cancer (CRC), not only via the pro-carcinogenic activities of specific pathogens but also via the influence of the wider microbial community, particularly its metabolome. Recent data have shown that the short-chain fatty acids acetate, propionate and butyrate function in the suppression of inflammation and cancer, whereas other microbial metabolites, such as secondary bile acids, promote carcinogenesis. In this Review, we discuss the relationship between diet, microbial metabolism and CRC and argue that the cumulative effects of microbial metabolites should be considered in order to better predict and prevent cancer progression.

J Clin Gastroenterol. 2011 Nov;45 Suppl:S120-7.

Fermentation in the human large intestine: its physiologic consequences and the potential contribution of prebiotics.

Macfarlane GT1, Macfarlane S.

Abstract

The human large intestine harbors a complex microbiota containing many hundreds of different bacterial species. Although structure/function relationships between different components of the microbiota are unclear, this complex multicellular entity plays an important role in maintaining homeostasis in the body. Many of the physiologic properties of the microbiota can be attributed to fermentation and the production of short-chain fatty acids (SCFAs), particularly acetate, propionate, and butyrate. In healthy people, fermentation processes are largely controlled by the amounts and different types of substrate, particularly complex carbohydrates that are accessible to bacteria in the colonic ecosystem. However, other factors impact on bacterial metabolism in the large gut, including large bowel transit time, the availability of inorganic terminal electron acceptors, such as nitrate and sulfate, and gut pH. They all affect the types and levels of SCFA that can be formed by the microbiota. This is important because to a large extent, acetate, propionate, and butyrate have varying physiologic effects in different body tissues. Prebiotics such as galactooligosaccharides together with inulins and their fructooligosaccharide derivatives have been shown to modify the species composition of the colonic microbiota, and in various degrees, to manifest several health-promoting properties related to enhanced mineral absorption, laxation, potential anticancer properties, lipid metabolism, and anti-inflammatory and other immune effects, including atopic disease. Many of these phenomena can be linked to their digestion and SCFA production by bacteria in the large gut.

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Nutr Res Rev. 2010 Dec;23(2):366-84.

From the gut to the peripheral tissues: the multiple effects of butyrate.

Guilloteau P, Martin L, Eeckhaut V, Ducatelle R, Zabielski R, Van Immerseel F.

Abstract

Butyrate is a natural substance present in biological liquids and tissues. The present paper aims to give an update on the biological role of butyrate in mammals, when it is naturally produced by the gastrointestinal microbiota or orally ingested as a feed additive. Recent data concerning butyrate production delivery as well as absorption by the colonocytes are reported. Butyrate cannot be detected in the peripheral blood, which indicates fast metabolism in the gut wall and/or in the liver. In physiological conditions, the increase in performance in animals could be explained by the increased nutrient digestibility, the stimulation of the digestive enzyme secretions, a modification of intestinal luminal microbiota and an improvement of the epithelial integrity and defence systems. In the digestive tract, butyrate can act directly (upper gastrointestinal tract or hindgut) or indirectly (small intestine) on tissue development and repair. Direct trophic effects have been demonstrated mainly by cell proliferation studies, indicating a faster renewal of necrotic areas. Indirect actions of butyrate are believed to involve the hormono-neuro-immuno system. Butyrate has also been implicated in down-regulation of bacteria virulence, both by direct effects on virulence gene expression and by acting on cell proliferation of the host cells. In animal production, butyrate is a helpful feed additive, especially when ingested soon after birth, as it enhances performance and controls gut health disorders caused by bacterial pathogens. Such effects could be considered for new applications in human nutrition.

Am J Clin Nutr. 2016 Aug;104(2):526-36.

Zinc carnosine works with bovine colostrum in truncating heavy exercise-induced increase in gut permeability in healthy volunteers.

Davison G, Marchbank T, March DS, Thatcher R, Playford RJ.

Abstract

BACKGROUND:

Heavy exercise causes gut symptoms and, in extreme cases, heat stroke that is due to the increased intestinal permeability of luminal toxins.

OBJECTIVE:

We examined whether zinc carnosine (ZnC), a health-food product taken alone or in combination with bovine colostrum (a natural source of growth factors), would moderate such effects.

DESIGN:

Eight volunteers completed a 4-arm, double-blind, placebo-controlled crossover protocol (14 d of placebo, ZnC, colostrum, or ZnC plus colostrum) before undertaking standardized exercise 2 and 14 d after the start of treatment. Changes in epithelial resistance, apoptosis signaling molecules, and tight junction (TJ) protein phosphorylation in response to a 2°C rise in body temperature were determined with the use of Caco-2 and HT29 intestinal cells.

RESULTS:

Body temperature increased 2°C, and gut permeability (5-h urinary lactulose:rhamnose ratios) increased 3-fold after exercise (from 0.32 ± 0.016 baseline to 1.0 ± 0.017 at 14 d; $P < 0.01$). ZnC or colostrum truncated the rise by 70% after 14 d of treatment. The combination treatment gave an

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additional benefit, and truncated exercise induced increase at 2 d (30% reduction; P < 0.01). A 2°C temperature rise in in vitro studies caused the doubling of apoptosis and reduced epithelial resistance 3-4-fold. ZnC or colostrum truncated these effects (35-50%) with the greatest response seen with the combination treatment (all P < 0.01). Mechanisms of action included increasing heat shock protein 70 and truncating temperature-induced changes in B cell leukemia/lymphoma-2 associated X protein α and B cell lymphoma 2. ZnC also increased total occludin and reduced phosphorylated tyrosine claudin, phosphorylated tyrosine occludin, and phosphorylated serine occludin, thereby enhancing the TJ formation and stabilization.

CONCLUSION:

ZnC, taken alone or with colostrum, increased epithelial resistance and the TJ structure and may have value for athletes and in the prevention of heat stroke in military personnel. This trial was registered at www.isrctn.com as ISRCTN51159138.

Scand J Gastroenterol. 2014 Feb;49(2):164-72.

Efficacy of zinc-carnosine chelate compound, Polaprezinc, enemas in patients with ulcerative colitis.

Itagaki M, Saruta M, Saijo H, Mitobe J, Arihiro S, Matsuoka M, Kato T, Ikegami M, Tajiri H.

Abstract

OBJECTIVES:

Ulcerative colitis (UC) is a chronic, relapsing and remitting intestinal inflammatory disorder. Zinc is known to be efficacious for the repair of damaged tissue and has been shown to protect against gastric ulceration. This study focused on Polaprezinc (PZ), N-(3-aminopropionyl)-L-histidinato zinc, which accelerates ulcer healing through actions such as prostaglandin-independent cytoprotection and antioxidative activity.

METHODS:

In this randomized, placebo-controlled, investigator-blinded trial, 28 patients with active UC at The Jikei University Hospital were randomly divided into two groups: one treated with a 150 mg PZ enema (n = 18) and the other not treated with a PZ enema (n = 10). All patients received usual induction therapy. Clinical symptoms, endoscopic findings and histological findings were evaluated at entry and one week later.

RESULTS:

In the PZ group, modified Matts' endoscopic scores were significantly improved after treatment compared to baseline in the rectum (p = 0.004), sigmoid colon (p = 0.03) and descending colon (p = 0.04). In the non-PZ group, scores were not significantly improved in the rectum (p = 0.14) and descending colon (p = 0.34), but were improved in the sigmoid colon (p = 0.04). In the PZ group, the Mayo scores at baseline and at Day 8 were 9.1 ± 1.6 and 5.8 ± 2.7 (p = 0.00004), respectively, and in the placebo group, the scores were 8.9 ± 1.7 and 7.4 ± 2.1 (p = 0.009), respectively. Clinical response or remission was significantly better in the PZ group (71%) than in the placebo group (10%).

CONCLUSIONS:

A zinc-carnosine chelate compound, PZ, enema may become a useful new add-on treatment to accelerate mucosal healing in UC.

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BMC Gastroenterol. 2013 Jul 4;13:108.

Effectiveness of polaprezinc for low-dose aspirin-induced small-bowel mucosal injuries as evaluated by capsule endoscopy: a pilot randomized controlled study.

Watari I, Oka S, Tanaka S, Aoyama T, Imagawa H, Shishido T, Yoshida S, Chayama K.

Abstract

BACKGROUND:

Treatment of low-dose aspirin (LDA)-induced small-bowel injury has not been established. Polaprezinc, a chelate of zinc and L-carnosine, may be efficacious for such injury. We conducted a pilot randomized controlled study to investigate whether polaprezinc is effective against LDA-induced small-bowel injuries.

METHODS:

Consecutive patients under long-term (>3 months) LDA treatment and who agreed to participate in our study underwent initial capsule endoscopy (CE). Patients with LDA-induced small-bowel injury apparent upon initial CE (n = 20) were randomized into a polaprezinc (150 mg/day for 4 weeks) group and a control (no polaprezinc treatment) group. All underwent follow-up CE after 4 weeks. Changes in the number and characteristics of small-bowel mucosal injuries were compared within and between the two groups.

RESULTS:

The median number of reddened lesions and erosions/ulcers upon follow-up CE in the polaprezinc group significantly decreased ($P < 0.05$). However, there was no significant difference in the median number of reddened lesions and erosions/ulcers upon follow-up CE in the control group.

CONCLUSIONS:

Co-administration of polaprezinc may be effective against small-bowel mucosal injury associated with long-term LDA therapy.

Gut. 2007 Feb;56(2):168-75.

Zinc carnosine, a health food supplement that stabilises small bowel integrity and stimulates gut repair processes.

Mahmood A, FitzGerald AJ, Marchbank T, Ntatsaki E, Murray D, Ghosh S, Playford RJ.

Abstract

BACKGROUND:

Zinc carnosine (ZnC) is a health food product claimed to possess health-promoting and gastrointestinal supportive activity. Scientific evidence underlying these claims is, however, limited.

AIM:

To examine the effect of ZnC on various models of gut injury and repair, and in a clinical trial.

METHODS:

In vitro studies used pro-migratory (wounded monolayer) and proliferation ([(3)H]-thymidine incorporation) assays of human colonic (HT29), rat intestinal epithelial (RIE) and canine kidney (MDCK) epithelial cells. In vivo studies used a rat model of gastric damage (indomethacin/restraint) and a mouse model of small-intestinal (indomethacin) damage. Healthy volunteers (n = 10) undertook a randomised crossover trial comparing changes in gut permeability (lactulose:rhamnose ratios) before and after 5 days of indomethacin treatment (50 mg three times a day) with ZnC (37.5 mg twice daily) or placebo

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coadministration.

RESULTS:

ZnC stimulated migration and proliferation of cells in a dose-dependent manner (maximum effects in both assays at 100 micromol/l using HT29 cells), causing an approximate threefold increase in migration and proliferation (both $p<0.01$). Oral ZnC decreased gastric (75% reduction at 5 mg/ml) and small-intestinal injury (50% reduction in villus shortening at 40 mg/ml; both $p<0.01$). In volunteers, indomethacin caused a threefold increase in gut permeability in the control arm; lactulose:rhamnose ratios were (mean (standard error of mean)) 0.35 (0.035) before indomethacin treatment and 0.88 (0.11) after 5 days of indomethacin treatment ($p<0.01$), whereas no significant increase in permeability was seen when ZnC was coadministered.

CONCLUSION:

ZnC, at concentrations likely to be found in the gut lumen, stabilises gut mucosa. Further studies are warranted.

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