ALL IN ONE DAY SEMINAR, CLINICAL EVIDENCE BASED PRACTICE OF CHIROPRACTIC: ETHICS & LAW, BASIC SCIENCE (NUTRITION), & ADVANCED CHIROPRACTIC ADJUSTIVE TECHNIQUE.

Presented by
Mark Cymerint D.C.

<u>California Approval Numbers:</u>
CA-D-24-06-05011 Advanced Adjustive Technique
CA-D-24-06-05010 Basic Science (Nutrition)
CA-D-24-06-05012 Ethics & Law

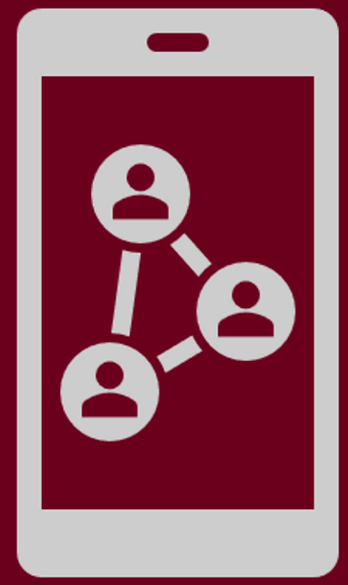
<u>Arizona Approval Number:</u>
AZCE23494
“All In One Day, Clinical Evidence Based Practice of Chiropractic: Principles of Practice, Ethics, and Chiropractic Adjustive Technique.”

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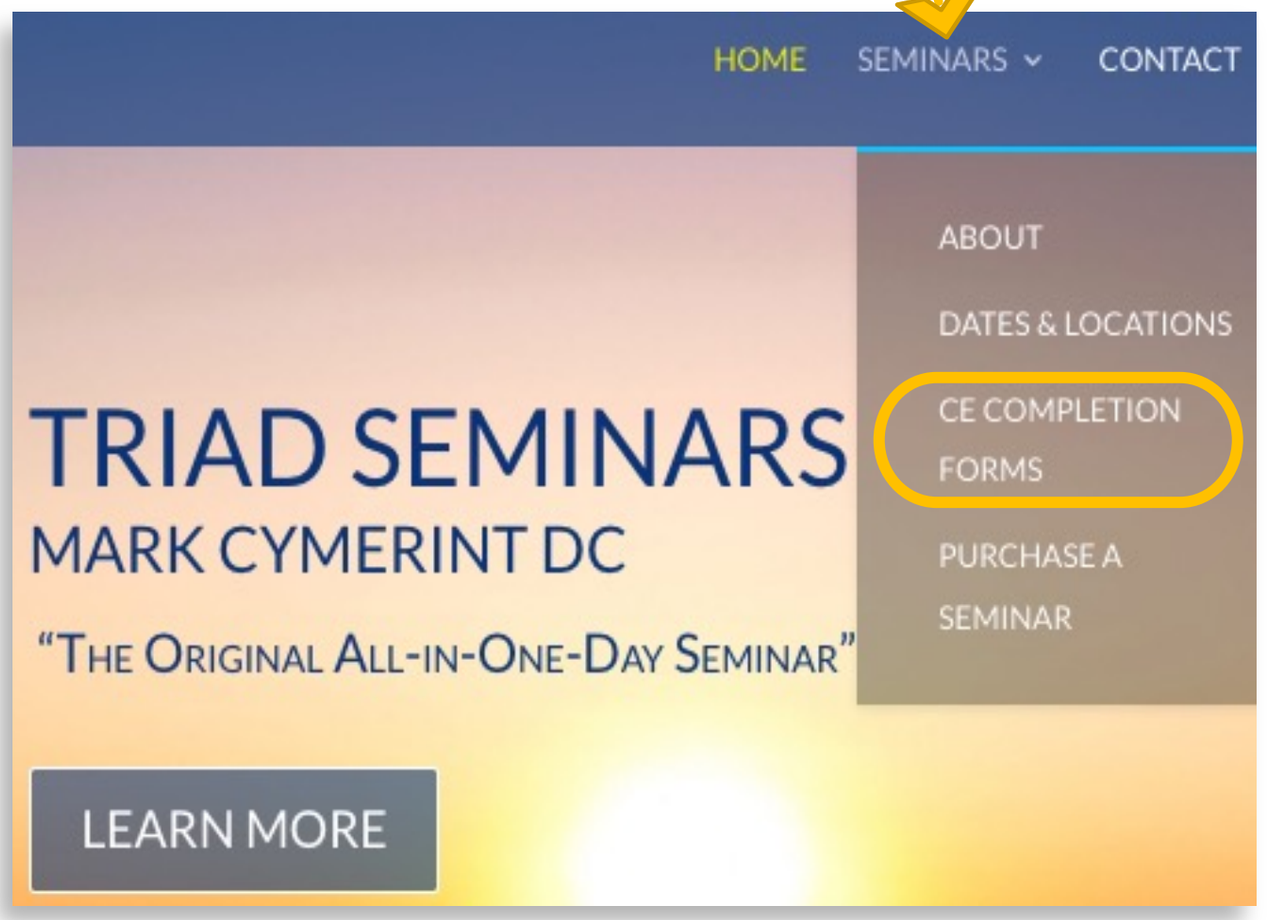
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II. BASIC SCIENCE (NUTRITION)

A. INFLAMMATION
   a) Natural inflammation reduction treatment options, including nutritional supplements and special dietary recommendations for an anti-inflammatory protocol, including legal hemp for anti-inflammatory management.
   b) Literature review
B. DIGESTION
   a) Green Alkaline foods for fiber and digestion
   b) Colon Health
   c) Minerals and Collagen Protein
D. AMINO ACIDS
   a) Definitions
   b) Amino acids for cardiovascular health
   c) Nitric oxide production

INFLAMMATION: WHAT IS IT?

Natural inflammation reduction treatment options, including nutritional supplements and special dietary recommendations for an anti-inflammatory protocol.

1. What is an inflammation?. *Institute for Quality and Efficiency in Health Care (IQWiG)*. 2015. Available at: https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0072482/. Accessed October 12, 2016

CAUSES OF INFLAMMATION

Possible Causes of Inflammation:

- Pathogens (germs) like bacteria, viruses
- External injuries (i.e. Sports, Work-related, or Trauma)
- Chemicals found in OTC or prescription medications, environmental and product exposure
- Any disease, disorder, condition ending in “-itis.”

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INFLAMMATION & AUTOIMMUNE DISEASE

Autoimmune Diseases: The immune system attacks itself causing harmful inflammatory responses (*i.e. AIDS/HIV*)

- Rheumatoid arthritis | Inflammation of joints
  - mainly hands
- Psoriasis | Inflammation of skin
  - mainly elbow
- Crohn's/ ulcerative colitis | Inflammation of bowel

What is an inflammation?. Institute for Quality and Efficiency in Health Care (IQWiG). 2015. Available at: https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0072482/. Accessed October 12, 2016.

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NATURAL INFLAMMATION REDUCTION TREATMENT OPTIONS

RESEARCH: CANNABIDIOL, CANNABINOL, & CANNABIGEROL FOR ANTI-INFLAMMATORY PROTOCOL



Natural inflammation reduction treatment options, including nutritional supplements and special dietary recommendations for an anti-inflammatory protocol, including legal hemp for anti-inflammatory management.

CBD: ANTI-INFLAMMATORY NUTRITIONAL OPTION

Cannabidiol: A Non-psychoactive cannabinoid

- *Analgesic*
- *Anti-inflammatory*
- *Neuroprotective*



Lucas, C. J., Galettis, P., & Schneider, J. (2018). The Pharmacokinetics and the Pharmacodynamics of Cannabinoids. *British Journal of Clinical Pharmacology*. doi:10.1111/bcp.13710

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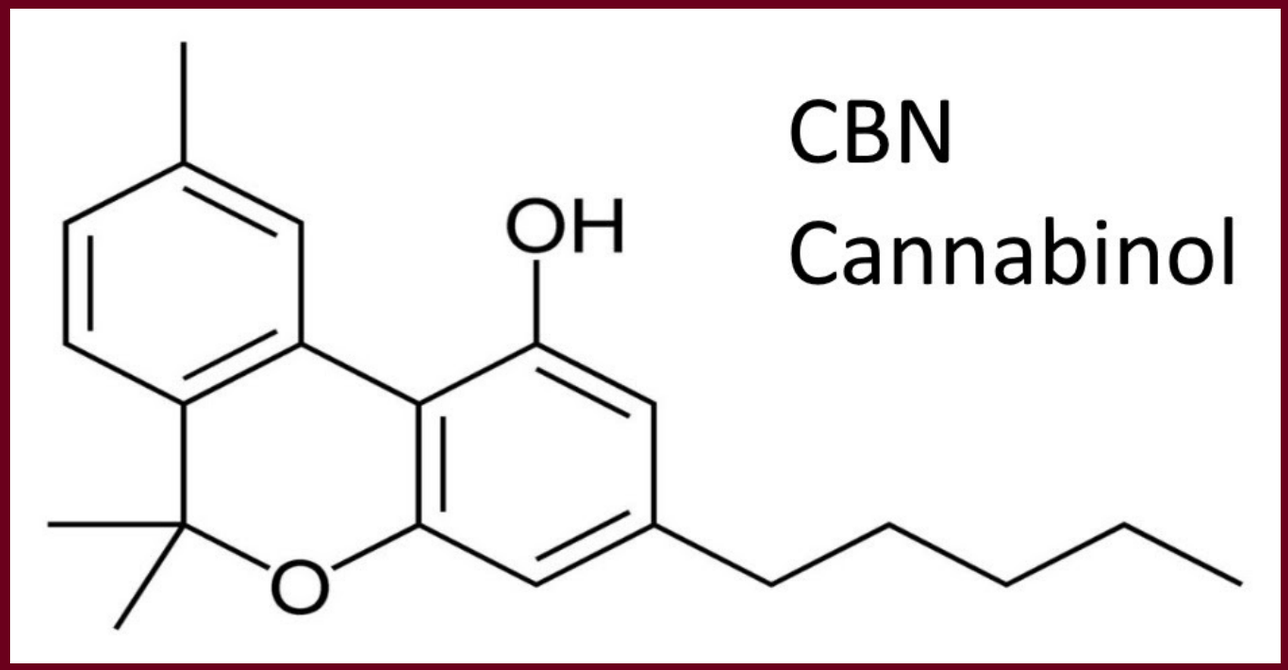
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CBN: ANTI-INFLAMMATORY NUTRITIONAL OPTION

Cannabinol: A Non-psychoactive cannabinoid

- Sedative
- Anti-inflammatory



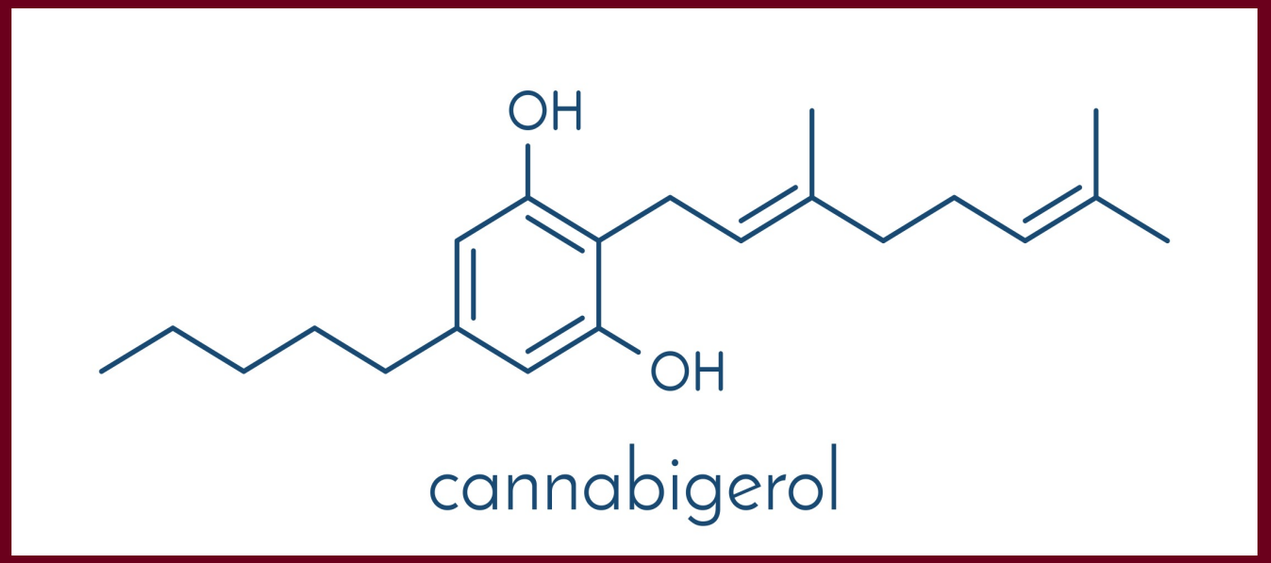
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Natural inflammation reduction treatment options, including nutritional supplements and special dietary recommendations for an anti-inflammatory protocol, including legal hemp for anti-inflammatory management.

CBG: AN ANTI-INFLAMMATORY NUTRITIONAL OPTION

Cannabigerol: A Non-psychoactive cannabinoid

- Anti-inflammatory
- Analgesic
- Effective for:
    - Psoriasis
    - Neuropsychiatric Disorders (ADHD, PTSD)
    - Inflammatory Bowel Disease



Lucas, C. J., Galettis, P., & Schneider, J. (2018). The Pharmacokinetics and the Pharmacodynamics of Cannabinoids. *British Journal of Clinical Pharmacology*. doi:10.1111/bcp.13710

The Human Endocannabinoid System

THC and CBN are known to "fit" like lock and key into network of existing receptors . The Endocannabinoid System exists to receive cannabinoids produced inside the body called "Anadnamide" and "2-Arachidonyl-glycerol". Stimulating the ECS with plant-based cannabinoids restores balance and helps maintain symptoms.

CB1 receptors are concentrated in the brain and central nervous system but also sparsely populates other parts of the human body.



THC

Tetrahydrocannibinol

CB1

CBD

Cannabidiol

CBD does not directly "fit" CB1 or CB2 receptors but has powerful indirect effects still being studied.

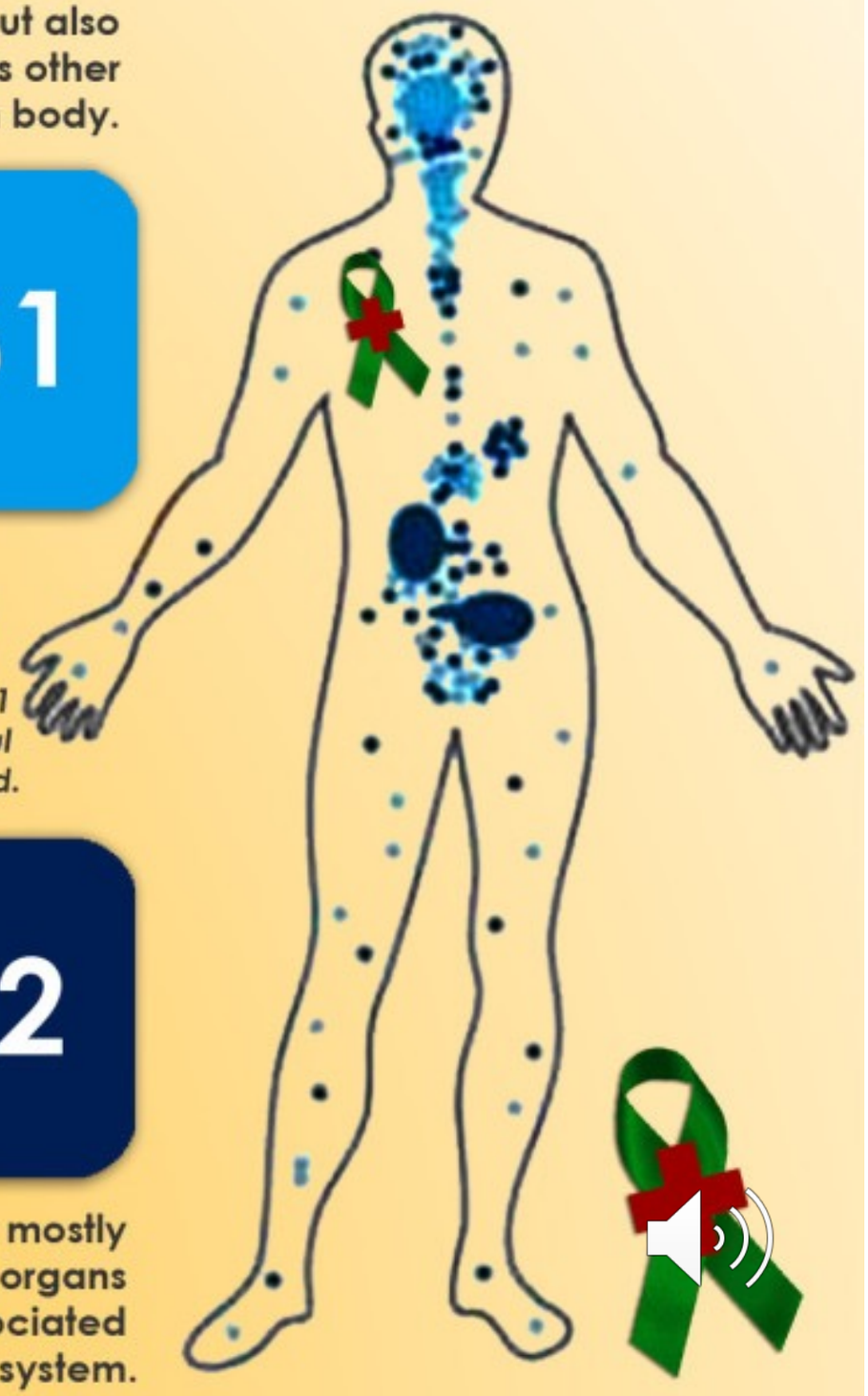
CBN

Cannabinol

CB2

CB2 receptors are mostly in the perepheral organs especially cells associated with the immune system.

Receptors are found on cell surfaces

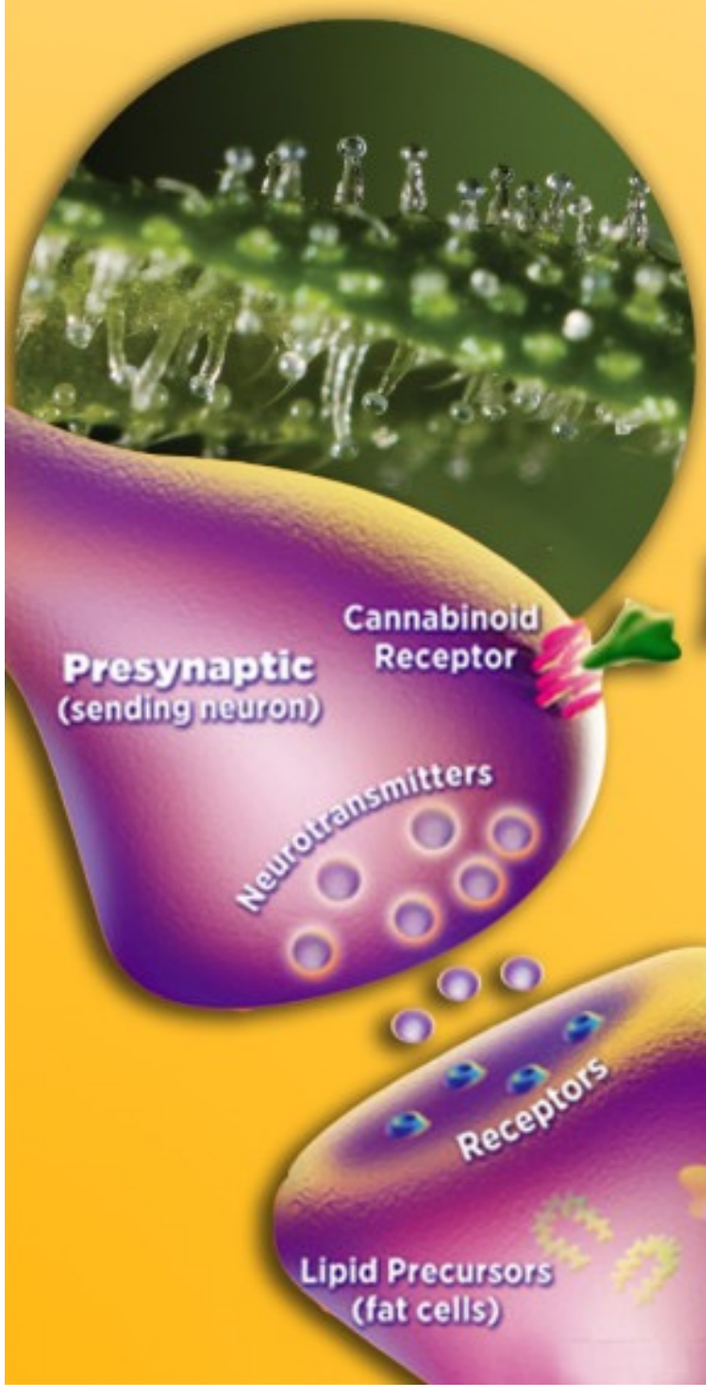


www.the-human-solution.org

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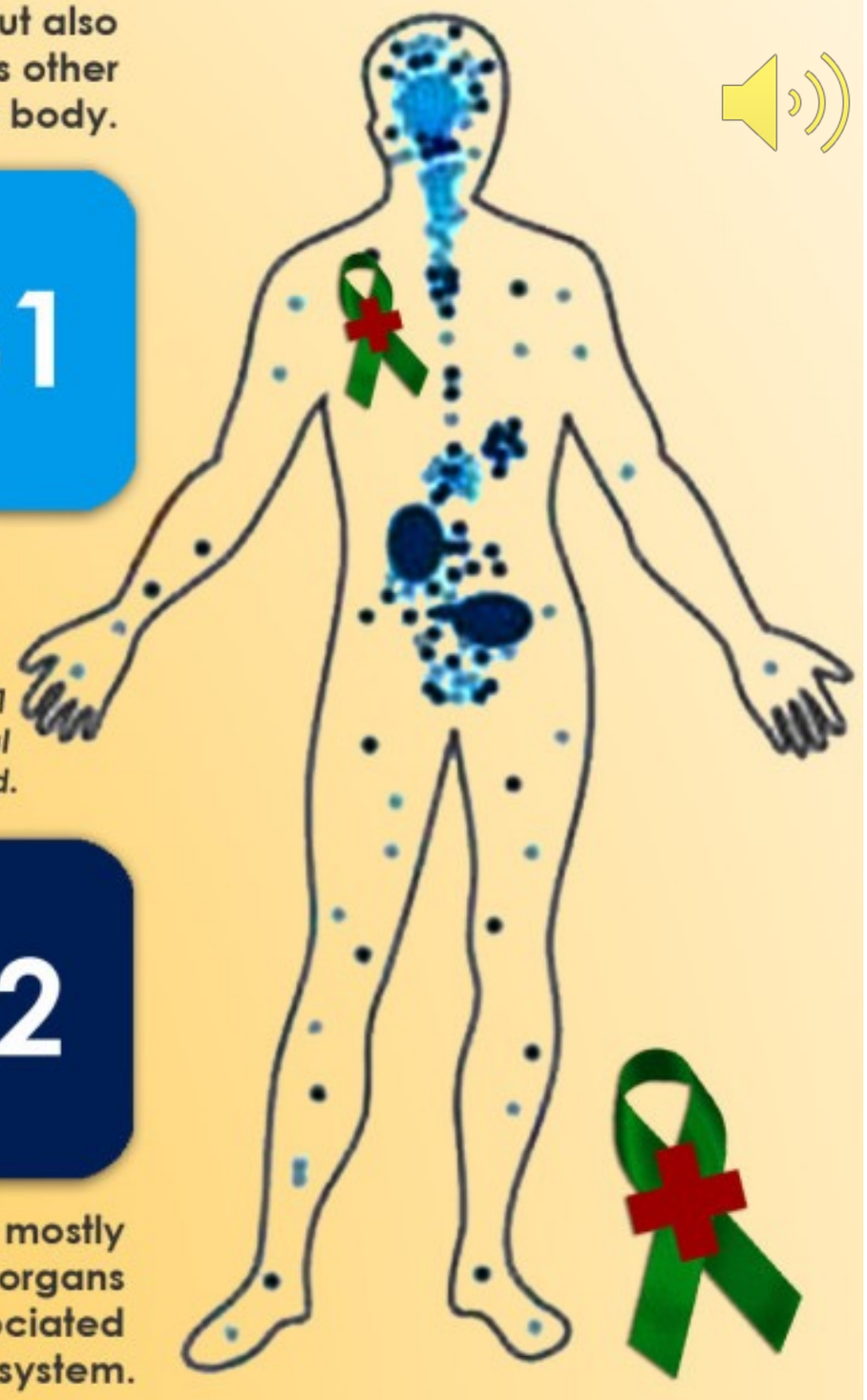
CBN

Cannabinol

CB2

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Receptors are found on cell surfaces



www.the-human-solution.org

WHAT SHOULD I LOOK FOR WHEN CONSIDERING CBD AS A THERAPEUTIC OPTION?



- Consider extraction methods:
  - Alcohol/Solvent Extraction
  - CO2 Extraction

- Be cautious of products with:
  - Flavors, sugars, unpronounceable ingredients

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ALCOHOL SOLVENT EXTRACTION (WORST METHOD)

- Ethanol, low-grade alcohol & butane (most-commonly used)
- Chlorophyll extracted together with cannabinoids & terpenes (leaves dark color and bitter flavor)
- Additional post processing required to remove the chlorophyll reducing potency of the oil
- Destroys plant waxes

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SUPERCRITICAL CO2 EXTRACTION

Most superior & expensive CBD extraction method

The pressure and temperature of carbon dioxide (CO2) is manipulated over time to reach supercritical phase

CO2 passed through high-quality hemp

CO2 extracts oils without denaturing the phytocannabinoids, terpenes & flavonoids



HOW MUCH CBD FOR INFLAMMATION MANAGEMENT?



- Start low dosage, go slow and increase as needed for symptomatic relief

- Start with recommended dosage
  - Assess how you feel after one week



CBD SAFETY PROFILE

- CBD Does not alter HR, BP, or body temperature
- No negative influence on food intake, gastrointestinal transit, psychomotor or psychological functions

Iffland, K., & Grotenhermen, F. (2017). An update on safety and side effects of cannabidiol: A review of clinical data and relevant animal studies. *Cannabis and Cannabinoid Research, 2*(1), 139-154. doi:10.1089/can.2016.0034

DIFFERENT OPTIONS OF DELIVERY & BIOAVAILABILITY FOR INFLAMMATION MANAGEMENT



Oral ~ 6% bioavailability
(gel capsules)

- Undergoes extensive hepatic first-pass metabolism
- Slow working & requires higher serving sizes

Inhalation ~ 31% bioavailability
(vaporizing)

- Avoids extensive hepatic first-pass metabolism
- More instantaneous
- Requires lower serving sizes
- Not recommended for people with asthma, SOB, respiratory issues

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DIFFERENT OPTIONS OF DELIVERY & BIOAVAILABILITY FOR INFLAMMATION MANAGEMENT

- **Oromucosal 30% bioavailability~**
  (CBD Oil with dropper recommendations on bottle)
  - Avoids extensive hepatic first-pass metabolism
  - Rapid absorption (useful for symptoms requiring rapid relief)
  - Drops under tongue
    Hold under the tongue 60-90 seconds



DIFFERENT OPTIONS OF DELIVERY & BIOAVAILABILITY FOR INFLAMMATION MANAGEMENT

- **Topical administration** **30% bioavailability**
  - HIGH ABSORPTION RATE

  - Avoids first-pass metabolism

  -- Used for:

    - Inflammation / pain

  --- Types:

    - Salve
    - Rollerball
    - Recovery stick

Most Popular with Chiropractors!



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WHAT CONCENTRATION OF CBD SHOULD BE CONSIDERED FOR INFLAMMATION MANAGEMENT?

500mg, 600mg, 750mg, 1000mg:

- Used by those trying to target a specific health concern

2500mg:

- For those who have experience with CBD
- Severe pain / accident
- Terminal illness pain



DIVERSITY OF MOLECULAR TARGETS AND SIGNALING PATHWAYS FOR CBD

Date & Journal: Pharmacology Research Perspectives . 2020 Dec

Abstract

Cannabidiol (CBD) is the second most abundant component of the Cannabis plant and is known to have effects distinct from Δ^9 -tetrahydrocannabinol (THC). Many studies that examined the behavioral effects of CBD concluded that it lacks the psychotomimetic effects attributed to THC. However, CBD was shown to have a broad spectrum of effects on several conditions such as anxiety, inflammation, neuropathic pain, and epilepsy. It is currently thought that CBD engages different targets and hence CBD's effects are thought to be due to multiple molecular mechanisms of action. A well-accepted set of targets include GPCRs and ion channels, with the serotonin 5-HT_{1A} receptor and the transient receptor potential cation channel TRPV1 channel being the two main targets. CBD has also been thought to target G protein-coupled receptors (GPCRs) such as cannabinoid and opioid receptors. Other studies have suggested a role for additional GPCRs and ion channels as targets of CBD. Currently, the clinical efficacy of CBD is not completely understood. Evidence derived from randomized clinical trials, in vitro and in vivo models and real-world observations support the use of CBD as a drug treatment option for anxiety, neuropathy, and many other conditions. Hence an understanding of the current status of the field as it relates to the targets for CBD is of great interest so, in this review, we include findings from recent studies that highlight these main targets.

de Almeida DL, Devi LA. Diversity of molecular targets and signaling pathways for CBD. Pharmacol Res Perspect. 2020 Dec;8(6):e00682. doi: 10.1002/prp2.682. PMID: 33169541; PMCID: PMC7652785.

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CANNABIS COMPOUNDS EXHIBIT ANTI-INFLAMMATORY ACTIVITY IN VITRO IN COVID-19-RELATED INFLAMMATION IN LUNG EPITHELIAL CELLS AND PRO-INFLAMMATORY ACTIVITY IN MACROPHAGES

Date & Journal: Scientific Report. 2021 Jan 14.

Abstract

Cannabis sativa is widely used for medical purposes and has anti-inflammatory activity. This study intended to examine the anti-inflammatory activity of cannabis on immune response markers associated with coronavirus disease 2019 (COVID-19) inflammation. An extract fraction from C. sativa Arbel strain (F_{CBD}) substantially reduced (dose dependently) interleukin (IL)-6 and -8 levels in an alveolar epithelial (A549) cell line. F_{CBD} contained cannabidiol (CBD), cannabigerol (CBG) and tetrahydrocannabivarin (THCV), and multiple terpenes. Treatments with F_{CBD} and a F_{CBD} formulation using phytocannabinoid standards ($F_{CBD:std}$) reduced IL-6, IL-8, C-C Motif Chemokine Ligands (CCLs) 2 and 7, and angiotensin I converting enzyme 2 (ACE2) expression in the A549 cell line. Treatment with F_{CBD} induced macrophage (differentiated KG1 cell line) polarization and phagocytosis in vitro, and increased CD36 and type II receptor for the Fc region of IgG (FcγRII) expression. F_{CBD} treatment also substantially increased IL-6 and IL-8 expression in macrophages. $F_{CBD:std}$, while maintaining anti-inflammatory activity in alveolar epithelial cells, led to reduced phagocytosis and pro-inflammatory IL secretion in macrophages in comparison to F_{CBD}. The phytocannabinoid formulation may show superior activity versus the cannabis-derived fraction for reduction of lung inflammation, yet there is a need of caution proposing cannabis as treatment for COVID-19.

Anil SM, Shalev N, Vinayaka AC, Nadarajan S, Namdar D, Belausov E, Shoval I, Mani KA, Mechrez G, Koltai H. Cannabis compounds exhibit anti-inflammatory activity in vitro in COVID-19-related inflammation in lung epithelial cells and pro-inflammatory activi

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Mandolini, G. M., Lazzaretti, M., Pigoni, A., Oldani, L., Delvecchio, G., & Brambilla, P. (2018). Pharmacological properties of cannabidiol in the treatment of psychiatric disorders: a critical overview. *Epidemiology and Psychiatric Sciences, 27*, 327-335. doi:10.1017/S2045796018000239

BASIC SCIENCE (NUTRITION)

NUTRITIONAL SUPPLEMENTS AND SPECIAL DIETARY RECOMMENDATIONS FOR AN ANTI-INFLAMMATORY PROTOCOL.

RESEARCH: TURMERIC, CURCUMIN, GINGER, BLACK PEPPER, SAFFRON, & BROMELAIN



CURCUMIN, CURCUMINOIDS, & TURMERIC RESEARCH



CURCUMINOIDS

THE GOLDEN SPICE CURCUMIN IN CANCER: A PERSPECTIVE ON FINALIZED CLINICAL TRIALS DURING THE LAST 10 YEARS

Date & Journal: J Cancer Res Ther . Jan-Mar 2022.

Abstract

Curcumin, the key bioactive phytochemical present in turmeric (Curcuma longa L.), is the most studied natural compound in cancer. Preclinical studies (in vitro and in vitro) and clinical trials have demonstrated curcumin's effectiveness as an anti-inflammatory agent. The existing evidence supports that curcumin inhibits the proliferation of many types of cancer cells and can play an important role in cancer therapy. This study analyses the existing evidence in the literature on finalized clinical trials (2010-2020) related to the effect of curcumin and turmeric-derived products that focused on different types of cancers, such as chronic myeloid leukemia, multiple myeloma, prostate, colorectal and pancreatic cancer as well as cancer therapy-related complications, including oral mucositis and radiation dermatitis. Original English language articles and clinical trials published between 2010 and 2020 were searched using mainstream scholarly databases, such as PubMed, ScienceDirect, Google Scholar, and ClinicalTrials.gov. The keywords, such as "curcumin," "turmeric," "cancer," "anti-inflammatory," and "clinical trials," were used in various combinations. A total of 21 clinical trials were selected, reviewed, and included in this study. Sixteen out of 21 clinical trials were associated with the effectiveness of curcumin or turmeric on various types of cancer, and the other five clinical trials were related to the evaluation of the efficacy of curcumin or turmeric in relieving the side effects of cancer chemotherapy and radiotherapy. The emerging data from the clinical trials confirm that curcumin has the potential for cancer prevention and intervention. However, it is not yet clear whether long-term curcumin supplementation has similar benefits.

Karaboga Arslan AK, Uzunhisarcıklı E, Yerer MB, Bishayee A. The golden spice curcumin in cancer: A perspective on finalized clinical trials during the last 10 years. J Cancer Res Ther. 2022 Jan-Mar;18(1):19-26. doi: 10.4103/jcrt.JCRT_1017_20. PMID: 353817

THE GOLDEN SPICE CURCUMIN IN CANCER: A PERSPECTIVE ON FINALIZED CLINICAL TRIALS DURING THE LAST 10 YEARS

Date & Journal: J Cancer Res Ther . Jan-Mar 2022.

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CURCUMIN SUPPLEMENTATION IMPROVES OXIDATIVE STRESS AND INFLAMMATION BIOMARKERS IN PATIENTS UNDERGOING HEMODIALYSIS: A SECONDARY ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL



Date & Journal: Int Urol Nephrol . 2022 Mar 26.

Abstract

Background and objectives: Recent studies have shed light on the potential role of curcumin in mitigating inflammation in patients with chronic kidney disease (CKD). This study aimed to evaluate the effects of curcumin supplementation on plasma levels of markers of inflammation and oxidative stress in patients with CKD undergoing hemodialysis (HD).

Results: After 12 weeks of supplementation with curcumin, the TNF-a plasma levels were significantly reduced [from 15.0 (8.23-73.3) to 6.17 (1.11-55.0) pg/mL, p = 0.01].

Conclusion: 12 weeks of treatment with curcumin in HD patients resulted in a reduction in the biomarker of inflammation (TNF-a), confirming our previous hypothesis that curcumin has an anti-inflammatory effect.



Alvarenga L, Cardozo LFMF, Da Cruz BO, Paiva BR, Fouque D, Mafra D. Curcumin supplementation improves oxidative stress and inflammation biomarkers in patients undergoing hemodialysis: a secondary analysis of a randomized controlled trial. Int Urol Nephrol

BENEFICIAL EFFECTS ON ABDOMINAL BLOATING WITH AN INNOVATIVE FOOD-GRADE FORMULATION OF *CURCUMA LONGA* AND *BOSWELLIA SERRATA* EXTRACTS IN SUBJECTS WITH IRRITABLE BOWEL SYNDROME AND SMALL BOWEL DYSBIOSIS

Date & Journal: Nutrients . 2022 Jan 18.

Abstract

Bloating is a symptom frequently reported by subjects with irritable bowel syndrome (IBS) and small bowel dysbiosis, and Low FODMAP's diet (LFD) has been used to treat them. Extracts of *Curcumalonga* and *Boswelliaserrata* share anti-inflammatory and antimicrobial effects that could be useful in the management of these clinical conditions. The aim of this study was to evaluate the efficacy of curcumin and boswellia extracts (as Curcumin Boswellia Phytosome, CBP) and LFD on the relief of abdominal bloating in IBS subjects with small bowel dysbiosis, in comparison to LFD alone, in a 30-day supplementation, randomized trial. IBS participants were randomized to either the intervention (500 mg bid of CBP and LFD) or control arm (LFD). Small bowel dysbiosis has been defined by an increase of urinary indican with normal urinary skatole. A total of 67 subjects were recruited. The intervention group (33 subjects) showed a significant decrease (*p* < 0.0001) of bloating, abdominal pain, and indican values at the end of the study, when compared to the control group (34 subjects). Moreover, the subjects of the intervention group showed a significantly better (*p* < 0.0001) global assessment of efficacy (GAE) as compared to controls. In conclusion, in subjects with IBS and small bowel dysbiosis, abdominal bloating can be successfully reduced with a supplementation with CBP and LFD.

Giacosa A, Riva A, Petrangolini G, Allegrini P, Fazia T, Bernardinelli L, Peroni G, Rondanelli M. Beneficial Effects on Abdominal Bloating with an Innovative Food-Grade Formulation of Curcuma longa and Boswellia serrata Extracts in Subjects with Irritable

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EFFECT OF TURMERIC SUPPLEMENTATION ON THE PHARMACOKINETICS OF PACLITAXEL IN BREAST CANCER PATIENTS: A STUDY WITH POPULATION PHARMACOKINETICS APPROACH

Date & Journal: Phytother Res . 2022 Apr.

Abstract

Turmeric is one of the most used herbal supplements among cancer patients. It reportedly modulates the function of CYP450 enzymes and drug transporters. This study investigates the effect of turmeric on the pharmacokinetics of paclitaxel in breast cancer patients. This is a prospective longitudinal study with 60 breast cancer patients on treatment with single-agent paclitaxel and turmeric. The patients were followed up for two consecutive chemotherapy cycles, and their blood samples were collected, first without turmeric (first cycle) and the next after a 21-day concomitant administration of 2 g/day turmeric (second cycle). Plasma samples were quantified for paclitaxel concentration using High Performance Liquid Chromatograph with UV detector (HPLC-UV) method. The sparse concentration-time data of paclitaxel were subjected to population pharmacokinetic modeling, and then noncompartmental analysis (NCA) was performed on the simulated data to estimate the pharmacokinetic parameters of paclitaxel, before and after turmeric supplementation, for comparisons. The population pharmacokinetic parameters of paclitaxel differed from before to after turmeric supplementation. NCA of simulated concentration-time profiles showed a statistically significant reduction of 7.7% and 12.1% in AUC_{inf} and Cmax, respectively. Given the small magnitude of the changes in pharmacokinetic parameters, the observed changes are not clinically relevant. Thereby, turmeric at the recommended dose can be combined safely with paclitaxel.

Kalluru H, Mallayasamy SR, Kondaveeti SS, Chandrasekhar V, Kalachaveedu M. Effect of turmeric supplementation on the pharmacokinetics of paclitaxel in breast cancer patients: A study with population pharmacokinetics approach. Phytother Res. 2022 Apr;36(4)

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CURCUMIN RELEASING EGGSHELL DERIVED CARBONATED APATITE NANOCARRIERS FOR COMBINED ANTI-CANCER, ANTI-INFLAMMATORY AND BONE REGENERATIVE THERAPY.

DATE & JOURNAL: J NANOSCI NANOTECHNOL. 2019 NOV

- Bone cancer or osteosarcoma is an aggressive cancer affecting the long bones and is treated by a combination of surgery and chemotherapy. Local drug delivery directly to the site of bone cancer and the use of plant-based drugs has been explored towards improving the efficacy and decreasing the toxicity of the anti-cancer drugs. Curcumin, derived from turmeric is highly effective against cancer cells and shows very low toxicity against normal cells. Bone repair is facilitated by use of bone substitutes such as bioceramics, amongst which the carbonated apatite (CA) nanocarriers closely mimic the natural bone mineral. In the current work, we have developed CA nanocarriers based local delivery of curcumin as an adjunct treatment for bone cancer. CA nanocarriers with 6 wt.% carbonate were prepared by wet chemical synthesis using synthetic derived (6SWCA) and eggshell derived (6EWCA) precursors along with hydroxyapatite (WHA) as a control. The X-ray diffraction (XRD) patterns showed the CAs to be phase pure with a mean crystallite size of 17 nm. The Fouriertransform infrared spectroscopy (FTIR) analysis of both CAs indicated the carbonate substitution as B-Type. The amount of carbonate substitution was observed to be around 6 wt.% using FTIR and CHNO elemental analyzer. The 6EWCA showed a greater loading (36%) and release (66%) of curcumin than 6SWCA and WHA nanocarriers. The bovine serum albumin (BSA) protein denaturation assay showed the curcumin loaded CAs to be highly anti-inflammatory while their anti-cancer activity was confirmed by the high cytotoxic activity against MG-63 human osteosarcoma cells. Conclusively, an eggshell derived apatite drug delivery system was found to be very suitable to cure osteosarcoma, prevent post-cancer inflammation and modulate bone repair and regeneration.

Verma AH, Kumar TSS, Madhumathi K, Rubaiya Y, Ramalingan M, Doble M. Curcumin Releasing Eggshell Derived Carbonated Apatite Nanocarriers for Combined Anti-Cancer, Anti-Inflammatory and Bone Regenerative Therapy. J Nanosci Nanotechnol. 2019 Nov 1;19(11):6872-6880. doi: 10.1166/jnn.2019.16640. PMID: 31039839.

THE IMPACT OF CURCUMIN AND ITS MODIFIED FORMULATIONS ON ALZHEIMER'S DISEASE.

DATE & JOURNAL: J CELL PHYSIOL. 2019 MAR 7

- Alzheimer's disease (AD) is a major health problem worldwide, with no effective treatment approach. Curcumin is the main ingredient of turmeric traditionally used in Asian medicine. Several experimental studies have indicated the protective effect of curcumin and its novel formulations in AD. Curcumin has antioxidant, anti-inflammatory and neurotrophic activities, proposing a strong potential to prevent neurodegenerative diseases. However, there are no sufficient clinical trials to confirm curcumin use in AD patients. Low bioavailability following oral administration of curcumin limits its usage in human. The present study was designed to gather the effects of curcumin and its modified formulations in human and experimental models of AD.

Farkhondeh T, Samarghandian S, Pourbagher-Shahri AM, Sedaghat M. The impact of curcumin and its modified formulations on Alzheimer's disease. J Cell Physiol. 2019 Aug;234(10):16953-16965. doi: 10.1002/jcp.28411. Epub 2019 Mar 7. PMID: 30847942.

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CURCUMA LONGA L. AMELIORATES ASTHMA CONTROL IN CHILDREN AND ADOLESCENTS: A RANDOMIZED, DOUBLE-BLIND, CONTROLLED TRIAL.

DATE & JOURNAL: J ETHNOPHARMACOL. 2019 APR 13

- ETHNOPHARMACOLOGICAL RELEVANCE: Roots of Curcuma longa L. are used as medicine for millennia. They possess several pharmacological properties, including anti-inflammatory action, and can be suitable for asthma treatment.

- AIM OF THE STUDY: We aimed to test the hypothesis that, in children and adolescents with persistent asthma, the administration of powdered roots of C. longa for 6 months, in addition to standard treatment, compared to placebo, will result in better disease control.

- CONCLUSION: The powdered roots of C. longa led to less frequent nighttime awakenings, less frequent use of short-acting β-adrenergic agonists, and better disease control after 3 and 6 months, when compared to placebo.

Manarin G, Anderson D, Silva JME, Coppede JDS, Roxo-Junior P, Pereira AMS, Carmona F. Curcuma longa L. ameliorates asthma control in children and adolescents: A randomized, double-blind, controlled trial. J Ethnopharmacol. 2019 Jun 28;238:111882. doi: 10.1016/j.jep.2019.111882. Epub 2019 Apr 13. PMID: 30991137.

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SYSTEMIC ADMINISTRATION OF CURCUMIN AFFECT ANXIETY- RELATED BEHAVIORS IN A RAT MODEL OF POST TRAUMATIC STRESS DISORDER VIA ACTIVATION OF SEROTONERGIC SYSTEMS

PUBLISHED: JUN 19, 2018

Posttraumatic stress disorder (PTSD) is a trauma-induced psychiatric disease characterized by impaired hyperarousal, fear extermination, depression, anxiety, and amnesic symptoms that may include the release of monoamines in the dread circuit. Curcumin (CUR), a major diarylheptanoid and polyphenolic component of Curcuma longa, reportedly possesses several pharmacological features, including antidiabetic, antiatherosclerotic, anticancer, and neuropsychiatric actions. But the anxiolytic-like effects of CUR and its mechanism of action in PTSD are unclear. The current research measured some anxiety-related behavioral responses to examine the effects of CUR on symptoms of anxiety in rats after single prolonged stress (SPS) exposure by reversing the serotonin (5-HT) dysfunction. Rats received CUR (20, 50, or 100 mg/kg, i.p., once daily) for 14 days after SPS exposure. Administration of CUR significantly increased the number of central zone crossings in the open field test and reduced grooming behavior in the elevated plus maze (EPM) test and increased the number of open-arm visits on the EPM test. CUR administration significantly reduced freezing response to contextual fear conditioning. CUR recovered neurochemical abnormalities and SPS-induced decreased 5-HT tissue levels in the hippocampus, amygdala, and striatum. These results suggested that CUR has anxiolytic-like effects on biochemical and behavioral symptoms associated with anxiety. Thus, CUR may be a useful agent to alleviate or treat psychiatric disorders similar to those observed in patients with PTSD.

Bombi Lee and Hyejung Lee· Acupuncture and Meridian Science Research Center, College of Korean Medicine, Kyung Hee University, Seoul 02447, Republic of Korea

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PIPERINE (BLACK PEPPER) RESEARCH



EFFECT OF A FIXED COMBINATION OF CURCUMIN, ARTEMISIA, BROMELAIN, AND BLACK PEPPER ORAL ADMINISTRATION ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY INDICES IN PATIENTS WITH DIABETIC MACULAR EDEMA

Date & Journal: Nutrients . 2022 Apr 6.

Abstract

Background: To investigate the effects of a fixed combination of Curcumin (200 mg), Artemisia (80 mg), Bromelain (80 mg), and Black pepper (2 mg) on vascular parameters in mild to moderate diabetic macular edema (DME).

Results: A significant improvement of BCVA and CRT reduction was recorded at 6 months follow-up in the dietary complementary supplementation group compared to control (respectively $p = 0.028$ and $p = 0.0003$). VD of the total capillary plexus, microaneurysms count, glycaemia and HbA1c did not vary over the follow-up period between groups. Within the Intravit® group, poor responders tended to show a larger FAZ area, more microaneurysms, and a lower VD in the DCP compared to the good responders group (p < 0.0001).

Conclusions: A fixed combination of Curcumin, Artemisia, Bromelain, and Black pepper oral administration may have a positive impact on central retinal thickness, visual acuity, and VD of the DCP in compensated type 2 diabetic patients with mild DME.

Chiosi F, Rinaldi M, Campagna G, Manzi G, De Angelis V, Calabrò F, D'Andrea L, Tranfa F, Costagliola C. Effect of a Fixed Combination of Curcumin, Artemisia, Bromelain, and Black Pepper Oral Administration on Optical Coherence Tomography Angiography Indic

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Virusdisease . 2020 Sep

Abstract: Ebola and Dengue are the critical diseases caused by RNA viruses, especially in the tropical parts of the globe, including Asia and Africa, and no prominent therapeutic options are available so far. Here, an effort was made to evaluate the efficacy of black pepper (*Piper nigrum* L.) alkaloid Piperine as a potential drug through computational docking simulation. Eight structurally essential proteins of Dengue and Ebola virus were selected as in silico docking targets for Piperine. Absorption, Distribution, Metabolism, and Excretion profile showed that Piperine was safe and possessed significant drug-like properties. Molecular dynamic simulation and binding free energy calculation showed that Piperine could inhibit Methyltransferase (PDB id 1L9K) of Dengue and VP35 Interferon Inhibitory Domain (PDB id 3FKE) of Ebola virus in comparison with the commercial antiviral Ribavirin. Furthermore, statistical analysis based on multivariate and clustering approaches revealed that Piperine had more affinity towards viral proteins than that of Ribavirin.

Nag A, Chowdhury RR. Piperine, an alkaloid of black pepper seeds can effectively inhibit the antiviral enzymes of Dengue and Ebola viruses, an in silico molecular docking study. Virusdisease. 2020 Sep;31(3):308-315. doi: 10.1007/s13337-020-00619-6. Epub 2020 Aug 5. PMID: 32904842; PMCID: PMC7458978.

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DATE & JOURNAL: PHYTOTHERAPY RESEARCH . 2020 AUG.

Abstract: Osteoarthritis is the most common articular disease that can lead to chronic pain and severe disability. Curcumin-an effective ingredient in turmeric with anti inflammatory property-plays an important role in protecting the joints against destructive factors. Gingerols and piperine, are the effective ingredients of ginger and black pepper, which may potentially enhance and sustain the effect of curcumin in this direction. To determine the effect of cosupplementation with turmeric extract, black pepper, and ginger on prostaglandin E2 (PGE2) in patients with chronic knee osteoarthritis, compared with Naproxen. Sixty patients with two different levels of knee osteoarthritis (Grade 2 and 3) were studied. Individuals were randomly assigned to receive daily turmeric extract, ginger, and black pepper together or Naproxen capsule for 4 weeks. PGE2 was evaluated by ELISA method. 24-hr recall was also assessed. All of participants completed the study. PGE2 decreased significantly in both groups ($p < .001$), but there was no significant differences between groups. The results of this study indicated that intake of the selected herbs twice a day for 4 weeks may improve the PGE2 levels in patients with chronic knee osteoarthritis similar to Naproxen drug.

Heidari-Beni M, Moravejolahkami AR, Gorgian P, Askari G, Tarrahi MJ, Bahreini-Esfahani N. Herbal formulation "turmeric extract, black pepper, and ginger" versus Naproxen for chronic knee osteoarthritis: A randomized, double-blind, controlled clinical trial. Phytother Res. 2020 Aug;34(8):2067-2073. doi: 10.1002/ptr.6671. Epub 2020 Mar 16. PMID: 32180294.

HERBAL FORMULATION "TURMERIC EXTRACT, BLACK PEPPER, AND GINGER" VERSUS NAPROXEN FOR CHRONIC KNEE OSTEOARTHRITIS: A RANDOMIZED, DOUBLE-BLIND, CONTROLLED CLINICAL TRIAL

DATE & JOURNAL: PHYTOTHERAPY RESEARCH . 2020 AUG.

Abstract: Osteoarthritis is the most common articular disease that can lead to chronic pain and severe disability. Curcumin-an effective ingredient in turmeric with anti inflammatory property-plays an important role in protecting the joints against destructive factors. Gingerols and piperine, are the effective ingredients of ginger and black pepper, which may potentially enhance and sustain the effect of curcumin in this direction. To determine the effect of cosupplementation with turmeric extract, black pepper, and ginger on prostaglandin E2 (PGE2) in patients with chronic knee osteoarthritis, compared with Naproxen. Sixty patients with two different levels of knee osteoarthritis (Grade 2 and 3) were studied. Individuals were randomly assigned to receive daily turmeric extract, ginger, and black pepper together or Naproxen capsule for 4 weeks. PGE2 was evaluated by ELISA method. 24-hr recall was also assessed. All of participants completed the study. PGE2 decreased significantly in both groups ($p < .001$), but there was no significant differences between groups. The results of this study indicated that intake of the selected herbs twice a day for 4 weeks may improve the PGE2 levels in patients with chronic knee osteoarthritis similar to Naproxen drug.

Heidari-Beni M, Moravejolahkami AR, Gorgian P, Askari G, Tarrahi MJ, Bahreini-Esfahani N. Herbal formulation "turmeric extract, black pepper, and ginger" versus Naproxen for chronic knee osteoarthritis: A randomized, double-blind, controlled clinical trial. Phytother Res. 2020 Aug;34(8):2067-2073. doi: 10.1002/ptr.6671. Epub 2020 Mar 16. PMID: 32180294.

A SYSTEMATIC REVIEW ON BLACK PEPPER (PIPER NIGRUM L.): FROM FOLK USES TO PHARMACOLOGICAL APPLICATIONS.

Date & Journal: Crit Rev Food Sci Nutr. 2019 Feb 11

Considered as the "King of spices", black pepper (Piper nigrum L.) is a widely used spice which adds flavor of its own to dishes, and also enhances the taste of other ingredients. Piper nigrum has also been extensively explored for its biological properties and its bioactive phyto-compounds. There is, however, no updated compilation of these available data to provide a complete profile of the medicinal aspects of P. nigrum. This study endeavors to systematically review scientific data on the traditional uses, phytochemical composition, and pharmacological properties of P. nigrum. The country with the highest number of traditional reports of P. nigrum for both human and veterinary medicine was India, mostly for menstrual and ear-nose-throat disorders in human and gastrointestinal disorders in livestock. The seeds and fruits were mostly used, and the preferred mode of preparation was in powdered form, pills or tablets, and paste. Piper nigrum and its bioactive compounds were also found to possess important pharmacological properties. Antimicrobial activity was recorded against a wide range of pathogens via inhibition of biofilm, bacterial efflux pumps, bacterial swarming, and swimming motilities. Studies also reported its antioxidant effects against a series of reactive oxygen and nitrogen species including the scavenging of superoxide anion, hydrogen peroxide, nitric oxide, DPPH, ABTS, and reducing effect against ferric and molybdenum (VI). Improvement of antioxidant enzymes in vivo has also been reported. Piper nigrum also exhibited anticancer effect against a number of cell lines from breast, colon, cervical, and prostate through different mechanisms including cytotoxicity, apoptosis, autophagy, and interference with signaling pathways. Its antidiabetic property has also been confirmed in vivo as well as hypolipidemic activity as evidenced by decrease in the level of cholesterol, triglycerides, and low-density lipoprotein and increase in high-density lipoprotein. Piper nigrum also has anti-inflammatory, analgesic, anticonvulsant, and neuroprotective effects. The major bioactive compound identified in P. nigrum is piperine although other compounds are also present including piperic acid, piperlonguminine, pellitorine, piperolein B, piperamide, piperettine, and (-)-kusunokinin, which also showed biological potency. Most pharmacological studies were conducted in vitro (n = 60) while only 21 in vivo and 1 clinical trial were performed. Hence, more in vivo experiments using a pharmacokinetic and pharmacokinetic approach would be beneficial. As a conclusive remark, P. nigrum should not only be regarded as "King of spices" but can also be considered as part of the kingdom of medicinal agents, comprising a panoply of bioactive compounds with potential nutraceutical and pharmaceutical applications.

Takooree H, Aumeeruddy MZ, Rengasamy KRR, Venugopala KN, Jeewon R, Zengin G, Mahomoodally MF. A systematic review on black pepper (Piper nigrum L.): from folk uses to pharmacological applications. Crit Rev Food Sci Nutr. 2019;59(sup1):S210-S243. doi: 10.1080/10408398.2019.1565489. Epub 2019 Feb 11. PMID: 30740986.

BIOLOGY-ORIENTED SYNTHESIS (BIOS) OF PIPERINE DERIVATIVES AND THEIR COMPARATIVE ANALGESIC AND ANTI-INFLAMMATORY ACTIVITIES.

PUBLISHED: MED CHEM . 2018.

Background: Serious side effects such as gastric intestinal ulcers, bleeding etc. are associated with most anti-inflammatory and analgesic drugs. So, there is a need to search novel, potent, and safer anti-inflammatory and analgesic drugs. Piperine alkaloid was isolated from Piper nigrum L. and some derivatives of piperine having azomethine, sulfamoyl, propanoyl, acetamoyl and heterocyclic oxadiazole were synthesized. The structures of synthetic derivatives were confirmed by using different spectroscopic techniques such as 1H-, 13C-NMR, EI-MS, and IR. Melting points were also determined for all compounds. Piperine and its all the synthetic derivatives were subjected to comparative in vivo evaluation of analgesic and anti-inflammatory activities at the oral dose of 6 mg/kg/day. Analgesic activity was evaluated by tail immersion, hot plate and acetic acid writhing methods, while antiinflammatory activity was evaluated by carrageenan-induced paw inflammation.

CONCLUSION: The newly identified molecules may serve as a lead for future research in connection of potent and safer anti-inflammatory and analgesic drug candidates.

Yasir A, Ishtiaq S, Jahangir M, Ajaib M, Salar U, Khan KM. Biology-Oriented Synthesis (BIOS) of Piperine Derivatives and their Comparative Analgesic and Antiinflammatory Activities. Med Chem. 2018;14(3):269-280. doi: 10.2174/1573406413666170623083810. PMID: 28641526.

RESEARCH ON GINGER



DOES DIET PLAY A ROLE IN REDUCING NOCICEPTION RELATED TO INFLAMMATION AND CHRONIC PAIN?

Date & Journal: Nutrition . 2019 Oct.

Abstract

Dietary habits are fundamental issues to assess when modulating health and well-being; however, different nutritional panels may help individuals prevent acute and chronic pain. Many substances, known to be active antioxidants and anti-inflammatory compounds, should serve this fundamental task. Antinociceptive and analgesic natural compounds include flavonoids, terumbone from ginger root, curcuminoids, ω-3 polyunsaturated fatty acids, and taurine. Furthermore, correct intake of trace elements and minerals is strategic to reduce inflammation-related pain. This review addresses these items in an effort to suggest new criteria for proper dietary supplementation to prevent pain.

Bjørklund G, Aaseth J, Doşa MD, Pivina L, Dadar M, Pen JJ, Chirumbolo S. Does diet play a role in reducing nociception related to inflammation and chronic pain? Nutrition. 2019 Oct;66:153-165. doi: 10.1016/j.nut.2019.04.007. Epub 2019 Apr 26. PMID: 313016

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GINGER EXTRACT HAS ANTI-LEUKEMIA AND ANTI-DRUG RESISTANT EFFECTS ON MALIGNANT CELLS

Date & Journal: J Cancer Res Clin Oncol . 2019 Aug.

Abstract

Purpose: Based on the poor prognosis of drug resistance in pediatric acute lymphoblastic leukemia (ALL) and adverse effects of chemotherapy, this study was aimed to evaluate the effect of several herbal extracts on leukemic cells.

Results: The IC_{50}s for cinnamon, ginger and green tea extracts on ALL cell lines were 300 µg/ml, 167 µg/ml and 70 µg/ml, respectively. Surprisingly, the methotrexate (MTX)-resistant sub-line showed more sensitivity to ginger. Combined treatment with ginger and MTX showed synergistic effects on CCRF-CEM, Nalm-6 and ALL primary cells. It was shown that ginger does not impair the high expression levels of ABCA2 or ABCA3 transporter genes in the ALL malignant cells, suggesting other molecular pathways involved in its anticancer potential.

Conclusion: To the best of our knowledge, this is the first study that reveals the antileukemic effect of ginger extract on both, pediatric ALL cell lines and primary cells.

Rahimi Babasheikhali S, Rahgozar S, Mohammadi M. Ginger extract has anti-leukemia and anti-drug resistant effects on malignant cells. J Cancer Res Clin Oncol. 2019 Aug;145(8):1987-1998. doi: 10.1007/s00432-019-02949-5. Epub 2019 Jun 18. PMID: 31214760.

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GINGER (ZINGIBER OFFICINALE ROSCOE) IN THE PREVENTION OF AGEING AND DEGENERATIVE DISEASES: REVIEW OF CURRENT EVIDENCE

Evid Based Complement Alternat Med . 2019 Aug 20

Abstract

Currently, the age of the population is increasing as a result of increased life expectancy. Ageing is defined as the progressive loss of physiological integrity, which can be characterized by functional impairment and high vulnerability to various types of diseases, such as diabetes, hypertension, Alzheimer's disease (AD), Parkinson's disease (PD), and atherosclerosis. Numerous studies have reported that the presence of oxidative stress and inflammation contributes to the development of these diseases. In general, oxidative stress could induce proinflammatory cytokines and reduce cellular antioxidant capacity. Increased oxidative stress levels beyond the production of antioxidant agents cause oxidative damage to biological molecules, including DNA, protein, and carbohydrates, which affects normal cell signalling, cell growth, differentiation, and apoptosis and leads to disease pathogenesis. Since oxidative stress and inflammation contribute to these diseases, ginger (*Zingiber officinale* Roscoe) is one of the potential herbs that can be used to reduce the level of oxidative stress and inflammation. Ginger consists of two major active components, 6-gingerol and 6-shogaol, which are essential for preventing oxidative stress and inflammation. Thus, this paper will review the effects of ginger on ageing and degenerative diseases, including AD, PD, type 2 diabetes mellitus (DM), hypertension, and osteoarthritis.

Mohd Sahardi NFN, Makpol S. Ginger (Zingiber officinale Roscoe) in the Prevention of Ageing and Degenerative Diseases: Review of Current Evidence. Evid Based Complement Alternat Med. 2019 Aug 20;2019:5054395. doi: 10.1155/2019/5054395. PMID: 31531114; PMC

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BLACK GINGER EXTRACT INCREASES PHYSICAL FITNESS PERFORMANCE AND MUSCULAR ENDURANCE BY IMPROVING INFLAMMATION AND ENERGY METABOLISM.

Published: Heliyon . 2016 May 24

We previously reported that polymethoxyflavones (PMFs) in black ginger (Kaempferia parviflora) extract (KPE) increased energy production by activating AMP-activated protein kinase (AMPK) in C2C12 myoblasts. We herein evaluated the effects of KPE on physical fitness performance and muscular endurance in mice. Male mice were orally administered KPE for 4 weeks, and then forced swimming test, open-field test, inclined plane test, and wire hanging test were performed. KPE significantly increased the swimming time, motility after swimming, and grip strength. IL-6 and TNF-α mRNA expression levels were decreased in the soleus muscle, whereas peroxisome proliferator-activated receptor γ coactivator (PGC)-1α and glycogen synthase mRNA expression levels, mitochondrial number, and glycogen content were increased. These results were in agreement with those obtained for KPE and PMFs in C2C12. Therefore, the activation of AMPK by PMFs may be one of the mechanisms by which KPE improves physical fitness performance and muscular endurance.

Toda K, Hitoe S, Takeda S, Shimoda H. Black ginger extract increases physical fitness performance and muscular endurance by improving inflammation and energy metabolism. Heliyon. 2016 May 24;2(5):e00115. doi: 10.1016/j.heliyon.2016.e00115. PMID: 27441286;

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ACUTE EFFECTS OF GINGER EXTRACT ON BIOCHEMICAL AND FUNCTIONAL SYMPTOMS OF DELAYED ONSET MUSCLE SORENESS.

Published: Med J Islam Repub Iran . 2015 Sep 12.

BACKGROUND: Inflammation and pain induced by delayed onset muscle soreness (DOMS) as a result of eccentric exercise (EE) or unaccustomed activity cause some difficulties in exercise for athletes. The purpose of this study was to survey the effect of ginger extract on biochemical and functional symptom of delayed onset muscle soreness.

CONCLUSION: The finding of this study suggests that 2 grams of ginger may have anti-inflammation and analgesic effect on DOMS

Hoseinzadeh K, Daryanoosh F, Baghdasar PJ, Alizadeh H. Acute effects of ginger extract on biochemical and functional symptoms of delayed onset muscle soreness. Med J Islam Repub Iran. 2015 Sep 12;29:261. PMID: 26793652; PMCID: PMC4715415.

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SAFFRON, BROMELAIN, & EDTA RESEARCH







THE POTENTIAL ROLE OF SAFFRON (CROCUS SATIVUS L.) AND ITS COMPONENTS IN OXIDATIVE STRESS IN DIABETES MELLITUS: A SYSTEMATIC REVIEW

Date & Journal: Clin Nutr ESPEN. 2022 April

Abstract

• **Background and aims:** Diabetes mellitus is one of the most important life-threatening metabolic diseases of the 21st century. The use of complementary and alternative medicine in diabetic patients seems to be increasing. Saffron, a valuable herbal medicine, has several pharmacological properties such as anti-oxidant effect, which can play important role in ameliorating the complications of diabetes. The aim of this study was to systematically review the therapeutic effects of saffron and its bioactive components on oxidative stress in diabetes mellitus.

• **Results:** In the end, only 31of the 389 articles met the criteria for analysis. Of the 31 articles, 4 were in-vitro studies, 25 were animal studies, and 2 were clinical trials studies. Saffron supplementation may activate insulin receptor substrate 1 (IRS1) and peroxisome proliferator-activated receptor gamma (PPAR-γ), which can improve hyperglycemia and insulin transduction signal in adipose tissue, and regulate glucose metabolism, leading to an increased nuclear factor erythroid 2-related factor 2 (Nrf2), HO-1 expression, amelioration of mitochondrial function, and an increased levels of antioxidant enzymes.

• **Conclusion:** Most studies have shown that saffron supplementation significantly enhanced the production and activity of antioxidant enzymes and decreased oxidative stress indices in diabetes mellitus. However, human pharmacokinetic and more accurate clinical trial studies are needed to determine dose ranges and the exact mechanisms of action of saffron and its active components in diabetes.

Moini Jazani A, Karimi A, Nasimi Doost Azgomi R. The potential role of saffron (Crocus Sativus L.) and its components in oxidative stress in diabetes mellitus: A systematic review. Clin Nutr ESPEN. 2022 Apr;48:148-157. doi: 10.1016/j.clnesp.2022.01.022. E

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EFFECTS OF SAFFRON SUPPLEMENTATION ON IMPROVING SLEEP QUALITY: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Date & Journal: Sleep Med. 2022 April.

Abstract

Objective: To compare the efficacy of different dosage regimens of saffron supplementation on improving sleep quality among healthy adults, patients with insomnia or type 2 diabetes and patients under Methadone maintenance treatment (MMT).

Results: The pooling of the effect sizes showed that saffron group achieve a notable treatment effect on PSQI (MD: -2.14; 95% CI: -2.86 to -1.42; P < 0.01), ISI (MD: -2.63; 95% CI: -3.70 to -2.55; P < 0.01) and RSQ (MD: 7.05; 95% CI: 1.48 to 12.62; P = 0.01) compared with placebo group.

Conclusion: Saffron supplementation as a treatment for improving sleep quality have promising clinical application as its great improvement on all efficacy outcomes and no serious adverse advents occurred as the dose was increased. The dose of 100 mg saffron supplementation per day was proved to achieve excellent and more stable curative effect on improving sleep quality in our subgroup analysis. However, further investigation is necessary to confirm the efficacy and long-term safety of different doses of saffron for insomnia.

Lian J, Zhong Y, Li H, Yang S, Wang J, Li X, Zhou X, Chen G. Effects of saffron supplementation on improving sleep quality: a meta-analysis of randomized controlled trials. Sleep Med. 2022 Apr;92:24-33. doi: 10.1016/j.sleep.2022.03.001. Epub 2022 Mar 6. P

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THE MECHANISMS OF SAFFRON (CROCUS SATIVUS') ON THE INFLAMMATORY PATHWAYS OF DIABETES MELLITUS: A SYSTEMATIC REVIEW

Date & Journal: Diabetes Metab Syndr . 2022 Jan.

Abstract

Background: Diabetes is one of the major medical problems, which can lead to damage to cells or organs in various parts of the body. Saffron as herbal medicine has contained several active ingredients, including safranal, flavonoids, crocetin, and crocin, which are effective in modulating oxidative stress and inflammation, which can play the main role in reducing the effects of diabetes. However, so far, the effect of saffron on diabetes inflammation has not been evaluated in the form of systematic review studies. The purpose of this systematic study was to evaluate the evidence obtained from in-vitro, animal, and clinical trials studies on the effects of saffron on inflammation in diabetes.

Results: In the end, only 20 of the 596 articles met the criteria for analysis. Of the 20 articles, 3 were in-vitro studies, 13 were animal studies, and 4 were human studies.

Conclusion: The findings of this systematic study (Except for two studies) suggest that saffron supplementation with potential anti-inflammatory properties may reduce the expression of the inflammatory pathway and the production of inflammatory products in diabetes.

Nasimi Doost Azgomi R, Karimi A, Zarshenas MM, Moini Jazani A. The mechanisms of saffron (Crocus sativus') on the inflammatory pathways of diabetes mellitus: A systematic review. Diabetes Metab Syndr. 2022 Jan;16(1):102365. doi: 10.1016/j.dsx.2021.102365.

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NEPHROPROTECTIVE ROLE OF BROMELAIN AGAINST OXIDATIVE INJURY INDUCED BY ALUMINIUM IN RATS

Environ Toxicol Pharmacol . 2020 Nov

Abstract

The present study was designed to investigate the nephroprotective effect of bromelain against oxidative stress stimulated by aluminium chloride in rats.

In addition, significant alterations in lipid and protein profiles were detected. Furthermore, histopathological and immunohistochemical variations were seen in kidney sections supporting the obtained biochemical changes. Otherwise, rats supplemented with bromelain singly declined lipid peroxidation and improved most of the studied parameters. Moreover, rats pretreated with bromelain followed by AlCl3 intoxication showed significant alleviation in lipid peroxidation, antioxidant status and biochemical indices with respect to AlCl3 treated group. Conclusively, bromelain has beneficial protective effects and has the capability to counteract the toxic influence of AlCl3. So, bromelain might represent a novel approach in the therapy of metal toxicity because of its antioxidant and chelating properties.

El-Demerdash FM, Baghdadi HH, Ghanem NF, Mhanna ABA. Nephroprotective role of bromelain against oxidative injury induced by aluminium in rats. Environ Toxicol Pharmacol. 2020 Nov;80:103509. doi: 10.1016/j.etap.2020.103509. Epub 2020 Oct 1. PMID: 33010469.

THE COMBINATION OF BROMELAIN AND CURCUMIN AS AN IMMUNE-BOOSTING NUTRACEUTICAL IN THE PREVENTION OF SEVERE COVID-19

Date & Journal: Metabol Open . 2020 Dec.

Abstract

The coronavirus disease 2019 (COVID-19) pandemic is still ongoing, while no treatment has been proven effective. COVID-19 pathophysiology involves the activation of three main pathways: the inflammatory, the coagulation and the bradykinin cascades. Here, we highlight for the first time the joint potential therapeutic role of bromelain and curcumin, two well-known nutraceuticals, in the prevention of severe COVID-19. Bromelain (a cysteine protease isolated from the pineapple stem) and curcumin (a natural phenol found in turmeric) exert important immunomodulatory actions interfering in the crucial steps of COVID-19 pathophysiology. Their anti-inflammatory properties include inhibition of transcription factors and subsequent downregulation of proinflammatory mediators. They also present fibrinolytic and anticoagulant properties. Additionally, bromelain inhibits cyclooxygenase and modulates prostaglandins and thromboxane, affecting both inflammation and coagulation, and also hydrolyzes bradykinin. Interestingly, curcumin has been shown in *silico* studies to prevent entry of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into cells as well as viral replication, while a recent experimental study has demonstrated that bromelain may also inhibit viral entry into cells. Notably, bromelain substantially increases the absorption of curcumin after oral administration. To the best of our knowledge, this is the first report highlighting the significance of bromelain and, most importantly, the potential preventive value of the synergistic effects of bromelain and curcumin against severe COVID-19.

Kritis P, Karampela I, Kokoris S, Dalamaga M. The combination of bromelain and curcumin as an immune-boosting nutraceutical in the prevention of severe COVID-19. Metabol Open. 2020 Dec;8:100066. doi: 10.1016/j.metop.2020.100066. Epub 2020 Nov 13. PMID: 33205039; PMCID: PMC7661945.

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Date & Journal: Metabol Open . 2020 Dec.

Abstract

The coronavirus disease 2019 (COVID-19) pandemic is still ongoing, while no treatment has been proven effective. COVID-19 pathophysiology involves the activation of three main pathways: the inflammatory, the coagulation and the bradykinin cascades. Here, we highlight for the first time the joint potential therapeutic role of bromelain and curcumin, two well-known nutraceuticals, in the prevention of severe COVID-19. Bromelain (a cysteine protease isolated from the pineapple stem) and curcumin (a natural phenol found in turmeric) exert important immunomodulatory actions interfering in the crucial steps of COVID-19 pathophysiology. Their anti-inflammatory properties include inhibition of transcription factors and subsequent downregulation of proinflammatory mediators. They also present fibrinolytic and anticoagulant properties. Additionally, bromelain inhibits cyclooxygenase and modulates prostaglandins and thromboxane, affecting both inflammation and coagulation, and also hydrolyzes bradykinin. Interestingly, curcumin has been shown in *silico* studies to prevent entry of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into cells as well as viral replication, while a recent experimental study has demonstrated that bromelain may also inhibit viral entry into cells. Notably, bromelain substantially increases the absorption of curcumin after oral administration. To the best of our knowledge, this is the first report highlighting the significance of bromelain and, most importantly, the potential preventive value of the synergistic effects of bromelain and curcumin against severe COVID-19.

Kritis P, Karampela I, Kokoris S, Dalamaga M. The combination of bromelain and curcumin as an immune-boosting nutraceutical in the prevention of severe COVID-19. Metabol Open. 2020 Dec;8:100066. doi: 10.1016/j.metop.2020.100066. Epub 2020 Nov 13. PMID: 33205039; PMCID: PMC7661945.

BROMELAIN: A REVIEW ON ITS POTENTIAL AS A THERAPY FOR THE MANAGEMENT OF COVID-19

Niger J Physiol Sci . 2020 Jun 30

Abstract

Coronavirus Disease 2019 is a wide-spreading severe viral disease caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2) virus that needs to be urgently eradicated. SARS-COV-2 has infected millions of people worldwide and results in more than three hundred thousand deaths. Several repurposed drugs have failed to successfully eradicate the infection. Multiorgan failure caused by pronounced inflammation and systemic coagulation accounts for severe complications and death associated with diseases. Bromelain appears to be a potential candidate that may be used to inhibit or prevent the symptoms of the diseases. Its anti-inflammatory and anticoagulatory properties make it a potential agent that may slow the progression of the disease. In this review, we highlighted the beneficial effects of bromelain based on both experimental and clinical evidence that make bromelain a good candidate for the treatment of symptoms of CoVID-19 infection.

Owoyele BV, Bakare AO, Ologe MO. Bromelain: A Review on its Potential as a Therapy for the Management of Covid-19. Niger J Physiol Sci. 2020 Jun 30;35(1):10-19. PMID: 33084621.

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Servings per container: 30

Serving Size: 3 capsules

Ingredient	Amount Per Serving
Organic Turmeric Powder	1100mg*
95% Standardized Curcuminoid	200mg*
Black Pepper Fruit Extract (Piperine)	10mg*

A proprietary blend of the following natural ingredients: Organic ginger root extract; saffron powder; bromelain. Other ingredients: Vegetable cellulose capsule; EDTA. Made with 72% organic ingredients. Daily value not established.

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II. BASIC SCIENCE (NUTRITION)

A. INFLAMMATION
   a) Natural inflammation reduction treatment options, including nutritional supplements and special dietary recommendations for an anti-inflammatory protocol, including legal hemp for anti-inflammatory management.
   b) Literature review
B. DIGESTION
   a) Green Alkaline foods for fiber and digestion
   b) Colon Health
   c) Minerals and Collagen Protein
D. AMINO ACIDS
   a) Definitions
   b) Amino acids for cardiovascular health
   c) Nitric oxide production

ALKALINE GREENS FOR FIBER AND DIGESTION

- Acid interferes with digestion as food stagnates and rots, lowering the pH of the body.

- A 16oz bottle of soda has a pH= 2. Very acidic. To bring the pH back up to our normal 7.3, we would have to dilute the soda with about 10 gallons of water.

- The blood must maintain a pH = 7.3-7.45. (Guyton) The body begins to sweep the extra acids into the tissues (muscles & joints). (lactic acid)

- Acidification will actually precipitate acids out of solution, in the form of crystals, salts, and stones (i.e. kidney & gall stones).

GUT MICROBIOTA-DERIVED INOSINE FROM DIETARY BARLEY LEAF SUPPLEMENTATION ATTENUATES COLITIS THROUGH PPARΓ SIGNALING ACTIVATION

Date & Journal: Microbiome . 2021 Apr 5.

Abstract

Background: Ulcerative colitis is a type of chronic inflammatory bowel disease closely associated with gut microbiota dysbiosis and intestinal homeostasis dysregulation. Barley leaf (BL) has a long history of use in Traditional Chinese Medicine with potential health-promoting effects on intestinal functions. However, its mechanism of action is not yet clear. Here, we explore the potential modulating roles of gut microbial metabolites of BL to protect against colitis and elucidate the underlying molecular mechanisms.

Results: Using 16S rRNA gene-based microbiota analysis, we first found that dietary supplementation of BL ameliorated dextran sulfate sodium (DSS)-induced gut microbiota dysbiosis. The mechanisms by which BL protected against DSS-induced colitis were resulted from improved intestinal mucosal barrier functions via the activation of peroxisome proliferator-activated receptor (PPAR)γ signaling. In addition, metabolomic profiling analysis showed that the gut microbiota modulated BL-induced metabolic reprograming in the colonic tissues particularly by the enhancement of glycolysis process. Notably, dietary BL supplementation resulted in the enrichment of microbiota-derived purine metabolite inosine, which could activate PPARγ signaling in human colon epithelial cells. Furthermore, exogenous treatment of inosine reproduced similar protective effects as BL to protect against DSS-induced colitis through improving adenosine 2A receptor ($A_{2A}R$)/PPARγ-dependent mucosal barrier functions.

Conclusions: Overall, our findings suggest that the gut microbiota-inosine-$A_{2A}R$/PPARγ axis plays an important role in the maintenance of intestinal homeostasis, which may represent a novel approach for colitis prevention via manipulation of the gut microbial purine metabolite.

Li D, Feng Y, Tian M, Ji J, Hu X, Chen F. Gut microbiota-derived inosine from dietary barley leaf supplementation attenuates colitis through PPARγ signaling activation. Microbiome. 2021 Apr 5;9(1):83. doi: 10.1186/s40168-021-01028-7. PMID: 33820558; PMCID

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OAT FIBER SUPPLEMENTATION ALLEVIATES INTESTINAL INFLAMMATION AND AMELIORATES INTESTINAL MUCOSAL BARRIER VIA ACTING ON GUT MICROBIOTA-DERIVED METABOLITES IN LDLR $^{-/-}$ MICE

Date & Journal: Nutrition . 2022 Mar.

Abstract

Objective: Gut microbiota-derived metabolites are involved in intestinal inflammation, which can affect the development of atherosclerotic plaques. Previous studies have shown that oat fiber can delay the progression of atherosclerosis via improving lipid metabolism. The aim of this study was to evaluate how oat fiber acted on gut microbiota-derived metabolites, inhibited intestinal inflammation, and protected the intestinal mucosal barrier.

Results: Pathologically, oat fiber reversed the increment of the atherosclerotic lesion and ameliorated intestinal mucosal barrier in LDLR$^{-/-}$ mice. Oat fiber regulated the levels of gut microbiota-derived metabolites along with a decrease in isobutyrylcarnitine, valerylcarnitine, 1-methylguanosine, and 2-methylguanosine, and an increase in l-tyrosine and niacinamide. Notably, oat fiber blocked the TLR4 signal pathway and decreased the expression of nuclear factor-κB p65 in both the aorta and gut tissues. Also, oat fiber raised the expression of tight junction proteins including ZO-1 and occludin.

Conclusion: Taken together, the present study revealed that oat fiber feeding effectively attenuated the development of atherosclerosis, at least partly via affecting gut microbiota-derived metabolites, inhibiting the intestinal inflammatory response, and maintaining the integrity of the intestinal mucosal barrier.

Gao H, Song RJ, Jiang H, Zhang W, Han SF. Oat fiber supplementation alleviates intestinal inflammation and ameliorates intestinal mucosal barrier via acting on gut microbiota-derived metabolites in LDLR-/- mice. Nutrition. 2022 Mar;95:111558. doi: 10.1016

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ALGAE SUPPLEMENTATION FOR EXERCISE PERFORMANCE: CURRENT PERSPECTIVES AND FUTURE DIRECTIONS FOR SPIRULINA AND CHLORELLA

Date & Journal: Front Nutr . 2022 Mar 7.

Abstract

Nutritional clinical trials have reported algae such as spirulina and chlorella to have the capability to improve cardiovascular risk factors, anemia, immune function, and arterial stiffness. With positive results being reported in clinical trials, researchers are investigating the potential for algae as an ergogenic aid for athletes. Initial studies found spirulina and chlorella supplementation to increase peak oxygen uptake and time to exhaustion, with the mechanistic focus on the antioxidant capabilities of both algae. However, a number of oxidative stress biomarkers reported in these studies are now considered to lack robustness and have consequently provided equivocal results. Considering the nutrient complexity and density of these commonly found edible algae, there is a need for research to widen the scope of investigation. Most recently algae supplementation has demonstrated ergogenic potential during submaximal and repeated sprint cycling, yet a confirmed primary mechanism behind these improvements is still unclear. In this paper we discuss current algae supplementation studies and purported effects on performance, critically examine the antioxidant and ergogenic differing perspectives, and outline future directions.

Gurney T, Spendiff O. Algae Supplementation for Exercise Performance: Current Perspectives and Future Directions for Spirulina and Chlorella. Front Nutr. 2022 Mar 7;9:865741. doi: 10.3389/fnut.2022.865741. PMID: 35321288; PMCID: PMC8937016.

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MACA COULD IMPROVE ENDURANCE CAPACITY POSSIBLY BY INCREASING MITOCHONDRIAL BIOGENESIS PATHWAYS AND ANTIOXIDANT RESPONSE IN EXERCISED RATS

Date & Journal: J Food Biochem . 2022 Mar 29

Abstract

The objective of this study was to shed light on the effect of a novel (Lepidium peruvianum) Maca blend on anti-fatigue capacities in exercised rats. Twenty-eight male albino rats were allocated into four groups (n = 7) at random: (i) Control (vehicle), (ii) Maca: (40 mg/kg/BW), (iii) WL-FST: weight-loaded forced swimming test group, and (iv) WL-FST + Maca group.) Maca supplementation increased swimming time to exhaustion ($p < .01$), while decreasing serum lactate and liver glycogen concentrations. Maca addition resulted in lower levels of serum, liver, and muscle MDA ($p < .05$). Muscle GPx activity increased in both Maca groups ($p < .001$). Moreover, NF-κB levels were less in the WL-FST + Maca compared to the WL-FST group ($p < .001$). Nrf1, Nrf2, PGC-1a, SIRT1, and TFAM levels were augmented in the WL-FST + Maca compared to the WL-FST ($p < .05$). Consequently, our Maca blend increased endurance capacity and prevented exercise-induced oxidative stress and lactic acid buildup.

PRACTICAL APPLICATIONS: Maca (the brassica species Lepidium peruvianum) has been consumed in Peru for centuries to enhance mood, libido, and energy. Although the positive effects of this plant on energy metabolism are accredited, the underlying molecular mechanisms of these effects have not been sufficiently elucidated. The current study's findings suggest that this innovative, exclusive maca powder blend can boost endurance while preventing oxidative stress and lactic acid buildup during acute exercise. The mechanism of this efficacy is thought to be caused by maca's regulatory properties on energy metabolism signaling receptors and strong antioxidant scavenging effects on the free radicals that are produced by prolonged exhaustive exercise periods.

Orhan C, Gencoglu H, Tuzcu M, Sahin N, Ojalvo SP, Sylla S, Komorowski JR, Sahin K. Maca could improve endurance capacity possibly by increasing mitochondrial biogenesis pathways and antioxidant response in exercised rats. J Food Biochem. 2022 Mar 29:e1415

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MATCHA TEA POWDER'S ANTIDEPRESSANT-LIKE EFFECT THROUGH THE ACTIVATION OF THE DOPAMINERGIC SYSTEM IN MICE IS DEPENDENT ON SOCIAL ISOLATION STRESS

Date & Journal: Nutrients. 2023 Jan 22

Abstract

Matcha tea powder is believed to have various physiological benefits; however, its detailed mechanism of action has been poorly understood. Here, we investigated whether the mental state of mice, due to social isolation stress, affects the antidepressant-like effect of Matcha tea powder by using the tail suspension test. Oral administration of Matcha tea powder reduced the duration of immobility in the stress-susceptible C57BL/6J strain, but not in BALB/c strain. In C57BL/6J mice, SCH23390, a dopamine D1 receptor blocker, prevented Matcha tea powder from exerting its antidepressant-like effect. Matcha tea powder also increased the number of c-Fos-positive cells in the prefrontal cortex (PFC) region and the nucleus accumbens (NAc) region in C57BL/6J mice, but not in BALB/c mice. In contrast, Matcha tea powder did not change the number of c-Fos-positive cells in the ventral tegmental area (VTA) region. Notably, C57BL/6J mice with a shorter immobility time had a higher number of c-Fos-positive cells in the PFC, NAc, and VTA regions. However, no such correlation was observed in the stress-tolerant BALB/c mice. These results suggest that Matcha tea powder exerts an antidepressant-like effect through the activation of the dopaminergic system including the PFC-NAc-VTA circuit and that mental states are important factors affecting the physiological benefits of Matcha tea powder.

Kurauchi Y, Ohta Y, Matsuda K, Sanematsu W, Devkota HP, Seki T, Katsuki H. Matcha Tea Powder's Antidepressant-like Effect through the Activation of the Dopaminergic System in Mice Is Dependent on Social Isolation Stress. Nutrients. 2023 Jan 22;15(3):581.

EFFECTS OF MATCHA GREEN TEA POWDER ON COGNITIVE FUNCTIONS OF COMMUNITY-DWELLING ELDERLY INDIVIDUALS

Date & Journal: Nutrients . 2020 Nov 26.

Abstract

Matcha Green Tea Powder contains a variety of active ingredients beneficial to health, such as tea catechins, lutein and vitamin K. It is also known that these ingredients confer benefits upon cognitive functions of elderly people. Therefore, we aimed to investigate the relationship between a daily supplementation of Matcha and the change in cognitive functions of community-dwelling elderly people. A randomized, double-blind, placebo-controlled 12-week trial was performed. Sixty-one participants were recruited and randomly assigned to receive test drink containing 3g powder from fresh Matcha or placebo powder per day. Changes in cognitive function were assessed utilizing a psychometric test battery. Daily food intake was assessed by a Brief-type Self-administered Diet History Questionnaire (BDHQ). In the gender-specific analysis, a significant cognitive enhancement was observed in the Montreal Cognitive Assessment (MoCA) score in the active group of women. In dietary analysis, we found a significant inverse correlation between consumption of vitamin K in daily diet, excluding test drinks, and change in MoCA. The present study suggests that daily supplementation of Matcha Green Tea Powder has protective effects against cognitive decline in community-dwelling elderly women.

Sakurai K, Shen C, Ezaki Y, Inamura N, Fukushima Y, Masuoka N, Hisatsune T. Effects of Matcha Green Tea Powder on Cognitive Functions of Community-Dwelling Elderly Individuals. Nutrients. 2020 Nov 26;12(12):3639. doi: 10.3390/nu12123639. PMID: 33256220; P

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MATCHA GREEN TEA ALLEVIATES NON-ALCOHOLIC FATTY LIVER DISEASE IN HIGH-FAT DIET-INDUCED OBESE MICE BY REGULATING LIPID METABOLISM AND INFLAMMATORY RESPONSES

Date & Journal: Nutrients . 2021 Jun 6.

Abstract

Lately, matcha green tea has gained popularity as a beverage and food additive. It has proved to be effective in preventing obesity and related metabolic syndromes. However, the underlying mechanisms of its control effects against non-alcoholic fatty liver disease (NAFLD) are complicated and remain elusive. In the present study, we performed an in vivo experiment using male C57BL/6 mice fed with a high-fat diet and simultaneously treated with matcha for six weeks. Serum biochemical parameters, histological changes, lipid accumulation, inflammatory cytokines, and relevant indicators were examined. Dietary supplementation of matcha effectively prevented excessive accumulation of visceral and hepatic lipid, elevated blood glucose, dyslipidemia, abnormal liver function, and steatosis hepatitis. RNA sequencing analyses of differentially expressed genes in liver samples indicated that matcha treatment decreased the activity of lipid droplet-associated proteins and increased the activity of cytochrome P450 enzymes, suggesting improved metabolic capacity and liver function. The current study provided evidence for new dietary strategies based on matcha supplementation to ameliorate lipotoxicity-induced obesity and NALFD.

Zhou J, Yu Y, Ding L, Xu P, Wang Y. Matcha Green Tea Alleviates Non-Alcoholic Fatty Liver Disease in High-Fat Diet-Induced Obese Mice by Regulating Lipid Metabolism and Inflammatory Responses. Nutrients. 2021 Jun 6;13(6):1950. doi: 10.3390/nu13061950. PMI

EFFICACY OF WITHANIA SOMNIFERA (ASHWAGANDHA) SUPPLEMENTATION ON ADULT'S COGNITION AND MOOD

Date & Journal: Journal Ayurveda Integrative Medicine. 2021 Nov 25.

Abstract

The present study examined the effects of a proprietary Ashwagandha (Withania somnifera) root and leaf extract (NooGandha® Specnova LLC, USA) supplement for improving cognitive abilities, cortisol levels, and self-reported mood, stress, food cravings, and anxiety with adults who have perceived stress. Healthy adults (n = 43 women and n = 17 men; mean age = 34.41 years) who reported experiencing perceived stress were randomized to the following groups: Ashwagandha (400 mg/d), Ashwagandha (225 mg/d), and placebo for 30 days. The following outcomes were assessed at Day 0, Day 15, and Day 30: saliva cortisol levels, cognitive performance (i.e., CNS vital signs), and the self-reported measures of Trait Anxiety Inventory, Depression Anxiety Stress Scale, Perceived Stress Scale, and Food Cravings Questionnaire-15. For the self-report assessments, significant main effects for time were evidenced for anxiety, depression, perceived stress, and food cravings, p's < 0.01. The main effect for group and the interactions were non-significant. For the CNS vital signs, significant differences were observed in cognitive flexibility, visual memory, reaction time, psychomotor speed, and executive functioning, p's < 0.05, with the Ashwagandha groups often out-performing the placebo group. Both Ashwagandha groups had reductions in cortisol levels over time, with significant reductions evidenced for the Ashwagandha 225 mg/d group from Day 0 to Day 15 to Day 30. The placebo group had a non-significant increase in cortisol levels from Day 0 to Day 15-30. No adverse events were reported. In conclusion, Ashwagandha supplementation may improve the physiological, cognitive, and psychological effects of stress.

Remenapp A, Coyle K, Orange T, Lynch T, Hooper D, Hooper S, Conway K, Hausenblas HA. Efficacy of Withania somnifera supplementation on adult's cognition and mood. J Ayurveda Integr Med. 2021 Nov 25;13(2):100510. doi: 10.1016/j.jaim.2021.08.003. Epub ahead

EFFICACY OF WITHANIA SOMNIFERA (ASHWAGANDHA) SUPPLEMENTATION ON ADULT'S COGNITION AND MOOD

Date & Journal: Journal Ayurveda Integrative Medicine. 2021 Nov 25.

Abstract

The present study examined the effects of a proprietary Ashwagandha (Withania somnifera) root and leaf extract (NooGandha® Specnova LLC, USA) supplement for improving cognitive abilities, cortisol levels, and self-reported mood, stress, food cravings, and anxiety with adults who have perceived stress. Healthy adults (n = 43 women and n = 17 men; mean age = 34.41 years) who reported experiencing perceived stress were randomized to the following groups: Ashwagandha (400 mg/d), Ashwagandha (225 mg/d), and placebo for 30 days. The following outcomes were assessed at Day 0, Day 15, and Day 30: saliva cortisol levels, cognitive performance (i.e., CNS vital signs), and the self-reported measures of Trait Anxiety Inventory, Depression Anxiety Stress Scale, Perceived Stress Scale, and Food Cravings Questionnaire-15. For the self-report assessments, significant main effects for time were evidenced for anxiety, depression, perceived stress, and food cravings, p's < 0.01. The main effect for group and the interactions were non-significant. For the CNS vital signs, significant differences were observed in cognitive flexibility, visual memory, reaction time, psychomotor speed, and executive functioning, p's < 0.05, with the Ashwagandha groups often out-performing the placebo group. Both Ashwagandha groups had reductions in cortisol levels over time, with significant reductions evidenced for the Ashwagandha 225 mg/d group from Day 0 to Day 15 to Day 30. The placebo group had a non-significant increase in cortisol levels from Day 0 to Day 15-30. No adverse events were reported. In conclusion, Ashwagandha supplementation may improve the physiological, cognitive, and psychological effects of stress.

Remenapp A, Coyle K, Orange T, Lynch T, Hooper D, Hooper S, Conway K, Hausenblas HA. Efficacy of Withania somnifera supplementation on adult's cognition and mood. J Ayurveda Integr Med. 2021 Nov 25;13(2):100510. doi: 10.1016/j.jaim.2021.08.003. Epub ahead

EFFECTS OF ASHWAGANDHA (WITHANIA SOMNIFERA) ON VO 2MAX: A SYSTEMATIC REVIEW AND META-ANALYSIS

Date & Journal: Nutrients . 2020 Apr 17.

Abstract

The purpose of this study was to systematically review the scientific literature about the effects of supplementation with Ashwagandha (*Withania somnifera*) on maximum oxygen consumption (VO_{2max}), as well as to provide directions for clinical practice. A systematic search was conducted in three electronic databases following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines (PRISMA). The inclusion criteria were: (a) VO_{2max} data, with means ± standard deviation before and after the supplement intervention, (b) the study was randomized controlled trial (RCT), (c) the article was written in English. The quality of evidence was evaluated according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. A meta-analysis was performed to determine effect sizes. Five studies were selected in the systematic review (162 participants) and four were included in the meta-analysis (142 participants). Results showed a significant enhancement in VO_{2max} in healthy adults and athletes ($p = 0.04$). The mean difference was 3.00 (95% CI from 0.18 to 5.82) with high heterogeneity. In conclusion, Ashwagandha supplementation might improve the VO_{2max} in athlete and non-athlete people. However, further research is need to confirm this hypothesis since the number of studies is limited and the heterogeneity was high.

Pérez-Gómez J, Villafaina S, Adsuar JC, Merellano-Navarro E, Collado-Mateo D. Effects of Ashwagandha (Withania somnifera) on VO2max: A Systematic Review and Meta-Analysis. Nutrients. 2020 Apr 17;12(4):1119. doi: 10.3390/nu12041119. PMID: 32316411; PMCID:

NOPAL FIBER (OPUNTIA FICUS-INDICA) IMPROVES SYMPTOMS IN IRRITABLE BOWEL SYNDROME IN THE SHORT TERM: A RANDOMIZED CONTROLLED TRIAL

Date & Journal: Neurogastroenterol Motil . 2021 Feb.

Abstract

Background: Clinical guidelines provide limited and conflicting recommendations regarding dietary fiber supplementation in irritable bowel syndrome (IBS). Nopal (Opuntia ficus-indica) is a cactus plant fiber containing both insoluble and soluble fibers that may have therapeutic potential in IBS. Our aim was to evaluate the dose-response effect of extracted nopal fiber powder on symptoms in IBS.

Methods: We performed a 4-arm, double-blind, parallel, randomized controlled trial in 60 patients fulfilling Rome IV criteria for IBS. Patients were randomized and blindly allocated to receive either nopal fiber (10, 20, or 30 g/day) or placebo (30 g/day dextrose) for one week and to keep their usual diet. Symptom severity (Global Symptom Question, IBS-SSS, Gastrointestinal Symptom Rating Scale), stool frequency and consistency (Bristol Stool Form Scale), breath hydrogen response, and stool short-chain fatty acids (SCFA) were measured at baseline and follow-up.

Conclusions and inferences: Nopal fiber supplementation at doses of 20 and 30 g/day was associated with short-term improvement in IBS symptoms, warranting a fully powered clinical trial of longer duration with symptomatic, physiological, and microbiological endpoints.

Remes-Troche JM, Taboada-Liceaga H, Gill S, Amieva-Balmori M, Rossi M, Hernández-Ramírez G, García-Mazcorro JF, Whelan K. Nopal fiber (Opuntia ficus-indica) improves symptoms in irritable bowel syndrome in the short term: a randomized controlled trial. Ne

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EFFECT OF FENUGREEK SUPPLEMENTATION ON BLOOD LIPIDS AND BODY WEIGHT: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Date & Journal: J Ethnopharmacol . 2020 May 10

Abstract:

Ethnopharmacological relevance: Fenugreek is a traditional herbal medicine that has been used for centuries to treat hyperglycemia, muscle spasms, gastritis, constipation, edema, and other metabolic disorders. Recently, lipid-lowering effects of fenugreek have been identified.

Aim of the study: The aim of this systematic review and meta-analysis was to determine and clarify the impact of fenugreek supplementation on anthropometric indices and serum lipid levels.

Conclusion: Fenugreek supplementation improved lipid parameters in adults. However, to confirm these results, more studies, particularly among hyperlipidemic patients, are needed.

Askarpour M, Alami F, Campbell MS, Venkatakrishnan K, Hadi A, Ghaedi E. Effect of fenugreek supplementation on blood lipids and body weight: A systematic review and meta-analysis of randomized controlled trials. J Ethnopharmacol. 2020 May 10;253:112538. doi: 10.1016/j.jep.2019.112538. Epub 2020 Feb 20. PMID: 32087319.

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A RANDOMIZED CLINICAL TRIAL OF THE EFFECTS OF LEAFY GREEN VEGETABLES AND INORGANIC NITRATE ON BLOOD PRESSURE

Date & Journal: Am J Clin Nutr . 2020 Apr.

Background: A diet rich in fruits and vegetables is associated with lowering of blood pressure (BP), but the nutrient(s) responsible for these effects remain unclear. Research suggests that inorganic nitrate present in leafy green vegetables is converted into NO in vivo to improve cardiovascular function.

Conclusions: A 5-wk dietary supplementation with leafy green vegetables or pills containing the same amount of inorganic nitrate does not decrease ambulatory SBP in subjects with elevated BP. This trial was registered at clinicaltrials.gov as NCT02916615.

Sundqvist ML, Larsen FJ, Carlström M, et al. A randomized clinical trial of the effects of leafy green vegetables and inorganic nitrate on blood pressure. Am J Clin Nutr. 2020;111(4):749-756. doi:10.1093/ajcn/nqaa024

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TARGETING THE GUT MICROBIOTA BY DIETARY NUTRIENTS: A NEW AVENUE FOR HUMAN HEALTH

Date & Journal: Crit Rev Food Sci Nutr . 2019.

Abstract:

The gut microbiota is a complex ecosystem consisted of trillions of microbes that have co-evolved with their host for hundreds of millions of years. During the last decade, a growing body of knowledge has suggested that there is a compelling set of connections among diet, gut microbiota and human health. Various physiological functions of the host, ranging from metabolic and immune regulation to nerve and endocrine development, are possibly mediated by the structural components of microbial cell or the products of microbial metabolism, which are greatly influenced by dietary macronutrients and micronutrients. Thus, governing the production and activity of these microbial-associated small molecules and metabolites through dietary intervention may provide promising strategies for the improvement of human health and disease. In this review article, we first provide an overview of current findings about the intimate interrelationships between diet and gut microbiota. We also introduce the physiological effects of some microbial-associated small molecules and metabolites on the host as well as the detailed signaling mechanisms.

Li D, Wang P, Wang P, Hu X, Chen F. Targeting the gut microbiota by dietary nutrients: A new avenue for human health. Crit Rev Food Sci Nutr. 2019;59(2):181-195. doi:10.1080/10408398.2017.1363708

IMPACT OF A PROBIOTIC PRODUCT ON BOWEL HABITS AND MICROBIAL PROFILE IN PARTICIPANTS WITH FUNCTIONAL CONSTIPATION: A RANDOMIZED CONTROLLED TRIAL

Date & Journal: Journal of Digestive Disorders. 2019 September 20.

Abstract

Objective: To investigate the clinical efficacy of a multi-strain probiotic product on bowel habits and microbial profile in participants with functional constipation.

Conclusions: No significant differences were observed in symptomology, with both groups showing a more than 20% improvement. However, the probiotic helped modulate bowel function earlier than the placebo, with a corresponding shift to a more fibrolytic microbiota.

Martoni CJ, Evans M, Chow CT, Chan LS, Leyer G. Impact of a probiotic product on bowel habits and microbial profile in participants with functional constipation: A randomized controlled trial. J Dig Dis. 2019;20(9):435-446. doi:10.1111/1751-2980.12797

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THE CHEMICAL COMPOSITION AND NUTRITIONAL VALUE OF CHIA SEEDS-CURRENT STATE OF KNOWLEDGE

Date & Journal: Nutrients . 2019 May 31

Abstract

Chia (Salvia hispanica) is an annual herbaceous plant, the seeds of which were consumed already thousands of years ago. Current research results indicate a high nutritive value for chia seeds and confirm their extensive health-promoting properties. Research indicates that components of chia seeds are ascribed a beneficial effect on the improvement of the blood lipid profile, through their hypotensive, hypoglycaemic, antimicrobial and immunostimulatory effects. This article provides a review of the most important information concerning the potential application of chia seeds in food production. The chemical composition of chia seeds is presented and the effect of their consumption on human health is discussed. Technological properties of chia seeds are shown and current legal regulations concerning their potential use in the food industry are presented.

Kulczyński B, Kobus-Cisowska J, Taczanowski M, Kmiecik D, Gramza-Michałowska A. The Chemical Composition and Nutritional Value of Chia Seeds-Current State of Knowledge. Nutrients. 2019;11(6):1242. Published 2019 May 31. doi:10.3390/nu11061242

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FLAXSEED BIOACTIVE COMPOUNDS AND COLORECTAL CANCER PREVENTION

Date & Journal: Curr Oncol Rep . 2018 Jun 5.

Abstract

Purpose of review: Flaxseed and its bioactive components have been associated with a decreased risk of colorectal cancer incidence and progression. This review aims to summarize recent research regarding the role of flaxseed and each of its major dietary bioactive components in reducing colorectal cancer.

Recent findings: In both human and animal model experiments, flaxseed consumption had beneficial effects on colon physiology associated with reduction in colorectal cancer risk or occurrence. Considered separately, each of flaxseed's major bioactive components, including fiber, alpha-linolenic acid, lignans, and other phytochemicals, is also associated with decreased risk of colonic neoplasms and regulation of cell growth through several potential mechanisms. Collectively, experimental data suggests that consumption of flaxseed and/or its bioactive components may reduce colorectal cancer risk by a variety of mechanisms. Future studies should focus on the mechanisms by which whole flaxseed can prevent colorectal cancer.

DeLuca JAA, Garcia-Villatoro EL, Allred CD. Flaxseed Bioactive Compounds and Colorectal Cancer Prevention. Curr Oncol Rep. 2018;20(8):59. Published 2018 Jun 5. doi:10.1007/s11912-018-0704-z

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Servings per container: 30
Serving Size: 4 capsules

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Organic Wheat Grass, Organic Barley Grass, Organic Oat Grass, Organic Spinach, Organic Alfalfa, Organic Spirulina, Organic Chlorella, Organic Nopal, Organic Maca, Organic Rose Hips, Organic Chia, Organic Fenugreek, Organic Gota Kola, Organic Hemp, Organic Mesquite Powder, Organic Sacha Inchi Seed Powder, Organic Flax Seed Powder, Organic Kale, Organic Green Tea (Matcha), Organic Eleuthero Root, Organic Reishi, Organic Holy Basil, Organic Ashwaganda, Organic Astragulus, Organic Licorice, Organic Ginger, Organic Kelp, Organic Orange Peel, Organic Dulse, Organic Beet Root, Organic Lemon Peel, Organic Dandelion Root.

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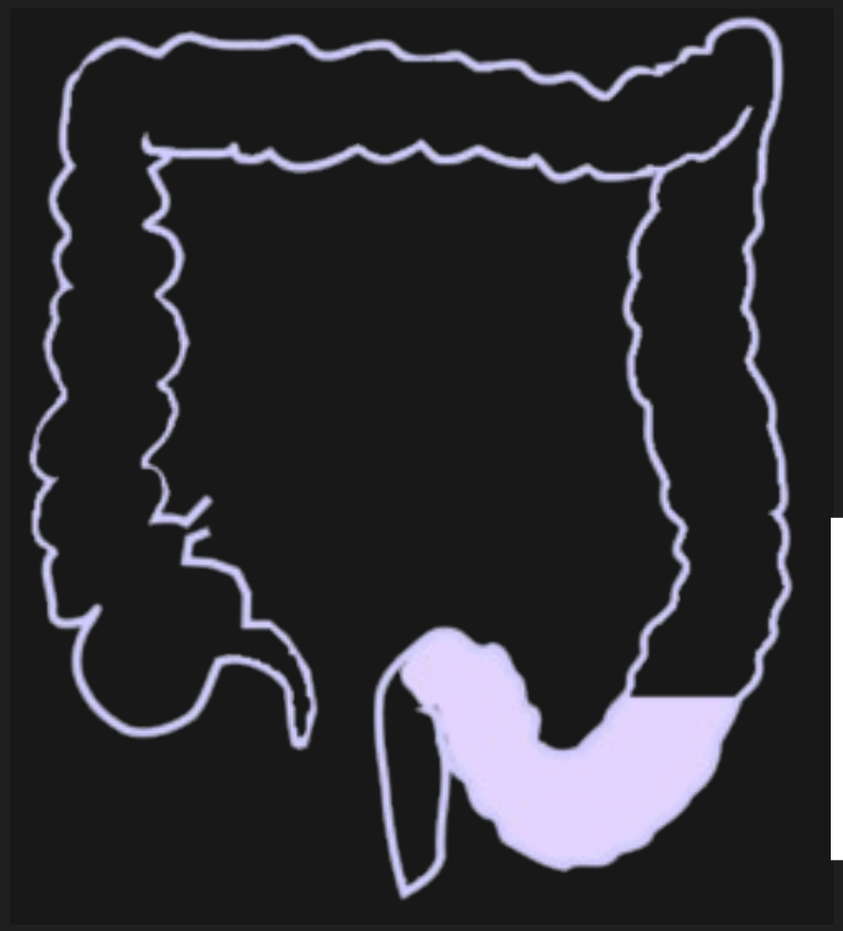
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COLON HEALTH

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COLON CLEANSING:
WHY THE NEED?

- ***We kill our friendly bacteria from an acidic diet.***

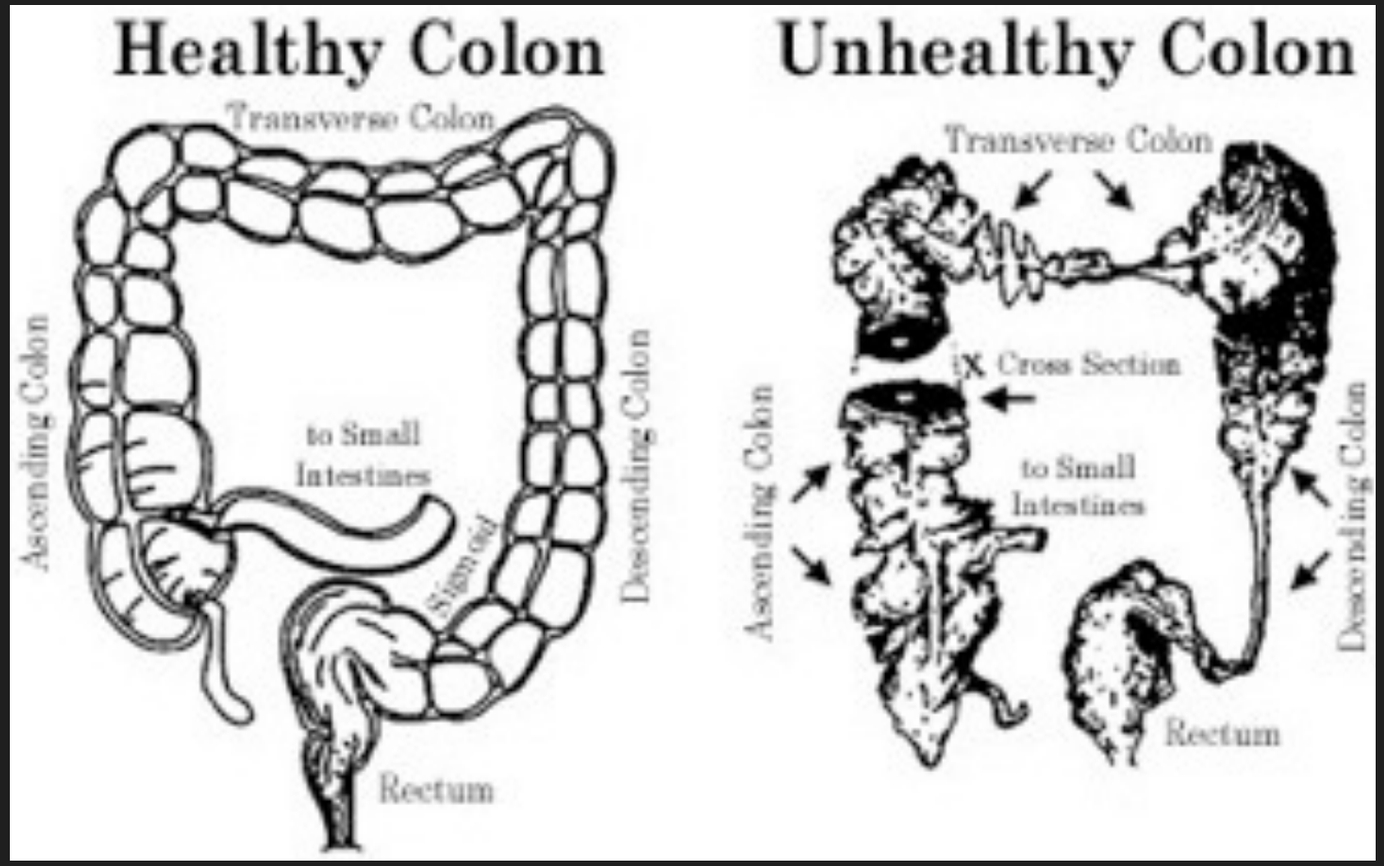
- ***Acidification of the body decreases enzyme production.***

- ***Mucoid plaque from rotting food in the intestinal lining halts peristalsis.***

TRANSIT TIME = 3 MEALS ONLY

- Transit time: We're only supposed to store three meals before a meal comes out (Jensen), but most Americans store nine, twelve, or even more.

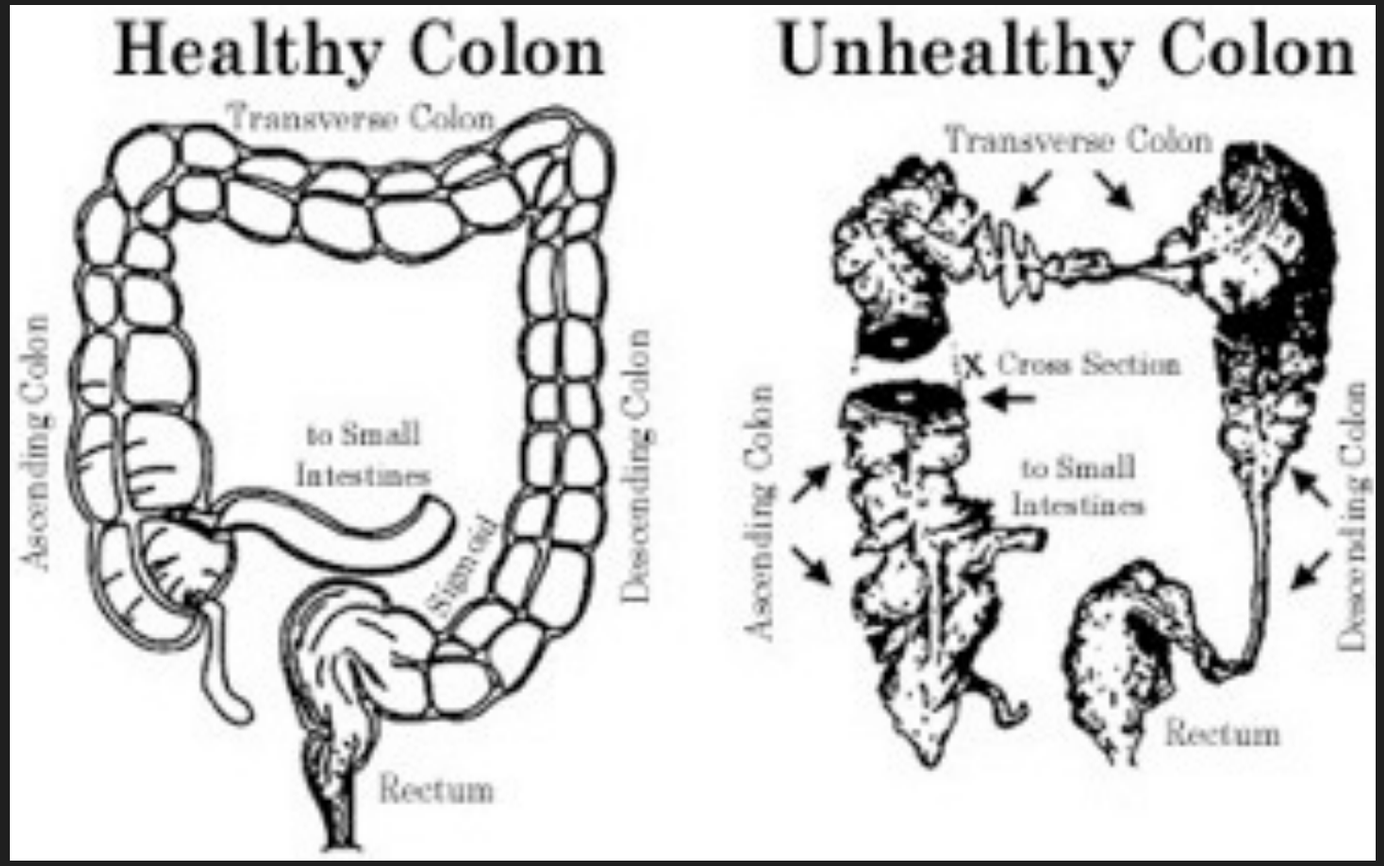
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COLON CLEANSING PROTOCOL IN CHILDREN: RESEARCH CONDITIONS VS. CLINICAL PRACTICE

Date & Journal: Endosc Int. Open. March 29, 2018

BACKGROUND & STUDY: Colon preparation rates are the limiting factor for a successful diagnostic colonoscopy in children. Different colon cleansing protocols have been published for use in children. Unfortunately, the applicability of those published research protocols has not been formally evaluated in routine clinical practice. We investigated the success rate of our previously published colon cleansing protocol as utilized in our clinical practice.

CONCLUSION: We recommend testing each new protocol under the routine conditions of clinical practice to confirm its applicability for general practitioners.

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THE COLON REVISITED OR THE KEY TO WELLNESS, HEALTH AND DISEASE!

Date & Journal: Med Hypotheses. 2017 Oct.

Abstract:

The hypothesis being advanced in this paper is that there is a new medical paradigm emerging from the biomedical research carried out in this century, mainly due to the explosion of the so called "omics" and associated techniques. The main idea is that there is a common pathway from wellbeing and health to chronic **disease** ("chronopathy") and even to death, which comprises following steps: 1) unhealthy diet, sedentary life style, permanent exposition to xenobiotics & all kinds of noxious stimuli; 2) intestinal dysbiosis;3) alteration of the intestinal mucus layer (especially the **colon**); 4) disruption of the endothelial tight junctions;5) metabolic endotoxemia+bacterial translocation; 6) inflammation; 7) exacerbation of the enteric nervous system (ENS) & consequent maladaptation/malfunctioning of the **colon**; 8) epigenetic manifestations; 9) "chronopathy" and premature death. In order to maintain a good health or to improve or even reverse chronic diseases in a person, the main outcome to look for is a homeostatic balance of the intestinal microbiota (eubiosis), most of which is located in the **colon**.

… Bacteria do not rely on other living beings for their existence, while the latter depend completely on the former. Humans are no exemption, and new evidence emerges each day about the pivotal role of intestinal microbiota in human health, **disease** and, in general, in its wellbeing. The following facts about intestinal microbiota are nowadays generally accepted: there are about 10 times more bacteria in the gut than human cells in every human being; the microbioma is about 100150 times bigger that the human genome, and there is a clear link between intestinal microbiota and many of the most common chronic diseases, from obesity and diabetes to depression and Parkinson **disease** and different kinds of cancer.

The main implication of this theory is that … we ought to be more conscious of our intestinal microbiota, take care of it and monitor it permanently. Thus, as part of our good life habits (healthy eating, physical exercise), we should probably undergo periodic seasons of fasting and **colon** cleansing, as it was common in older times.

Gonzalez-Correa CA, Mulett-Vásquez E, Miranda DA, Gonzalez-Correa CH, Gómez-Buitrago PA. The colon revisited or the key to wellness, health and disease. Med Hypotheses. 2017 Oct;108:133-143. doi: 10.1016/j.mehy.2017.07.032. Epub 2017 Jul 29. PMID: 29055387.e

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Diverticulitis: An Update From the Age Old Paradigm

Curr Probl Surg . 2020 Oct

Abstract: For a disease process that affects so many, we continue to struggle to define optimal care for patients with diverticular disease. Part of this stems from the fact that diverticular disease requires different treatment strategies across the natural history- acute, chronic and recurrent.

Diverticular disease was rarely described in the literature prior to the 1900's. In the late 1960's and early 1970's, Painter and Burkitt popularized the theory that diverticulosis is a disease of Western civilization based on the observation that diverticulosis was rare in rural Africa but common in economically developed countries. Previous surgical guidelines focused on early operative intervention to avoid potential complicated episodes of recurrent complicated diverticulitis (e.g., with free perforation) that might necessitate emergent surgery and stoma formation. More recent data has challenged prior concerns about decreasing effectiveness of medical management with repeat episodes and the notion that the natural history of diverticulitis is progressive. It has also permitted more accurate grading of the severity of disease and permitted less invasive management options to attempt conversion of urgent operations into the elective setting, or even avoid an operation altogether. The role of diet in preventing diverticular disease has long been debated. A high fiber diet appears to decrease the likelihood of symptomatic diverticulitis. The myth of avoid eating nuts, corn, popcorn, and seeds to prevent episodes of diverticulitis has been debunked with modern data. Overall, the recommendations for "diverticulitis diets" mirror those made for overall healthy lifestyle – high fiber, with a focus on whole grains, fruits and vegetables.

Diverticulosis is one of the most common incidental findings on colonoscopy and the eighth most common outpatient diagnosis in the United States. Over 50% of people over the age of 60 and over 60% of people over age 80 have colonic diverticula. Of those with diverticulosis, the lifetime risk of developing diverticulitis is estimated at 10–25%, although more recent studies estimate a 5% rate of progression to diverticulitis. Diverticulitis accounts for an estimated 371,000 emergency department visits and 200,000 inpatient admissions per year with annual cost of 2.1–2.6 billion dollars per year in the United States. The estimated total medical expenditure (inpatient and outpatient) for diverticulosis and diverticulitis in 2015 was over 5.4 billion dollars. The incidence of diverticulitis is increasing.

Continued…

Diverticulitis: An Update From the Age Old Paradigm

Curr Probl Surg . 2020 Oct

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Besides increasing age, other risk factors for diverticular disease include use of NSAIDS, aspirin, steroids, opioids, smoking and sedentary lifestyle. Diverticula most commonly occur along the mesenteric side of the antimesenteric taeniae resulting in parallel rows. These spots are thought to be relatively weak as this is the location where vasa recta penetrate the muscle to supply the mucosa. The exact mechanism that leads to diverticulitis from diverticulosis is not definitively known.

The most common presenting complaint is of left lower quadrant abdominal pain with symptoms of systemic unwellness including fever and malaise, however the presentation may vary widely. The gold standard cross-sectional imaging is multi-detector CT. It is minimally invasive and has sensitivity between 98% and specificity up to 99% for diagnosing acute diverticulitis. Uncomplicated acute diverticulitis may be safely managed as an out-patient in carefully selected patients. Hospitalization is usually necessary for patients with immunosuppression, intolerance to oral intake, signs of severe sepsis, lack of social support and increased comorbidities. The role of antibiotics has been questioned in a number of randomized controlled trials and it is likely that we will see more patients with uncomplicated disease treated with observation in the future. Acute diverticulitis can be further sub classified into complicated and uncomplicated presentations. Uncomplicated diverticulitis is characterized by inflammation limited to colonic wall and surrounding tissue. The management of uncomplicated diverticulitis is changing. Use of antibiotics has been questioned as it appears that antibiotic use can be avoided in select groups of patients. Surgical intervention appears to improve patient's quality of life. The decision to proceed with surgery is recommended in an individualized manner.

Complicated diverticulitis is defined as diverticulitis associated with localized or generalized perforation, localized or distant abscess, fistula, stricture or obstruction. Abscesses can be treated with percutaneous drainage if the abscess is large enough. The optimal long-term strategy for patients who undergo successful non-operative management of their diverticular abscess remains controversial. There are clearly patients who would do well with an elective colectomy and a subset who could avoid an operation all together however, the challenge is appropriate risk-stratification and patient selection. Management of patients with perforation depends greatly on the presence of feculent or purulent peritonitis, the extent of contamination and hemodynamic status and associated comorbidities. Fistulas and strictures are almost always treated with segmental colectomy.

Click Source to Read Article: Curr Probl Surg . 2020 Oct;57(10) :100862. doi: 10.1016/j.cpsurg.2020.100862. Epub 2020 Jul 18.

MINERALS & COLLAGEN RESEARCH



FUNCTIONS OF MINERALS

Structural: bones, teeth, ligaments

Solutes and electrolytes in the blood

Nerve transmission

Muscle action

Enzyme actions



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Structural: bones, teeth, ligaments

Solutes and electrolytes in the blood

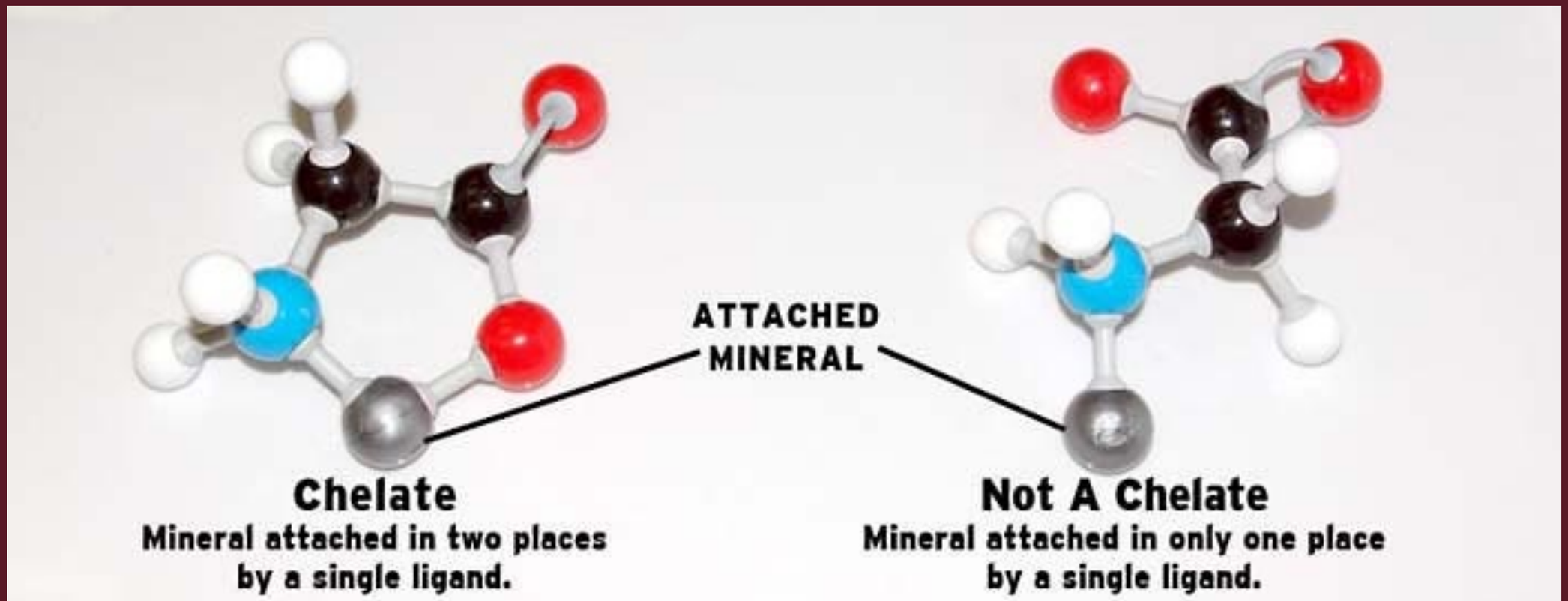
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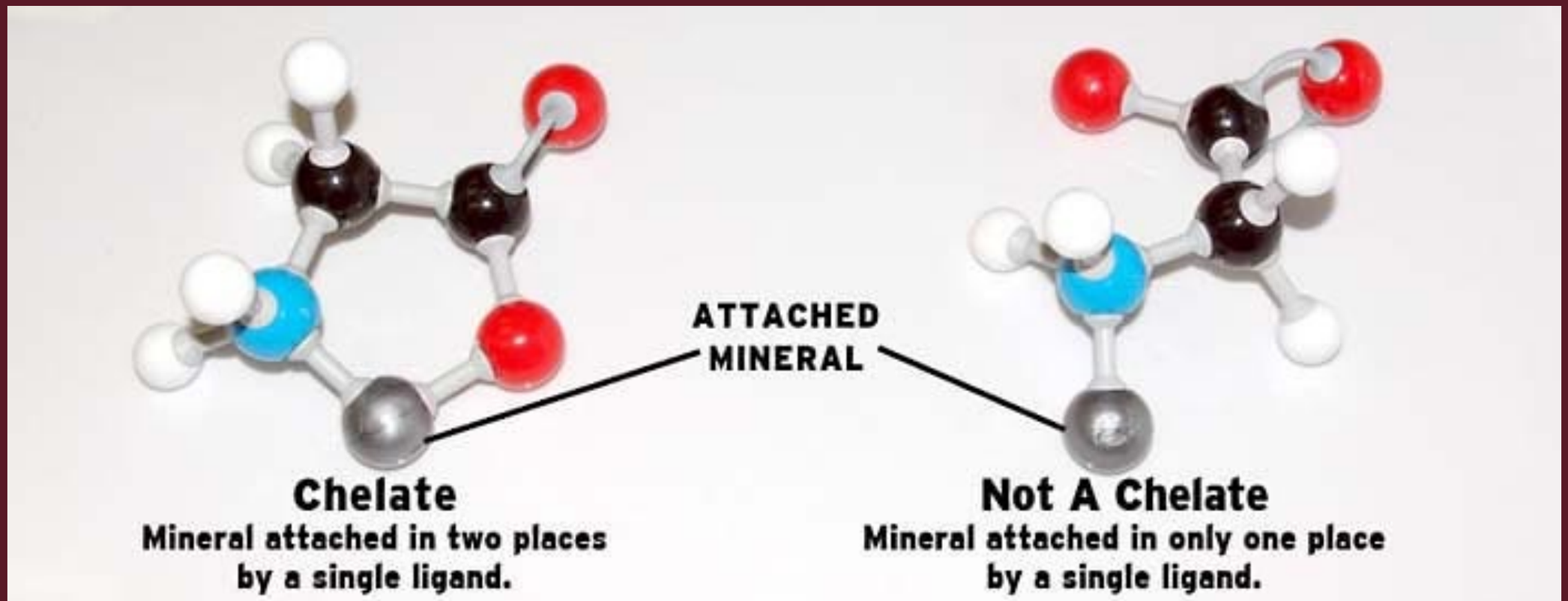


BEST TYPE OF MINERAL SUPPLEMENTS



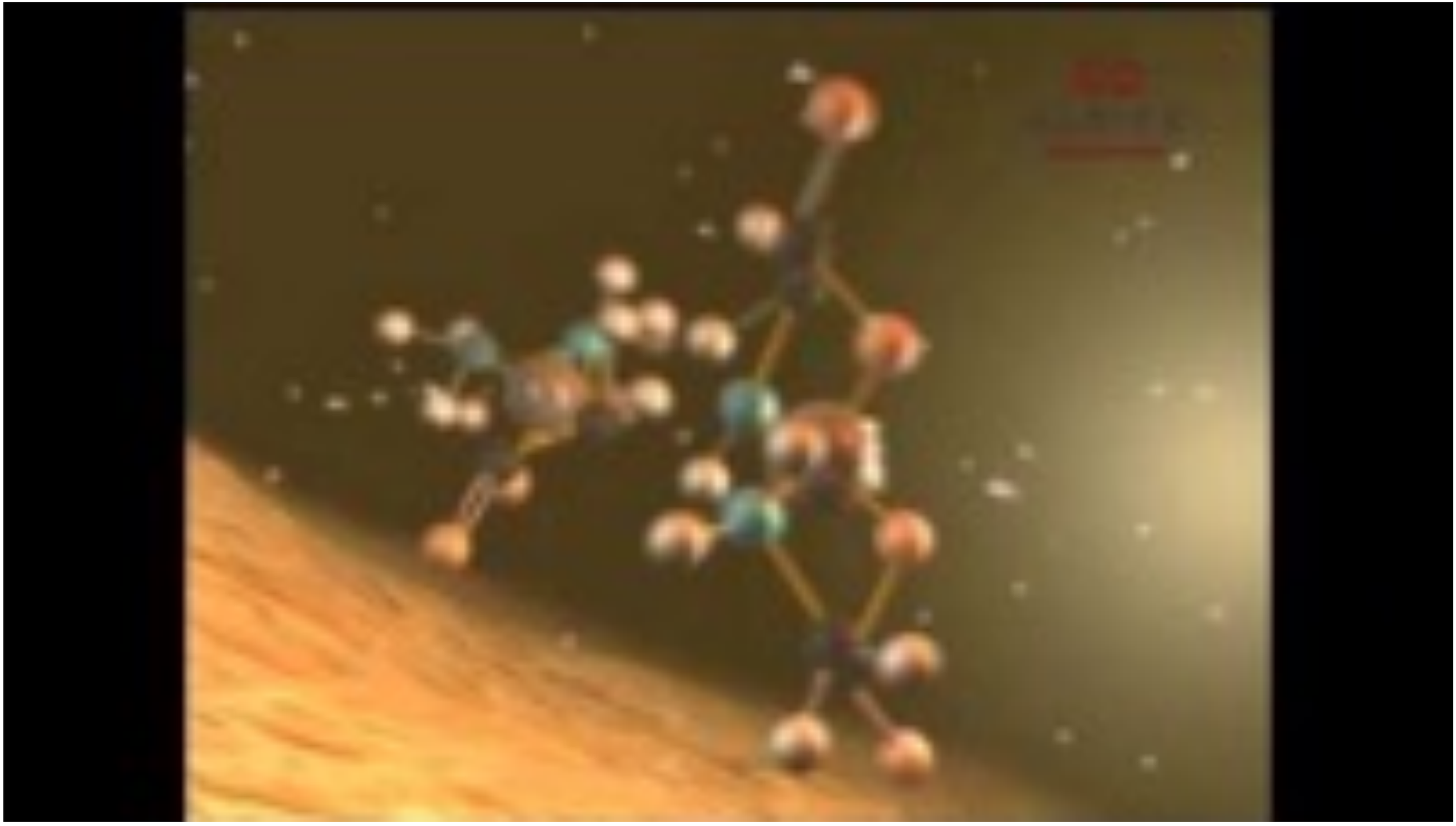
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  - Chelation can include minerals, vitamins, or enzymes. Minerals in food may be bound with organic molecules already in a chelated state.
  - Albion Labs - TRAACS – "The Real Amino Acid Chelate System"
  - Chelation Therapy = treatment for removing heavy metals from the blood. The toxic metals are bound to a therapeutic amino acid ligand called EDTA.

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ALBION AMINO ACID CHELATE ABSORPTION



A SHORT VIDEO

IMPACT OF BONE MINERAL DENSITY IN REDUCING FRACTURE RISK IN PATIENTS RECEIVING ALENDRONATE PLUS ALFACALCIDOL THERAPY

Date & Journal: J Orthop Sci . 2021 Nov.

Abstract

●**Background:** Changes in bone mineral density (BMD) are a potential surrogate marker for fracture endpoints in clinical trials. However, little is known whether the increase in BMD in response to combination treatment with alendronate plus alfacalcidol is associated with fracture risk reduction. We aimed to evaluate the impact of BMD on fracture risk in osteoporosis patients, using the data from the randomized clinical trial comparing alendronate plus alfacalcidol with alendronate alone.

●**Methods:** We selected 412 patients with two or more prevalent vertebral fractures and who had BMD measurements at baseline and after 6, 12, and/or 24 months out of 2022 patients from the database of the Japanese Osteoporosis Intervention Trial. Patients in this subset who received combination treatment with alendronate plus alfacalcidol had shown a lower risk of fracture than patients treated with alendronate alone. We used Poisson regression model analysis to calculate the proportion of treatment effect (PTE) that was attributable to BMD increases in patients receiving combination treatment.

Results: The highest PTE attributable to changes in BMD was 1.2% in patients with a BMD increase of 3% or more in the lumbar spine. For BMD measurements of the radius, the highest PTE was 2.8% with a BMD increase of 0% or more. For BMD measurements of the metacarpal bone, the highest PTE was 1.2% with a BMD increase of 3% or more. In patients with a BMD greater than or equal to 70% of the young adult mean in the lumbar spine, the PTE attributable to BMD was 0.2%. In patients with a BMD greater than or equal to 70% of the young adult mean in the radius, the PTE attributable to BMD was 0.3%.

●**Conclusions:** The additional effects of alfacalcidol in reducing fracture risk do not likely result from increased BMD; other mechanisms remain a possibility.

Itoi E, Uemura Y, Ohta H, Nakamura T, Fukunaga M, Orimo H, Shiraki M. Impact of bone mineral density in reducing fracture risk in patients receiving alendronate plus alfacalcidol therapy. J Orthop Sci. 2021 Nov;26(6):1085-1093. doi: 10.1016/j.jos.2020.10.

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SELENIUM CONCENTRATION IS ASSOCIATED WITH OCCURRENCE AND DIAGNOSIS OF THREE CARDIOVASCULAR DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Date & Journal: J Trace Elem Med Biol . 2022 Mar.

Abstract

Background: Selenium (Se) is a vital trace element playing its biological functions through selenoprotein, which has been implicated in various physiological and pathological processes. A growing number of studies indicate that low Se increases the risk of cardiovascular diseases (CVDs). This meta-analysis aimed to compare and analyze differences in Se levels between patients with heart failure (HF), myocardial infarction (MI), coronary heart disease (CHD), and healthy people. This will provide ideas with the potential to improve clinical intervention and prevention of CVDs.

Results: A total of 49 eligible studies (including 61 cohorts) were obtained. Results of the meta-analysis showed that there was a significant difference in Se levels between HF, MI, CHD patients and healthy people. Analysis of the correlation between Se level and publication year showed that SMD of Se levels in HF and controls was positively correlated with time. Se level was found to be a good diagnostic marker of MI (AUC = 0.7107, P = 0.0167, Sensitivity = 77.27 %, Specificity = 72.73 %).

Conclusions: This meta-analysis shows that Se levels in patients with HF, MI, and CHD are generally lower compared with healthy controls. However, due to the small number of included studies, further studies are needed to confirm the present results.

Yang L, Qi M, Du X, Xia Z, Fu G, Chen X, Liu Q, Sun N, Shi C, Zhang R. Selenium concentration is associated with occurrence and diagnosis of three cardiovascular diseases: A systematic review and meta-analysis. J Trace Elem Med Biol. 2022 Mar;70:126908. d

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Date & Journal: J Trace Elem Med Biol . 2022 Jan

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Background: Normal fetal growth is associated with maternal nutrition. Trace elements play important roles in fetus growth. This review aims to provide a summary of the literature evaluating the relation between selenium, zinc and copper levels during pregnancy with birth weight.

Result: Significant differences were found between pooled standardized mean differences (SMD) of umbilical cord blood copper levels in small-for-gestational age birth weight (SGA) and appropriate-for-gestational age birth weight (AGA) (SMD: 0.34 μg/L, 95 % CI: 0.13 to 0.56). There was a significant pooled correlation between umbilical cord blood selenium concentrations and birth weight (r: 0.08, 95 % CI: 0.01 to 0.16). A significant pooled correlation was found between umbilical cord blood zinc concentrations and birth weight (r: 0.09, 95 % CI: 0.04 to 0.15), with significant heterogeneity (I^2 % = 0.63). There was significant positive association between maternal blood zinc concentrations and birth weight.

Conclusion: Findings showed the association of trace elements including selenium, zinc and copper during pregnancy with birth weight. There was significant correlation between umbilical cord and maternal blood selenium and zinc levels with birth weight. The umbilical cord blood copper levels in SGA birth weight was higher than copper levels in AGA birth weight.

Atazadegan MA, Heidari-Beni M, Riahi R, Kelishadi R. Association of selenium, zinc and copper concentrations during pregnancy with birth weight: A systematic review and meta-analysis. J Trace Elem Med Biol. 2022 Jan;69:126903. doi: 10.1016/j.jtemb.2021.12

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DO MULTIVITAMIN/MINERAL DIETARY SUPPLEMENTS FOR YOUNG CHILDREN FILL CRITICAL NUTRIENT GAPS?

Date & Journal: J Acad Nutr Diet . 2022 Mar.

Abstract

- **Background:** Nearly a third of young US children take multivitamin/mineral (MVM) dietary supplements, yet it is unclear how formulations compare with requirements.

- **Objective:** Describe the number and amounts of micronutrients contained in MVMs for young children and compare suggested amounts on product labels to micronutrient requirements.

- **Results:** The 288 MVMs contained a mean of 10.1 ± 2.27 vitamins and 4.59 ± 2.27 minerals. The most common were, in rank order, vitamins C, A, D, E, B_6, B_{12}; zinc, biotin, pantothenic acid, iodine, and folic acid. For micronutrients denoted by the DGA 2015 and DGA 2020 of public health concern, 56% of the 281 products containing vitamin D, 4% of the 144 with calcium, and none of the 60 containing potassium provided at least half of the DV. The upper tolerable intake level was exceeded by 49% of 197 products with folic acid, 17% of 283 with vitamin A, and 14% of 264 with zinc. Most MVMs contained many of 16 other vitamins and minerals identified in national surveys as already abundant in children's diets.

- **Conclusions:** A reexamination of the amounts and types of micronutrients in MVMs might consider formulations that better fill critical gaps in intakes and avoid excess.

Dwyer JT, Saldanha LG, Bailen RA, Gahche JJ, Potischman N, Bailey RL, Jun S, Long Y, Connor E, Andrews KW, Pehrsson PR, Gusev PA. Do Multivitamin/Mineral Dietary Supplements for Young Children Fill Critical Nutrient Gaps? J Acad Nutr Diet. 2022 Mar;122(3)

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Date & Journal: Bone . 2022 Jan.

Abstract

- **Background:** Magnesium plays a key role in bone health and may, therefore, represent an interesting nutrient for the prevention of bone loss and osteoporosis. The aim of this systematic review and meta-analysis was to investigate the impact of magnesium intake from any source on bone mineral density (BMD), bone mineral content (BMC), bone turnover markers, and fracture risk in older adults.

- **Results:** Once 787 records were screened, six cohort studies, one case-control study and five cross-sectional studies were included. Qualitative evaluation demonstrated a positive trend between higher magnesium intake and higher hip and femoral neck BMD. Meta-analysis of four studies showed a significant positive association between magnesium intake and hip BMD (pooled beta: 0.03, 95% CI: 0.01-0.06, $p < 0.05$).

- **Conclusions:** This systematic review indicates that a higher magnesium intake may support an increase in hip and femoral neck BMD. Due to limited research no associations with BMD at other sites or fractures were found. There is a need for properly designed cohort studies to determine the association between magnesium intake and bone health in older adults. Next, large and long-term randomized controlled trials in older adults are needed to determine whether an increase in magnesium (supplementation) intake can improve bone health. The combination of several bone nutrients (calcium, vitamin D, protein, magnesium and potentially more) may be needed for the most optimal effect on bone health and to delay or prevent the development of osteoporosis.

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Servings per container: 30
Serving Size: 3 capsules

Ingredient	Amount Per Serving	% Daily Value
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Magnesium Bisglycinate Chelate TRAACS®	500mg	125%
Potassium Glycinate complex TRAACS®	300mg	6%
Calci-K® (Calcium Potassium Phosphate Citrate)TRAACS®	50mg	1%
Ferrochel® (Ferrous Bisglycinate Chelate)TRAACS®	5mg	2%
Vitamin D3 (Cholecalciferol)	400 IU	100%
Sodium (as bicarbonate)	100 mg	4%
Zinc Bisglycinate Chelate TRAACS®	15mg	136%

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Calci-K® (Calcium Potassium Phosphate Citrate)TRAACS®	50mg	1%
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WHAT IS COLLAGEN PROTEIN?

- Largest Protein in our body. 70% of our total protein.

- Collagen Protein make up heart, lungs, blood vessels, discs, muscle, bone, internal organs.

- Ptosis = loss of collagen, droopy organs and skin.

  Caused by hormonal changes, drugs, alcohol, processed foods, white sugar, hydrogenated oils, fluoridated water, dehydration, stress, and trauma.

Collagen is concentrated in the **extracellular matrix (ECM)**, a network that supports the cells of every single tissue in your body.

By dry weight, collagen makes up:



90% of the sclera (white part of your eye)



80% of tendons



70-80% of the skin



60% of cartilage



30% of bones



1–10% of muscle mass

COLLAGEN TYPES USED IN NUTRITIONAL PRODUCTS FOR PAIN MANAGEMENT & INFLAMMATION REDUCTION

SEVERAL DIFFERENT TYPES OF PROTEIN HAVE BEEN IDENTIFIED, BUT MOST OF THE COLLAGEN IN THE BODY IS TYPE I, II, OR III.

TYPE I – Most Common. In the bones, teeth, ligaments, & tendons.
Also present in skin and is responsible for the skin's elasticity & strength.
Loss of Type I Collagen results in wrinkles & aged appearance.

Source: Hides of Organic Grass Fed Cows

TYPE II – Found in the cartilage.

Source: Feet of GMO Fed Chickens or Hooves of GMO Fed Cows

TYPE III - Most prevalent in skin, blood vessels, and internal organs.

Source: Feet of Caged, GMO Fed Chickens

León-López, Arely et al. "Hydrolyzed Collagen-Sources and Applications." *Molecules (Basel, Switzerland)* vol. 24,22 4031. 7 Nov. 2019, doi:10.3390/molecules24224031

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WHY HYDROLYZED COLLAGEN TYPE I ?

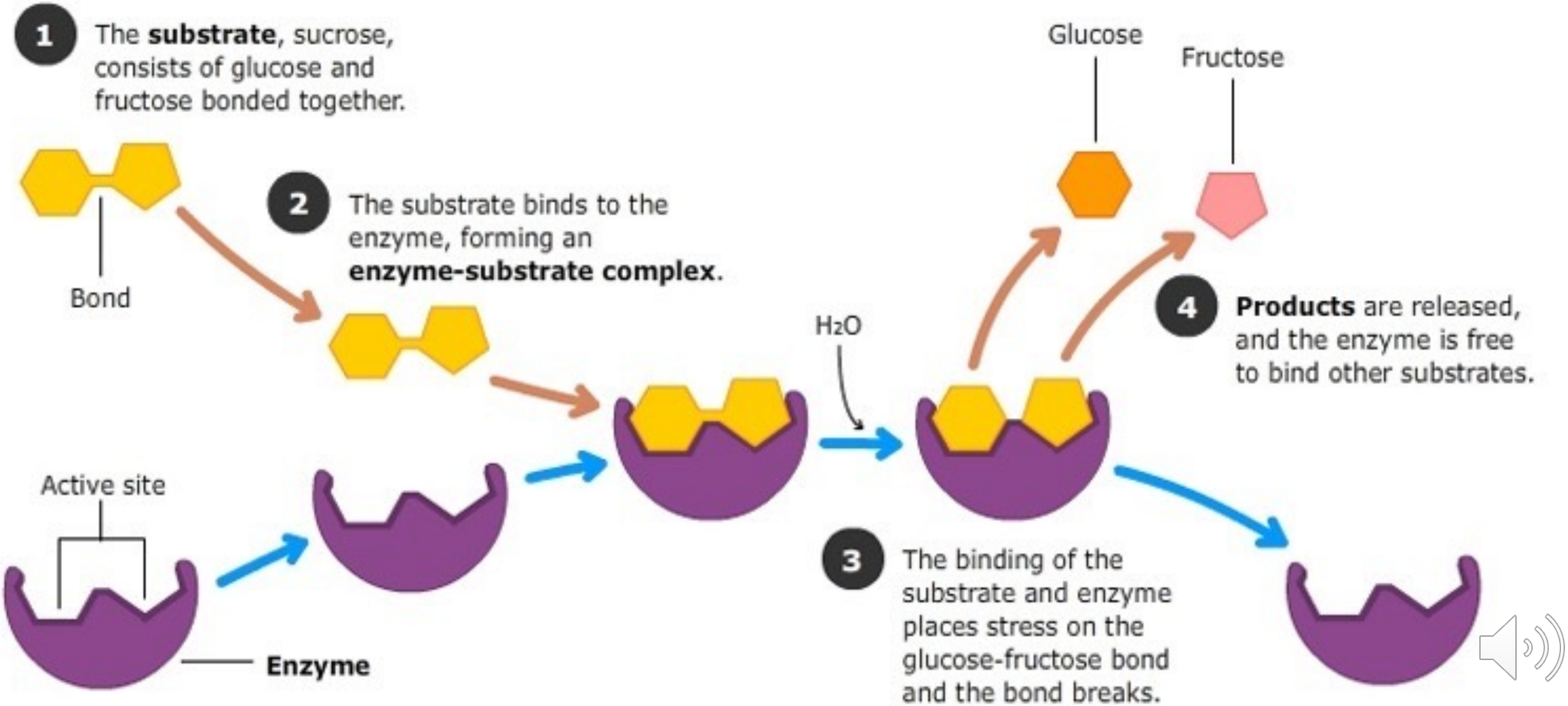
- The body can't absorb collagen in whole form.
- This protein must be broken down during the digestive process before it can be absorbed.
- To increase bioavailability, we use *Hydrolyzed* collagen
  - Collagens long amino acid chain is broken down into peptides
  - Resulting in a much easier absorption process in the GI tract.
  - Capsules are better for this digestion process than powder due to the lack of clumping.

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PROCESS OF ENZYMATIC HYDROLYSIS

Definition: Catalytic decomposition of a chemical compound by reaction with water.

In supplements it is used for the breakdown of proteins into amino acids by the addition of the enzyme protease.



HYDROLYZED COLLAGEN TYPE I

Results of Clinical Studies Suggest:

- Increase of lean muscle, muscle tone, skin tone, joint rebuilding, stronger arteries, increased energy, and organ rebuilding.

Long Term Improvements Suggest:

- Reduction in: Osteoporosis, high blood pressure, arthritis, weak bladder, obesity, chronic fatigue, and autoimmune diseases.

Nutritional option that I use in my practice for Rehabilitation of Injuries, and Muscle & Tissue Strengthening.

Scan with your smartphone!

ORGANICCS
ABSOLUTELY PURE ®

TYPE-1 COLLAGEN PROTEIN

ALL-NATURAL AID FOR STRENGTHENING HAIR, SKIN, NAILS, MUSCLES & JOINTS

180 VEGGIE CAPSULES

MADE IN USA

" A dietary supplement"



Supplement Facts

Suggested Dosage: Up to 6 capsules per day or as recommend by your healthcare provider.

Servings per container: 30
Serving Size: 6 capsules

Ingredient	Amount Per Serving	% Daily Value
Type 1 Hydrolyzed Collagen Kosher(Bovine)	3000 mg	120%
Vitamin C (Ascorbic Acid)	200 mg	333%

A proprietary blend of 320 mg of the following natural ingredients:
Glucosamine sulfate; Horsetail herb; Citrus Bioflavonoids. Made with organic ingredients when possible.

Other ingredients: Vegetable capsule.

Distributed by:
Organiccs Absolutely Pure, LLC
Laguna Hills, CA. 92653
(949) 707-5785
USP Inc. Facility Code 20181

Lot:

Exp:

Manufactured by PHS Oxnard CA

Nutritional option that I use in my practice for Rehabilitation of Injuries, and Muscle & Tissue Strengthening.

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Date & Journal: J Drugs Dermatol . 2019 Jan 1.

Abstract

The use of nutraceuticals such as collagen for skincare has been rising, but regulations are lacking on quality, absorption, and efficacy. To address this knowledge gap, clinical studies regarding the potential effects of collagen-based dietary supplements on skin are being completed. The objective of this article is to review the literature and assess available randomized-controlled trials using collagen supplementation for treatment efficacy regarding skin quality, anti-aging benefits, and potential application in medical dermatology.

Findings: Eleven studies with a total of 805 patients were included for review. Eight studies used collagen hydrolysate, 2.5g/d to 10g/d, for 8 to 24 weeks, for the treatment of pressure ulcers, xerosis, skin aging, and cellulite. Two studies used collagen tripeptide, 3g/d for 4 to 12 weeks, with notable improvement in skin elasticity and hydration. Lastly, one study using collagen dipeptide suggested anti-aging efficacy is proportionate to collagen dipeptide content.

Conclusions and Relevance: Preliminary results are promising for the short and long-term use of oral collagen supplements for wound healing and skin aging. Oral collagen supplements also increase skin elasticity, hydration, and dermal collagen density. Collagen supplementation is generally safe with no reported adverse events. Further studies are needed to elucidate medical use in skin barrier diseases such as atopic dermatitis and to determine optimal dosing regimens.

Choi FD, Sung CT, Juhasz ML, Mesinkovsk NA. Oral Collagen Supplementation: A Systematic Review of Dermatological Applications. J Drugs Dermatol. 2019 Jan 1;18(1):9-16. PMID: 30681787.

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Date & Journal: Nutr Hosp . 2015 Jul 18.

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Introduction: Hydrolysate Collagen (HC) consists of small peptides with a molecular weight lower than 5.000 Dalton units (Da), produced from gelatinization and subsequent enzymatic hydrolysis of native collagen which is found in rich collagenic animal tissues. There is much evidence about the HC ingestion positive effect over degenerative joint and bones diseases.

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Results: Up to date, there are more than 60 scientific studies (in vitro, in vivo, clinics and on bioavailability) about HC ingestion efficacy on reducing collagen damage and loss consequences as joint pain and erosion (osteoarthritis), bone density loss (osteoporosis) and skin ageing.

Conclusions: Preclinical studies show that HC stimulates collagenic tissue regeneration by increasing not only collagen synthesis but minor components (glycosaminoglycans and hyaluronic acid) synthesis as well. Clinical studies show that HC continual ingestion helps to reduce and prevent joint pain, bone density loss and skin ageing. These results as well as its high level of tolerance and safety make HC ingestion attractive for a long-term use in bone and joint degenerative diseases and in fight against skin ageing.

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Date & Journal: PLoS One . 2017 Apr 6

Osteoarthritis (OA) is a degenerative joint disease for which there are no disease modifying therapies. Thus, strategies that offer chondroprotective or regenerative capability represent a critical unmet need. Recently, oral consumption of a hydrolyzed type 1 collagen (hCol1) preparation has been reported to reduce pain in human OA and support a positive influence on chondrocyte function. To evaluate the tissue and cellular basis for these effects, we examined the impact of orally administered hCol1 in a model of posttraumatic OA (PTOA). In addition to standard chow, male C57BL/6J mice were provided a daily oral dietary supplement of hCol1 and a meniscal-ligamentous injury was induced on the right knee. At various time points post-injury, hydroxyproline (hProline) assays were performed on blood samples to confirm hCol1 delivery, and joints were harvested for tissue and molecular analyses were performed, including histomorphometry, OARSI and synovial scoring, immunohistochemistry and mRNA expression studies. Confirming ingestion of the supplements, serum hProline levels were elevated in experimental mice administered hCol1. In the hCol1 supplemented mice, chondroprotective effects were observed in injured knee joints, with dose-dependent increases in cartilage area, chondrocyte number and proteoglycan matrix at 3 and 12 weeks post-injury. Preservation of cartilage and increased chondrocyte numbers correlated with reductions in MMP13 protein levels and apoptosis, respectively. Supplemented mice also displayed reduced synovial hyperplasia that paralleled a reduction in Tnf mRNA, suggesting an anti-inflammatory effect.

Findings: These findings establish that in the context of murine knee PTOA, daily oral consumption of hCol1 is chondroprotective, anti-apoptotic in articular chondrocytes, and anti-inflammatory. While the underlying mechanism driving these effects is yet to be determined, these findings provide the first tissue and cellular level information explaining the already published evidence of symptom relief supported by hCol1 in human knee OA. These results suggest that oral consumption of hCol1 is disease modifying in the context of PTOA.

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Topical Collagen Research

HYALURONIC ACID-CROSS-LINKED FILLER STIMULATES COLLAGEN TYPE I AND ELASTIC FIBER SYNTHESIS IN SKIN THROUGH THE TGF-B/SMAD SIGNALING PATHWAY IN A NUDE MOUSE MODEL.

Publication: Journal of Plastic Reconstructive Aesthetic Surgery. 2019 Apr 11.

Compared to pure hyaluronic acid filler, cross-linked hyaluronic acid (HAc) exhibits superior biocompatibility and longevity as a dermal filler. We previously developed composite HAc-hydroxyapatite (HAp) fillers. Herein, we systematically compared the protein-level increase and gene expression between HAc-micro-HAp and HAc-nano-HAp in mice and determined the mechanisms underlying the biological responses to HAc and HAp. Five-week-old female BALB/c-nude mice were classified into five groups: normal skin, Radiesse, Restylane, HAc-nano-HAp, and HAc-micro-HAp. Fillers (200 µl) were injected to evenly fill the back of mice. Skin biopsies were performed to investigate collagen and elastic fiber synthesis after filler injections. Western blot analysis, real-time polymerase chain reaction analysis, and immunohistochemistry were performed to investigate protein and gene expression changes.

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Date & Journal: Int J Biol Macromol. 2018 Dec

Hyaluronic acid (HA) plays multifaceted roles in regulating the various biological processes such as skin repairmen, diagnosis of cancer, wound healing, tissue regeneration, anti-inflammatory, and immunomodulation. Owing to its remarkable biomedical and tissue regeneration potential, HA has been numerously employed as one of the imperative components of the cosmetic and nutricosmetic products. The present review aims to summarize and critically appraise recent developments and clinical investigations on cosmetic and nutricosmetic efficacy of HA for skin rejuvenation. A thorough analysis of the literature revealed that HA based formulations (i.e., gels, creams, intra-dermal filler injections, dermal fillers, facial fillers, autologous fat gels, lotion, serum, and implants, etc.) exhibit remarkable anti-wrinkle, anti-nasolabial fold, anti-aging, space-filling, and face rejuvenating properties. This has been achieved via soft tissue augmentation, improved skin hydration, collagen and elastin stimulation, and face volume restoration. HA, alone or in combination with lidocaine and other co-agents, showed promising efficacy in skin tightness and elasticity, face rejuvenation, improving aesthetic scores, reducing the wrinkle scars, longevity, and tear trough rejuvenation. Our critical analysis evidenced that application/administration of HA exhibits outstanding nutricosmetic efficacy and thus is warranted to be used as a prime component of cosmetic products.

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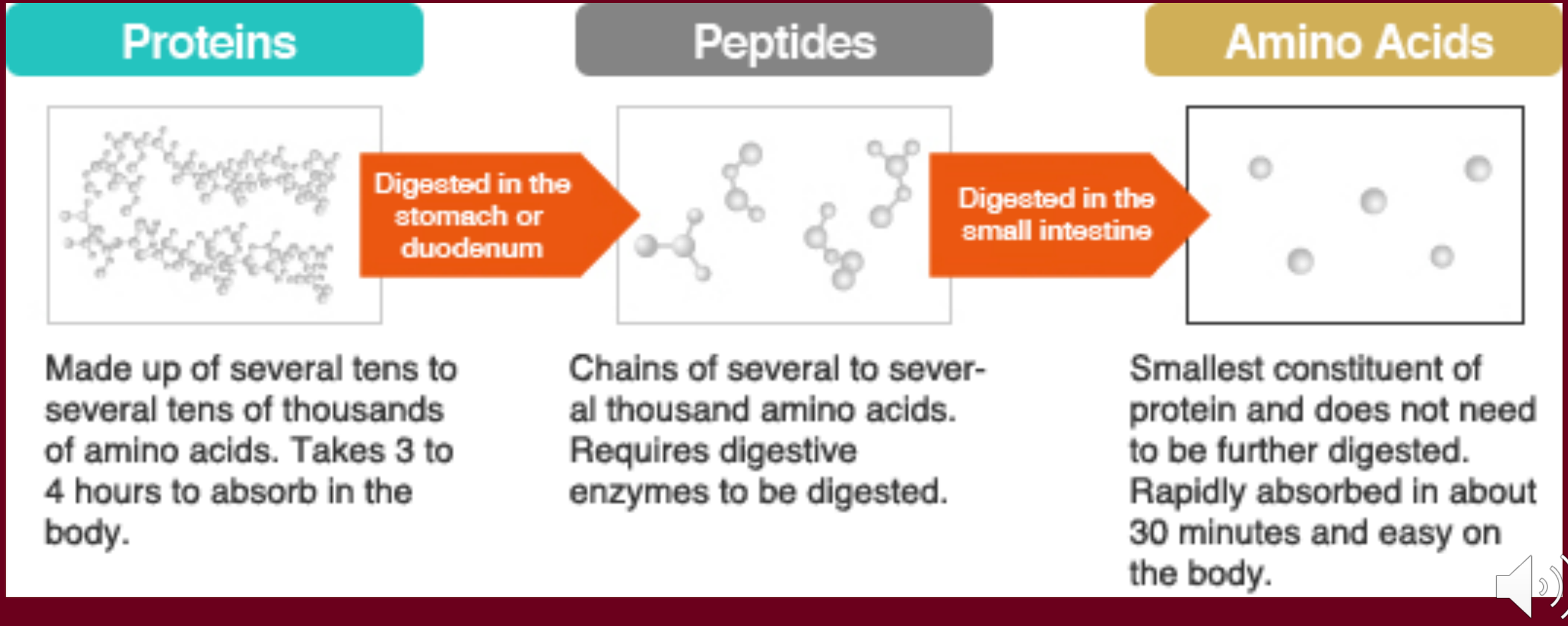
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II. BASIC SCIENCE (NUTRITION)

A. INFLAMMATION
   a) Natural inflammation reduction treatment options, including nutritional supplements and special dietary recommendations for an anti-inflammatory protocol, including legal hemp for anti-inflammatory management.
   b) Literature review
B. DIGESTION
   a) Green Alkaline foods for fiber and digestion
   b) Colon Health
   c) Minerals and Collagen Protein
C. AMINO ACIDS
   a) Definitions
   b) Amino acids for cardiovascular health
   c) Nitric oxide production

WHAT IS AN AMINO ACID?

- Building blocks of protein
- Basis of all life, essential to all metabolic processes



INTERNATIONAL REGULATIONS ON AMINO ACID USE IN FOODS AND SUPPLEMENTS AND RECOMMENDATIONS TO CONTROL THEIR SAFETY BASED ON PURITY AND QUALITY

Date & Journal: J Nutr . 2020 Oct 1

Abstract

We examined international regulatory developments related to the use of proteinogenic amino acids in human nutrition and concluded that the current risk-assessment practices tend to focus exclusively on setting maximum daily limits. In this brief review we argue that controlling the standards of purity and ingredient quality are the key safety issues that should be considered during risk assessment. Moreover, if maximum intake limits on amino acids are implemented, they should be defined using a well-established rationale for the health risks associated with high intakes. This would avoid setting limits that are so low that they render the dietary supplements ineffective and which, therefore, could mislead the consumer. We further suggest that there should be greater regional concordance in how the use of amino acids as ingredients is regulated and use the capacity of industry to oversee pre-competitive issues, such as standards of purity and scientific research on the safety of generic ingredients. Our arguments are based on clinical safety scientific research and oversights of amino acid purity standards conducted in the last decade by the not-for-profit international association, the International Council on Amino Acid Science.

Smriga M. International Regulations on Amino Acid Use in Foods and Supplements and Recommendations to Control Their Safety Based on Purity and Quality. J Nutr. 2020 Oct 1;150(Suppl 1):2602S-2605S. doi: 10.1093/jn/nxaa093. PMID: 33000158.

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THE RENAL SAFETY OF L-CARNITINE, L-ARGININE, AND GLUTAMINE IN ATHLETES AND BODYBUILDERS

Date & Journal: J Ren Nutr . 2019 May

Abstract

One of the major concerns about taking amino acid supplements is their potential adverse effects on the kidney as a major organ involved in the metabolism and excretion of exogenous substances. The aim of this study is to review available data about renal safety of the most prominent amino acid supplements including L-arginine, glutamine and also L-carnitine as well as creatine (as amino acid derivatives) in athletes and bodybuilders. The literature was searched by keywords such as "L-carnitine", "L-arginine", "glutamine", and "kidney injury" in databases such as Scopus, Medline, Embase, and ISI Web of Knowledge. Articles published from 1950 to December 2017 were included. Among 3171, 5740, and 1608 records after primary search in the relevant databases, 8, 7, and 5 studies have been finally included, respectively, for L-carnitine, L-arginine, and glutamine in this review. Arginine appears to have both beneficial and detrimental effects on kidney function. However, adverse effects are unlikely to occur with the routine doses (from 3 to >100 g/day). The risks and benefits of L-carnitine on the athletes' and bodybuilders' kidney have not been evaluated yet. However, L-carnitine up to 6000 mg/day is generally considered to be a safe supplement at least in healthy adults. Both short-term (20-30 g within a few hours) and long-term (0.1 g/kg four times daily for 2 weeks) glutamine supplementation in healthy athletes were associated with no significant adverse effects, but it can cause glomerulosclerosis and serum creatinine level elevation in the setting of diabetic nephropathy. Creatine supplementation (ranged from 5 to 30 g/day) also appears to have no detrimental effects on kidney function of individuals without underlying renal diseases. More clinical data are warranted to determine the optimal daily dose and intake duration of common supplemental amino acids associated with the lowest renal adverse effects in sportsmen and sports women.

Davani-Davari D, Karimzadeh I, Sagheb MM, Khalili H. The Renal Safety of L-Carnitine, L-Arginine, and Glutamine in Athletes and Bodybuilders. J Ren Nutr. 2019 May;29(3):221-234. doi: 10.1053/j.jrn.2018.08.014. Epub 2018 Oct 16. PMID: 30341034.

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AMINO ACIDS IN INTESTINAL PHYSIOLOGY AND HEALTH

Adv Exp Med Biol . 2020

Abstract:

Dietary protein digestion is an efficient process resulting in the absorption of amino acids by epithelial cells, mainly in the jejunum. Some amino acids are extensively metabolized in enterocytes supporting their high energy demand and/or production of bioactive metabolites such as glutathione or nitric oxide. In contrast, other amino acids are mainly used as building blocks for the intense protein synthesis associated with the rapid epithelium renewal and mucin production. Several amino acids have been shown to support the intestinal barrier function and the intestinal endocrine function. In addition, amino acids are metabolized by the gut microbiota that use them for their own protein synthesis and in catabolic pathways releasing in the intestinal lumen numerous metabolites such as ammonia, hydrogen sulfide, branched-chain amino acids, polyamines, phenolic and indolic compounds. Some of them (e.g. hydrogen sulfide) disrupts epithelial energy metabolism and may participate in mucosal inflammation when present in excess, while others (e.g. indole derivatives) prevent gut barrier dysfunction or regulate enteroendocrine functions. Lastly, some recent data suggest that dietary amino acids might regulate the composition of the gut microbiota, but the relevance for the intestinal health remains to be determined. In summary, amino acid utilization by epithelial cells or by intestinal bacteria appears to play a pivotal regulator role for intestinal homeostasis. Thus, adequate dietary supply of amino acids represents a key determinant of gut health and functions.

Beaumont M, Blachier F. Amino Acids in Intestinal Physiology and Health. Adv Exp Med Biol. 2020;1265:1-20. doi: 10.1007/978-3-030-45328-2_1. PMID: 32761567.

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BENEFICIAL PROPERTIES OF GREEN TEA CATECHINS

- Publication: International Journal of Molecular Science. 2020 Mar 4

Abstract:

Green tea (*Camellia sinesis*) is widely known for its anticancer and anti-inflammatory properties. Among the biologically active compounds contained in *Camellia sinesis*, the main antioxidant agents are catechins. Recent scientific research indicates that the number of hydroxyl groups and the presence of characteristic structural groups have a major impact on the antioxidant activity of catechins. The best source of these compounds is unfermented green tea. Depending on the type and origin of green tea leaves, their antioxidant properties may be uneven. Catechins exhibit the strong property of neutralizing reactive oxygen and nitrogen species. The group of green tea catechin derivatives includes: epicatechin, epigallocatechin, epicatechin gallate and epigallocatechin gallate. The last of these presents the most potent anti-inflammatory and anticancer potential. Notably, green tea catechins are widely described to be efficient in the prevention of lung cancer, breast cancer, esophageal cancer, stomach cancer, liver cancer and prostate cancer. The current review aims to summarize the potential anticancer effects and molecular signaling pathways of major green tea catechins. It needs to be clearly emphasized that green tea as well as green tea catechols cannot replace the standard chemotherapy. Nonetheless, their beneficial effects may support the standard anticancer approach.

Musial C, Kuban-Jankowska A, Gorska-Ponikowska M. Beneficial Properties of Green Tea Catechins. Int J Mol Sci. 2020 Mar 4;21(5):1744. doi: 10.3390/ijms21051744. PMID: 32143309; PMCID: PMC7084675.

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FUNCTIONAL NITRIC OXIDE NUTRITION TO COMBAT CARDIOVASCULAR DISEASE

- Publication: Current Atherosclerotic Report . 2018 Mar 17.

Purpose: To reveal the mechanisms of nitric oxide (NO) production in humans and how lifestyle, drug therapy, and hygienic practices can decrease NO production. Furthermore, to show how functional nitric oxide nutrition can overcome these limitations to restore endogenous NO production and combat cardiovascular disease.

Findings: Research over the past decade has revealed that inorganic nitrate and nitrite found naturally in green leafy vegetables and other vegetables such as beets can provide the human body with a source of bioactive nitric oxide. NO is one of the most important molecules produced within the cardiovascular system that maintains normal blood pressure and prevents inflammation, immune dysfunction, and oxidative stress, hallmarks of cardiovascular disease. This pathway is dependent upon the amount of inorganic nitrate and nitrite in the foods we eat, the presence of oral nitrate-reducing bacteria, and sufficient stomach acid production. The concept of food being medicine and medicine being food has lost its place in the practice and implementation of modern medicine over the past century. Certain dietary patterns and specific foods are known to confer very significant protective effects for many human diseases, including cardiovascular disease, the number one killer of men and women in the developed world. However, identification of single or multiple bioactive molecules that are responsible for these effects has escaped scientists and nutritionists for many years. This review will highlight the biochemical, physiological, and epidemiological basis for functional nitric oxide nutrition that can be safely and effectively utilized in patients.

Bryan NS. Functional Nitric Oxide Nutrition to Combat Cardiovascular Disease. Curr Atheroscler Rep. 2018;20(5):21. Published 2018 Mar 17. doi:10.1007/s11883-018-0723-0

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Supplement Facts

Suggested Dosage: Up to 4 capsules per day or as recommended by your healthcare provider.

Servings per container: 30
Serving Size: 4 capsules

Ingredients	Amount Per Serving	% Daily Value
Vitamin C (Ascorbic Acid)	100mg	167%
Vitamin B1 Thiamine	20 mg	1333%
Vitamin B2 Riboflavin	40 mg	1765%
Vitamin B3 Niacinimide	65 mg	325%
Pantothenic Acid	10 mg	100%
Vitamin B6 Pyridoxine HCl	20 mg	1000%
Folic Acid	400 mcg	100%

A proprietary blend of 2955 mg total of the following ingredients: L-Arginine; L-Taurine, L-Lysine, L-Glutamine; L-Leucine; L-Isoleucine; L-Valine; Green tea leaf extract (Camelia sinensis); Organic American Ginseng (Panax ginseng); Organic Maca Root Powder (Lipidium Meyenii); L-Phenylalanine; N-Acetyl Tyrosine; L-Phenylethylamine; Caffeine from Coffee Bean (natural source) 150mg. Made with organic ingredients when possible.
Other ingredients: Vegetable capsule.

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Other ingredients: HPMC vegetable capsule.

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   b) Nutritional options
   c) Objective nutritional questionnaire
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   a) Molecular hydrogen, constipation, ionization
   b) Filtration and nutritional benefits
   c) Water pH & safety
F. EVIDENCE BASED DIET RELATED RESEARCH
   a) Intermittent Fasting
   b) Ketogenic Diet
   c) Plant Based Nutrition

A COMPREHENSIVE REVIEW OF HERBAL SUPPLEMENTS USED FOR PERSISTENT SYMPTOMS ATTRIBUTED TO LYME DISEASE



Date & Journal: Integr Med (Encinitas). 2023 Mar

Abstract

Context: Lyme disease is the most common, tick-borne disease in the USA. While most patients successfully recover with antibiotics, some patients experience persistent symptoms for months to years. Patients who attribute chronic symptoms to Lyme disease commonly use herbal supplements. The complexity, variability in dose and formulation, and lack of data for these herbal compounds make it difficult to assess their efficacy and safety.

Objective: This review examines the evidence for the antimicrobial activity, safety, and drug-drug interactions of 18 herbal supplements that patients commonly use for treatment of persistent symptoms attributed to Lyme disease.

Results: Seven of the 18 herbs reviewed had evidence for in-vitro activity against B. burgdorferi. These compounds included: (1) cat's claw (2) cryptolepis, (3) Chinese skullcap, (4) Japanese knotweed, (5) sweet wormwood, (6) thyme, and (7) oil of oregano. With the exception of oil of oregano these compounds also have anti-inflammatory activity. In vivo data and clinical trials are lacking. Clinicians should be cautious as many of the identified compounds have drug interactions and additive effects that could lead to increased risks for bleeding, hypotension, and hypoglycemia.

Conclusions: Many of the herbs that alternative and integrative practitioners use to treat Lyme disease have anti-inflammatory effects that may contribute to patients' perceptions of symptomatic improvement. Some herbs have limited demonstrated anti-borrelial activity in vitro, but in-vivo data and clinical trial data is lacking. Further research is required to determine the efficacy, safety and appropriate use of these herbs for this patient population.



Alehagen U, Johansson P, Svensson E, Aaseth J, Alexander J. Improved cardiovascular health by supplementation with selenium and coenzyme Q10: applying structural equation modelling (SEM) to clinical outcomes and biomarkers to explore underlying mechanisms

IMPROVED CARDIOVASCULAR HEALTH BY SUPPLEMENTATION WITH SELENIUM AND COENZYME Q10: APPLYING STRUCTURAL EQUATION MODELLING (SEM) TO CLINICAL OUTCOMES AND BIOMARKERS TO EXPLORE UNDERLYING MECHANISMS IN A PROSPECTIVE RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED INTERVENTION PROJECT IN SWEDEN

Date & Journal: Eur J Nutr . 2022 Apr 6.

Abstract

Purpose: Selenium and coenzyme Q10 have synergistic antioxidant functions. In a four-year supplemental trial in elderly Swedes with a low selenium status, we found improved cardiac function, less cardiac wall tension and reduced cardiovascular mortality up to 12 years of follow-up. Here we briefly review the main results, including those from studies on biomarkers related to cardiovascular risk that were subsequently conducted. In an effort, to explain underlying mechanisms, we conducted a structured analysis of the inter-relationship between biomarkers.

Results: In addition to positive clinical effects, the intervention with selenium and coenzyme Q10 was also associated with favourable effects on biomarkers of cardiovascular risk. Using these results in the SEM model, we showed that the weights of the first-order factors inflammation and oxidative stress were high, together forming a second-order factor inflammation/oxidative stress influencing the factors, fibrosis ($\beta = 0.74$; $p < 0.001$) and myocardium ($\beta = 0.65$; $p < 0.001$). According to the model, the intervention impacted fibrosis and myocardium through these factors, resulting in improved cardiac function and reduced CV mortality.

Conclusion: Selenium reduced inflammation and oxidative stress. According to the SEM analysis, these effects reduced fibrosis and improved myocardial function pointing to the importance of supplementation in those low on selenium and coenzyme Q10.

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ZINC IN CANCER THERAPY REVISITED ★

Date & Journal: Isr Med Assoc J . 2022 Apr

Abstract

Zinc is a trace element, which is abundant in nature. It is also an essential and important micronutrient found in many foods. It has a role in multiple bodily processes including wound healing and boosting of the immune system. This review shows evidence of zinc deficiency in cancer patients of all types, a deficiency that correlates with disease severity and negatively correlates with survival rates. Lower zinc levels led to more severe and advanced disease symptoms and to lower survival rates. Zinc is a nanoparticle and acts as a photosensitizer in photodynamic therapy in various combinations with other substances. It also shows incredible cytotoxicity and tumor suppressive ability in studies conducted both in vitro and in vivo as well as in studies conducted in humans. This result is shown in all types of cancer tested. Zinc shows incredible toxicity toward cancer cells without showing any side effects toward healthy cells. It is recommended that zinc be added to cancer treatment regimens to alleviate zinc deficiency in cancer patients and perhaps to treat cancer as a whole.

Gelbard A. Zinc in Cancer Therapy Revisited. Isr Med Assoc J. 2022 Apr;24(4):258-262. PMID: 35415986.

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HOST AND VIRAL ZINC-FINGER PROTEINS IN COVID-19

Date & Journal: Int J Mol Sci . 2022 Mar 28.

Abstract

An unprecedented effort to tackle the ongoing COVID-19 pandemic has characterized the activity of the global scientific community over the last two years. Hundreds of published studies have focused on the comprehension of the immune response to the virus and on the definition of the functional role of SARS-CoV-2 proteins. Proteins containing zinc fingers, both belonging to SARS-CoV-2 or to the host, play critical roles in COVID-19 participating in antiviral defenses and regulation of viral life cycle. Differentially expressed zinc finger proteins and their distinct activities could thus be important in determining the severity of the disease and represent important targets for drug development. Therefore, we here review the mechanisms of action of host and viral zinc finger proteins in COVID-19 as a contribution to the comprehension of the disease and also highlight strategies for therapeutic developments.

Esposito S, D'Abrosca G, Antolak A, Pedone PV, Isernia C, Malgieri G. Host and Viral Zinc-Finger Proteins in COVID-19. Int J Mol Sci. 2022 Mar 28;23(7):3711. doi: 10.3390/ijms23073711. PMID: 35409070; PMCID: PMC8998646.

HOST AND VIRAL ZINC-FINGER PROTEINS IN COVID-19

Date & Journal: Int J Mol Sci . 2022 Mar 28.

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CALCIUM, MAGNESIUM, AND ZINC SUPPLEMENTATION DURING PREGNANCY: THE ADDITIVE VALUE OF MICRONUTRIENTS ON MATERNAL IMMUNE RESPONSE AFTER SARS-COV-2 INFECTION

Date & Journal: Nutrients . 2022 Mar 30.

Abstract

Magnesium may contribute to the immune response during and after SARS-CoV-2 infection by acting as a cofactor for immunoglobulin production and other processes required for T and B cell activity. Considering magnesium as a recommended dietary supplement during pregnancy and the possible role of magnesium deficiency in COVID-19 and its complications, the current study sought to determine the effect of magnesium and magnesium-containing nutritional supplements on the immune response following SARS-CoV-2 infection in pregnant women, as well as to observe differences in pregnancy outcomes based on the supplements taken during pregnancy. The study followed a cross-sectional design, where patients with a history of SARS-CoV-2 infection during their pregnancy were surveyed for their preferences in nutritional supplementation and their profile compared with existing records from the institutional database. A cohort of 448 pregnant women with COVID-19 during 22 months of the pandemic was assembled, out of which 13.6% took a magnesium-only supplement, and 16.5% supplemented their diet with a combination of calcium, magnesium, and zinc. Around 60% of patients in the no-supplementation group had the SARS-CoV-2 anti-RBD lower than 500 U/mL, compared with 50% in those who took magnesium-based supplements. A quantity of magnesium >450 mg in the taken supplements determined higher levels of antibody titers after COVID-19. Low magnesium dosage (<450 mg) was an independent risk factor for a weak immune response (OR-1.25, *p*-value = 0.003). The observed findings suggest supplementing the nutritional intake of pregnant women with magnesium-based supplements to determine higher levels of SARS-CoV-2 anti-RBD antibodies, although causality remains unclear.

Citu IM, Citu C, Margan MM, Craina M, Neamtu R, Gorun OM, Burlea B, Bratosin F, Rosca O, Grigoras ML, Motoc A, Malita D, Neagoe O, Gorun F. Calcium, Magnesium, and Zinc Supplementation during Pregnancy: The Additive Value of Micronutrients on Maternal Imm

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MULTIPLE MICRONUTRIENT SUPPLEMENTATION: AS A SUPPORTIVE THERAPY IN THE TREATMENT OF COVID-19

Date & Journal: Biomed Res Int . 2022 Mar 14

Abstract

During the infection and treatment of the SARS-CoV-2 viral infection, age and comorbidities play a major role in the successful management of COVID-19. The nutritional status changes which occur in the body vary with the age and underlying conditions and has a vital role in the functioning of the immune system and cellular membrane integrity, thus minimizing the vulnerability to the infection. Considering the data already published by eminent researchers, a few micronutrients have shown outstanding results as supportive therapies in the treatment of viral infections. Micronutrient like zinc improves the membrane barrier integrity, has anti-inflammatory activity, and is involved in antibody production. Vitamin A supports the phagocytic activity of macrophages, while vitamin C reduces the worsening of respiratory tract infections by restoring the dysfunctional epithelial barrier of the lungs. Vitamin D, vitamin E, selenium, and omega-3 fatty acid metabolites play a major role in immunomodulation and in the inhibition of proinflammatory cytokine production. Magnesium is involved in the synthesis of antibodies, while copper, vitamin B12, and folate have significant effects on immune cells. A few researchers suggest that iron supplementation has reduced the risk of acquiring respiratory tract infections in children. As the age of the patient increases, the need for micronutrients increases, thus leading to an imbalanced nutritional status which in turn increases the risk and fatality of the infections. The use of micronutrients in modulating the inflammatory, immune responses, and the epithelial barrier integrity is explored during the treatment of viral infections for faster recovery.

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HYPERTONIC SOLUTION IN SEVERE COVID-19 PATIENT: A POTENTIAL ADJUVANT THERAPY

Date & Journal: Front Med (Lausanne). 2022 Jun 21

Abstract

Coronavirus disease 2019 (COVID-19) features hyper-inflammation, cytokine storm, neutrophil function changes, and sodium chloride (NaCl) homeostasis disruption, while the treatment with NaCl hypertonic solutions (HS) controls electrolytic body homeostasis and cell functions. HS treatment is a simple, popular, economic, and feasible therapy to regulate leukocyte function with a robust anti-inflammatory effect in many inflammatory diseases. The purpose of this narrative review is to highlight the knowledge on the use of HS approaches against viral infection over the past years and to describe the mechanisms involved in the release of neutrophil extracellular traps (NETs) and production of cytokine in severe lung diseases, such as COVID-19. We reported the consequences of hyponatremia in COVID-19 patients, and the immunomodulatory effects of HS, either *in vitro* or *in vivo*. We also described the relationship between electrolyte disturbances and COVID-19 infection. Although there is still a lack of clinical trials, hypertonic NaCl solutions have marked effects on neutrophil function and NETs formation, emerging as a promising adjuvant therapy in COVID-19.

Gennari-Felipe M, Borges L, Dermargos A, Weimann E, Curi R, Pithon-Curi TC, Hatanaka E. Hypertonic Solution in Severe COVID-19 Patient: A Potential Adjuvant Therapy. Front Med (Lausanne). 2022 Jun 21;9:917008. doi: 10.3389/fmed.2022.917008. PMID: 35801207; PMCID: PMC9253300.

OLIVE LEAF EXTRACT SUPPLEMENTATION COMBINED WITH CALORIE -RESTRICTED DIET ON REDUCING BODY WEIGHT AND FAT MASS IN OBESE WOMEN: RESULT OF A RANDOMIZED CONTROL TRIAL

Date & Journal: Clin Nutr Res . 2021 Oct 31.

Abstract

The present trial aims to evaluate a supplementation of the olive leaf extract (OLE) in adjunct with a weight loss diet on anthropometric indices, glycemic indices, lipid profile, as well as the level of adipokines, and free fatty acid in obese women. We carried out an 8-week randomized, placebo-controlled, double-blind, parallel-group, clinical trial. The participants were randomly stratified according to age and they were assigned to one of the two study groups: Standard weight loss diet (estimated daily energy requirements minus 500 kcal) + OLE supplementation (n = 35) in intervention group or Standard weight loss diet (estimated daily energy requirements minus 500 kcal) + placebo (n = 35) in placebo group. The study groups were homogeneous regarding the baseline age, height, weight, body mass index (BMI), waist circumferences, married status, and physical activity levels ($p > 0.05$). The results of analysis of covariance presented significant decreases in BMI, fat mass, and body weight in the OLE group compared to those in the placebo group ($p < 0.05$). At the end of the study, the serum levels of fasting blood sugar, insulin, low-density lipoprotein cholesterol, total cholesterol, leptin, fatty free acid, and homeostasis model assessment-insulin resistance significantly decreased, and serum levels of high-density lipoprotein cholesterol and adiponectin elevated in the intervention group ($p < 0.05$). Based on results it seems that the addition of OLE to a hypocaloric diet for 8-week compared with a hypocaloric diet alone may be more effective in modifying obesity and metabolic risk factors.

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Olive leaves are rich in bioactive substances which exert anti-inflammatory, antioxidant, insulin-sensitizing and antihypertensive effects. The aim of this study was to analyze the possible beneficial effects of an olive leaf extract (OLE) rich in secoiridoids and phenolic compounds on the aging-induced metabolic and vascular alterations. Three experimental groups of rats were used: 3-month-old rats, 24-month-old rats and 24-month-old rats supplemented 21 days with OLE (100 mg/kg). Administration of OLE to aged rats decreased the weight of adrenal glands and prevented the aging-induced loss of body weight and muscle mass. In the serum, OLE reduced the circulating levels of LDL-cholesterol and IL-6 and increased the concentrations of leptin and adiponectin. In the liver OLE attenuated the decreased gene expression of SOD-1, GSR, GCK and GSK-3β and reduced the aging-induced overexpression of NOX-4, Alox-5, iNOS and TNF-α. In aorta segments, OLE prevented endothelial dysfunction and vascular insulin resistance and improved vasoconstriction in response to KCl and NA. Improvement in vascular function was associated with the attenuation of the alterations in the gene expression of COX-2, IL-6, GPx, NOX-1 and IL-10. In conclusion, OLE exerts anti-inflammatory and antioxidant effects in aged rats and attenuates the alterations in vascular function associated with aging.

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Date & Journal: Int J Mol Sci . 2020 May 14.

Abstract

Although medicinal mushroom extracts have been proposed as promising anti-cancer agents, their precise impacts on metastatic breast cancer are still to be clarified. For this purpose, the present study exploited the effect of a novel medicinal mushroom blend, namely Micotherapy U-care, in a 4T1 triple-negative mouse breast cancer model. Mice were orally administered with Micotherapy U-care, consisting of a mixture of *Agaricus blazei, Ophiocordyceps sinensis, Ganoderma lucidum, Grifola frondosa*, and *Lentinula edodes*. The syngeneic tumor-bearing mice were generated by injecting 4T1 cells in both supplemented and non-supplemented mice. After sacrifice 25 days later, specific endpoints and pathological outcomes of the murine pulmonary tissue were evaluated. (i) Histopathological and ultrastructural analysis and (ii) immunohistochemical assessment of TGF-ß1, IL-6 and NOS2, COX2, SOD1 as markers of inflammation and oxidative stress were performed. The QoL was comparatively evaluated. Micotherapy U-care supplementation, starting before 4T1 injection and lasting until the end of the experiment, dramatically reduced the pulmonary metastases density, also triggering a decrease of fibrotic response, and reducing IL-6, NOS, and COX2 expression. SOD1 and TGF-ß1 results were also discussed. These findings support the valuable potential of Micotherapy U-care as adjunct therapy in the critical management of triple-negative breast cancer.

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Date & Journal: Int J Med Mushrooms . 2020.

Abstract

Lentinus edodes (=Lentinula edodes) is a culinary-medicinal mushroom with a long tradition of use in Asia. The major active substance in L. edodes is a beta-(1-3,1-6)-glucan (lentinan). GlycaNova produces Lentinex®, which contains this beta-glucan from L. edodes mycelia, in a proprietary process that maintains the triple helix molecular structure and high molecular weights. This study was carried out to investigate the effect of Lentinex supplementation on the well-being of adults. We evaluated the effect of Lentinex in healthy adult subjects in a randomized, placebo-controlled, double-blind trial. Sixty-three subjects, randomly allocated to two groups, took orally either 1-2 mL/day Lentinex (1-2 mg beta-glucan) or placebo for four weeks. The participants completed a well-being questionnaire prior to commencing supplementation and again at the end of the in-home study. The results showed an important and statistically significant improvement in well-being over the period in the treated group compared with the placebo group. The degree of improvement in the treated group, including relative to placebo, was higher for subjects who had lower initial well-being than for subjects with higher initial well-being. In conclusion, the lower an individual's initial well-being, the more Lentinex helped.

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ANDROGRAPHOLIDE SUPPRESSES NON-SMALL-CELL LUNG CANCER PROGRESSION THROUGH INDUCTION OF AUTOPHAGY AND ANTITUMOR IMMUNE RESPONSE

Date & Journal: Pharmacol Res . 2022 Mar 31.

Abstract

Despite recent advances in diagnosis and therapeutic strategies, treatment of non-small-cell lung cancer (NSCLC) remains unsatisfactory in terms of prognosis. Andrographolide (AD), a principal active component of Andrographis paniculata (Burm.f.) Nees, exerts anti-cancer therapeutic properties. AD has been used for centuries in China for clinical treatment of viral infections. However, the pharmacological biology of AD in NSCLC remains unknown. In this study, AD regulated autophagy and PD-L1 expression in NSCLC. Molecular dynamics simulations indicated that AD bound directly to signal transducer and activator of transcription-3 (STAT3) with high affinity. Proteomics analysis indicated that AD reduced the expression of tumour PD-L1 in NSCLC by suppressing JAK2/STAT3 signalling. AD modulated the P62-dependent selective autophagic degradation of PD-L1 by inhibiting STAT3 phosphorylation. In vivo study revealed that AD suppressed tumour growth in H1975 xenograft mice and Lewis lung carcinoma cell models, and better efficacy was obtained at higher concentrations. AD prolonged the survival time of the mice and enhanced the treatment efficacy of anti-PD-1 mAb immunotherapy by stimulating $CD8^+$ T cell infiltration and function. This work elucidated the specific mechanism by which AD inhibited NSCLC. Treatment with the combination of AD and anti-PD-1 mAb immunotherapy could be a potential strategy for patients with NSCLC.

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Date & Journal: Biologia (Bratisl) . 2022 Feb 28.

Abstract

The COVID-19 infection by Novel Corona Virus (SARS-CoV-2) has become one of the largest pandemic diseases, with cumulative confirmed infections of 275,233,892 and 5,364,996 deaths to date according to World Health Organization. Due to the absence of any approved antiviral drug to treat COVID-19, its lethality is getting severe with time. The main protease of SARS-CoV-2, M^{pro} is considered one of the potential drug targets because of its role in processing proteins translated from viral RNA. In the present study, four of the plant metabolites, 14-deoxy-11,12-didehydroandrographolide, andrograpanin, quinine, cinchonine from two eminent medicinal plants *Andrographis paniculata and Cinchona officinalis*, have been evaluated against the main protease of SARS-CoV-2 through *in-silico* molecular docking and molecular dynamics simulation study. From the result interpretations, it is found that andrograpanin has strong binding affinities with the target protein in its active site with potential negative energies. Molecular Dynamic simulation and MMGBSA studies suggest that earlier reported N3 inhibitor and andrograpanin exhibit effective binding interactions involving identical amino acid residues with the same binding pockets of the main protease of SARS-CoV-2. Therefore, the theoretical experiment suggests that andrograpanin, could be considered the promising inhibitor against SARS-CoV-2 M^{pro}.

Majumdar M, Singh V, Misra TK, Roy DN. In silico studies on structural inhibition of SARS-CoV-2 main protease Mpro by major secondary metabolites of Andrographis paniculata and Cinchona officinalis. Biologia (Bratisl). 2022 Feb 28:1-17. doi: 10.1007/s1175

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Date & Journal: Biologia (Bratisl) . 2022 Feb 28.

Abstract

The COVID-19 infection by Novel Corona Virus (SARS-CoV-2) has become one of the largest pandemic diseases, with cumulative confirmed infections of 275,233,892 and 5,364,996 deaths to date according to World Health Organization. Due to the absence of any approved antiviral drug to treat COVID-19, its lethality is getting severe with time. The main protease of SARS-CoV-2, M^{pro} is considered one of the potential drug targets because of its role in processing proteins translated from viral RNA. In the present study, four of the plant metabolites, 14-deoxy-11,12-didehydroandrographolide, andrograpanin, quinine, cinchonine from two eminent medicinal plants *Andrographis paniculata and Cinchona officinalis*, have been evaluated against the main protease of SARS-CoV-2 through *in-silico* molecular docking and molecular dynamics simulation study. From the result interpretations, it is found that andrograpanin has strong binding affinities with the target protein in its active site with potential negative energies. Molecular Dynamic simulation and MMGBSA studies suggest that earlier reported N3 inhibitor and andrograpanin exhibit effective binding interactions involving identical amino acid residues with the same binding pockets of the main protease of SARS-CoV-2. Therefore, the theoretical experiment suggests that andrograpanin, could be considered the promising inhibitor against SARS-CoV-2 M^{pro}.

Majumdar M, Singh V, Misra TK, Roy DN. In silico studies on structural inhibition of SARS-CoV-2 main protease Mpro by major secondary metabolites of Andrographis paniculata and Cinchona officinalis. Biologia (Bratisl). 2022 Feb 28:1-17. doi: 10.1007/s1175

Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis

Nutrients. 2020 May 27

Abstract

The coronavirus-disease 2019 (COVID-19) was announced as a global pandemic by the World Health Organization. Challenges arise concerning how to optimally support the immune system in the general population, especially under self-confinement. An optimal immune response depends on an adequate diet and nutrition in order to keep infection at bay. For example, sufficient protein intake is crucial for optimal antibody production. Low micronutrient status, such as of vitamin A or zinc, has been associated with increased infection risk. Frequently, poor nutrient status is associated with inflammation and oxidative stress, which in turn can impact the immune system. Dietary constituents with especially high anti-inflammatory and antioxidant capacity include vitamin C, vitamin E, and phytochemicals such as carotenoids and polyphenols. Several of these can interact with transcription factors such as NF-kB and Nrf-2, related to anti-inflammatory and antioxidant effects, respectively. Vitamin D in particular may perturb viral cellular infection via interacting with cell entry receptors (angiotensin converting enzyme 2), ACE2. Dietary fiber, fermented by the gut microbiota into short-chain fatty acids, has also been shown to produce anti-inflammatory effects. In this review, we highlight the importance of an optimal status of relevant nutrients to effectively reduce inflammation and oxidative stress, thereby strengthening the immune system during the COVID-19 crisis.

Iddir M, Brito A, Dingeo G, Fernandez Del Campo SS, Samouda H, La Frano MR, Bohn T. Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis. Nutrients. 2020 May 27;12(6):1562. doi: 10.3390/nu12061562. PMID: 32471251; PMCID: PMC7352291.

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SELENIUM AND AUTOIMMUNE DISEASES: A REVIEW ARTICLE

- Curr Rheumatol Rev . 2019

Abstract

Background: Selenium is an essential trace element with fundamental effects on human biology. Trace elements deficiency is not an uncommon finding in autoimmune diseases. This deficiency may be a consequence of autoimmune diseases or may contribute to their etiology. With regard to evidence showing the association between selenium deficiency and generation of reactive oxygen species and subsequent inflammation, reviewing the role of selenium in collagen vascular diseases could help researchers to devise strategies for managing these diseases.

Objective: The present study aimed to evaluate the role of selenium and autoimmune rheumatic diseases.

Study eligibility criteria: All the studies on the use of selenium without any limitations in terms of the preparation method, administration route, or formulation process were included in the study. The exclusion criteria were: 1) Articles published in languages other than English, 2) Administration of chemical and hormonal drugs rather than selenium, 3) Investigation of the effects of selenium on the autoimmune problems in animal models, and 4) Insufficiency of the presented data or poor description of the applied methods. Furthermore, review articles, meta-analyses, expert opinions, editorial letters, case reports, consensus statements, and qualitative studies were excluded from the study.

Sahebari M, Rezaieyazdi Z, Khodashahi M. Selenium and Autoimmune Diseases: A Review Article. Curr Rheumatol Rev. 2019;15(2):123-134. doi:10.2174/1573397114666181016112342

DOES LARCH ARABINOGALACTAN ENHANCE IMMUNE FUNCTION? A REVIEW OF MECHANISTIC AND CLINICAL TRIALS

Nutr Metab (Lond). 2016 April.

Abstract

The common cold is a viral infection with important economic burdens in Western countries. The research and development of nutritional solutions to reduce the incidence and severity of colds today is a major focus of interest, and larch arabinogalactan seems to be a promising supportive agent. Arabinogalactan has been consumed by humans for thousands of years and is found in a variety of common vegetables as well as in medicinal herbs. The major commercial sources of this long, densely branched, high-molecular-weight polysaccharide are North American larch trees. The aim of this article is to review the immunomodulatory effects of larch arabinogalactan derived from Larix laricina and Larix occidentalis (North American Larix species) and more specifically its role in the resistance to common cold infections. In cell and animal models, larch arabinogalactan is capable of enhancing natural killer cells and macrophages as well as the secretion of pro-inflammatory cytokines. In humans a clinical study demonstrated that larch arabinogalactan increased the body's potential to defend against common cold infection. Larch arabinogalactan decreased the incidence of cold episodes by 23 %. Improvements of serum antigen-specific IgG and IgE response to Streptococcus pneumoniae and tetanus vaccination suggesting a B cell dependent mechanism have been reported in vaccination studies with larch arabinogalactan, while the absence of response following influenza vaccination suggests the involvement of a T cell dependent mechanism. These observations suggest a role for larch arabinogalactan in the improvement of cold infections, although the mode of action remains to be further explored.

Dion C, Chappuis E, Ripoll C. Does larch arabinogalactan enhance immune function? A review of mechanistic and clinical trials. Nutr Metab (Lond). 2016;13:28. Published 2016 Apr 12. doi:10.1186/s12986-016-0086-x

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ASTRAGALUS MEMBRANACEUS NANOPARTICLES MARKEDLY IMPROVE IMMUNE AND ANTI-OXIDATIVE RESPONSES; AND PROTECTION AGAINST AEROMONAS VERONII IN NILE TILAPIA OREOCHROMIS NILOTICUS

Fish Shellfish Immunol. 2020 Feb.

Abstract: The effects of dietary administration of Astragalus membranaceus nanoparticles (ANP) on immune and anti-oxidative responses, growth performance and disease resistance of Oreochromis niloticus were evaluated in the present study. Fish were divided into three groups and received the ANP at rates of 0 (control), 1, and 2%/kg diet for four weeks. After the four-week feeding trial, three fish from each replicate were sampled for immune and anti-oxidative responses evaluation, ten fish from each group were challenged with A. veronii, and nine fish from each group were subjected to cold and hypoxia challenges. It was obvious from the results that ANP significantly enhanced lysozyme activity and nitrous oxide (NO) activities, as well as improved superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activities. Also, aspartate aminotransferase, alanine transaminase, glucose, and cortisol measurements showed significantly lower levels in incorporated groups compared to the control. Growth performance; and amylase and lipase digestive enzymes activities also showed markedly improved results. Expression of heat shock protein 70 (HSP70) and interleukin 1, beta (IL-1β) genes were significantly upregulated throughout the entire experimental period. When challenged with A. veronii, the mortality of treated groups was significantly ($P < 0.05$) lower than the control. Current results prove that dietary ANP had a synergistic effect on immune and anti-oxidative responses, growth performance and disease resistance of Oreochromis niloticus.

Elabd H, Wang HP, Shaheen A, Matter A. Astragalus membranaceus nanoparticles markedly improve immune and anti-oxidative responses; and protection against Aeromonas veronii in Nile tilapia Oreochromis niloticus. Fish Shellfish Immunol. 2020;97:248-256. doi:10.1016/j.fsi.2019.12.025

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ASTRAGALUS POLYSACCHARIDES ENHANCE THE IMMUNE RESPONSE TO AVIAN INFECTIOUS BRONCHITIS VIRUS VACCINATION IN CHICKENS

Microb Pathog. 2017 Oct.

Abstract

Astragalus polysaccharides (APS) are biological macromolecules extracted from Astragalus species that have strong immunoregulatory properties. In this study, APS were employed as an adjuvant for an avian infectious bronchitis virus (IBV) vaccine, and its effects on the cellular immune and humoral immune responses to vaccination in chickens were investigated. One hundred and fifty chicken were randomly divided into five groups (n = 30, each group). The chickens in all groups, except for the unvaccinated control group, were vaccinated with an IBV DNA vaccine. Three of the four vaccinated groups were administered different doses of APS (APSL, 10 mg/kg; APSM, 50 mg/kg; and APSH, 100 mg/kg) after the first vaccination, and the remaining vaccinated group served as a control, without any additional treatment. At 14, 28, and 42 days after the first vaccination, serum anti-IBV antibody titers; peripheral lymphocyte proliferation; and the mRNA expression of IL-1β, IL-2, IL-8, and TNF-α in the spleen were assessed by enzyme-linked immunosorbent assay (ELISA), the cell counting kit-8 (CCK-8), and real time quantitative RT-PCR (qRT-PCR), respectively. At most time points, the titer of IBV-specific antibodies, lymphocyte proliferation, and IL-1β, IL-2, IL-8, and TNF-α mRNA expression levels were higher in three APS groups than in the vaccine control group, and these increases were dose-dependent. These data suggest that APS could be used as an adjuvant for IBV vaccination to provide better protection against IBV infection.

Zhang P, Wang J, Wang W, et al. Astragalus polysaccharides enhance the immune response to avian infectious bronchitis virus vaccination in chickens. Microb Pathog. 2017;111:81-85. doi:10.1016/j.micpath.2017.08.023

EFFECT OF MUSHROOM AGARICUS BLAZEI ON IMMUNE RESPONSE AND DEVELOPMENT OF EXPERIMENTAL CEREBRAL MALARIA

Malar J. 2015 Aug 11.

Background: Cerebral malaria (CM) is debilitating and sometimes fatal. Disease severity has been associated with poor treatment access, therapeutic complexity and drug resistance and, thus, alternative therapies are increasingly necessary. In this study, the effect of the administration of Agaricus blazei, a mushroom of Brazilian origin in a model of CM caused by Plasmodium berghei, strain ANKA, was investigated in mice.

Results: Mice treated with A. blazei aqueous extract or fraction C, that shows antioxidant activity, displayed lower parasitaemia, increased survival, reduced weight loss and protection against the development of CM. The administration of A. blazei resulted in reduced levels of TNF, IL-1β and IL-6 production when compared to untreated P. berghei-infected mice. Agaricus blazei (aqueous extract or fraction C) treated infected mice displayed reduction of brain lesions. Although chloroquine treatment reduced parasitaemia, there was increased production of proinflammatory cytokines and damage in the CNS not observed with A. blazei treatment. Moreover, the in vitro pretreatment of infected erythrocytes followed by in vivo infection resulted in lower parasitaemia, increased survival, and little evidence of clinical signs of disease.

Conclusions: This study strongly suggests that the administration of A. blazei (aqueous extract or fraction C) was effective in improving the consequences of CM in mice and may provide novel therapeutic strategies.

Val, C.H., Brant, F., Miranda, A.S. et al. Effect of mushroom Agaricus blazei on immune response and development of experimental cerebral malaria. Malar J 14, 311 (2015). https://doi.org/10.1186/s12936-015-0832-y

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ANTIGENOTOXIC AND ANTIOXIDANT POTENTIAL OF MEDICINAL MUSHROOMS (IMMUNE ASSIST) AGAINST DNA DAMAGE INDUCED BY FREE RADICALS: AN IN VITRO STUDY

Mutat Res Genet Toxicol Environ Mutagen. 2019 Sep.

Abstract

Immune Assist (IA) is produced from extract of six species of medical mushrooms: Agaricus blazei - Cordyceps sinensis - Grifola frondosa - Ganoderma lucidum - Coriolus versicolor - Lentinula edodes. The genoprotective potential of IA was evaluated for the first time. Significant antigenotoxic effects were detected in human peripheral blood cells against H2O2 induced DNA damage, in the pretreatment and in the posttreatment. The most efficient concentration of IA in pretreatment was 500 μg/mL, while in posttreatment it was the concentration of 250 μg/mL. Kinetics of attenuation of H2O2 induced DNA damage in posttreatment with the optimal concentration of IA showed significant decrease in the number of damaged cells at all time periods (15-60 min), reaching the greatest reduction after 15 and 45 min. Remarkable ·OH scavenging properties and moderate reducing power, together with the modest DPPH scavenging activity, could be responsible for the great attenuation of DNA damage after 15 min of exposure to IA, while reduction of DNA damage after 45 min could be the result in additional stimulation of the cell's repair machinery. Our results suggest that IA displayed antigenotoxic and antioxidant properties. A broader investigation of its profile in biological systems is needed.

Živković L, Bajić V, Bruić M, et al. Antigenotoxic and antioxidant potential of medicinal mushrooms (Immune Assist) against DNA damage induced by free radicals-an in vitro study. Mutat Res. 2019;845:403078. doi:10.1016/j.mrgentox.2019.06.008

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THE EFFECT OF OLIVE LEAF EXTRACT ON UPPER RESPIRATORY ILLNESS IN HIGH SCHOOL ATHLETES: A RANDOMIZED CONTROL TRIAL

Nutrients. 2019 Feb 9.

Abstract

Upper respiratory illness (URI) has a major impact on both training and competition in an athletic setting. High school athletes are a sub-category who have reported higher illness rates than professional and sub-elite high school athletes of the same sport. Olive leaf extract (OLE) is an over-the-counter supplement that contains polyphenols, notably oleuropein and hydroxytyrosol, that have antiviral, antibacterial, anti-inflammatory and antioxidant properties that may reduce URI rates. Thirty-two high school students who play sport for the elite team at their school were recruited to a randomised controlled trial and allocated to a daily placebo or OLE (extent equivalent to 20 g of olive leaf, containing 100 mg oleuropein) supplementation for nine weeks during their competitive season. Twice weekly measures of wellbeing, training load and respiratory illness (sporting upper respiratory illness (SUPPRESS) questionnaire) were recorded at trainings, meetings or games. There was no significant difference in illness incidence (odds ratio (OR): 1.02 (95% confidence interval (CI) 0.21⁻4.44)), but there was a significant 28% reduction in sick days (OR: 0.72 (95% CI 0.56⁻0.93) p-value = 0.02) when supplemented with OLE. The dietary intakes of the athletes were sub-optimal with regard to immune support. OLE supplementation over a season did not significantly reduce URI incidence, but did decrease duration in high school athletes, potentially aiding return to play.

Somerville V, Moore R, Braakhuis A. The Effect of Olive Leaf Extract on Upper Respiratory Illness in High School Athletes: A Randomised Control Trial. Nutrients. 2019;11(2):358. Published 2019 Feb 9. doi:10.3390/nu11020358

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VITAMIN C AND SARS CORONAVIRUS

- J Antimicrob Chemother. 2003 Dec.

Sir,

Recently, a new coronavirus was identified as the cause of the severe acute respiratory syndrome (SARS).1 In the absence of a specific treatment for SARS, the possibility that vitamin C may show non-specific effects on severe viral respiratory tract infections should be considered. There are numerous reports indicating that vitamin C may affect the immune system,2,3 for example the function of phagocytes, transformation of T lymphocytes and production of interferon. In particular, vitamin C increased the resistance of chick embryo tracheal organ cultures to infection caused by an avian coronavirus.4 Studies in animals found that vitamin C modifies susceptibility to various bacterial and viral infections,3 for example protecting broiler chicks against an avian coronavirus.5 Placebo-controlled trials have shown quite consistently that the duration and severity of common cold episodes are reduced in the vitamin C groups,3 indicating that viral respiratory infections in humans are affected by vitamin C levels. There is also evidence indicating that vitamin C may affect pneumonia.3 In particular, three controlled trials with human subjects reported a significantly lower incidence of pneumonia in vitamin C-supplemented groups,6 suggesting that vitamin C may affect susceptibility to lower respiratory tract infections under certain conditions. The possibility that vitamin C affects severe viral respiratory tract infections would seem to warrant further study, especially in light of the recent SARS epidemic.

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Published: Nutrients. Nov. 2017

Abstract

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

Carr AC, Maggini S. Vitamin C and Immune Function. Nutrients. 2017;9(11):1211. Published 2017 Nov 3. doi:10.3390/nu9111211

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ZINC AND IMMUNITY: AN ESSENTIAL INTERRELATION

Published: Arch Biochem Biophys . 2016 Dec.

Abstract

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Maares M, Haase H. Zinc and immunity: An essential interrelation. Arch Biochem Biophys. 2016;611:58-65. doi:10.1016/j.abb.2016.03.022

ZINC AND IMMUNITY: AN ESSENTIAL INTERRELATION

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ZINC AS A GATEKEEPER OF IMMUNE FUNCTION

Published: Nutrients . 2017 Nov 25

Abstract

After the discovery of zinc deficiency in the 1960s, it soon became clear that zinc is essential for the function of the immune system. Zinc ions are involved in regulating intracellular signaling pathways in innate and adaptive immune cells. Zinc homeostasis is largely controlled via the expression and action of zinc "importers" (ZIP 1-14), zinc "exporters" (ZnT 1-10), and zinc-binding proteins. Anti-inflammatory and anti-oxidant properties of zinc have long been documented, however, underlying mechanisms are still not entirely clear. Here, we report molecular mechanisms underlying the development of a pro-inflammatory phenotype during zinc deficiency. Furthermore, we describe links between altered zinc homeostasis and disease development. Consequently, the benefits of zinc supplementation for a malfunctioning immune system become clear. This article will focus on underlying mechanisms responsible for the regulation of cellular signaling by alterations in zinc homeostasis. Effects of fast zinc flux, intermediate "zinc waves", and late homeostatic zinc signals will be discriminated. Description of zinc homeostasis-related effects on the activation of key signaling molecules, as well as on epigenetic modifications, are included to emphasize the role of zinc as a gatekeeper of immune function.

Wessels I, Maywald M, Rink L. Zinc as a Gatekeeper of Immune Function. Nutrients. 2017;9(12):1286. Published 2017 Nov 25. doi:10.3390/nu9121286

FUTURE PERSPECTIVES IN ADDRESSING THE GLOBAL ISSUE OF VITAMIN D DEFICIENCY

Published: Proc Nutr Soc . 2020 May

Abstract

Vitamin D is a fundamentally critical nutrient that the human body requires to function properly. It plays an important role in musculoskeletal health due to its involvement in the regulation of calcium and phosphorus. Having a low level of vitamin D in the body may be detrimental for a wide range of health outcomes, including risk of osteoporotic and stress fractures, risk of CVD and some cancers, and lowering of the capability of the immune system. Vitamin D is an unusual nutrient; it is not a vitamin, in the true sense of the word but a pro-hormone. The main source of vitamin D is UV exposure, not dietary intake. Interestingly, there are two forms of vitamin D, vitamin D2 and vitamin D3, both of which are metabolised into 25-hydroxyvitamin D (25(OH)D) in the liver, the biomarker of vitamin D status. Vitamin D deficiency is a global public health problem, especially amongst older people and ethnic minority groups. The newest publication from the UK Government's Public Health England Department recommends that vitamin D intake should be 10 µg daily and this recommendation compares well (albeit lower) with other guidelines such as the Institute of Medicine recommendation of 15 µg for those aged 1-70 years and 20 µg for those 70 years or over. Few countries, however, have a specific vitamin D policy to prevent deficiency in populations. Finland leads the way, demonstrating impressive results in reducing population-level vitamin D deficiency through mandatory food fortification programmes. Collaboration between academia, government and industry, including countries from varying latitudes, is essential to identify long-term solutions to the global issue of vitamin D deficiency. This paper provides a narrative review of the evidence related to the role of vitamin D deficiency in health outcomes, outlines controversies regarding setting levels of adequacy, identifies the prevalence of vitamin D deficiency across the globe, and identifies population-level strategies adopted by countries to prevent vitamin D deficiency.

Mendes MM, Charlton K, Thakur S, Ribeiro H, Lanham-New SA. Future perspectives in addressing the global issue of vitamin D deficiency. Proc Nutr Soc. 2020;79(2):246-251. doi:10.1017/S0029665119001538

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"A dietary supplement"



Supplement Facts

Suggested Dosage: Up to 3 capsules per day or as recommended by your healthcare provider.

Servings per container: 30
Serving Size: 3 capsules

Ingredient	Amount Per Serving	% Daily Value
Vitamin B6 (as pyridoxine HCL)	50 mg	2941%
Vitamin D3 (as cholecalciferol)	5000 IU	1250%
Vitamin C (as ascorbyl palmitate)	300 mg	333%
Magnesium BisGlycinate Chelate TRAACS®	500 mg (90 mg elemental)	21%
Selenium Glycinate TRAACS®	200 mcg	1110%
Zinc Bisglycinate Chelate TRAACS®	26 mg	236%

A proprietary blend of 900 mg the following natural ingredients: Organic olive leaf powder, Organic maitake mushroom powder, Shiitake mushroom powder, Reishi mushroom powder, Agaricus blazei mushroom powder, Organic ginger root powder, Organic licorice root powder, Andrographis powder, Arabinogalactan powder, Ashwagandha powder, and Astragalus powder. Other ingredients: Silicon dioxide, Magnesium stearate, vegetable capsule. Made with organic ingredients when possible.

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RESEARCH & DEVELOPMENT

TREATMENT OF COVID-19 PATIENTS WITH QUERCETIN: A PROSPECTIVE, SINGLE CENTER, RANDOMIZED, CONTROLLED TRIAL

Date & Journal: Turk J Biol . 2021 Aug 30.

Abstract

Scientific research continues on new preventive and therapeutic strategies against severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2). So far, there is no proven curative treatment, and a valid alternative therapeutic approach needs to be developed. This study is designed to evaluate the effect of quercetin in COVID-19 treatment. This was a single-centre, prospective randomized controlled cohort study. Routine care versus QCB (quercetin, vitamin C, bromelain) supplementation was compared between 429 patients with at least one chronic disease and moderate-to-severe respiratory symptoms. Demographic features, signs, laboratory results and drug administration data of patients were recorded. The endpoint was that QCB supplementation was continued throughout the follow-up period from study baseline to discharge, intubation, or death. The most common complaints at the time of hospital admission were fatigue (62.4%), cough (61.1%), anorexia (57%), thirst (53.7%), respiratory distress (51%) and chills (48.3%). The decrease in CRP and ferritin levels was higher in the QCB group (all Ps were < 0.05). In the QCB group, the increase in platelet and lymphocyte counts was higher (all Ps were < 0.05). QCB did not reduce the risk of events during follow-up. Adjustments for statistically significant parameters, including the lung stage, use of favipiravir and presence of comorbidity did not change the results. While there was no difference between the groups in terms of event frequency, the QCB group had more advanced pulmonary findings. QCB supplement is shown to have a positive effect on laboratory recovery. While there was no difference between the groups in terms of event frequency, QCB supplement group had more advanced pulmonary findings, and QCB supplement is shown to have a positive effect on laboratory recovery/results. Therefore, we conclude that further studies involving different doses and plasma level measurements are required to reveal the dose/response relationship and bioavailability of QCB for a better understanding of the role of QCB in the treatment of SARS CoV-2.

Önal H, Arslan B, Üçüncü Ergun N, Topuz Ş, Yilmaz Semerci S, Kurnaz ME, Molu YM, Bozkurt MA, Süner N, Kocataş A. Treatment of COVID-19 patients with quercetin: a prospective, single center, randomized, controlled trial. Turk J Biol. 2021 Aug 30;45(4):518-

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DIETARY SUPPLEMENTS FOR TREATMENT OF ENDOMETRIOSIS: A REVIEW

Date & Journal: Acta Biomed. 2022 Mar 14.

Abstract

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Yalçın Bahat P, Ayhan I, Üreyen Özdemir E, İnceboz Ü, Oral E. Dietary supplements for treatment of endometriosis: A review. Acta Biomed. 2022 Mar 14;93(1):e2022159. doi: 10.23750/abm.v93i1.11237. PMID: 35315418; PMCID: PMC8972862.

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POTENTIAL OF NATURAL PRODUCTS IN THE TREATMENT OF MYOCARDIAL INFARCTION: FOCUS ON MOLECULAR MECHANISMS

Date & Journal: Crit Rev Food Sci Nutr . 2022 Jan 3.

Abstract

Although conventional drugs are widely used in the prevention and treatment of cardiovascular disease (CVD), they are being used less frequently due to concerns about possible side effects over the long term. There has been a renewed research interest in medicinal plant products, and their role in protecting the cardiovascular system and treating CVD, which are now being considered as potential alternatives to modern drugs. The most important mechanism causing damage to the myocardium after heart attack and reperfusion, is increased levels of free radicals and oxidative stress. Therefore, treatment approaches often focus on reducing free radicals or enhancing antioxidant defense mechanism. It has been previously reported that bioactive natural products can protect the heart muscle in myocardial infarction (MI). Since these compounds are readily available in fruits and vegetables, they could prevent the risk of MI if they are consumed daily. Although the benefits of a healthy diet are well known, many scientific studies have focused on whether pure natural compounds can prevent and treat MI. In this review we summarize the effects of curcumin, resveratrol, quercitin, berberine, and tanshinone on MI and CVD, and focus on their proposed molecular mechanisms of action.

Sheida A, Taghavi T, Shafabakhsh R, Ostadian A, Razaghi Bahabadi Z, Khaksary Mahabady M, Hamblin MR, Mirzaei H. Potential of natural products in the treatment of myocardial infarction: focus on molecular mechanisms. Crit Rev Food Sci Nutr. 2022 Jan 3:1-18

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Objective Nutritional / Metabolic Questionnaire

Name: _____ **Date:** _____

Do you Eat:	
Do you eat 5 or more servings of vegetables in a day?	Yes or No
Do you eat 4 or more servings of fruit in a day?	Yes or No
Do you drink more than 1 sugar sweetened beverage (sodas energy drinks, sweetened tea) in a day?	Yes or No
Do you drink more than 2 cups of coffee in a day?	Yes or No
Do you eat more than 3 servings candy, cookies, cakes, sweetened rolls in a week?	Yes or No
Do you eat bread all 7 days of the week?	Yes or No
Do you eat whole grain bread & pasta?	Yes or No
Do you eat more than 2 servings a day of packaged snack foods i.e.-potato chips, crackers, corn chips, Cheetos etc. daily?	Yes or No
Do you eat more than 2 packaged entrees and side dishes daily?	Yes or No
Do you purchase/eat regular store bought meat (not grass-fed)?	Yes or No
Do you purchase/eat farm raised fish (not wild caught)?	Yes or No
Do you eat almonds, walnuts, cashews, pistachio, macadamia, pecans more than 2 times a week?	Yes or No
Do you eat chia, flaxseed, or hempseed more than 5 times week?	Yes or No
Total Yes's :	

Cooking	
What oils do you cook with? ☐ olive oil ☐ coconut oil ☐ grass-fed butter ☐ corn oil ☐ sunflower oil ☐ vegetable oil	
Do you eat Yogurt?	Yes or No
Do you consume cheese or milk products?	Yes or No

Objective Nutritional / Metabolic Questionnaire

Name: _____ **Date:** _____

Do you Eat:	
Do you eat 5 or more servings of vegetables in a day?	Yes or No
Do you eat 4 or more servings of fruit in a day?	Yes or No
Do you drink more than 1 sugar sweetened beverage (sodas energy drinks, sweetened tea) in a day?	Yes or No
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Do you eat more than 2 packaged entrees and side dishes daily?	Yes or No
Do you purchase/eat regular store bought meat (not grass-fed)?	Yes or No
Do you purchase/eat farm raised fish (not wild caught)?	Yes or No
Do you eat almonds, walnuts, cashews, pistachio, macadamia, pecans more than 2 times a week?	Yes or No
Do you eat chia, flaxseed, or hempseed more than 5 times week?	Yes or No
Total Yes's :	

Cooking	
What oils do you cook with? ☐ olive oil ☐ coconut oil ☐ grass-fed butter ☐ corn oil ☐ sunflower oil ☐ vegetable oil	
Do you eat Yogurt?	Yes or No
Do you consume cheese or milk products?	Yes or No

Objective Nutritional / Metabolic Questionnaire

Do you cook at home more than 5 times in a week?	Yes or No
Total Yes's :	

Do you feel?	
Do you have muscle cramping?	Yes or No
Do you have restless leg syndrome?	Yes or No
Are you nervous or have anxiety?	Yes or No
Do you get headaches often?	Yes or No
Are you constipated frequently?	Yes or No
Do you suffer from osteoporosis or osteopenia?	Yes or No
Do you suffer from chronic pain?	Yes or No
Have you been diagnosed with an autoimmune disease?	Yes or No
Do you have muscle stiffness or pain?	Yes or No
Total Number of Yes':	

Exercise	
Do you exercise?	Yes or No
Do you exercise 5 days a week?	Yes or No
What types of exercises ?	
Are you more of a couch potato?	Yes or No
Do you ever get sore from exercising?	Yes or No
Total Number of Yes':	

Immune	
Do you get a cold or the flue each season?	Yes or No
Do you believe that you have a strong immune system?	Yes or No
Do you have more than 1 bowl movement in a day?	Yes or No
Do you have allergies ?	Yes or No

Objective Nutritional / Metabolic Questionnaire

Do you get a sore throat and/or stuffy/runny nose more than once a month?	Yes or No
Do you eat dairy products – ice cream?	Yes or No
Do you eat sugar foods? i.e. candy/cakes	Yes or No
Would you like to strength your immune response?	Yes or No
Total Number of Yes':	

Cardio-Metabolic Health	
Are you currently diagnosed with ?	
Cholesterol Problems?	Yes or No
High Blood Pressure	Yes or No
Diabetes ?	Yes or No
Pre-diabetes ?	Yes or No
Metabolic Syndrome?	Yes or No
Any other diagnosis please list below:	

Do you take medications for:	
Cholesterol	Yes or No
High Blood Pressure	Yes or No
Diabetes / Pre-diabetes?	Yes or No
Total Yes's :	
Please list all medications:	

Are you under the care of a physician for these conditions?
If yes, who is your physician currently managing these conditions?(Name, Address, Phone #)

Objective Nutritional / Metabolic Questionnaire

How important is it to you function at your optimum 100% health? On a scale of 1-10 (10 being ready to change today) _____

How ready are to change? On a scale of 1-10 (10 being ready to change today) _____

_____ Your Diet
_____ Supplementation
_____ Consistent Chiropractic Care
_____ Exercise

For Practitioner Use Only:

Note- Yes = 1 point No= 0 points (ex. 5 yes' = 5 points)

	Totals:	**Supplement Recommendations**
Do you eat?		> 5 **Greens- If yes is the primary answer this shows that the diet may be a very acidic diet. To counter balance the acidity, we recommend the Greens product which is an alkaline superfood which will help improve digestion, immunity, inflammation, energy, and aiding in weight loss.** **Turmeric- With the increased amount of processed foods and sugary foods the body is undergoing an overwhelming amount of inflammation which could lead to pain, chronic disease, or autoimmune disease. Turmeric helps the body fight inflammation with the curcuminoids, ginger, curcumin, bromelain, and saffron. Turmeric will also help if the patient has any current pain or chronic conditions by supporting the body with an anti- inflammatory product.**
Cooking		> 2 & corn oil & vegetable oil are chosen **With the increase in saturated fats, eating out, and the need for energy the patient is a great candidate for the Ultra Amino Energy.** **Why? This supplement is full of amino acids specifically L-arginine which is a vasodilator. This is why it is great for our cardiovascular system. It is also full of B- vitamins that will supply the patients with energy & no crash. Educate patient on cooking methods to incorporate more healthy fats. Also, great to improve brain function.**

Objective Nutritional / Metabolic Questionnaire

Do you feel		>1 **Minerals Chelated- This formula uses chelated minerals with Albion and TRACCS (The Real Amino Acid Chelate System) a highly bioavailable and absorptive form of the minerals. This supplement is formulated with ferrous gluconate (iron) to aid with hemoglobin formation, an oxygen carrier, muscle function, and brain function. This supplement has magnesium which helps prevent muscle aches and spasms, helps increase energy, calms nerves and anxiety, aids digestion by relieving constipation, important in heart health, and helps prevent migraine headaches. These minerals are also essential in building & maintaining strong bones.** **Turmeric- Turmeric helps the body fight inflammation which is the underlying root of a lot of diseases. Patients who suffer from chronic pain, autoimmune disease, and muscle stiffness/pain may benefit from this supplement by adding in an anti-inflammatory product like our Turmeric product.**
Exercise		>2 **Turmeric- With turmeric being an anti-inflammatory supplement, it can be great for post work out inflammation and recovery/ soreness .** **Type One Collagen- Working out helps strengthen our muscles, tendons, and ligaments. Type One Collagen Protein is important for growth and maintenance of tendons and ligaments. It also helps with joint health and improves our muscle mass.** **Ultra Amino Energy- Aminos are a great aid for the cardiovascular system. By adding these into your daily supplement regiment it can be a great aid in improving stamina during a working out and provide you sustained energy throughout the day without any crash or added sugars!** **Minerals - Helps with cramping during and after exercise. Great for bone health to keep bones strong!**
Immune		< 2 **Mega Immune- This is a daily immune product that helps maintain the integrity of the immune system by a synergistic blend of ingredients. This product is a great immune support supplement to keep the immune system strong all year long.**

Objective Nutritional / Metabolic Questionnaire

Cardio-Metabolic Health		> 2 **ALL (Greens, Minerals, Turmeric, Type 1 Collagen Protein, & Ultra Amino Energy) SUPPLEMENTS TO SUPPORT THE BODY & CURRENT DISEASES.**

Dr. Mark Cymerint D.C. Recommendations:

For Patient: _____

Supplement Recommendations:

- □ **Total Turmeric -** _____
- □ **Chelated Minerals -** _____
- □ **Type-1 Collagen -** _____
- □ **Ultra Amino Energy -** _____
- □ **Ultra Amino Energy (Caffeine Free) -** _____
- □ **Alkaline Greens -** _____
- □ **Mega Immune -** _____

Exercise Recommendations:

Dietary Recommendations:

CASE REPORT







CHIROPRACTIC PATIENT
JAN. 2016

- COMORBIDITIES –
HEIGHT: 5’8”
WEIGHT: 225LBS (OBESITY)
MEDS: 5 DIFFERENT CARDIOVASCULAR MEDS.
LIFESTYLE: SEDENTARY
DIET: POOR
MENTAL HEALTH: DEPRESSION

CASE REPORT







CHIROPRACTIC PATIENT
DEC. 2016

- COMORBIDITIES –
HEIGHT: 5’8”
WEIGHT: 153LBS (WNL)
MEDS: REPLACED BY 6 DIETARY SUPPLEMENTS DAILY
LIFESTYLE: ACTIVE (WALKS 3-4 MILES PER DAY)
DIET: VERY GOOD. REDUCED SUGAR, DAIRY, CARBS.
MENTAL HEALTH: STABLE AND HEALTHY

ADDITIONAL IMMUNE SYSTEM RESEARCH 2020

CRITICAL CARE MANAGEMENT OF ADULTS WITH COMMUNITY-ACQUIRED SEVERE RESPIRATORY VIRAL INFECTION

Published: Intensive Care Med | 2020 Feb.

Abstract

With the expanding use of molecular assays, viral pathogens are increasingly recognized among critically ill adult patients with community-acquired severe respiratory illness; studies have detected respiratory viral infections (RVIs) in 17-53% of such patients. In addition, novel pathogens including zoonotic coronaviruses like the agents causing Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and the 2019 novel coronavirus (2019 nCoV) are still being identified. Patients with severe RVIs requiring ICU care present typically with hypoxemic respiratory failure. Oseltamivir is the most widely used neuraminidase inhibitor for treatment of influenza; data suggest that early use is associated with reduced mortality in critically ill patients with influenza. At present, there are no antiviral therapies of proven efficacy for other severe RVIs. Several adjunctive pharmacologic interventions have been studied for their immunomodulatory effects, including macrolides, corticosteroids, cyclooxygenase-2 inhibitors, sirolimus, statins, anti-influenza immune plasma, and vitamin C, but none is recommended at present in severe RVIs. Evidence-based supportive care is the mainstay for management of severe respiratory viral infection. Non-invasive ventilation in patients with severe RVI causing acute hypoxemic respiratory failure and pneumonia is associated with a high likelihood of transition to invasive ventilation. Limited existing knowledge highlights the need for data regarding supportive care and adjunctive pharmacologic therapy that is specific for critically ill patients with severe RVI. There is a need for more pragmatic and efficient designs to test different therapeutics both individually and in combination.

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CRITICAL CARE MANAGEMENT OF ADULTS WITH COMMUNITY-ACQUIRED SEVERE RESPIRATORY VIRAL INFECTION

Published: Intensive Care Med | 2020 Feb.

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PLATELET-TO-LYMPHOCYTE RATIO IS ASSOCIATED WITH PROGNOSIS IN PATIENTS WITH CORONAVIRUS DISEASE-19

Published: J Med Virol . 2020 Sep

Abstract

Since December 2019, novel coronavirus infected pneumonia emerged in Wuhan city and rapidly spread throughout China. In severe novel coronavirus pneumonia cases, the number of platelets, their dynamic changes during the treatment, platelet-to-lymphocyte ratio (PLR) were a concern. We sought to describe the platelet feature of these cases. Single-center case series of the 30 hospitalized patients with confirmed coronavirus disease (COVID)-19 in Huizhou municipal central hospital from January 2020 to February 2020 were retrospectively analyzed. Demographic, clinical, blood routine results, other laboratory results, and treatment data were collected and analyzed. Outcomes of severe patients and nonsevere patients were compared. Univariate analysis showed that: age, platelet peaks, and PLR at peak platelet were the influencing factors in severe patients, multivariate analysis showed that the PLR value at peak platelet during treatment was an independent influencing factor in severe patients. The average hospitalization day of patients with platelet peaks during treatment was longer than those without platelet peaks ($P < .05$). The average age of patients with platelet peaks during treatment was older than those without platelet peaks ($P < .05$). The patients with significantly elevated platelets during treatment had longer average hospitalization days. And the higher PLR of patients during treatment had longer average hospitalization days. Single-center case series of the 30 hospitalized patients with confirmed COVID-19 in Huizhou Municipal Central Hospital, presumed that the number of platelets and their dynamic changes during the treatment may have a suggestion on the severity and prognosis of the disease. The patient with markedly elevated platelets and longer average hospitalization days may be related to the cytokine storm. The PLR of patients means the degree of cytokine storm, which might provide a new indicator in the monitoring in patients with COVID-19.

Qu R, Ling Y, Zhang YH, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19 [published online ahead of print, 2020 Mar 17]. J Med Virol. 2020;10.1002/jmv.25767. doi:10.1002/jmv.25767

GUIDE TO THE FORENSIC PATHOLOGY PRACTICE ON DEATH CASES RELATED TO CORONA VIRUS DISEASE 2019 （COVID-19)

Published Review: Fa Yi Xue Za Zhi . 2020 Feb

Abstract

Autopsy is of great significance to the elucidation of the pathological changes, pathogeneses and causes of death of corona virus disease 2019 （COVID-19） and can provide theoretical basis for more scientific and accurate prevention and control of the outbreak. Based on related laws and regulations, such as the Law of the People's Republic of China on Prevention and Control of Infectious Diseases, the clinical manifestations and epidemiological characteristics of COVID-19, and the related guidelines on the prevention and control of the outbreak, combined with the practical work of forensic pathology examination, the Guide to the Forensic Pathology Practice on Death Cases Related to Corona Virus Disease 2019 （COVID-19） （Trial Draft） has been developed. This guide includes information on the background investigation of the cases, autopsy room requirements, personal prevention and protections, external examinations, autopsy, auxiliary examinations, and so on. This guide can be used as a reference by forensic and pathological examination institutions, as well as examination staff.

Mao DM, Zhou N, Zheng D, et al. Guide to the Forensic Pathology Practice on Death Cases Related to Corona Virus Disease 2019 （COVID-19） （Trial Draft. Fa Yi Xue Za Zhi. 2020;36(1):6-5. doi:10.12116/j.issn.1004-5619.2020.01.003

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REVIEW AND PROSPECT OF PATHOLOGICAL FEATURES OF CORONA VIRUS DISEASE

Published Review: Fa Yi Xue Za Zhi . 2020 Feb

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Since 2003, coronavirus has caused multiple major public health events that resulted in global epidemics, such as severe acute respiratory syndrome （SARS）, Middle East respiratory syndrome （MERS） and corona virus disease 2019 （COVID-19）. Especially since COVID-19 outbroke in Wuhan, Hubei, in December 2019, coronavirus has had a significant impact on people's health and lives. But so far, the pathological diagnosis of COVID-19 has been relatively deficient： it is still confined to the pathological findings of punctured organs, and the majority of medical workers have poor awareness of its pathological characteristics. The COVID-19, as same as SARS and MERS, is caused by coronaviruses and can cause viral pneumonia. They have certain similarities. This article comprehensively reviews the pathological features observed in the autopsies of the aforementioned three diseases, in order to provide reference to the analysis of pathological changes of COVID-19.

Wang HJ, Du SH, Yue X, Chen CX. Review and Prospect of Pathological Features of Corona Virus Disease. Fa Yi Xue Za Zhi. 2020;36(1):16-20. doi:10.12116/j.issn.1004-5619.2020.01.004

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PUTATIVE ROLES OF VITAMIN D IN MODULATING IMMUNE RESPONSE AND IMMUNOPATHOLOGY ASSOCIATED WITH COVID-19

Virus Res . 2021 Jan 15

Abstract

The first incidence of COVID-19 was reported in the Wuhan city of Hubei province in China in late December 2019. Because of failure in timely closing of borders of the affected region, COVID-19 spread across like a wildfire through air travel initiating a pandemic. It is a serious lower respiratory track viral infection caused by highly contagious, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Coronavirus including COVID-19 causing SARS-CoV-2 causes zoonotic diseases and thought to be originated from bats. Since its first incidence, the virus has spread all across the world, causing serious human casualties, economic losses, and disrupting global supply chains. As with SARS-CoV, COVID-19 causing SARS-CoV-2 follows a similar path of airborne infection but is less lethal and more infectious than SARS and MERS. This review focusses on the pathogenesis of SARS-CoV-2, especially on the dysfunctional immune responses following a cytokine storm in severely affected persons. The mode of entry of SARS-CoV-2 is via the angiotensin converting enzyme 2 (ACE-2) receptors present on the epithelial lining of lungs, gastrointestinal tract, and mucus membranes. Older persons with weaker immune systems and associated co-morbidities are more vulnerable to have dysfunctional immune responses, as most of them concomitantly have severe hypovitaminosis D- consequently, causing severe damage to key organs of the body including lungs and the cardiovascular system. A vast majority of persons who were entered to intensive care units and died were found to have had severe vitamin D deficiency; thus, this area must be investigated seriously. In addition, this article assesses the role of vitamin D in reducing the risk of COVID-19. Vitamin D is a key regulator of the renin-angiotensin system that is exploited by SARS-CoV-2 for entry into the host cells. Further, vitamin D modulates multiple mechanisms of the immune system to contain the virus that includes dampening the entry and replication of SARS-CoV-2, reduces concentration of pro-inflammatory cytokines and increases levels of anti-inflammatory cytokines, enhances the production of natural antimicrobial peptide and activates defensive cells such as macrophages that could destroy SARS-CoV-2. Thus, this article provides the urgency of needed evidences through large population based randomized controlled trials and ecological studies to evaluate the potential role of vitamin D in COVID-19.

Kumar R, Rathi H, Haq A, Wimalawansa SJ, Sharma A. Putative roles of vitamin D in modulating immune response and immunopathology associated with COVID-19. Virus Res. 2021 Jan 15;292:198235. doi: 10.1016/j.virusres.2020.198235. Epub 2020 Nov 21. PMID: 33232783; PMCID: PMC7680047.

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THREE NOVEL PREVENTION, DIAGNOSTIC, AND TREATMENT OPTIONS FOR COVID-19 URGENTLY NECESSITATING CONTROLLED RANDOMIZED TRIALS

Medical Hypotheses . 2020 Oct

Abstract:

Purpose: Asymptomatic or minimally symptomatic infection with COVID-19 can result in silent transmission to large numbers of individuals, resulting in expansion of the pandemic with a global increase in morbidity and mortality. New ways of screening the general population for COVID-19 are urgently needed along with novel effective prevention and treatment strategies.

Hypothesis: A hypothetical three-part prevention, diagnostic, and treatment approach based on an up-to-date scientific literature review for COVID-19 is proposed. Regarding diagnosis, a validated screening questionnaire and digital app for COVID-19 could help identify individuals who are at risk of transmitting the disease, as well as those at highest risk for poor clinical outcomes. Global implementation and online tracking of vital signs and scored questionnaires that are statistically validated would help health authorities properly allocate essential health care resources to test and isolate those at highest risk for transmission and poor outcomes. Second, regarding prevention, no validated protocols except for physical distancing, hand washing, and isolation exist, and recently ivermectin has been published to have anti-viral properties against COVID-19. A randomized trial of ivermectin, and/or nutraceuticals that have been published to support immune function including glutathione, vitamin C, zinc, and immunomodulatory supplements (3,6 Beta glucan) could be beneficial in preventing transmission or lessening symptomatology but requires statistical validation. Third, concerning treatment, COVID-19 induced inflammation and "cytokine storm syndrome" with hemophagocytic lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS) have resulted in extreme morbidity and mortality in those with certain comorbidities, secondary to "acute respiratory distress syndrome" (ARDS) and multiorgan dysfunction with disseminated intravascular coagulation (DIC).Deficiency in red blood cell, serum and alveolar glutathione has been published in the medical literature for ARDS, as well as viral and bacterial pneumonias, resulting from increased levels of free radical/oxidative stress.

Conclusion and implications: A three-part prevention, diagnostic, and treatment plan is proposed for addressing the severe complications of COVID-19. Digital monitoring of symptoms to clinically diagnose early exposure and response to treatment; prevention with ivermectin as well as nutritional therapies that support a healthy immune response; treatment with anti-inflammatory therapies that block NF-κB and activate Nrf2 pathways, as well as novel therapies that address COVID-19 pneumonia and ARDS with DIC including anticoagulation and/or novel respiratory therapies with or without acetazolamide and sildenafil. These three broad-based interventions urgently need to be subjected to randomized, controlled trials.

Horowitz RI, Freeman PR. Three novel prevention, diagnostic, and treatment options for COVID-19 urgently necessitating controlled randomized trials. Med Hypotheses. 2020 Oct;143:109851. doi: 10.1016/j.mehy.2020.109851. Epub 2020 May 22. PMID: 32534175; PMCID: PMC7242962.

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RETEST POSITIVE FOR SARS-COV-2 RNA OF "RECOVERED" PATIENTS WITH COVID-19: PERSISTENCE, SAMPLING ISSUES, OR RE-INFECTION?

J Med Virol . 2020 Nov.

Abstract

"Retest Positive" for severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) from "recovered" coronavirus disease-19 (COVID-19) has been reported and raised several important questions for this novel coronavirus and COVID-19 disease. In this commentary, we discussed several questions: (a) Can SARS-CoV-2 re-infect the individuals who recovered from COVID-19? This question is also associated with other questions: whether or not SARS-CoV-2 infection induces protective reaction or neutralized antibody? Will SARS-CoV-2 vaccines work? (b) Why could some recovered patients with COVID-19 be re-tested positive for SARS-CoV-2 RNA? (c) Are some recovered patients COVID-19 with re-testing positive for SARS-CoV-2 RNA infectious? and (d) How should the COVID-19 patients with retest positive for SARS-CoV-2 be managed?

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A NEW POSITIVE SARS-COV-2 TEST MONTHS AFTER SEVERE COVID-19 ILLNESS: REINFECTION OR INTERMITTENT VIRAL SHEDDING?

British Medical Journal Case Rep . 2021 Feb 4.

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We present a case of a patient who had a history of severe coronavirus disease (COVID-19) 4 months prior to this current presentation and, after a long asymptomatic period, subsequently tested positive for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by a RNA PCR assay, after several interval negative SARS-CoV-2 RNA tests. We present this potential case of SARS-CoV-2 reinfection in order to incite discussion around differentiating persistent infection with intermittent viral shedding and reinfection, as well as to discuss evolving knowledge and approaches to the clinical management, follow-up molecular testing and treatment of COVID-19 reinfection.

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CYTOKINE STORM INDUCED BY SARS-COV-2 INFECTION: THE SPECTRUM OF ITS NEUROLOGICAL MANIFESTATIONS

Cytokine . 2021 Feb

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Thepmankorn P, Bach J, Lasfar A, Zhao X, Souayah S, Chong ZZ, Souayah N. Cytokine storm induced by SARS-CoV-2 infection: The spectrum of its neurological manifestations. Cytokine. 2021 Feb;138:155404. doi: 10.1016/j.cyto.2020.155404. Epub 2020 Dec 11. PMID: 33360025; PMCID: PMC7832981.

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A NETWORK-BASED ANALYSIS REVEALS THE MECHANISM UNDERLYING VITAMIN D IN SUPPRESSING CYTOKINE STORM AND VIRUS IN SARS-COV-2 INFECTION

Front Immunol . 2020 Dec 9

Abstract

Background: SARS-CoV-2 causes ongoing pandemic coronavirus disease of 2019 (COVID-19), infects the cells of the lower respiratory tract that leads to a cytokine storm in a significant number of patients resulting in severe pneumonia, shortness of breathing, respiratory and organ failure. Extensive studies suggested the role of Vitamin D in suppressing cytokine storm in COVID-19 and reducing viral infection; however, the precise molecular mechanism is not clearly known. In this work, bioinformatics and systems biology approaches were used to understand SARS-CoV-2 induced cytokine pathways and the potential mechanism of Vitamin D in suppressing cytokine storm and enhancing antiviral response.

Conclusion: This comprehensive study identified the pathways associated with cytokine storm in SARS-CoV-2 infection. The proposed underlying mechanism of Vitamin D could be promising in suppressing the cytokine storm and inducing a robust antiviral response in severe COVID-19 patients. The finding in this study urgently needs further experimental validations for the suitability of Vitamin D in combination with IFN-α to control severe COVID-19.

Ahmed F. A Network-Based Analysis Reveals the Mechanism Underlying Vitamin D in Suppressing Cytokine Storm and Virus in SARS-CoV-2 Infection. Front Immunol. 2020 Dec 9;11:590459. doi: 10.3389/fimmu.2020.590459. PMID: 33362771; PMCID: PMC7756074.

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DECODING THE SILENT WALK OF COVID-19: HALTING ITS SPREAD USING OLD BULLETS

Biomed Pharmacother . 2021 Jan

Abstract

Severe acute respiratory syndrome (SARS) develops within 3-14 days when CoV2 invades epithelial, myeloid cells in the nasopharynx and pneumocytes in the respiratory tract through angiotensin converting enzyme (ACE2). Infection swiftly disseminates to gastrointestinal, cardiovascular, renal organs as well as immune system to deregulate their normal functioning through unique and distinct mechanisms. The health system and economy has been intensely thwarted by the rapid spread and exorbitant mortality caused by COVID-19 disease across the globe. The acute progression of the disease and high infection rate pose an enormous challenge for its therapeutic management and critical care. The viral structure, genome and proteome have been deciphered which yielded cues for targeting already available therapeutic entities. More than 200 compounds have been screened and till date approximately 69 therapeutic agents are undergoing clinical trials across the world. Among these, Remdesivir (RMD), chloroquine (CQ), hydroxychloroquine (HCQ), noscapine (NOS) and heparin have demonstrated fairly promising results in preclinical and clinical studies. Recently, RMD has been approved by USFDA for the management of COVID 19. However, intense research is going on to screen and ace the 'magic bullets' for the management of SARS-CoV2 infection worldwide. The current review illustrates the plausible therapeutic targets in SARS-CoV2 important for inhibition of virus cycle. In addition, the role of RMD, CQ, HCQ, NOS and heparin in combating infection has been addressed. The importance of vitamin C and D supplements as adjunct therapies in the prevention of SARS-CoV2 virus infection have also been summarized.

Kumar M, Madan J, Sodhi RK, Singh SB, Katyal A. Decoding the silent walk of COVID-19: Halting its spread using old bullets. Biomed Pharmacother. 2021 Jan;133:110891. doi: 10.1016/j.biopha.2020.110891. Epub 2020 Oct 19. PMID: 33227700; PMCID: PMC7572089.

DECODING THE SILENT WALK OF COVID-19: HALTING ITS SPREAD USING OLD BULLETS

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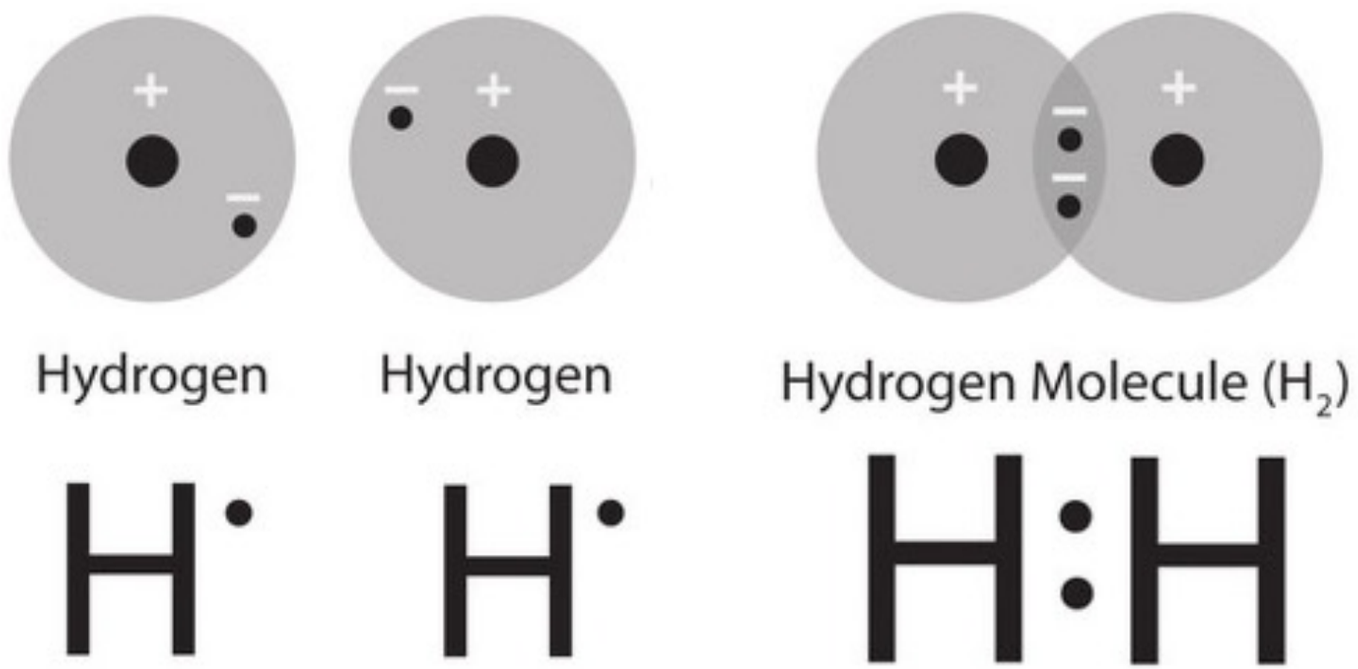
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II. BASIC SCIENCE (NUTRITION)

D. IMMUNE SYSTEM RESEARCH
   a) Recent studies from the NIH/PubMed
   b) Nutritional options
   c) Objective nutritional questionnaire
E. WATER
   a) Molecular hydrogen, constipation, ionization
   b) Filtration and nutritional benefits
   c) Water pH & safety
F. EVIDENCE BASED DIET RELATED RESEARCH
   a) Intermittent Fasting
   b) Ketogenic Diet
   c) Plant Based Nutrition

MOLECULAR HYDROGEN

- The chemical formula H2:
  - Composed of (2) bonded hydrogen atoms
  - The smallest molecule in existence
  - Its size enables molecular hydrogen to be dispersed readily in the body & cross through the blood/brain barrier.



MOLECULAR HYDROGEN

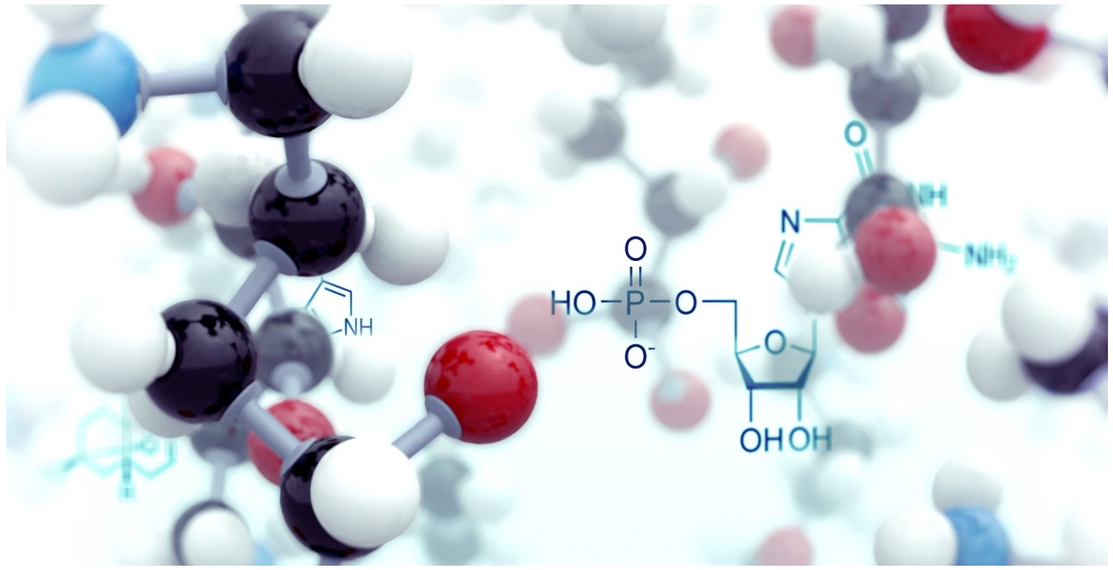
- The smallest element and lightest molecule in the universe

- Contains two (2) protons and two (2) electrons, thus making it neutrally-charged.

- It can affect our bodies at a cellular level. With antioxidant and cytoprotective properties, molecular hydrogen is capable of entering the energy-generating mitochondria of our cells, and mopping up any unwanted free radicals, therefore boosting our overall well-being.

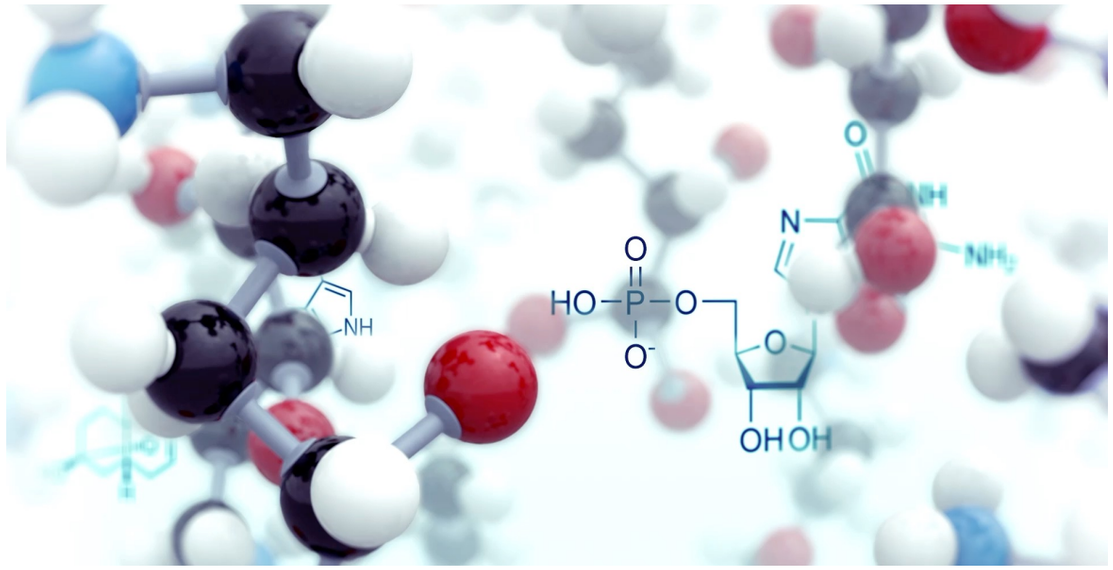
- Hydrogen-rich ionized alkaline water has a negative *ORP (Oxidation Reduction Potential)* to counter the positive ORP of our degenerating cells and oxidization of our bodies as we become older.

MOLECULAR HYDROGEN BENEFITS



- Reduced inflammation
- Pain relief
  - Pain relief in joints
- Decelerated aging process
- Decreased muscle fatigue

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Molecular hydrogen: An inert gas turns clinically effective

Annals of Medicine. 2015 June.

Abstract

Molecular hydrogen (H2) appeared as an experimental agent in biomedicine approximately 40 years ago, yet the past 5 years seem to confirm its medicinal value in the clinical environment. H2 improves clinical end-points and surrogate markers in several clinical trials, from metabolic diseases to chronic systemic inflammatory disorders to cancer. However, less information is available concerning its medicinal properties, such as dosage and administration, or adverse reactions and use in specific populations. The present paper overviews the clinical relevance of molecular hydrogen and summarizes data from clinical trials on this innovative medical agent. Clinical profiles of H2 provide evidence-based direction for practical application and future research on molecular hydrogen for the wider health care community.

Ostojic SM. Molecular hydrogen: An inert gas turns clinically effective. Ann Med. 2015 Jun;47(4):301-4. doi: 10.3109/07853890.2015.1034765. Epub 2015 May 4. PMID: 25936365.

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Pilot study: Effects of drinking hydrogen-rich water on muscle fatigue caused by acute exercise in elite athletes

Medical Gas Research . 2012 Jul 12.

Background: Muscle contraction during short intervals of intense exercise causes oxidative stress, which can play a role in the development of overtraining symptoms, including increased fatigue, resulting in muscle microinjury or inflammation. Recently it has been said that hydrogen can function as antioxidant, so we investigated the effect of hydrogen-rich water (HW) on oxidative stress and muscle fatigue in response to acute exercise.

Methods: Ten male soccer players aged 20.9 ± 1.3 years old were subjected to exercise tests and blood sampling. Each subject was examined twice in a crossover double-blind manner; they were given either HW or placebo water (PW) for one week intervals. Subjects were requested to use a cycle ergometer at a 75 % maximal oxygen uptake (VO2) for 30 min, followed by measurement of peak torque and muscle activity throughout 100 repetitions of maximal isokinetic knee extension. Oxidative stress markers and creatine kinase in the peripheral blood were sequentially measured.

Results: Although acute exercise resulted in an increase in blood lactate levels in the subjects given PW, oral intake of HW prevented an elevation of blood lactate during heavy exercise. Peak torque of PW significantly decreased during maximal isokinetic knee extension, suggesting muscle fatigue, but peak torque of HW didn't decrease at early phase. There was no significant change in blood oxidative injury markers (d-ROMs and BAP) or creatine kinase after exercise.

Conclusion: Adequate hydration with hydrogen-rich water pre-exercise reduced blood lactate levels and improved exercise-induced decline of muscle function. Although further studies to elucidate the exact mechanisms and the benefits are needed to be confirmed in larger series of studies, these preliminary results may suggest that HW may be suitable hydration for athletes.

Aoki K, Nakao A, Adachi T, Matsui Y, Miyakawa S. Pilot study: Effects of drinking hydrogen-rich water on muscle fatigue caused by acute exercise in elite athletes. Med Gas Res. 2012 Jul 12;2:12. doi: 10.1186/2045-9912-2-12. PMID: 22520831; PMCID: PMC33955

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Hydrogen-Rich Water Improves Cognitive Ability and Induces Antioxidative, Antiapoptotic, and Anti-Inflammatory Effects in an Acute Ischemia-Reperfusion Injury Mouse Model

Biomed Res Int . 2021 Oct 27

Background: Cerebral ischemia and its reperfusion injury facilitate serious neurodegenerative diseases such as dementia due to cell death; however, there is currently no treatment for it. Reactive oxygen species is one of the many factors that induce and worsen the development of such diseases, and it can be targeted by hydrogen treatment. This study examined the effect of molecular hydrogen in cerebral ischemia-reperfusion injury, which is emerging as a novel therapeutic agent for various diseases.

Methods: Ischemia-reperfusion injury was generated through bilateral common carotid artery occlusion in C57BL/6 mice. The test group received hydrogen-rich water orally during the test period. To confirm model establishment and the effect of hydrogen treatment, behavioural tests, biochemical assays, immunofluorescence microscopy, and cytokine assays were conducted.

Results: Open field and novel object recognition tests revealed that the hydrogen-treated group had improved cognitive function and anxiety levels compared to the nontreated group, while hematoxylin and eosin stain showed abundant pyknotic cells in a model mouse brain, and this was attenuated in the hydrogen-treated mouse brain. Total antioxidant capacity and thiobarbituric acid reactive substance assays revealed that hydrogen treatment induced antioxidative effects in the mouse brain. Immunofluorescence microscopy revealed attenuated apoptosis in the striatum, cerebral cortex, and hippocampus of hydrogen-treated mice. Western blotting showed that hydrogen treatment reduced Bax and TNFα levels. Finally, cytokine assays showed that IL-2 and IL-10 levels significantly differed between the hydrogen-treated and nontreated groups.

Conclusion: Hydrogen treatment could potentially be a future therapeutic strategy for ischemia and its derived neurodegenerative diseases by improving cognitive abilities and inducing antioxidative and antiapoptotic effects. Hydrogen treatment also decreased Bax and TNFα levels and induced an anti-inflammatory response via regulation of IL-2 and IL-10. These results will serve as a milestone for future studies intended to reveal the mechanism of action of molecular hydrogen in neurodegenerative diseases.

Lee D, Choi JI. Hydrogen-Rich Water Improves Cognitive Ability and Induces Antioxidative, Antiapoptotic, and Anti-Inflammatory Effects in an Acute Ischemia-Reperfusion Injury Mouse Model. Biomed Res Int. 2021 Oct 27;2021:9956938. doi: 10.1155/2021/9956938

Molecular hydrogen is protective against 6-hydroxydopamine-induced nigrostriatal degeneration in a rat model of Parkinson's disease

Neuroscience Letters . 2009 Apr 3

Abstract

Molecular hydrogen serves as an antioxidant that reduces hydroxyl radicals, but not the other reactive oxygen and nitrogen species. In the past year, molecular hydrogen has been reported to prevent or ameliorate eight diseases in rodents and one in human associated with oxidative stress. In Parkinson's disease, mitochondrial dysfunction and the associated oxidative stress are major causes of dopaminergic cell loss in the substantia nigra. We examined effects of approximately 50%-saturated molecular hydrogen in drinking water before or after the stereotactic surgery on 6-hydroxydopamine-induced nigrostriatal degeneration in a rat model of Parkinson's disease. Methamphetamine-induced behavioral analysis showed that molecular hydrogen prevented both the development and progression of the nigrostriatal degeneration. Tyrosine hydroxylase staining of the substantia nigra and striatum also demonstrated that pre- and post-treatment with hydrogen prevented the dopaminergic cell loss. Our studies suggest that hydrogen water is likely able to retard the development and progression of Parkinson's disease.

Fu Y, Ito M, Fujita Y, Ito M, Ichihara M, Masuda A, Suzuki Y, Maesawa S, Kajita Y, Hirayama M, Ohsawa I, Ohta S, Ohno K. Molecular hydrogen is protective against 6-hydroxydopamine-induced nigrostriatal degeneration in a rat model of Parkinson's disease. N

WATER & CONSTIPATION

Up to one half of all Americans have it.

Drinking Chlorinated water = Constipation

Chlorine compounds in tap water kill the helpful good gut bacteria, leading to overgrowth of harmful bacteria, yeasts, or even parasites.

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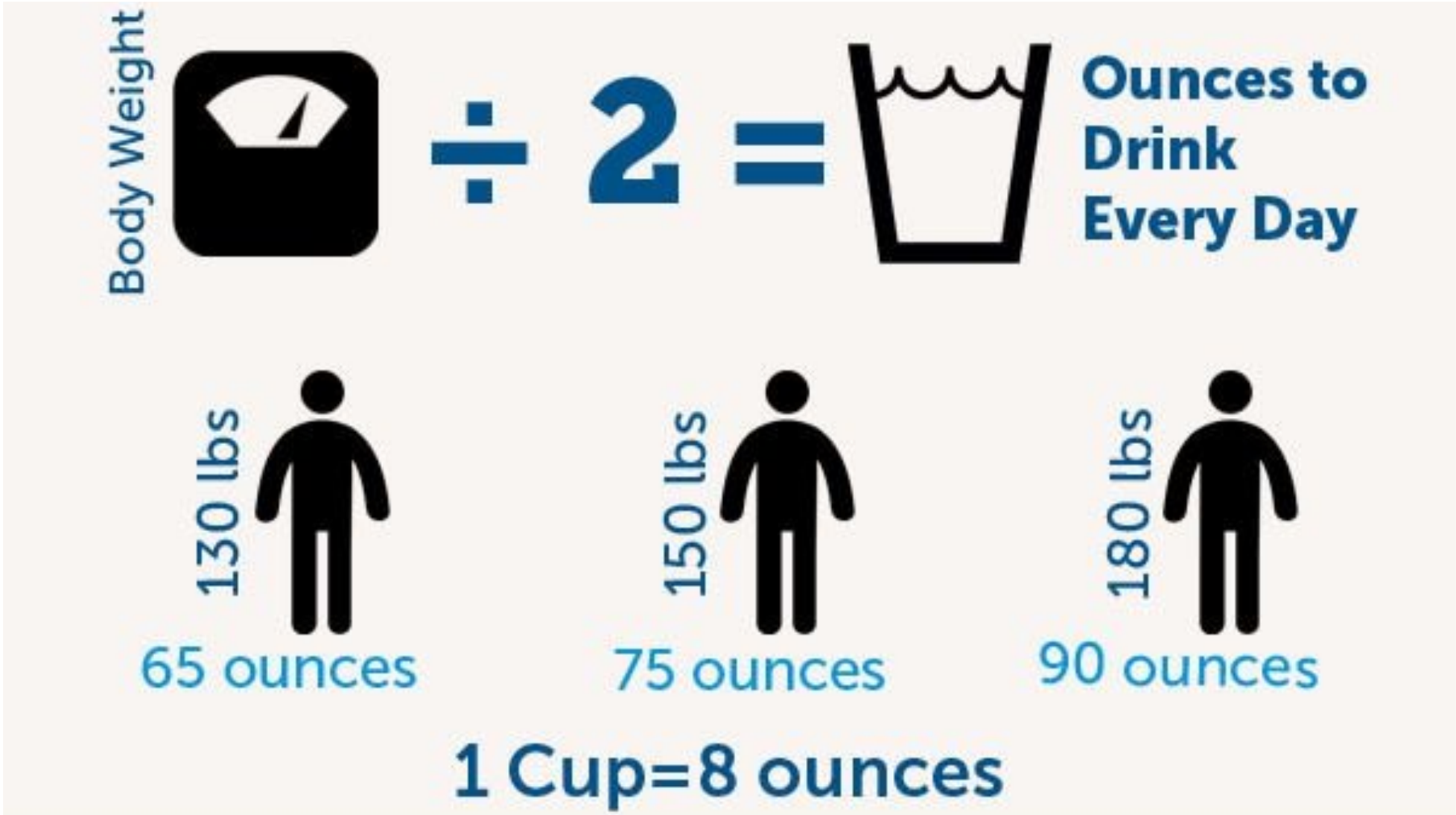
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HOW MUCH WATER SHOULD WE DRINK?

Half your body weight in oz. per day minimum!

Hydration usually takes about **8 weeks** to achieve if drinking the proper amount.



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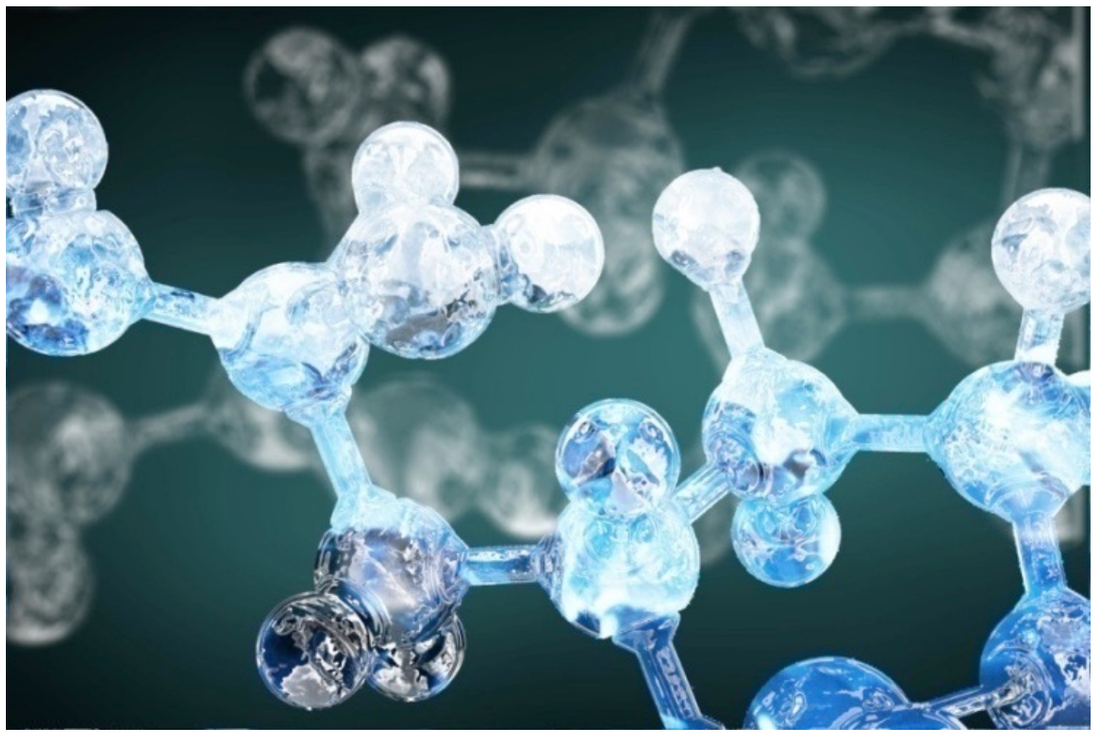
PH & IONIZATION

- **Filtration (Carbon Ceramic Fiber Filter)**
- **Being able to control the pH/acid/alkalinity**
- **Number of plates in the machine (9-13 preferred)**
- **Less molecules per cluster**
- **Self Cleaning**
- **No adding of minerals**
- **Lifetime Warranty**



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UNHEALTHY WATER IN YOUR HOME!
DO YOU DRINK ANY OF THESE?



BOTTLED WATER

- There have been more than 100 recalls on contaminated bottled water.
- According to the FDA, "contaminated bottled water can harm your health."



BOTTLED ALKALINE WATER

Did you know that even though some bottled water is marketed as being alkaline, it is impossible for this type of water to contain the antioxidant known as molecular hydrogen? That's because molecular hydrogen cannot be contained in a plastic bottle (the hydrogen is too small and therefore dissipates too quickly).



TAP WATER

The EPA states that tap water sources may contain over 90 dangerous contaminants which can cause cancer and learning disorders in children.

Some of the EPA's list of tap water contaminants include:

- E. Coli
- Lead
- Arsenic
- Organic chemicals
- Pharmaceuticals
- Chromium-6
- Chloroform

Sources:

https://www.epa.gov/sites/default/files/2015-10/documents/ace3_drinking_water.pdf

https://www.cdc.gov/healthywater/drinking/bottled/index.html#

https://www.usnews.com/news/business/articles/2021-05-21/us-enacts-real-water-recall-amid-reports-of-death-illness#

UNHEALTHY WATER CONTINUED...



FILTERED WATER (WATER PITCHERS/ FAUCET ATTACHMENTS)

- Most of these devices lack premium filtration materials, and they do not add any health benefits like antioxidants, alkaline pH levels or molecular hydrogen to your water.
- Look at the packaging of these filter pitchers and you'll notice that they only remove a few contaminants and 2-3 heavy metals (some not including lead) – leaving consumers with a false sense of security.



REVERSE OSMOSIS WATER (R.O.)

- Water is intended to provide essential minerals (like calcium and magnesium) to protect your teeth and bones. By drinking water that is devoid of these minerals (like R.O.) your body will naturally pull these minerals from your teeth and bones, thus weakening them.
- The World Health Organization (WHO) made a statement about R.O. water: "long term RO consumption has a definite adverse influence on the animal and human organisms."

HTTPS://WWW.FDA.GOV/SAFETY/RECALLS-MARKET-WITHDRAWALS-SAFETY-ALERTS/REAL-WATER-INC-ISSUES-PRECAUTIONARY-RECALL-ALL-SIZES-REAL-WATER-BRAND-DRINKING-WATER-DUE-POSSIBLE

DID YOU KNOW?

- Vitamin C and Molecular Hydrogen can BOTH neutralize free radicals. However, studies show that Molecular Hydrogen provides greater protection than Vitamin C because ONLY Molecular Hydrogen can increase powerful antioxidant enzymes in the body.

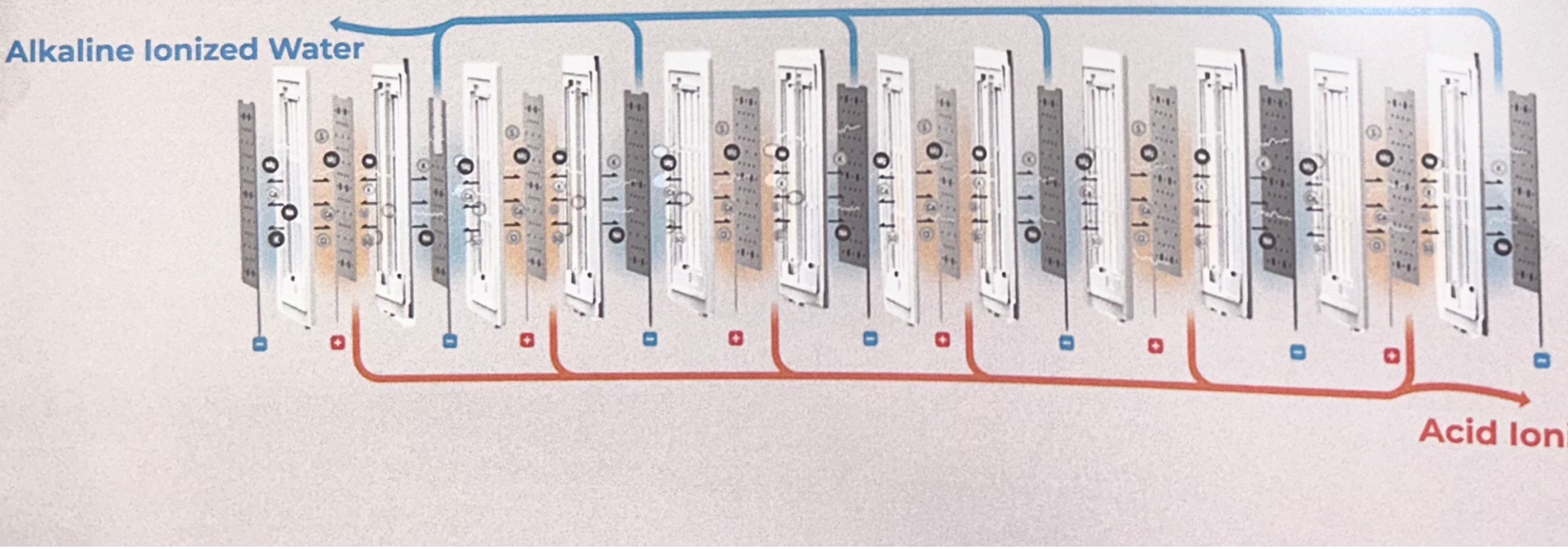
HOW IT WORKS

The secret is the water cell...

When your tap water enters the Tyent water ionizer, it runs through two filters and is filtered to 99% purity.

Next, it runs through our proprietary electrolysis process where “free” and available hydrogen gas (H2 molecular hydrogen) is dissolved into the water. Then, the water molecules are split into two unique streams of water. One stream becomes acidic, which is great for your skin and hair. We call it Beauty Water!

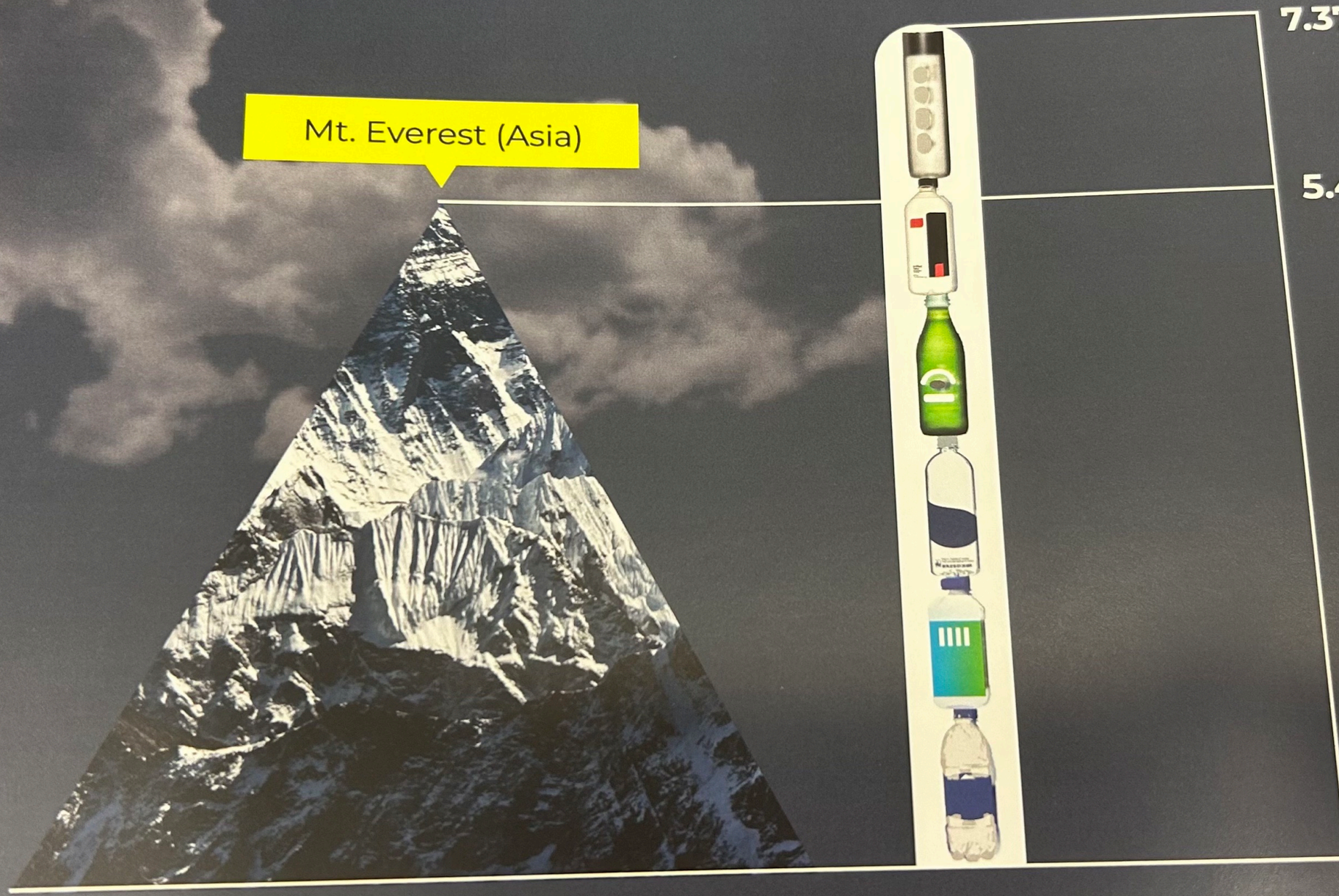
The other water stream becomes the perfect drinking water! It’s alkaline, ultra-hydrating and filled with therapeutic antioxidants called molecular hydrogen.





IS YOUR WATER ECO-FRIENDLY?

1 family + 10 years = a tower of bottles as high as Mt. Everest!



HIGHER THAN MT. EVEREST!

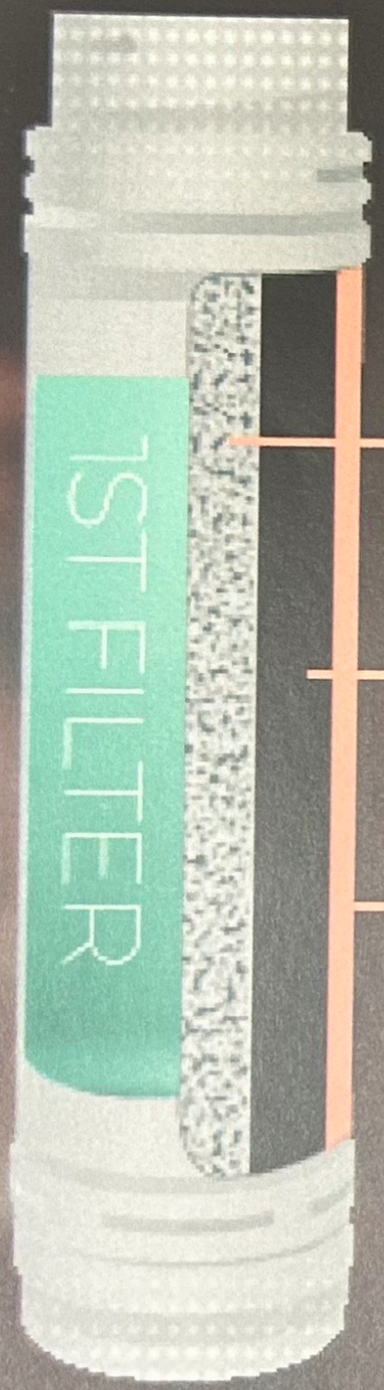
BOTTLED WATER VS. TYENT WATER
DOES IT MAKE CENT$?

Bottled Alkaline Water costs between **$2.00 to $5.00 on average!**





Tyent water ONLY costs about **6¢ a glass!**



TM Filtration

Carbon block

Membrane



.01 Micron UF

TM Ceramic

Carbon block

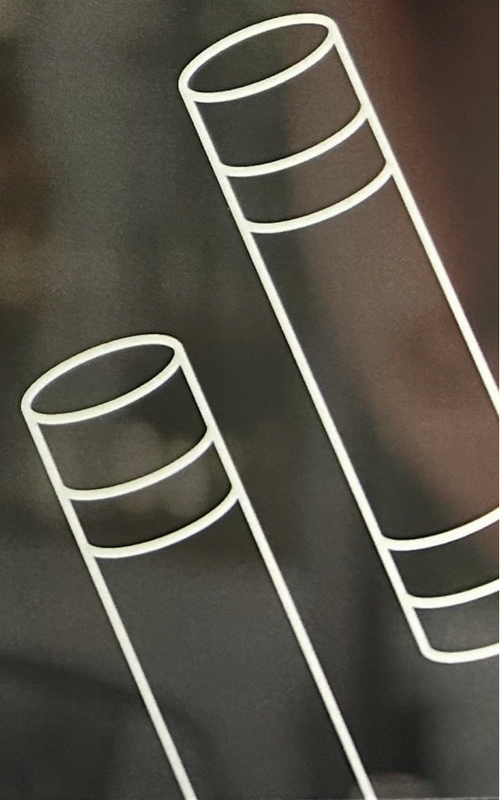
Membrane

DUAL FILTRATION

Removes over 99% of unhealthy contaminants...
To help take care of what matters most!

Tyent engineers designed the most advanced water filtration technology in the world. All Tyent units have two large state-of-the-art filters with Ultra .01 Micron Filtration technology. It's the same filtration found in some dialysis machines.

Tyent filters have been tested by an EPA certified lab and have been shown to reduce MORE THAN 200 CONTAMINANTS found in tap water by over 99%!



PH, IONIZATION & MOLECULAR HYDROGEN

With Molecular Hydrogen Boost



Auto fill Quantity Selector

3 Alkaline Levels & 3 Acidic Levels + Turbo Modes

Outstanding Electrolysis

Smartphone Touch Technology

TM Ceramic & Carbon Block filtration

PH, IONIZATION & MOLECULAR HYDROGEN

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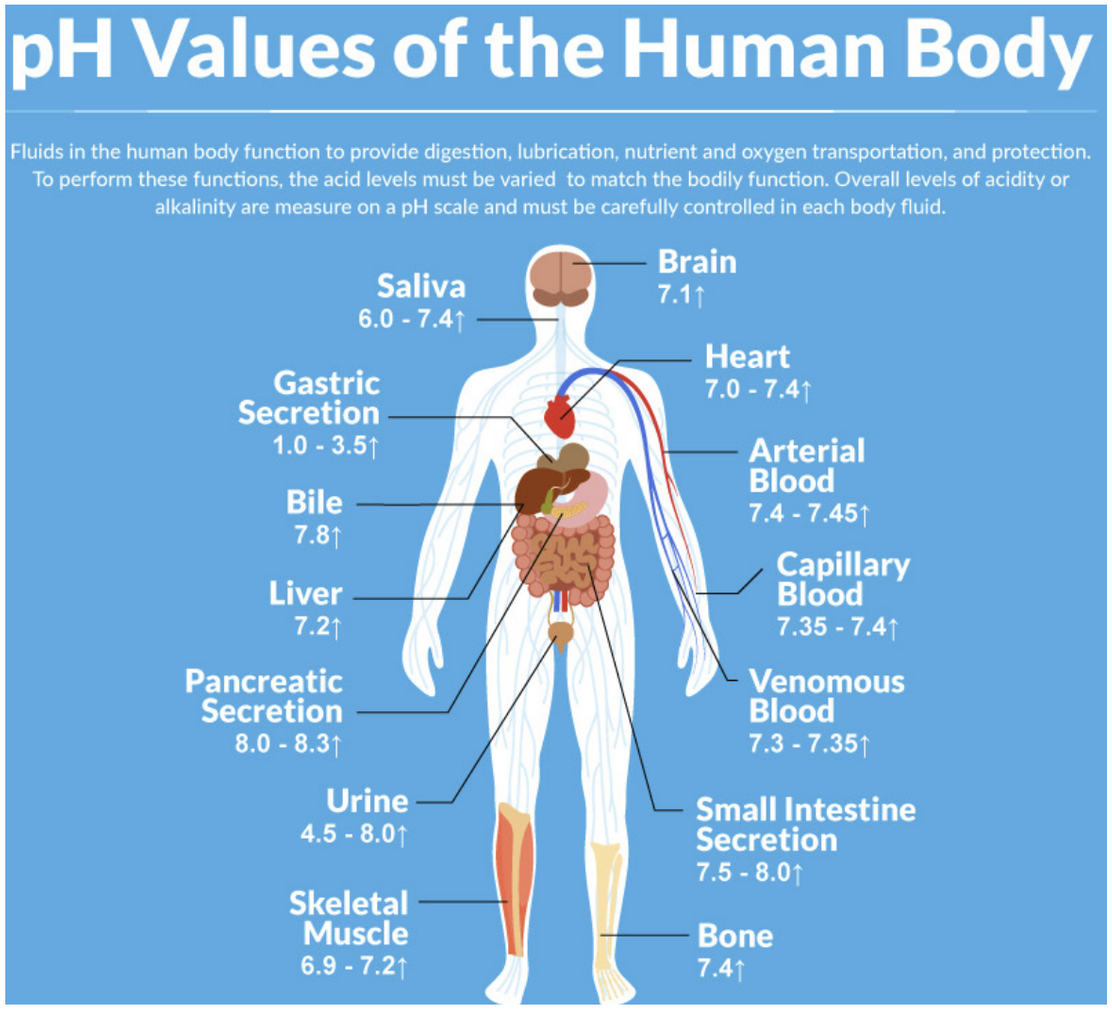
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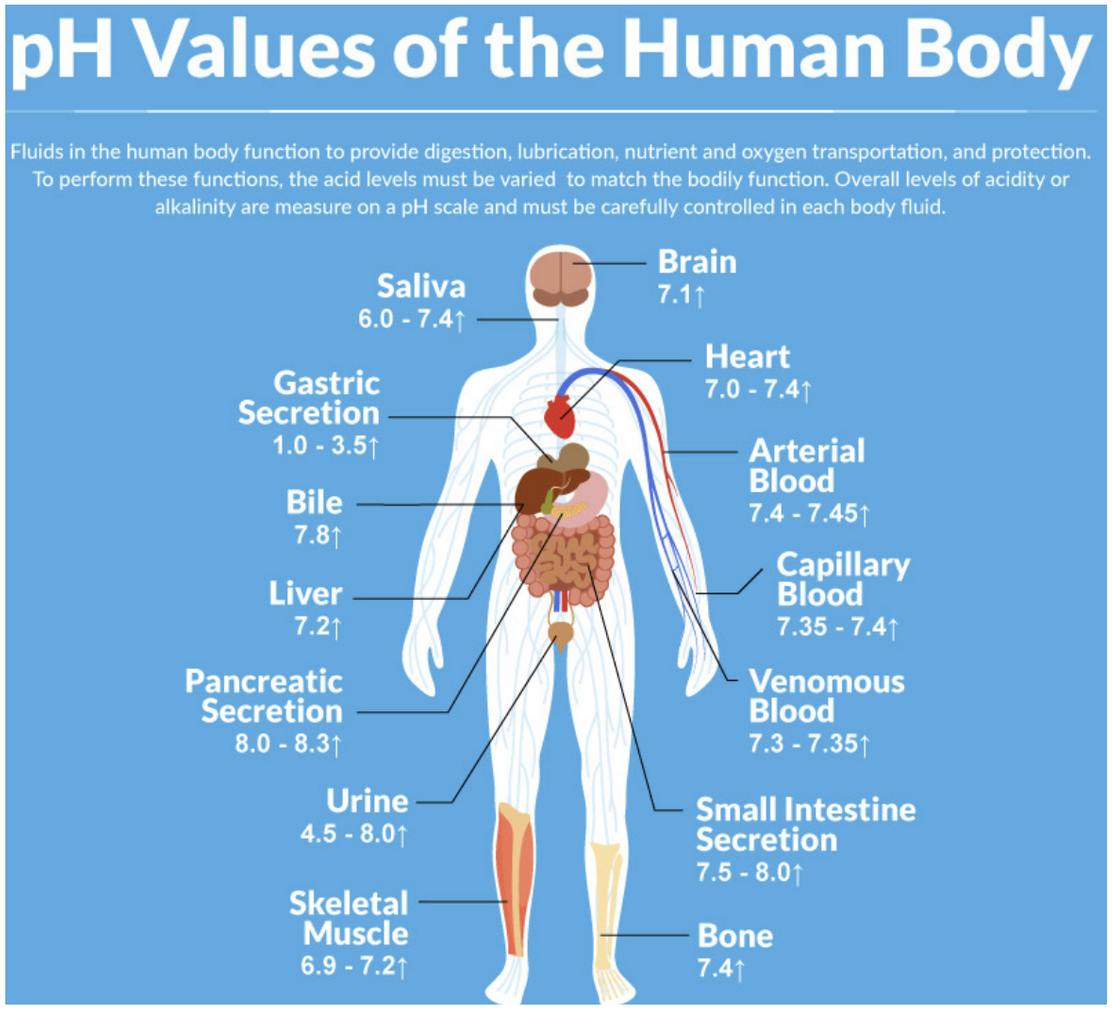
PH: ACIDIC WATER, SKIN & HAIR ARE BETWEEN 4.5 TO 5.5 PH



Benefits of Acidic Water:

- Natural astringent & skin cleanser
- Helps clear up bacteria that causes acne
- Soothes the itch & sting of insect bites, eczema & psoriasis
- Removes tooth plaque
- Improves plant growth

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NUTRITION DISCLAIMER

Just Remember…
Nutrition Is One Of The Hardest Topics To Cover As Guidelines Are Always Changing & Diets Are Open To Different Interpretation.

Evidence Based Diet Related Research: Fasting & Intermittent Fasting

Complete Alternate Day Fasting	Involves alternating fasting days (no energy-containing foods or beverages consumed) with eating days.
Time Restricted Feeding	No eating anything but water after dinner. No snacking in the evening. Eating can be resumed the following day any time before noon. Eating is permitted until after dinner.
Religious Fasting	Variety of fasting regimens undertaken for religious or spiritual purposes, ie. Yom Kippur (Judaism) 25.5hr fast - no food or water.
Ramadan Fasting	A fast from sunrise to sunset during the holy month of Ramadan; the most common dietary practice is to consume one large meal after sunset and one lighter meal before dawn. Thus, the feast and fast periods of Ramadan are approximately 12 hours in length
Other Religious Fasts	Members of the Church of Jesus Christ of Latter-Day Saints routinely abstain from food and drink for extended periods of time. Some Seventh-day Adventists consume their last of two daily meals in the afternoon, resulting in an extended nighttime fasting interval that may be biologically important

Source: https://academic.oup.com/nutritionreviews/article/73/10/661/1849182

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METABOLIC EFFECTS OF INTERMITTENT FASTING

Published: Annu. Rev. Nutr . 2017 Aug 21

The objective of this review is to provide an overview of intermittent fasting regimens, summarize the evidence on the health benefits of intermittent fasting, and discuss physiological mechanisms by which intermittent fasting might lead to improved health outcomes. A MEDLINE search was performed using PubMed and the terms "intermittent fasting," "fasting," "time-restricted feeding," and "food timing." Modified fasting regimens appear to promote weight loss and may improve metabolic health. Several lines of evidence also support the hypothesis that eating patterns that reduce or eliminate nighttime eating and prolong nightly fasting intervals may result in sustained improvements in human health. Intermittent fasting regimens are hypothesized to influence metabolic regulation via effects on (a) circadian biology, (b) the gut microbiome, and (c) modifiable lifestyle behaviors, such as sleep. If proven to be efficacious, these eating regimens offer promising nonpharmacological approaches to improving health at the population level, with multiple public health benefits.

Patterson RE, Sears DD. Metabolic Effects of Intermittent Fasting. Annu Rev Nutr. 2017;37:371-393. doi:10.1146/annurev-nutr-071816-064634

IMPACT OF INTERMITTENT FASTING ON THE LIPID PROFILE: ASSESSMENT ASSOCIATED WITH DIET AND WEIGHT LOSS

Published: Clinical Nutrition ESPEN. April 2018

Intermittent fasting, whose proposed benefits include the improvement of lipid profile and the body weight loss, has gained considerable scientific and popular repercussion. This review aimed to consolidate studies that analyzed the lipid profile in humans before and after intermittent fasting period through a detailed review; and to propose the physiological mechanism, considering the diet and the body weight loss.

Normocaloric and hypocaloric intermittent fasting may be a dietary method to aid in the improvement of the lipid profile in healthy, obese and dyslipidemic men and women by reducing total cholesterol, LDL, triglycerides and increasing HDL levels. However, the majority of studies that analyze the intermittent fasting impacts on the lipid profile and body weight loss are observational based on Ramadan fasting, which lacks large sample and detailed information about diet. Randomized clinical trials with a larger sample size are needed to evaluate the IF effects mainly in patients with dyslipidemia.

Santos HO, Macedo RCO. Impact of intermittent fasting on the lipid profile: Assessment associated with diet and weight loss. Clin Nutr ESPEN. 2018;24:14-21. doi:10.1016/j.clnesp.2018.01.002

IMPACT OF INTERMITTENT FASTING ON THE LIPID PROFILE: ASSESSMENT ASSOCIATED WITH DIET AND WEIGHT LOSS

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EVIDENCE BASED DIET RELATED RESEARCH: KETOGENIC DIET

A diet moderate in proteins (lean meats, fish) and high fats, low in carbohydrates. i.e. healthy fats avocado, nuts, and olive oil.

In absence of circulating blood sugar from food, we start breaking down stored fat into ketone bodies to generate energy.

Difficult to sustain over a long period of time.

HISTORY OF THE KETOGENIC DIET

Date & Journal: Epilepsia . 2008 Nov

Abstract

Fasting and other dietary regimens have been used to treat epilepsy since at least 500 BC. To mimic the metabolism of fasting, the ketogenic diet (KD) was introduced by modern physicians as a treatment for epilepsy in the 1920s. For two decades this therapy was widely used, but with the modern era of antiepileptic drug treatment its use declined dramatically. By the end of the twentieth century this therapy was available in only a small number of children's hospitals. Over the past 15 years, there has been an explosion in the use, and scientific interest in the KD. This review traces the history of one of the most effective treatments for childhood epilepsy.

Wheless JW. History of the ketogenic diet. Epilepsia. 2008;49 Suppl 8:3-5. doi:10.1111/j.1528-1167.2008.01821.x

INFLUENCE OF THE MEDITERRANEAN AND KETOGENIC DIETS ON COGNITIVE STATUS AND DECLINE: A NARRATIVE REVIEW

Date & Journal: Nutrients . 2020 Apr 8.

Abstract

Alzheimer's disease (AD) is the most common form of senile dementia, accounting for up to 70% of dementia cases. AD is a slowly progressive disease, which causes global mental deterioration by affecting various cognitive areas. A growing body of evidence has demonstrated that lifestyle habits and nutritional patterns could delay the natural course of the neurodegeneration process. There is no single dietary pattern unequivocally proven to prevent AD. Nevertheless, epidemiological data suggest that by adopting several dietary habits, especially if accompanied with a healthy lifestyle, the negative consequences of AD could potentially be delayed. Alongside with others, two specific eating patterns have been well investigated concerning their potential beneficial effect on cognitive status: the Mediterranean diet (MedDi) and the Ketogenic Diet (KD). Despite the different underlying mechanisms, both of them have demonstrated a fairly profitable role in reducing or delaying cognitive impairment. The aim of the present narrative review is to overview the existing research on the efficacy of MedDi and KD against AD-related cognitive decline, focusing on the proposed protective mechanisms of action. Although the current knowledge on this complex topic does not allow us, at this point, to make exhaustive conclusions, this information could be of help in order to better characterize the possible role of MedDi and KD as nonpharmacological therapies in the treatment of AD and, more generically, of neurodegenerative disorders.

Vinciguerra F, Graziano M, Hagnäs M, Frittitta L, Tumminia A. Influence of the Mediterranean and Ketogenic Diets on Cognitive Status and Decline: A Narrative Review. Nutrients. 2020;12(4):1019. Published 2020 Apr 8. doi:10.3390/nu12041019

THE KETOGENIC DIET AND SPORT: A POSSIBLE MARRIAGE?

Date & Journal: Exerc Sport Sci Rev. 2015 Jul

Abstract

The ketogenic diet (KD) is used widely as a weight loss strategy and, more rarely, as therapy for some diseases. In many sports, weight control is often necessary (boxing, weightlifting, wrestling, etc.), but the KD usually is not considered. Our hypothesis is that KD might be used to achieve fat loss without affecting strength/power performance negatively.

Paoli A, Bianco A, Grimaldi KA. The Ketogenic Diet and Sport: A Possible Marriage?. Exerc Sport Sci Rev. 2015;43(3):153-162. doi:10.1249/JES.0000000000000050

KETOGENIC DIET IN ALZHEIMER'S DISEASE

Date & Journal: Int J Mol Sci . 2019 Aug 9.

Abstract

At present, the prevalence of Alzheimer's disease, a devastating neurodegenerative disorder, is increasing. Although the mechanism of the underlying pathology is not fully uncovered, in the last years, there has been significant progress in its understanding. This includes: Progressive deposition of amyloid β-peptides in amyloid plaques and hyperphosphorylated tau protein in intracellular as neurofibrillary tangles; neuronal loss; and impaired glucose metabolism. Due to a lack of effective prevention and treatment strategy, emerging evidence suggests that dietary and metabolic interventions could potentially target these issues. The ketogenic diet is a very high-fat, low-carbohydrate diet, which has a fasting-like effect bringing the body into a state of ketosis. The presence of ketone bodies has a neuroprotective impact on aging brain cells. Moreover, their production may enhance mitochondrial function, reduce the expression of inflammatory and apoptotic mediators. Thus, it has gained interest as a potential therapy for neurodegenerative disorders like Alzheimer's disease. This review aims to examine the role of the ketogenic diet in Alzheimer's disease progression and to outline specific aspects of the nutritional profile providing a rationale for the implementation of dietary interventions as a therapeutic strategy for Alzheimer's disease.

Rusek M, Pluta R, Ułamek-Kozioł M, Czuczwar SJ. Ketogenic Diet in Alzheimer's Disease. Int J Mol Sci. 2019;20(16):3892. Published 2019 Aug 9. doi:10.3390/ijms20163892

KETOGENIC DIET AS A METABOLIC THERAPY FOR MOOD DISORDERS: EVIDENCE AND DEVELOPMENTS

Date & Journal: Neurosci Biobehav Rev . 2018 Nov.

Abstract

Despite significant advances in pharmacological and non-pharmacological treatments, mood disorders remain a significant source of mental capital loss, with high rates of treatment resistance, requiring a coordinated effort in investigation and development of efficient, tolerable and accessible novel interventions. Ketogenic diet (KD) is a low-carb diet that substantially changes the energetic matrix of the body including the brain. It has been established as an effective anticonvulsant treatment, and more recently, the role of KD for mental disorders has been explored. Ketogenic diet has profound effects in multiple targets implicated in the pathophysiology of mood disorders, including but not limited to, glutamate/GABA transmission, monoamine levels, mitochondrial function and biogenesis, neurotrophism, oxidative stress, insulin dysfunction and inflammation. Preclinical studies, case reports and case series have demonstrated antidepressant and mood stabilizing effects of KD, however, to date, no clinical trials for depression or bipolar disorder have been conducted. Because of its potential pleiotropic benefits, KD should be considered as a promising intervention in research in mood disorder therapeutics, especially in treatment resistant presentations.

Brietzke E, Mansur RB, Subramaniapillai M, et al. Ketogenic diet as a metabolic therapy for mood disorders: Evidence and developments. Neurosci Biobehav Rev. 2018;94:11-16. doi:10.1016/j.neubiorev.2018.07.020

EVIDENCE BASED DIET RELATED RESEARCH: PLANT BASED NUTRITION

- Focuses on vegetables, fruits, grains (especially whole grains), beans and peas, lentils, nuts, and seeds (rather than on meat, poultry, fish, eggs, and dairy foods). It is not necessarily meatless or vegan. (Plant based burgers.)

- Min. 70% of every plate ate is plant based.



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A PLANT-BASED DIET, ATHEROGENESIS, AND CORONARY ARTERY DISEASE PREVENTION

Date & Journal: Perm J . Winter 2015.

Abstract

A plant-based diet is increasingly becoming recognized as a healthier alternative to a diet laden with meat. Atherosclerosis associated with high dietary intake of meat, fat, and carbohydrates remains the leading cause of mortality in the US. This condition results from progressive damage to the endothelial cells lining the vascular system, including the heart, leading to endothelial dysfunction. In addition to genetic factors associated with endothelial dysfunction, many dietary and other lifestyle factors, such as tobacco use, high meat and fat intake, and oxidative stress, are implicated in atherogenesis. Polyphenols derived from dietary plant intake have protective effects on vascular endothelial cells, possibly as antioxidants that prevent the oxidation of low-density lipoprotein. Recently, metabolites of L-carnitine, such as trimethylamine-N-oxide, that result from ingestion of red meat have been identified as a potential predictive marker of coronary artery disease (CAD).

Tuso P, Stoll SR, Li WW. A plant-based diet, atherogenesis, and coronary artery disease prevention. Perm J. 2015;19(1):62-67. doi:10.7812/TPP/14-036

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PLANT-BASED DIETS: CONSIDERATIONS FOR ENVIRONMENTAL IMPACT, PROTEIN QUALITY, AND EXERCISE PERFORMANCE

Date & Journal: Nutrients . 2018 Dec 1.

Abstract

Plant-based diets provide well-established physical and environmental health benefits. These benefits stem in part from the degree of restriction of animal-derived foods. Historically, meat and other animal-derived proteins have been viewed as an integral component of athletes' diets, leading some to question the adequacy of vegetarian or vegan diets for supporting athletic performance. The purpose of this review is to examine the impact of plant-based diets on human physical health, environmental sustainability, and exercise performance capacity. Based on currently available literature, it is unlikely that plant-based diets provide advantages, but do not suffer from disadvantages, compared to omnivorous diets for strength, anaerobic, or aerobic exercise performance. However, plant-based diets typically reduce the risk of developing numerous chronic diseases over the lifespan and require fewer natural resources for production compared to meat-containing diets. As such, plant-based diets appear to be viable options for adequately supporting athletic performance while concurrently contributing to overall physical and environmental health. Given the sparse literature comparing omnivore, vegetarian, and vegan athletes, particularly at the elite level, further research is warranted to ascertain differences that might appear at the highest levels of training and athletic performance.

Lynch H, Johnston C, Wharton C. Plant-Based Diets: Considerations for Environmental Impact, Protein Quality, and Exercise Performance. Nutrients. 2018;10(12):1841. Published 2018 Dec 1. doi:10.3390/nu10121841

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CARDIO-METABOLIC BENEFITS OF PLANT-BASED DIETS

Date & Journal: Nutrients . 2017 Aug 9.

Abstract

Cardio-metabolic disease, namely ischemic heart disease, stroke, obesity, and type 2 diabetes, represent substantial health and economic burdens. Almost one half of cardio-metabolic deaths in the U.S. might be prevented through proper nutrition. Plant-based (vegetarian and vegan) diets are an effective strategy for improving nutrient intake. At the same time, they are associated with decreased all-cause mortality and decreased risk of obesity, type 2 diabetes, and coronary heart disease. Evidence suggests that plant-based diets may reduce the risk of coronary heart disease events by an estimated 40% and the risk of cerebral vascular disease events by 29%. These diets also reduce the risk of developing metabolic syndrome and type 2 diabetes by about one half. Properly planned vegetarian diets are healthful, effective for weight and glycemic control, and provide metabolic and cardiovascular benefits, including reversing atherosclerosis and decreasing blood lipids and blood pressure. The use of plant-based diets as a means of prevention and treatment of cardio-metabolic disease should be promoted through dietary guidelines and recommendations.

Kahleova H, Levin S, Barnard N. Cardio-Metabolic Benefits of Plant-Based Diets. Nutrients. 2017;9(8):848. Published 2017 Aug 9. doi:10.3390/nu9080848

ASSOCIATION BETWEEN RED MEAT CONSUMPTION AND COLON CANCER: A SYSTEMATIC REVIEW OF EXPERIMENTAL RESULTS

Date & Journal: Exp Biol Med (Maywood) . 2017 Apr.

Abstract

A role for red and processed meat in the development of colorectal cancer has been proposed based largely on evidence from observational studies in humans, especially in those populations consuming a westernized diet. Determination of causation specifically by red or processed meat is contingent upon identification of plausible mechanisms that lead to colorectal cancer. We conducted a systematic review of the available evidence to determine the availability of plausible mechanistic data linking red and processed meat consumption to colorectal cancer risk. Forty studies using animal models or cell cultures met specified inclusion criteria, most of which were designed to examine the role of heme iron or heterocyclic amines in relation to colon carcinogenesis. Most studies used levels of meat or meat components well in excess of those found in human diets. Although many of the experiments used semi-purified diets designed to mimic the nutrient loads in current westernized diets, most did not include potential biologically active protective compounds present in whole foods. Because of these limitations in the existing literature, there is currently insufficient evidence to confirm a mechanistic link between the intake of red meat as part of a healthy dietary pattern and colorectal cancer risk. Impact statement Current recommendations to reduce colon cancer include the reduction or elimination of red or processed meats. These recommendations are based on data from epidemiological studies conducted among cultures where meat consumption is elevated and consumption of fruits, vegetables, and whole grains are reduced. This review evaluated experimental data exploring the putative mechanisms whereby red or processed meats may contribute to colon cancer. Most studies used levels of meat or meat-derived compounds that were in excess of those in human diets, even in cultures where meat intake is elevated. Experiments where protective dietary compounds were used to mitigate the extreme levels of meat and meat-derived compounds showed protection against colon cancer, with some essentially negating the impact of meat in the diet. It is essential that better-designed studies be conducted that use relevant concentrations of meat or meat-derived compounds in complex diets representative of the foods consumed by humans.

Turner ND, Lloyd SK. Association between red meat consumption and colon cancer: A systematic review of experimental results. Exp Biol Med (Maywood). 2017;242(8):813-839. doi:10.1177/1535370217693117

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RED AND PROCESSED MEATS AND HEALTH RISKS: HOW STRONG IS THE EVIDENCE?

Date & Journal: Diabetes Care . 2020 Feb.

Abstract

Prevailing dietary guidelines have widely recommended diets relatively low in red and processed meats and high in minimally processed plant foods for the prevention of chronic diseases. However, an ad hoc research group called the Nutritional Recommendations (NutriRECS) consortium recently issued "new dietary guidelines" encouraging individuals to continue their current meat consumption habits due to "low certainty" of the evidence, difficulty of altering meat eaters' habits and preferences, and the lack of need to consider environmental impacts of red meat consumption. These recommendations are not justified, in large part because of the flawed methodologies used to review and grade nutritional evidence. The evidence evaluation was largely based on the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria, which are primarily designed to grade the strength of evidence for clinical interventions especially pharmacotherapy. However, the infeasibility for conducting large, long-term randomized clinical trials on most dietary, lifestyle, and environmental exposures makes the criteria inappropriate in these areas. A separate research group proposed a modified and validated system for rating the meta-evidence on nutritional studies (NutriGRADE) to address several limitations of the GRADE criteria. Applying NutriGRADE, the evidence on the positive association between red and processed meats and type 2 diabetes was rated to be of "high quality," while the evidence on the association between red and processed meats and mortality was rated to be of "moderate quality." Another important limitation is that inadequate attention was paid to what might be replacing red meat, be it plant-based proteins, refined carbohydrates, or other foods. In summary, the red/processed meat recommendations by NutriRECS suffer from important methodological limitations and involve misinterpretations of nutritional evidence. To improve human and planetary health, dietary guidelines should continue to emphasize dietary patterns low in red and processed meats and high in minimally processed plant foods such as fruits and vegetables, whole grains, nuts, and legumes.

Qian F, Riddle MC, Wylie-Rosett J, Hu FB. Red and Processed Meats and Health Risks: How Strong Is the Evidence?. Diabetes Care. 2020;43(2):265-271. doi:10.2337/dci19-0063

Thank you, Docs!

A brief evaluation survey will be emailed to you in the coming days.
Please fill out the evaluation ASAP & press “submit”.

Hope you enjoyed the seminar and I thank you for your continued support!
We really appreciate all of you!

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