STM JOURNALS

Research & Reviews: A Journal of
Pharmaceutical Science

ISSN: 2229-7006
Volume 15, Issue 3, 2024
September–December
DOI (Journal): 10.37591/RRJoPS

https://journals.stmjournals.com/rrjops

Review RRJoPS

# An Overview of *Berberis Lycium Royle's* Medicinal Significance

Deepika[1], Komal Pathania[2], Lovish Sharma[3,*], Ankur Thakur[4]

***Abstract***

*Natural medication substances are acknowledged as essential and play important roles in the current medical system because their therapeutic effects are dependent upon the availability of these bioactive molecules. Natural medicines are extremely helpful since they provide necessary bioactive compounds that are less harmful but nonetheless more potent because of their ability to prevent disease. In 1837, John Forbes Royle wrote the first description of the B. lycium plant. The Berberidaceae family comprises 450–500 deciduous and evergreen shrub species. This genus holds significant importance in diverse Indian Himalayan medical traditions. Indigenous to South Asia, including India, Nepal, Pakistan, and Afghanistan, the plant yields berries as its fruits. The flowers are initially bright yellow, turning purplish as the fruits ripen. The berries are oval, measuring approximately 7mm in length, 4mm in diameter, and weighing 227 mg. Flowering of this plant takes place in April to May and fruiting occurs in September to October and June to July. Whereas, abundant in various chemicals, the plant contains Glycosides, Alkaloid, Tannins, Flavonoids, Saponins, Triterpenoids, Carbohydrates, Phenolic Acid, Steroids, and Reducing sugar. With a wide array of beneficial properties, this medicinal plant exhibits antibacterial effects, anti-inflammatory effects, efficient microorganism elimination, acts as an aperient with a gentle laxative effect, and possesses various pharmacological properties.*

**Keywords:** *Berberis lycium, berberine,* alkaloids, pharmacological properties, medicinal plant.

## INTRODUCTION

Jussieu A.L. first recognised the family *Berberidaceae* as "*Berberides*" [1, 2]. John Forbes Royle first characterized the *Berberis lycium* plant in 1837. A less well-known plant, *Berberis lycium* (Berberidaceae), is referred to as Barberry in English, while its fruit is referred to as "Kashmal" and its roots as "Darhald" [3–5]. The family Berberidaceae includes 450–500 species of deciduous and evergreen shrubs under the genus *Berberis*. India is said to be home to 77 different species [6]. Since ancient times, the genus *Berberis* has been used in traditional systems of medicine [7]. In various Indian Himalayan medical systems, this genus has gained significant status.

***Author for Correspondence**
Lovish Sharma
E-mail: Lovishsharma0178@gmail.com

[1,2]Assistant Professor, School of Pharmacy and Emerging Sciences, Baddi University of Emerging Sciences & Technology, Baddi, District Solan, Himachal Pradesh, India
[3]Assistant Professor, Department of Pharmaceutical Chemistry, School of Pharmacy, Chitkara University, Baddi, District Solan, Himachal Pradesh, India
[4]Assistant Professor, Department of Pharmaceutical Chemistry, Himachal Pharmacy College, Nalagarh, Himachal Pradesh, India

Received Date: September 17, 2024
Accepted Date: September 23, 2024
Published Date: September 28, 2024

**Citation:** Deepika, Komal Pathania, Lovish Sharma, Ankur Thakur. An Overview of *Berberis Lycium Royle's* Medicinal Significance. Research & Reviews: A Journal of Pharmaceutical Science. 2024; 15(3): 61–71p.

### Taxonomic Classification of Medicinal Plant

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

 

## The Region of Occurrence of Medicinal Plant

*Berberis lycium* is a plant native to South Asia, including India, Nepal, Pakistan, and Afghanistan. It is widely distributed throughout temperate and subtropical areas of the world. In India, it grows subtropical and temperate regions from Kashmir to Uttaranchal in the outer northern and western Himalayas at altitudes of 850 and 3500 meters [8].

### Morphology of Medicinal Plant

*B. lycium* is a sharp-tipped deciduous shrub that grows to a height of 2–4 meters. On the stem of the plant, there are oblong leaves arranged alternately [9]. The plant has androgynous blooms that are self-pollinating; however insects help facilitate pollen dispersal [10].

*Berberis lycium* produces fruits known as berries. The flowers are bright yellow in color which acquire purplish color on ripening of fruits. The fruits are oval. The fruit length is about 7 mm, 4 mm in diameter and weigh 227 mg. The months of April to May are flowering season and September to October and June to July is marked as fruiting season. The fruit is used either raw or cooked and used as a preservative. The fruit is succulent and has a little acidic quality [11] (Figures 1, 2).

**Figure 1.** *B. Lycium* leaves.

**Figure 2.** *B. Lycium* flowers.

### The Microscopic Characters of Root and Stem of Medicinal Plant

The roots are greyish brown with shining on the outside. Warty, brittle, and up to 3 mm thick bark that is easily detached. Deep yellow on the cut surface. Hard to break, phenolic in smell, and bitter in flavor. The cork cells are dark brown and 8–11 layered. Cork cambium is 2 or 3 layered. Cortical Zone is 17–22 layered. Sclereids is 2–4 in groups. Pericyclic fibers are frequently present. Vessels are solitary or present in group of 3 or 4. Medullary rays are 2–5 cells broad. The stem's outer surface is greyish brown with a shine. Bark that is easily separated, thin, fragile, and twisted. Canary yellow on the cut surface. Hard and bitter to the taste. The cork cells are dark brown and 7–19 layered. Cork cambium is 2 or 3 layered. Cortical zone is 20–26 layered. Sclereids is scattered or sometimes in linear groups. Pericyclic fibers are frequently present. Vessels are solitary or present in group of 3 or 4. Medullary rays are 1–3 cells broad and pith is present (Figures 3, 4) [12].

**Figure 3.** *B. Lycium* fruits.

**Figure 4.** *B. Lycium* roots.

 

**Phytochemical Constituents of Medicinal Plant**

The plant is rich in many chemicals, contains Glycosides, Alkaloid, Tannins, Flavonoids, Saponins, Triterpenoids, Carbohydrates, Phenolic Acid, Steroids and Reducing sugar. Whole plant contains Berberine, Berbamine, Palmatine, Jhelumine, Punjabine, Sindamine, Maleic acid, Ascorbic acid [13, 14]. The leaves contain Berberine, Saponins, Potassium, Iron, Sodium, Phosphorus, Zinc and Calcium [15]. The stem contains Berberine, Copper, Manganese [16, 17, 18]. The fruit of the plant contains Saponins, Tannins, Alkaloids, Berbamine, Chinamine, Balauchistanamine, Sindamine berberine, Zinc and Sulphur [17, 19, 20] and have a significant amount of dry matter (62.5%), moisture (12.5%), protein (2.5%), fat (1.8%), sugar (4.5%), fiber (1.5%), and vitamin C (0.8%) [21]. The root of *B. lycium* have a composition that consists of 61.2% dry matter, 20.5% moisture, 4.5% protein, 2.6% fat, 3.5% sugar, 2.5% fiber, and 0.3% Vitamin C, Alkaloids, Tannins, Saponins, Flavonoids, Terpenoids, Steroids, Carbohydrates, Fat, Anthocyanin, Berberine, Palmatine, β-sitosterol, Jatrorrhizine, Butyl-3-hydroxypropyl phthalate, 4,4-dimethylhexadeca-3-ol, 4-methyl-7-hydroxycoumarin, and 3-(4′-(6-methyl butyl) phenyl) Propan-1-ol, Sulphur, Zinc, Manganese, Copper, Sodium, Potassium, Iron, Phosphorus [14, 15, 18, 22, 23]. The shoot contains Sodium, Iron, Potassium, Phosphorus [15]. The plant possesses large amounts of the alkaloid Berberine, which belongs to the isoquinoline alkaloid family. This compound is typically derived from the root or root bark of *B. lycium* [24]. The roots of *B. lycium* consist of approximately 4.0% berberine, while its stembark contains about 2.8% berberine [25] (Figures 5–18).

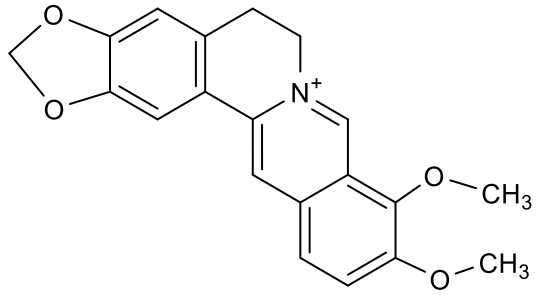


**Figure 5.** Berberine [14].

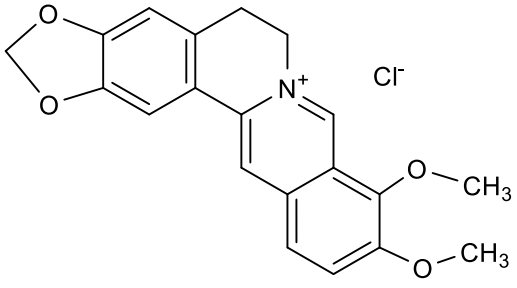


**Figure 6.** Plamatine [14].

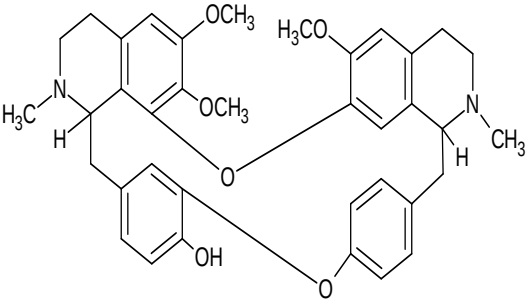


**Figure 7.** Berbamine [14].

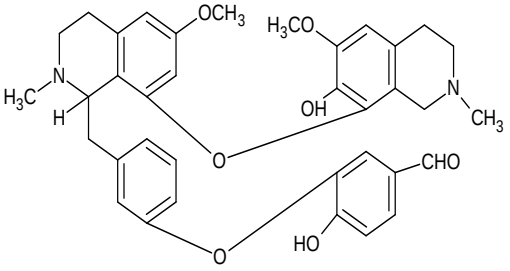


**Figure 8.** Jhelunine [15].

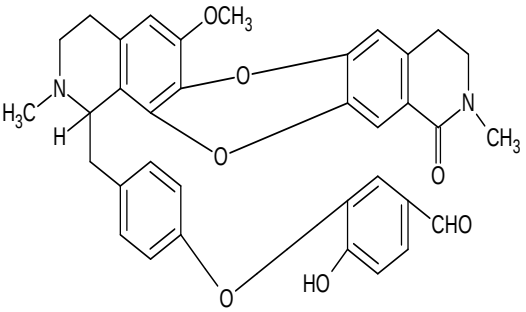


**Figure 9.** Punjabine [15].

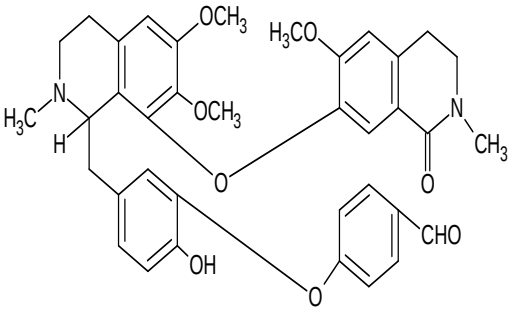


**Figure 10.** Sindamine [18].

 

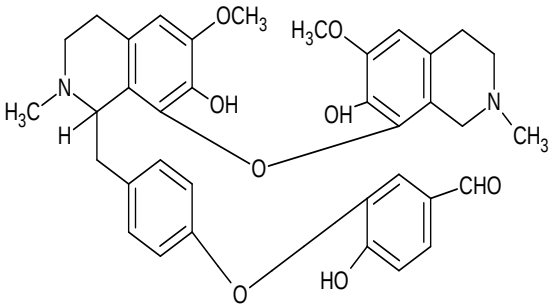


**Figure 11.** Chenabine [18].

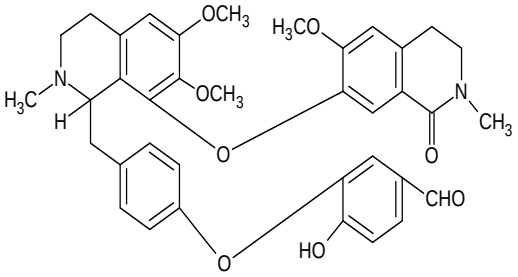


**Figure 12.** Balauchistanamine [18].

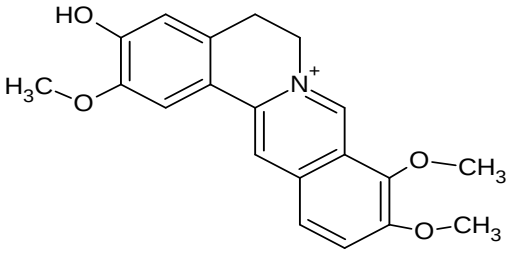


**Figure 13.** Jatrorrhizine [18].

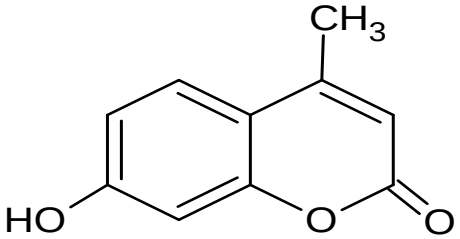


**Figure 14.** 4-methyl-7-hydroxycoumarin [22].

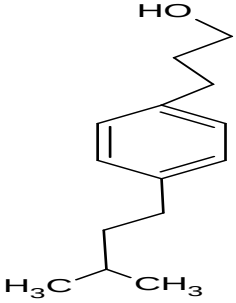


**Figure 15.** 3-(4′-(6-Methyl butyl) phenyl) propan-1-ol [22].

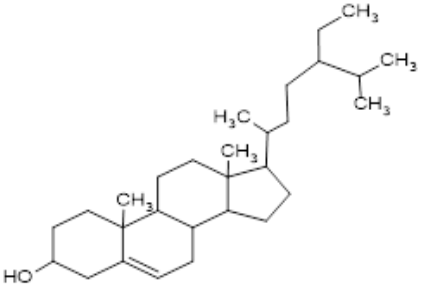


**Figure 16.** β-Sitosterol [23].


**Figure 17.** 4,4-Dimethylhexadecan-3-ol [23].

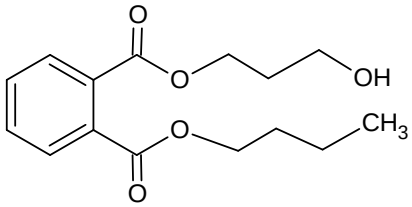


**Figure 18.** Butyl-3-hydroxypropyl phthalate [23].

**Figures 5–18.** Structures of chemical constituents which have been reported from *B. Lycium.*

**Therapeutic Uses of Medicinal Plant**

*Berberis lycium* has many beneficial properties. It shows antibacterial effects, anti-inflammatory effect, effectively eliminating microorganisms, an aperient and offering a gentle laxative effect. Moreover, it exhibits anticarcinogenic properties, helping to combat cancer. Furthermore, it acts as a febrifuge, aiding in the reduction of fever, and serves as an ophthalmic remedy for treating eye complaints. Different parts of the plant have distinct therapeutic applications:

- *Leaves:* The leaves of *B. lycium* are utilized for the treatment of Ophthalmia, jaundice and backache [26].
- *Fruits:* The *Berberis lycium* fruit's cooling and laxative properties make it useful for treating pharyngitis and intestinal colic. Whereas, Typhoid and fever are also treated with the fruit decoction [27].

 

- *Stem:* The *Berberis lycium* stem is useful for rheumatism since it possesses diaphoretic and laxative qualities. Additionally, ear injuries, whooping cough, headaches, and other diseases can all be successfully treated using the stem bark in conjunction with the root. The stem is also used to treat jaundice and ophthalmia [27].
- *Root:* The root of this plant possesses remarkable medicinal properties and is highly valued in India. The aqueous extract derived from the root serves as an effective treatment for ophthalmia, providing relief for swollen and sore eyes, as used by the local community. Additionally, it is used to cure Jaundice, Diabetes. Another use is to massage shattered bones to speed up their recovery by combining powdered root bark and mustard oil. Additionally, this adaptable root is used as a treatment for several ailments, including wounds, Gonorrhea, healing Piles, unhealthy ulcers, and acute Conjunctivitis. It also has bitter tonic, Astringent, Diaphoretic, and Febrifuge properties. The effectiveness of the dried root extract as a treatment for Sun blindness serves as more evidence of its significance in traditional medicine. The plant's roots, along with the root bark and lower stem wood, are crushed and then boiled to create a crude extract. For this procedure, water (and milk) is both used. The mixture is then filtered and condensed to create "Rasaut," a dark brown, sticky mass. Rasaut dissolves quite well in water. This preparation is combined with either butter and alum or opium and lime-juice, and it is applied externally to the eyelids for the treatment of ophthalmia and other eye ailments. It acts as an anti-inflammatory drug, helping to treat enlarged liver and spleen. Scrofula, fistula, acute spreading suppurations, and numerous Skin disorders are also treated with it [27].

**Pharmacological Activities of Medicinal Plant *Antidiabetic Activity***

Berberies have been discovered to possess antidiabetic properties. Extracts from the roots of *Berberis lycium* were found to significantly decrease glucose levels [28]. The plant's various extracts (water, methanolic, aqueous methanolic, n-hexane, and chloroform) were prepared for the study to test their antidiabetic effects on rabbits with diabetes brought on by alloxan. The aqueous extract, when taken orally at 500 mg/kg, demonstrated the greatest hypoglycemic action for up to 6 hours. Methanolic, Aqueous Methanolic, and n-Hexane extracts of 500 mg/kg lowered the blood sugar levels within 4 hours. Additionally, the effects of the water extract and insulin were examined, and the findings showed that 500 mg/kg of water extract mixed with 2 units of insulin produced effects like those of 6 units of insulin [29]. The extracts were as effective as pure Berberine and showed substantial benefits on body weight, glucose tolerance, serum lipid profiles, and glycosylated Haemoglobin [30]. 50 mg/kg extract of *Berberis* and Berberine was given to the normal, experimental diabetic rats by oral route and result showed decrease in blood glucose levels within 3 to 7 days of treatment. The experimental animals' body weight, serum lipid profiles, glucose tolerance, and glycosylated haemoglobin were all significantly affected, according to the study. The effects of *Berberis* extract and Berberine were equivalent across all assessed parameters, with the extract demonstrating efficacy like berberine without any supplementary effects. Berberine strongly influences the metabolism of lipids and carbohydrates, notably in the control of glucose [31, 32]. Moreover, Berberine has shown protective effects against β-cell destruction and oxidative stress in the pancreas of diabetic rats subjected to a high-carbohydrate/high-fat diet and a diabetic and hyper-lipidemic state induced by Streptozotocin administration [33, 34].

***Anti-Cancer Activity***

The effectiveness of berberine in fighting Cancer was investigated through experiments using cell lines. A surprise cytotoxic effect of berberine, which results in cell death in a dose-dependent manner at doses ranging from 5 μM to 200 μM, was discovered using the trypan blue exclusion experiment. Notably, an LD50 was produced after 5 hours of treatment with berberine at a 200 μM concentration. Additionally, the comet assay was used to assess the effect of berberine at doses ranging from 0 μM to 100 μM on DNA damage and repair. An increase in tail DNA content demonstrated irreversible cell damage caused by berberine exposure up to 20 μM. Additionally, DNA damage repair happened

 

within 1.5 hours after the cells were exposed to $H_2O_2$, indicating that berberine had a part in slowing DNA repair and ultimately causing cell death [35]. Berberine can help to kill cancer cells in various cancer cell types, including breast, lung and liver cancer. Apoptosis was frequently reported to be the mechanism of berberine-induced cancer cell death, and it was seen in both cancer cell xenografts and cell lines [36]. Nevertheless, autophagy and necrosis were also associated with berberine-induced cancer cell death, as reported in the studies [37, 38].

***Anti-Microbial Activity***

The roots of *Berberis* species contain several alkaloids, with berberine being the most significant, and are essential for their antibacterial effects. A study indicated that the root extract of *Berberis lycium* had inhibitory effects against certain bacteria, although the solvents used for extraction did not enhance this activity [39]. To evaluate its antibacterial properties, a 50% hydroalcoholic extract derived from air-dried roots and stems of *B. lycium* was examined against multiple bacterial strains, including Micrococcus luteum, Bacillus subtilis, Bacillus cereus, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, Salmonella typhimurium, and Streptococcus pneumoniae. The root extract demonstrated antifungal efficacy against Aspergillus spinulosus and Aspergillus flavus, with minimum inhibitory concentrations (MIC) of 0.62 µg/ml and 1.25 µg/ml, respectively [40]. The hydroalcoholic extract exhibited a more powerful and wider range of action against bacterial strains than fungal strains [41]. *B. lycium* helps fight off diseases and infections in animals. Furthermore, it was observed to substantially diminish Coccidial oocysts per gram of feces [42]. Berberine, often found in chloride and sulfate salts, has significant bacteriostatic efficacy against Staphylococcus epidermidis, Neisseria meningitidis, and *E. coli*. [43]. Berberine was tested against 17 types of bacteria to see if it can stop their growth. The results showed measuring the following parameters: IC50, MIC, minimum microbicidal concentration (MMC), and minimum microbistatic concentration (MMS). The IC50 value for S. aureus was established at 14.6 mg/ml, but that for Bacillus subtilis was 43 mg/ml, perhaps due to the emergence of spore-based resistance. The impact of berberine on Gram-Positive and Gram-Negative organisms was minimal [44]. The National Institute of Health demonstrated notable antibacterial activity of berberine extracts against bacteria, fungi, viruses, and Chlamydia, therefore reinforcing its effectiveness as an antimicrobial agent [45]. Besides its extensive antibacterial capabilities, berberine may impede Aspergillus fumigatus by affecting the ergosterol production pathway [46]. Furthermore, Berberine chloride has anti-Leishmanial activity in macrophages by activating p38 MAPK and suppressing ERK1/2 [47]. It also produces apoptosis-like death in Leishmania donovani promastigotes, along with elevated reactive oxygen species production [48].

***Hepatoprotective Activity***

In hepatoprotective activity, crude powder and methanolic extract of *Berberis lycium* were used. Paracetamol was used to produce hepatotoxicity in rabbits, and the results showed that the treated rabbits had significantly lower levels of the increased enzymes Alkaline Phosphatase, Serum Glutamic Pyruvic Transaminase, and Serum Goxaloacetic Transaminase [49]. Another study involving mice, six poly herbal formulations, including Livokin (Herbomed, Kolkata), which contains *B. lycium*, were investigated for their hepatoprotective effects on Paracetamol-induced hepatotoxicity. In these animals, the formulation was discovered to have a hepatoprotective effect [50]. Furthermore, a mixture of *B. lycium* bark, *Pistacia integerrima*, and *Gallium aparine* was prepared and administered to male Sprague-Dawley rats with Hepatotoxicity induced by Carbon Tetrachloride. According to the research, these medicinal herbs had a stronger therapeutic impact than a preventive one [51]. Alanine aminotransferase and aspartate aminotransferase activities were also significantly inhibited, and superoxide dismutase activity was elevated when rats were given Berberine and Coptidis rhizomes aqueous extract after receiving $CCl_4$ treatment. Coptidis rhizome aqueous extract displayed Hepatoprotective effects against acute liver injuries induced by $CCl_4$, and its effectiveness was attributed to its antioxidant properties [52]. Furthermore, it was discovered that Berberine prevented liver fibrosis in mouse models. By boosting the antioxidant system, preventing Lipid Peroxidation, and decreasing Hepatic Satellite Cell Proliferation, it demonstrated protective effects against experimental Liver Fibrosis [53, 54].

 

***Wound Healing Property***

In this activity, three models of wound repair: excision, incision, and dead wound space will be treated. Both the aqueous and methanol extracts of the plant showed promising results in promoting wound healing. They showed an improvement in breaking strength and enhanced the area of epithelialization. In the group treated with the aqueous extract, moderate collagen deposition, macrophages, and fibroblasts were observed. Other group treated with the methanol extract and resulted in an increase in collagen deposition with fewer macrophages and fibroblasts. These results demonstrated that the methanol extract promoted wound healing more effectively than the aqueous extract [55].

***Anti-Bacterial Activity***

Berberine, the active constituent of Hydrastis canadensis root extract, demonstrated effectiveness against a multidrug-resistant strain of Mycobacterium TB [56]. Furthermore, it has been shown to have inhibitory effects on Helicobacter pylori [57]. Moreover, Berberine showed effectiveness against other intestinal infections, including Shigella dysenteriae, Salmonella paratyphi, and several Klebsiella species, which may induce severe diarrhea. The efficacy of Berberine Sulfate in inhibiting the adhesion of Streptococcus pyogenes and E.coli to host cells may play a role in its mode of action against various infections [58].

***Anti-Hypertensive Activity***

Berberine induces vasorelaxation by influencing both the endothelium and the underlying vascular smooth muscle via several cellular processes. At reduced doses, berberine-induced aortic relaxation seems to depend on its impact on the endothelium, whereas at elevated concentrations, its effects are independent of the existence of intact endothelium [59]. Various other mechanisms have been suggested, such as an ACE-inhibitor effect, direct release of NO/cGMP from rat aortic rings, heightened sensitivity to Acetylcholine, and activation of K+ channels [60–62]. Berberine was beneficial to individuals with chronic heart failure, resulting in a reduction of ventricular premature complexes and an enhancement of left ventricular ejection percent. Berberine significantly reduced ventricular premature contractions in a substantial number of individuals with Ventricular Tachyarrhythmia [63]. Moreover, berberine or its alkaloids induced a dose-dependent, sustained reduction in blood pressure in trials with rabbits and cats. Moreover, varying dosages of Berberine had both beneficial and detrimental effects on feline cardiac health [64, 65]. Furthermore, intravenous berberine infusion in rats resulted in a reduction in blood pressure [66].

***Anti-Diarrheal Activity***

In humans, Berberine has shown to markedly diminish smooth muscle contraction, intestinal motility, and prolong intestinal transit time by directly blocking several enterotoxins generated by Vibrio cholera and *E. coli* [67, 68]. Laboratory investigations have shown that Berberine Sulfate may inhibit bacterial adherence to mucosal or epithelial surfaces, the first stage in the infection process. This outcome may be ascribed to berberine's capacity to inhibit the formation of fimbrial structures on the bacterial surface [58]. Moreover, Berberine has shown limited effectiveness in mice against E. histolytica, suggesting its potential use in the treatment of biliary disorders [69].

**Antihyperlipidemic Activity**

Researchers explored the antihyperlipidemic properties of *B. lycium* by collecting its roots for the study. The results showed oral treatment with the plant’s powder significantly reduced: Cholesterol and triglyceride levels by up to 30% in just 4 weeks [70–75].

**Anti-Inflammatory Activity**

In this activity, Wistar Rats were used and in vivo and in vitro experiments were conducted on the Berberine. When oral cancer cell lines OC2 and KB cells were treated with Berberine at concentrations of 1, 10, and 100 mM for 12 hours, there was a gradual decrease in prostaglandin E2

 

(PGE2) production, regardless of the presence or absence of 12-O-tetradecanoylphorbol-13-acetate (TPA) induction at 10nM. This reduction in PGE2 production was dependent on the dose of berberine used. The Anti-Inflammatory effect of Berberine was observed as early as 3 hours after treatment. The mechanism behind this effect involved a decrease in the COX-2 protein, rather than a significant inhibition of its enzyme activity. This suggests that Berberine's mode of action involves targeting the COX-2 protein to exert its anti-inflammatory influence [76].

**Anti-Fungal activity**

In this activity research showed the effect of Berberine Hydrochloride on Candida species, i.e., color stability of dental materials and surface surface roughness of acrylic resin plates. Result indicates that the experimental denture cleaner removed 64% to 89% of adhering cells from acrylic resin surfaces. Furthermore, it did not affect the measured physical properties of the materials [77]. Furthermore, rats subjected to an extract from *Berberis* vulgaris, including 80% berberine and other alkaloids, exhibited a 72% increase in bile excretion. Furthermore, studies indicate that berberine aids in reducing bilirubin levels [78].

## CONCLUSION

Natural products have played a critical role in both the advancement of human development and the preservation of life on Earth. These amazing occurrences often represent significant turning points in the search for novel herbal medicines. Natural medicines are very helpful since they provide vital bioactive ingredients that are less harmful but more potent in that they efficiently prevent illnesses. The *Berberis lycium Royle* plant is an important botanical species with a variety of characteristics. As a member of the Berberidaceae family, this plant is highly valued in several Indian Himalayan traditional medicinal systems. The *Berberis lycium Royle* plant possesses a wide range of advantageous features and is rich in varied substances, including Glycosides, Alkaloid, Tannins, Flavonoids, Saponins, Triterpenoids, Carbohydrates, Phenolic Acid, Steroids, and Reducing sugar. These characteristics include aperient features with a mild laxative impact, antibacterial and anti-inflammatory benefits, effective microorganism removal, and diverse pharmacological capabilities. This abundance of qualities highlights the plant's potential influence on human health and well-being and establishes it as a useful resource in both conventional medicine and pharmaceutical research.

## REFERENCES

1. Jussieu JD. Berberidaceae, nom. cons. Genera Plantarum. 1789;286.
2. Brückner C. Clarification of the carpel number in Papaverales, Capparales, and Berberidaceae. Bot Rev. 2000;66:155–307.
3. Anwar AK, Ashfaq M, Nasveen MA. Pharmacognostic studies of selected indigenous plants of Pakistan. Peshawar: Pakistan Forest Institute; 1979. p. 15–35.
4. Baquar SR. Medicinal and poisonous plants of Pakistan. 1989.
5. Usmanghani K, Saeed A, Alam MT. Indusyunic medicine. Karachi: University of Karachi Press; 1997. p. 120.
6. Nadkarni KM. Indian Material Medica. Bombay: Popular Prakashan Depot; 1980. p. 180–90.
7. Rajasekaran A, Pant J. The genus Berberis Linn.: A review. Pharmacogn Rev. 2008;2(4).
8. Bhardwaj D, Kaushik N. Phytochemical and pharmacological studies in genus Berberis. Phytochem Rev. 2012;11:523–42.
9. Sharma R. Medicinal plants of India: an encyclopaedia. Daya Books; 2003.
10. Dhar U, Kachroo P. Alpine Flora of Kashmir Himalaya. Brittonia. 1983 Oct;35(4):379.
11. Irshad AH, Pervaiz AH, Abrar YB, Fahelboum I, Awen BZ. Antibacterial activity of Berberis lycium root extract. Trakia J Sci. 2023;1:88–90.
12. Parra SA, Gaur K, Ranawat LS, Rather MI. An overview on various aspects of plant Berberis lycium Royale. Am J Pharmacol Sci. 2008;6:19–24.
13. Srivastava S, Rawat AKS. Quality evaluation of ayurvedic crude drug daruharidra, its allied species, and commercial samples from herbal drug markets of India. Evid Based Complementary Altern Med. 2013;2013:472973.

 

14. Furrianca MC, Alvear M, Zambrano T, Barrientos L, Fajardo V, Salazar LA. Medicinal value of the Berberis genus as a hypoglycemic agent. Bol Latinoam Caribe Plantas Med Aromat. 2015;14:423–41.
15. Sood P, Modgil R, Sood M. Physico-chemical and nutritional evaluation of indigenous wild fruit Kasmal, Berberis lycium Royle. Indian J Nat Prod Resour. 2010;1(3):362–6.
16. Ahmed M, Alamgeer A, Sharif T, Zabta CH M, Akbar A. Effect of Berberis lycium Royle on lipid profile in alloxan induced diabetic rabbits. Ethnobotanical leaflets. 2009;2009(6):4.
17. Wang H, Zhu C, Ying Y, Luo L, Huang D, Luo Z. Metformin and berberine, two versatile drugs in treatment of common metabolic diseases. Oncotarget. 2018 Feb;9(11):10135.
18. Srivastava SK, Rai V, Srivastava M, Rawat AKS, Mehrotra S. Estimation of heavy metals in different Berberis species and its market samples. Environ Monit Assess. 2006;116:315–20.
19. Mustafa K, Mohamed H, Yu AM, Shah MS, Akhlaq M, Xiao H, Song Y. In vitro anticancer potential of Berberis lycium Royle extracts against human hepatocarcinoma (HepG2) cells. Biomed Res Int. 2020;2020:8256809.
20. Ahmed S, Shuaib M, Ali K, Ali S, Hussain F. Evaluation of different parts of Berberis lyceum and their biological activities: a review. Pure Appl Biol. 2017;6(3):897–907.
21. Gulfraz M, Arshad M, Nayyer N, Kanwal N, Nisar U. Investigation for bioactive compounds of Berberis lyceum Royle and Justicia adhatoda L. Ethnobot Leaflets. 2004;2004:5.
22. Shaista S, Kalim T, Naghmana R, Sidra N, Bilal M, Muhammad Ajmal S, Mohammad S. Phytochemical and antioxidant studies of Berberis lycium. Pak J Pharm Sci. 2013;26(6):1165–72.
23. Sharma P, Awasthi A, Gupta I. Phytochemical investigation and evaluation of antioxidant potential of Berberis lycium roots from Himachal Pradesh. J Pharmacogn Phytochem. 2019;8(3):4740–5.
24. Ahmed M, Alamgeer A, Sharif T, Zabta CHM, Akbar A. Effect of Berberis lycium Royle on lipid profile in alloxan-induced diabetic rabbits. Ethnobot Leaflets. 2009;2009:4.
25. Garhwal S. Analysis of berberine content using HPTLC fingerprinting of root and bark of three Himalayan Berberis species. Asian J Biotechnol. 2010;2(4):239–45.
26. Uniayal K, Singh KN, Jamwal P, Lal B. Traditional use of medicinal plants among the tribal communities of Chhota Bhangal, Western Himalaya. J Ethnobiol Ethnomed. 2006;2:14.
27. Hasanuzzaman SM. Guide on medicinal and aromatic plants of SAARC countries. Dhaka: SAARC Agricultural Information Center; 2006.
28. Hassan M, Dar BN, Rather SA, Akhter R, Huda AB. Physico-chemical, sensory and microbial characteristics of fruit-flavored milk-based beverages during refrigerated storage. Adv Biomed Pharma. 2015;2:32–9.
29. Ahmed M, Sharif T, Alamgeer A, Zabta CHM, Akbar A. Effect of Berberis lycium on lipid profile in alloxan-induced diabetic rabbits. Ethnobot Leaflets. 2009;13:702–8.
30. Gulfraz M, Qadir G, Nosheen F, Parveen Z. Antihyperglycemic effects of Berberis lyceum Royle in alloxan-induced diabetic rats. Diabetologia Croatica. 2007;36:49–54.
31. Gulfraz M, Mehmood S, Ahmad A, Fatima N, Praveen Z, Williamson EM. Comparison of the antidiabetic activity of Berberis lycium root extract and berberine in alloxan-induced diabetic rats. Phytother Res. 2008;22:1208–12.
32. Kong WJ, Zhang H, Song DQ, Xue R, Zhao W, Wei J, Jiang JD. Berberine reduces insulin resistance through protein kinase C–dependent up-regulation of insulin receptor expression. Metabolism. 2009;58:109–19.
33. Zhou J, Zhou S, Tang J, Zhang K, Guang L, Huang Y, Li D. Protective effect of berberine on beta cells in streptozotocin- and high-carbohydrate/high-fat diet-induced diabetic rats. Eur J Pharmacol. 2009;606:262–8.
34. Yin J, Xing H, Ye J. Efficacy of berberine in patients with type 2 diabetes mellitus. Metabolism. 2008 May;57(5):712–7.
35. Szeto S, Yow CMN, Fung KW. Characterization of berberine on human cancer cells in culture. Turkish J Med Sci. 2002;32(5):363–8.
36. Choi MS, Oh JH, Kim SM, Jung HY, Yoo HS, Lee YM, Moon DC, Han SB, Hong JT. Berberine inhibits p53-dependent cell growth through induction of apoptosis of prostate cancer cells. Int J Oncol. 2009 May;34(5):1221–30.

 

37. Letašiová S, Jantová S, Čipák LU, Múčková M. Berberine—antiproliferative activity in vitro and induction of apoptosis/necrosis of the U937 and B16 cells. Cancer Lett. 2006 Aug;239(2):254–62.
38. Hou Q, Tang X, Liu H, Tang J, Yang Y, Jing X, Wang Z. Berberine induces cell death in human hepatoma cells in vitro by downregulating CD147. Cancer Sci. 2011 Jul;102(7):1287–92.
39. Irshad AH, Pervaiz AH, Abrar YB, Fahelboum I, Awen BZ. Antibacterial activity of Berberis lycium root extract. Trakia J Sci. 2013;1:88–90.
40. Singh M, Srivastava S, Rawat AK. Antimicrobial activities of Indian Berberis species. Fitoterapia. 2007 Dec;78(7-8):574–6.
41. Singh M, Srivastava S, Rawat AKS. Antimicrobial studies of stem of different Berberis species. Nat Prod Sci. 2009;15(2):60–5.
42. Nidaullah H, Durrani FR, Ahmad S, Jan IU, Gul S. Aqueous extract from different medicinal plants as anticoccidial, growth promotive and immunostimulant in broilers. J Agric Biol Sci. 2010;5(1):53–9.
43. Chevalier A. Encyclopedia of medicinal plants. Revised Edition. Sydney (AUS): Dorling Kindersley; 2001.
44. Čerňáková M, Košťálová D. Antimicrobial activity of berberine—a constituent of Mahonia aquifolium. Folia Microbiol. 2002;47:375–8.
45. Sack RB, Froehelich JL. Berberine—one herb in many ways. Altern Med Rev. 2000;5:175–7.
46. Lei G, Dan H, Jinhua L, Wei Y, Song G, Li W. Berberine and itraconazole are not synergistic in vitro against Aspergillus fumigatus isolated from clinical patients. Molecules. 2011;16:9218–33.
47. Saha P, Bhattacharjee S, Sarkar A, Manna A, Majumder S, Chatterjee M. Berberine chloride mediates its anti-leishmanial activity via differential regulation of the mitogen activated protein kinase pathway in macrophages. PLoS One. 2011 Apr;6(4):e18467.
48. Saha P, Sen R, Hariharan C, Kumar D, Das P, Chatterjee M. Berberine chloride causes a caspase-independent, apoptotic-like death in Leishmania donovani promastigotes. Free Radic Res. 2009 Jan;43(11):1101–10.
49. Ahmad M. Hepatocurative effect of Barberry Lycium (Royle) in hepatotoxic rabbits. Gomal Univ J Res. 2008 Jun;24(1):1–9.
50. Girish C, Koner BC, Jayanthi S, Rao KR, Rajesh B, Pradhan SC. Hepatoprotective activity of six polyherbal formulations in paracetamol induced liver toxicity in mice. Indian J Med Res. 2009 May;129(5):569–78.
51. Khan MA, Khan J, Ullah S, Malik SA, Shafi M. Hepatoprotective effects of Berberis lycium, Galium aparine and Pistacia integerrima in carbon tetrachloride (CCl4)-treated rats. J Postgrad Med Inst. 2008;22(2).
52. Ye X, Feng Y, Tong Y, Ng KM, Tsao S, Lau GK, Kobayashi S. Hepatoprotective effects of Coptidis rhizoma aqueous extract on carbon tetrachloride-induced acute liver hepatotoxicity in rats. J Ethnopharmacol. 2009 Jul;124(1):130–6.
53. Sun X, Zhang X, Hu H, Lu Y, Chen J, Yasuda K, Wang H. Berberine inhibits hepatic stellate cell proliferation and prevents experimental liver fibrosis. Biol Pharm Bull.. 2009 Sep;32(9):1533-7.
54. Zhang BJ, Xu D, Guo Y, Ping J, Chen LB, Wang H. Protection by and anti-oxidant mechanism of berberine against rat liver fibrosis induced by multiple hepatotoxic factors. Clin Exp Pharmacol Physiol.2008 Mar;35(3):303–9.
55. Asif A, Kakub G, Mehmood S, Khunum R, Gulfraz M. Wound healing activity of root extracts of Berberis lyceum Royle in rats. Phytother Res. 2007 Jun;21(6):589–91.
56. Gentry EJ, Jampani HB, Keshavarz-Shokri A, Morton MD, Vander Velde D, Telikepalli H, Mitscher LA, Shawar R, Humble D, Baker W. Antitubercular natural products: Berberine from the roots of commercial Hydrastis c anadensis powder. Isolation of inactive 8-oxotetrahydrothalifendine, canadine, β-hydrastine, and two new quinic acid esters, hycandinic acid esters-1 and-2. J Nat Prod. 1998 Oct;61(10):1187–93.
57. Bae EA, Han MJ, Kim NJ, KIM DH. Anti-Helicobacter pylori activity of herbal medicines. Biol Pharm Bull. 1998 Sep;21(9):990-2.990–992.
58. Sun DA, Courtney HS, Beachey EH. Berberine sulfate blocks adherence of Streptococcus pyogenes to epithelial cells, fibronectin, and hexadecane. Antimicrob Agents Chemother. 1988 Sep;32(9):1370–4.

 

59. Wong KK. Mechanism of the aortic relaxation induced by low concentrations of berberine. Planta Med. 1998 Dec;64(08):756–7.
60. Wen-Fei C, Mao-Hsiung Y, Chieh-Fu C. Mechanism of vasodilatory effect of berberine in rat mesenteric artery. Eur J Pharmacol. 1991 Oct;204(1):35–40.
61. Olmez E, Ilhan M. Evaluation of the alpha-adrenoceptor antagonistic action of berberine in isolated organs. Arzneimittelforschung. 1992 Sep;42(9):1095–7.
62. Kang DG, Sohn EJ, Kwon EK, Han JH, Oh H, Lee HS. Effects of berberine on angiotensin-converting enzyme and NO/cGMP system in vessels. Vasc Pharmacol. 2002 Dec;39(6):281–6.
63. Lau CW, Yao XQ, Chen ZY, Ko WH, Huang Y. Cardiovascular actions of berberine. Cardiovasc Drug Rev. 2001 Sep;19(3):234–44.
64. Watt G. Dictionary of the Economic Products of India, reprinted edition, Periodical Expert, Delhi. 1972;6(4):83.
65. Lahiri SC. Positive and negative inotropic effects of berberine on the cats' heart. Ann. Biochem. Exper. Med. 1958;18:95.
66. Anonymous, Wealth of India, Raw Materials, Publications and Information Directorate, SIR New Delhi. 1976;10:36.
67. Sack RB, Froehlich JL. Berberine inhibits intestinal secretory response of Vibrio cholerae and Escherichia coli enterotoxins. Infect Immun. 1982;35:471–5.
68. Yuan J, Shen XZ, Zhu XS. Effect of berberine on transit time of human small intestine. Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi Jiehe Zazhi= Chinese J Integ Trad West Med. 1994 Dec;14(12):718–20.
69. Hostettmann K, Marston A, Maillard M, Hamburger M, editors. Phytochemistry of plants used in traditional medicine. 1995.
70. Chand N, Durrani FR, Qureshi M, Durrani Z. Role of Berberis lycium in reducing serum cholesterol in broilers. Asian-Australas J Anim Sci. 2007;20(4):563-8.
71. Abidi P, Zhou Y, Jiang JD, Liu J. Extracellular signal-regulated kinase–dependent stabilization of hepatic low-density lipoprotein receptor mRNA by herbal medicine berberine. Arterioscler Thromb Vasc Biol.. 2005 Oct;25(10):2170–6.
72. Lee S, Lim HJ, Park JH, Lee KS, Jang Y, Park HY. Berberine-induced LDLR up-regulation involves JNK pathway. Biochem Biophys Res Commun. 2007 Nov;362(4):853–7.
73. Kulkarni SK, Dhir A. Possible involvement of L-arginine-nitric oxide (NO)-cyclic guanosine monophosphate (cGMP) signaling pathway in the antidepressant activity of berberine chloride. Eur .J Pharmacol 2007 Aug;569(1-2):77–83.
74. Kulkarni SK, Dhir A. On the mechanism of antidepressant-like action of berberine chloride. Eur J Pharmacol. 2008 Jul;589(1–3):163–72.
75. Kulkarni SK, Dhir A. Current investigational drugs for major depression. Expert Opin Investig Drugs. 2009 Jun;18(6):767–88.
76. Kuo CL, Chi CW, Liu TY. The anti-inflammatory potential of berberine in vitro and in vivo. Cancer Lett. 2004 Jan;203(2):127–37.
77. Nakamoto K, Tamamoto M, Hamada T. In vitro study on the effects of trial denture cleansers with berberine hydrochloride. J Prosthet Dent. 1995 Jun;73(6):530–3.
78. Chan MY. The effect of berberine on bilirubin excretion in the rat. Am J Chin Med. 1977;5(02):161–8.

 