Review Article

Evaluation of different parts of *Berberis lycium* and their biological activities: a review

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Abstract

Berberis lycium is a common medicinal plant which belongs to family Berberidaceae. It is native to Pakistan and India. It is used medicinally for diarrhea, internal wounds, jaundice, internal colic, piles, diabetes, backache, rheumatism, throat pain, scabies, pustules, gingivitis, sub blindness, remittent fever and eye disorder. The various parts of *Berberis lycium* such as roots, stem, leaves, and fruit contain bioactive compounds like carbohydrates, proteins, fats, vitamin C, tannins, saponins, alkaloids, anthocyanins, berberine, berbamine, chinabine, baluchistanamine and sindamine. It contains various minerals i.e. sodium, phosphorus, copper, potassium, Iran, and zinc. The plant have shown many biological activities including anti-diabetic property, antimicrobial property, antihyperlipidemic property, hepatoprotective property, pesticidal property, antioxidant properties and wound healing properties. In light of current review there is a need of additional investigation and exploration regarding the medicinal value of this plant.

Keywords: *Berberis lycium*; Phytochemical; Biological activities; Medicinal uses

Introduction

Berberis lycium belongs to family Berberidaceae, [1] established this family as “Berberides” and is considered as one of the oldest angiosperms which possess a high number of discontinues genera [2]. This family is comprised of 17 genera and 650 species. The English name of *Berberis lycium* is barberry [3], while “Kashmal” is

the word used for the fruit of this plant [4, 5], and roots are called as “Darhald” [6]. The plant is a native species of Nepal [3], however, the species has been reported throughout Himalayas Mountains, temperate and semi-temperate localities of Afghanistan, Bangladesh, India, and Pakistan [7]. In Pakistan grows in KPK,

Baluchistan, Punjab and Azad Kashmir at an altitude of 900-2900 meters [8].

Berberis lycium is a spiny deciduous shrub with an average height of 2-4 meters. The plant bears lanceolate leaves which are alternately arranged on the stem [9]. The plant is self-fertile with hermaphrodite bright yellow colored flowers. The flowers are entomophilous, 11 to 16 in number and possess corymbs racemes inflorescence [10]. March to July mark the flowering season of this species. The color of the flowers changes from yellow to purple on ripening (that is fruits).

Berberis lycium produces an ovoid fruit which is up to 7 millimeter long and is known as Berries. The fruits start ripening from the 2nd week of May and remain to do so throughout June. Its fruit is usually used either cooked or raw and prepared into preserves. The fruit is slightly acidic and juicy in nature. The plant possesses wide ecological amplitude and seeds can be grown in sandy, silty or loamy soils. The plant has a hard and branched root with a diameter ranging from 3 to 8 cm. The root bark is thick which is fissured externally and smooth internally [11]. The cork is 5-10 cells thick, xylem with spiral, cambium, reticulate and pitted tracheae [12]. Examination of pollen morphology through scanning electron microscope revealed that the Pollen diameter in *Berberis kunawurensis* is around 38.71 μm and exine thickness is about 2.25 μm [13]. Honey bees also visit this plant for nectar [14].

B. lycium species have been declared vulnerable by the International Union for Conservation of Nature (IUCN) [15]. It is one of the endangered species of Pakistan [16]. *B. lycium* has been reported to contain important alkaloids like berberine [8, 17-19], berbamine [20], Palmitine [18, 19], karakoramine, baluchistanamine, jhelumine, gilgitine, umbellatine [5] and chinabine [21]. The plant is recognized to have

Carbohydrates, Proteins, Lipids, and Vitamins [10], hydrolysable tannins, saponins and cardioactive glycosides [22]. Fruits are known to have moisture, phytic acid, hemicelluloses, β carotene, vitamin A, cellulose and anthocyanins [10]. The plant is also recognized to have various minerals including zinc, copper, sulphur, sodium, calcium, iron [19], lead, magnesium, copper [23], potassium and phosphorus [10].

B. lycium is found to be effective against microorganisms. It is confirmed to have efficient antifungal and antibacterial activity [24]. The plant is also reported to be anticoccidial and immunostimulant [25], antimutagenic [26], hypoglycemic [22], antihyperlipidemic [27], pesticidal [28], hepatoprotective [29]. The plant is also proved efficient in healing wounds [30]. Moreover, the alkaloid berberine from this species is confirmed to be antipyretic [31], anti-inflammatory [32], anti hypercholesterolemia [33], antitumor [34], antidiarrheal [35] and antidiabetic [36].

Taxonomy

Berberis lyceum belongs to kingdom Plantae, Phylum: Tracheophyta, Class: Magnoliopsida, Order: Ranunculales, Family: Berberidaceae, Genus: *Berberis*, Species: *lyceum*, Scientific name: *Berberis lycium*.

Phytochemical profile

Berberis lycium is extensively studied for its phytochemical constituents. Various essential phytochemicals including alkaloids, saponins, minerals, and carbohydrates have been reported from this species. Modern technology such as atomic absorption spectrophotometer has made it easy to study mineral contents of plants. [19] Studied root and fruit of *B. lycium* for mineral contents by using atomic absorption spectrophotometer. His findings revealed that the root contains 0.2% zinc (Zn) and 0.2% sulphur (S), while the sulphur (S) and zinc (Zn) contents in fruit were 0.1% and

0.8%, respectively. Similarly [23] examined roots and stem of *B. lycium* for lead (Pb), copper (Cu) and manganese (Mn) through atomic absorption spectrophotometer. According to their results, the quantity of Lead (Pb) found in stem and roots of the plant were 7.992 ± 0.106 and 4.360 ± 0.176 ppm, respectively. Result for Copper (Cu) quantity in stem and roots were 5.031 ± 0.176 and 4.360 ± 0.176 ppm, individually. Manganese (Mn) in the stem and root of the plant was 18.272 ± 0.212 and 15.500 ± 0.212 ppm correspondingly.

In another study, Atomic absorption spectrophotometer was used by [10] to examine Phosphorous, Potassium, Iron, and Sodium, while by flame photometer Calcium quantity in the fruit of the said plant. The results showed the presence of Sodium (14.5 ± 0.11 mg/100 g), Potassium (161.42 ± 0.41 mg/100 g), Calcium (18.272 ± 0.212 mg/100 g), Iron (2.61 ± 0.06 mg/100 g) and Phosphorus (38.0 ± 0.24 mg/100 g) in healthy amount. Leaves have also been reported to be plentiful in Iron (528.47 ± 0.02 μ gg-1), Potassium (4077.00 ± 0.58 μ gg-1), Mn (136.12 ± 0.01 μ gg-1), Phosphorous (1315.00 ± 0.01 μ gg-1), Cu (53.41 ± 0.09 μ gg-1), Zinc (37.71 ± 0.02 μ gg-1), Sodium (79.00 ± 0.01 μ gg-1) and Calcium (2389.00 ± 0.04 μ gg-1). It was shown by [37] that Copper, Zinc, and Sodium were concentrated in root, Potassium in shoot, while Phosphorous, Mn and Calcium in leaves shown in (Table 1).

B. lycium is also screened for moisture, proteins, sugars, fibers, vitamin and dry matter. According to [19], roots of *B. lycium* possess moisture (20.5%), sugar (3.5%), dry matter (61.2%), fat (2.6%), protein (4.5%), Vitamin C (0.3%) and fiber (2.5%) in the given percentages. Fruits comprise moisture (12.5%), Vitamin C (0.8%), dry matter (62.5%), fat (1.8%), protein (2.5%), sugar (4.5%) and fiber (1.5%) in the given percentages. Roots showed the highest amount of fiber and fats while leaves showed highest amount of crude proteins [37] shown in (Table 2).

Phytochemical screening of water extract of *B. lycium* by [22] showed the presence of Cardiac glycosides, Saponins, Hydrolysable Tannins, and Alkaloids. Analysis of fruit revealed the presence of tannins (8.9 ± 0.15 mg/100g), Phytic acid (2.5 ± 0.04 mg/100 g), β - Carotene (343.0 ± 0.89 μ g/100 g), Phytate phosphorus (0.78 ± 0.06 mg/100 g), Hemicellulose (6.01 ± 0.41 %), Anthocyanin (82.47 ± 0.29 mg/100 ml juice), Vitamin A (85.65 ± 0.17 μ g/100 g) and Cellulose (7.94 ± 0.60 %) [10]. Essential alkaloids such as Berberine (Figure 1) and palmitine (Figure 1) in roots of *B. lycium* are found in a concentration of 4.5% and 3.1%, respectively, while in fruits 2.9% Berberine is present [19], Berbamine [20], baluchistanamine, karakoramine, sindamine, gilgitine, jhelumine, punjabine, umbellatine [5] and Chinabine [21] are other alkaloids that have been recognized in *B. lycium* Shown in (Table 2).

Table 1. Minerals in different parts of *Berberis lycium*

S. No	Minerals	Parts available	References
1	Sulphur(S) and Zinc (Zn)	Root, Fruit	[19]
2	Copper(Cu) and manganese(Mn)	Stem, root	[23]
3	Phosphorous (P), Potassium (K), Iron (Fe) and Sodium(Na)	Roots, Shoots, Leaves	[10]

Table 2. Bioactive compounds in different parts of *Berberis lycium*

S. No	Phytochemical	Part available	References
1	Carbohydrates	Roots	[19,10]
2	Fats	Roots	[19]
3	Proteins	Roots	[19]
4	Vitamins C,	Roots	[19]
5	Tannins	Fruit	[22]
6	Alkaloids	Fruit	[22]
7	Saponins	Fruit, leaves	[22]
8	Anthocyanin	Roots	[10]
9	Berberine	Roots	[19]
10	Berbamine	Roots, fruit	[20]
11	Chinabine	Fruit	[21]
12	Baluchistanamine	Fruit	[5]
13	Sindamine	Fruit	[5]

Figure 1. Structures of the major constituents of *B. lycium*. (a) Berberine [38] (b) Palmitine [38] (c) Berbamine [39] (d) Phytic acid [40] and (e) Vitamin A [41]**Folk medicines and *Berberis lycium***

A plant which possesses medicinal properties is known as a Medicinal plant. World Health Organization (WHO) defines medicinal plants as any plant whose organs contain medicinally active constituents with a therapeutic value or is used as a precursor to synthesize drugs (WHO). Usually, the

extract of the plant is used to treat various ailments. The extract obtained is a kind of Traditional Medicine. Thus in developing countries, in order to maintain health, people use these medicinal plants and traditional medicines to cure their ailments and maintain good health [42]. Scientists are working to further explore the priceless

properties of medicinal plants since a long time. Furthermore, more than 30% of modern medicines preparations are grounded on plants [43].

B. lycium Royle has also been used in folk medicine against diarrhea [4, 5, 16, 44-47], internal wounds [16, 46, 48,], jaundice [4, 14, 16, 46,], intestinal colic [16, 45], piles [4, 10, 16, 44, 47], diabetes [15, 48, 49], ophthalmia [4, 26, 44, 45, 50], backache [14] rheumatism [14, 45], manorrhagia [5], gingivitis [46], intermittent fever, sun blindness and remittent fever [45] Shown in (Table 3).

Plant is also febrifuge [5, 10, 51, 52] diuretic, expectorant [16] and diaphoretic [45]. Different organs of plants are used according to preparation. In the treatment of internal wounds, throat pain and dysentery, powder of the plant bark is used. Aqueous extract of root bark is used in the treatment of scabies, pustules, and diabetes whereas a paste made from root powder is used in bone fractures. A decoction of the plant roots is known as ‘Rasaunt’ which is used to treat

eyes infections. Furthermore, the sap of young vegetative shoot is also used to treat eye disorders [50]. Jaundice is traditionally treated by rhizome decoction [14]. So far, traditional medicines have provided many valuable clues in the expansion of modern medicines against various diseases. Nevertheless, rediscovery of old-fashioned medicine is needed in light of modern knowledge of medicines [53] Shown in (Table 3).

In traditional medication system, *B. lycium* has been widely used to treat diabetics. Recent pharmacological investigations revealed that this plant decrease hyperglycemia and the possible mechanism of this plant to have antidiabetic activity are attributed to its insulin-like mechanism. Moreover, the plant has been used traditionally to treat wounds, gingivitis, and rheumatism. One of the major alkaloids from this plant is called Berberine. Berberine is anti-inflammatory [53] shown in (Table 3).

Table 3. Medicinal uses of different parts of *Berberis lycium*

S. No	Medicinal uses	Part uses	References
1	Diarrhea	Roots	[4, 5, 16, 44-47]
2	Internal wounds	Roots	[16, 45, 48]
3	Jaundice	Roots	[5, 14, 46]
4	Intestinal colic	Roots, barks	[16, 44]
5	Piles	Roots	[5, 16, 18, 44, 47]
6	Diabetes	Roots	[15, 48, 49]
7	Ophthalmia	Root, leaves	[5, 26, 44, 45, 50]
8	Backache	Roots and leaves	[14]
9	Rheumatism	Roots	[45, 14]
10	Throat pain, Scabies, pustules	Roots	[48]
11	Gingivitis	Roots	[46]
12	Sun blindness, remittent fever	Roots, fruit	[45]
13	Eye disorder	Roots	[50]
14	Anti-inflammatory	Whole	[53]

Pharmacological properties

Antidiabetic property of *B. lycium*

B. lycium is known to have antidiabetic property. [9] conducted an experiment to study the effect of *B. lycium* on alloxan induced diabetic rats. Crude powder and extracts of *B. lycium* were used in the study. The extracts used in the study were aqueous, methanolic, n-hexane, aqueous methanolic and chloroform. Results from his study revealed that the blood glucose level was declined by crude powder in both normal and diabetic rabbits. Aqueous extract caused maximum hypoglycemic activity for about 6 hours. While n-hexane, methanolic and aqueous methanolic extracts lowered blood glucose level for about 4 hours. The results obtained from chloroform extracts showed non-significant activity against diabetics. To further study the effect, water extract was compared insulin. Results revealed that water extract (500mg/kg) with insulin (2 units) was comparable with many insulin units (6 units). Similarly, [19] evaluated the effect of aqueous and ethanolic extracts of root on normal and alloxanized rats. In the study, the reference drug was glibenclamide

(20 mg/kg). Blood glucose level was evaluated from serum by glucose oxidase method. Results revealed lowered hyperglycemia at 50 and 100 mg/kg dose after 3 to 5 hours of treatment. The dose of 100 mg/kg showed the more pronounced effect on the subjects. Serum glucose level was decreased in oral glucose tolerance test in a dose-dependent manner by the plant extracts. Insulin-like effect was observed in hypoglycemia which could be due to peripheral glucose consumption. Behavioral changes and acute toxicity were not observed in the experimental animals at the given doses. A comparative study of pure berberine and ethanolic root extract of *B. lycium* was performed on alloxan induced diabetics rats and normal rats. Same doses of berberine (50 mg/kg) and ethanolic root extract were provided to the rats. Surprisingly, plant extract in comparison with berberine showed the same efficiency in reducing blood glucose level. An efficient effect was also seen on serum lipid profile, body weight and glycosylated hemoglobin [19] Shown in (Table 4).

Table 4. Pharmacological and biological activities of *Berberis lycium*

S.No	Biological activity	References
1	Anti-diabetic property	[19,22]
2	Antimicrobial property	[24, 25, 54]
3	Hepatoprotective property	[29, 55]
4	Antihyperlipidemic property	[22, 27]
5	Pesticidal property	[28]
6	Wound healing property	[30]
7	Antioxidant properties	[56-58]

Antimicrobial property of *B. lycium*

Medicinal plants have the potential to kill bacteria and fungus pathogens. Antimicrobial activities of medicinal plants are due to the phytochemicals. *B. lycium* has a rich profile of phytochemicals, thus this plant is also tested against various pathogens. Microdilution method was used

to study the antimicrobial activity of hydroalcoholic (50%) extract of root and stem (air dried) of *B. lycium* by [24]. *Enterobacter aerogenus*, *Klebsiella pneumonia*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Micrococcus luteum*, *Escherichia coli*, *Bacillus cereus*, *Proteus mirabilis*, *Staphylococcus aureus*,

Streptococcus pneumonia and *Salmonella typhimurium* were the species against which the plant extract showed antimicrobial activity. Minimum inhibitory concentration (MIC) showed against each organism by root extract was 2.50, 1.25, 0.62, 0.62, 1.25, 0.31, 2.50, 1.25, 0.62, 0.62 and 2.5 µg/ml, respectively. MIC showed by stem extract was 1.25, 0.31, 0.31, 0.31, 0.31, 0.62, 2.50, 0.31, 0.62, 1.25 and 0.62 µg/ml, respectively. Hydroalcoholic extract of *B. lycium* has been proved to be effective against bacterial strains as compared to fungal strains [54].

The fungal strain of *Aspergillus terreus* was also inhibited by the stem and root extract at MIC 0.62 and 0.31 µg/ml, respectively. Root extract also showed activity against *Aspergillus flavus* and *Aspergillus spinulosus* at MIC 1.25 and 0.62 µg/ml, respectively. *B. lycium* showed better immune performance against infectious bursal disease, newcastle disease, and infectious bronchitis. Coccidial oocysts/gram of feces showed a significant reduction in response to this plant [25]. The plant was also mixed in containers of drinking water along with other medicinal plants to reduce pathogens and kill germs Shown in (Table 4).

Hepatoprotective property

B. lycium is known to have hepatoprotective property. Methanolic extract and crude powder were used to study the hepatoprotective property of this plant in rabbits. Hepatotoxicity was induced by paracetamol in the experimental organism. Results revealed that the elevated amount of serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase alkaline phosphatase enzymes were significantly reduced by the plant in treated rabbits [55]. *B. lycium* significantly reduced hepatotoxicity in hepatotoxic mice (Paracetamol induced hepatotoxicity). *B. lycium* bark powder is also confirmed to

have hepatoprotective activity [29] Shown in (Table 4).

Antihyperlipidemic property

B. lycium roots were used to study antihyperlipidemic property in male albino rabbits. From the results, it was concluded that oral use of crude powder (250 and 500 mg/kg) for four weeks significantly decreased triglyceride level, total cholesterol level and low-density lipids (LDLs) while high-density lipids (HDLs) were increased in rabbits. It was also observed that the weight of diabetic rabbits was highly stabilized by the provided doses [22].

[27] Studied the hypolipidemic effect of root bark of *B. lycium* in broilers. Result showed significant decrease in the triglyceride, LDL, and total cholesterol while a dose dependent significant increase in HDL Shown in (Table 4).

Pesticidal property

Through Soxhlet apparatus, Petroleum ether and aqueous methanol extracts of *B. lycium* root were prepared and further dried under vacuum. Two higher doses (5000 and 10000 ppm) were used to study the activity of plant extract against pests. At the dose of 5000 ppm, the mortality rate shown by petroleum ether extracts were 25% against *Helicoverpa armigera* Hub and 92% against *Aphis craccivora* Koch. On the other hand at the dose of 10000ppm, the mortality rate was 26% against *Tetranychus urticae* Koch, 96% against *A. craccivora* Koch and 28% against *H. armigera* Hub and *Plutella xylostella* L. Extract of Petroleum ether repressed *A. craccivora* Koch at 458.65 ppm fatal amount at 50% (LC50) after 24 hours engagement time and 57.79 ppm LC50 after 48 hours. The LC50 at 48-hour contact was almost similar with to a chemical insecticide called Dimethoate at 24 h contact. The mortality rate shown by aqueous methanolic extract at the dose of 5000 ppm was 26% against *A. craccivora* Koch. Extract also displayed 44% death rate against *H.*

armigera Hub, 43% against *T. urticae* Koch, 41% against *P. xylostella* L. and 68% against *A. craccivora* Koch [28] Shown in (Table 4).

Wound healing property

Swiss Wister rats were used to study wound healing property of *B. lycium* root extract. The models of wound repair used in the study were excision, incision and dead wound space while methanolic and aqueous extracts were used. Epithelialization and breaking strength of wounds were increased by both extracts. Collagen deposition, fibroblasts, and macrophages were found in aqueous treated rats. In methanolic treated rats, a significant amount of collagen deposition but with low fibroblast and macrophage was detected. Similarly, hydroxyproline content of granulation tissue and dry weight was also increased. In nutshell, it was concluded that methanolic extract was more efficient than the aqueous extract [30] Shown in (Table 4).

Antioxidant properties

Reactive oxygen species (ROS) such as hydrogen peroxide, $\cdot\text{OH}$ (hydroxyl radical) and superoxide anion are well known for their potential of causing diseases like Inflammation, Cancer, Rheumatoid arthritis, Aging and Atherosclerosis [56]. However, the formation of ROS and related disorders in humans can be averted by Natural antioxidants [57]. The root extract of *B. lycium* is known for antioxidant properties and strong reduction potential. Root extract converts potassium ferricyanide (Fe^{3+}) to potassium ferrocyanide (Fe^{2+}), which then reacts with ferric chloride and form a ferric ferrous complex that has an absorption maximum at 700 nm. This test is comparatively inexpensive and simple. Reducing power assay does not measure the 'Thiol group' comprising reagents [58] shown in (Table 4).

Conclusion

In the present review, various aspects of *B. lycium* have been discussed. *B. lycium* is a native species of Nepal but is also found throughout the Himalayas. It is a multi-potential plant with many characteristics. The plant contains essential phytochemicals such as alkaloids, saponins, tannins, carbohydrates, phenols, glycosides, proteins and essential elements like zinc, copper, magnesium, potassium, sulfur, phosphorous, iron. Alkaloid berberine which has many pharmacological effects is also found in this plant. Berberine is anti-diarrheal but the exact mechanism of action is uncertain. Therefore, *in vivo* anti-diarrheal activities and *in vitro* spasmolytic activities of plant extracts are required to find the underlying mechanism. The plant extracts have been proved to possess pharmacological properties. The extracts are known to be antidiabetic, antimicrobial, antioxidants, pesticidal, antihyperlipidemic, hepatoprotective and wounded healers. However, the active constituents responsible for these pharmacological activities are unknown. Similarly, clinical data regarding the authenticity and efficiency of these pharmacological activities is very limited which pose a serious limitation to our knowledge and understanding. Thus more work is required to point out the underlying phytochemicals which are responsible for various activities of this plant. Also, a strong clinical data regarding these activities is also needed.

Authors' contributions

Plant selection & idea: S Ahmed & M Shuaib Analyzed the Data: K Ali & S Ali, Contributed reagents/ materials/ tools: M Shuaib, K Ali, S Ali & F Hussain, Wrote the paper: S Ahmed, M Shuaib & F Hussain.

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