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# Role of Berberine and Other Alkaloids in the Antimicrobial Activity of Berberis Lyceum

**Yelmame Vinod Bhaurao[1] and Dr. Krishan Pal[2]**
[1]Research Scholar, Department of Botany
[2]Research Guide, Department of Botany
Sunrise University Alwar, Rajasthan

**Abstract:** *Berberis lyceum Royle, a medicinal shrub belonging to the family Berberidaceae, has long been used in traditional Ayurvedic and Unani medicine for the treatment of infectious diseases, inflammation, wounds, gastrointestinal disorders, and skin infections. The antimicrobial potential of B. lyceum is primarily attributed to its bioactive alkaloids, particularly berberine, along with other isoquinoline alkaloids such as palmatine, jatrorrhizine, berbamine, and oxyacanthine. This review examines the phytochemical composition of B. lyceum, focusing on berberine and related alkaloids, and discusses their mechanisms of antimicrobial action against bacterial, fungal, and protozoal pathogens. The review also highlights experimental evidence supporting the therapeutic potential of these alkaloids and outlines future research directions.*

**Keywords*:*** Berberis lyceum, berberine, isoquinoline alkaloids, antimicrobial activity

## I. INTRODUCTION

Medicinal plants have served as an essential source of therapeutic agents for centuries. Among them, *Berberis lyceum* Royle is widely distributed in the Himalayan regions of India and Pakistan. Traditionally, its roots and bark have been used for treating infections, fever, diarrhea, and wound healing (Kirtikar & Basu, 2006). The plant is rich in isoquinoline alkaloids, especially berberine, which is considered the principal bioactive compound responsible for its antimicrobial properties (Imanshahidi & Hosseinzadeh, 2008).

With increasing antimicrobial resistance, there is renewed interest in plant-derived compounds as alternative or complementary therapies. Alkaloids from *B. lyceum* have shown broad-spectrum activity against Gram-positive and Gram-negative bacteria, fungi, and protozoa (Cowan, 1999). This review synthesizes current knowledge regarding the antimicrobial activity of berberine and other alkaloids present in *B. lyceum*.

## PHYTOCHEMICAL COMPOSITION OF BERBERIS LYCEUM

The roots, stem bark, and leaves of *B. lyceum* contain various alkaloids, flavonoids, tannins, and phenolic compounds. However, alkaloids represent the major pharmacologically active constituents. Berberis lyceum, a medicinal plant traditionally used in the Himalayan region, is well-known for its rich phytochemical profile, particularly its isoquinoline alkaloids, phenolics, and flavonoids, which contribute to its therapeutic potential. Among these bioactive constituents, berberine is the most prominent and extensively studied alkaloid.

Berberine is reported to possess significant antimicrobial properties, acting against a broad spectrum of bacteria, fungi, and protozoa. Mechanistically, berberine disrupts microbial cell walls and membranes, inhibits nucleic acid synthesis, and interferes with essential enzymatic activities in pathogens, leading to cell death (Ahmad et al., 2020; Khan et al., 2019). In addition to berberine, B. lyceum contains other important alkaloids such as berbamine, palmatine, jatrorrhizine, and oxyacanthine, each contributing synergistically to the overall antimicrobial effect.

These alkaloids have been observed to enhance the efficacy of berberine by targeting multiple pathways in microbial cells, thereby reducing the likelihood of resistance development (Sharma & Kaur, 2018). The antimicrobial activity of these alkaloids is not limited to bacteria; studies have demonstrated their effectiveness against fungal strains such as Candida albicans and Aspergillus niger, suggesting broad-spectrum potential (Verma et al., 2021).

Phytochemical analyses indicate that the concentration of berberine in different parts of B. lyceum, particularly roots and stems, is higher compared to leaves, correlating with the stronger antimicrobial activity observed in root extracts (Singh et al., 2017). In addition, the synergistic presence of flavonoids and phenolic compounds enhances the antibacterial effects, possibly by facilitating the uptake of alkaloids into microbial cells and generating oxidative stress within pathogens (Kumar et al., 2020).

Traditional usage of B. lyceum in folk medicine for treating gastrointestinal infections, urinary tract infections, and skin diseases aligns with these pharmacological findings, highlighting the clinical relevance of its bioactive constituents (Rai & Chandra, 2019). Recent in vitro studies have also explored the potential of berberine and related alkaloids in combination with conventional antibiotics, reporting additive or synergistic effects against multidrug-resistant strains, which could offer an alternative strategy to combat antimicrobial resistance (Tiwari et al., 2022).

Overall, the phytochemical composition of Berberis lyceum, dominated by berberine and supplemented by other alkaloids, constitutes a potent natural antimicrobial system. The plant's multi-component profile ensures diverse mechanisms of action, enhancing its therapeutic utility. Given the increasing global concern over antibiotic resistance, B. lyceum and its alkaloids present promising candidates for the development of plant-based antimicrobial agents, warranting further pharmacological and clinical investigations to optimize dosage, bioavailability, and safety profiles (Ahmad et al., 2020; Verma et al., 2021). Thus, the antimicrobial efficacy of Berberis lyceum is a result of the combined and complementary actions of berberine and other structurally related alkaloids, supported by synergistic interactions with additional phytochemicals present in the plant.

## MAJOR ALKALOIDS IDENTIFIED IN *B. LYCEUM*

- Berberine
- Palmatine
- Jatrorrhizine
- Berbamine
- Oxyacanthine
- Columbamine

Among these, berberine is the most extensively studied and pharmacologically significant compound (Kulkarni & Dhir, 2010).

## ROLE OF BERBERINE IN ANTIMICROBIAL ACTIVITY

### A. Antibacterial Activity

Berberine exhibits significant antibacterial activity against both Gram-positive and Gram-negative bacteria such as *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, and *Pseudomonas aeruginosa* (Kong et al., 2004).

### B. Mechanisms of Action

**Inhibition of DNA replication** – Berberine intercalates into DNA, inhibiting nucleic acid synthesis.
**Disruption of cell membrane integrity** – It alters membrane permeability.
**Inhibition of efflux pumps** – Berberine suppresses bacterial multidrug resistance pumps.
**Protein synthesis inhibition** – It interferes with ribosomal function.
These mechanisms contribute to its broad-spectrum antibacterial effect (Stermitz et al., 2000).

## ANTIFUNGAL ACTIVITY

Berberine has demonstrated antifungal effects against *Candida albicans*, *Aspergillus* spp., and dermatophytes. It disrupts fungal cell wall synthesis and mitochondrial function, leading to growth inhibition (Imanshahidi & Hosseinzadeh, 2008).

## ANTIPROTOZOAL ACTIVITY

Berberine exhibits activity against *Leishmania* spp. and *Plasmodium* spp. It interferes with protozoal DNA and enzyme systems, reducing parasitic growth (Birdsall & Kelly, 1997).

## ROLE OF OTHER ALKALOIDS IN ANTIMICROBIAL ACTIVITY

Although berberine is the principal alkaloid, other alkaloids also contribute synergistically. Berberis lyceum, a medicinal plant widely distributed in the Himalayan region, has long been recognized for its therapeutic potential, particularly due to its rich content of bioactive alkaloids. Among these, berberine is the most extensively studied and is known for its potent antimicrobial properties against a broad spectrum of bacterial, fungal, and protozoal pathogens (Kumar et al., 2020).

Berberine exerts its antimicrobial activity primarily by intercalating into microbial DNA, disrupting replication and transcription processes, and interfering with the function of key enzymes essential for microbial survival (Imenshahidi & Hosseinzadeh, 2016). Beyond berberine, B. lyceum contains several other alkaloids, including berbamine, oxyacanthine, palmatine, and jatrorrhizine, each contributing synergistically to the plant's antimicrobial efficacy (Singh et al., 2018).

Berbamine, for instance, exhibits antibacterial activity by altering bacterial cell membrane permeability, thereby enhancing the susceptibility of pathogens to environmental stressors and other antimicrobial compounds (Rauf et al., 2019). Similarly, palmatine has been reported to inhibit the growth of Gram-positive and Gram-negative bacteria by targeting bacterial cell wall synthesis and disrupting membrane potential (Khan et al., 2021).

The presence of multiple alkaloids in B. lyceum contributes not only to the additive antimicrobial effect but also to a synergistic interaction where the combined activity of berberine with minor alkaloids amplifies the overall inhibitory effect on pathogenic microbes (Chaudhary & Sharma, 2017). In addition to antibacterial properties, these alkaloids demonstrate antifungal and antiviral potential, with jatrorrhizine showing significant inhibition against fungal strains such as Candida species by disrupting ergosterol synthesis and affecting cell membrane integrity (Ahmad et al., 2015).

Oxyacanthine, another minor alkaloid, enhances the antimicrobial profile of B. lyceum by modulating microbial biofilm formation, which is critical for persistent infections and resistance development (Sharma et al., 2019). Collectively, the spectrum of alkaloids in B. lyceum contributes to a multi-targeted antimicrobial mechanism, reducing the likelihood of microbial resistance compared to single-compound therapies (Imenshahidi & Hosseinzadeh, 2016). Furthermore, these alkaloids also exhibit anti-inflammatory and immunomodulatory effects, which may support the host defense system in combating infections (Singh et al., 2018).

Recent studies emphasize that the holistic antimicrobial activity of B. lyceum is not solely due to berberine but arises from the concerted action of multiple alkaloids, suggesting that standardized extracts containing the full complement of these compounds may offer enhanced therapeutic efficacy (Kumar et al., 2020). Therefore, exploring the role of both major and minor alkaloids in B.

lyceum is essential for understanding its pharmacological potential and for developing novel antimicrobial agents that could serve as alternatives or complements to conventional antibiotics (Chaudhary & Sharma, 2017). Overall, the interplay of berberine with other alkaloids such as berbamine, palmatine, jatrorrhizine, and oxyacanthine underscores the importance of studying the entire alkaloid profile for comprehensive antimicrobial evaluation and potential clinical applications.

## PALMATINE

Palmatine shows moderate antibacterial activity and enhances the effect of berberine when used in combination (Kong et al., 2004).

## JATRORRHIZINE

Jatrorrhizine exhibits antimicrobial and anti-inflammatory properties, particularly against Gram-positive bacteria.

## BERBAMINE

Berbamine has been reported to possess antibacterial and antifungal activity and may modulate immune responses.

## OXYACANTHINE

Oxyacanthine demonstrates mild antimicrobial effects and contributes to the overall pharmacological profile of *B. lyceum* extracts. Berberis lyceum, a member of the Berberidaceae family, has long been recognized for its medicinal properties, largely attributed to its rich content of alkaloids, particularly berberine and oxyacanthine. Berberine, a well-studied isoquinoline alkaloid, exhibits broad-spectrum antimicrobial activity against bacteria, fungi, and protozoa, making it a key bioactive constituent in Berberis species (Kumar et al., 2019). Its mechanism of action involves the disruption of microbial cell walls and membranes, inhibition of nucleic acid synthesis, and interference with key enzymatic pathways critical for microbial survival (Zhang et al., 2020).

Oxyacanthine, another prominent alkaloid present in Berberis lyceum, complements berberine's antimicrobial effects by targeting microbial enzymes and disrupting energy metabolism, thereby enhancing the overall antimicrobial efficacy of the plant extract (Singh & Sharma, 2018). Studies have demonstrated that the combination of berberine and oxyacanthine produces a synergistic effect, reducing the minimum inhibitory concentration (MIC) required to inhibit common pathogenic bacteria such as Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa (Rashid et al., 2021).

Moreover, the antimicrobial potency of Berberis lyceum is not limited to bacteria; berberine and related alkaloids also show significant antifungal activity, particularly against Candida species, by interfering with ergosterol synthesis and fungal cell membrane integrity (Ahmad et al., 2017). Phytochemical analyses reveal that other minor alkaloids present in Berberis lyceum, including berbamine and palmatine, contribute to a multi-targeted antimicrobial action, which is particularly important in combating antibiotic-resistant strains (Gupta & Verma, 2019).

Additionally, the inherent antioxidant and anti-inflammatory properties of these alkaloids enhance host defense mechanisms, indirectly supporting microbial inhibition (Khan et al., 2020). Research comparing crude extracts with isolated berberine and oxyacanthine indicates that while isolated compounds show potent antimicrobial activity, the whole plant extract often demonstrates superior efficacy, suggesting a synergistic interplay among various alkaloids and phytochemicals (Sharma et al., 2018).

This synergism is particularly evident in traditional medicinal applications of Berberis lyceum, where decoctions and extracts have been effectively used to treat gastrointestinal infections, skin wounds, and respiratory ailments, highlighting the practical relevance of its alkaloid content (Jabeen et al., 2019). Further studies on the pharmacokinetics and bioavailability of berberine and oxyacanthine emphasize their potential for therapeutic development, as they not only inhibit microbial growth but also modulate host immune responses (Patel & Singh, 2020).

Berberis lyceum represents a valuable natural source of antimicrobial agents, with berberine and oxyacanthine playing central roles in its efficacy. Their synergistic interactions, broad-spectrum activity, and additional health-promoting properties underscore the importance of further exploring Berberis lyceum as a potential alternative or adjunct to conventional antimicrobial therapies, particularly in the face of rising antibiotic resistance.

## SUMMARY OF ALKALOIDS AND THEIR ANTIMICROBIAL EFFECTS

| **Alkaloid** | **Major Source (Plant Part)** | **Target Microorganisms** | **Mechanism of Action** | **Key References** |
|---|---|---|---|---|
| Berberine | Root, bark | *S. aureus*, *E. coli*, *Candida* spp., *Leishmania* | DNA intercalation, membrane disruption, efflux pump inhibition | Kong et al., 2004; Stermitz et al., 2000 |
| Palmatine | Root, stem | Gram-positive bacteria | Membrane interference | Kong et al., 2004 |
| Jatrorrhizine | Root bark | *Staphylococcus* spp. | Enzyme inhibition | Imanshahidi & Hosseinzadeh, 2008 |
| Berbamine | Root | Fungi, bacteria | Cell membrane alteration | Kulkarni & Dhir, 2010 |
| Oxyacanthine | Stem bark | Mild antibacterial spectrum | Unknown (probable membrane effects) | Cowan, 1999 |

## SYNERGISTIC EFFECTS OF ALKALOIDS

Studies suggest that whole plant extracts of *B. lyceum* often show stronger antimicrobial activity than isolated berberine alone. This indicates synergistic interactions between alkaloids and other phytochemicals (Cowan, 1999). Combination therapy involving berberine and conventional antibiotics has shown enhanced efficacy against resistant strains, suggesting potential use in combating antimicrobial resistance (Stermitz et al., 2000).

## CLINICAL AND THERAPEUTIC IMPLICATIONS

The antimicrobial properties of berberine and related alkaloids support their traditional use in treating:

Gastrointestinal infections
Skin infections
Eye infections
Wound healing
Urinary tract infections

However, despite promising in vitro results, clinical studies remain limited. Further pharmacokinetic and toxicity evaluations are necessary before standardized therapeutic applications can be recommended (Kulkarni & Dhir, 2010).

## LIMITATIONS AND FUTURE DIRECTIONS

Although numerous in vitro studies demonstrate antimicrobial potential, challenges remain:

Limited human clinical trials
Variability in alkaloid concentration depending on geography
Poor bioavailability of berberine
Need for standardized extraction protocols

Future research should focus on nanoformulations to enhance bioavailability, clinical validation studies, and exploration of synergistic drug combinations.

## II. CONCLUSION

*Berberis lyceum* is a valuable medicinal plant with significant antimicrobial properties primarily attributed to berberine and other isoquinoline alkaloids. Berberine acts through multiple mechanisms, including DNA intercalation, membrane disruption, and efflux pump inhibition, making it effective against a wide range of pathogens. Other alkaloids such as palmatine, jatrorrhizine, berbamine, and oxyacanthine contribute synergistically to the plant's antimicrobial activity. While promising, further clinical investigations are required to fully establish its therapeutic applications in modern medicine.

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