Pharmacognosy Reviews, 2025; 19(38):225-235.
www.phcogrev.com

Review Article

Phytochemistry and Pharmacological Insights on *Berberis napaulensis* (DC.) Spreng.: An Updated Review

Sapna Tamang[1], Saurav Moktan[2,*]

[1]Department of Botany, Santipur College, N.S. Road, Santipur, Nadia, West Bengal, INDIA.
[2]Department of Botany, University of Calcutta, 35, B.C. Road, Kolkata, West Bengal, INDIA.

ABSTRACT

In the temperate and sub-temperate zones of the eastern Himalayas, the abundance of medicinal flora, notably *Berberis napaulensis*, assumes substantial significance. *Berberis napaulensis* is a member of the Berberidaceae family, which encompasses 500 species world wide under the genus *Berberis*, each possessing considerable significance. Notably, one such species, *B. napaulensis*, is particularly impactful in ongoing medicinal research. This review elucidates the botany, traditional uses, phytochemical, biosynthesis of phytochemicals and pharmacological attributes of *Berberis napaulensis*, illuminating its potential within traditional medicine. Photographs were captured during the extensive field surveys conducted in the Darjeeling district, and a comprehensive literature review was undertaken for the purpose of this study. This approach highlights the global importance of the plant in addressing various health concerns. The recognized phytochemical compounds in *Berberis napaulensis* demonstrate significant pharmacological effectiveness, highlighting the need for careful recognition. The integration of traditional knowledge and pharmacological understanding holds promise for addressing a range of conditions, cancer, viral diseases, and neurological disorders and many others.

Keywords: Berberine, *Berberis napaulensis*, Isoquinoline alkaloids, Jatrorrhizine, Pharmacological activities, Traditional applications.

Correspondence:
Dr. Saurav Moktan
Department of Botany, University of Calcutta, 35, B.C. Road, Kolkata-700019, West Bengal, INDIA.
Email: smbot@caluniv.ac.in

Received: 02-05-2025;
Revised: 30-06-2025;
Accepted: 18-08-2025.

INTRODUCTION

Plant natural products hold significant importance in various aspects of human life and the natural world.[1-3] The Himalayas have always been a treasure house for several medicinal plant and many species from eastern Himalaya have been reported to show immense medicinal prospects.[4-7] One such plant taxon is *Berberis napaulensis*, a prominent member of the *Berberis* genus, contributing to the diverse flora of Nepal, which boasts a rich array of 21 species.[8] The first description of the genus *Berberis* was provided by Linnaeus in his publication Genera Plantarum.[9] It is native to eastern Himalaya and China and is placed under family Berberidaceae, which comprises both herbaceous and woody taxa and is represented by 13 accepted genera and about 733 species.[10] The name 'berberys' originates from its Arabian designation for the fruit.[11] The species *Berberis napaulensis* (DC.) Spreng., currently accepted, was initially described by Candolle in 1821, using Buchanan-Hamilton's Nepal data[12] noted early 19th-century descriptions for *Berberis acanthifolia* and *Berberis napaulensis* based on Hamilton and Wallich's specimens from 1802. *B. napaulensis* was assigned to the orientales group based on biogeographic and leaf type criteria.[13] The current accepted name is *Berberis napaulensis* (DC.) Spreng., published in 1825. In Nepal and the Darjeeling-Sikkim eastern Himalaya, it is known as 'Chutro', while its English name is 'Nepal Barberry.[14] *Berberis napaulensis* encompasses chemical diversity, traditional uses, and pharmacological potential, bridging traditional knowledge with modern medicinal applications. The following review delves deeper into the multifaceted aspects of these plants, drawing insights from a diverse range of studies and research endeavours.

METHODOLOGY

In this review, a comprehensive information on *Berberis napaulensis* has been compiled from multiple peer-reviewed research articles accessed through electronic databases such as ScienceDirect, Scopus, Google Scholar, PubMed, Google, and ResearchGate. The keywords used during the literature search included, *Berberis napaulensis*, Isoquinoline alkaloids, berberine, jatrorrhizine, Traditional applications, Pharmacological activities. Traditionally used as an ethnomedicine for treating various ailments, *B. napaulensis* owes its therapeutic value to the presence of diverse bioactive compounds. Its promising pharmacological profile highlights significant potential for future research and

DOI: 10.5530/phrev.20252353

clinical applications. Additionally, photographs depicting the plant's habit were taken during field visits in the Darjeeling region.

RESULTS

Morphology and distribution

B. napaulensis (syn. *Mahonia napaulensis* DC.) is an early winter blooming plant that blooms around October to December. It is an evergreen shrub or small tree that can reach heights upto 2-7 m, though it typically develops to be shorter, and the leaves have fewer, more elongated leaflets approximately 61cm long. The terminal leaflet is often not noticeably bigger than the rest. The racemes of fragrant flowers are approximately 20-22 cm long and carried in protracted clusters at the terminal ends (Figure 1). The colours of the petals range from pale orange to deep yellow. The outer sepals measure 3-4 x 2 mm, and the style is around 0.4 mm long. The dark blue, extremely pruinose fruit, measuring about 9 x 6 mm, ripens during April to June. *B. napaulensis* is distributed in temperate and sub-temperate regions of eastern Himalaya, western Himalaya, south-central and south-east China, Myanmar, Nepal, Thailand, Tibet, Bhutan, Vietnam, NE India at altitudes of 2000-2900 m, and Southern Western Ghats.[10-14]

Traditional uses

Traditionally, plants containing a variety of secondary metabolites such as tannins, terpenoids, alkaloids, and polyphenols are known to exhibit potent antimicrobial activities, which are well-documented in phytochemical research.[15,16] *M napaulensis*, rich in isoquinoline alkaloids such as berberine (0.173%±0.03), has been highlighted in comparative pharmacognostic studies as a potential substitute for the Ayurvedic drug Daruharidra (*Berberis aristata*).[17] This species is traditionally used in Ayurveda, Homeopathy, Unani, Chinese medicine, and Allopathy for the treatment of various ailments.[17-19] In the Chinese medicinal system, the stem and root of *M. napaulensis* have traditionally been used to treat dysentery, likely due to the antimicrobial properties of its alkaloid compounds.[20] A decoction made by boiling 20 g of *M. napaulensis* bark in 200 mL of water for 10-15 min is traditionally used in the treatment of ophthalmological conditions such as eye boils and irritation, possibly due to its anti-inflammatory and wound-healing properties.[21,22] Additionally, the stem of *B. napaulensis* provides a natural dye, used traditionally by the Apatani tribe, with scientific evidence supporting its effectiveness as a textile dye due to the presence of bioactive compounds.[23,24]

Phytochemicals in *B. napaulensis*

To further elucidate the medicinal potential of *Berberis napaulensis*, its phytochemical profile has been thoroughly investigated. *B. napaulensis* reveals distinct bright yellow colorants visible on the underside of bark as shown in Figure 1D. Berberidaceae plants, notably the genus *Berberis* are known for various isoquinoline alkaloids[25,26] and it has been observed that alkaloid production occurs during the active growth phase and gets stored within the cortex and bark.[27] Govindachari *et al*., first extracted *B. napaulensis* bioactives, revealing significant isoquinoline alkaloids berberine ($C_{20}H_{18}NO_4^+$) (Figure 3A) and jatrorhizzine ($C_{20}H_{20}NO_4^+$) (Figure 3B) from root and stem bark of the plant.[28] Isoquinoline alkaloids, notable for wide bioactivities, including antitumor and neuroprotection, have captured global research interest.[29] After a long gap of research on *B. napaulensis* phytochemicals, Vankar *et al*., identified additional bioactive compounds from stem of the plant such as coptisine ($C_{19}H_{14}NO_4^+$) (Figure 3D) palmatine ($C_{21}H_{24}NO_4^+$) (Figure 3C) and columbamine ($C_{20}H_{20}NO_4^+$) (Figure 3E) along with berberine and jatrorhizzine.[30] Furthermore, Mai *et al*., isolated and characterized two bisbenzylisoquinoline compounds homoaromoline ($C_{37}H_{40}N_2O_6$) (Figure 3N) and isotetrandrine ($C_{38}H_{42}N_2O_6$) (Figure 3O) from wood of the plant.[31] Berberine has many metabolites such as berberrubine ($C_{20}H_{18}NO_4^+$) (Figure 3G), thalifendine ($C_{19}H_{16}NO_4^+$) (Figure 3H), demethyleneberberine ($C_{19}H_{18}NO_4^+$) (Figure 3I), and jatrorhizzine ($C_{20}H_{20}NO_4^+$) is also one of them, and comparatively, berberrubine and jatrorhizzine are pharmacologically more active metabolites than berberine.[32] Subsequently, Singh *et al*., identified eight bioactive chemicals from roots of the plants, magnoflorine ($C_{20}H_{24}NO_4^+$) (Figure 3J), isocorydine ($C_{20}H_{23}NO_4^+$) (Figure 3K), glaucine ($C_{21}H_{25}NO_4^+$) (Figure 3L), tetrahydropalmatine ($C_{21}H_{25}NO_4^+$) (Figure 3M), tetrahydroberberine ($C_{20}H_{21}NO_4^+$) (Figure 3F), jatrorrhizine ($C_{20}H_{20}NO_4^+$), palmatine ($C_{21}H_{22}NO_4^+$), and berberine ($C_{20}H_{18}NO_4^+$) using UHPLC-ESI-MS/MS technique from the root part of *B. napaulensis*.[33] When compared, *B. napaulensis* showed the greatest concentration of berberine i.e., 86580.00 µg/g, followed by the concentrations of palmatine 13877.50 µg/g and jatrorrhizine 47765.00 µg/g.[33] Thusa and Mulmi (2017) identified isoquinoline compounds, quinones, glycosides, terpenoids, cardiac glycosides, and steroids. Berberine and β-sitosterol were confirmed through.[34] Chaudhary *et al*., found flavonoids, phenols, starch, sugars, and tannins from the roots of the plant.[35] In 2022, Khang *et al*., isolated the 1-C-syringylglycerol 4-O-β-D-glucopyranoside, 5,6-dihydro-2,3,9,12-tetramethoxydibenzoquinolizinium, 7-hydroxy-6-methoxyisochroman-1-one, 6,7-dimethoxyisochroman-1-one, and 4',7-dihydroxyflavanone from the stems of *Mahonia napaulensis*.[36] Furthermore, this review provides an in-depth analysis of various isoquinoline compounds, including berberine and jatrorhizine, focusing on their bioactivities, biosynthesis, chemical structures, and molecular mechanisms of action. Figure 2 represents the different compounds presents in *B. napaulensis* and Figure 3 represents the structural representation of different isoquinoline alkaloids.

DISCUSSION

Biosynthesis of berberine and jatrorrhizine

These alkaloids, mainly derived from the amino acids phenylalanine and L-tyrosine, generate the intermediate dopamine (3, 4-dihydrophenylalanine) via reaction with an aldehyde or ketone, and the basic pathway of biosynthesis, which runs from norcoclaurine to reticuline, is shared by all alkaloid-producing plant species and widely dispersed for isoquinoline alkaloids.[37] Enzymological research on biosynthesis is widely conducted, with a focus on cultured plant cells. Almost all of the enzyme genes in the biosynthesis pathway for berberine have been identified and described.[38] Dopamine undergoes a Mannich reaction to produce (S)- Norcocauline when it condenses with 4-hydroxy-phenylacetaldehyde[39] (4HPAA) with the enzyme Norcocauline Synthase (NCS).[40] S-adenosyl methionine (S)-reticuline is produced after further oxidation and methylation, which is an essential stage in the formation of isoquinoline alkaloids in plants.[41] Common first stages in biosynthesis lead to the formation of (S)-reticuline and the branch point intermediate in the biosynthesis of several isoquinoline alkaloids is this crucial step.[40] A well-known flavin-dependent enzyme called Berberine Bridge Enzyme (BBE) converts (S)-reticuline to (S)-scoulerine in one important route.[42,43] Scoulerine 9-Omethyltransferase (SOMT) then methylates (S)-scolerine to produce (S)-Tetrahydrocolumbamine (THCB). The enzyme produced by heterologous expression had the anticipated substrate selectivity.[44] The methylene dioxy bridge of (S)-canadine is produced by the substrate-specific cytochrome P-450 oxidase canadine synthase.[45] S-Tetrahydroprotoberberine Oxidase (STOX), a substrate-specific oxidase whose sequence has not yet been determined, catalyses the last stage of berberine production.[46] The discovery of several biosynthetic enzymes has also been made possible by earliest examples of the creation of a benzylisoquinoline alkaloid in cell culture at levels required for commercial manufacturing is the overproduction of Berberine in *Coptis japonica*.[47,48] According to Rueffer *et al*., 3-O-demethylation of (S)-scoulerine coupled with 2-O and 9-O methylation may result in the formation of jatrorrhizine and other way is from the oxidation of Berberine.[49] The diagrammatic representation of the biosynthesis of Berberine and Jatrorrhizine is presented in Figure 4.

Pharmacology of isoquinoline alkaloids

The *Berberis napaulensis* roots are reservoirs of isoquinoline alkaloids and modern medicine also confirms the pharmacological advantages of isoquinoline alkaloids as anticancer, antitumour, anti-inflammatory, wound healing, antidiabetic, antioxidant, antimicrobial, antibacterial, heptaprotective, hypolipedemic and more.[38,51,52] The compounds, berberine and jatrorhizzine with others isoquilonine alkaloids have a potential of various anticancers activities that make this compounds truly beneficial in the field of pharmacology.[38,50-53] Table 1, includes several bioactive compounds identified in *Berberis napaulensis*; however, detailed discussions on pharmacological activities in this review primarily focus on berberine and jatrorhizine. The chemical structures of these compounds were retrieved from PubChem.[54]

Antitumor and anticancer properties

Yang *et al*., evaluated the methanolic stem extract of *M. napaulensis*, followed by BuOH fractionation, and identified the antiproliferative effects of compounds, particularly berberine and palmatine, using the MTT assay. The results showed a significant reduction in cell viability of more than 70% in human colon carcinoma CoLo 205 cells at the highest tested concentration (200 µg/mL).[139] Earlier studies shows that the Berberine treatment at concentrations of 2.5, 5.0, 10, and 20 µM for 24 hr reduced the levels of transcription factors NF-κB, c-Fos, and c-Jun in A549 cells.[55] Additionally, Bao *et al*., demonstrated that the Low-dose berberine (1.25-5 µM) promoted cancer cell proliferation, while

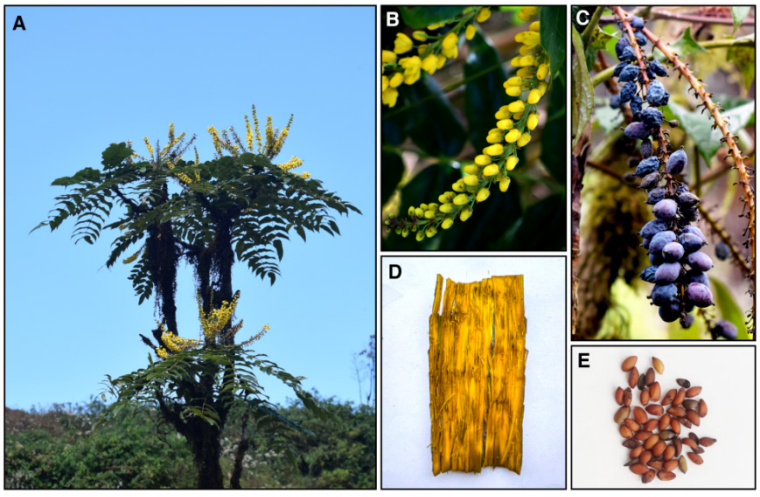


Figure 1: A. *B. napaulensis* in bloom B. portion of inflorescence C. ripened fruits D. underside of bark E. Seeds.

high doses (10-80 μM) inhibited it. Co-treatment with low-dose berberine weakened the anticancer effects of Fluorouracil (5-FU), Camptothecin (CPT), and Paclitaxel (TAX).[56] The anticancer activity of Methanol extract of *M. napaulensis* bark moderate against human lung cancer A549 cells (IC_{50} value of 228.97 μg/mL)[57] and human cervical cancer HeLa cells (IC_{50} value of 367.72 μg/mL).[58] Many researchers have concluded that berberine is effective against various cancers, including prostate, cervical, pancreatic, and bladder cancer, by regulating the proliferation mechanisms of human cancer cell lines.[58-60] Similarly, Berberine alleviates insulin resistance in women with PCOS, enhancing fertility and pregnancy outcomes.[61] Moreover Jatrorrhizine anticancer potential has been widely investigated. Qin *et al.*, found platinum (II) complexes with jatrorrhizine derivatives to be highly cytotoxic to HeLa cells, showing selectivity and strength via HL-7702 cells.[76] Furthermore, Qin *et al.*, found that a jatrorrhizine-berberine platinum (II) complex induced apoptosis in bladder tumor cells and jatrorrhizine itself inhibits colorectal carcinoma proliferation.[78]

Anti-inflammatory activities

Berberine, a natural compound with both anti-inflammatory and anti-tumor activities, holds promise for cancer treatment, particularly in the digestive system. Although its effects are moderate, structural modifications-especially at positions like C-8, C-9, C-12, and C-13 - have shown potential to enhance its efficacy, bioavailability, and metabolic stability.[63] Future drug development should aim to optimize both anti-inflammatory and anti-cancer properties through targeted structural changes.[63]

Bone regeneration

Berberine and Jatrorrhizine promotes osteoblast proliferation and differentiation while inhibiting osteoclast formation to aid bone regeneration hinting at its potential for osteoporosis treatment.[64,140]

Cardiovascular effects

Berberine has shown potential in managing heart failure and arrhythmias through its circulatory effects, primarily by blocking Potassium (K^+) channels and activating the Na^+/Ca^{2+} exchanger, which influence cardiac excitability and contractility.[68] Similarly, Jatrorrhizine also demonstrates cardioprotective properties by reducing cardiomyocyte apoptosis and fibrosis via modulation of the p53/Bax/Bcl-2 apoptotic pathway and the TGF-β1/Smad2/3 signaling cascade, as observed in myocardial infarction animal models.[141]

Anti-diabetic

Berberine has been shown to significantly lower fasting and postprandial blood glucose levels, supporting its therapeutic potential in managing type 2 diabetes mellitus.[71]

In addition to berberine, other isoquinoline alkaloids such as jatrorrhizine, coptisine, and palmatine also exhibit antidiabetic properties, possibly through modulation of gut microbiota and glucose metabolism pathways.[81]

Anti-obesity and lipid regulation

Several studies have demonstrated the anti-obesity potential of berberine.[65,66] It acts as a novel cholesterol-lowering agent by stabilizing LDLR mRNA, thereby enhancing cholesterol clearance.[142] Recent findings also suggest that berberine alleviates lipid dysregulation in obesity by modulating central pathways, possibly through neuronal regulation.[66] Similarly, jatrorrhizine exhibits antihyperglycemic effects by inhibiting α-glucosidase and aldose reductase.[143] It also demonstrates lipid-lowering properties by upregulating LDLR and CYP7A1

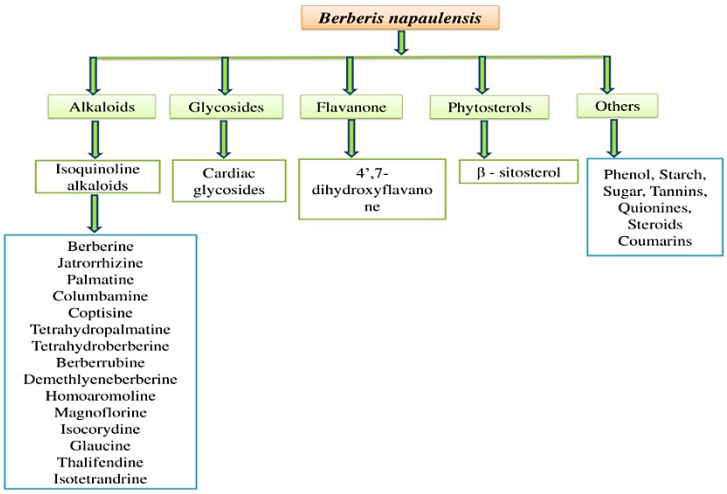
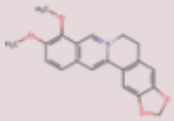
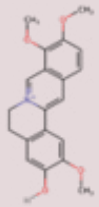
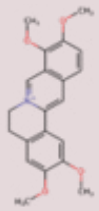
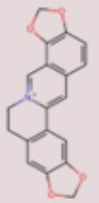
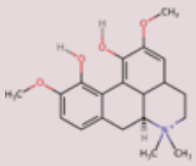
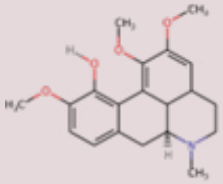
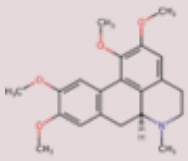
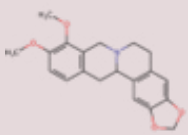
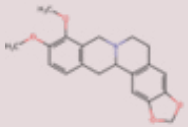
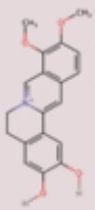
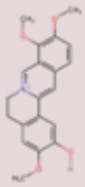
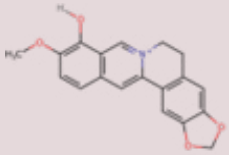


Figure 2: Compounds presents in *Berberis napaulensis.*

Table 1: Isoquinoline alkaloids of *B. napaulensis* with various pharmacological activities and bioactivities.

Phytochemical constituents	Chemical structure	Bioactivities of active constituents
(A) Berberine		Antitumor and anticancer;[55-61] Anti-inflammatory;[62,63] Bone regeneration;[64] Anti-obesity;[65-67] Cardiovascular effects;[68-70] Antidiabetic;[71] Antiviral;[72] Antifungal;[73] Neuroprotective activity;[74] Hypolipidemic.[75]
(B) Jatrorrhizine		Antitumor and anticancer;[76-78] Anti-inflammatory;[79] Antiobesity;[80] Antidiabetic;[81] Anti hypercholesterolemic;[82] Anti-microbial, antiviral, Antibacterial effects;[83] Neuroprotective;[84] Effects on the Central Nervous System;[85-87] Hepatoprotective.[88,89]
(C) Palmatine		Antitumor and anticancer;[90,91] Anti-inflammatory;[92] Neuroprotective;[93] Regulate lipid activity;[94] Antiviral;[95,96] Antibacterial.[97,98]
(D) Coptisine		Antitumor and anticancer;[99-102] Anti-inflammatory;[103,104] Antibacterial activity;[105,106] Antiviral,[107,108] Antifungal;[109,110] Antioxidant;[111] Cardioprotective[112] Neuroprotective.[113,114]
(E) Magnoflorine		Anti-inflammatory;[115] Antifungal[116,117] Immunomodulatory;[118] Anticancer;[119,120] Antitumor.[121]
(F) Isocorydine		Anticancer and antitumor.[122,123]
(G) Glaucine		Anti-inflammatory;[124] Anticancer;[125] Antioxidant.[126]
(H) Tetrahydropalmatine		Anti-inflammatory;[127,128] Antioxidant.[129]

Phytochemical constituents	Chemical structure	Bioactivities of active constituents
(I) Tetrahydroberberine		Neuroprotective.[130]
(J) Demethyleneberberine		Anti-inflammatory;[131,132] Neuroprotective;[133] Antioxidant.[134]
(K) Columbamine		Anticancer;[135,136] Antimicrobial.[137]
(L) Berberrubine		Antifungal.[138]

expression, promoting cholesterol utilization and excretion.[82] These actions collectively improve lipid profiles and contribute to weight management. Moreover, jatrorrhizine therapy has been shown to reverse liver alterations in hyperlipidemic mice, suggesting its potential to treat hyperlipidemia by suppressing fatty acid synthesis and enhancing fatty acid oxidation.[80]

Neuroprotective activity

Oren-Gedoku-To (OGT), a traditional Chinese medicinal formula, contains key ingredients such as jatrorrhizine, berberine, palmatine, and baicalein.[84] In a study by Yu *et al.*, these components, especially jatrorrhizine were found to exhibit strong Indoleamine 2,3-Dioxygenase (IDO1) inhibitory activity, highlighting their potential in treating Alzheimer's disease. Jatrorrhizine showed IC_{50} values of 206 μM for recombinant human IDO1 and 17.8 μM for HEK 293-hIDO1 cells, indicating its effectiveness.[84] Additionally, jatrorrhizine has been identified as a potent PMAT (plasma membrane monoamine transporter) inhibitor, suggesting its role as a promising antidepressant agent by modulating monoamine neurotransmission through uptake-2 inhibition.[86]

Anti-microbial, antiviral and anti-bacterial effects

Shrestha *et al.*, reported that the methanolic stem extract of *Mahonia napaulensis* exhibited weak antimicrobial activity, with Minimum Inhibitory Concentrations (MICs) of 100.22 mg/mL against *Staphylococcus aureus*, 50.15 mg/mL against *Escherichia coli*, and 25.08 mg/mL against *Candida albicans*.[57] In contrast, Deng *et al.*, found that the alkaloids jatrorrhizine and palmatine showed significant antimicrobial activity against both plant and animal pathogens.[144] Yu *et al.*, observed that jatrorrhizine alone exhibited minimal antibacterial activity at a MIC of 64 mg/L. However, when combined with Norfloxacin (NFX), it significantly enhanced the antimicrobial efficacy against Methicillin-Resistant *Staphylococcus aureus* (MRSA) strain SA1199B in mice, suggesting a synergistic *in vivo* interaction between jatrorrhizine and NFX.[83] Similarly, berberine has demonstrated strong antibacterial potential against multi-drug-resistant *E. coli* strains.[145] In addition to its antibacterial activity, berberine exhibits anti-viral effects by targeting various stages of the viral life cycle, including inhibition of DNA synthesis, modulation of key signaling pathways, and enhancement of host immune responses. These mechanisms position berberine as a promising candidate for the development of novel antiviral therapies, including potential applications against SARS-CoV-2.[72] Furthermore, several studies have reported the antifungal activity of *M. napaulensis* extracts against

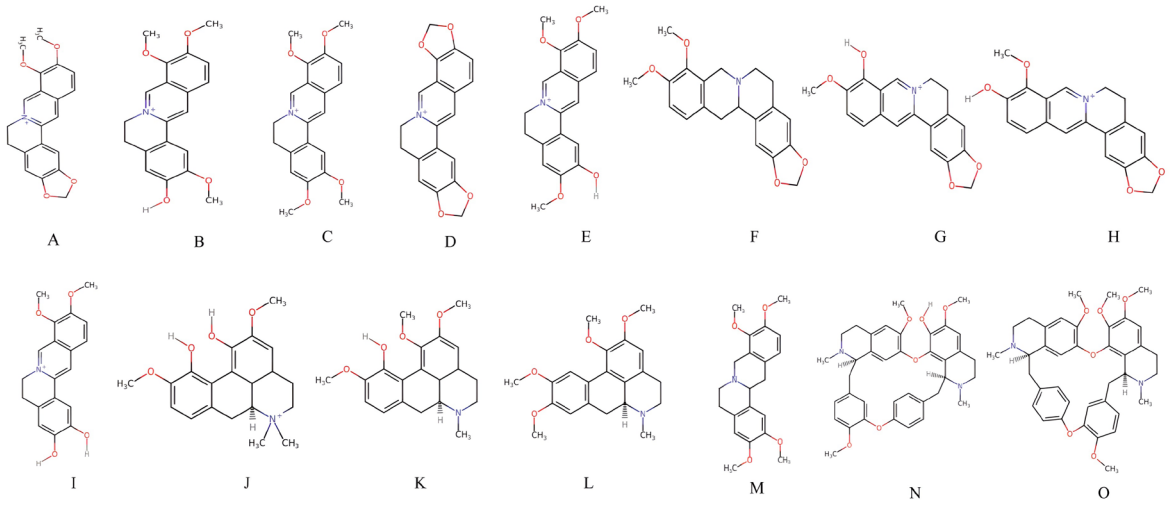


Figure 3: Structural representation of isoquinoline alkaloids in *Berberis napaulensis*. (A) Berberine, (B) Jatrorrhizine, (C) Palmatine, (D) Coptisine, (E) Columbamine, (F) Tetrahydroberberine, (G) Berberrubine, (H) Thalifendine, (I) Demethyleneberberine, (J) Magnoflorine, (K) Isocorydine, (L) Glaucine, (M) Tetrahydropalmatine, (N) Homoaromoline, (O) Isotetrandrine.

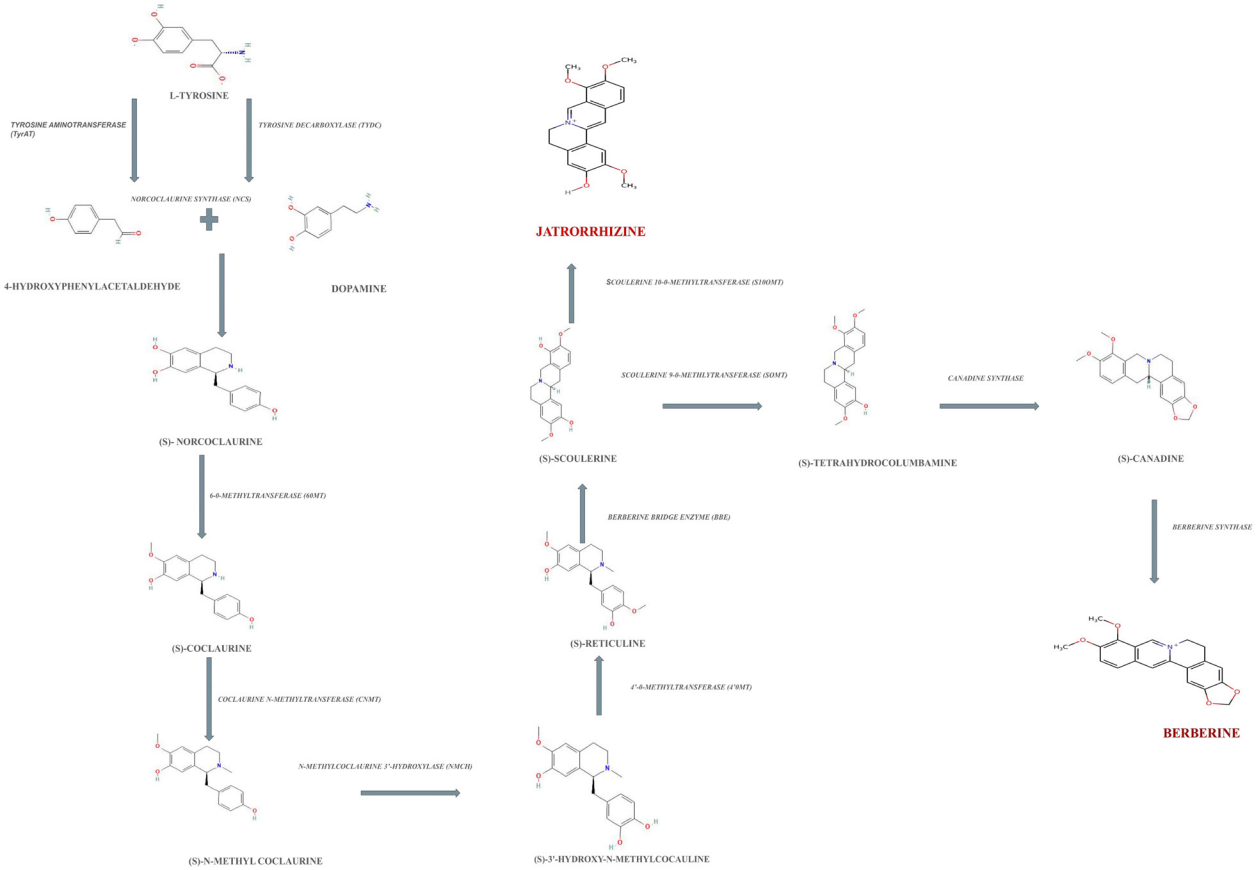


Figure 4: Biosynthetic pathway for Berberine and Jatrorrhizine.

pathogenic fungi such as *Colletotrichum capsici, Leptosphaerulina trifolii, Alternaria brassicicola*, and *Helminthosporium solani* at concentrations ranging from 20 to 100 µg/mL. A significant reduction in colony growth was also observed in *Trichoderma* species.[20]

Hepatoprotective activity

Berberine provides hepatoprotective effects against CCl_4-induced liver damage by exerting antioxidant activity, reducing oxidative stress, and suppressing inflammation.[88] Similarly, jatrorrhizine, used in traditional Chinese medicine formulations, shows liver-protective potential by lowering lactate dehydrogenase release and preventing oxidative injury.[89]

Antioxidant activity

Paudel *et al*., reported that the methanolic extract of *Mahonia napaulensis* bark exhibited DPPH radical scavenging activity with an IC_{50} value of 230.89 µg/mL, compared to 182.73 µg/mL for ascorbic acid.[146] Similarly, Shrestha observed moderate antioxidant activity with an IC_{50} of 212.97 µg/mL for the bark extract.[57] Yang *et al*., demonstrated that the ethyl acetate fraction of the stem extract showed strong antioxidant potential, with an IC_{50} of 48.93±0.59 µg/mL.[139] Additionally, Racková *et al*. found that jatrorrhizine and magnoflorine exhibit significant antioxidant activity.[147,148] Furthermore, studies suggest that the presence of catechol rings in berberine and its derivatives enhances their antioxidant capacity.[148]

Safety and toxicity considerations

Berberine, a major active constituent of *Berberis napaulensis*, is associated with adverse effects such as cramping, diarrhoea, gas, constipation, stomach pain, nausea, and abdominal distention.[149,150] High doses of berberine have also been linked to stomach lesions, flu-like symptoms, arterial hypotension, and dyspnea.[151] Furthermore, due to the risk of bilirubin-induced brain damage, the use of berberine-containing plants is not recommended for jaundiced new borns, pregnant women, and nursing mothers.[152] In contrast, jatrorrhizine demonstrates a better safety profile. A 90-day subchronic toxicity study in rats receiving jatrorrhizine at 70.05 mg/kg/day reported no changes in body or organ weights, and no abnormalities in urinalysis, hematological parameters, gross necropsy, or histological assessments.[153]

CONCLUSION

Berberis napaulensis holds significant promise as a valuable medicinal plant due to its rich phytochemical profile, especially the presence of isoquinoline alkaloids such as berberine and jatrorrhizine. Traditionally used across various medical systems-Ayurveda, Chinese medicine, and local ethnomedicinal practices-for treating ailments like dysentery, ophthalmic issues, and skin diseases, this plant is now gaining scientific validation. Studies highlight its wide-ranging pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, antidiabetic, hepatoprotective, and cardiovascular protective effects. Berberine and jatrorrhizine, in particular, have demonstrated strong bioactivity in areas such as lipid and glucose regulation, neuroprotection, and cancer therapy, often through well-characterized molecular pathways. While the review focuses mainly on these two compounds, the plant contains several other bioactives with therapeutic potential, warranting deeper exploration.

Going forward, a more detailed understanding of its lesser-known constituents, mechanisms of action, and structure-activity relationships will enhance its clinical relevance. With further pharmacological, toxicological, and clinical investigations, *B. napaulensis* may emerge as a sustainable natural source for novel therapeutic agents.

ACKNOWLEDGEMENT

The authors are grateful to the Department of Botany, University of Calcutta for all the necessary facilities. The authors also wish to thank the anonymous reviewer.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

UHPLC-ESI-MS/MS: Ultra High-Performance Liquid Chromatography-Electrospray Ionization-Tandem Mass Spectrometry; **LDLR:** Low-Density Lipoprotein Receptor; **ROS:** Reactive Oxygen Species; **MRSA:** Methicillin-Resistant *Staphylococcus aureus*; **NFX:** Norfloxacin; **MIC:** Minimum Inhibitory Concentration; **IDO1:** Indoleamine 2, 3-Dioxygenase 1; **NF-κB:** Nuclear Factor Kappa B; **MAPK:** Mitogen-Activated Protein Kinase; **OGT:** Oren-Gedoku-To; **MIC:** Minimum Inhibitory Concentration; **IC_{50}:** Inhibitory concentration 50; **DPPH:** 2-2-Diphenyl-1-Picrylhydrazyl.

ETHICAL STATEMENTS

We, the authors of this review paper, confirm that the manuscript is our original work. It has not been published previously and is not under consideration for publication elsewhere. All sources of information, ideas, and/or words that are not our own have been properly acknowledged through appropriate citations and quotations. As this is a review article, it does not involve any studies with human participants or animals conducted by us.

REFERENCES

1. Mukherjee AK, Basu S, Sarkar N, Ghosh AC. Advances in cancer therapy with plant-based natural products. Curr med chem. 2001; 8(12): 1467-86.
2. Aniszewski T. The ecological role of alkaloids, in Alkaloids-Secrets of Life: Alklaloid Chemistry, Biological Significance, Applications and Ecological Role. Elsevier; 2007. p. 205-12.

3. Porras G, Chassagne F, Lyles JT, Marquez L, Dettweiler M, Salam AM, *et al.*, Ethnobotany and the role of plant natural products in antibiotic drug discovery. Chem rev. 2020; 121(6): 3495-560.
4. Salick J, Fang Z, Byg A, Eastern Himalayan alpine plant ecology, Tibetan ethnobotany, and climate change. Glob Env Chan. 2009; 19(2): 147-55.
5. Mukherjee D, Chakraborty S, Roy A, Mokthan MW, Differential approach of germplasm conservation of high value of medicinal plants in north eastern Himalayan region. Inter J Agri Env Biotech. 2009; 2(4): 332-40.
6. Singh A, Bajpai V, Kumar S, Rawat AK S, Kumar B, Analysis of isoquinoline alkaloids from *Mahonia leschenaultia* and *Mahonia napaulensis* roots using UHPLC-Orbitrap-MSn and UHPLC-QqQLIT-MS/MS. J Pharma Anal.2017; 7(2): 77-86.
7. Semy K, Kuotsu R. Ethnobotanical Study of Medicinal Herbs Used by the Naga Tribes of Eastern Himalayas. In: Arunachalam K, Yang X, Sasidharan SP, editors. *Bioprospecting of Tropical Medicinal Plants*. Cham: Springer Nature Switzerland AG; 2023. p. 1-23.
8. Adhikari B, Pendry C, Pennington R, Milne R. A revision of *Berberis* s.s. (berberidaceae) in nepal. Edin J Bot. 2012; 69(3): 447-522.
9. Linnaeus C, Genera plantarum. Leiden; Conrad Wishoff; 1737.
10. Plants of the World Online [https://powo.science.kew.org/], Royal Botanic Gardens, Kew, [updated 2025 March 8; cited 2025 March 9]. Available from http://www.plantsoftheworldonline.org/.
11. Quattrocchi U. CRC world dictionary of medicinal and poisonous plants: common names, scientific names, eponyms, synonyms, and etymology. 1st ed. Boca Raton (FL): CRC press; 2012.
12. Schilling T and Watson M, Clarifying the identities of two Nepalese Mahonia. Plantsm. 2014; 13(2): 94-100.
13. Huang J, Su T, Lebereton-Anberree J, Zhang ST, Zhou ZK. The oldest *Mahonia* (Berberidaceae) fossil from East Asia and its biogeographic implications. J Pl Res. 2016; 129(2016): 209-23.
14. Paudel K, Ramamurthy A, Sharma G. Pharmacognostical and phytochemical standardization on stem bark of *Mahonia nepalensis* DC: An extra pharmacopoeial plant. J Ind Syst Med.2022; 10(3): 155-63.
15. Cushnie TT, Cushnie B, Lamb AJ, Alkaloids: An overview of their antibacterial, antibiotic-enhancing and antivirulence activities, Inter J antimicro agents. 2014; 44(5): 377-86.
16. Cowan MM, Plant products as antimicrobial agents, Clin Mic Rev. 1999; 12(4): 564-82
17. Chaudhary MK, Misra A, Srivastava S, Comparative Pharmacognostical Studies Of Three *Mahonia* Species: Exploring the possibilities as a substitute of Ayurvedic drug "Daruharidra", Ind J Trad Know. 2022; 21(4): 774-81
18. Tiwari AK, Dwivedi N, Tripathi MK. Scientific evaluation of Darvyadi Kvatha Curna-A classical Ayurvedic compound formulation, IJ Nat Prod Res. 2015; 6(4); 314-19.
19. Tiwari AK, Dwivedi N, Tripathi MK, Tripathi SP. Standardization and quality control of Darvyadi Pravahi Kvatha-An Ayurvedic formulation, IJ Nat Prod Res. 2016; 15(4); .
20. He JM, Mu Q. The medicinal uses of the genus *Mahonia* in traditional Chinese medicine: an ethnopharmacological, phytochemical and pharmacological review. J Ethnopharmacol. 2015 Dec 4; 175: 668-83.
21. Thapa S, Medico-ethnobotany of Magar Community in Salija VDC of Parbat District, Central Nepal. Our Nat. 2012; 10(1): 176-90
22. Dulal K, Chaudhary S, Uprety Y, Shrestha N, Shakya S, Ethnomedicinal plants used by the local people of Changunarayan Municipality, Bhaktapur, Nepal. Ethnobot Res App. 2022; 23: 1-27.
23. Vankar PS, Shanker R, Dixit S, Mahanta D, Tiwari SC. Sonicator dyeing of modified cotton, wool and silk with *Mahonia napaulensis* DC. and identification of the colorant in *Mahonia*. Indust Crops Prod. 2008; 27(3): 371-9
24. Jha KK, Some marketing aspects of important non-timber forest products in a proposed UNESCO heritage site of Arunachal Pradesh, India J Plant Chem Ecophysio. 2016; 1(1): 1007-12.
25. Guinaudeau H, Leboeuf M, Cavé A. Aporphine alkaloids II, J Nat Prod 1979; 42(4): 325-360.
26. Shamma M. The isoquinoline alkaloids chemistry and pharmacology. Academic Press; New York; 2012; p. 241-43.
27. Chatterjee R. 1944, A chemical study of *Mahonia nepalensis* DC. (*Berberis nepalensis* Spreng.), J America Pharm Ass.1944; 33(7): 210-12.
28. Govindachari TR, Pai BR, Rajadurai S, Ramadas Rao U. Alkaloids of *Mahonia nepalensis* DC.In; Proceedings of the Indian Academy of Sciences, 1958; Springfield, India. Springer. 1958; p. 41-48.
29. Shang XF, Yang CJ, Morris-Natschke SL, Li JC, Yin XD, Biologically active isoquinoline alkaloids covering 2014-2018, Med Res Rev. 2020; 40(6): 2212-89.
30. Vankar PS, Shanker R, Dixit S, Mahanta D, Tiwari SC, Sonicator dyeing of modified cotton, wool and silk with *Mahonia napaulensis* DC. and identification of the colorant in *Mahonia*, Indust Crops Prod. 2008; 27(3): 371-79.
31. Mai NT, Tuan TA, Huong HT, Van Minh C, Ban NK, Van Kiem, *et al.*, Bisbenzylisoquinoline alkaloids from *Mahonia nepalensis*, Viet J Chem, 2009; 47(3): 368.
32. Spinozzi S, Colliva C, Camborata C, Roberti M, Ianni C, Neri F, *et al.* Berberine and its metabolites: relationship between physicochemical properties and plasma levels after administration to human subjects, J Nat Prod. 2014; 766(4): 772.
33. Singh A, Bajpai V, Kumar S, Rawat A, Kumar B, Analysis of isoquinoline alkaloids from *Mahonia leschenaultia* and *Mahonia napaulensis* roots using UHPLC-Orbitrap-MSn and UHPLC-QqQLIT-MS/MS, J Pharm Anal. 2016; 77(2): 86.
34. Thusa R, Mulmi S. Analysis of phytoconstituents and biological activities of different parts of *Mahonia nepalensis* and *Berberis aristata*, Nep J Biotech. 2017; 5(1): 5-13.
35. Chaudhary MK, Misra A, Srivastava S. Comparative Pharmacognostical Studies of Three *Mahonia* Species: Exploring the possibilities as a substitute of Ayurvedic drug "Daruharidra", Ind J Trad Know. 2022; 21(4): 774-81.
36. Khang NHD, Ho DT, Kiem N, Duong T, Thien T, *et al.*, Chemical constituents from the chloroform extract of the stem of *Mahonia nepalensis* DC., berberidaceae, Anal J Chem Phy Bio. 2022; 9: 222-5.
37. Sato F, Hashimoto T, Hachiya A, Tamura KI, Choi KB, Morishige T, *et al.* Metabolic engineering of plant alkaloid biosynthesis, Pro Nat Acad Sci. 2001; 98(1): 367-72
38. Singh S, Pathak N, Fatima E, Negi AS, Plant isoquinoline alkaloids: Advances in the chemistry and biology of berberine, Eur J Med Che. 2021; 226: 113839.
39. Wink M. Biochemistry of plant secondary metabolism. Sheffield Academic Press, UK 1999.
40. He SM, Liang YL, Cong K, Chen G, Zhao X, Zhao QM, *et al.* Identification and characterization of genes involved in benzylisoquinoline alkaloid biosynthesis in *Coptis* species, Fron Pl Sci, 2018: 9: 731.
41. Sato F, Inui T and Takemura T, Metabolic engineering in isoquinoline alkaloid biosynthesis, Curr Pharma Biotech. 2007; 8(4): 211-8.
42. Wang S, Wang M, Duan C, Yao Y, Ren J, Liu L, Pan Y, Liu G. A berberine bridge enzyme-like oxidase mediates the cage-like acresorbicillinol C biosynthesis. Org Lett. 2024; 26(3): 642-6.
43. Hauschild K, Pauli H H and Kutchan T M, Isolation and analysis of a gene bbe1 encoding the berberine bridge enzyme from the California poppy *Eschscholzia californica*, Pl Mol Bio.1998; 36: 473-78.
44. Takeshita N, Fujiwara H, Mimura H, Fitchen JH, Yamada Y, Sato F. Molecular cloning and characterization of S-adenosyl-L-methionine: scoulerine-9-O-methyltransferase from cultured cells of *Coptis japonica*, Pl Cell Physio. 1995; 36(1): 29-36.
45. Ikezawa N, Tanaka M, Nagayoshi M, Shinkyo R, Sakaki T, Inouye K, *et al.* Molecular cloning and characterization of CYP719, a methylenedioxy bridge-forming enzyme that belongs to a novel P450 family, from cultured *Coptis japonica* cells, J Bio Chem. 2003; 278(40): 38557-65.
46. Amann M, Nagakura N, Zenk MH. Purification and properties of (S)-tetrahydroprotoberberine oxidase from suspension-cultured cells of *Berberis wilsoniae*. Europea, J Biochem, 1988: 175(1); 17-25.
47. Sato F, Yamada Y, High berberine-producing cultures of *Coptis japonica* cells. Phytochem, 1984; 23(2): 281-5.
48. Matsubara K, Kitani S, Yoshioka T, Morimoto T, Fujita Y, Yamada Y. High density culture of *Coptis japonica* cells increases berberine production, J Chem Tech Biotech. 1989; 46(1): 61-9.
49. Rüffer M, Ekundayo O, Nagakura N, Zenk M H, Biosynthesis of the protoberberine alkaloid jatrorrhizine, Tetrahed Let. 1983; 24(26): 2643-4.
50. Zhong F, Chen Y, Chen J, Liao H, Li Y, Ma Y. Jatrorrhizine: a review of sources, pharmacology, pharmacokinetics and toxicity, Front Pharma, 2022; 12: 783127.
51. Liu Q, Liu Y, Li Y, Yao S, Nonaqueous capillary electrophoresis coupled with laser-induced native fluorescence detection for the analysis of berberine, palmatine, and jatrorrhizine in Chinese herbal medicines, J Sep Sci. 2006; 29(9): 1268-74.
52. Kuepeli E, Koşar M, Yeşilada E, Hüsnü, Başer C. A comparative study on the anti-inflammatory, antinociceptive and antipyretic effects of isoquinoline alkaloids from the roots of Turkish *Berberis* species, Life sci, 2002; 72(6): 645-57.
53. Janbaz K, Gilani A, Studies on preventive and curative effects of berberine on chemical-induced hepatotoxicity in rodents. Fitoter. 2000; 71(1): 25-33.
54. National Center for Biotechnology Information. PubChem; Compound Summary. NCBI; 2023 [cited 2025 March 04] Available from: https://pubchem.ncbi.nlm.nih.gov/compound
55. Peng PL, Hsieh YS, Wang CJ, Hsu JL, Chou FP. Inhibitory effect of berberine on the invasion of human lung cancer cells via decreased productions of urokinase-plasminogen activator and matrix metalloproteinase-2, Toxico App Pharmacol, 2006; 214(1): 8-15
56. Bao J, Huang B, Zou L, Chen S, Zhang C, Zhang Y, Hormetic effect of berberine attenuates the anticancer activity of chemotherapeutic agents. PloS One, 2015; 10(9): 0139298.
57. Shrestha RK, Nayak S, Maharjan PS, Pokharel B, Jhingan GD, Singh RP, Bhavesh NS, Shrestha BG. Chemical composition, antioxidant, antimicrobial, and anticancer activities of *Mahonia napaulensis* DC. bark from Nepal. BMC Complementary Medicine and Therapies. 2025; 25(1): 105.
58. Li X, Zhang A, Sun H, Liu Z, Zhang T, Qiu S, *et al.* Metabolic characterization and pathway analysis of berberine protects against prostate cancer, Oncotar. 2017; 8(39): 65022.
59. Agnarelli A, Natali M, Garcia-Gil M, Pesi R, Tozzi MG, Ippolito C, *et al.*Cell-specific pattern of berberine pleiotropic effects on different human cell lines, Sci Rep. 2018; 8(1): 10599.
60. Xia Y, Chen S, Cui J, Wang Y, Liu X, Shen Y, *et al.* Berberine suppresses bladder cancer cell proliferation by inhibiting JAK1-STAT3 signaling via upregulation of miR-17-5p, Biochem Pharmacol. 2021; 188: 114575.

61. Ionescu OM, Frincu F, Mehedintu A, Plotogea M, Cirstoiu M, *et al.*, Berberine-A promising therapeutic approach to polycystic ovary syndrome in infertile/pregnant women, Life. 2023; 13(1): 125.
62. Chao J, Lu TC, Liao JW, Huang TH, Lee MS, Cheng HY, *et al.*, Analgesic and anti-inflammatory activities of ethanol root extract of *Mahonia oiwakensis* in mice, J Ethnopharm, 2009; 125(2): 297-303.
63. Zou K, Li Z, Zhang Y, Zhang HY, Li B, Zhu WL, *et al.* Advances in the study of berberine and its derivatives: a focus on anti-inflammatory and anti-tumor effects in the digestive system, Acta Pharma Sin. 2017; 38(2): 157-67.
64. Zhang Y, Ma J, Zhang W, Berberine for bone regeneration: Therapeutic potential and molecular mechanisms, J Ethnopharm, 2021; 277: 114249.
65. Ilyas Z, Perna S, Al-Thawadi S, Alalwan TA, Riva A, Petrangolini G, *et al.* The effect of Berberine on weight loss in order to prevent obesity: A systematic review, Biomed Pharmacol. 2020; 127: 110137.
66. Park HJ, Jung E, Shim I. Berberine for appetite suppressant and prevention of obesity, Biomed Res Int. 2020; 2020: 1-7.
67. Habtemariam S. Berberine pharmacology and the gut microbiota: A hidden therapeutic link, Pharma Res. 2020; 155: 104722.
68. Lau CW, Yao XQ, Chen ZY, Ko WH, Huang Y, Cardiovascular actions of berberine, Cardiovas Drug Rev. 2001; 19(3): 234-44.
69. Sanchez-Chapula J, Increase in action potential duration and inhibition of the delayed rectifier outward current IK by berberine in cat ventricular myocytes, Brit J Pharmacol. 1996; 117(7): 1427.
70. Fang J, Lai J, Lichtenberg J, Chen H, Zhang Y, Wu X, *et al.* Efficacy and safety of berberine for chronic congestive heart failure: a randomized, double-blind, placebo-controlled trial. Am J Cardiol. 2025; 145: 112-20.
71. Tilak AV, Vaidya MU, Limaye MV. An observational study of the antidiabetic activity of berberine in newly diagnosed type 2 diabetes mellitus patients. Biomed Sci. 2016; 6(3): 230-233.
72. Warowicka A, Nawrot R, Goździcka-Józefiak A. Antiviral activity of berberine, Arch Viro. 2020; 165: 1935-45.
73. Park KD, Lee JH, Kim SH, Kang TH, Moon JS, Kim SU. Synthesis of 13-(substituted benzyl) berberine and berberrubine derivatives as antifungal agents, Bioorg med chem. 2006; 16(15): 3913-16.
74. Akbar M, Shabbir A, Rehman K, Akash MSH, Shah MA. Neuroprotective potential of berberine in modulating Alzheimer's disease via multiple signaling pathways, J Food Biochem. 2021; 45(10): e13936.
75. Brusq JM, Ancellin N, Grondin P, Guillard R, Martin S, Saintillan Y, *et al.*, Inhibition of lipid synthesis through activation of AMP kinase: an additional mechanism for the hypolipidemic effects of berberine, J lip res. 2006; 47(06): 1281-8.
76. Qin QP, Wang ZF, Huang XL, Tan MX, Luo ZH, Wang SL, *et al.*, Two Telomerase-Targeting Pt(ii) Complexes of Jatrorrhizine and Berberine Derivatives Induce Apoptosis in Human Bladder Tumor Cells, Dalton Trans 2019a; 48(40): 15247-54.
77. Qin QP, Zou BQ, Wang ZF, Huang XL, Zhang Y, Tan MX, *et al.*, High *In vitro* and *In vivo* Antitumor Activities of Luminecent Platinum (II) Complexes with Jatrorrhizine Derivatives, Eur J Med Chem. 2019b;183: 111727.
78. Wang P, Gao XY, Yang SQ, Sun ZX, Dian LL, Qasim M, *et al.*, Jatrorrhizine inhibits colorectal carcinoma proliferation and metastasis through Wnt/β-catenin signaling pathway and epithelial-mesenchymal transition, Drug Des Dev Ther. 2019; 2019: 2235-47.
79. Chao J, Lu TC, Liao JW, Huang TH, Lee MS, Cheng HY, *et al*, Analgesic and anti-inflammatory activities of ethanol root extract of *Mahonia oiwakensis* in mice, J Ethnopharm. 2009; 125(2): 297-303.
80. Yang W, She L, Yu K, Yan S, Zhang X, Tian X, *et al.* Jatrorrhizine hydrochloride attenuates hyperlipidemia in a high-fat diet-induced obesity mouse model, Mol Med Rep. 2016; 14(4): 3277-84.
81. Lyu Y, Lin L, Xie Y, Li D, Xiao M, Zhang Y, *et al.* Blood-glucose-lowering effect of *Coptidis rhizoma* extracts from different origins via gut microbiota modulation in db/db mice, Front Pharma. 2021; 12: 684358.
82. Wu H, He K, Wang Y, Xue D, Ning N, Zou Z, *et al.* The antihypercholesterolemic effect of jatrorrhizine isolated from Rhizoma coptidis, Phytomed, 2014; 21(11): 1373-81.
83. Yu H, Wang Y, Wang X, Guo J, Wang H, Zhang H, *et al.*, Jatrorrhizine suppresses the antimicrobial resistance of methicillinresistant *Staphylococcus aureus*. Exp Therap Med. 2019; 18(5): 3715-22.
84. Yu J, Piao BK, Pei Y X, Qi X, Hua BJ, Protective effects of tetrahydropalmatine against γ-radiation induced damage to human endothelial cells. Life Sci. 2010; 87: 55-63.
85. Zhang S, Tang MB, Luo HY, Shi CH, Xu YM, Necroptosis in neurodegenerative diseases: a potential therapeutic target. Cell Death Dis. 2017; 8: e2905
86. Sun S, Zhou S, Lei S, Zhu S, Wang K, Jiang H, *et al.* Jatrorrhizine reduces 5-HT and NE uptake via inhibition of uptake-2 transporters and produces antidepressant-like action in mice. Xenobiot. 2019; 49(10): 1237-43.
87. Röhrig UF, Reynaud A, Majjigapu SR, Vogel P, Pojer F, Zoete V, *et al.*, Inhibition mechanisms of indoleamine 2, 3-dioxygenase 1 (IDO1). J Med Chem. 2016; 62(19): 8784-95.
88. Domitrovic R, Jakovac H, Blagojević G. Hepatoprotective activity of berberine is mediated by inhibition of TNF-α, COX-2, and iNOS expression in CCl4-intoxicated mice. Toxico. 2011: 280: 33-43.
89. Wang S, Li X, Niu Y, Liu Y, Zhu Y, Lu X, *et al.*, Identification and screening of chemical constituents with hepatoprotective effects from three traditional Chinese medicines for treating jaundice. J Sep Sci. 2016; 39(19): 3690-9.
90. Zhang L, Li J, Ma F, Yao S, Li N, Wang J, *et al.* Synthesis and cytotoxicity evaluation of 13-n-alkyl berberine and palmatine analogues as anticancer agents. Mol. 2012; 17(10): 11294-302.
91. Ali H, Dixit S. Extraction optimization of *Tinospora cordifolia* and assessment of the anticancer activity of its alkaloid palmatine. Sci World J. 2013; 2013(1): 1-10.
92. Chao J, Lu TC, Liao JW, Huang TH, Lee MS, Cheng HY, *et al.*, Analgesic and anti-inflammatory activities of ethanol root extract of *Mahonia oiwakensis* in mice. J Ethnopharm, 2009; 125(2): 297-303.
93. Jia W, Su Q, Cheng Q, Peng Q, Qiao A, Luo X, *et al.* Neuroprotective effects of palmatine via the enhancement of antioxidant defense and small heat shock protein expression in aβ-transgenic *Caenorhabditis elegans*. Oxi Med Cell Long. 2021; 2021(1): 1-18.
94. Ning N, He K, Wang Y, Zou Z, Wu H, Li X, *et al.* Hypolipidemic effect and mechanism of palmatine from *Coptis chinensis* in hamsters fed high-fat diet. Phytother Res. 2015; 29(5): 668-73.
95. Ho YJ, Lu JW, Huang YL, Lai ZZ, Palmatine inhibits Zika virus infection by disrupting virus binding, entry, and stability. Biochem. Biophy Res Comm. 2019; 518(4): 732-8.
96. Jadhav V, Ingle Sujata, Ahmed R, Inhibitory activity of palmatine on main protease complex (mpro) of SARS-CoV-2, Rom J Biophys. 2021; 31: 27-40.
97. Fan T, Guo X, Zeng Q, Wei W, You X, Pang J, *et al.* Synthesis and Structure-Activity Relationship of Palmatine Derivatives as a Novel Class of Antibacterial Agents against Helicobacter pylori, Mole. 2020; 25(6): 1352.
98. Wang S, Li X, Niu Y, Liu Y, Zhu Y, Lu X, *et al.* Identification and screening of chemical constituents with hepatoprotective effects from three traditional Chinese medicines for treating jaundice, J Sep Sci. 2016; 39(19): 3690-9.
99. Zhou L, Yang F, Li G, Huang J, Liu Y, Zhang Q, *et al.* Coptisine induces apoptosis in human hepatoma cells through activating 67-kDa laminin receptor/cGMP signalling, Front Pharma. 2018; 9: 517.
100. Kim SY, Hwangbo H, Lee H, Park C, Kim GY, Moon SK. *et al.* Induction of apoptosis by coptisine in Hep3B hepatocellular carcinoma cells through activation of the ROS-mediated JNK signaling pathway, Int J Mole Sci, 2020; 21(15): 5502.
101. Kim SY, Hwangbo H, Kim MY, Ji SY, Lee H, Kim GY, *et al.* Coptisine induces autophagic cell death through down-regulation of PI3K/Akt/mTOR signaling pathway and up-regulation of ROS-mediated mitochondrial dysfunction in hepatocellular carcinoma Hep3B cells, Arc Biochem Biophys, 2021; 697: 108688.
102. Nakonieczna S, Grabarska A, Gawel K, Wróblewska-Łuczka P, Czerwonka A, Stepulak A, *et al.* Isoquinoline Alkaloids from *Coptis chinensis* Franch: Focus on Coptisine as a Potential Therapeutic Candidate against Gastric Cancer Cells, Int J Mol Sci. 2022; 23(18): 10330.
103. Lee JW, Iwahashi A, Hasegawa S I, Yonezawa T, Jeon W B, Cha BY, *et al.* Coptisine inhibits RANKL-induced NF-κB phosphorylation in osteoclast precursors and suppresses function through the regulation of RANKL and OPG gene expression in osteoblastic cells. J Nat Med. 2012; 66: 8-16.
104. Chen HB, Luo CD, Liang JL, Zhang ZB, Lin GS, Wu JZ, *et al.* Anti-inflammatory activity of coptisine free base in mice through inhibition of NF-κB and MAPK signaling pathways. Eur J Pharma. 2017; 811: 222-31.
105. Li C, Huang P, Wong K, Xu Y, Tan L, Chen H, *et al.* Coptisine-induced inhibition of *Helicobacter pylori*: elucidation of specific mechanisms by probing urease active site and its maturation process. J Enz Inhib Med Chem. 2018; 33(1): 1362-75.
106. Zhang R, Tian S, Zhang T, Zhang W, Lu Q, Hu Q, *et al.*, Antibacterial activity mechanism of coptisine against *Pasteurella multocida*. Front Cell Inf Microbio, 2023; 13: 1207855.
107. Sadeghi M, Miroliaei M, Inhibitory effects of selected isoquinoline alkaloids against main protease (Mpro) of SARS-CoV-2. *in silico* study. In Sil Pharm; 2022; 10(1): 5.
108. He MF, Liang JH, Shen YN, Zhang CW, Yang KY, Liu LC, *et al.* Coptisine Inhibits Influenza Virus Replication by Upregulating p21, Mole. 2023; 28(14): 5398.
109. Kong WJ, Zhao YL, Xiao XH, Li ZL, Jin C, Li HB. Investigation of the anti-fungal activity of coptisine on Candida albicans growth by microcalorimetry combined with principal component analysis, J App Microbio. 2009; 107(4): 1072-80.
110. Akash S, Hossain A, Mukerjee N, Sarker MM, Khan MF, *et al.* Modified coptisine derivatives as an inhibitor against pathogenic *Rhizomucor miehei, Mycolicibacterium smegmatis* (Black Fungus), Monkeypox, and Marburg virus by molecular docking and molecular dynamics simulation-based drug design approach, Front Phar. 2023; 14: 1140494.
111. Hu YR, Ma H, Zou ZY, He K, Xiao YB, Wang Y, *et al.*, Activation of Akt and JNK/Nrf2/NQO1 pathway contributes to the protective effect of coptisine against AAPH-induced oxidative stress, Biomed Pharm. 2017; 85: 313-22.
112. Gong LL, Fang LH, Wang SB, Sun JL, Qin HL, Li XX, *et al.*, Coptisine exert cardioprotective effect through anti-oxidative and inhibition of RhoA/Rho kinase pathway on isoproterenol-induced myocardial infarction in rats, Atherosc. 2012; 222(1): 50-8.
113. Friedemann T, Schumacher U, Tao Y, Leung AK, Schröder S, Neuroprotective activity of coptisine from *Coptis chinensis* (Franch), Evid Based Complement Alternat Med. 2015; 2015(1): 827308.
114. Yu D, Tao BB, Yang YY, Du LS, Yang SS, He XJ, *et al.* The IDO inhibitor coptisine ameliorates cognitive impairment in a mouse model of Alzheimer's disease. J Alz Dis. 2015; 43(1): 291-302.

115. Shen Y, Fan X, Qu Y, Tang M, Huang Y, Peng Y et al. *Magnoflorine attenuates* inflammatory responses in RA by regulating the PI3K/Akt/NF-κB and Keap1-Nrf2/HO-1 signalling pathways *in vivo* and *in vitro*. Phytomed. 2022; 104: 154339.
116. Kim J, Ha Quang, Bao T, Shin YK, Kim KY, Antifungal activity of magnoflorine against *Candida strains*. World J Microbio Biotech. 2018; 34: 1-7.
117. Luo N, Jin L, Yang C, Zhu Y, Ye X, *et al.* Antifungal activity and potential mechanism of magnoflorine against *Trichophyton rubrum*. J Antibio. 2021; 74(3): 206-14.
118. Ahmad W, Jantan I, Haque MA, Arsyad L, Magnoflorine from *Tinospora crispa* upregulates innate and adaptive immune responses in Balb/c mice. Int Immunopharm. 2022; 111: 109081.
119. Sun XL, Zhang XW, Zhai HJ, Zhang D, Ma SY. Magnoflorine inhibits human gastric cancer progression by inducing autophagy, apoptosis and cell cycle arrest by JNK activation regulated by ROS. Biomed Pharm. 2020; 125: 109118.
120. Okon E, Kukula-Koch W, Halasa M, Jarzab A, Baran M, Dmoszynska-Graniczka M, *et al.* Magnoflorine—Isolation and the Anticancer Potential against NCI-H1299 Lung, MDA-MB-468 Breast, T98G Glioma, and TE671 Rhabdomyosarcoma Cancer Cells, Biomole. 2020; 10(11): 1532.
121. Baran M, Miziak and Bonio M, Magnoflorine-a compound with anti-tumour activity, J Pre-Clin Cli Res. 2020; 14(3): 98-101.
122. Chen L, Tian H, Li M, Ge C, Zhao F, Zhang L, *et al.* Derivate isocorydine inhibits cell proliferation in hepatocellular carcinoma cell lines by inducing G2/M cell cycle arrest and apoptosis, Tumor Bio. 2016; 35: 5951-61.
123. Yan Q, Li RX, Xin AY, Liu JX, Li WG, *et al.*, Research on anticancer activity of isocorydine and its derivatives. Zhong. Zhong China Journal of Chinese Materia Medica. 2017; 42(16): 3152-8.
124. Remichkova M, Dimitrova P, Philipov S, Ivanovska N, Toll-like receptor-mediated anti-inflammatory action of glaucine and oxoglaucine. Fitoter. 2009; 80(7): 411-4.
125. Kang H, Jang SW, Pak JH, Shim S. Glaucine inhibits breast cancer cell migration and invasion by inhibiting MMP-9 gene expression through the suppression of NF-κB activation, Mole Cell Biochem. 2015; 403(1): 85-94.
126. Spasova M, Philipov S, Milkova T. Amino acid Derivatives of Aporphinic Alkaloid Glaucine and their antioxidant activity. InLebl M, editor. Peptides for Youth: New York: Springer;2009; p. 267-8.
127. Zhao G, Etherton TD, Martin KR, Heuvel JPV, Gillies PJ, West SG, *et al.*, Anti-inflammatory effects of polyunsaturated fatty acids in THP-1 cells. Biochem Biophys Res Commun. 2005; 336(3): 909-17.
128. Speranza L, Franceschelli S, Pesce M, Reale M, Menghini L, Vinciguerra I, *et al.*, Antiinflammatory effects in THP-1 cells treated with verbascoside. Phytother Res. 2010; 24(9): 1398-404.
129. Yu CJ, Zheng F, Kuang CX, Huang WD, Yang Q, Oren-gedoku-to and its constituents with therapeutic potential in Alzheimer's disease inhibit indoleamine 2, 3-dioxygenase activity *in vitro*, J Alz Dis. 2010; 22(1): 257-66.
130. Wu C, Yang K, Liu Q, Wakui M, Jin GZ, Zhen X, *et al.* Tetrahydroberberine blocks ATP-sensitive potassium channels in dopamine neurons acutely-dissociated from rat substantia nigra pars compacta. Neuropharma. 2010; 59: 567-72.
131. Chen HB, Luo CD, Liang JL, Zhang ZB, Lin GS, Wu JZ, *et al.* Anti-inflammatory activity of coptisine free base in mice through inhibition of NF-κB and MAPK signaling pathways. Eur J Pharma.2017; 811: 222-31.
132. Zhang M, Li Q, Zhou C, Zhao Y, Li R, Zhang Y, *et al.*, Demethyleneberberine attenuates concanavalin A-induced autoimmune hepatitis in mice through inhibition of NF-κB and MAPK signalling, Int Immunopharma. 2020; 80: 106137.
133. Gupta S, Khan A, Vishwas S, Gulati M, Singh TG, Dua K. *et al.* Demethyleneberberine: A possible treatment for Huntington's disease. Med Hypo. 2021; 153: 110639.
134. Zhang P, Qiang X, Zhang M, Ma D, Zhao Z, Zhou C, *et al.*, Demethyleneberberine, a natural mitochondria-targeted antioxidant, inhibits mitochondrial dysfunction, oxidative stress, and steatosis in alcoholic liver disease mouse model. J Pharm Exp Ther. 2015; 352(1): 139-47.
135. Lei C, Yao Y, Shen B, Liu J, Pan Q, Liu N, *et al.* Columbamine suppresses the proliferation and malignization of colon cancer cells via abolishing Wnt/β-catenin signaling pathway. Can Manag Res. 2019; 11: 8635-645.
136. Bao J, Huang B, Zou L, Chen S, Zhang C, Zhang Y, *et al.*, Hormetic effect of berberine attenuates the anticancer activity of chemotherapeutic agents. PloS One. 2015; 10(9): e0139298.
137. Alamzeb M, Khan MR, Ali S, Shah S Q, Rashid M U, Antimicrobial properties of extracts and compounds isolated from *Berberis jaeschkeana*, Bangla Pharma. 2013; 8(2): 107-109.
138. Park KD, Lee JH, Kim SH, Kang TH, Moon JS, Kim SU, *et al.* Synthesis of 13-(substituted benzyl) berberine and berberrubine derivatives as antifungal agents. Bioorg med chem. 2006; 16(15): 3913-6.
139. Yang J, TLA N, Kim MJ, Seong ES, Kwon YS, Yoo NH. Biological activity and alkaloid compounds of *Mahonia napaulensis* DC. extracts. ScienceAsia. 2023; 49(4): 603-09
140. Li P, Yang Q, Dong L, Zhang D, Xiao Q, Jatrorrhizine Ameliorates Osteogenic Differentiation in Dexamethasone Induced MC3T3-E1 Cells by Regulating Histone Deacetylase 4. Cur Top Nutral Res. 2022; 20(3): 567.
141. Hao M, Jiao K, Jatrorrhizine reduces myocardial infarction-induced apoptosis and fibrosis through inhibiting p53 and TGF-β1/Smad2/3 pathways in mice. Acta Cir Bras. 2022; 37(7): 1-9.
142. Kong WJ, Wei J, Zuo ZY, Wang YM, Song DQ, You XF, *et al.* Combination of simvastatin with berberine improves the lipid-lowering efficacy. Meta. 2008; 57(8): 1029-37.
143. Patel MB, Mishra S. Isoquinoline alkaloids from *Tinospora cordifolia* inhibit rat lens aldose reductase, Phytother Res. 2012; 26(9): 1342-7.
144. Deng Y, Zhang M, Luo H. Identification and antimicrobial activity of two alkaloids from traditional Chinese medicinal plant *Tinospora capillipes*. Industl Crops Prod.2012; 37(1): 298-302.
145. Bandyopadhyay S, Patra PH, Mahanti A, Mondal DK, Dandapat P, Bandyopadhyay S, *et al.* Potential antibacterial activity of berberine against multi drug resistant enterovirulent *Escherichia coli* isolated from yaks (*Poephagus grunniens*) with haemorrhagic diarrhoea. Asian Pac J trop med. 2013; 6(4): 315-9.
146. Paudel R, Sharma RK, Bhandari S, Koirala M, Bhandari G, Bhandari NL. Phytochemical screening and evaluation of antimicrobial and antioxidant activity of *Mahonia napaulensis* (Jamanemandro) bark extract. Nepal Journal of Science and Technology. 2020; 19(2): 55-61.
147. Račková L, Májeková M, Košt'álová D, Štefek M. Antiradical and antioxidant activities of alkaloids isolated from *Mahonia aquifolium*. Structural aspects Bioorganic and medicinal chemistry. 2004; 12(17): 4709-15.
148. Roselli M, Cavalluzzi MM, Bruno C, Lovece A, Carocci A, Franchini C, *et al.*, Synthesis and evaluation of berberine derivatives and analogs as potential antiacetylcholinesterase and antioxidant agents. Phytochem Lett. 2016; 18: 150-6.
149. Yin J, Xing H, Ye J. Efficacy of berberine in patients with type 2 diabetes mellitus, Metabo, 2008; 57(5): 712-7.
150. Dong H, Wang N, Zhao L, Lu F, Berberine in the treatment of type 2 diabetes mellitus: a systemic review and meta-analysis. Evid Based Complement Alternat Med. 2012; 2012(1): 1-12.
151. Bagade A, Tumbigeremutt V and Pallavi G, Cardiovascular effects of berberine: a review of the literature. J Rest Med. 2017; 6(1); 37-45.
152. Tan YZ, Wu AC, Tan BY, Wu JH, Tang LF, Li JH, *et al.* Study on the interactions of berberine displaces other drug from their plasma proteins binding sites. Chi Pharm Bull. 2002; 18(5): 576-8.
153. Wu H, He K, Wang Y, Xue D, Ning N, Zou Z, *et al.* The antihypercholesterolemic effect of jatrorrhizine isolated from *Rhizoma coptidis*, Phytomed. 2014; 21(11): 1373-81.

Cite this article: Tamang S, Moktan S. Phytochemistry and Pharmacological Insights on *Berberis napaulensis* (DC.) Spreng.: An Updated Review. Pharmacog Rev. 2025;19(38):225-35.