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An Overview on Various Aspects of Plant *Berberis Lycium* Royale

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Abstract Herbal medicine is getting popularized in developing and developed countries owing to its natural origin. *Berberis Lycium* also famous as Indian Barberry, Kashmal in Hindi and Ishkeen in Urdu belongs to the family Berberidaceae. Its local name is Kawdach in Kashmir valley. Traditionally, *Berberis lycium* is used by the Tribal peoples in J&K, India, since the time immemorial. It is an evergreen spiny shrub 2-3 m in height growing mainly in Himalayan regions. The various parts of the plant like root, bark, stem, leaves and fruits are used by the people as a medicine or food. In traditional system of medicine, the plant is used for various affliction and diseases. This plant has also gained wide acceptance for its medicinal value in ayurvedic drugs. The plant is known to prevent liver disorders, abdominal disorders, skin diseases, cough, ophthalmic, oral ulcers, kidney, conjunctivitis, piles, leprosy etc. The pharmacological studies have shown that plant has hypoglycemic, antihyperlipidemic, hepatoprotective, antipyretic, wound healing, anticancer, antimicrobial, antifungal, pesticidal properties.In the present article we have summarized various aspects of the plant *Berberis lycium.*

Keywords: *Berberis Lycium, Berberidaceae, Berberine, Traditional medicine, Phytochemical, Pharmacological activity*

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1. Introduction

The use of plants as medicines is as old as the origin of mankind. The plant based, conventional medicine systems continues to play an essential role in health care, with about 80% of the world's inhabitants relying mainly on traditional medicines for their primary health care [1]. Since the origin of mankind people have mainly relied on plants for their food as well as their medicines for their treatment. Through trial and error they discovered that some plants were good for food, some were poisonous and some were also helpful in treatment of different diseases. Medicinal plants are getting attraction of most of the researches for the evaluation of new drugs, because of the polyvalent action and lesser side effects of plant products [2].

2. Plant Profile

The family Berberidaceae was first established by (Jussieu A.L.) [3] as 'Berberides' and was considered one of the most primitive angiosperms having a high number of disjunct or discontinuous genera (Bruckner C 2000) [4]. *Berberis lycium* was described in 1837 by John Forbes Royle. Berberidaceae is a heterogeneous assemblage of angiosperms represented by around 12 genera and 600 species. About 77 species of Berberis are reported from India [5].

Kingdom-Plantae Phylum-Tracheophyta
Class-Magnoliopsida Order-Ranunculales
Family-Berberidaceae Genus-Berberis
Species-*Berberis lycium*

3. Occurrence

Berberis lycium is found throughout the temperate and subtropical regions of the world (apart from Australia). *Berberis lycium* is native to India, Nepal, Pakistan and globally distributed in various parts of world. In India, It occurs in sub-tropical and temperate regions from Kashmir to Uttaranchal on the outer northern-western Himalayas between altitude ranges of 850 - 3500 metres. The plant possesses wide ecological amplitude and seeds can be grown in sandy, silty or loamy soils.

4. Morphology Aspects

The shrub of *Berberis lycium* is attractive and is easily grown shrub 2 to 3 m high, which is erect or suberect and semideciduous with dimorphic shoot (the long shoot forming the structure of the plant and short shoot 1-2 mm long) the stem and branches are pale whitish to grayish and contain spines arranged alternately on the stem. Leaves of this plant are leaves 2.5 to 7.5 by 8.18 mm, lanceolate or narrowly obovate-oblong and coriaceous in shape entire or with a few large spinous teeth that are arranged alternately on the stem [6]. The leaves of the plant are dull green above, pale and glaucous beneath. Secondary nerves are not prominent on the upper surface. The plant has androgynous (containing both sex organs) flowers which are self pollinated but pollination occurs via insects too [7].The plant blooms from May to June. The flowers have a cupped shape which are arranged in racemes and are mostly pale yellow in color, and are larger than the leaves [8].The fruits of the plant are called as berries and are ovoid or obovoid-subglobose which acquire bright red colour or purplish colour on ripening. On an average they are 7 mm long, 4 mm in diameter and weighing 227 mg. The colour of the pulp or juice is plum purple. On an average the fruit contain 2-5 seeds colour varying from yellow to pink. The fruit is slightly acidic and juicy in nature. Root is hard 3-8 cm in diameter, branched and gradually tapering and occasionally split longitudinally however its wood is smooth and bright yellow in colour. Root bark can be up to 3mm thick, externally fissured and internally smooth [9].

5. Anatomical Characters of *Berberis Lycium*

Table 1. Botanical analysis of the roots of*Berberis lycium*

Characters	
Macroscopic	Outer surface grayish brown with shinnings. Bark up to 3 mm thick, brittle, warty and easily detachable. Cut surface deep yellow. Fracture hard, odour phenolic and bitter in taste
Cork cells	Dark brown, 8–11 layered
Cork Cambium	2 or 3 layered
Cortical zone	17–22 layered
Sclereids	2 to 4 in groups
Pericyclic fibers	Frequently present
Vessels	Solitary or in group of 3 or 4
Medullary Rays	2 to 5 cells broad

Table 2. Botanical analysis of the stems of *Berberis lycium*

Characters	
Macroscopic	Outer surface grayish brown with shining. Bark easily detachable, thin, brittle, and twisted. Cut surface canary yellow. Fracture hard and bitter in taste
Cork cells	Dark brown, 7–19layered
Cork Cambium	2 or 3 layered
Cortical zone	20–26 layered
Sclereids	Scattered or sometimesin linear groups
Pericyclic fibers	Frequently present
Vessels	Solitary or in group of 3or 4
Medullary Rays	1 to 3 cells broad
Pith	Present

[10].

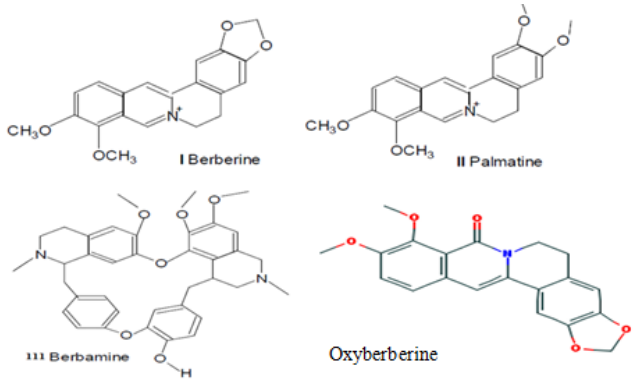
6. Flowering and Fruiting Season

The flowering and fruiting season of *Berberis lycium* is from the month of March-July. The flowers start appearing from the first fortnight of March and ends up to April. The fruits of *Berberis lycium* are relished from the month of June- July.The fruits or berries acquire bright red colour or purplish colour on ripening. The fruits start ripening from the second week of May and continue to do so throughout June. They can be retained on the shrub for a longer period after ripening but fall off soon after the onset of rain so, the fruiting season ends abruptly with the commencement of rain.

7. Chemical Constituent

The various chemical constituent of *Berberis lycium* are berberine, berbamine, chinabine, karakoramine, palmatine, balauchistanamine, gilgitine, jhelumine, punjabine, sindamine, chinabine acetic acid, maleic acid, ascorbic acid [11]. The plant contains major alkaloid berberine which is an isoquinoline alkaloid and umbellitine. This is usually taken from root or root bark of the Berberis lycium, and other Berberis species abundantly available in local forests. Phytochemical screening of water extract of *Berberis lycium* by showed the presence of Cardiac glycosides, Saponins, Hydrolysable Tannins, and Alkaloids [12]. The fruits contain malic, tartaric, citric acids and tannins [13]. Fruits also contain moisture, vitamin A, fibercontent, cellulose, hemicelluloses, β carotein, anthocyanins, phytic acid and phytate phosphorous [14]. Leaves are abundant in Zinc, Mn, Iron, Cu, Phosphorous, Potassium, Sodium and Calcium. It was revealed that Zinc, Cu and Sodium were maximum in root, while Mn, Phosphorous, Calcium in leaves, whereas, Potassium in shoot [15].Roots of B. lycium possess dry matter (61.2%), moisture (20.5%), protein (4.5%), fat (2.6%), sugar (3.5%), fiber (2.5%) and vitamin C (0.3%). Fruits also contain dry matter (62.5%), moisture (12.5%), protein (2.5%), fat (1.8%), sugar (4.5%), fiber (1.5%) and vitamin C (0.8%) in considerable amount. A wide variety of minerals are also documented such as sodium, calcium, sulphur, iron, zinc,vitamin C[16], copper, lead and manganese [17]. The plant is also documented to possess hydrolysable tannins, cardioactive glycoside and saponins [18]. Three new

alkaloids are also found in the roots of *Berberis lycium*-baberine, berbericine hydrochloride and berbericine hydroiodide. Two artefact alkaloids berberine-chloroform, palmitine-chloroform along with oxyberberine, Umbellatine, berberine and berbamine was also identified in the roots of same species.Kara-koramine $C_{25}H_{27}O_5N$, monophenolic chenabine $C_{37}H_{40}O_7N_2$ and diphenolic jhelumine $C_{36}H_{38}O_7N_2$ (more polar than chenabine) [19,20,21].



8. Traditional Medicinal Uses

Berberis lycium roots form areputed drug in the ayurvedic medicines. Every part of this plant has some medicinal value. Its root, bark, stem and fruits are used invarious ayurvedic preparations. In Unani system of medicine, it is used for the treatment of leprosy. A common recipe is to boilsliced pieces of root and its bark in water. The water extract is strained and further boiled until a semi solidmass, called “Rasaut” is obtained. The extract of roots is used for the treatment of urinary tract infections, enlargement of spleen, gastric and duodenal ulcer andliver disorders. The product is mixed with butter and alum to be used as an external application for the eyelids in acute conjunctivitis. Similar ointment containing camphor is used against acne, pimples and other skin infections [22]. The local inhabitants also use the dried mass of the root bark in powder form after mixing with molten animal fat as bandage for bone fractures.

The fruits of the plant are also very nutritious and are rich source of vitamins, minerals, antioxidants, anthocyaninetc. These fruits are consumed in raw form or are utilized in the preparation of juices, jams, preserve etc. by the local inhabitants. In Indochina, the fruit is given as a cure for renal disorder. The fruit juice is used for gums and teeth ailments. Decoction of fruit is used in typhoid and common cold. The fruits are in the form of berries and are used as fresh or indried form. Fruits of *Berberis lycium* are cool and laxative and are used for the relief of intestinal colic and pharyngitis. Decoction of fruit is also used in typhoid and fever [23].

Stems of the plant are used for the stomach pain, diarrhea, jaundice and in the inhibition of melanohialdehyde [24]. The bark of the plant shows wound healing activity [25]. Dried powdered plant bark is used for dysentery, internal wounds and throat pain. The plant leaves are used in jaundice and as tea substitute. The plant on the whole is used by the local inhabitants for the treatment of swollen and sore eyes, broken bones, internal injuries, ulcer, jaundice and rheumatism [26]. Berberine is the major alkaloid present in the rhizomes of *Berberis lycium* which has antibacterial effect. But this berberine is not appreciably absorbed by the body so it is used externally for the treatment of various enteric infections especially bacterial dysentery.

9. Pharmacological Activity

Antidiabetic Activity: *Berberis lycium* has shown antidiabetic activity in rabbits hence it helps in the reduction of sugar intensity in the blood. The root bark extract of Effect of *Berberis lycium* was determined in an alloxan induced diabetic rabbits. Simple powder of *Berberis lycium* reduced the level of blood glucose in both diabetic and normal rabbits. Water, methanolic, aqueous methanolic, n-hexane and chloroform extracts of plant were made to screen their antidiabetic activity in alloxanized rabbits. Results showed that amongst the extracts, water extract (500 mg/kg) showed greatest hypoglycemic activity when administered orally, for almost 6 hours. Similar dosage of methanol, aqueous methanol and n-hexane extract decreased glucose intensity in the blood for 4 hours. There was no significant change showed by the chloroform extract [27].

Ethanolic and aqueous extracts of the roots of the plant were administered in normal and alloxanized rats and 20 mg/kg glibenclamide was utilized as a control drug. The 50 and 100 mg/kg dosage quantity reduced the blood glucose level after 3 to 5 hours of administration but there was more prominent effect of the dose used later on. Oral glucose tolerance test showed that the plant extracts decreased serum glucose intensity in a dose-reliant behavior. This observed procedure concerned in hypoglycemia has insulin-like effect, maybe due to the peripheral glucose utilization [28].

Hepatoprotective Effect: *Berberis lycium* is known to have hepatoprotective property effect. *Berberis lycium* was mixed with Galium aparine and *Pistacia integerrima* and was tested in rats that were treated with carbon tetra chloride; the results showed that the combination of these three medicinal plants encompasses anti-hepatotoxicity effects. The three medicinal plants used in the present study showed high curative effect as a therapeutic agent relatively than protective agent [29].

To estimate potential hepatoprotective effect of *Berberis lycium*, methanolic extract of crude powder were used. Hepatotoxicity was induced by giving Paracetamol was to the rabbits. Results showed that plant considerably decreased the elevated levels of serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase and alkaline phosphatase enzymes in hepatotoxic rabbits [30].

Anti-hyperlipidemic Effect: Male albino rabbits were used to studyanti-hyperlipidemic effect of *Berberis lycium* Royle by utilizing its roots. Results showed that oral administration of 250 and 500 mg/kg crude powder showed a major decrease in the levels of low density lipids (LDLs), total cholesterol and triglyceride, while high density lipids (HDLs) were elevated. Also the same doses were successful in stabilizing the weight of diabetic rabbits. An increase in HDL and decrease in LDL levels was found when treated with root of the plant and this

effect most likely prevents the patients suffering from diabetes from having heart problems. Plant root bark powder when frequently administrated showed a positive result on hyperlipidaemia linked with high blood glucose levels [27].

Berberine have been screened in lipid metabolism, it has been observed that berberine is capable of lowering lipid concentration by increasing the transcriptional activity of LDLR promoter by a JNK pathway and stabilization of hepatic LDL-C receptor (LDLR) by an extracellular signal-regulated kinase (ERK)-dependent pathway [31].

Wound Healing Activity: The root extract of *Berberis lycium* was examined to study its wound healing ability in Swiss Wistar rats. Methanolic and aqueous extracts of the roots were tested in Swiss Wistar rats. The models of wound repair used in the study were excision, incision and deceased wound space forms of wound repair. Both extracts enhanced the region of epithelialization and also displayed enhancement in breaking potency. Results revealed that aqueous extract was less efficient than the methanolic extract [25].

Pesticidal Activity: Petroleum ether and aqueous methanol extracts of *Berberis lycium* root was prepared through Soxhlet apparatus and dried under vaccum. To check the activity, plant extracts were tested at two higher doses (5000 and 10000 ppm) against pests. Petroleum ether extract showed 25% mortality rate against *Helicoverpa armigeraHub* and 92% mortatlity rate against *Aphis craccivora Koch* at the dose of 5000 ppm. [32].

Antimutagenic property: p53 deficient HL-60 cells along with berberine and palmatinewere used to evaluateanti-neoplastic activities of *Berberis lycium* root extracts. The n-butanol extract showed maximum toxicity against HL-60 cells (IC_{50} 2.3 µg extract / ml medium after 48 h of treatment), followed by the ethanol extract (23.5 µg/ml) and then water extract (110 µg/ml). Berberine showed IC_{50} 1.2 µg/ml after 48 h of treatment, while palmatine did not show inhibitory effect on cell growth. HL-60 cells were exposed to 5.5 µg butanol extract/ml and 0.6 µg berberine/ml for 48 h to evaluate the cell cycle distribution which resulted in reduction of G1 cells and accumulation of cells in the S-phase by both plant extract and berberine. The butanol extract induced maximumapoptosis and was found to be superior in activity followed by the ethyl acetate and the water extracts [33].

Antioxidant properties: Reactive oxygen species (ROS) such as -OH (hydroxyl radical),hydrogen peroxide and superoxide anion are known for their potential of causing diseases likeRheumatoid arthritis, Inflammation, Cancer, Aging and Atherosclerosis [34].The root extract of *Berberis lycium* is known for antioxidant properties and strong reduction potential. Root extract converts potassium ferricyanide (Fe3+) to potassium ferrocyanide (Fe2+), which then reacts with ferric chloride and form a ferric ferrous complex that has an absorption maximum at 700 nm. This test is inexpensive and simple. [35]

Antidiarrheal activity: Berberine reduces smooth muscle contraction, intestinal motility and delays intestinal transit time in humans. It also directly inhibits some *E. coli*and *Vibrio cholera*enterotoxins significantly [36]. In-vitro study has shown that berberine sulphate inhibits bacterial adherences to mucosal or epithelial surfaces, which is the first step in the infective process. This may be a result of berberine's inhibitory effect on fimbrial structure formation on the surface of the bacteria [37].

Anti-arrhythmic activity: Berberine and its derivatives, 8-oxoberberine and tetrahydroberberine effects are attributed to the blockade of K^+ channels (delayed rectifier and K (ATP)) and stimulation of Na^+ -$Ca^{(2+)}$ exchanger. Berberine has been shown to prolong the duration of ventricular action potential. The vasodilatoractivityof berberine has been attributed to multiple cellular mechanisms. Theeffect ofberberine oncardiovascular system suggests its possible clinical usefulness in the treatment of arrhythmias [38].

Antidepressant activity: Neuropsychiatric research on berberine investigated its CNS effects. Thisresearch demonstrated that berberine also possesses an antidepressant activity. It was found that the drug affected the signalling pathway of L-arginine-NO cGMP, which resulted in the antidepressant activity of the drug. The antidepressant activity was confirmed by conducting forced-swim test (FST) and tail-suspension test (TST) [39]. Total immobility period was recorded during a 6-min test. Berberine (5-20 mg/kg, i. p.) produced a reduction in immobility period in both tests. When berberine (5 mg/kg, i. p.) was co-administered with other typical antidepressant drugs such as mianserin (32 mg/kg, i. p.) or trazodone (2mg/kg, i. p.) it was found to improve the anti-immobility effect of sub effective doses of the two antidepressant in FST but did not modify their effects. Berberine (5mg/kg, i.p.) in mouse whole brain increased the levels of nor epinephrine, serotonin or dopamine.

Berberine is well known to bind sigma receptors like many synthetic antidepressant drugs. Also as a natural compound it has been safely administered to humans, preliminary results suggests the initiation of clinical trials in patients with depression, bipolar affective disorder, schizophrenia in which cognitive capabilities are affected with either the extract or pure berberine [40].

Antimicrobial property: *Berberislycium* is very effective against many micro-organisms especially bacteria and fungi. Medicinal plants have the potential to kill bacteria and fungus pathogens *Berberislycium* is used against different bacteria such as Bacillus subtilis, Pseudomonas aeruginosa, Bacillus cereus, Enterobactoraerogenus, Micrococcusluteum, Escherichia coli, Klebsiella pneumonia, Proteusmirabilis, Staphylococcus aureusand Streptococcus pneumonia. Thehydroalcoholic extract of*Berberislycium* has been reported toexhibit stronger and broad spectrum effect against bacterialstrains as compared to fungal strains [41].

Antiprotozoal activity: The crude extracts of berberine had proven to be more effective than its salts [42]. In a clinical trial, berberine administration improved gastrointestinal symptoms and resulted in a marked reduction Giardia positive stools and it was effective at half the dose of the popular Giardiasis medication, metronidazole [43].

10. Conclusion

In the present review, various aspects of *Berberis lycium* have been discussed. It is a multi-potential plant

with many characteristics. In this article we havediscussed and highlighted the morphological, anatomical characters, phytochemical constituents, traditional uses and the pharmacological properties of this herb. The various pharmacological studies reported in this review support its traditional use and may prove to be useful in the development of some commercial drugs. Thus more work is required to point out the underlying phytochemicals which are responsible for various activities of this plant. The literature also showed that the plant has a leading capacity for the development of new good efficacy drugs in future. These plants are hardy in nature and grown in nature 'premaculture' so does not require chemical or pesticides and are ecofriendly.

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