IAG Enhancement of Immune Function References

1) Review

Nutr Metab (Lond)

. 2016 Apr 12;13:28.
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Does larch arabinogalactan enhance immune function? A review of mechanistic and clinical trials

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Free PMC article

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. Different hypotheses can be envisaged as larch arabinogalactan can possibly act indirectly through microbiota-dependent mechanisms and/or have a direct effect on the immune system via the gut-associated lymphoid tissue (GALT).

2) Review

Altern Med Rev

. 1999 Apr;4(2):96-103.

Larch arabinogalactan: clinical relevance of a novel immune-enhancing polysaccharide

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- PMID: 10231609

Free article

Abstract

Larch arabinogalactan is composed of greater than 98-percent arabinogalactan, a highly branched polysaccharide consisting of a galactan backbone with side-chains of galactose and arabinose sugars. Larch arabinogalactan is an excellent source of dietary fiber, and has been approved as such by the FDA. It has been shown to increase the production of short-chain fatty acids, principally butyrate and propionate, and has been shown to decrease the generation and absorption of ammonia. Evidence also indicates human consumption of larch arabinogalactan has a significant effect on enhancing beneficial gut microflora, specifically increasing anaerobes such as Bifidobacteria and Lactobacillus. Larch arabinogalactan has several interesting properties which appear to make it an ideal adjunctive supplement to consider in cancer protocols. Experimental studies have indicated larch arabinogalactan can stimulate natural killer (NK) cell cytotoxicity, enhance other functional aspects of the immune system, and inhibit the metastasis of tumor cells to the liver. The immune-enhancing properties also suggest an array of clinical uses, both in preventive medicine, due to its ability to build a more responsive immune system, and in clinical medicine, as a therapeutic agent in conditions associated with lowered immune function, decreased NK activity, or chronic viral infection.

Clinical Trial

3) Altern Med Rev

. 2002 Apr;7(2):138-49.

Immunological activity of larch arabinogalactan and Echinacea: a preliminary, randomized, double-blind, placebo-controlled trial

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Free article

Abstract

The immunomodulating effects of two Echinacea species, E. purpurea and E. angustifolia and larch arabinogalactan extracted from Larix occidentalis were examined in a randomized, double-blind, placebo-controlled, prospective four-week clinical trial at a naturopathic medical school research center.

Subjects/materials: Forty-eight healthy female volunteers (22-51 y) were randomly assigned to one of six groups: standardized extract of E. purpurea (EP); ultra-refined E. purpurea/E. angustifolia (urEPA); E. purpurea/E. angustifolia (EPA); E. purpurea/E. angustifolia plus larch arabinogalactan (EPALA); larch arabinogalactan (LA); or placebo.

Methods: Immunological tests with enumerative measurements, stool cultures for Lactobacillus acidophilus and yeast, and health-related quality of life (HRQoL) using the Medical Outcomes Study derived SF-36

self-administered questionnaire were assessed at baseline and at four weeks.

Results: Complement properdin increased by 21 percent in the EPA group ($p<0.05$) and by 18 percent in the EPALA group ($p<0.05$), compared to the placebo group ($p>0.05$). SF-36 showed improvements in overall physical health, vitality, and emotional health in the same two groups (EPA and EPALA).

Discussion: Volunteers in the EPA and EPALA groups had increased production of complement properdin after four weeks of intervention. The increased complement properdin may be an indication of one aspect of immune system stimulation in patients treated with either E. purpurea/E. angustifolia or E. purpurea/E. angustifolia plus larch arabinogalactan.

4) Clinical Trial

Curr Med Res Opin

. 2013 Mar;29(3):251-8.
doi: 10.1185/03007995.2013.765837. Epub 2013 Jan 22.

Larch arabinogalactan effects on reducing incidence of upper respiratory infections

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- DOI: 10.1185/03007995.2013.765837

Abstract

Objective: Larch arabinogalactan (ResistAid *) may prevent cold infections due to its immune-stimulatory properties. In a placebo-controlled, double-blind, randomized clinical trial, the effect of a proprietary larch arabinogalactan preparation on the incidences of common colds and its effect on cold symptoms, as a well established model for immune function, was compared to placebo.

Research design and methods: A total of 199 healthy participants who had a self reported cold infection rate of three in 6 months were randomly assigned to receive a total of either 4.5 g of an arabinogalactan preparation (n = 101) or placebo (n = 98) over a period of 12 weeks.

Main outcome measures: The participants documented each common cold episode in a diary, and rated 10 predefined infection symptoms on a 4 point rating scale during an infection period, resulting in an infection score. The common cold episodes were confirmed by medical doctors.

Clinical trial registration: ISRCTN41183655.

Results: In the full analysis set (FAS), arabinogalactan tended to decrease the incidence of common cold ($p = 0.055$). The number of participants affected by a cold was significantly reduced by arabinogalactan supplementation ($p = 0.038$). Concerning the per protocol (PP) collective, the incidences of common cold ($p = 0.040$) and the number of participants affected by the infection ($p = 0.033$) were significantly fewer after arabinogalactan compared to placebo consumption. The severity of symptoms at episode start as experienced by the participants was significantly higher after arabinogalactan supplementation ($p = 0.028$). The treatment was well tolerated with no significant differences between the study groups.

Conclusion: The present study demonstrated that larch arabinogalactan increased the body's potential to defend against common cold infection.

While the immunomodulatory effect of arabinogalactan can be assumed, its mechanism of action remains to be elucidated.

5) Randomized Controlled Trial

Nutr J

. 2010 Aug 26;9:32.
doi: 10.1186/1475-2891-9-32.

Proprietary arabinogalactan extract increases antibody response to the pneumonia vaccine: a randomized, double-blind, placebo-controlled, pilot study in healthy volunteers

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- PMCID: PMC2939641
- DOI: 10.1186/1475-2891-9-32

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Abstract

Background: Arabinogalactan from Larch tree (Larix spp.) bark has previously demonstrated immunostimulatory activity. The purpose of this study was to test the hypothesis that ingestion of a proprietary arabinogalactan extract, ResistAid™, would selectively enhance the

antibody response to the pneumococcal (pneumonia) vaccine in healthy adults.

Methods: This randomized, double-blind, placebo-controlled, parallel group pilot study included 45 healthy adults who had not previously been vaccinated against Streptococcus pneumoniae. The volunteers began taking the study product or placebo (daily dosage 4.5 g) at the screening visit (V1-Day 0) and continued over the entire 72 day study period. After 30 days the subjects received the 23-valent pneumococcal vaccine (V2). They were monitored the following day (V3-Day 31), as well as 21 days (V4-Day 51) and 42 days (V5-Day 72) after vaccination. Responses by the adaptive immune system (antigen specific) were measured via pneumococcal IgG antibodies (subtypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and salivary IgA levels. Responses by the innate immune system (non-specific) were measured via white blood cell counts, inflammatory cytokines and the complement system.

Results: Vaccination significantly increased pneumococcal IgG levels as expected. The arabinogalactan group demonstrated a statistically significant greater IgG antibody response than the placebo group in two antibodies subtypes (18C and 23F) at both Day 51 ($p = 0.006$ and $p = 0.002$) and at Day 72 ($p = 0.008$ and $p = 0.041$). These same subtypes (18C and 23F) also demonstrated change scores from baseline which were significant, in favor of the arabinogalactan group, at Day 51 ($p = 0.033$ and 0.001) and at Day 72 ($p = 0.012$ and $p = 0.003$). Change scores from baseline and mean values were greater in the arabinogalactan group than placebo for most time points in antibody subtypes 4, 6B, 9V, and 19F, but these differences did not reach statistical significance. There was no effect from the vaccine or arabinogalactan on salivary IgA, white blood cell count, inflammatory cytokines or complement.

Conclusions: The proprietary arabinogalactan extract (ResistAid), tested in this randomized, double-blind, placebo-controlled, parallel-group

pilot study, increased the antibody response of healthy volunteers to the 23-valent pneumococcal vaccine compared to placebo.

6) Randomized Controlled Trial

J Am Coll Nutr

. 2013;32(5):331-8.
doi: 10.1080/07315724.2013.839907.

Immunomodulatory effects of ResistAid™: A randomized, double-blind, placebo-controlled, multidose study

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- DOI: 10.1080/07315724.2013.839907

Free PMC article

Abstract

Objective: To evaluate the ability of a proprietary arabinogalactan extract from the larch tree (ResistAid, Lonza Ltd., Basel, Switzerland) to change the immune response in healthy adults to a standardized antigenic challenge (tetanus and influenza vaccines) in a dose-dependent manner compared to placebo.

Methods: This randomized, double-blind, placebo-controlled trial included 75 healthy adults (18-61 years old). Subjects were randomized to receive either 1.5 or 4.5 g/day of ResistAid or placebo for 60 days. At day 30, subjects were administered both tetanus and influenza vaccines. Serum antigenic response (tetanus immunoglobulin G [IgG], influenza A and B IgG and immunoglobulin M [IgM]) was measured at days 45 (15 days after vaccination) and 60 (30 days after vaccination) of the study and compared to baseline antibody levels. Frequency and intensity of adverse events were monitored throughout the study.

Results: As expected, all 3 groups demonstrated an expected rise in tetanus IgG levels 15 and 30 days following the vaccine. There was a strongly significant difference in the rise in IgG levels at day 60 in the 1.5 g/day group compared to placebo ($p = 0.008$). In the 4.5 g/day group, there was significant rise in tetanus IgG at days 45 and 60 compared to baseline ($p < 0.01$) but these values were not significant compared to placebo. Neither group demonstrated any significant elevations in IgM or IgG antibodies compared to placebo following the influenza vaccine. There were no clinically or statistically significant or serious adverse events.

Conclusions: ResistAid at a dose of 1.5 g/day significantly increased the IgG antibody response to tetanus vaccine compared to placebo. In conjunction with earlier studies, this validates the effect of ResistAid on the augmentation of the response to bacterial antigens (in the form of vaccine).

7) Cancer Immunol Immunother

. 1993;36(4):237-44.
doi: 10.1007/BF01740905.

Mechanism of stimulation of human natural killer cytotoxicity by arabinogalactan from Larix occidentalis

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- PMID: 8439987

- DOI: 10.1007/BF01740905

Abstract

Cultures of human peripheral blood mononuclear cells (PBMC) as well as cultures of preseparated peripheral non-adherent cells (PNAC) and monocytes showed enhancement of natural killer (NK) cytotoxicity against K562 tumor cells when pretreated with arabinogalactan from Larix occidentalis for 48-72 h. Lack of enhanced responses of PBMC (37% of donors) did not necessarily mean that PNAC and monocyte cultures were also non-responsive to arabinogalactan treatment. Moreover, PBMC, PNAC and monocytes of individual donors could exhibit various responses to arabinogalactan when cultures derived from bleedings after intervals of several months were assayed. Arabinogalactan-mediated enhancement of NK cytotoxicity was not initiated directly but was found to be governed by the cytokine network. Generally, arabinogalactan pretreatment induced an increased release of interferon gamma (IFN gamma), tumor necrosis factor alpha, interleukin-1 beta (IL-1 beta) and IL-6 but only IFN gamma was involved in enhancement of NK cytotoxicity since cytotoxicity enhancement of PBMC and PNAC but not that of monocytes could be blocked when anti-IFN gamma antibodies were present during pretreatment. The presence of anti-IL-2 antibodies

completely blocked NK cytotoxicity enhancement of PBMC and only moderately that of PNAC and monocytes. This blocking effect was also observed when no detectable increase of IL-2 release could be recorded. The receptor specificity of arabinogalactan is not well characterized. Initial information obtained from comparative studies indicated that arabinogalactan presumably interacts with a receptor that showed specificity for a NK-cytotoxicity-enhancing oligo-saccharide from Viscum album extracts since the action of both components was not synergistic but rather competitive.