

Research On Goji Berries (Lycium Barbarum)

Effects of Lycium barbarum polysaccharide on tumor microenvironment T-lymphocyte subsets and dendritic cells in H22-bearing mice

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OBJECTIVE: To study the effects of Lycium Barbarum polysaccharide (LBP) on tumor microenvironment T-lymphocyte subsets and dendritic cells in H22-bearing mice and the mechanisms for intervention of tumor immune escape by LBP. **METHODS:** H22-bearing mice were given LBP orally for two weeks. T-lymphocyte subsets and the phenotypes of dendritic cells in tumor-infiltrating lymphocytes (TIL) were detected by flow cytometry (FCM).

RESULTS: LBP could significantly increase the numbers of CD4(+) and CD8(+) T cells in TIL as compared with those in model control group ($P < 0.05$). In model control group, the number of dendritic cells in tumor microenvironment decreased markedly, while in LBP-treated group, the increased number of dendritic cells and B7-1 expression were observed, but there were no significant differences between these two groups. **CONCLUSION:** LBP has anti-tumor effect probably by increasing the numbers of CD4(+) and CD8(+) T cells in TIL to relieve the immunosuppression and enhance the anti-tumor function of the immune system. But whether LBP can recover the phenotype and function of dendritic cells in H22-bearing mice should be further studied.

Therapeutic Effects of Lycium barbarum Polysaccharide (LBP) on Irradiation or Chemotherapy-Induced Myelosuppressive Mice.

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Aim: The aim of this study was to investigate the effects of Lycium Barbarum polysaccharide (LBP) on irradiation- or chemotherapy-induced myelosuppressive mice and cultured peripheral blood mononuclear cells (PBMCs).

Methods: In an in vivo experiment, mice were irradiated with a sublethal dose of 550 cGy X-ray or intraperitoneally (i.p.) injected with carboplatin (CB) 125 mg/kg to produce severe myelosuppression. Four to 6 hours after the irradiation or injection, mice were subcutaneously (s.c.) injected with LBP (50, 100, and 200 mg/kg) daily from day 0 to day 6. Blood samples were collected from the tail veins of mice at different time points, and peripheral white blood cells (WBC), red blood cells (RBC), and platelet (PLT) counts were monitored. In an in vitro experiment, human PBMCs were incubated with LBP at different concentrations in combination with phytohemagglutinin (PHA), and the production of granulocyte colony-stimulating factor (G-CSF) was tested.

Results: Compared to the control, 50 mg/kg LBP (LBP-L) significantly ameliorated the decrease of peripheral WBC of irradiated myelosuppressive mice on day 13, and 100 mg/kg LBP (LBP-M) did the same on days 17 and 21. All dosages of LBP significantly ameliorated the decrease of peripheral RBC of irradiated myelosuppressive mice on days 17 and 25. Two-hundred mg/kg LBP (LBP-H) and LBP-M significantly enhanced peripheral PLT counts of irradiated myelosuppressive mice on days 10, 13, 17, and 21, as did LBP-L on days 13 and 17. All dosages of LBP increased peripheral WBC counts of chemotherapy-induced myelosuppressive mice to some extent, but there was no statistic difference when compared to the control. LBP-H significantly ameliorated the decrease of peripheral RBC of chemotherapy-induced myelosuppressive mice on days 13, 15, 17, and 20, and LBP-M and LBP-L did the same on days 15 and 17. All dosages of LBP significantly enhanced peripheral PLT counts of chemotherapy-induced myelosuppressive mice on days 7 and 10, as did LBP-H on days 13, 15, and 17, and LBP-M on days 13 and 15. Also, LBP could obviously stimulate human PBMCs to produce G-CSF.

Conclusions: LBP promoted the peripheral blood recovery of irradiation or chemotherapy-induced myelosuppressive mice, and the effects may be the result of the stimulation of PBMCs to produce G-CSF.

Neuroprotective effects of anti-aging oriental medicine *Lycium barbarum* against b-amyloid peptide neurotoxicity.

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Abstract

As aged population dramatically increases in these decades, efforts should be made on the intervention for curing age-associated neurodegenerative diseases such as Alzheimer's disease (AD). Natural plant extracts of *Lycium Barbarum* are well-known to exhibit antiaging effects. We therefore hypothesized that they exhibit neuroprotective effects against toxins in aging-related neurodegenerative diseases. In this study, we aimed to investigate whether extracts from *L. Barbarum* have neuroprotective effects against toxicity of fibrillar Ab1–42 and Ab25–35 fragments. Primary rat cortical neurons exposed to Ab peptides resulted in apoptosis and necrosis. Pre-treatment with extract isolated from *L. Barbarum* significantly reduced the release of lactate dehydrogenase (LDH). In addition, it attenuated Ab peptide-activated caspases-3-like activity. The extract elicited a typical dose-dependent neuroprotective effect. Effective dosage of this extract was wider than that of a well-known western neuroprotective medicine lithium chloride (LiCl). We have further examined the underlying mechanisms of the neuroprotective effects. In agreement with other laboratories, Ab peptides induce a rapid activation of c-Jun N-terminal kinase (JNK) by phosphorylation. Pre-treatment of aqueous extract markedly reduced the phosphorylation of JNK-1 (Thr183/Tyr185) and its substrates c-Jun-I (Ser 73) and c-Jun-II (Ser 63). **Taken together, we have proved our hypothesis by showing neuroprotective effects of the extract from *L. barbarum*. Study on anti-aging herbal medicine like *L. barbarum* may open a new therapeutic window for the prevention of AD.**

Observation of the Effects of *Lycium Barbarum* Polysaccharides (LBP) In Combination with LAK/IL-2 Therapy In the Treatment of 75 Cancer Patients

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Abstract: Seventy-nine advanced cancer patients in a clinical trial were treated with *Lycium Barbarum* polysaccharides (LBP) in combination with Lymphokine Activated Killer cell (LAK) and Interleukin-2 (IL-2). Initial results of the treatment indicated that regression of cancer was achieved in 75 of the 79 patients with various cancers. Cancers treated in this trial included malignant melanoma, renal cell carcinoma, colorectal carcinoma, lung cancer, nasopharyngeal carcinoma, and malignant hydrothorax. The response rate of patients treated with the LBP/LAK/IL-2 combination was 40.9% while that of patients treated with LAK/IL-2 only was 16.1% ($P < 0.05$). In addition, the mean length of time patients treated with the LBP/LAC/IL-2 combination therapy remained in remission was significantly greater than for patients in the **LAK/IL-2 only treatment group. The LBP combination treatment led to a considerable increase in Natural Killer (NK) and LAK cell activity. These results indicate that LBP can be used as an adjuvant in the biotherapy of cancer.**

Effect of *lycium barbarum* polysaccharide on human hepatoma QGY7703 cells: inhibition of proliferation and induction of apoptosis.

Life Sci. 2005 Mar 18; 76(18):2115-24.

Lycium Barbarum polysaccharide, extracted from *Lycium Barbarum* that is a kind of traditional Chinese herb, is found to have anticancer activity. In this study, the effect of lycium on the proliferation rate, cell cycle distribution and apoptosis in the human hepatoma QGY7703 cell line were investigated. **The study suggests that the induction of cell cycle arrest and the increase of intracellular calcium in apoptotic system may participate in the antiproliferative activity of lycium in human hepatoma QGY7703 cells.**

Fasting plasma zeaxanthin response to *Lycium barbarum* (wolfberry; Kei Tze) in a food-based human supplementation trial.

Br J Nutr. 2005 Jan;93(1):123-30.

Age-related macular degeneration (AMD) is a common disorder that causes irreversible loss of central vision. Increased intake of foods containing zeaxanthin may be effective in preventing AMD because the macula accumulates zeaxanthin and lutein, oxygenated carotenoids with antioxidant and blue light-absorbing properties. *Lycium Barbarum* L. is a small red berry known as *Fructus lycii* and wolfberry in the West, and Kei Tze and Gou Qi Zi in Asia. *Lycium* is rich in zeaxanthin dipalmitate, and is valued in Chinese culture for being good for vision. The aim of this study, which was a single-blinded, placebo-controlled, human intervention trial of parallel design, was to provide data on how fasting plasma zeaxanthin concentration changes as a result of dietary supplementation with whole wolfberry. Fasting blood was collected from healthy, consenting subjects; fourteen subjects took 15 g/d lycium (estimated to contain almost 3 mg zeaxanthin) for 28 d. Repeat fasting blood was collected on day 29. Age- and sex-matched controls (n 13) took no lycium. After lycium supplementation, plasma zeaxanthin increased 2.5-fold. **This human supplementation trial shows that zeaxanthin in whole lycium is bioavailable and that intake of a modest daily amount markedly increases fasting plasma zeaxanthin levels. These new data will support further study of dietary strategies to maintain macular pigment density.**

Hypoglycemic and hypolipidemic effects and antioxidant activity of fruit extracts from *Lycium barbarum*.

Life Sci. 2004 Nov 26;76(2):137-49.

The hypoglycemic and hypolipidemic effects of *Lycium Barbarum* fruit water decoction, crude polysaccharide extracts (crude LBP), and purified polysaccharide fractions (LBP-X) in alloxan-induced diabetic or hyperlipidemic rabbits were investigated. Total antioxidant capacity assay showed that all three *Lycium Barbarum* extracts/fractions possessed antioxidant activity. However, water and methanol fruit extracts and crude polysaccharide extracts exhibited stronger antioxidant activity than purified polysaccharide fractions because crude extracts were identified to be rich in antioxidants (e.g., carotenoids, riboflavin, ascorbic acid, thiamine, nicotinic acid). *Lycium Barbarum* polysaccharides (glycocojugates), containing several monosaccharides and 17 amino acids, were major bioactive constituents of hypoglycemic effect. **Both polysaccharides and vitamin antioxidants from *Lycium barbarum* fruits were possible active principles of hypolipidemic effect.**

Comparison of plasma responses in human subjects after the ingestion of 3R,3R'-zeaxanthin dipalmitate from wolfberry (*Lycium barbarum*) and non-esterified 3R,3R'-zeaxanthin using chiral high-performance liquid chromatography.

Br J Nutr. 2004 May;91(5):707-13.

Age-related macular degeneration (AMD) is one of the most common eye diseases of elderly individuals. It has been suggested that lutein and zeaxanthin may reduce the risk for AMD. Information concerning the absorption of non-esterified or esterified zeaxanthin is rather scarce. Furthermore, the formation pathway of meso (3R,3'S)-zeaxanthin, which does not occur in plants but is found in the macula, has not yet been identified. Thus, the present study was designed to assess the concentration of 3R,3R'-zeaxanthin reached in plasma after the consumption of a single dose of native 3R,3'R-zeaxanthin palmitate from *Lycium Barbarum* or non-esterified 3R,3'R-zeaxanthin in equal amounts.

2-O-(beta-D-Glucopyranosyl)ascorbic acid, a novel ascorbic acid analogue isolated from *Lycium* fruit.

J Agric Food Chem. 2004 Apr 7;52(7):2092-6.

A novel stable precursor of ascorbic acid (vitamin C), 2-O-(beta-D-glucopyranosyl)ascorbic acid, was isolated from both the ripe fresh fruit and dried fruit of *Lycium Barbarum* L., a plant of the Solanaceae family. The chemical structure was inferred by instrumental analyses and confirmed by chemical synthesis. The dried fruit of *Lycium Barbarum* L. contained ca. 0.5% of it, which is comparable to the ascorbic acid content of fresh lemons. **It increased the blood ascorbic acid by oral administration to rats, and it was also detected in blood from the portal vein.**

Study on protective action of *lycium barbarum* polysaccharides on DNA imparments of testicle cells in mice.

Wei Sheng Yan Jiu. 2003 Nov;32(6):599-601.

To investigate the protective effect of *Lycium Barbarum* polysaccharides on DNA oxidative damage of testicle cells induced by hydrogen peroxide (H₂O₂). The single cell gel electrophoresis(SCGE) was used to detect the breakage of DNA strand and analyze lycium protection against oxidation damage in testicle cells treated by different concentrations of lycium for 1 hour firstly, and then cultured with 100 μmol/L H₂O₂ for 25 min. The results showed that a certain moment action by H₂O₂ could induce the breakage of DNA strand. The pretreatment of lycium significantly decreased the frequencies of cells with tail moment and the tail length of testicle cells treated by H₂O₂. It is suggested that lycium itself could not cause the oxidation damage, but it could clean out the free-radical and restrain the DNA damage of testicle cells caused by the oxidative stress.

Effect of lycium fruit and epimedium on DNA synthesis of the aging-youth 2BS fusion cells

Zhongguo Zhong Xi Yi Jie He Za Zhi. 2003 Dec;23(12):926-8.

OBJECTIVE: To study the effect of water extracts of lycium fruit and Epimedium (EM) on DNA synthesis of the aging-youth 2BS fusion cells.

METHODS: Human embryonic lung diploid fibroblasts 2BS national standard strain, were used as an aging model. Cell denucleation and cell fusion techniques were applied to observe the effect of lycium and EM on DNA synthesis of 2BS fusion cells.

CONCLUSION: Both lycium and EM can accelerate the DNA synthesis rate of the aging youth 2BS fusion cells and prolong the life span of 2BS cells.

A polysaccharide-protein complex from Lycium barbarum upregulates cytokine expression in human peripheral blood mononuclear cells.

Eur J Pharmacol. 2003 Jun 27;471(3):217-22.

The production of cytokine is a key event in the initiation and regulation of an immune response. Many compounds are now used routinely to modulate cytokine production, and therefore the immune response, in a wide range of diseases, such as cancer. Interleukin-2 and tumor necrosis factor-alpha are two important cytokines in antitumor immunity. In this study, the effects of Lycium Barbarum polysaccharide-protein complex on the expression of interleukin-2 and tumor necrosis factor-alpha in human peripheral blood mononuclear cells were investigated. Administration of Lycium increased the expression of interleukin-2 and tumor necrosis factor-alpha at both mRNA and protein levels in a dose-dependent manner. **The results suggest that Lycium polysaccharide may induce immune responses and possess potential therapeutic efficacy in cancer.**

Hepatoprotective pyrrole derivatives of Lycium chinense fruits.

Bioorg Med Chem Lett. 2003 Jan 6;13(1):79-81.

As a part of our search for hepatoprotective compounds from Lycium chinense fruits, three new pyrrole derivatives (1-3) were isolated. These compounds and a related synthetic methylated compound (4) were evaluated for their biological activity and structure-activity relationship, and compounds 1 and 2 showed hepatoprotective effects comparable to silybin at the concentration of 0.1 microM (64.4 and 65.8%, respectively).

Isolation and purification of Lycium barbarum polysaccharides and its antifatigue effect

Wei Sheng Yan Jiu. 2000 Mar 30;29(2):115-7.

A purified component of Lycium Barbarum polysaccharide was isolated from Lycium Barbarum. Lycium was tested on five different doses (5, 10, 20, 50 and 100 mg.kg-1.d-1) in mice. The results showed that lycium induced a remarkable adaptability to exercise load, enhanced resistance and accelerated elimination of fatigue. Lycium could enhance the storage of muscle and liver glycogen, increase the activity of LDH before and after swimming, decrease the increase of blood urea nitrogen (BUN) after strenuous exercise, and accelerate the clearance of BUN after exercise. The dosage of lycium 10 mg.kg-1.d-1 was the best amount among the five tested doses.

Inhibition the growth of human leukemia cells by Lycium barbarum polysaccharide

Wei Sheng Yan Jiu. 2001 Nov;30(6):333-5.

The effect and the mechanism of Lycium Barbarum polysaccharide on inhibiting the growth of human leukemia HL-60 cells were examined. Lycium polysaccharide could inhibit the growth of HL-60 cells in dose-dependent manner and decrease the membrane fluidity of the cell. Agarose gel electrophoresis of DNA from the cells treated with LBP-X revealed a "DNA ladder" and positive TUNEL test. **The results showed that the apoptosis of HL-60 cells induced by lycium maybe its important mechanism on anti-tumorigenesis.**

The protective effects of total flavonoids from Lycium Barbarum L. on lipid peroxidation of liver mitochondria and red blood cell in rats

Wei Sheng Yan Jiu. 1999 Mar 30;28(2):115-6.

The protective effects of total flavonoids from Lycium Barbarum L. on lipid peroxidation in mitochondria and red blood cells (RBC) induced by oxygen radicals produced by Fe²⁺-cysteine system were investigated. The mitochondria lipid peroxidation (measured as malondialdehyde, MDA) was significantly inhibited by lycium, and the fluidity of mitochondria membrane was also protected effectively. It was observed by scan electron microscope, that the shape of RBC in the Fe²⁺ system was damaged significantly. The shape of RBC was remained with the addition of Lycium Barbarum.

Radiosensitizing effects of Lycium barbarum polysaccharide for Lewis lung cancer.

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The radiosensitizing effects of the Lycium Barbarum polysaccharide (LBP) were observed by the model transplanted Lewis lung cancer on C57 BL mice. When LBP alone was administered, it was not obvious that LBP inhibited the growth of Lewis lung cancer. The significant radiosensitizing effects were obtained by combination of LBP and radiation. The mean numerical value of the dose modifying factors (DMF) was 2.05. The results also showed certain radiation enhancement effects of LBP to acute hypoxic cells of Lewis lung cancer. LBP presented few toxicity to the mice.

Study on the composition of Lycium barbarum polysaccharides and its effects on the growth of weanling mice.

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In order to observe the effects of Lycium Barbarum polysaccharides (LBP-4) on the growth of weanling mice and the absorption of some metals in the their body, the composition of LBP-4 is determined. 120 female weanling mice are divided in random into 4 groups. They are fed on LBP-4 at the dose of 5, 10 and 20 mg/(kg.d) respectively. The taken feed weight and the body weight of mice are recorded everyday. After 21 days, the content of calcium, magnesium, zinc and iron in pygal muscles and femora of mice is determined. **The results showed that LBP-4 is composed of six kinds of monosaccharides that can enhance food conversion rate and the content of zinc and iron in body of mice, and reduce the body weight.**

These are just a few that we have listed. To find more go to:

<http://www.ncbi.nlm.nih.gov/entrez/>