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LYCIUM BARBARUM (GOJI BERRY) AND ITS EFFECTS IN HEALTH
LYCIUM BARBARUM AND HEALTH

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ABSTRACT

Lycium barbarum or gojy berry (or wolfberry) is a plant popularly known for its benefits to the health, including hypoglicemic effects, body weight control and as anti-cancer. The purpose of this review was to investigate the properties and medicinal applications of *L. barbarum*. Although there are still many characteristics that need to be studied about this plant, several benefic effects have been reported. Literature shows that there are several compounds in gojy berry that may prevent oxidant and inflammatory process, hyperglycemia, dyslipidemia and obesity. We suggest that this plant should be more researched in order to evaluate the possibility of application in the pharmaceutical industry and to obtain enough information to consider validation for its medicinal use.

KEYWORDS: *Lycium barbarum*, oxidative stress, inflammation, weight control, hhyperglycemia.

INTRODUCTION

Lycium barbarum (Gouqi, goji berry or wolfberry) belongs to the plant family Solanaceae and its red berries have been used for more than 2500 years as a traditional herb and food supplement including medicinal beverages and healthy soups. The traditional Chinese medicine have been using *L. barbarum* polyssaccharide (LBP) as the active ingredient.[1, 2]

The use of this plant is based on effects such as antiaging, antioxidant, anticancer antihypertensive, antidiabetics, antihyperlipidemia, antithrombosis, treatment of infections, inflammatory bowel disease and improvement of immune system.[3, 4]

In Brazil, goji berries are commonly used for reduction of body weight and in the treatment of dyslipidemia and diabetes and its consumption is increasing year by year due to these medicinal applications.[5]

Natural plants or its products are related to low toxicity to the liver and kidney and may work as an alternative for prevention or treatment of several diseases since the available allopathic therapies are usually associated with high costs and different side effects that bring discomfort for the patients. Due to the several positive effects that plant may promote in health, the objective of this review was to investigate the properties and applications of goji berry.

***Lycium barbarum* composition and health benefits**

L. barbarum contains polysaccharides, scopoletin, the glucosylated precursor and stable vitamin C analog 2-O-β-d-glucopyranosyl-l-ascorbic acid, carotenoids, betaine, cerebroside, β-sitosterol, flavonoids, amino acids, minerals, and vitamins. Table 1 shows some compounds present in this plant and its effects in health. The berries are known as the richest natural source of zeaxanthin, performing a high antioxidant capacity.[6, 7]

Table 1. *Lycium barbarum* compounds and their effects.

Goji berry	Compounds	Effects
Fruit extract.[8,9]	Phenolic content, flavonoids, quercetin, rutin, carotenoids and anthocyanins.	Anti-oxidant and Anti-inflammatory.
Ethanolic extract.[10]	Phenolic compounds.	Anticancer activity and non-toxicity effect against normal human skin fibroblasts (chemopreventive potential in breast cancer treatment).
Dried mature fruit.[8,11,12,13]	LBP, scopoletin, the glucosylated precursor, and stable vitamin C analog 2-O-*β*-d-glucopyranosyl-l-ascorbic acid, carotenoids, betaine, cerebroside, *β*-sitosterol, flavonoids, amino acids, minerals, and vitamins.	Protection of nervous system, improvement of immunity and regulation of glycaemia, protection of the eyes. Modulation of central nervous system and amplification of positive adaptive changes with improvement of function recovery and induction of selective target re-innervation in high fructose-diet animals with sciatic nerve crush-injury.

LBP: *Lycium barbarum* polysaccharides

Lycium barbarum polysaccharides (LBP)

L.barbarum polysaccharides (LBP) have multiple biological and pharmacological functions and are widely used in the manufacture of health care products to improve immunity, neuronal protection, and anti-aging.[7, 11, 12, 14-16] Figure 1 shows some effects of LBP.

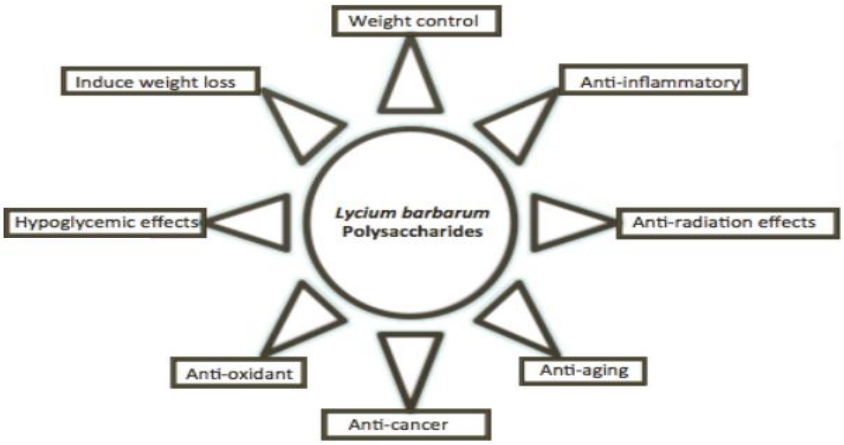

Figure 1. *L. barbarum* polysaccharides (LBP) and their biological effects.

LBP fractions present fucose, ribose, rhamnose, arabinose, xylose, mannose, galactose and lucose. It may also contain uronic acid and proteins.[4] Studies indicate that LBP act such as anti-inflammatory[17], anti-cancer[18,19], anti-fatigue[20], neuroprotective[16,21], anti-oxidant[11,17,22-26], hypoglycemic[17,27,28], fertility-protective[29], immunomodulating[30] and anti-radiation effects, most of which are related to the reproductive[29,31] and immune systems.[1] Studies show that the *L. barbarum* exhibits immune enhancing, hepatoprotective and neuroprotective properties and protect the eyes.[2, 12, 32] The neuroprotective effects may be used for neurological disorders prevention[15], although the specific mechanism of the compound remains uncertain. Table 2 show summarizes some effects of LBP.

Table 2. *Lycium barbarum* polysaccharides and some effects in health.

Model	Effects
Rats and mice.[7, 9,11, 20, 33]	Anti-inflammatory, anti-oxidant and ant-aging
Mice.[11]	Anti-radiation effects.
Diabetic rabbits.[34]	Generation and development of new neurons and inhibition of methylmercury induced damage in hippocampus neural stem

	cells. Improvement of renal function and inflammatory process in the kidneys.
Sprague-Dawley rats.[35]	Huntington's disease treatment.
Sprague-Dawley diabetic rats and humans.[17,36]	Hypoglycemic effects.
Review.[37]	Neuronal protection and ameliorative effects on inflammatory and oxidative processess, apoptosis and cell death.

LBP: anti-oxidant effects

Oxidative stress occurs due to an imbalance between pro-oxidants and anti-oxidants and it has been recognized as a contributing factor in several diseases such as inflammation, hypertension, cancer, diabetes, aging and neurodegenerative disorders. The excessive production of reactive oxygen species (ROS) are implicated in disease processes causing damage to cell structures, changing the normal physiological process.[8, 38]

Superoxide dismutase (SOD) is an anti-oxidant enzyme, one of the primary choice for elimination of ROS and prevent cell damages[39] Free radicals and lipids generate malondialdehyde (MDA) by peroxidation, which content is an indirect indicator of membrane damage. Oxidative stress is closely related to apoptosis and neurodegenerative disorders.[40-42]

Studies have shown that LBP could scavenge free radicals and reduce lipid peroxidation.[26] Berries are source of polyphenols and anthocyanins that show effects in the modulation of cell functions related to oxidative stress and/or anti-oxidant protection.[8, 36] LBP increases the activity of SOD, reduces the content of MDA, thus, bring protection to the cells.[1, 11, 29] An experiment using mice exposed to radiation showed better activity of SOD and decreased the MDA content after treatment with LBP.[11]

L. barbarum has attenuated oxidative stress and inflammation in streptozitocin induced diabetic rats (17). In high-fat diet-induced insulin resistance animal models, LBP is confirmed to be an anti-oxidant against insulin resistance and increases insulinogenic index and high density lipoprotein (HDL-c) levels in patients with type II diabetes.[36]

Until this time, the effects of berries on DNA damage and endogenous anti-oxidant enzyme activities and their effects on the inflammation are poorly understood.[43]

LBP: anti-inflammatory effects

Inflammatory process is a significant hallmark of diseases or pathological conditions and some plants have demonstrated anti-inflammatory effects by modulating oxidative stress.[44,45]

In fact, several studies demonstrate that berries show anti-inflammatory properties.[8, 11, 17] and protected DNA damage induced by H2O2 in mouse testicular cells and decreased the production of inflammatory mediators, such as prostaglandin E2, nitric oxide, interleukin 1β (IL-1β), and IL-6 in macrophages.[46, 47]

The over expression of IL-2 in inflammatory process enhanced the expression of endogenous cytokines.[17, 48] IL-6 and Tumor Necrosis Factor-α (TNF-α) elevation contributed to cell damage[17, 49] and studies using diabetic induced rats showed that LBP normalized IL-2, IL-6, TNF-α and interferon-α.[17]

The activation of neutrophils in inflammation process increases ROS production and its high level contributed to microvascular inflammation responses, including leukocyte recruitment and increased vascular permeability. LBP reduces the infiltration of neutrophils, improving the inflammation process.[8, 50]

LBP: anti-radiation effects

The degree of damage of ionizing radiation on humans is an increasingly serious issue and it is related to the dose of radiation and damage of exposure, but it may also confers benefits for humans such as X-rays, computed tomography and cancer therapies. There is a search for nontoxic or low-toxic anti-radiation drugs derived from traditional herbs.[11,29]

LBP have shown a protective effect against ionizing radiation-induced damage cells, including *in vivo* studies that assayed apoptosis (regulated genetically and induce by physiological and pathological stimuli, such as radiation). LBP may protect the reproductive function and prevent spermatogenic cell apoptosis induced by radiation. Kunming mice were exposed to X-rays to establish radiation injury models and treatment with an increase in dosage and duration of exposure to LBP dose decreased the apoptotic rate drastically and significantly.[11, 29, 31]

Furthermore, LBP may promote improvement in immune function.[1, 29] The overexpression of adhesion molecules such as CD44 and CD49dis related to the redistribution of

hematopoietic stem cells and homing, important in leukemia and hematological disease, respectively.[51] A mice model showed overexpression of CD44 and CD49d in the group which was exposed to ionizing radiation. Increasing the duration and dosage of LBP, there was significant suppression in the CD44 and CD49d expression.[11]

As pointed before, the increase the activity of SOD promoted by LBP results in anti-oxidative effects, improving cells response to radiation. With the increase in dosage and duration of the treatment, the anti-oxidative effects were better, but additional studies are needed to further establish the underlying mechanisms.[1, 11, 29]

LBP and Diabetes mellitus

Diabetes mellitus is characterized by hyperglycemia and metabolic disturbance and may cause several complications, such as nephropathy, the major cause of end-stage renal disease. Due to the limitation of treatment agents that focus on regulating blood glucose levels, insulin injection and some oral anti-hyperglycemic agents, a search for alternative treatment is highly demanded.[11,52,53,54] The disequilibrium of physical function in diabetic patients causes accumulation of ROS. In high-fat diet-induced insulin resistance animal models, LBP is confirmed to be an anti-oxidant against insulin resistance; its activity may be related to the normalization of oxidative system.[17, 55]

Patients with type II diabetes treated with LBP showed increased insulinogenic index and HDL-c. Inflammatory and immunosuppressive factors are involved in hyperglycemia that causes glomerular hypertrophy and glomerular basement membrane thickening. The over expression of IL-2, IL-6 and TNF-αmay be normalized with LBP in induced diabetic rats. These data suggest that LBP possesses anti-diabetic nephropathy actions, regulating inflammatory factors reducing oxidative stress.[17, 36]

Peroxisome proliferator-activated receptors (PPARs) have been implicated to participate in physiological and pathological processes, important in the treatment of diabetes mellitus, obesity, and atherosclerosis. They play important roles in the expression of various genes, which are crucial to lipid and glucose metabolism. A study showed that the ethyl acetate extracts of root bark of *L. barbarum* could active PPARs effects and the anti-diabetic activity of them could in part be mediated by this nuclear receptor, improving glucose and lipid metabolism.[56-59]

***Lycium barbarum* and weight control**

As we pointed before, the use of *L. barbarum* interferes in PPAR. A study that developed a cell-based PPARs screening model indicated that the ethyl acetate extracts of root bark of *L. barbarum* could significantly activate PPARγ, showing that this plant maybe used to promote the activation of PPARs effects on the glucose homeostasis and lipid metabolism. Thus, it may be important in the treatment of risk factor for cardiovascular diseases.[59]

Anthocyanins and other polyphenolic phytochemicals contained in *L. barbarum* and other berry fruits extracts have, in addition to anti-oxidant, anti-diabetic effects, hypolipidemic action effects and may control the weight.[8,9]

Bueno et al[5] realized an experimental research with Wistar rats treated with gojy berry tea. After 60 days, the animals presented weight loss even not reducing the food consumption. At the same time this study showed that animals treated with not pure gojy berry products, the results are not significant in lipid profile and may increase glicemia.

LBP and ethanol extract isolated: anti-cancer properties

Many researches have focused on searching for anti-cancer drugs with higher activities and lower toxicity from nature. Studies with medicinal plants have reveled anti-cancer activities probably to their capacity to induce apoptosis in cancer cells.[33, 60-61]

The mechanism of apoptosis is different from cell death in which a programmed sequence of events leads to the elimination of cells without releasing harmful substances into the surrounding area. When apoptosis does not work correctly, cells that should be eliminated may persist and become immortal. Therefore many kinds of tumor are related on blockage of apoptosis channel. Apoptosis inducing activities is one of the most important target of anti-tumors drugs.[63]

Authors identified that LBP inhibit the proliferation of human QGY7703 hepatoma cells, and human MGC-803 and SGC-7901 gastric cancer cells.[64, 65]

There is a anti-cancer activity also in ethanol extract isolated from gojy berry. This substance inhibited the proliferation of T47D human breast cancer cell line. The main proprieties is the reduction of anti-apoptotic proteins and the increase of pro-apoptotic proteins. No cytotoxic effects was found in normal cells.[10]

CONCLUSIONS

There are several compounds in gojy berry that may prevent hyperglycemia, dyslipidemia, obesity, cancer and oxidant and inflammatory processes. Due to its several effects in health, we suggest that *L. barbarum* should be more studied in order to evaluate the possibility of application in the pharmaceutical industry and to obtain enough information as the dose, the best delivery vehicle, pharmaceutical formulation and route of administration. All these information could give validation for its medicinal use.

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