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Medicinal value of wolfberry (*Lycium barbarum* L.)

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Abstract

Wolfberry is a kind of the multipurpose medicinal plant. In world the genus *Lycium* (family *Solanaceae*) has eighty species. *Lycium* species hold diverse varieties of nutrients and bioactive elements, for example vitamins, carotenoids, flavonoids, polyunsaturated fatty acids, free amino acids and elemental components. It appears very effective in treatment of liver, eyes and many other diseases. It has a plenty of several pharmacological and therapeutic actions such as antioxidant, immunomodulatory, anti-inflammatory, anti-atherogenic, anti-fibrotic, anti-mutagenic, anti-tumor, anti-radiation, anti-fatigue, anti-aging, anti-stress, anti-yeast, cardio protective and wound healing. Wolfberry has attracted attention world over due to its nutritional and medicinal values. This review paper highlights the importance of *Lycium* plant parts, i.e., Fruit, flower, leaves, bark and root for curing, also encourages the upcoming researchers to work on wonder species.

Keywords: Wolfberry, pharmacological, *Lycium*, medicine

Introduction

The plant *Lycium barbarum* (belonging to the Solanaceae family) has many names, but its English name is Wolfberry, in China it is called “Gouqizi”. On the basis of Chinese ethnobotanical knowledge the traditional Chinese medicine “Wolfberry” used for nourish liver and kidney. Wolfberry (*Lycium barbarum*) was assigned by the Swedish botanist, Carolus Linnaeus in 1753 [1]. It is mainly used for economic and ecological purposes due to its exceptional nutritional value and medicinal benefits [2]. It is a deciduous woody perennial plant with spearhead shaped leaf (25-50mm long), flower grow in groups of one to three in leaf axils, with pedicels (6-15 mm long), and fruits bright orange red ellipsoid berry (1-2 cm diameter) [3, 4]. The plant have tap and extensive root system, heat tolerant (survive up to 100 °F), grow on slightly alkaline soil (pH7-8.2) [5].

Fruits of *Lycium* plant contain a variety of bioactive secondary metabolites, as a result, they are used to develop drugs, dietary supplements and functional foods, because It has a plenty of several pharmacological and therapeutic actions such as antioxidant, immunomodulatory, anti-inflammatory, anti-atherogenic, anti-fibrotic, anti-mutagenic, anti-cancer, anti-radiation, anti-fatigue, anti-aging, anti-stress, anti-yeast, cardio protective and wound healing [6-8]. The wolfberry fruit has highest potentiality to prevent against the different types of disease [9]. The leaves of plant are very popular energizer and traditional Chinese medicine. Leaves of *Lycium barbarum* is rich in source of bioactive compounds, it contains polyphenols, flavonoids, alkaloids, minerals, and vitamins, therefore it has antioxidant, enzyme inhibitors, antimicrobial, and antimutagenic activities [10-13]. Flower tissues of wolfberry is a sources of mineral elements, polysaccharides (LBP) and phenolic compounds, this also have antioxidant activity so that flower can be a potential resource of nutrients [14]. Phytochemical variety consists of LBP, carotenoids, flavonoids, alkaloids, amides, peptides, anthraquinones, coumarins, lignanoids, terpenoids, sterols, steroids, natural acids, anthocyanins, essential oils, glycolipids, and others from leaves, fruits, and root bark of *Lycium chinense*, *Lycium barbarum*, and *Lycium ruthenicum* [15]. The large amount of dicaffeoylspermine/spermidines was found in root barks of wolfberry. It has strong antioxidative activity, anti-aging, neuroprotective, anti-Alzheimer's disease and cytotoxicity are beneficial for health care of human being [16, 17]. The root of wolfberry is treated with fever, night sweats, anxiety, gynecological diseases, night sweats, kidney false back pain, palpitations, insomnia, tears and spermatorrhea [18, 19]. It strongly suggests that consumption of *Lycium barbarum* fruits could serve as a potential source of natural antioxidant compounds and that *Lycium barbarum* phenolic extracts could be exploited for nutritional pharmaceutical purposes.

These all evidence clearly shows that the whole plant (fruits, roots, leaves, barks and flower) have medicinal value as well as plant is economically important. Hence, the biological impacts of wolfberry have progressively received attention. Its value in Chinese and herbal medicine are high and significant, as long as we can provide much scientific evidence with modern technology.

Materials and Methods

The article was written based on the reviewing of published papers available on CrossRef, PubMed, Web of Science and Google Scholar. All together 90 articles from the date of 1993 to 2019 were reviewed.

Pharmacology value of *Lycium barbarum*-derived products

In very recent years, awareness of consumers about the health benefits of different kinds of berry products has rapidly amplified, *Lycium barbarum* extracts of high phytochemical value for food industrial applications, the inhibitory effect of *Lycium barbarum* juices over a series of bacteria, i.e., *B. cereus*, *S. aureus*, *E. coli* and *P. aeruginosa* shown to be effective against the antiviral and antimicrobial activities [20]. Similarly, present investigation on *S. aureus*, *E. coli*, *Salm. Typhimurium*, *L. Monocytogenes*, *C. Perfigens*, and *C. Jejuni* noticeably shown that *Lycium barbarum* fruit and particularly the pomegranate peels demonstrated a significant anti-yeast, antibacterial and anti-fungi activity [21]. The leaves of *Lycium barbarum* is rich source of bioactive compounds, and many studies have shown that leaves have the morphology of phenolic compounds, antioxidants, enzyme inhibition, antibacterial and anti-aging activities [22]. In HIV infection, cell culture and antiviral activity have shown inhibitory effects [23]. The yield of *Lycium barbarum* oils extraction, fatty acid and carotenoid compositions identified the phytochemicals linoleic acid and zeaxanthin dipalmitate and this clearly indicate that *Lycium barbarum* have high antioxidant and antimicrobial activities [24], the research specify that this fruit is suitable for cosmetic, pharmaceutical and food applications. The plant chemical analysis and antioxidant activity of the cultivated *Lycium barbarum* in

Greece were preliminarily identified 17 phenolic compounds and this result was the first report of quercetin 3-O-hexose coumaric ester and quercetin 3-O-hexose-O-hexose-O-rhamnose in the fruit of wolfberry berries [25]. It demonstrates that the consumption of *Lycium barbarum* fruit can be a potential source of natural antioxidant compounds, and can be used for nutritional pharmaceutical purposes. Gas chromatography–mass spectrometry (GC-MS) analysis confirmed that the *Lycium barbarum* has high content of linoleic acid, palmitic acid and oleic acid in fruit, which clearly indicated the high concentration of bioactivity and antioxidant molecules in *Lycium barbarum* [26]. The *Lycium barbarum* has the highest quantity of free radical scavenging, i.e. 2,2-diphenyl-1-picrylhydrazyl and 2,2'-azino-bis (3-ethyl-benzthiazoline-sulfonic acid) [26]. The LBP of wolfberry grafted with doxorubicin nanoparticles has high cytotoxicity to tumor cells [27]. Pharmacological experiments shown that the fruit of wolfberry has anti-fatigue, anti-blood glucose, antioxidant and other characteristics [28-30]. The widespread use of *Lycium barbarum* in many oriental and traditional medicines for treatment of many inflammatory disorders and immunomodulatory activities has scientifically proven its use. Genetic studies on the treatment of inflammatory bowel disease have shown that the preventive effect of *Lycium barbarum* fruit on healthy intestines has the potential to reduce its preventive effect and the degree of inflammatory symptoms in inflammatory bowel disease patients [31]. The infusion of *Chrysanthemum morifolium* flower heads and *Lycium barbarum* fruit in 1:1 ratio shows the highest anti-inflammatory activity [32]. The mechanistic studies of *Lycium barbarum* have identified the beneficial effects of these phytochemicals in preventing the ethanol-induced hepatotoxicity is mediated by the antioxidant, free radical scavenging, antiinflammatory, antifibrotic, antimutagenic, and lipotropic effects [33]. From the different researches evident, it is clear that *Lycium barbarum* phytochemical value for anti-oxidative stress, anti-tumor, anti-radiation, anti-fatigue, anti-aging, anti-inflammatory and anti-tumor, anti-radiation, anti-fatigue, anti-aging, anti-inflammatory and immunomodulatory properties [8].

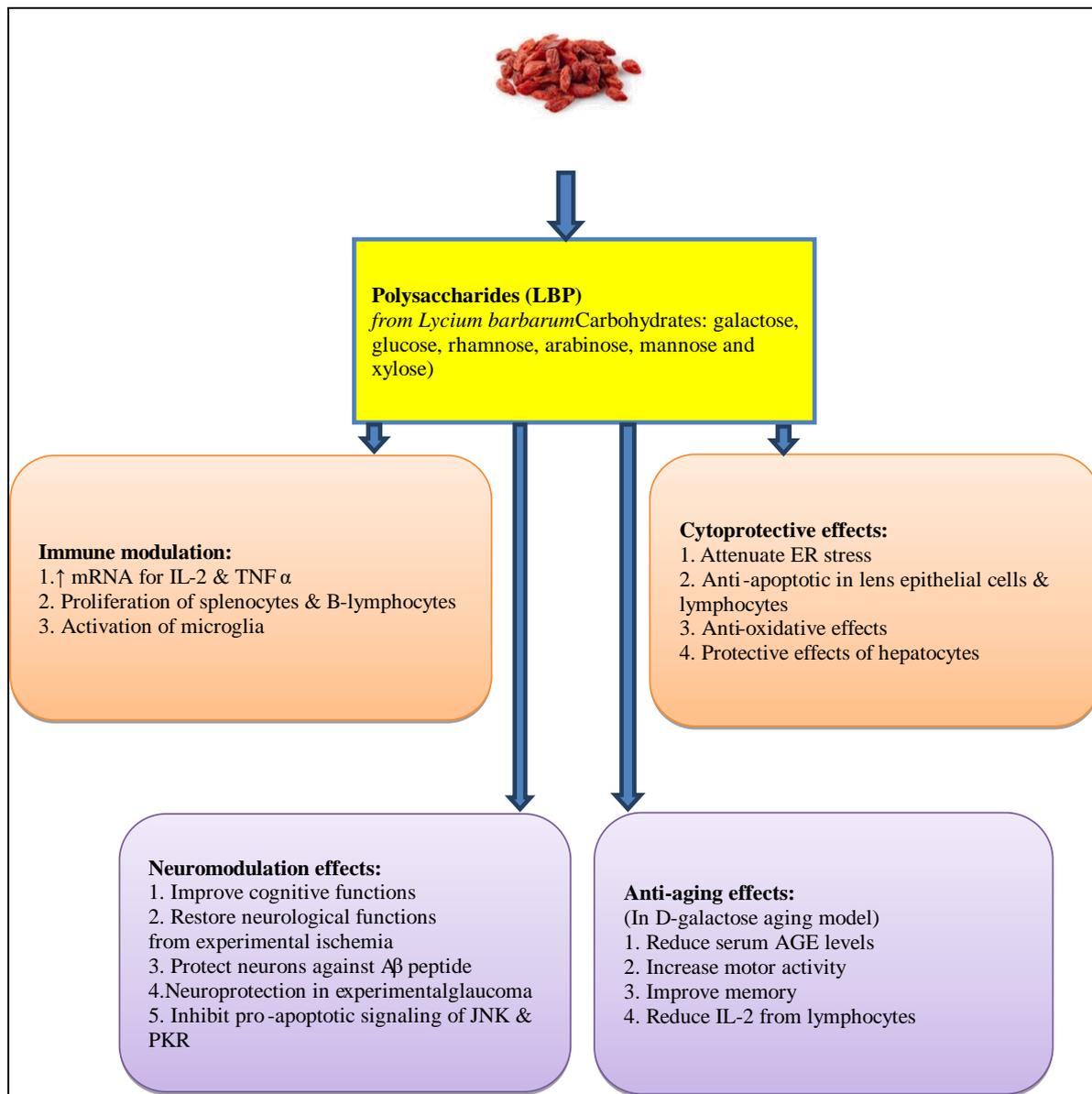


Fig 1: Summary of biological effects of LBP from *Lycium barbarum*. Source: [34]

Fruits

The *Lycium barbarum* fruits contain very low in sodium, saturated fat and cholesterol [35]. It consider as a supplement food for protein, thiamin and calcium, dietary fiber, vitamin A, vitamin C, riboflavin, iron, potassium, zinc, copper and selenium [36-38]. The 28 grams of dried *Lycium barbarum* contain calories (98 Kcal), carbohydrate (21.6g), fiber (3.6g), sugar (12.8 g), fat (291 mg) and protein (4g) [38]. X. Xiao *et al.*, 2019, found 5,6-dihydrosolasonine in *Lycium barbarum* plants [16]. It is a functional food of China, Chinese people from Northwest cultivate it, and utilize fruits and bark as a medicinal purpose [39]. The *Lycium barbarum* fruits contain both LBP (glycocojugates) and vitamin antioxidants because it contains several monosaccharides and amino acids, and are the major bioactive constituents of hypoglycemic effect [40]. *Lycium barbarum* fruits, isolation with boiling water shows carbohydrate content is up to 97.54%, the LBP extracted from fruits clearly indicate the anti-diabetic, antioxidant and anti-aging properties because the fruit mainly composed by of d-rhamnose, d-xylose, d-arabinose, d-fucose, d-glucose, d-galactose and β -amyloid [41, 42, 43]. The lab experiment after extracted LBP from dried fruits of *Lycium barbarum* displays that, it is effective in the protection of liver and kidney tissue from the damage of streptozotocin-induced diabetic rats that

the LBP may be of use as a antihyperglycemia agent [44]. Due to its anti-aging properties, the use of fruits can protect against the toxicity and retinal ganglion cells [42]. *Lycium barbarum* fruits have highest potentiality to increase the endogenous lipid peroxidation, but it can decreased the antioxidant activities [45]. The daily consumption of this fruits effect on scavenging hydroxy free radicals and superoxide anions because of the protective effects of the zeaxanthin fraction and LBP serve as stores of energy, as in glycogen [46]. The functional activity of fruits play role to protect against cancer and its antioxidant and immune function work on age related problem, fruits rich in superoxide dismutase, catalase, glutathione peroxidase and free of toxicity agent have potentiality to use for a chemopreventive (bladder, lungs and others cancer treatment) [45, 47, 48]. The bioactivity of *Lycium barbarum* fruits depends upon the extraction conditions and origin of fruits [49]. With comparison to steam, fruits have low activity against gram-positive and gram-negative bacteria so it's better use in proper ratio [50]. The *Lycium barbarum* ranked as a useful food due to its antioxidant properties so that its systematic pattern of study may be useful to well understand the nutraceutical characters for upcoming study [51]. Because of its low mycotoxins after contamination with toxic metals, dry *Lycium barbarum* fruits is consider as a

being the most safe and profitable for consumers [52]. The comparative analysis of different types of *Lycium barbarum* shows that the black Goji berry (*Lycium ruthenicum*) has higher phenolics and antioxidant capacities [53]. Therefore, further more comparative analysis is necessary to understand it and also promote the *Lycium ruthenicum* production by development of industry and agriculture [25, 54, 55].

Leaves

In context of traditional Chinese medicine, the leaves of *Lycium barbarum* called as “Tianjingcao”, because of its high ethno botanical value in China and the leaves were found to cure for nourishing the liver and enhancing eyesight [56]. Huge researches had been conducted on LBP from *Lycium barbarum* fruits, but the LBP from the leaves were rarely reported. The LBP from the leaves also beneficial effect on immunostimulating activity [57]. Leaves of *Lycium barbarum* have medicine value in China. The quality analysis between wild and domestic leaves of *Lycium ruthenicum* demonstrate that domestic has higher flavonoids than wild, these indicate that cultivated *Lycium ruthenicum* leaves are a suitable source for medicine vegetables and functional tea [58]. Leaves of *Lycium barbarum* holding enormous quantity of bio-flavonoids shows the *Lycium barbarum* leaves have significant substance that inhibits oxidation, as well as leaves contain bacterial strains i.e., gram-positive and gram-negative, so it is evidently specified that leaves of *Lycium barbarum* are valuable sources of flavonoids with relevant antioxidant and antimicrobial activities [59]. The far infrared-assisted extraction from the leaves of *Lycium barbarum* shows that bioactive constituents in real plant samples [60]. The leaves of *Lycium barbarum* is a Calcium (Ca) rich LBP mainly composed of mannose and xylose, And the endogenous Ca attenuates leaves immunomodulatory activity [13]. Like wish fruit leaves also has high amount dicaffeoyl-spermidine isomers [16]. Also, the fruit and leaves of *Lycium ruthenicum* are potential therapeutic agents against inflammation [61]. Via the usage of a fast and delicate ultra-high performance liquid chromatography coupled with triple quadrupole tandem mass spectrometry (UPLC-TQ-MS) technique became discovered leaves of *Lycium barbarum* has 10 phenolic acids and flavonoids (together with neochlorogenic acid, protocatechuic aldehyde, p-hydroxybenzoic acid, chlorogenic acid, cryptochlorogenic acid, caffeic acid, p-coumaric acid, ferulic acid, rutin and kaempferol-3-O-rutinoside) (X. Q. Zhao *et al.*, 2019). The chlorophyll removal extract of *Lycium barbarum* leaf may be developed as elements of utilitarian nourishment and cosmetics (J. E. Kim, Bae, Nam, Bae, & Ly, 2019). The hydroxycinnamic acid amides had been recognized from the leaves and root barks of *Lycium barbarum*, and serve as a potential anti-inflammatory function by using root barks and leaves [62]. The flavonoids extract from *Lycium barbarum* leaves might considerably inhibit lipid oxidation in minced mutton, so one can offer a new direction and theoretical foundation for the deep processing and utilization of *Lycium barbarum* leaves and the development of meat products rich in n-3 polyunsaturated fatty acids (L. Han, Shen, Tian, & Fan, 2018). The purification novel polysaccharides (LBP5-A) starting with *Lycium barbarum* leaves exhibited a grate scavenging ability for superoxide, hydroxyl, and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals (Gong *et al.*, 2016). First time in 2017, twelve compounds extracted through the usage of high-performance liquid chromatography coupled with high-resolution mass spectrometry, i.e., chlorogenic acids, flavonoids, phenolic

acids, neochlorogenic acid, chlorogenic acid, cryptochlorogenic acid, isochlorogenic acid B, isochlorogenic acid A, and isochlorogenic acid C those suggests *Lycium barbarum* leaves, deliver polyphenols with appropriate antioxidant activity [63].

Flower

The flower of *Lycium barbarum* is a source of (i) diosgenin; use on synthesis of steroid hormones, (ii) β -sitosterol; help to control blood cholesterol levels and (iii) lanosterol; useful for human eyes treatment, but no other data regarding their composition is available. *Lycium barbarum* flowers contain phenolic compounds, chlorogenic compounds, coumarin, ferulic acid, isoquercitrin, rutin and quercitrin, but the Gram-positive bacteria have mild antibacterial activity, the lack of antimicrobial activity on *Escherichia coli* [64]. Beta-carotene plays an important role in maintaining the source of vitamin A, and studies on the leaves and flowers of two medicinal plants i.e., *Lycium barbarum* and *Gentiana lutea* showing the content of beta-carotene in its leaves and flowers and its effects on genetically modified tobacco (nicotine) plants [65]. Flower of *Lycium barbarum* may have protective effects in diabetic retinopathy [66]. This traditional Chinese medicinal plants associated with anticancer may be probable sources of powerful natural antioxidants and useful chemopreventive agents [67]. Flower have low phenylpropanoid and chlorogenic acid with comparisons to the fruits and leaves [68]. Even low contain of phenylpropanoid and chlorogenic acid it has antitumor activity and immunomodulatory effect [69]. It has a rich source of bioactive molecules with nutraceutical properties [70]. The flowers of *Lycium barbarum* not only rich on rutin and chlorogenic acid but also, a formerly undescribed N,N-dicaffeoylspermidine derivative was recognized in flowers so that flowers and trimmed shoots as sources of valuable compounds [71]. Above evident shows that there is limited research work on the medicinal value of *Lycium barbarum* flower, to lead the knowledge gaps of medicinal value of *Lycium barbarum* flower further more deep research is needed.

Bark

The ethno botanical knowledge from the Xia Dynasty to present year, dried fruits and the root bark of *Lycium barbarum* become a commonly used traditional medicine plant in China [72, 73]. The ethnic groups of different parts of China used the bark of *Lycium barbarum* to cure cough, diabetes, dizziness, fever, gynecopathy, night sweat, lumbar genu aching and limp, leukorrhea, headache, amnesia, agrypnia, tuberculosis and spermatorrhea, asthma, hyperlipidemia and tuberculosis [18, 19]. Research conducted on *Lycium barbarum* root bark and fruit have found LBP, organic acids and alkaloids and it have a certain effect on lipid metabolism and oxidative recovery in diabetic animals [40, 74, 75]. The fruit and root bark of *Lycium barbarum* are the most commonly used materials in pharmacopoeia, while the aerial part of *Lycium barbarum* recorded by the officially published pharmacopoeia of Indian traditional medicinal plant [19]. An 80 year old Chinese women used *Lycium barbarum* bark, leaves, flower and fruits as a tea and cure from anticoagulation [76]. The *Lycium barbarum* bark has been studied for chemo-endocrine therapy for estrogen receptor positive (ER+) breast cancer [77]. The researches on *Lycium barbarum* bark shown hypoglycemic and hypolipidemic potential and could be useful for diabetic therapy because it decreases of fasting blood glucose, increases in blood glucose and lipid levels associated with

diabetes, improve abnormal glucose metabolism and increase insulin secretion and improve in body weight gain [78]. The findings of recent research on bark of *Lycium barbarum* root suggest that bark has an anti-hyperlipidemia effect [79]. The root bark of *Lycium barbarum* used for to clean heart. At present, *Lycium barbarum* is widely used in all over the world because of its anti-aging characteristics and as a health food [80].

Roots

Recently, most of the phytochemical and pharmacological studies have been focusing on the fruits and root bark of *Lycium barbarum* species even the research work on this species is not sufficient. The rehmannia glutinosa LBP isolated from the dried root have anti-inflammatory activity in the central nervous system curing some pathological disease states [81]. The roots of *Lycium barbarum* help to increase on humoral immunity [82]. It clearly indicate that roots also have properties of immunomodulation like others parts of *Lycium barbarum* plant. The effect of low molecular weight Rehmannia glutinosa LBP on the expression of PA 53 gene, that is, *Lycium barbarum* root has anti-tumor activity mechanism [83]. The study on the antioxidant activity of 30 kinds of traditional Chinese medicine shows that the root system of *Lycium barbarum* has the highest antioxidant activity [84]. Similar studies on the antioxidant activity and phenolic compounds of 112 kinds of traditional Chinese medicines with anticancer effect also indicated on *Lycium barbarum* roots. [67]. The root of *Lycium barbarum* is treated with fever, night sweats, anxiety, gynecological diseases, night sweats, kidney false back pain, palpitations, insomnia, tears and spermatorrhea [18, 19]. Research conducted on root bark and fruit in *Lycium barbarum* have found that water extracts, LBP, organic acids and alkaloids have a certain effect on lipid metabolism and oxidative recovery in diabetic animals [40, 74, 75]. In addition, in recent years root of *Lycium barbarum* has also shown the role of anti-fatigue and liver protection [85-88]. Currently, three new types of lignanamides have anti-inflammatory activity from root [89]. Similarly, a new lignanamides has been reported from the roots and its antioxidant activity [90].

Conclusion

Lycium barbarum appears to be a gifted plant consuming possible beneficiary character in successful human healthiness. In China researches to identify the potential of this plant are going on especially in cold desert area of Tibet and Inner-Mongolia. This review paper highlights medicinal value of different parts of *Lycium barbarum* plant i.e., fruits, flowers, roots, barks and leaves and also update the achievements of different research works. *Lycium barbarum* has a large population and very old trediational medicinal value in China but despite of this fact its true pharmacology potential is still under explored. The review paper presented above is an effort to highlight *Lycium barbarum* as a medicinally important plant which is also found in abundance in other region but has failed to gain importance. Moreover, people living in the area which shows a huge population of *Lycium barbarum* are unaware of the importance of this plant. Due to the lack of a proper scientific systematic study this plant remains underutilized and only few people know the importance of this plant. This review may also help for upcoming researchers to work on this valuable medicinal plant species.

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Conflict of interest

The authors declare no interest or any conflict of interest exists.

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