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Research Advances on the Anti-aging Profile of Fructus lycii: an Ancient Chinese Herbal Medicine

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Research Advances on the Anti-aging Profile of Fructus lycii: an Ancient Chinese Herbal Medicine*

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Abstract

Fructus lycii is a common Chinese herbal medicine used in China for nearly 2000 years. It has beneficial effects on eyes, liver and kidneys; and it has long been considered to be an anti-aging herb in ancient Chinese medicine. Modern studies have partially probed the magic anti-aging property of F. lycii. The beneficial effects of F. lycii on aging are largely attributed to its bioactive components such as polysaccharides, carotenoids and flavonoids. This review focuses on the anti-aging aspect of F. lycii, elaborating the bioactive ingredients accounting for the property, anti-aging pharmacology in terms of its antioxidation capacity, immunomodulative effect and neuroprotective activity.

KEYWORDS: Fructus lycii, anti-aging, Chinese herbal medicine

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Introduction

Although aging may be an inescapable natural process, pursuit of youth and longevity is a propensity in human nature. Today's ever growing elderly population worldwide has put anti-aging medicine and treatment for age-related diseases on the agenda. The view of aging as an extremely complex multifactorial process has replaced the earlier search for a distinct cause such as a single gene or the decline of a key body system. Each theory proposed for aging may only account for one aspect of the whole picture (Weinert and Timiras 2003). Therefore, herbal medicine that has multi-functional properties may fit better with the multifactorial characteristics of aging and looks promising in amelioration, prevention or treatment for aging and age-related diseases (Anekonda and Reddy 2005). There are quite a lot of medicinal plants and prescriptions in Chinese medical literatures aim at the prevention of diseases and the prolongation of life-span (Xiao et al. 1993). For example, in the earliest Chinese Herbal --- *Shen-nong Ben-cao Jing* or *Spirit Farmer's Herbal*, 120 among total 365 drugs, regarded as being of a superior category possessing the potential of "improving vital energy of the body and maintaining youth" via proper administration. The studies of traditional anti-aging medicinal herbs in China are now under way and some effective drugs and compound prescriptions have been explored. Their effects on cell generation, survival time, immunomodulation, improvement of visceral and metabolic functions, and anti-infection, and their trace element contents have been summarized and analyzed (Chen and Li 1994).

Fructus lycii, the dried fruit of *Lycium barbarum* L. in the Solanaceae family, is well-known in traditional Chinese herbal medicine. In Chinese, *F. lycii* is called *Gouqizi*, with *zi* meaning "seed" or specifically "berry." "Wolfberry" is the common English name for the plant, while the name "Goji berry" is in common use in the health food market for berries from this plant (Helmer 2006; Marchuck 2005). *F. lycii* has been used in traditional Chinese medicine for nearly 2,000 years. Its undocumented legend, however, is considerably older as *F. lycii* is often linked in Chinese lore to *Shennong*, China's legendary First Emperor, mythical father of agriculture, and herbalist who lived circa 2,800 BC. Ancient Chinese medical texts extolled wolfberries for strengthening the eyes, liver, and kidneys as well as fortifying the "*Qi*" or life force. An early medical work, *Spirit Farmer's Herbal* (475-221 B.C.), noted that *F. lycii* benefits ranging from replenishing vital essence to strengthening and restoring major organs. It was described as a superior herb in the *Spirit Farmer's Herbal*. According to "*Commentary on the*

Spirit Farmer's Herbal", a book written by *Tao Hong Jing* (456-536 AD), a Taoist master and physician, "*Lycium* tonifies *Jing* and *Qi* and strengthens the *Yin Tao* within the body." Documentation of *F. lycii* continued in the 7th century Tang Dynasty treatise *Yaoxing Lun*. The physician's handbook, *Compendium of Materia Medica* (*Ben Cao Gang Mu*), written during the Ming Dynasty (1368-1644 A.D.) reported that "taking in Chinese wolfberry regularly may regulate the flow of vital energy and strengthen the physique, which can lead to longevity."

Today, the majority of commercially produced *F. lycii* comes from the Ningxia Hui Autonomous Region of north-central China and the Xinjiang Uyghur Autonomous Region of western China, where they are grown according to the Good Agricultural Practice (GAP). *F. lycii* is sweet in taste which possesses tonic action such as invigorating the liver and kidney, plenishing vital essence and improving vision. Since *F. lycii* was described as a potent anti-aging agent in the above Chinese herbals, lots of studies have been conducted to confirm and demonstrate its chemical ingredients and pharmacological properties in recent years. In the present paper, the active components in *F. lycii,* the anti-aging profile including antioxidant effect, immunomodulation effect and neuroprotective effect of *F. lycii* will be reviewed.

Medicinal chemistry---bioactive components in *F. lycii*

Polysaccharides

Experiment results from several research groups have suggested that the main bioactive ingredient in *F. lycii* may be polysaccharides named *Lycium barbarum* polysaccharides (LBPs) or *Lycium barbarum* Glycopeptide (LbGp). Five glycoconjugates (from LbGp1 to LbGp5) have been obtained via the separation and purification of *F. lycii* and their physical and chemical properties, such as molecular weight, saccharine content, the composition of monosaccharide, the composition of amino acid and the analysis of elements, have been explored. And the structure of glycochains LbGpl-OL to LbGp5-OL have been elucidated (Huang et al. 1999a; Peng and Tian 2001; Tian 2003). Meanwhile, four fractions of LBP--- LBP-I, LBP-II, LBP-III and LBP-IV--- were obtained from *F. lycii* by DEAE ion-exchange cellulose and gel Chromatography by He *et al*. (He and Zhang 1996). Their structural composition was also studied. The results showed that these water-soluble LBPs are complex polysaccharides consisting of acidic heteropolysaccarides and polypeptides. Other polysaccharides fractions such as

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LBP 1a-1, LBP 1a-2, LBP 3a-1 and LBP 3a-2 (Duan et al. 2001), LBPA3, LBPB1, LBPC2 and LBPC4 (Zhao et al. 1997) were also extracted from *L. barbarum*.

Carotenoids

F. lycii contains a wide spectrum of antioxidant carotenoids, including β-carotene, zeaxanthin and lutein. It is the richest source of carotenoids of all known foods (Benzie et al. 2006; Cheng et al. 2005; Lam and But 1999; Weller and Breithaupt 2003). Most of carotenoids in *F. lycii* existed as esterified forms (Li et al. 1998). It is reported that total carotenoid concentrations of *F. lycii* from different sources are within the range of 0.03–0.5%. Zeaxanthin dipalmitate is a predominant carotenoid, comprising 31–56% of the total carotenoids in *F. lycii* (Peng et al. 2005). *F. lycii* is a good dietary source of zeaxanthin supplement. Leung *et al* (Leung et al. 2001) used rhesus monkeys to study the serum and tissue levels of zeaxanthin and lutein after feeding *F. lycii* extracts. Serum levels and macular density of zeaxanthin was raised by feeding a carotenoid-containing fraction of *F. lycii*. A study was designed to assess the concentration of 3R, 3'R-zeaxanthin reached in plasma after the consumption of a single dose of native 3R, 3'R-zeaxanthin palmitate from *L. barbarum* or non-esterified 3R, 3'R-zeaxanthin in equal amounts in twelve volunteers (Breithaupt et al. 2004). Enhanced bioavailability of 3R, 3'R-zeaxanthin dipalmitate was observed compared with the non-esterified form (Breithaupt et al. 2004). A possible explanation could be the apolar nature of 3R, 3'R-zeaxanthin dipalmitate in comparison with the more polar non-esterified form, which allows for the effective formation of micelles, needed before lipase activity (Breithaupt et al. 2004). Zeaxanthin and lutein are two carotenoids contained within the retina and may protect the macula and photoreceptor outer segments throughout the retina from oxidative stress and play a role in an antioxidant cascade that safely antagonize the energy of reactive oxygen species (ROS) (Semba and Dagnelie 2003). Lutein and zeaxanthin supplementation could protect the eyes against the development or progression of age-related macular degeneration (AMD) and other eye diseases (Landrum and Bone 2001).

Flavonoids

F. lycii is rich in flavonoids (Le et al. 2007). Three flavonol compounds---kaempferol, quercetin and myricetin---were obtained from the ethanol extract of *F. lycii* using reversed-phase HPLC and their structures were confirmed by electrospray ionization-mass spectroscopy. The three flavonols accounted for 43% of total flavonoid content (Le et al. 2007).

Amino acids and trace elements

L. barbarum contains 18 kinds of amino acids, of which 8 are indispensable amino acids for the human body. 50% of the amino acids are free amino acids. Taurine, a nonessential free amino acid, was found abundantly in *L. barbarum* (Cao et al. 2003; Xie and Zhang 1997). The content of taurine detected in *L. barbarum* is more than 3 mg/g (Cao et al. 2003). Although the function of taurine is the formation of bile salts, other functions including effects on retinal development, antioxidation, neuroinhibition, maintenance of excitatory activity in muscle, modulation of inflammatory cytokines in the brain and osmotic regulation of cell volume have been reported. (Cao et al. 2003; Chang et al. 2001). *L. barbarum* contains numerous trace elements, of which the main ones are zinc, iron and copper.

Fatty acids

L. barbarum contains essential fatty acids, which are required for the production of hormones and for the smooth functioning of the brain and nervous system. It is reported that fatty acids and their esters: hexadecanoic acid (47.5%), linoleic acid (9.1%), myristic acid (4.2%), and ethyl hexadecanoate (4.0%) were found to be the main constituents in the essential oil of *L. barbarum* (Altintas et al. 2006).

Vitamin

L. barbarum contains vitamin C at higher level than that found in oranges. A novel stable precursor of vitamin C, 2-O-(β-D-glucopyranosyl) ascorbic acid, was isolated from both the ripe fresh fruit and dried fruit of *L. barbarum* (Toyoda-Ono et al. 2004). B-complex vitamins, which are necessary for converting food into energy, and vitamin E, which is very rarely found in fruits, were also rich in *L. barbarum.*

Other bioactive components, such as β-sitosterol, betaine and scopoletin were identified in the fruit of *L. barbarum* (Xie et al. 2001). Betaine, which is used by the liver to produce choline, can inhibit the lipid peroxidation of RBC membrane (Ren et al. 1995). Scopoletin is the active component of the fruit of *L. barbarum* for inhibiting cell proliferation of human prostate cancer PC3 cells (Liu et al. 2000).

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Anti-aging effect of *F. lycii* as an antioxidant against oxidative damage

In 1956, Harman proposed the free radical theory for aging. The basic idea behind this theory is the assumption that aging results from random deleterious effects to tissues brought about by free radicals (Nohl 1993). Free radicals such as $\bullet O_2^-$ (superoxide anion), $\bullet OH$ (hydroxyl radical), H_2O_2 (hydrogen peroxide) and $^1O_2$ (singlet oxygen) attack the unsaturated fatty acids in the biomembranes resulting in membrane lipid peroxidation, a decrease in membrane fluidity, loss of enzymes, receptor activity and damage to membrane proteins leading to cell inactivation (Dhuley et al. 1993). The tissue injury includes DNA damage, protein damage and oxidation of enzymes in the human body.

Aerobic organisms are protected from oxygen toxicity by a natural antioxidant defence system involving enzymatic and non-enzymatic mechanisms (Ames et al. 1993). In the enzymatic defence mechanism, the major antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px) are regarded as the antioxidant defence system against reactive oxygen species generated in vivo during oxidative stress. SOD dismutates superoxide radicals to form hydrogen peroxide, which in turn is decomposed to water and oxygen by GSH-Px and CAT, thereby preventing the formation of hydroxyl radicals (Yao et al. 2005). These enzymes act cooperatively at different sites in the metabolic pathway of free radicals. Non-enzymatic antioxidants such as ascorbic acid, α-tocopherol, carotenoids, flavonoids and micronutrients such as zinc and selenium are present in notably high levels in a number of medicinal plants (Polidori et al. 2001). Restriction on the use of synthetic antioxidants is being imposed because of their carcinogenicity (Guyton et al. 1991). Therefore, the development and utilization of more effective antioxidants of natural origin are desired. Current research into free radicals has confirmed that foods rich in antioxidants play an essential role in the prevention of cancers (Serafini et al. 2002) and neurodegenerative diseases, including Parkinson’s and Alzheimer’s diseases (Di et al. 2002). *F. lycii* contains polysaccharides, ascorbic acids, vitamin E, carotenoids, flavonoids, betaine and micronutrients, all of which are potent antioxidants.

***Anti-oxidation effect of F. lycii* polysaccharides (LBP)**
LBPs have been identified as one of the active ingredients responsible for its biological activities. Both *in vitro* and *in vivo* studies have confirmed that polysaccharides have potent antioxidant activity. The antioxidant activity of the polysaccharides extracted from *L. barbarum* fruits has been evaluated by six *in vitro* methods (Li et al. 2007b). The multiple antioxidant activity of the polysaccharides is evident as it shows significant reducing power, superoxide scavenging ability, inhibition of mice erythrocyte hemolysis mediated by peroxyl free radicals and also ferrous ion chelating potency (Li et al. 2007b). In aged mice, changes in the antioxidant enzyme activity and lipid peroxidation product were investigated and effect of LBPs on oxidative stress in different organs was checked (Li et al. 2007c). Results showed that increased endogenous lipid peroxidation, and decreased antioxidant activities, as assessed by SOD, CAT, GSH-Px and total antioxidant capacity (TAOC) were observed in aged mice and restored to normal levels in the polysaccharides-treated groups. Moreover, addition of vitamin C to the polysaccharides further increased the *in vivo* antioxidant activity of the latter (Li et al. 2007c). In oxidative injured rat liver mitochondria induced by γ-irradiation, LBP significantly protects against loss of protein thiols and inactivation of SOD, CAT and GSH-Px in mitochondrial membranes. Moreover, the polysaccharide was more effective than a-tocopherol (Vit E) in inhibiting γ-irradiation-induced oxidative injury (Li et al. 2007a).

Increased oxidative stress is a widely accepted factor in the development and progression of diabetes and its complications (Ceriello 2000). In the streptozotocin (STZ) rat model of diabetes, administration of LBP can restore abnormal oxidative index to normal in its liver and kidney tissues, which also dose-dependently reduced malondialdehyde (MDA) level or increased antioxidase activities (SOD, CAT, GSH-Px, GR) compared with untreated diabetic control group (Li 2007). Also, LBP can control the level of blood glucose and modulate its metabolism, leading to significant decline in oxidative stress in rats with non-insulin-dependent diabetes mellitus (NIDDM) (Wu et al. 2006) and protect isolated rat islet cells from alloxan-induced damage (Xu et al. 2002). These studies also provide some scientific evidences for development of LBPs as potential natural oral anti-diabetic agents.

Oxidative stress has been reported to be a major cause of structural degradation and apoptosis in testes under hyperthermic stress. Testicular germ cells are vulnerable to heat stress and undergo apoptosis in response to increased

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scrotal temperature (Miura et al. 2002). SOD is the most heat-sensitive antioxidant enzyme; therefore heat exposure leads to the decrease of its activity in rat testicular tissues. SOD depletion in spermatozoa is thought to be associated with male infertility. H_2O_2, one of the main ROS, has been demonstrated to cause lipid peroxidation and DNA damage in cells (Halliwell and Aruoma 1991). LBP can effectively scavenge free radicals, suppress lipid peroxidation, and alleviate the damage to spermatogenic cells induced by heat exposure. LBP had significant protective effects against H_2O_2-induced DNA damage in the mouse testicular cells either by directly removing H_2O_2, scavenging •OH induced by H_2O_2 or by activating antioxidant defence system in the testicular tissues (Luo et al. 2006; Wang et al. 2002). These findings provide some scientific evidences for the extensive use of *L. barbarum* fruits as a traditional remedy for male infertility in China.

Antioxidative effect of flavonoids in F. lycii

The flavonoid is an important class of plant antioxidant (Heims et al. 2002). *F. lycii* is rich in flavonoids and contains substantial amounts of the three anti-oxidative activities (radical-scavenging activity, reducing capacity and chelating activity) *in vitro* (Le et al. 2007). Total flavonoids of *L. barbarum* (TFL) (0-217 mg/L) could scavenge O^{2-} in xanthine/xanthine oxidase (Xan/XO) system, with scavenging rate of 0-51%. TFL (7.5-200 mg/L) could scavenge OH produced in Fenton reaction and the scavenging rate is between 20% to 72% (Huang et al. 1998). Lipid peroxidation (measured as malondialdehyde, MDA) was significantly inhibited by TFL with a dose-response relation between the concentrations of 0.025 and 2.0 mg/ml, and the fluidity of mitochondria membrane was also protected effectively (Huang et al. 1999b).

Anti-aging effect of *F. lycii* as an immunomodulator against tumor

A variety of changes are observed in the immune system in both animal and human with increasing age. There is a decline in the functional capacity of immune responses and production of immunocompetent cells to regulatory signals and proteins. These changes translate into less effective innate and adaptive immune responses, increased reactivity against self-antigens in vivo, and an increased incidence of infection (Burns and Goodwin 2004).

Reduction of proliferative response of lymphocytes with age is one of the earliest qualitative changes. Quantitative analysis of T cells with aging appears to primarily involve shifts in the proportion of subpopulations such as CD4+ T helper and CD8+ T suppressor cell compartments. T helper cells from old mice are less capable of generating cytotoxic T lymphocytes (CTLs) to participate in delayed hypersensitivity reactions. Cytotoxic lymphocytes from aged mice are less effective in binding targets (Burns and Goodwin 2004). Studies revealed that LBP can obviously augment T cell-mediated immunity by increasing T lymphocyte proliferation and enhancing the activity of CTL (Deng et al. 2003; Du et al. 2004; Wang et al. 1990). LBP can significantly increase the numbers of CD4+ and CD8+ T cells in tumor-infiltrating lymphocytes (TILs) to relieve the immunosuppression and enhance the anti-tumor function of the immune system of H22-bearing mice (He et al. 2005). Dendritic cells (DC) are potent antigen-presenting cells that play pivotal roles in the initiation of the primary immune response of both helper and cytotoxic T lymphocytes. After capturing antigen, the DC precursors migrate to T cell regions of draining lymph nodes where they mature into functional DC. The functional DC further stimulate naive T cells by triggering the signalling pathway for antigen presentation and expression of co-stimulatory molecules. Study has proven that LBP can increase the number of dendritic cells in TILs of H22-bearing mice (He et al. 2005). Further study confirmed that LBPs are capable of promoting both the phenotypic and functional maturation of bone marrow derived dendritic cells (BMDC) *in vitro*. The co-expression of I-A/I-E, CD11c and secretion of IL-12 p40 by BMDC stimulated with LBPs (100 mg/ml) are increased (Zhu et al. 2007).

Both the primary and secondary antibody responses are affected in aging. Specific Antibody production to primary and secondary antigens was decreased with advancing age (Burns and Goodwin 2004). Immune-promoting effect of LBP on humoral immunity may be one of its actions against aging. The enhancing effect of LBP on antibody production response and IgG production by splenocytes in senescence-accelerated mouse (SAMP8) is also found by Qi *et al* (Qi et al. 2001) and the pure LBP at lower doses show higher immunological activity than crude LBP (Luo et al. 1999).

Senescence of the immune system may have a greater influence on tumor growth than on initial occurrence (Ershler 1993). Protective immunity against tumor is composed of both cellular and humoral immunity. Cell-mediated immune defense was mediated specifically by T cells including cytotoxic T cells. T cells can kill tumors and produce many lymphocyte factors consisting of macrophage mobile factor, lymphotoxin, transfer factor and interferon, which can enhance macrophage phagocytosis and the capacity of killing target cells. The

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humoral defence via antibody response is mediated by B cells and other immune cells involved in antigen processing and immunization. The antigen–antibody complex can counteract toxin and defend the infection induced by pathogen. Study has shown that water extracts of *L. barbarum* can promote the immune function recovery of radiated mice (Wang et al. 1995). The thymus and spleen index, proliferation reactions of spleen cells to concanavalin (Con A) or lipopolysaccharide (LPS), mixed lymphocyte culture (MLR), delayed type hypersensitive reaction (DTH) and plaque forming unit counts (PFC) of mice were enhanced by LBP treatment 30 days post ^{60}Co radiation (Wang et al. 1995).

Furthermore, LBP can markedly increase the natural killer (NK) and lymphokine-activated killer (LAK) cell activity and can be used as an adjuvant in the LAK/IL-2 biotherapy of cancer (Cao et al. 1994). LBP3p can significantly inhibit the growth of transplantable sarcoma S180 and increase macrophage phagocytosis, the form of antibody secreted by spleen cells, spleen lymphocyte proliferation, CTL activity and IL-2 mRNA expression level in S180-bearing mice (Gan et al. 2004). IL-2 and tumor necrosis factor-α (TNFα) are two important cytokines in antitumor immunity. IL-2 plays a vital role in activating T or B lymphocytes, proliferation of CTLs, helper T lymphocytes, NK cells, LAK cells and macrophages. The activity of IL-2 to promote the proliferation of the lymphocytes in aged mice was significantly lower than that of the adult mice. LBP can increase and restore the activity of IL-2 of aged mice (Geng et al. 1989). Administration of LBP3p increased the expression of IL-2 and TNFα at both mRNA and protein levels in a dose-dependent manner in human peripheral blood mononuclear cells (Gan et al. 2003).

Neuroprotective effect of *F. lycii* on aging-related neurodegenerative diseases

Beta-amyloid (Aβ) is one of the pathological factors leading to neuronal loss and apoptosis. Aβ-triggered neuronal cell death has been suggested in the involvement of caspase activation, stress kinase activation, ion channels formation, membrane destabilization, membrane receptor-mediated response, oxidative stress and intracellular calcium imbalance. The neuroprotective effects from aqueous and alkaline extract of *L. barbarum* to attenuate Aβ peptide neurotoxicity has been investigated by Yu *et al* (Ho et al. 2007; Yu et al. 2007; Yu et al. 2005). Primary cultured cortical neurons were exposed to Aβ peptides which induced apoptosis. Pretreatment of the aqueous extract (LBA) and alkaline extract (LBB) significantly reduce the level of lactate dehydrogenase (LDH) release and the activity of caspase-3 triggered by Aβ (Ho et al. 2007). LBA has wider effective dosages than that of the well-known western neuroprotective drug LiCl. Western blot analysis revealed that the neuroprotection mechanism of LBA relies on inhibition of c-Jun N-terminal (JNK) signalling pathway but subfractions of LBB showed a different mechanism by enhancing the phosphorylation of Akt, which can protect neurons from Aβ-induced apoptosis (Yu et al. 2005). These findings may open up a new avenue for drug discovery in neurodegenerative diseases such as Alzheimer's disease (AD)

Experiments have also indicated that polysaccharide from *L. barbarum* elicits neuroprotection to eye (Chan et al. 2007). In ocular hypertension (OH) model, rats fed with the *L. barbarum* extract could nearly totally escape from pressure-induced loss of retinal ganglion cells (RGCs). The results demonstrate that this extract may be a potential candidate for the development of neuroprotective drug against the loss of RGCs in glaucoma. Studies have also confirmed that *L. barbarum* is not simply an antioxidant in order to function as a neuroprotective agent, its aqueous extract can also protect neurons from dithiothreitol (DTT)-induced endoplasmic reticulum reducing stress (Yu et al. 2006).

Conclusion

F. lycii is an effective Chinese herb against aging and age-related diseases. The main ingredients accounting for its potent effect are polysaccharides, carotenoids and flavonoids. The mechanism underlying its anti-aging effect and applications are concluded into three aspects: First, polysaccharides, carotenoids and flavonoids in *F. lycii* could scavenge free radicals accumulated with age and amelierate the deleterious effects to tissues brought about oxidative damage. The antioxidant activity of *F. lycii* makes it a promising candidate for the therapy of male infertility, age-related macular degeneration and other oxidative stress-induced diseases. Second, polysaccharides in *F. lycii* is a potent immunostimulator which could obviously augment both the cellular and humoral immunity declined with increasing age, indicating that LBP can be used as an adjuvant in the biotherapy of cancer. Third, owing to its neuroprotective effect, *F.*

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lycii could be employed as new drug for aging-related neurodegenerative diseases such as Alzheimer's disease and the loss of RGCs in glaucoma.

Modern research on the anti-aging aspect of *F. lycii* is a successful model which integrated the experience-based traditional Chinese medicine and western evidence-based medicine and reflects the advantage the employing the multi-functional herbal materials in the prevention and treatment of age-related diseases. More anti-aging herbs according to Chinese literature need to be studied and developed using new theories and methodologies to benefit the increasing geriatric community worldwide and treat age-related diseases.

List of abbreviations

AD: Alzheimer's disease
AMD: age-related macular degeneration
Aβ: Beta-amyloid
BMDC: bone marrow derived dendritic cells
CAT: catalase
Con A: concanavalin A
CTLs: cytotoxic T lymphocytes
DC: Dendritic cells
DTH: delayed type hypersensitive reaction
DTT: dithiothreitol
F. lycii: Fructus lycii
GSH-Px: glutathione peroxidase
IL-2: interleukin-2
JNK: c-Jun N-terminal
L. barbarum: Lycium barbarum L.
LAK cells: lymphokine-activated killer cells
LbGp: *Lycium barbarum* Glycopeptide
LBPs: *Lycium barbarum* polysaccharides
LDH: lactate dehydrogenase
LPS: lipopolysaccharide
MDA: malondialdehyde
MHC: major histocompatibility complex
MLR: mixed lymphocyte culture
NIDDM: non-insulin-dependent diabetes mellitus
NK cells: natural killer cells

PFC: plaque forming unit counts
RGCs: retinal ganglion cells
ROS: reactive oxygen species
SOD: superoxide dismutase
STZ: streptozotocin
TAOC: total antioxidant capacity
TFL: flavonoids of *Lycium barbarum* L.
TIL: tumor-infiltrating lymphocytes
TNF: tumor necrosis factor

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