OPEN ACCESS
Saudi Journal of Biomedical Research
Abbreviated Key Title: Saudi J Biomed Res
ISSN 2518-3214 (Print) |ISSN 2518-3222 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article

Beneficent Role of Lycium Barbarum on Liver Health

Aisha Malik[1*], Irum Naureen[2], Aisha Saleem[1]

[1]M. Phil Researcher, School of Zoology, Minhaj University Lahore, Pakistan
[2]Assistant Professor, School of Zoology, Minhaj University Lahore, Pakistan

DOI: 10.36348/sjbr.2021.v06i12.003 | **Received:** 04.11.2021 | **Accepted:** 09.12.2021 | **Published:** 19.12.2021

***Corresponding author:** Aisha Malik

Abstract

Lycium Barbarum (wolfberry, goji berry, gouqizi, 枸杞) is a Chinese herbal drug located in Asia and South east Europe. The fruits of Lycium Barbarum are 1 to 2 cm long and are bright orange red in color. The speedy increase in the occurrence diseases has led to more research which contributes in the prevention and treatment. Goji berries contain many nutrients and bioactive compounds which allowed classifying them as superfruits. A short description of the fruits is presented together with cultivation requirements. The chemical composition of the berries and their health-promoting properties are described later in this literature review. There are potentially, very beneficial in dietary prevention of diseases, and affluence, such as diabetes, cardiovascular diseases and cancer. Lycium Barbarum is beneficial in all aspects including hepatoprotective, anti-cancer, anti-tumor, anti-aging, immunological, neuroprotection, and ant fatigue, control of glucose, anti-tumor and anti-oxidant properties. Lycium Barbarum juice is beneficial in many aspects including cardiovascular effects, blood pressure and pulse rate, neurological and psychological effects and musculoskeletal complaints. Goji ingredients that is potentially beneficial, and harmful for the human health, show allergic reactions and the interactions with other substances. High dietary fat intake has been shown to be associated with the development of obesity, diabetes, hypertension, cardiovascular disease and other physically degenerative disease.

Keywords: Lycium Barbarum, Gogi berries, bioactive compounds, Antioxidants, polyphenols, Health benefits.

INTRODUCTION

Lycium Barbarum (wolfberry, gogi berry, gouqizi, 枸杞) is a Chinese herbal drug located in Asia and South east Europe. The fruits of Lycium Barbarum are 1 to 2 cm long and are bright orange red in color [3]. The speedy increase in the occurrence diseases has led to more research which contribute in the prevention and treatment. LBP intake is associated with a number of therapeutic effects, including antiaging, neuroprotective effects in neurodegeneration owing to their antioxidizing properties, ocular neuroprotective effects [18], metabolic effect and neurotoxicity [17]. Furthermore, there is evidence that LBP may even improve male fertility [19].

Lycium Barbarum polysaccharides is one the most active component of this plant and involve a lot of biological activities such as neuroprotection, control of glucose, anti-tumor and anti-oxidant properties. In North America, Newzeland and Australia Lycium Barbarum fruits have been used as food and dietary supplements. Lycium Barbarum is characterized for its clinical and photochemistry properties. Lycium Barbarum juice is beneficial in many aspects including cardiovascular effects, blood pressure and pulse rate, neurological and psychological effects and musculoskeletal complaints [1].

Lycium Barbarum belongs to family *Solanaceae* and contains seventy species which grows in different areas of the world from temperate to subtropical regions including South America, North America, Australia and Southern Africa. Lycium Barbarum is also named as Barbary wolfberry or Chinese Boxothorn. Lycium Barbarum is beneficial to increase the life span and it also lowers the risk of arteriosclerosis and arterial hypertension [7]. Bioactive food components are physiologically active constituents in foods or dietary supplements derived from both animal and plant sources, including those needed to meet basic human nutrition needs, that have been demonstrated to have a role in health and to be safe for human consumption"[25].

Lycium Barbarum have been conducted on humans, laboratory animals and livestock animals especially mice and rabbits but very few research have been done on rabbits due to the less reproductive rate of rabbits. Rabbit is perfect livestock animal and the reproductive rate of rabbits depends on the amount and type of dose given to rabbits [2]. Goji berries or wolf berries have been used as a natural drug for improving the productive rate of rabbits. Negative balance of energy due to the lap over between the pregnancy and lactation period is the major reason for the less productive farm rates of rabbits. High costs of medicine and antibodies for curing disease are the other main reason for less productive rate. Studies revealed that Lycium Barbarum is effective to reduce infections, inflammations and thus act directly on the immune system, regulate secretions of hormones and improve oxidative status of organs [2]. The plant is extremely popular in China, where it has been used as a meal for generations due to its numerous health advantages and influence on lifespan [7].

Wolfberries ("goji", Lycium barbarum) Zhongning, Ningxia, China [26]

Composition

Lycium Barbarum contains high percentage of dietary fibers, proteins, micro and macro nutrients, carbohydrates and low level of fats. Lycium Barbarum also contains high nutritional value and biologically essential components such as phenolic, carotenoids, polysaccharides and flavonoids. Lycium Barbarum polysaccharides are the most important water soluble chemical component of this plant and comprised approximately 5 to 8% of dried fruit. Lycium Barbarum leaves find its usage in the form of spices and tea infusions. 0.03%-0-5% of this plant is composed of zeaxanth and esters. Other important components of Lycium Barbarum are alkaloids, glycoproteins, tocopherols, phenolic acids, sterols and betain etc. Goji berry (Lycium barbarum) contains over 15% of proteins, 21 essential minerals and 19 amino acids [34].

It includes: polysaccharides, carotenoids (such as zeaxanthin, fysalien and cryptoxanthin), calcium, iron, copper, calcium, zinc, selenium, isoleucine, tryptophan, germanium, potassium, phosphorus, and vitamin: B1, B2, B6 and E. Lycium Barbarum grows in dry, semiarid, and slightly semi saline areas in Mongolia, the Himalayas, western China, and Tibet. Lycium Barbarum contains a variety of coloured berries ranging from orange to dark red, while Lycium ruthenicum has tiny black berries. [4] The leaves of Lycium Barbarum are long and elliptic, the pedicel is 1–2 cm long, the calyx has two lobes that are 2- or 3-ribbed at the end, the corolla tube is 8–10 mm long and longer than the lobes, and the berries are red or orange, yellow, rectangular, and oval.

Lycium Barbarum contains fleshy, linear, or somewhat cylindrical leaves. The calyx has 2–4 lobes, the pedicel is 5–10 mm long, the berries are spherical purple and black, the head or border of the berry is occasionally notched, and the seeds are notably brown Gojji berry bushes grow at elevations ranging from 700 to 2700 meters and are very resistant to harsh climatic conditions [7]. Lycium Barbarum polysaccharides are the most important water soluble chemical component of this plant and comprised approximately 5 to 8% of dried fruit. 0.03%-0-5% of this plant is composed of zeaxanth and esters.

Other important components of Lycium Barbarum are alkaloids, glycoproteins, tocopherols, phenolic acids, sterols and betain etc. coloured berries ranging from orange to dark red, while Lycium ruthenicum has tiny black berries.. Gojji berry bushes grow at elevations ranging from 700 to 2700 meters and are very resistant to harsh climatic conditions [5].

Table-1: Energy and nutrients content of edible fresh and dried Lycium Barbarum fruit (100 g) [37]

Energy and nutrients content	Dried	Fresh
Energy (kcal)	349	-
Protein (g)	14.26	4.49
Fat (g)	0.39	2.33
Carbohydrate (g)	77.06	9.12
Pulp (g)	13.0	-
Ca (mg)	190	-
Fe (mg)	6.8	-

Energy and nutrients content	Dried	Fresh
Na (mg)	298	-
Vitamin C (mg)	48.4	-
Vitamin A (IU)	26822	-
Thiamin (mg)	-	0.23
Riboflavin (mg)	-	0.33
Niacin (mg)	-	1.7

Table-2: Polysaccharide Components Isolated from Lycium Barbarum [36]

Glycoconjugates	Carbohydrate Content (%)	Monosaccharides
LbGp2	90.71	Arabinose, galactose
LbGp3	93.6	Arabinose, galactose
LbGp4	85.6	Arabinose, galactose, Rhamnose, glucose
LbGp5	8.6	Rhamnose, arabinose, Xylose, galactose, mannose, Glucose
LbG5B		Rhamnose, arabinose, Glucose, galactose, Galactose (u)
LBP1a-1		Glucose
LBP1a-2		Glucose
LBP3a-1		GalactoseA
LBP3a-2		GalactoseA
LBP3p	92.4	Galactose, glucose, Rhamnose, arabinose, Mannose, xylose
LBPA1		Heteroglycan
LBPA3		Arabinose, galactose
LBPB1		Arabinose, glucose
LBPC2		Xylose, rhamnose, mannose
LBPC4		Glucose
LBPF1		-

Carotenoids have also been shown to defend against chronic illnesses. Carotenoid, the root of Lycium barbarum's red-orange colour and the focus of attention as the second key bioactive component, is found in the dried fruit in amounts ranging from 2-4 mg per grams of weight. The carotenoid zeaxanthin dipalmitate accounts for 56% of the total Carotenoid content in the fruit. -cryptoxanthin palmitate, zeaxanthin monopalmitate, and negligible levels of free zeaxanthin and -carotene are also found in Lycium barbarum. This fruit differentiates out among other fruits because of its high levels of dipalmitates and the increased bioavailability of esterified zeaxanthin (1143.7 g/g dried fruit) compared to free carotenoid [35, 1].

Health Benefits of Lycium Barbarum

A Gojji berry has been used for about thousands of years in the form of Traditional Chinese Medicine TCM as a food product and a natural curable herbal plant for the treatment of different diseases. Lycium Barbarum contains a variety of traditional, nutritional and economical values which then meets the demand of industrial sustainability in organic life [13]. Some common scientific names of Lycium Barbarum are Goji berries, wolf berries, Chinese herbalism etc. In TCM, Chinese herbalism or Gojji berries are effective for boosting sperm production in man, improves eyesight, enhances immunity, protects liver and kidney, regulates blood circulation along with other factors.

Lycium Barbarum can be crushed into fine powder and then given in the form of dose. Gojji berries contain a lot of health biologically active components like thiamine, absorbic acid, riboflavin's, carbohydrates, calcium, zinc, selenium, magnesium, potassium, phosphorus, sodium and a lot of other minerals. This research clarifies the nutritional and bioactive properties of Lycium Barbarum [21].

Fruits from the Lycium genus have long been utilized for medicinal purposes and health benefits in the healing of liver, kidney, eye, immunological, circulation, and lifespan diseases. The nutritional profile, sugars, organic acids, fatty acids, and tocopherols of Lycium Barbarum L. (Gojji) fruits and stems were stated in this study. Furthermore, bioactive capabilities such as antioxidant, hepatotoxic, and antibacterial activities were linked with phenolic profile of their hydromethanolic extracts [7, 8].

Energy, MUFA (monounsaturated fatty acids), tocopherols, and flavonols were mostly greater in stems. Antioxidant and antibacterial (against Gram-negative bacteria) activity were also higher in stems. Fruits, on the other hand, have more sugar, PUFA (polyunsaturated fatty acids), and hydroxycinnamic acid derivative content, as well as better action against Gram-positive bacteria. This study demonstrates the great potential of Gojji stems and fruits as bioactive chemical sources that may be employed in nutraceutical formulations or included into functional food items. Gogi berries may interact with certain drugs, including

blood thinners and medications for diabetes or high blood pressure.

Hypoglycemic properties

Goji fruit and the levels of glucose in blood, effects of L. barbarum preparations in alloxan-induced diabetic rabbits have been investigated by measuring a blood 3.9 mmol/L)≥glucose level. Decreased blood glucose levels (were recognized as substantial hypoglycemic effects. Results of the experiment were unambiguous. Moreover, the hypoglycemic effect of purified polysaccharide fractions was more significant than those of water decoction and crude polysaccharide fractions, implying that L. barbarum polysaccharides were major bioactive components in the hypoglycemic effect [29]. That animals on high-fat diets supplemented with polysaccharide fractions had statistically lower levels of glucose, compared to mice on high-fat diets only [30].

Antioxidant activity

The antioxidant activities of LBP have been widely studied in vitro previously. LBP exhibited moderate concentration-dependent inhibition of the 1,1-diphenyl-2 picrylhydrazyl radical, and significant reducing power, superoxide scavenging ability, inhibition of mice erythrocyte hemolysis mediated by peroxyl free radicals, and also ferrous ion chelating patency [31]. High dietary fat intake has been shown to be associated with the development of obesity, diabetes, hypertension, cardiovascular disease and other physically degenerative disease [32-33].

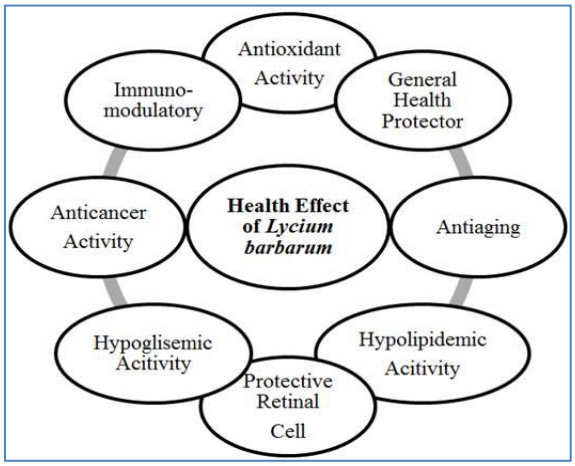

Fig-1: Health Effects of Lycium Barbarum [27].

Fruits from the Lycium genus have long been utilized for medicinal purposes and health benefits in the healing of liver, kidney, eye, immunological, circulation, and lifespan diseases. The nutritional profile, sugars, organic acids, fatty acids, and tocopherols of Lycium Barbarum L. (Gojji) fruits and stems were stated in this study. Furthermore, bioactive capabilities such as antioxidant, hepatotoxic, and antibacterial activities were linked with phenolic profile of their hydromethanolic extracts.

Hepatoprotective Role of Lycium Barbarum

Lycium Barbarum is a traditional Chinese medicine and herbal drug which have been widely used in china and other countries as a natural curable medicine. Lycium Barbarum polysaccharides are the active biological components of this plant. This research was done to find the effect and mechanism of Lycium Barbarum polysaccharides and its mechanism on Hepatic Encephalopathy HE [10].

The experiment was performed on thioacetamide induced acute mouse model. Some clinical phenotypic changes of HE are increased hepatic oxidative stress, high mortality rate, and severe hepatic histology injury, enhanced circulating levels of pro-inflammatory cytokines, ammonia, repressed tryptophan hydroxylase and deficiency in locomotors activity. Oral dose of LBP (5 mg/kg, oral gavage, and every day) effectively alleviated the histological changes, which were mediated via regulating MAPK pathways in both the liver and the brain. The knockout of the pro-inflammatory cytokines TNF- or IL-6 enhanced mice locomotor activity and MAPK activation in the brain [23].

Lycium Barbarum liver fibrosis, olive oil polysaccharides were found to be hepatoprotective. The anti-apoptotic, anti-inflammatory, and anti-fibrotic effects of olive oil and/or Lycium Barbarum were investigated in this research. CCl4-induced liver fibrosis in rats was investigated utilizing polysaccharides (LBP) [15]. The results reveal that CCl4 produced fatty liver abnormalities, cell death, inflammation, and collagen aggregation in the liver. TGF-1 and tissue inhibitors of metalloproteinase (TIMP)-1 level in the liver were decreased in the olive oil-treated groups [16]. Hepatic caspase-9 and caspase-3 activities were suppressed in the LBP-treated groups, as were hepatic tumour necrosis factor (TNF) - levels, IL-10 levels and IL-10/TNF- ratios, and hepatic TGF-1 and TIMP-1 levels. Olive oil mixed with LBP impaired

hepatic TGF-1 levels, reduced liver apoptotic markers, and inhibited liver inflammatory markers. In rats with CCl4-induced liver fibrosis, LBP improves liver apoptotic, inflammatory, and fibrotic markers, whereas olive oil coupled with LBP has significant anti-apoptosis and anti-inflammation effects than olive oil individually [17].

The goal of this study is to see whether pretreatment using Lycium Barbarum polysaccharides (LBP) would protect rats against cadmium (Cd)-induced hepatotoxicity. Wistar rats were split into four groups: control, LBP (300 mg/kg orally, once a day, for 30 days), Cd (CdCl2 4 mg/kg i.p. once), and LBP + Cd (300 mg/kg orally, once a day, for 30 days + CdCl2 4 mg/kg i.p. 24 hours after the previous treatment). Morphological/histological alterations, transaminases, total protein concentration, and oxidative stress as measured by MDA, 3NT, GSH, SOD, and TEAC activities were all used to investigate Cd liver damage. Pretreatment with LBP resulted in a little improvement in morphological architecture and 3NT quantity, as well as a significant improvement in hematic parameters. Based on the research findings, we may conclude that LBP pretreatment can alleviate liver conditions, however more research is needed to continually review LBP's defensive antioxidant activities against Cd-induced damage [16].

Lycium Barbarum polysaccharide (LBP) is a wolfberry water fraction and has been shown to have a hepatoprotective effect in a range of liver disease models. The anti-ALD (alcoholic liver disease) mechanism of LBP, on the other hand, has not been thoroughly explained. This experiment was performed on both male and female mice [12]. The impact of LBP in male and female mice was studied using a chronic ethanol-fed ALD in vivo model. Researchers discovered that ethanol produced more severe liver damage in female mice than in male mice, and that LBP's ameliorative effects were therefore more prominent in female mice that had their ovaries removed completely. The major mediator of LBP-inducer of protection, hepatic SCD1 expression, was shown to be closely linked with the degree of liver injury. LBP also stimulated the AMPK-CPT pathway to rebalance the deregulated lipid metabolism during ALD progression. Researchers identified that LBP directly interacted with ER instead of ER to activate the SCD1-AMPK-CPT pathway in the AML-12 cell line. Thus it was concluded that LPB is safe hepatoprotective agent [25].

Plant	Research models	Results	References
Lycium barbarum (Goji) juice,	Research was conducted on healthy adults for about 14 days	Increased ratings for calmness, energy levels, improvement of eye sight, ease of awakening, feeling of health and happiness, athletic performance, improvement of gastrointestinal function along with reduced stress and fatigue was observed. The body weight and musculoskeletal was not changes significantly from day 1 to day 15 throughout the experiment.	[20]
Lycium Barbarum plant	Effect of LBP on peritonitis mice was observed by recording the influence of behavioral scores, examining the pathological damage of the gut and liver, and measuring the levels of inflammatory cytokines utilizing acute peritonitis in mice as the inflammatory model.	LBP reduced the behavioral score of inflammatory mice, restricted the production of pro-inflammatory cytokines, and reduced liver and intestinal damage. Decrease cytokine production (TNF-, IL-1, and IL-6). LBP has anti-inflammatory properties in RAW264 cells caused by LPS.	[29]
Lycium Barbarum fruit	Impact of a hot water extract of Lycium Chinese fruit (LFE) on liver regeneration in rats.	Collapse, re-arrangement, and re-modeling of hepatic tissue after PH. In the number of PCNA-positive hepatocytes rose significantly. The experimental and control groups' PCNA-positive hepatocyte ratios peaked at 2 and 3 days, respectively. Thus it was concluded that regeneration ability of residual liver was improved by administering LFE.	[26]
Lycium Barbarum plant	Lycium Barbarum polysaccharide (LBP) using an ultrafiltration membrane technique to study the structure–bioactivity interaction of LBP. Experiment was conducted on human liver cancer cells (SMMC-7721).	However, LBP-p8 to enhance the development of SMMC-7721 cells. LBP-a4 (10.2 kDa), which contains 11.5 percent uronic acid, 0.34 percent protein, and 39.02 percent neutral sugar, may arrest SMMC-7721 cells in the G0/G1 phase and dramatically increase intracellular Ca2+ concentration.	[24]

CONCLUSION

Lycium Barbarum contains a variety of traditional, nutritional and economical values which then meets the demand of industrial sustainability in organic life. Lycium Barbarum grows in different areas of the world from temperate to subtropical regions. Beneficial role of Lycium Barbarum is beneficial in all aspects including hepatoprotective, anti-cancer, anti-tumor, anti-aging, immunological, neuroprotection, and ant fatigue, control of glucose, anti-tumor and anti-oxidant properties.

REFERENCES

1. Amagase, H., & Farnsworth, N. R. (2011). A review of botanical characteristics, phytochemistry, clinical relevance in efficacy and safety of Lycium barbarum fruit (Goji). *Food research international*, *44*(7), 1702-1717.
2. Andoni, E., Curone, G., Agradi, S., Barbato, O., Menchetti, L., Vigo, D., & Brecchia, G. (2021). Effect of Goji Berry (Lycium barbarum) Supplementation on Reproductive Performance of Rabbit Does. *Animals*, *11*(6), 1672.
3. Chiang, Y. Y., & Chao, J. C. J. (2018). Olive oil combined with Lycium barbarum polysaccharides attenuates liver apoptosis and inflammation induced by carbon tetrachloride in rats. *Journal of Functional Foods*, *48*, 329-336.
4. ÇOLAK, A. M., Okatan, V., Polat, M., & GÜÇLÜ, S. F. (2019). Different harvest times affect market quality of Lycium barbarum L. berries. *Turkish Journal of Agriculture and Forestry*, *43*(3), 326-333.
5. Kocyigit, E., & Sanlier, N. (2017). A review of composition and health effects of Lycium barbarum. *International Journal of Chinese Medicine*, *1*(1), 1.
6. Liu, Z. C., Yu, W. W., Zhou, H. C., Lan, Z. C., Wu, T., Xiong, S. M., ... & Liu, H. B. (2021). Lycium barbarum polysaccharides ameliorate LPS-induced inflammation of RAW264. 7 cells and modify the behavioral score of peritonitis mice. *Journal of Food Biochemistry*, e13889.
7. Mocan, A., Vlase, L., Vodnar, D. C., Bischin, C., Hanganu, D., Gheldiu, A. M., & Crișan, G. (2014). Polyphenolic content, antioxidant and antimicrobial activities of Lycium barbarum L. and Lycium chinense MillLeaves. *Molecules*, *19*(7), 10056-10073.
8. Pires, T. C., Dias, M. I., Barros, L., Calhelha, R. C., Alves, M. J., Santos-Buelga, C., & Ferreira, I. C. (2018). Phenolic compounds profile, nutritional compounds and bioactive properties of Lycium barbarum L: A comparative study with stems and fruits. Industrial crops and products, 122, 574-581.
9. Skenderidis, P., Lampakis, D., Giavasis, I., Leontopoulos, S., Petrotos, K., Hadjichristodoulou, C., & Tsakalof, A. (2019). Chemical properties, fatty-acid composition, and antioxidant activity of goji berry (Lycium barbarum L. and Lycium chinense Mill.) fruits. *Antioxidants*, *8*(3), 60.
10. Sun, X., Lv, Y., Huang, L., Gao, H., Ren, C., Li, J., & Xiao, J. (2020). Pro-inflammatory cytokines serve as communicating molecules between the liver and brain for hepatic encephalopathy pathogenesis and Lycium barbarum polysaccharides protection. *Journal of ethnopharmacology*, *248*, 112357.
11. Varoni, M. V., Pasciu, V., Gadau, S. D., Baralla, E., Serra, E., Palomba, D., & Demontis, M. P. (2017). Possible antioxidant effect of Lycium barbarum polysaccharides on hepatic cadmium-induced oxidative stress in rats. *Environmental Science and Pollution Research*, *24*(3), 2946-2955.
12. Wang, F., Tipoe, G. L., Yang, C., Nanji, A. A., Hao, X., So, K. F., & Xiao, J. (2018). Lycium barbarum Polysaccharide Supplementation Improves Alcoholic Liver Injury in Female Mice by Inhibiting Stearoyl-CoA Desaturase 1. *Molecular nutrition & food research*, *62*(13), 1800144.
13. Wenli, S., Shahrajabian, M. H., & Qi, C. (2021). Health benefits of wolfberry (Gou Qi Zi, Fructus barbarum L.) on the basis of ancient Chineseherbalism and Western modern medicine. *Avicenna Journal of Phytomedicine*, *11*(2), 109.
14. H. B. Deng, D. P., Cui, J. M., Jiang, Y. C., Feng, N. S. Cai, and D. D. Li., "Inhibiting effects of Achyranthes bidentata polysaccharide and Lycium barbarum polysaccharide on nonenzyme glycation in D-galactose induced mouse aging model," *Biomedical and Environmental Sciences*, *16*(3), 267–275.
15. Luo, Q., Cai, Y., Yan, J., Sun, M., & Corke, H. (2004). Hypoglycemic and hypolipidemic effects and antioxidant activity of fruit extracts from Lycium barbarum. *Life sciences*, *76*(2), 137-149.
16. Ho, Y. S., Yu, M. S., Lai, C. S. W., So, K. F., Yuen, W. H., & Chang, R. C. C. (2007). Characterizing the neuroprotective effects of alkaline extract of Lycium barbarum on β-amyloid peptide neurotoxicity. *Brain research*, *1158*, 123-134.
17. Ho, Y. S., Yu, M. S., Yik, S. Y., So, K. F., Yuen, W. H., & Chang, R. C. C. (2009). Polysaccharides from wolfberry antagonizes glutamate excitotoxicity in rat cortical neurons. *Cellular and molecular neurobiology*, *29*(8), 1233-1244.
18. Chiu, K., Chan, H. C., Yeung, S. C., Yuen, W. H., Zee, S. Y., Chang, R. C. C., & So, K. F. (2009). Modulation of microglia by Wolfberry on the survival of retinal ganglion cells in a rat ocular hypertension model. *Journal of ocular biology, diseases, and informatics*, *2*(2), 47-56.
19. Shi, G. J., Zheng, J., Wu, J., Qiao, H. Q., Chang, Q., Niu, Y., ... & Yu, J. Q. (2017). Protective effects of Lycium barbarum polysaccharide on male sexual dysfunction and fertility impairments

by activating hypothalamic pituitary gonadal axis in streptozotocin-induced type-1 diabetic male mice. *Endocrine journal*, EJ16-0430.
20. Amagase, H., & Nance, D. M. (2008). A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized Lycium barbarum (Goji) juice, GoChi™. *The Journal of Alternative and Complementary Medicine*, *14*(4), 403-412.
21. Liu, Z. C., Yu, W. W., Zhou, H. C., Lan, Z. C., Wu, T., Xiong, S. M., & Liu, H. B. (2021). Lycium barbarum polysaccharides ameliorate LPS-induced inflammation of RAW264. 7 cells and modify the behavioral score of peritonitis mice. Journal of Food Biochemistry, e13889.
22. Skenderidis, P., Lampakis, D., Giavasis, I., Leontopoulos, S., Petrotos, K., Hadjichristodoulou, C., & Tsakalof, A. (2019). Chemical properties, fatty-acid composition, and antioxidant activity of goji berry (Lycium barbarum L. and Lycium chinense Mill.) fruits. *Antioxidants*, *8*(3), 60.
23. Kocyigit, E., & Sanlier, N. (2017). A review of composition and health effects of Lycium barbarum. *International Journal of Chinese Medicine*, *1*(1), 1.
24. Zhang, M., Tang, X., Wang, F., Zhang, Q., & Zhang, Z. (2013). Characterization of Lycium barbarum polysaccharide and its effect on human hepatoma cells. *International journal of biological macromolecules*, *61*, 270-275.
25. Saldanha, G. L. (2004). Summary of comments received in response to the Federal Register notice defining bioactive food components. *Fed. Regist*, *69*(179), 55821-55822.
26. Ahn, Y. M., Lee, G. S., Yang, H. G., Jung, E. G., Han, K. I., Deuk, M., & Han, W. J. K. (2018). Antioxidant and proliferative activity of the fruit extract of Lycium chinense in regenerating liver after partial hepatectomy in rats. *Biomedical Research*, *29*(12), 2590-2596.
27. Nobuo, Kawahara, E.D. (2011): "Comparative Studies on Pharmacopoeia Definitions, Requirements and Information for Crude Drugs among FHH Member Countries in 2007". Western Pacific Regional Forum for the Harmonization of Herbal Medicines (FHH). Online document, accessed on 12 June 2018.
28. Jin, M., Lu, Z., Huang, M., Wang, Y., Wang, Y. (2012). International Journal of Biological Macromolecules, 50; 48–352
29. Luo, Q., Cai, Y., Yan, J., Sun, M., & Corke, H. (2004). Hypoglycemic and hypolipidemic effects and antioxidant activity of fruit extracts from Lycium barbarum. *Life sciences*, *76*(2), 137-149.
30. Ming, M., Guanhua, L., Zhanhai, Y., Guang, C., & Xuan, Z. (2009). Effect of the Lycium barbarum polysaccharides administration on blood lipid metabolism and oxidative stress of mice fed high-fat diet in vivo. *Food Chemistry*, *113*(4), 872-877.
31. Li, X. M., Li, X. L., & Zhou, A. G. (2007). Evaluation of antioxidant activity of the polysaccharides extracted from Lycium barbarum fruits in vitro. *European Polymer Journal*, *43*(2), 488-497.
32. Li, X. L., & Zhou, A. G. (2007). Evaluation of the antioxidant effects of polysaccharides extracted from Lycium barbarum. *Medicinal Chemistry Research*, *15*(9), 471-482.
33. Lin, C. L., Wang, C. C., Chang, S. C., Inbaraj, B. S., & Chen, B. H. (2009). Antioxidative activity of polysaccharide fractions isolated from Lycium barbarum Linnaeus. *International journal of biological macromolecules*, *45*(2), 146-151.
34. Marrazzo*, G., Barbagallo*, I., Galvano, F., Malaguarnera, M., Gazzolo, D., Frigiola, A., ... & Li Volti, G. (2014). Role of dietary and endogenous antioxidants in diabetes. *Critical reviews in food science and nutrition*, *54*(12), 1599-1616.
35. Zhong, Y., Shahidi, F., & Naczk, M. (2013). Phytochemicals and health benefits of goji berries. *Dried Fruits*, 133-144.
36. Tian, X., Liang, T., Liu, Y., Ding, G., Zhang, F., & Ma, Z. (2019). Extraction, Structural Characterization, and Biological Functions of Lycium Barbarum Polysaccharides: A Review. *Biomolecules*, *9*(9), 389. doi:10.3390/biom9090389
37. Kocyigit, E., & Sanlier, N. (2017). A review of composition and health effects of Lycium barbarum. *International Journal of Chinese Medicine*, *1*(1), 1.