Randomized Controlled Trial

Zhongguo Zhong Xi Yi Jie He Za Zhi

. 2009 Apr;29(4):305-8.

[Effect of Compound Astragalus Recipe on Lymphocyte Subset, Immunoglobulin and Complements in Patients With Myasthenia Gravia]

[Article in Chinese]

Guang-Hua Niu, Xu Sun, Chun-Ming Zhang

Affiliations expand

PMID: 19526753

Abstract

Objective: To investigate the effect and mechanisms of Compound Astragalus Recipe (CAR) for regulating cellular immune in patients with myasthenia gravis (MG).

Methods: Sixty MG patients were equally assigned to two groups randomly, the test group administered with CAR and the control group with prednisone for 3 months. Changes of patients' symptoms and adverse reactions were observed. The peripheral lymphocyte subsets distribution was examined by flow cytometry, and the levels of immunoglobulins and complements in the peripheral blood were measured by immuno-turbidimetry before and after treatment.

Results: The total effective rate in the test group after 12-week treatment reached 80% (24/30), while that of the control group reached 83.3% (25/30), difference between them showed no statistical significance ($P > 0.05$). CD4+ and CD4+/CD8+ ratio were lowered significantly in both groups, but the decrement of CD4+/CD8+ ratio in the test group was more significant than that in the control group, showing significance between groups ($P < 0.05$). While CD8+ in the test group after treatment was significantly increased as compared

with that before treatment (P < 0.05), but with no significant difference in comparing with that in the control group (P > 0.05). Serum levels of IgM and IgA in MG patients were significantly higher than normal range (P < 0.01). Levels of C3 and C4 were significantly increased in both groups after treatment (P < 0.05). Moderate high level of ALT and AST revealed transiently at the 2nd week in 5 patients of the control group, while no adverse reaction was found in the test group.

Conclusion: One of the mechanisms for CAR in playing its immuno-modulate effect may be its regulation on lymphocyte subsets distribution and humoral immune function.

Clinical Trial

Zhongguo Zhong Xi Yi Jie He Za Zhi

. 2003 May;23(5):351-3.

[Effect of Astragalus Injection on Immune Function in Patients With Congestive Heart Failure]

[Article in Chinese]
Zhi-gao Liu[1], Zheng-ming Xiong, Xi-yong Yu
Affiliations expand

- PMID: 12800417

Abstract

Objective: To study the effect of Astragalus Injection (AI) on the humoral immunity (IgG, IgA and IgM), cellular immunity (T-lymphocyte subsets) and soluble interleukin-2 receptor (sIL-2R) in patients with congestive heart failure (CHF).

Methods: Sixty-two in-patients with CHF, whose heart function belonged to NYHA grade II-IV, were randomly divided into two groups. The treated group was treated with AI 30 ml (equivalent to 60 g crude drug), and the control group was treated by nitroglycerine injection 10 mg, the drugs were administered respectively by adding in 5% glucose solution 500 ml for intravenous dripping, once a day, 20 days as one therapeutic course. Venous blood from

cubital vein was collected before and after treatment to detect the IgG, IgA, IgM, T-lymphocyte subsets and sIL-2R, and the clinical effect of treatment was evaluated.

Results: The clinical heart function markedly improved rate and total effective rate in the treated group was 25.8% and 74.2% respectively, significantly better than those in the control group respectively ($P < 0.05$ or $P < 0.01$), the left ventricular ejecting fraction (LVEF) and end syctolic volume (ESV) were improved in both groups ($P < 0.05$, $P < 0.01$), and the improvement in the treated group was superior to that in the control group ($P < 0.05$). In the treated group after treatment, the CD4 level and CD4/CD8 ratio increased ($P < 0.05$), levels of sIL-2R, IgG and IgA lowered ($P < 0.05$) significantly, while those in the control group were not changed significantly ($P > 0.05$).

Conclusion: AI could improve the immune function of CHF patients, and can be taken as an important auxiliary treatment for CHF.

Clinical Trial

Zhongguo Zhong Xi Yi Jie He Za Zhi

. 2001 May;21(5):349-50.

[Observation on Effect of Supplementary Treatment by Astragalus Injection in Treating Senile Pulmonary Tuberculosis Patients]

[Article in Chinese]

H R Niu, Z H Lai, L Yuan
Affiliations expand

PMID: 12577419

Abstract

Objective: To observe the clinical therapeutic supplementary effect of Astragalus injection (ASI) as anti-tuberculosis agents in treating senile tuberculosis (ST).

Methods: Seventy-six ST patients were divided according to their hospitalization order into two groups randomly, 39 in the ASI group and 37 in the control group. The anti-tuberculosis regimen applied on all patients were HRE (S)Z for first treated patients and KHZ1321 TH for retreated patients. In the ASI group, ASI was given additionally by adding ASI 20 ml into 500 ml 5% glucose solution for intravenous dripping, once a day. The therapeutic course was 2 months. The changes of focal size, bacteria in sputum, and erythrocyte immune function (EIF) were observed before and after treatment, and the EIF obtained from 30 healthy subjects was taken for control.

Results: EIF in patients of both groups was lower than that in healthy subjects ($P < 0.01$). Rosette rate of RBC-C3b receptor in both groups was all increased after treatment, the increment was higher in the ASI group than that in the control group significantly ($P < 0.01$). After 2 months ASI treatment, the effective rate of focal absorption examined by X-ray was 84.6% and the negative conversion rate of bacteria in sputum was 79.4%.

Conclusion: ASI has the effect of elevating erythrocyte immunity in senile pulmonary tuberculosis patients, it is able to enhance the therapeutic effect of treatment.

Clinical Trial

Zhongguo Zhong Xi Yi Jie He Za Zhi

. 2004 Feb;24(2):121-3.

[Modulatory Effect of Astragalus Membranaceus on Th1/Th2 Cytokine in Patients With Herpes Simplex Keratitis]

[Article in Chinese]
Su-ping Mao[1], Kai-ling Cheng, Yun-fen Zhou
Affiliations expand

- PMID: 15015443

Abstract

Objective: To explore the influence of Astragalus membranaceus (AM) on serum cytokines, Th1, including interleukin-2 (IL-2) and gamma-interferon (gamma-IFN), and Th2, including interleukin-4 (IL-4) and interleukin-10 (IL-10), in patients with herpes simplex keratitis (HSK).

Methods: One hundred and six HSK patients were randomly divided into the AM treated group and the ribavirin treated group. Levels of serum IL-2, IL-4, IL-10 and gamma-IFN of all the patients and 62 healthy person, selected from donors for control group, were determined by sandwich enzyme-linked immunosorbent assay (ELISA) technique.

Results: Levels of serum IL-4 and IL-10 in HSK patients were significantly higher and those of IL-2 and gamma-IFN were significantly lower than those in the healthy control (all $P < 0.01$). These parameters were significantly improved in the patients of the AM group after treatment, but with no change in patients of the ribavirin group.

Conclusion: AM can modulate the imbalance state of Th1/Th2 in HSK patients, improve their immune function disturbance, that shows important significance in treating HSK.

Randomized Controlled Trial

Zhongguo Zhong Xi Yi Jie He Za Zhi

. 2006 May;26(5):443-5.

[Effects of Radix Astragali Injection on Apoptosis of Lymphocytes and Immune Function in Patients With Systemic Lupus Erythematosus]

[Article in Chinese]

Xiao-yan Cai, Yan-li Xu, Xiao-jun Lin
Affiliations expand

- PMID: 16883914

Abstract

Objective: To investigate the effect of Radix Astragali Injection on apoptosis of lymphocytes and immune function in treating patients with systemic lupus erythematosus (SLE).

Methods: Eighty SLE patients were randomly assigned into the routine treatment group (RT) treated with conventional therapy and the Radix Astragali treated group (RA) treated with Radix Astragali Injection besides routine treatment. The expressions of Fas and Bcl-2 antigen on lymphocytes and the changes of T lymphocyte subsets in peripheral blood before and after treatment were observed.

Results: After treatment, the expression of Fas antigen on lymphocytes significantly lowered ($P < 0.01$), and that of Bcl-2 antigen, CD4+ lymphocyte subset and CD4+ / CD8+ ratio significantly increased in both groups (all $P < 0.01$). However, the changes of Fas antigen expression, CD4+ and CD4+ / CD8+ ratio were more significant in the RA group than those in the RT group ($P < 0.05$).

Conclusion: Radix Astragli Injection can enhance the inhibitory function of corticosteroid/immunosuppressant on apoptosis, and regulate the ratio and function of T lymphocyte subsets to normal range, which may be a useful approach for enhancing the efficacy of treatment to SLE.

Randomized Controlled Trial

Zhongguo Zhong Xi Yi Jie He Za Zhi

. 2011 Nov;31(11):1487-90.

[Effects of Radix Astragali on IL-1beta, TNF-alpha and Antigen Expression of Peripheral Blood Mononuclear Cells in Patients With Graves Disease]

[Article in Chinese]

Juan Wu[1], Dong-fang Liu, Yu Chen
Affiliations expand

PMID: 22303710

Abstract

Objective: To study the effects of Radix Astragali on serum cytokines IL-1beta, TNFalpha and antigen expression of peripheral blood mononuclear cells (PBMCs) in patients with Graves disease (GD).

Methods: Eighty GD patients at their first visit were randomly assigned to the methimazole (MMI) group (Group A) and the MMI combined Radix Astragali group (Group B), 40 in each. The improvement of clinical symptoms and thyroid functions were observed after one-month treatment. The serum IL-1beta and TNF-alpha levels in the peripheral blood were determined using radioimmunoassay. The expression levels of surface antigen CD80, CD54, and HLA-DR of PBMCs were detected using flow cytometry.

Results: The improvement of the thyroid gland function was similar in the two groups. There was no obvious change in the levels of autoantibody TGAb or TPOAb of the two groups. Symptoms such as fear of heat, hidrosis, palpitation, and so on were more obviously improved in Group B than in Group A ($P < 0.05$). The serum IL-betaP, TNFalphaa, CD00 levels in the peripheral blood were all improved in the two groups after treatment when compared with before treatment ($P < 0.05$ or $P < 0.01$). But the serum levels of IL-beta and TNFalpha decreased more obviously in Group B than in Group A ($P < 0.05$). The expression of CD54 decreased more obviously in Group B ($P < 0.01$), showing statistical difference when compared with Group A at the same time point ($P < 0.05$).

Conclusion: Radix Astragali could significantly relieve the clinical symptoms such as hidrosis and palpitation, regulate the immune function of GD patients, playing an important role in the adjuvant therapy for GD.

Clinical Trial

Zhongguo Zhong Xi Yi Jie He Za Zhi

. 1995 Jun;15(6):328-30.

[Effect of Astragalus Membranaceus on T-lymphocyte Subsets in Patients With Viral Myocarditis]

[Article in Chinese]

Z Q Huang[1], N P Qin, W Ye
Affiliations expand

- PMID: 7549379

Abstract

The efficacy of Astragalus membranaceus (AM) oral liquor combined with routine therapy and routine therapy alone on T-lymphocyte subsets of peripheral blood in viral myocarditis patients have been studied. The results showed that the T-lymphocyte subsets profile and OKT4/OKT8 ratio of peripheral blood were significantly lower in viral myocarditis patients than that in healthy control ($P < 0.05, 0.01$). Routine therapy combined with AM could significantly enhance OKT3, OKT4 and OKT4/OKT8 ratio in the above-mentioned patients ($P < 0.05, 0.01$). The possible pharmacodynamic mechanism of improved cell immunity in viral myocarditis patients by combining routine therapy with AM was discussed.

Randomized Controlled Trial

Biomed Mater Eng

. 2015;26 Suppl 1:S2113-21.
doi: 10.3233/BME-151517.

Milkvetch Root Improves Immune Function in Patients With Acute Exacerbation of COPD

Donglin Jiang[1,2], Xu Wang[2], Qiang Su[2], Shengyang Jiang[1], Fenglai Yuan[1], Caidi Zhang[2], Fang Gong[1], Qiaojing Dong[2], Jianping Shi[2], Baohua Chen[2]
Affiliations expand

- PMID: 26405990

- DOI: 10.3233/BME-151517

Abstract

Milkvetch root as a medicine has been used for more over 2000 years in China, can strengthen immune function, protect liver, promote urination, resist aging and stress, reduce blood pressure and extensively resist bacterium. This study explored the effects of milkvetch root on the immune function of patients with a definitive diagnosis of acute exacerbation of chronic obstructive pulmonary disease (COPD). The patients were randomly assigned to either the experimental or control group. All patients received conventional clinical therapy; those in the experimental group were also administered milkvetch root. The serum levels of cytokines including tumor necrosis factor alpha (TNF-α), interleukin-8 (IL-8), IL-1β, and IL-32 and immunocytes including T helper (Th), cytotoxic T (Tc), natural killer (NK), regulatory T (Treg) and B cells were measured 1 day before treatment and 7 and 14 days post-treatment. After bronchodilator inhalation, pulmonary function was evaluated at these same time points. The serum TNF-α, IL-8, IL-1β, and IL-32 levels were significantly lower in the experimental group than in the control group 14 days post-treatment. The Th/Tc ratio and NK cell ratio was significantly higher but the Treg cell ratio was significantly lower in the experimental group than in the control group. The forced expiratory volume in 1 second (FEV1) and FEV1/forced vital capacity (FVC) were significantly higher in the experimental group than in the control group 14 days post-treatment. These results indicate that milkvetch root can improve the immune function of patients with acute exacerbation of COPD.

ASTRAGALUS PRECLINICAL TRIALS

Review

Integr Cancer Ther

. 2003 Sep;2(3):247-67.
doi: 10.1177/1534735403256419.

Immune System Effects of Echinacea, Ginseng, and Astragalus: A Review

Keith I Block[1], Mark N Mead
Affiliations expand

PMID: 15035888

- DOI: 10.1177/1534735403256419

Abstract

Traditional herbal medicine provides several remedies for strengthening the body's resistance to illness through effects on immune system components. This review article examines 3 popular herbal immune stimulants that are often of interest to cancer patients. Echinacea, a native of North America, is widely used to prevent, or provide early treatment for, colds. Preclinical studies lend biological plausibility to the idea that echinacea works through immune mechanisms. Numerous clinical trials have been carried out on echinacea preparations: it appears that the extracts shorten the duration and severity of colds and other upper respiratory infections (URIs) when given as soon as symptoms become evident. However, trials of long-term use of echinacea as a preventive have not shown positive results. Ginseng has been studied in some depth as an antifatigue agent, but studies of immune mechanisms have not proceeded so far. Preclinical evidence shows some immune-stimulating activity. There have been several clinical trials in a variety of different diseases. Astragalus is the least-studied agent. There are some preclinical trials that show intriguing immune activity. The herbs discussed appear to have satisfactory safety profiles. Cancer patients may wish to use these botanicals to inhibit tumor growth or to boost resistance to infections. However, passive immunotherapy with herbs, with no mechanism to expose tumor antigens, is unlikely to be effective in inhibiting tumor growth. Although the margin of safety for these herbs is large, more research is needed to demonstrate the clear value of using herbs to improve resistance to infections.

ASTRAGALUS AND ANTIOXIDANT

Curr Drug Targets. 2016;17(12):1331-40.

The Antioxidant Effects of Radix Astragali (Astragalus membranaceus and Related Species) in Protecting Tissues from Injury and Disease.

Shahzad M, Shabbir A, Wojcikowski K, Wohlmuth H, Gobe GC[1].
Author information

Abstract

Oxidative stress plays a key role in the pathogenesis of various diseases. Antioxidants protect the cells and tissues from oxidative stress by scavenging free radicals and reactive oxygen species. These antioxidants may

be endogenous or exogenous. Plants are considered as potential and powerful exogenous source of antioxidants. Astragalus species (spp.), especially Astragalus membranaceus, have a long history of medicinal use in traditional Chinese medicine. Specifically, constituents of the dried roots of Astragalus spp. (Radix Astragali) provide significant protection against heart, brain, kidney, intestine, liver and lung injury in various models of oxidative stress-related disease. Different isolated constituents of Astragalus spp., such as astragalosides, flavonoids and polysaccharides also displayed significant prevention of tissue injury via antioxidant mechanisms. In this article, the antioxidant benefits of Astragalus spp. and its isolated components in protecting tissues from injury are reviewed, along with identification of the various constituents that possess antioxidant activity.

ASTRAGALUS IN VITRO

Phytother Res

. 2018 Aug;32(8):1521-1529.
doi: 10.1002/ptr.6080. Epub 2018 Apr 19.

Astragalus Polysaccharides Exerts Anti-Infective Activity by Inducing Human Cathelicidin Antimicrobial Peptide LL-37 in Respiratory Epithelial Cells

Lin Zhao[1], Shuai Tan[1], Hai Zhang[2], Peng Liu[3], Yu-Zhu Tan[2], Jia-Chuan Li[4], Da Jia[1], Xiao-Fei Shen[1]
Affiliations expand

- PMID: 29672953

- DOI: 10.1002/ptr.6080

Abstract

Astragalus polysaccharides (APS), one of the major active components in Astragalus membranaceus, is an effective immunomodulator used in the treatment of immunological diseases in China. However, the anti-infective action and mechanism of APS is not fully known. In the present study, we found that APS induced the expression of human cathelicidin antimicrobial peptide LL-37, a key host anti-infective molecule, in both mRNA and protein levels in respiratory epithelial cells HBE16 and A549. Furthermore, the lysate and supernatant from APS-treated HBE16 cells both exhibited an obvious antibacterial action, which was partially neutralizated by LL-37 monoclonal antibody. In addition, APS also significantly elevated the phosphorylation of p38 MAPK and JNK and caused the degradation of IκBα. Specific inhibitors of p38 MAPK, JNK, or NF-κB obviously abolished APS-induced LL-37 synthesis and antibacterial activity, respectively. Taken together, our results confirmed the enhancement of APS on LL-37 induction and antibacterial action in respiratory epithelial cells, which may be attributed to activation of p38 MAPK/JNK and NF-κB pathways. Furthermore, these results also supported the clinical application of APS in the treatment of infectious diseases.

Evid Based Complement Alternat Med

. 2019 Dec 31;2019:2971604.
doi: 10.1155/2019/2971604.eCollection 2019.

Astragalus Membranaceus Treatment Protects Raw264.7 Cells From Influenza Virus by Regulating G1 Phase and the TLR3-Mediated Signaling Pathway

Yuxi Liang[1], Qiuyan Zhang[1], Linjing Zhang[1], Rufeng Wang[1], Xiaoying Xu[2], Xiuhua Hu[1]
Affiliations expand

- PMID: 31975996

- PMCID: PMC6955127

- DOI: 10.1155/2019/2971604

Abstract

Influenza is an acute respiratory infection disease caused by the influenza virus. At present, due to the high mutation rate of influenza virus, it is difficult for the existing antiviral drugs to play an effective antiviral effect continually, so it is urgent to develop a new anti-influenza drug. Recently, more and more studies have been conducted on the antiviral activity of *Astragalus membranaceus*, but the specific antiviral mechanism of this traditional Chinese medicine is not clear. In this study, the results proved that the *Astragalus membranaceus* injection showed obvious anti-influenza virus activity. It could improve the survival rate of Raw264.7 cells which were infected with influenza virus, while it improved the blocking effect of influenza virus on cell cycle after infection, increased the SOD activity, and reduced the MDA content. At the same time, the innate immunity was affected by regulating the expression of TLR3, TAK1, TBK1, IRF3, and IFN-β in the TLR3-mediated signaling pathway, thus exerting its antiviral effect in vitro.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6955127/

ASTRAGALUS ANIMAL STUDIES

J Anim Sci Biotechnol

. 2013 Jun 21;4(1):22.
doi: 10.1186/2049-1891-4-22.

Astragalus Polysaccharide Enhances Immunity and Inhibits H9N2 Avian Influenza Virus in Vitro and in Vivo

Sanpha Kallon[#1], Xiaorong Li[#1], Jun Ji[1], Cuiying Chen[1], Qianyun Xi[1], Shuang Chang[2], Chunyi Xue[3], Jingyun Ma[1], Qingmei Xie[1], Youngliang Zhang[1]
Affiliations expand

- PMID: 23786718

- PMCID: PMC3729712

- DOI: 10.1186/2049-1891-4-22

Abstract

This study investigated the humoral immunization of Astragalus polysaccharide (APS) against H9N2 avian influenza virus (H9N2 AIV) infection in chickens.The effects of APS treatment on H9N2 infection was evaluated by an MTT [3(4, 5-dimethylthiazol-2-yl)-2, 3-diphenyl tetrazolium bromide] assay and analysis of MHC and cytokine mRNA expression. The effect on lymphocyte and serum antibody titers in vivo was also investigated. IL-4, IL-6, IL-10, LITAF, IL-12 and antibody titers to H9N2 AIV were enhanced in the first week after APS treatment. The results indicated that APS treatment reduces H9N2 AIV replication and promotes early humoral immune responses in young chickens.

ASTRAGALUS NULL EVIDENCE

Review

Cochrane Database Syst Rev

. 2016 Dec 1;12(12):CD011958.
doi: 10.1002/14651858.CD011958.pub2.

Oral Astragalus (Huang Qi) for Preventing Frequent Episodes of Acute Respiratory Tract Infection in Children

Guobin Su[1,2], Xiankun Chen[3], Zhuangzhu Liu[1,4], Lihong Yang[5], La Zhang[1], Cecilia Stålsby Lundborg[2], Zehuai Wen[6], Xinfeng Guo[5], Xindong Qin[1], Jueyao Liang[7], Xusheng Liu[1]
Affiliations expand

- PMID: 27905672

- PMCID: PMC6463872

- DOI: 10.1002/14651858.CD011958.pub2

Abstract

Background: Acute respiratory tract infections (ARTIs) are common in children and can involve both upper and lower airways. Many children experience frequent ARTI episodes or recurrent respiratory tract infections (RRTIs) in early life, which creates challenges for paediatricians, primary care physicians, parents and carers of children.In China, Astragalus (Huang qi), alone or in combination with other herbs, is used by Traditional Chinese Medicine (TCM) practitioners in the form of a water extract, to reduce the risk of ARTIs; it is believed to stimulate the immune system. Better understanding of the therapeutic mechanisms of Astragalus may provide insights into ARTI prevention, and consequently reduced antibiotic use.

Objectives: To assess the effectiveness and safety of oral Astragalus for preventing frequent episodes of acute respiratory tract infections (ARTIs) in children in community settings.

Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 12, 2015), MEDLINE (Ovid) (1946 to 31 December 2015), Embase (Elsevier) (1974 to 31 December 2015), AMED (Ovid) (1985 to 31 December 2015), Chinese National Knowledge Infrastructure (CNKI) (1979 to 31 December 2015) and Chinese Scientific Journals full text database (CQVIP) (1989 to 31 December 2015), China Biology Medicine disc (CBM 1976 to 31 December 2015) and Wanfang Data Knowledge Service Platform (WanFang) (1998 to 31 December 2015).

Selection criteria: We included randomised controlled trials (RCTs) comparing oral Astragalus as a sole Chinese herbal preparation with placebo to prevent frequent episodes of ARTIs in children.

Data collection and analysis: We used standard Cochrane methodological procedures for this review. We assessed search results to identify relevant studies. We planned to extract data using standardised forms. Disagreements were to be resolved through discussion. Risk of bias was to be assessed using the Cochrane 'Risk of bias' tool. We planned to use mean difference (MD) or standardised mean difference (SMD) for continuous data and risk ratio (RR) or odds ratio (OR) to analyse dichotomous data, both with 95% confidence intervals (CIs).

Main results: We identified 6080 records: 3352 from English language databases, 2724 from Chinese databases, and four from other sources. Following initial screening and deduplication, we obtained 120 full-text papers for assessment. Of these, 21 were not RCTs; 55 did not meet the

inclusion criteria because: participants were aged over 14 years; definition was not included for recurrent or frequent episodes;Astragalus preparation was not an intervention; Astragalus preparation was in the formula but was not the sole agent; the Astragalus preparation was not administered orally; or Astragalus was used for treatment rather than prevention of ARTI. A further 44 studies were excluded because they were not placebo-controlled, although other inclusion criteria were fulfilled.No RCTs met our inclusion criteria.

Authors' conclusions: We found insufficient evidence to enable assessment of the effectiveness and safety of oral Astragalus as a sole intervention to prevent frequent ARTIs in children aged up to 14 years.

EPICOR

J Med Food. 2011 Sep;14(9):1002-10. doi: 10.1089/jmf.2010.0174. Epub 2011 Apr 18.

Antioxidant bioavailability and rapid immune-modulating effects after consumption of a single acute dose of a high-metabolite yeast immunogen: results of a placebo-controlled double-blinded crossover pilot study.

Jensen GS[1], Redman KA, Benson KF, Carter SG, Mitzner MA, Reeves S, Robinson L.

Author information

Abstract

The objective of this pilot study was to investigate the acute effects on circulating lymphocyte subsets, antioxidant status, and cytokine profile after consumption of EpiCor(®) (EP) (Embria Health Sciences, Ankeny, IA, USA), a dried fermentate produced from Saccharomyces cerevisiae, using a placebo-controlled randomized crossover study design with 12 healthy adult human subjects. EP contains high levels of bioavailable antioxidants and strongly activates natural killer (NK) cells in vitro. EP consumption has been shown to increase erythrocyte hematocrit levels, boost mucosal immune protection, reduce cold/flu symptoms, reduce seasonal allergy symptoms and the need for rescue medication, and increase salivary secretory immunoglobulin A levels. This warranted further study on immune effects in humans. A within-subject analysis of data collected before and at 1 and 2 hours after consumption of a single dose of 500 mg of EP versus placebo was performed. A transient reduction in circulating T and NK cell numbers was observed 2 hours post-consumption, suggesting that homing and recirculation of these cells, as part of healthy immune surveillance, were supported by EP. The increased expression of activation markers on the CD3(-) CD56(+) NK cell population was significant for CD69 at 1 hour post-consumption (CD25, P<.07; CD69, P<.05), whereas for CD25 it was significant at 2 hours after consumption (CD25, P<.03; CD69, P<.15). A rapid increase in

serum interferon-γ was observed at 1 hour post-consumption (P<.07; after removal of two outlying data sets, P<.05) and may have contributed to the effects seen on NK and T cell subsets. Significant increase in serum antioxidant protection was seen 2 hours after consumption (P<.04). Thus consumption of a single 500 mg dose of EP provides a rapid and transient effect on the trafficking and activation status of specific lymphocyte subsets, as well as increased antioxidant protection.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157306/

Evid Based Complement Alternat Med. 2012;2012:973041. doi: 10.1155/2012/973041. Epub 2012 Apr 5.

A dried yeast fermentate prevents and reduces inflammation in two separate experimental immune models.

Evans M[1], Reeves S, Robinson LE.

Author information

Abstract

Diverse and significant benefits against cold/flu symptoms and seasonal allergies have been observed with a dried fermentate (DF) derived from Saccharomyces cerevisiae (EpiCor) in multiple published randomized trials. To determine if DF may influence other immune conditions, two separate animal studies were conducted. Study 1 examined the ability of DF to prevent or reduce inflammation when given orally for 14 days to rats prior to receiving 1% carrageenan (localized inflammation model). DF significantly ($P < 0.05$) reduced swelling at all time points (1, 2, 3, 6, 12, and 24 hours) versus the control. Edema severity and PGE2 levels were reduced by approximately 50% and 25% ($P < 0.05$), respectively. Study 2 examined the ability of DF to treat established inflammation induced by type-2 collagen in mice over 4 weeks (autoimmune arthritis model). Significantly reduced arthritis scores, antibody response to type-2 collagen, and interferon-gamma levels were observed compared to controls (all parameters $P < 0.05$). DF favorably impacts multiple acute and potentially chronic immunologic inflammatory control mechanisms and should be further tested in clinical trials.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3328167/

J Altern Complement Med. 2010 Feb;16(2):213-8. doi: 10.1089/acm.2009.0310.

Immunogenic yeast-based fermentate for cold/flu-like symptoms in nonvaccinated individuals.

Moyad MA[1], Robinson LE, Zawada ET, Kittelsrud J, Chen DG, Reeves SG, Weaver S.

Author information

Abstract

BACKGROUND:

The common cold has a profound impact on employee attendance and productivity. Seasonal influenza is responsible for approximately 200,000 hospitalizations and 36,000 deaths per year in the United States alone. Over-the-counter medication efficacy has been questioned, and seasonal vaccination compliance issues abound. Our previously reported randomized trial of an oral fermentation product found an adjuvant benefit for vaccinated individuals in terms of a significantly reduced incidence and duration of cold and flu-like symptoms.

METHODS:

A concurrent 12-week, randomized, double-blind, placebo-controlled clinical trial of 116 subjects with no recent history of seasonal influenza vaccination was conducted. Participants received once-daily supplementation with 500 mg of a dried modified Saccharomyces cerevisiae oral fermentate (EpiCor) or placebo. Clinical outcome measurements included periodic interval-based in-clinic examinations and serologic analysis at baseline, 6 weeks, and 12 weeks. Participants utilized a standardized self-report symptom diary.

RESULTS:

Subjects receiving the intervention experienced a statistically significant reduction in the incidence ($p = 0.01$), a nonsignificant reduction in duration ($p = 0.10$), and no impact on the severity ($p = 0.90$) of colds or flu-like symptoms, but a more favorable safety profile compared with subjects receiving placebo.

CONCLUSIONS:

This nutritional-based fermentate appeared to be safe and efficacious in a unique at-risk population and should receive more clinical research as a potential method to reduce the incidence of cold and flu-like symptoms, in individuals with and without a history of influenza vaccination.

See PubMed for full article.

Adv Ther. 2009 Aug;26(8):795-804. doi: 10.1007/s12325-009-0057-y. Epub 2009 Aug 12.

Immunogenic yeast-based fermentation product reduces allergic rhinitis-induced nasal congestion: a randomized, double-blind, placebo-controlled trial.

Moyad MA[1], Robinson LE, Kittelsrud JM, Reeves SG, Weaver SE, Guzman AI, Bubak ME.
Author information

Abstract

INTRODUCTION:

Allergic rhinitis (AR) impacts around 25% of the worldwide population. However, cost, safety, and a high dissatisfaction rate with numerous conventional medications continues to be an issue in the largest patient surveys, due primarily to a lack of efficacy on nasal congestion. Our previously published randomized trial demonstrated a significant reduction in cold and flu-like symptoms, and a secondary potential observation of a decrease in nasal congestion with an oral yeast-derived compound; therefore, the objective of this study was to test the effects of this same product on nasal congestion and other notable AR symptoms.

METHODS:

A 12-week, randomized, double-blind, placebo-controlled clinical trial of 96 healthy subjects with a recent clinically documented history of seasonal allergies and AR was conducted. Participants received once-daily supplementation with 500 mg of a dried, modified Saccharomyces cerevisiae oral fermentation product (EpiCor, Embria Health Sciences, Ankeny, Iowa, USA) or placebo during the 12-week period of the highest recorded concentrations of total pollen counts for this Midwest geographic area. Clinical outcome measurements included in-clinic examinations, validated questionnaire and standard diary, and serologic analysis at baseline, 6 and 12 weeks.

RESULTS:

During the highest pollen count period (weeks 1-6), EpiCor significantly reduced the mean severity of specific AR symptoms, including a significant reduction in nasal congestion (P=0.04), rhinorrhea (P=0.005), and a nonsignificant reduction in ocular discharge symptoms. A significantly (P=0.04) reduced total number of days with nasal congestion (12.5 fewer days) favored EpiCor compared with placebo, as did the nasal congestion section of the quality of life questionnaire (P=0.04). Subjects receiving the intervention also experienced significantly (P=0.03) higher salivary IgA levels. Adverse events were similar to placebo.

CONCLUSION:

This yeast-derived product appeared to be safe and efficacious, and should receive more clinical research with and without standard medications to reduce the impact of seasonal allergies, especially AR-induced nasal congestion.

Urol Nurs. 2008 Apr;28(2):146-8, 145.

Lessons learned from the 2007-2008 cold and flu season: what worked and what was worthless.

Moyad MA[1], Robinson LE.

Author information

Abstract

The 2007-2008 cold and flu season had a feeble beginning but a dramatic end. Most states in the U.S. were reporting their highest number of flu cases well into February and March. It is concerning that not only the public but health care professionals have not embraced widespread vaccination because approximately 200,000 hospitalizations and 36,000 deaths a year continue to make this condition one of the leading preventable causes of morbidity and mortality. The real question that needs to be asked next year is who should not be vaccinated rather than who needs to be vaccinated. Preventive measures with soap and water and 62% ethyl alcohol hand gels continue to make sense, whereas the antibacterial soaps seem to provide no added protection and theoretically increase the risk of bacterial resistance. A few dietary supplements garnered some attention. Among products with clinical research, an oral 500 mg qd immunogenic fermentate (Epicor) reduced the risk and duration of cold and flu symptoms in subjects vaccinated for seasonal influenza. Two novel prescription medications (zanamivir [Relenza], and oseltamivir [Tamiflu]) are available for the prevention and/or treatment of influenza and also have demonstrated minimal resistance compared to the older medications. These FDA-approved medications should receive more attention because of their overall effectiveness in treating the flu during the first stages of the disease process.

Urol Nurs. 2008 Feb;28(1):50-5.

Effects of a modified yeast supplement on cold/flu symptoms.

Moyad MA[1], Robinson LE, Zawada ET Jr, Kittelsrud JM, Chen DG, Reeves SG, Weaver SE.

Author information

Abstract

A yeast-based product (EpiCor, a dried Saccharomyces cerevisiae fermentate) was compared to placebo to determine effects on the incidence and duration of cold and flu-like symptoms in healthy subjects recently vaccinated for seasonal influenza. In a 12-week, randomized, double-blind, placebo-controlled clinical trial, 116 participants received daily supplementation with 500 mg of EpiCor or placebo for 12 weeks. Data collected included periodic in-clinic examinations and serologic evaluations at baseline, 6- and 12-weeks. Subjects also utilized a standardized self-report symptom diary during the study. Participants receiving the yeast-based product had significantly fewer symptoms and significantly shorter duration of symptoms when compared with subjects taking a placebo.

Randomized Controlled Trial

Nutrients

. 2019 Feb 9;11(2):358.
doi: 10.3390/nu11020358.

The Effect of Olive Leaf Extract on Upper Respiratory Illness in High School Athletes: A Randomised Control Trial

Vaughan Somerville [1], Rachel Moore [2], Andrea Braakhuis [3]
Affiliations expand

- PMID: 30744092
- PMCID: PMC6412187
- DOI: 10.3390/nu11020358

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.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6412187/

OLIVE LEAF IN VITRO STUDIES

Comparative Study

Endocr Metab Immune Disord Drug Targets

. 2018;18(1):85-93.
doi: 10.2174/1871530317666171116110537.

Olive Leaf Extracts Act as Modulators of the Human Immune Response

Thea Magrone[1], Anna Spagnoletta[1], Rosaria Salvatore[1], Manrico Magrone[1], Francesco Dentamaro[2], Matteo A Russo[3], Graziana Difonzo[4], Carmine Summo[4], Francesco Caponio[4], Emilio Jirillo[1]
Affiliations expand

- PMID: 29149822

- DOI: 10.2174/1871530317666171116110537

Abstract

Background: Olive tree leaves have been used in the Mediterranean area as traditional medicine in virtue of their healthy effects. Olive leaf extracts (OLEs) contain higher amounts of polyphenols than those detected in the extra virgin olive oil and fruit. Several lines of evidence support the cardioprotective, anti-oxidant and anti-inflammatory activities exerted by OLEs.

Methods: Peripheral blood mononuclear cells from twenty-five healthy donors were cultured in the presence of 3 µg of two OLE extracts, extract A (resuspended in water) and extract B (resuspended in 70% ethanol). After harvesting, cell pellets were used for cytofluorimetric phenotyping, while supernatants were assayed for cytokine release by means of ELISA. Furthermore, in the same supernatants nitric oxide (NO) content was determined.

Results: Both extracts, but especially extract A, increased absolute numbers of CD8+ and natural killer (NK) cells. In addition, an increased production of interferon (IFN)-γ by both extracts as an expression of T helper (h)1 activation was observed. Finally, both extracts enhanced NO release.

Conclusion: OLEs, and mostly extract A, are able to in vitro modify healthy human immune response by increasing IFN-γ production which seems to be associated to the higher absolute numbers of CD8+ and NK cells and this may suggest a reinforcement of the anti-tumor activity. Furthermore, increased levels of NO may indicate the potential cardioprotective effects exerted by OLEs in virtue of their vasodilation dependent activity. Finally, OLEs are able to maintain the equilibrium between T regulatory cells and Th17 cells as evidenced by unmodified levels of interleukin (IL)-IL-10 and IL-17, respectively. In the light of these results, OLEs are potential therapeutic compounds for the treatment of chronic inflammatory disease, also preventing cardiovascular event outcome.

Biochem Biophys Res Commun

. 2003 Aug 8;307(4):1029-37.
doi: 10.1016/s0006-291x(03)01292-0.

Anti-HIV Activity of Olive Leaf Extract (OLE) and Modulation of Host Cell Gene Expression by HIV-1 Infection and OLE Treatment

Sylvia Lee-Huang[1], Li Zhang, Philip Lin Huang, Young-Tae Chang, Paul L Huang
Affiliations expand

- PMID: 12878215

- DOI: 10.1016/s0006-291x(03)01292-0

Abstract

We investigated the antiviral activity of olive leaf extract (OLE) preparations standardized by liquid chromatography-coupled mass spectrometry (LC-MS) against HIV-1 infection and replication. We find that OLE inhibits acute infection and cell-to-cell transmission of HIV-1 as assayed by syncytia formation using uninfected MT2 cells co-cultured with HIV-1-infected H9 T lymphocytes. OLE also inhibits HIV-1 replication as assayed by p24 expression in infected H9 cells. These anti-HIV effects of OLE are dose dependent, with EC(50)s of around 0.2 microg/ml. In the effective dose range, no cytotoxicity on uninfected target cells was detected. The therapeutic index of OLE is above 5000. To identify viral and host targets for OLE, we characterized gene expression profiles associated with HIV-1 infection and OLE treatment using cDNA microarrays. HIV-1 infection modulates the expression patterns of cellular genes involved in apoptosis, stress, cytokine, protein kinase C, and hedgehog signaling. HIV-1 infection up-regulates the expression of the heat-shock proteins hsp27 and hsp90, the DNA damage inducible transcript 1 gadd45, the p53-binding protein mdm2, and the hedgehog signal protein patched 1, while it down-regulates the expression of the anti-apoptotic BCL2-associated X protein Bax. Treatment with OLE reverses many of these HIV-1 infection-associated changes. Treatment of HIV-1-infected cells with OLE also up-regulates the expression of the apoptosis inhibitor proteins IAP1 and 2, as well as the calcium and protein kinase C pathway signaling molecules IL-2, IL-2Ralpha, and ornithine decarboxylase ODC1.

OLIVE LEAF EXTRACT MECHANISM OF ACTION

Randomized Controlled Trial

Int J Mol Sci

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. 2016 Dec 2;17(12):2019.
doi: 10.3390/ijms17122019.

Human Intervention Study to Assess the Effects of Supplementation With Olive Leaf Extract on Peripheral

Blood Mononuclear Cell Gene Expression

Anna Boss [1], Chi Hsiu-Juei Kao [2 3], Pamela M Murray [4], Gareth Marlow [5], Matthew P G Barnett [6], Lynnette R Ferguson [7 8]
Affiliations expand

- PMID: 27918443

- PMCID: PMC5187819

- DOI: 10.3390/ijms17122019

Abstract

Olive leaf extract (OLE) has been used for many years for its putative health benefits, but, to date, scientific evidence for the basis of these effects has been weak. Although recent literature has described a link between ailments such as cardiovascular disease, diabetes and cancer and a protective effect of polyphenols in the OLE, the mode of action is still unclear. Here, we describe a double-blinded placebo (PBO)-controlled trial, in which gene expression profiles of peripheral blood mononuclear cells from healthy male volunteers (*n* = 29) were analysed to identify genes that responded to OLE, following an eight-week intervention with 20 mL daily consumption of either OLE or PBO. Differences between groups were determined using an adjusted linear model. Subsequent analyses indicated downregulation of genes important in inflammatory pathways, lipid metabolism and cancer as a result of OLE consumption. Gene expression was verified by real-time PCR for three genes (*EGR1*, *COX-2* and *ID3*). The results presented here suggest that OLE consumption may result in health benefits through influencing the expression of genes in inflammatory and metabolic pathways. Future studies with a larger study group, including male and female participants, looking into direct effects of OLE on lipid metabolism and inflammation are warranted.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5187819/

ASTRAGALUS, GARLIC, OLIVE LEAF, NAC ETC.

Review

Altern Med Rev

. 2007 Mar;12(1):25-48.

Colds and Influenza: A Review of Diagnosis and Conventional, Botanical, and Nutritional Considerations

Mario Roxas [1], Julie Jurenka
Affiliations expand

PMID: 17397266

Abstract

The common cold is the leading cause of doctor visits in the United States and annually results in 189 million lost school days. In the course of one year the U.S. population contracts approximately 1 billion colds. Influenza infection is still a leading cause of morbidity and mortality, accounting for 20-25 million doctor visits and 36,000 deaths per year in the United States. Conventional therapies for colds and flu focus primarily on temporary symptom relief and include over-the-counter antipyretics, anti-inflammatories, and decongestants. Treatment for influenza also includes prescription antiviral agents and vaccines for prevention. This article reviews the common cold and influenza viruses, presents the conventional treatment options, and highlights select botanicals (Echinacea spp., Sambucus nigra, larch arabinogalactan, Astragalus membranaceous, Baptisia tinctoria, Allium sativa, Panax quinquefolium, Eleutherococcus senticosus, Andrographis paniculata, olive leaf extract, and Isatis tinctoria) and nutritional considerations (vitamins A and C, zinc, high lactoferrin whey protein, N-acetylcysteine, and DHEA) that may help in the prevention and treatment of these conditions.

Although clinical research examining garlic's effect on colds and flu is minimal, one study did evaluate an allicin-containing garlic supplement on cold incidence and duration in 146 volunteers. Subjects received one capsule daily for 12 weeks between November and February, and symptoms were assessed via a symptom diary using a five-point scale. In the garlic-supplemented group, 24 colds were reported compared to 65 in the placebo group; the treatment group experience shorter duration of cold symptoms compared to placebo – 1.5

versus 5.0 days, respectively.[144]

Olive Leaf Extract

Constituents of the olive tree, Olea europaea, have been studied and utilized in folk medicine for centuries. Olive leaf extract, derived from the leaves of the olive tree, contains phenolic compounds, specifically oleuropein, that have demonstrated potent antimicrobial, antioxidant, and anti-inflammatory activity.

Oleuropein and derivatives such as elenolic acid have been shown to be effective in in vitro and animal studies against numerous microorganisms, including retroviruses, coxsackie viruses,[150] influenza, and parainfluenza 3,[150,151] as well as some bacteria.[152] Research suggests that olive leaf constituents interact with the protein of virus particles and reduce the infectivity and inhibit replication of viruses known to cause colds, influenza, and lower respiratory infection.[150,151,153] Olive leaf extract has also been shown to stimulate phagocytosis, thereby enhancing the immune response to viral infection. Anecdotal reports indicate olive leaf extract taken at the onset of cold or flu symptoms prevents or shortens the duration of the disease. For viral sore throats, gargling with olive leaf tea may alleviate symptoms, possibly by decreasing inflammation and viral infectivity.

Astragalus (Astragalus membranaceus)

Astragalus membranaceus has traditionally been used as a tonic and treatment for colds and flu, either alone or in conjunction with other herbs.[154] Astragalus is rich in polysaccharides, flavonoids, multiple trace minerals, and amino acids, all of which contribute to its immuno-supportive properties. Animal studies demonstrated oral administration of Astragalus root extract to mice infected with Japanese encephalitis virus increased survival rates by 30-40 percent compared to 20 percent in the untreated control group.[155] The researchers attribute this to increased phagocytic activity.

In a small, double-blind, placebo-controlled trial participants took oral extracts of Echinacea purpurea, Astragalus membranaceus, or Glycyrrhiza glabra singly, a combination of the three herbs, or placebo twice daily for seven days, to determine whether intake of the herbal tinctures (singly and/or in combination) stimulated activation and/or proliferation of immune cells. Of the herbs tested, Astragalus demonstrated the strongest activation and proliferation of immune cells, particularly CD8 and CD4 T-cells, compared to placebo. Furthermore, the combination herbal formula demonstrated an additive effect regarding activation, but not proliferation, of T-cells.[156]

ACS Omega

. 2020 Mar 31;5(14):8312-8320.
doi: 10.1021/acsomega.0c00772.eCollection 2020 Apr 14.

Investigation Into SARS-CoV-2 Resistance of Compounds in Garlic Essential Oil

Bui Thi Phuong Thuy [1], Tran Thi Ai My [2], Nguyen Thi Thanh Hai [2], Le Trung Hieu [2], Tran Thai Hoa [2], Huynh Thi Phuong Loan [2], Nguyen Thanh Triet [3], Tran Thi Van Anh [4], Phan Tu Quy [5], Pham Van Tat [6], Nguyen Van Hue [7], Duong Tuan Quang [8], Nguyen Tien Trung [9], Vo Thanh Tung [10], Lam K Huynh [11 12], Nguyen Thi Ai Nhung [2]
Affiliations expand

- PMID: 32363255

- PMCID: PMC7123907

- DOI: 10.1021/acsomega.0c00772

Abstract

Eighteen active substances, including 17 organosulfur compounds found in garlic essential oil (T), were identified by GC-MS analysis. For the first time, using the molecular docking technique, we report the inhibitory effect of the considered compounds on the host receptor angiotensin-converting enzyme 2 (ACE2) protein in the human body that leads to a crucial foundation about coronavirus resistance of individual compounds on the main protease (PDB6LU7) protein of SARS-CoV-2. The results show that the 17 organosulfur compounds, accounting for 99.4% contents of the garlic essential oil, have strong interactions with the amino acids of the ACE2 protein and the main protease PDB6LU7 of SARS-CoV-2. The strongest anticoronavirus activity is expressed in allyl disulfide and allyl trisulfide, which account for the highest content in

the garlic essential oil (51.3%). Interestingly, docking results indicate the synergistic interactions of the 17 substances, which exhibit good inhibition of the ACE2 and PDB6LU7 proteins. The results suggest that the garlic essential oil is a valuable natural antivirus source, which contributes to preventing the invasion of coronavirus into the human body.

BERBERINE AND H. PYLORI

Clinical Trial

Medicine (Baltimore)

. 2017 Aug;96(32):e7697.
doi: 10.1097/MD.0000000000007697.

Berberine Containing Quadruple Therapy for Initial Helicobacter Pylori Eradication: An Open-Label Randomized Phase IV Trial

Di Zhang[1], Li Ke, Zhen Ni, Yu Chen, Lin-Hui Zhang, Shao-Hua Zhu, Chan-Juan Li, Lei Shang, Jie Liang, Yong-Quan Shi
Affiliations expand

- PMID: 28796053
- PMCID: PMC5556219
- DOI: 10.1097/MD.0000000000007697

Abstract

Background: Due to increasing antimicrobial resistance, a bismuth-based quadruple regimen has been recommended as an alternative first-line therapy for Helicobacter

pylori (H pylori) eradication. However, different results are varied greatly and the availability of bismuth was limited in some countries. We assessed the efficacy and safety of 14-day berberine-containing quadruple therapy as an alternative regimen for H pylori eradication.

Methods: In a randomized, open-label, non-inferiority, phase IV trial between November 25, 2014, and October 15, 2015, 612 treatment-naive patients were randomly assigned to 14-day berberine-containing (n = 308) or 14-day bismuth-containing (n = 304) quadruple therapy. The primary outcomes were eradication rates determined by the C urea breath test (C-UBT) 28 days after the end of treatment. The secondary outcomes were adverse events and compliance.

Results: The baseline demographic data including age, gender, body mass index (BMI), general condition and severity score were not statistically different in both groups. The eradication rates in bismuth and berberine groups were 86.4% (266/308) and 90.1% (274/304) in intention-to-treat (ITT) analysis (P = .149), and 89.6% (266/297) and 91.3% (273/299) in per-protocol (PP) analysis (P = .470), respectively. No statistically significant difference was found in the overall incidence of adverse events between both groups (35.7% vs 28.6%, P = .060).

Conclusions: Both regimens achieved the recommended efficacy for H pylori eradication. The berberine-containing quadruple regimen was not inferior to bismuth-containing quadruple regimen and can be recommended as an alternative regimen for H pylori eradication in the local region.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5556219/

BERBERINE AND ANTIMICROBIAL

Randomized Controlled Trial

J Endod

. 2012 Aug;38(8):1114-7.
doi: 10.1016/j.joen.2012.04.023. Epub 2012 Jun 7.

Efficacy of Berberine, an Antimicrobial Plant Alkaloid, as an Endodontic Irrigant Against a Mixed-

Culture Biofilm in an in Vitro Tooth Model

Qian Xie[1], Bradford R Johnson, Christopher S Wenckus, Mohamed I Fayad, Christine D Wu
Affiliations expand

- PMID: 22794217

- DOI: 10.1016/j.joen.2012.04.023

Abstract

Introduction: Berberine, a plant alkaloid isolated from many medicinal plants, has shown antimicrobial activity against selected oral pathogens. The purpose of this investigation was to evaluate the antimicrobial efficacy of berberine solution against selected endodontic pathogens using a multispecies biofilm tooth model.

Methods: The bacterial species used in the multispecies biofilm tooth model were Fusobacterium nucleatum, Enterococcus faecalis, and Prevotella intermedia. Extracted human anterior teeth were collected and standardized to a length of 14.0 mm. Teeth were cultured in Schaedler broth with the 3 test bacteria strains for 21 days and then randomly assigned to 6 treatment groups (ie, sterile saline, 5.25% NaOCl, 2% chlorhexidine [CHX], 1% CHX, 2 mg/mL berberine, and 1 mg/mL berberine plus 1% CHX). The teeth were instrumented to size 35/.06 and irrigated with 6 mL irrigant for 2 minutes. Surviving bacteria were sampled before and after instrumentation. Data were analyzed using analysis of variance ($P < .05$) followed by the Scheffé test.

Results: The minimal inhibitory concentration of berberine against F. nucleatum, P. intermedia, and E. faecalis was 31.25 μg/mL, 3.8 μg/mL, and 500 μg/mL, respectively. Instrumentation and irrigation resulted in 99% bacterial reduction in all groups. All tested solutions resulted in a statistically significant reduction in bacteria when compared with the saline control. When used alone, berberine (2 mg/mL) was less effective than the other test irrigants. However, when combined with 1% CHX, berberine (2 mg/mL) was comparable in bactericidal activity with 5.25% NaOCl, 2% CHX, and 1% CHX (Table 2).

Conclusions: Berberine was more effective than saline as an endodontic irrigant against selected endodontic pathogens in vitro and, when combined with CHX, was comparable with NaOCl in its bactericidal efficacy.

BERBERINE AND CANCER

. 2018 Jan 1;143:1858-1868.
doi: 10.1016/j.ejmech.2017.10.078.Epub 2017 Nov 11.

Synthesis and Biological Evaluation of New Berberine Derivatives as Cancer Immunotherapy Agents Through Targeting IDO1

Yan-Xiang Wang [1], Wei-Qiang Pang [1], Qing-Xuan Zeng [1], Zhe-Song Deng [2], Tian-Yun Fan [1], Jian-Dong Jiang [1], Hong-Bin Deng [3], Dan-Qing Song [4]
Affiliations expand

- PMID: 29133053

- DOI: 10.1016/j.ejmech.2017.10.078

Abstract

To discover small-molecule cancer immunotherapy candidates through targeting Indoleamine 2,3-dioxygenase 1 (IDO1), twenty-five new berberine (BBR) derivatives defined with substituents on position 3 or 9 were synthesized and examined for repression of IFN-γ-induced IDO1 promoter activities. Structure-activity relationship (SAR) indicated that large volume groups at the 9-position might be beneficial for potency. Among them, compounds 2f, 2i, 2n, 2o and 8b exhibited increased activities, with inhibition rate of 71-90% compared with BBR. Their effects on IDO1 expression were further confirmed by protein level as well. Furthermore, compounds 2i and 2n exhibited anticancer activity by enhancing the specific lysis of NK cells to A549 through IDO1, but not cytotoxicity. Preliminary mechanism revealed that both of them inhibited IFN-γ-induced IDO1 expression through activating AMPK and subsequent inhibition of STAT1 phosphorylation. Therefore, compounds 2i and 2n have been selected as IDO1 modulators for small-molecule cancer immunotherapy for next investigation.

. 2018 Dec;32(12):2560-2567.
doi: 10.1002/ptr.6196. Epub 2018 Oct 11.

Anti-influenza Activity of Berberine Improves Prognosis by Reducing Viral Replication in Mice

Yu-Qi Yan[1,2,3], Ying-Jie Fu[1,2,3], Sha Wu[1,2,3], Hong-Qiong Qin[1,2,3], Xiao Zhen[1,2,3], Bi-Mei Song[1,2,3], Yuan-Shu Weng[1,2,3], Peng-Cheng Wang[1,2,3], Xiao-Yin Chen[4], Zhen-You Jiang[1,2,3]
Affiliations expand

PMID: 30306659

DOI: 10.1002/ptr.6196

Abstract

Berberine, a natural isoquinoline alkaloid isolated from the berberis species, has a wide array of biological properties such as anti-inflammatory, antibacterial, antifungal, and antihelminthic effects. We evaluated the antiviral effect of berberine against influenza A/FM1/1/47 (H1N1) in vivo and in vitro. The results showed that berberine strongly suppressed viral replication in A549 cells and in mouse lungs. Meanwhile, berberine relieved pulmonary inflammation and reduced necrosis, inflammatory cell infiltration, and pulmonary edema induced by viral infection in mice when compared with vehicle-treated mice. Berberine suppressed the viral infection-induced up-regulation of TLR7 signaling pathway, such as TLR7, MyD88, and NF-κB (p65), at both the mRNA and protein levels. Furthermore, berberine significantly inhibited the viral infection-induced increase in Th1/Th2 and Th17/Treg ratios as well as the production of inflammatory cytokines. Our data provide new insight into the potential of berberine as a therapeutic agent for viral infection via its antiviral activity.

Chin J Integr Med

. 2011 Jun;17(6):444-52.
doi: 10.1007/s11655-011-0640-3. Epub 2011 Jun 10.

In Vivo and in Vitro Antiviral Effects of Berberine on Influenza Virus

Ying Wu[1], Ji-qian Li, Ye-ji Kim, Jun Wu, Qian Wang, Yu Hao
Affiliations expand

- PMID: 21660679

- DOI: 10.1007/s11655-011-0640-3

Abstract

Objective: To explore the potential effects of berberine on influenza virus infection both in vitro and in vivo.

Methods: In vitro anti-influenza virus assays were performed by cytopathogenic effect and neuraminidase assays in Madin Darby canine kidney cells. In vivo anti-influenza virus assays were performed on the viral pneumonia model of mice. The numbers of mice that died within day 2 to day 14 postinfection were recorded to calculate the mortality. On days 2, 4, and 6, the viral titers in the lungs were determined by hemagglutination assay; hematoxylin/eosin staining was used to assess the pathogenic changes of lung tissues; the concentrations of tumor necrosis factor-alpha (TNF-α) and monocyte specific chemoattractant molecule (MCP-1) were measured by radio immunoassay or enzyme-linked immunosorbent assay; the concentrations of nitric oxide (NO) and inducible nitric oxide synthetase (iNOS) were detected by colorimetric method; reverse transcription polymerase chain reaction was used to detect the mRNA level of TNF-α and MCP-1.

Results: Berberine showed inhibitory effects on cytopathogenic effects and neuraminidase activity of virus, with the therapeutic index 9.69. In vivo, berberine decreased mice mortality from 90% to 55%, reduced virus titers in the lungs on day 2 postinfection ($P<0.05$). The lung histology scores were 1.50 ± 0.67, 4.50 ± 1.00, and 5.50 ± 1.00 in the berberine group on days 2, 4, and 6, respectively, which were significantly reduced compared to 2.17 ± 0.22, 6.83 ± 0.44, and 8.50 ± 0.33 in the infected group ($P<0.05$). The productions of NO and iNOS were repressed by berberine compared with those in the infected group ($P<0.01$). The transcription and expression of TNF-α were inhibited by berberine on day 4 ($P<0.01$) and day 6 ($P<0.05$), and those of MCP-1 were inhibited on day 6 ($P<0.01$) compared with the infected group.

Conclusions: Berberine exhibited antiviral effects on the influenza virus both in vitro and in vivo. The possible therapeutic mechanism of berberine on influenza-induced viral pneumonia might be inhibiting the virus infection, as well as improving the pathogenic changes by repressing inflammatory substances release.

Viruses

. 2020 Mar 21;12(3):344.
doi: 10.3390/v12030344.

Berberine Hampers Influenza A Replication Through Inhibition of MAPK/ERK Pathway

Paweł Botwina[1,2], Katarzyna Owczarek[1], Zenon Rajfur[3], Marek Ochman[4], Maciej Urlik[4], Maria Nowakowska[5], Krzysztof Szczubiałka[5], Krzysztof Pyrc[1]
Affiliations expand

- PMID: 32245183

- PMCID: PMC7150991

- DOI: 10.3390/v12030344

Abstract

Background: Berberine (BBR) is an isoquinoline alkaloid which exhibits a variety of biological and therapeutic properties, and has been reported by some to block replication of the influenza virus. However, contradictory results have also been presented, and the mechanistic explanation is lacking.

Methods: A panel of cell lines (Madin-Darby canine kidney (MDCK), adenocarcinoma human alveolar basal epithelial cells (A549), lung epithelial type I (LET1)) and primary human airway epithelial cells (HAE) susceptible to influenza virus infection were infected with a seasonal influenza A virus in the presence or absence of BBR. Cytotoxicity towards cell lines was measured using XTT assay. The yield of the virus was analyzed using RT-qPCR. To study the molecular mechanism of BBR, confocal microscopy and Western blot analyses of cellular fractions were applied.

Results and conclusions: Our results show cell-type-dependent anti-influenza properties of BBR in vitro which suggests that the compound acts on the cell and not

the virus. Importantly, BBR hampers influenza replication in primary human airway epithelium 3D cultures that mimic the natural replication site of the virus. Studies show that the influenza A virus upregulates the mitogen-activated protein kinase/extracellular signal-related kinase (MAPK/ERK) pathway and hijacks this pathway for nucleolar export of the viral ribonucleoprotein. Our results suggest that BBR interferes with this process and hampers influenza A replication.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7150991/

CITRUS BIOFLAVONOIDS AND IMMUNITY

Planta Med

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. 2001 Aug;67(6):548-9.
doi: 10.1055/s-2001-16484.

Flavanone Glycosides From Citrus Junos and Their Anti-Influenza Virus Activity

H K Kim, W K Jeon, B S Ko

- PMID: 11509977

- DOI: 10.1055/s-2001-16484

Abstract

By bioactivity-guided fractionation, a new flavanone triglycoside, naringenin 7-O-(2",6"-di-O-alpha-rhamnopyranosyl)-beta-glucopyranoside (1), as well as hesperetin 7-O-(2", 6"-di-O-alpha-rhamnopyranosyl)-beta-glucopyranoside (2), hesperidin (3) and narirutin (4) have been isolated from the fruits of Citrus junos Tanaka (Rutaceae). In addition, hesperetin 7-O-(2",6"-di-O-alpha-rhamnopyranosyl)-beta-glucopyranoside (2) is reported for the first time from this plant and inhibits the influenza A virus.

Biol Pharm Bull

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. 2009 Jul;32(7):1188-92.
doi: 10.1248/bpb.32.1188.

Glucosyl Hesperidin Prevents Influenza a Virus Replication in Vitro by Inhibition of Viral Sialidase

Repon Kumer Saha[1], Tadanobu Takahashi, Takashi Suzuki
Affiliations expand

PMID: 19571383

DOI: 10.1248/bpb.32.1188

Abstract

Hesperidin, a flavonoid obtained from citrus fruits, is known to have multiple biological activities and antimicrobial activities for human viruses; however, hesperidin has very low solubility in water and the target molecule of hesperidin for influenza virus remains unknown. A water-soluble derivative of hesperidin, glucosyl hesperidin (GH), which was synthesized by regioselective transglycosylation with cyclodextrin glucanotransferase, has been reported to have biological activities that are as or stronger than those of hesperidin. To determine the inhibitory effect of GH on influenza A virus (IAV) infection, Madin-Darby canine kidney (MDCK) cells were treated with GH before, at the same time as, and after IAV inoculation. GH treatment before IAV inoculation had no effect on virus replication, whereas, treatment with GH at the same time as or after IAV inoculation induced distinct reduction in IAV replication. Inhibition analysis of GH against two surface glycoprotein spikes of IAV revealed that GH prevents IAV replication by inhibition of viral sialidase activity that is involved in the entry and release stages on IAV infection but not by receptor binding inhibition. GH had no cytotoxic effects on MDCK cells in a dose range of 0-25 mM. Our results provide useful information for the development of novel sialidase inhibitors for influenza prevention.