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Review article:

A REVIEW ON BIOLOGICAL AND CHEMICAL DIVERSITY IN *BERBERIS* (BERBERIDACEAE)

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ABSTRACT

Berberis is an important genus and well known in the Indian as well as European systems of traditional medicine. It is used since ancient times for curing eye disease, fever, jaundice, rheumatism, vomiting during pregnancy, kidney and gall balder stones and various other ailments due to the presence of biologically active alkaloid berberine. Action of the root extracts of few species are believed to be as powerful as quinine in the treatment of malarial fever.

A plethora of literature pertaining to the taxonomy, biology, chemistry, traditional and ethnic uses of *Berberis* in different countries and indigenous cultures was collected by both offline (library, journals, textbooks etc.) and online mode (electronic search of available databases). In addition to this, books on traditional medicine and ethno pharmacological knowledge were also referred to extract ancient uses of *Berberis* in different traditional medicine systems. Most of the folklore, traditional and ethno botanical claims about *Berberis* species were validated by broad spectrum *in vitro* and *vivo* pharmacological studies. The present article summarizes its usage in eye and liver disorder, fever, kidney and gall stones along with anticancer activity.

This comprehensive review will not only help researchers for further evaluation but also provide substantial information for future exploitation of species to develop novel herbal formulations.

Keywords: *Berberis*, berberine, pharmacology, ethno botany

INTRODUCTION

The genus *Berberis* has an important place in various traditional systems of medicine worldwide for their efficacious medicinal properties. The ancient Ayurvedic literature of India records uses of *Rasaut* (*Ras* = juice; *out* = frothing and foaming when boiling; hence *Rasaut* means concentrated juice), an extract of either stem or root of *Berberis* sp. The specific uses of *Rasaut* for curing eye diseases and indolent ulcers earned a great fame. In the British Pharmacopoeia, the alkaloid berberine- the active principle in several species of *Berberis* and *Mahonia*, has been incorporated for its successful use in the treatment of oriental sore.

The roots of *Berberis* species are employed as an anti-periodic, diaphoretic and antipyretic, and its action was believed to be as powerful as quinine. The bark is used as a tonic and anti-periodic. This plant is also well proven for cardio vascular, hepato-protective, antimicrobial and anti-cancerous activities. Hence, a review of genus *Berberis* has been done to put all its activities, ethno botanical claims, pharmacological action along with chemistry. The scientific information compiled in this review is gathered by extensive

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search of several electronic databases *viz*. SCOPUS, Google scholar, NOPR, Pub med, Elsevier, ACs, Medline plus, Web of science, etc. Additionally, the library search and ancient medicinal treatises/text books were also referred for gathering information on the traditional uses of *Berberis*. The review of *Berberis* was also done with an end in view of identifying the knowledge gaps in traditional uses, pharmacological studies, toxicity profiling, clinical trials and other relevant research in this medicinally important genus. Previous reviews on individual species of *Berberis* are available, but a comprehensive update on the entire genus is still lacking. This review will help researchers to identify the latent and patent potentials of *Berberis* and explore further studies on the biological and chemical properties of various species of this genus.

TAXONOMIC HISTORY OF *BERBERIS*

Berberis belongs to the family Berberidaceae, which was first established by A.L. Jussieu in 1789 as 'Berberides' and was considered one of the most primitive families of Angiosperms having a high number of disjunction or discontinuous genera. There is a general agreement among botanists (Kumazawa, 1938; Hutchinson, 1959; Airy Shaw, 1966; Takhtajan, 1969; Meacham, 1980; Nowicke and Skvarla; 1981) that the genera of Berberidaceae are not closely related but are separable into 4 distinct families, namely Lardizabalaceae (*Decaisnea*, *Holboellia, Parvatia*), Nandinaceae (*Nandina*), Podophyllaceae (*Podophyllum*) and Berberidaceae (*Berberis*, *Mahonia*, *Epimedium*). Berberidaceae was placed in the order Ranales (Bentham and Hooker, 1862). Several other works (Takhtajan, 1969; Cronquist, 1968) placed it in the order Ranunculales, while one worker (Hutchinson, 1959) included this family under a separate order Berberidales.

First taxonomic account of the family Berberidaceae for the Indian subcontinent (Hooker and Thomson, 1875) included six genera and 17 species. A revision of the genus *Berberis* was made by Schneider during 1905 and 1908 and recorded 13 new species and one variety from Indian region. Subsequently (Schneider, 1942) a monograph of section *Wallichianae* was published in which he recognized 71 species in 8 subsections. Chatterjee (1953) included 68 species of *Berberis*, 11 species of *Mahonia*, one species of *Epimedium* and two species of *Podophyllum*. In a survey (Ahrendt, 1941/45) the *Berberis* spp. from Bhutan, Assam, South Tibet, Upper Burma and Northwest Yunnan and later (Ahrendt, 1961) published a detailed revision of *Berberis* and *Mahonia* species. He included 52 species with 43 infra specific categories under *Berberis* and 11 species under *Mahonia* from the Indian region. It was again revised by including one new species (*B. victoriana*) from the Indian region (Chamberlain and Hu, 1985). Jafri (1975) while dealing with the Berberidaceae for the *Flora of West Pakistan* included only one species of *Mahonia* and 15 species of *Berberis* from Kashmir region. In a more recent study (Rao and Hajra, 1993) while revising the family for the *Flora of India* included 54 species of *Berberis,* one species of *Epimedium* and 13 species of *Mahonia* from the present political boundaries of India.

Singh et al. (1974, 1978) discussed the significance of epidermal structure and leaf architecture in the taxonomy of Berberidaceae. They have studied hardly 5-6 species of the family. Palynologically only five species of *Berberis* have been studied (Nair, 1965) and chromosome numbers in only nine species with five infraspecific categories of *Berberis* and three species of *Mahonia* have been reported (Kumar and Subramaniam, 1986). Some commercially important *Berberis* spp. from Indian region is shown in Figure 1.

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B. aristata

B. asiatica

B. lycium

B. chitria

Figure 1: Some important species of genus *Berberis* collected from India

ETHNOBOTANICAL AND TRADITIONAL USES

There has been an increasing interest towards the scientific study of human-plant interaction in the natural environment among the botanists, social scientists, anthropologists, practitioners of indigenous systems of medicine. Jain (1981) undertook intensive field study among tribes of central India and devised methodology for ethno- botany, particularly in the Indian context. Different species of genus *Berberis* are used ethno botanically and medicinally by various tribes and in different traditional medical systems. A detailed pharmacognostic study of some common Himalayan *Berberis* species has been done by Srivastava et al., 2001, 2004, 2006, 2010; Singh et al., 2009, 2012; Srivastava and Rawat, 2013, 2014. The ethno botanical uses of *Berberis* by different tribal communities in India and some other countries are provided in Table 1.

PHARMACOLOGICAL ACTIVITIES OF *BERBERIS* SPECIES

Berberis has diverse pharmacological potential. Various pharmacological activities of the *Berberis* species make them an important part of polyherbal formulations for the treatment of several diseases and disorders (Figure 2, Table 2).

Table 1: Ethno botanical uses of different species of *Berberis*

Species	Ethno botanical Information	References
B. aristata	In Raithal locality of Uttarkashi (Uttaranchal), India, *Rasaut*- a popular medicine prepared for eye disorders from the roots of *B. aristata*	Kirtikar and Basu, 1935; Anonymous, 1948; Hayashi, 1950; Küpeli et al., 2002; Uniyal, 1964
	In Kumaon region of India, the decoction of root bark from *B. aristata* and *B. asiatica* is used for curing eye troubles and boils. A sauce is also prepared from its acidic flower buds	Shah and Joshi, 1971
	The decoction of the root of *B. aristata* is used in piles, gastric disorders and other allied complaints by Tibetan people and the plant is known there as *Kershuen*	Chauhan et al., 1978/79
	Local inhabitants of DehraDun district of Uttaranchal, India use *B. aristata* as fish poison	Jain and Suri, 1979/80
	Used in snake and scorpion bite by the tribal's in Uttaranchal, India	Mittre, 1981
B. asiatica	Inhabitants of Assam, India, use root extract with butter for the treatment of bleeding piles. About 2 ml of the extract of its root is taken with butter daily for two weeks	Bhattacharjee et al., 1980
B. lycium	In Lahul province of HP, India, *B. lycium* and *B. pachyacantha* fruit is used medicinally for stomachache. Roots yield a yellow dye for textiles. The twigs are important in ceremonials of *Priests* and *Lamas.* In the *Burial ceremony,* barberry nails are used. For *Losar* (New Year) celebrations barberry wood and buck wheat straw is used.	Koetz and Walter, 1979
	In Rajouri district of Jammu, India, fruits of *B. lycium* are used as coagulant, branches made into broom for removing husk from grains	Virjee et al., 1984
B. *petiolaris*	In Kumaon region of Uttaranchal hills, India, the flowers of *B. petiolaris* are mixed with spinach, mashed and taken as salad	Bhargava, 1959
B. tinctoria	Todas of Nedimand tribes, Nilgiris, India, grind the roots of *B. tinctoria* with water and administer it for stomachache, especially in the treatment of worms. Bark is used for stomach disorders of Buffaloes, along with butter. Fruits are eaten by Kotas of Kollimalai	Abraham, 1981
B. wallichiana	*B. wallichiana* is used by the tribes of various ethnic groups like Nishi, Apatani, Hill-Miri, Adi, etc. of Subansiri district of Arunachal Pradesh, India. A bunch of spines is used for tattooing on chin and forehead. The tattoo locally called *te* is significant and is a traditional custom. Skin is pricked with spines. A mixture of rice starch and root is applied on the wound. The rice starch pierces the skin and the root gives the colour	Pal, 1984

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Species	Ethno botanical Information	References
B. jaeshkeana	Root extract of *B. jaeshkeana* and *B. kumaonesis*, commonly called as Kingora and Jhuri respectively in Garhwal Himalayas, India, used as an astringent, diuretic, blood purifier and alternative. It is also used in eye disorders, menorrhea, jaundice and skin diseases by the local tribes	Gaur et al., 1976
B. vulgaris	Berries are used for sore throat and fever. Poultice of pounded root or bark used for sore throat	Speck, 1998
	Cold and compound decoctions of berries are taken in fever	Tantaquidgeon, 1928
	Decoction of leaves taken three times a day for jaundice	Carr and Carlos, 1945
	Bark and root is used for ulcerated gums and sore throat	Chandler et al., 1979
	Roots of *B. vulgaris* are boiled in water and decoction is used in both human and cattle for the treatment of internal injuries and also used for tanning skin	Chaudhary et al., 1980
B. holstii	African endemic species in northern Malawi. Leaves and stem bark infusion is used for coughs, malaria, stomachache, sexually transmitted infections and pneumonia	Maliwichi-Nyirenda, 2011

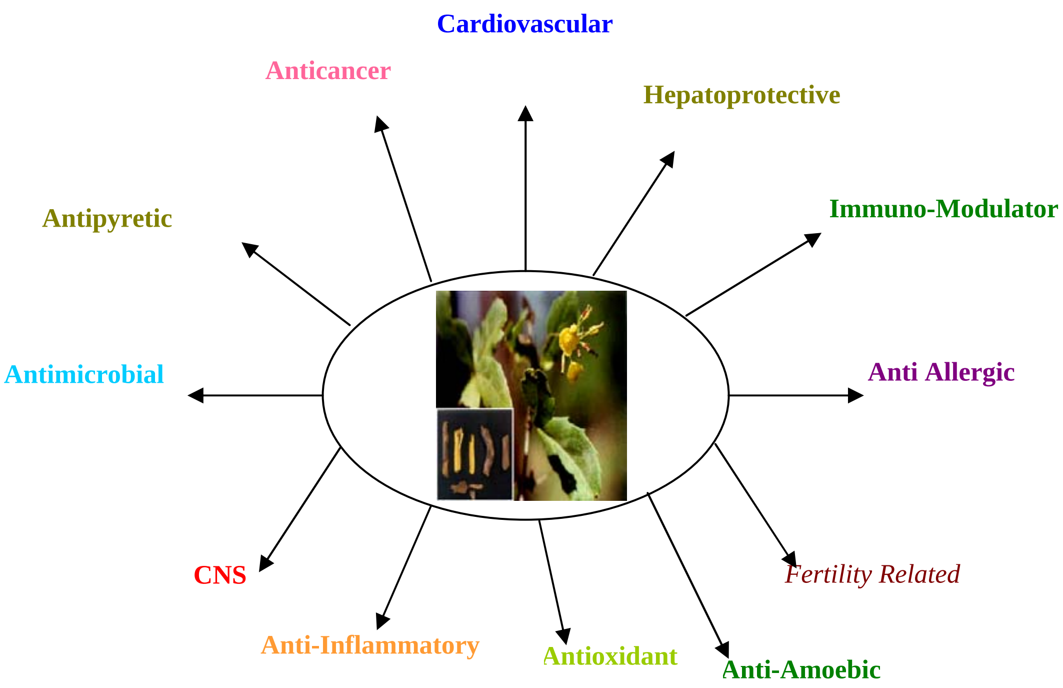

Figure 2: A broad spectrum of pharmacological activities of *Berberis*

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Table 2: Pharmacological activities of various *Berberis* species

Activity	Source/species	Plant part	Type of extract/ fraction/ Isolate tested	Experimental procedures/animals/ organism studied/type of study	References
Cardio vascular activity	*B. darwinii*	Stem bark	Methanol extract	*In vitro* acetyl cholinesterase inhibition assay	Habtemariam, 2011
	B. aristata	Root	Aqueous-methanol extract	Ovari-ectomized rats	Yogesh et al., 2011
	B. lycium	Root bark	Hydro-alcoholic extract	Guinea pigs	Fang et al., 1986
		Root bark	Hydro-alcoholic extract	Guinea pigs	Wang et al., 1987
		Root	Isolated Berberine	Microelectrode techniques were used for intracellular recordings of the trans-membrane electrical potentials on canine cardiac purkinje and ventricular muscle fibers and on rabbit atrial fibers	Neto, 1993
		Root	Isolated Berberine	Guinea pigs	Wang et al., 1993
	B. orthobotrys	Root bark	Isolated Berbamine	Guinea pigs	Li et al., 1985
		Root bark	Isolated Berbamine	Rabbits & Rats	Fang et al., 1986
		Root bark	Isolated Berbamine	Guinea pigs	Li et al., 1991
		Root bark	Isolated Berbamine	Guinea pigs	Li et al., 1986
	B. chitria	Root bark	Isolated Berberine	Guinea pigs	Xiong and Fang, 1989
	B. chilensis	Root bark	Total Alkaloid	Electrical activity of frog cardiac pacemaker cells	Morales et al., 1989
		Root bark	Total Alkaloid	Guinea pigs	Morales et al., 1993
		Root bark	Isolated Berberidine and Tetrahydroberberine	Rat muscles	Han et al., 1990
	B. paraspecta	Root	Aqueous extracts	Chorio allantoic membrane (CAM) assay and In vitro bovine aortic endothelial cells (BAECs) culture and crystal violet assay	Wang et al., 2004

Activity	Source/species	Plant part	Type of extract/ fraction/ Isolate tested	Experimental procedures/animals/ organism studied/type of study	References
Anti-inflammatory activity	*B. aristata*	Root	Aqueous methanol extracts	Rats	Akhter et al., 1977
	B. vulgaris	Roots	Ethanol extract	Carrageenan- and zymosan-induced paw edema	Invanovska and Philipov, 1996
	B. crataegina	Root bark	Methanol extract	Carrageenan-induced edema and Serotonin-induced edema	Yeilada and Küpeli, 2002
		Root bark	Isolated Berberine	Cell proliferation and activation of NF-κB. The protein levels of ICAM-1, TGF-β1, iNOS and FN in rat MCs by Western blot	Jiang et al., 2011
		Root bark	Isolated Berberine	LPS- and IFN-γ-induced neuro-inflammation in microglia cells	Chen et al., 2012
		Root bark	Isolated Berberine	Nitric oxide (NO) expression and high-mobility group box 1 (HMGB1) release in lipopolysaccharide (LPS)-induced macrophages.	Lee et al., 2013
Central Nervous System activity	*Berberis* sp.	-	Isolated Berberine	Behavioral effects in conscious cats and mice, Pento barbitone sleeping time, Amphetamine toxicity, Pain threshold	Shanbhag et al., 1970
Anti-convulsion activity	*B. integerrima*	Root	Methanol extract, and hydromethanolic, and chloroform fractions	Pentylenetetrazole (PTZ) and maximal electroshock (MES)-induced seizure models	Hosseinzadeh et al., 2013
Anti-histaminic and anti-cholinergic activity	*B. vulgaris*	Fruits	Aqueous extract	Isolated guinea-pig ileum	Shamsa et al., 1999
Anti-microbial activity	*B. vulgaris*	Root	Isolated Berberine	Intestinal loop model	Sack and Frochlich, 1982
	B. chitria	Root	Water soluble & alcoholic extract	Antimicrobial	Dobhal et al., 1988
	B. heterophylla	Leaves, stems and root	Aqueous extracts	*In vitro* assay on Gram-positive and Gram-negative bacteria, fungi and different *Candida* species	Freile et al., 2003
	B. aetnensis	Root and Leaves	Ether, Ethanol and Chloroform extracts	*In vitro* assay on Gram positive and Gram negative bacteria	Musumeci et al., 2003

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Activity	Source/species	Plant part	Type of extract/ fraction/ Isolate tested	Experimental procedures/animals/ organism studied/type of study	References
Hepato protective activity	*Berberis* sp.	Root	Isolated Berberine chloride	Rats	Chan, 1977
	B. integerrima	Root bark	Isolated Berberine	CCl_4 induced toxicity model	Jamshidzadeh and Niknahad, 2006
		Root bark	Isolated Berberine	TNF-α, COX-2 and iNOS in CCL_4 induced toxicity	Domitrović et al., 2011
	B. aristata,	crude extract	Ethanol extract	amoebic liver abscess in golden hamsters and in immune modulation studies	Sohni and Bhatt, 1996
	B. aristata	crude extract	Ethanol extract	*In vitro* amoebicidal activity against *Entamoeba histolytica*	Sohni et al., 1995
Anti-cancer activity	*Berberis* sp.	Root	Isolated berberine	Activity on AP-1 using a reporter gene assay in human hepatoma cells	Fukuda et al., 1999a,b
	B. amurensis	Root bark	Isolated Berbamine	Apoptosis of Gleevec-sensitive and -resistant Ph^+CML cells	Xu et al., 2006
	B. koreana	Root bark	Water extract	Human cancer cell lines A549, AGS, MCF-7 and Hep 3B	Qadir et al., 2009
Hepato-carcinoma	*Berberis* sp.	Root	Isolated Berberine	Anticancer actions in hepatocellular carcinoma SMMC-7721 cells	Li et al., 2013
		Root	Isolated Berberine	MMP-1 and MMP-9 mRNA expressions by real-time PCR	Kim et al., 2012
		Root	Isolated Berberine	Streptozotocin-induced apoptosis in mouse pancreatic islets through down-regulating *Bax*/*Bcl-2* gene expression ratio	Chueh and Lin, 2012
Antipyretic activity	*Berberis* sp.	Root	Isolated Berberine sulfate	In vivo model on rats, dog, rabbit and guinea pig	Sabir et al., 1978
Immuno-stimulant activity	*Berberis* sp.	Root bark	Isolated Berbamine	I.P. injection of berbamine in mice inoculated with influenza virus	Li and Sui, 1986
	B. koreana	fruit	Aqueous Extract	Immunoassays	Qadir et al., 2008
Fertility related activity	*B. vulgaris*	Leaves and bark	Acetone extracts	In-vivo effect on uterus of guinea pig, cat and rabbit	Aliev and Yuzbashinskaya, 1953

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Fertility related activity	*B. chitria*	Roots	Isolated Palmitine	Administered orally to dogs for 60 days to check the impairment of primary and secondary spermatocytes and elongated spermatids (Stages IV-VIII).	Gupta and Dixit, 1989
Anti-oxidant activity	*Berberis* sp.	Roots	Isolated Berbamine	Colorimetric estimation of (MDA) malonaldehyde formation method and ESR-spin trapping technique.	Ju and Han, 1990
Anti-diabetic activity	*B. vulgaris*	Fruits and roots	Aqueous ethanol extract	Rats	Rajaei et al., 2011; Meliani et al., 2011
Urolithiasis	*B. vulgaris*	Root bark	Aqueous methanol extract	Animal model of urolithiasis, developed in male Westar rats by adding 0.75 % ethylene glycol in drinking water.	Jyothilakshmi et al., 2013; Bashir and Gilani, 2011
Osteolytic and Hyper choletrolemic	*B. aristata*	Root	Berberine	Rats	Zhou et al., 2012; Rahigude et al., 2012; Dong et al., 2011; Huang et al., 2012

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CHEMICAL DIVERSITY IN *BERBERIS*

Isoquinoline alkaloids are the major bioactive constituents in *Berberis* (Figure 3). Berberine is a major representative of the protoberberine alkaloids which are a structural class of organic cations, characteristically yellow, having four linked benzene rings with a nitrogen atom joining two rings pairs, and modified via two oxygen atoms at each end. A vast array of alkaloids has been isolated from various *Berberis* species, among which, berberine, berbamine, Palmitine, jatrorrhizine and isotetrandrine are the most common ones (Figure 4).

The histological distribution of berberine has been well studied; alkaloids of *Berberis* are located chiefly in the cortical tissues of the roots and stems. The bark of old roots contains the highest concentration of alkaloids. In the upper parts of the stem, concentration is low and in young leaves alkaloids could not be detected (Greathouse and Rigler, 1940; Greathouse and Watkins, 1938). Histological distribution of berberine, umbellatine and nepiotime has also been examined in Indian species of *Berberis* (Chatterjee, 1952; Chatterjee et al., 1954). Mean value of berberine content for young actively growing shoots is 0.04 % and for young parenchymatous roots is 1.41 %. Thus there is a progressive increase in the berberine content of the plants with an increase in age.

Chemical analysis of the traditional preparation '*Rasaut*' from Punjab market showed 1.67-4.26 % total alkaloid. The yield of *Rasaut* from *B. lycium* was found to be 15.4 % w/v and contained about 9.4 %w/v berberine (Anonymous, 1948).

Berberine exists in three tautomeric forms (I-III) in solution. Later on, these tautomeric structures and the evidence for the existence and structures of the ammonium (I) and pseudo-base form (II) were established (Anonymous, 1967). Chemical diversity of various *Berberis* species is illustrated in Table 3.

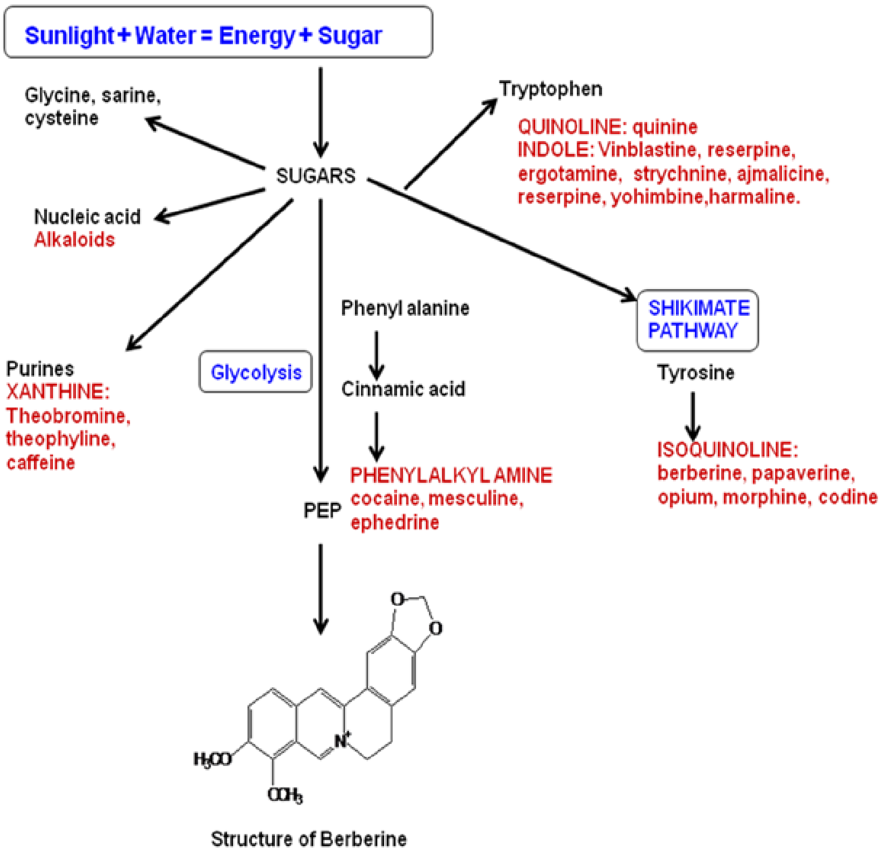

Figure 3: Biosynthetic pathway of Berberine and allied alkaloids

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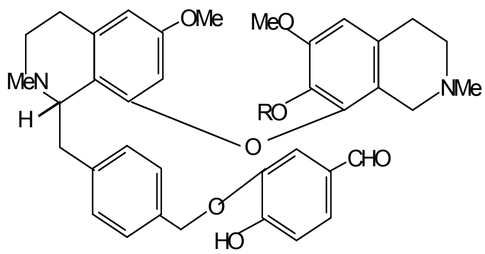
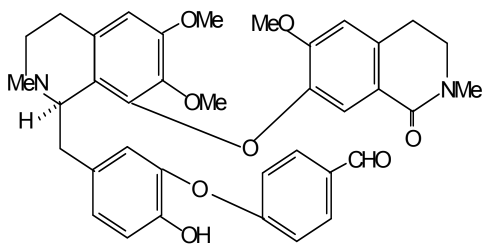
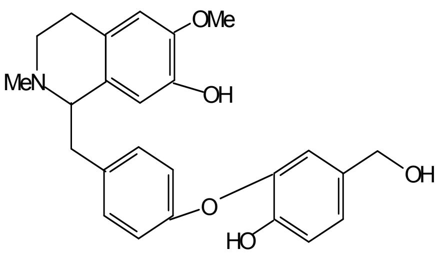


(+) Chenabine
R= Me
(+) Jhelumine
R = H

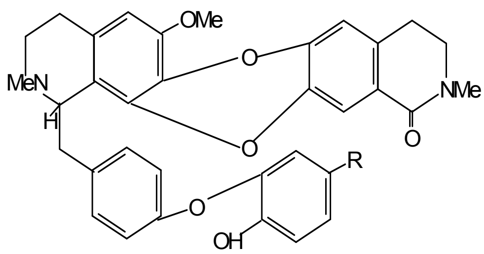
Berberine-chloroform
R, R=-OCH$_2$O-,
R'=H,CCl$_3$
Palmatine -chloroform
R, R=Ome, R'=H,CCl$_3$
Oxy-berberine
R,R= -OCH$_2$O -, R'=O



Sindamine



Karakoramine



Punjabine
R = CHO
Gilgitine
R = COOMe

Figure 4: Some other important active principles of *Berberis*

Table 3: Phyto constituents of various *Berberis* species

Species	Isolated active principals	Plant parts	Reference
B. aristata	• Karachine ($C_{26}H_{27}O_5N$), melting point 146-148 °C • Taxilamine	Roots	Blasko et al., 1982; Potdar et al., 2012
B. asiatica	• Berberine, Palmitine, jatrrohirine, colunbamamine tetrahydropalmitine, berbamine, oxyberberine and oxyacanthine	Leaves & Root	Chatterjee, 1952; Chandra and Puro-hit, 1980

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Species	Isolated active principals	Plant parts	Reference
B. chitria	• A new aporphine base-o-methyl corydine N-oxide, along with berberine; palmitine, jatrorrhizine and oxyacanthine • Benzene extracts yielded hentriacontane, tri-acontane, cetyl alcohol, β-sitosterol, β-sitosterol, dihydro kaempferol, quercetin, and oleic, steric, palmitic and linoleic acids. • Alcoholic extract revealed 5 alkaloidal components of which three closely related alkaloids separated and named as chitrian A, B, C. • Water extract revealed the presence of glucose, fructose and rhamnose • Dihydropalmitine N-oxide (I) jatrorrhizine detected from its chloride (5, 6-dihydro 3-hydroxy-2, 9, 10-trimethoxyl dibenzo [a, g] quinoliziaium chloride dihydrate) consists of 4 fused rings. • Berlambine lambertine, berbamunine, berberine, berbamine, yuziphine (a new alkaloid), columbamine, palmitine and hydroxyacanthine. • Umbellatine, berberine and berbamine	Roots	Bhakuni et al., 1968; Hussain and Shoeb, 1958; Ghosh et al., 1993; Yasupov et al., 1990; Ali and Khan, 1978
B. lycium	• Three new alkaloids-baberine, melting point 152 °C ($C_{19}H_{21}NO_3$), berbericine hydrochloride, mp. 199 °C ($C_{20}H_{17}NO_4Cl$) and berbericine hydroiodide, m.p. 205 °C ($C_{21}H_{22}NO_4I$). • Two artefact alkaloids berberine-chlorofrom, palmitine-chloroform along with oxyberberine • Umbellatine, berberine and berbamine was also identified in the roots of same species • Berberine chloride • Three new seco-bisbenzylisoquinolines (+)-sindamine (monophenolic base) $C_{37}H_{38}O_8N_2$; (-) -Punjabine (Secodimer Monophenolic base) $C_{35}H_{32}O_7N_2$; (-) - Gilgitine (Secodimer monophenolic base) $C_{36}H_{34}O_8N_2$. • Punjabine and gilgitine are the first secodimeric alkaloids derived from *in vivo* oxidation of bis benzylisoquinoline precursor in corporating three diaryl ether bridges. • (+) - Kara-koramine $C_{25}H_{27}O_5N$, monophenolic (+) chenabine $C_{37}H_{40}O_7N_2$ and diphenolic (+) - jhelumine $C_{36}H_{38}O_7N_2$ (more polar than chenabine)	Roots	Ikram et al., 1996; Miana, 1973; Datta et al., 1976; Leet et al., 1983; 1982
B. pachy-cantha	• Oxyacanthine, mp. 212-14 °C, oxyberberine, mp. 200-1 °C; berbamine-C_6H_6 adduct, melting point 124-6 °C; isotetrandrine mp. 180-2 °C; jatrorrhizine mp. 217-20 °C (decomposition); magnoflorine picrate mp 217-23 °C and isodide mp. 228-30 °C. • Two anthocyanin pigments were isolated and identified as polar gonidin - 3 glucoside and cyanidin - 3 glucoside.	Roots	Tomita and Yong, 1960; Du and Francis, 1974

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Species	Isolated active principals	Plant parts	Reference
B. concinna	• Berberine and Palmitine were isolated as tetrahydro derivatives. • Alkaloid 9, 9-dimetlytetracosan-6 - one $Me(CH_2)_4COCH_2CH_2CMe_2(CH_2)_{14}Me$	Stem bark	Tiwari and Masood, 1977; 1978
B. corearia	• 1, 4-Bis (2' - hydroxy-5'-methylphenyl)-butan-1, 4-dione (I) (a ketone). • A new ketone -7 methyltetracosan - 6 - one (II), along with berberine • Anthocyanins -cyanidin, pelargonidin, petunidin, peonidin and delphinidin aglycons bounded with glucose and rutinose.	Stem bark Fruits	Tiwari and Masood, 1979; Majumdar and Saha, 1978 Vereskovskii and Sapiro, 1985
B. vulgaris	• 8 pigments that were identified with the percentage of the total carotenoids are β -carotene, 0.8; β -carotene 5-7; lutein 39.0; zea xanthin, 8.6; chrysanthemaxanthin, 7.6; flavoxanthin 11.7; auroxanthin 5.7; capsanthin 1.9 and there were two unidentified fractions constituting 15.2 %. • Tannin (5.56), carbohydrates (5.82). Organic acids (3.69), Mn (7.20) and pectic substances (0.48) percent and Vitamin C 156.50 mg. • Thalifoline mp.195-197 °C, [8]-Oxyberberine mp. 191-193 °C, Chilenine mp. 135°-137 °C, Baluchistanamine mp. 115-118 °C, Tejedine mp.132-134 °C, Obaberine mp.136°-138 °C. Isotetrandrine mp 171-174 °C, Oxycanthine mp. 205-208 °C, Berbamine mp.145-147 °C, Aromoline mp. 166-169 °C, Obamegine mp. 197°-198 °C, Thaligrisine mp. 120-122 °C, Jatrorrhizine Chloride mp. 203-205 °C, Palmitine Chloride 201-202 °C. Berberine Chloride mp.202°-206 °C.	Fruits Root bark	Wierzchowski and Budicz, 1969; Parlamarchulk et al., 1973; Suau et al., 1998
B. kawakamii	• Berberine - C_6H_6 adduct mp. 124- 6 °C; isotetrandrine mp. 179-81 °C; jatrorrhizine; berberine; shobakunine and magnolosine picrate mp 224- 6 °C (decomposition)	Roots	Tsang-Hsiumg and Lu, 1960
B. mingetsensis	• Berbamine -C_6H_6 adduct mp 125-7 °C; a new base mp 240-2 °C; isotetrandrine mp 179-81°; oxyberberine mp 199-201 °C; berberine and shobakunine	Roots	Tsang-Hsiumg and Lu, 1960
B. calliobotrys	• New dimeric aporphine benzylisoquinoline- *Khyberine* pakistanamine, 1-0-methylpakistanine, pakistanine, chitraline and kalashine.	Roots	Hussain and Shamma, 1980
B. orthobotrys	• A new dimer kalashine together with the pakistanamine and pakistanine. • Kalashine is the first aporphine benzylisoquinoline known to be substituted at C-H Acid catalyzed rearrangments of pakistanaminein 3 N-HCl leads to 1-0-methyl pakistanine, together with small amounts of 1-0 methyl kalashine and (+) armeparvine	Roots	Hussain and Shamma, 1980

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Species	Isolated active principals	Plant parts	Reference
B. umbellata	• An alkaloid $C_{20}H_{20}O_3$ mp 108-110 °C and was characterized as 2, 5-Bis (2'-methoxy-5'-methylphenyl) furan (I)	Roots	Masood and Tiwari, 1981
B. brandi-siana	• A new alkaloid (+) - berbamine-2'-β-N-oxide ($C_{37}H_{40}N_2O_7$) along with berbamine, palmitine, (+) berbernine, thalifoline, (+) reticuline, (+) apo-glaziovine, (+) isoboldine and (+) isotetrandrine.	Aerial part	Hussain et al., 1986
B. pseudo-umbellata	• Berberine and palmitine as the major and the bisbenzyisoquinoline alkaloid oxyaoanthine and O-methyl oxyacanthine as minor bases	Aerial part	Pant et al., 1986
B. flori-bunda	• Oxyacanthine, berbamine, berberine, epi-berberine, palmitine, dihydrocoridaline, jatror-rhizine and coulambine.This species appears to be the first instance of bearing epi-berberine	Roots	Chatterjee et al., 1953
B. laurina	• Two new alkaloid diastereomer (absolute configu-ration-+) (5) of O-methyl thalicberine (++) (5), which is O-methyl iso-thalicberine (1) and other is lauberine (III a), • Two new phenolic alkaloid which have been named espinine (I a) $C_{36}H_{40}N_2O_6$ m.p. 123-5, R_f. 0.08 and Espinidine (I d) $C_{37}H_{42}N_2O_6$ R_f. 0.15. • Extracts of *B. laurina* roots yielded only 0.536 % Et_2O solution alkaloid hydrastinine	Roots	Falco et al., 1969; 1968; Krets, 1956
B. baluchi-stanica	• Free base baluchistanamine mp. 122-124 °C. • Phenolic aprophine benzylisoquinoline alkaloid pakistanine $C_{37}H_{40}O_6N_2$ mp. 156 and first known proaphorphine benzylisoquinoline alkaloid paki-stanamine $C_{38}H_{42}O_6N_2$ mp. 158-162 °C.	Roots	Shamma et al., 1974; 1972
B. amur-sensis	• Berbamine (as C_6H_6 adduct) mp. 124-6 °C; a new phenolic tertiary base mp. 190-1 °C; hydroxy ber-berine mp. 197-9 °C; jatrorrhizine and shobaku-nine. Berberine, ferulic acid and vanillinic acid	Stem & Roots	Tomita and Kugo, 1955
B. thun-bergii	• Two picrates - jatorrhizine picrate mp. 217-20 °C monoflorine picrate mp. 224-5 °C	Roots	Tomita and Kikuchi, 1956
B. tschono-skyana	• Oxyacantheine, 2.40, 206-8 °C Obamegine ($C_{18}H_{19}O_3N$), 1.00, 164-6 °C, 98· 90; oxyberberine, 0.20, 197-90 °C, a new tertiary non phenolic base, 0.01, 89-92 °C, Obaberine ($C_{20}H_{23}O_4N$), 0.40, - , 178–180 °C; Jatrorrhirine 1.12, 214-15 °C - ; magnoflorine, 3.11, 3.11, - 231 – 2 °C; Shoba-kanine, 0.93, 138-40° • Another alkaloid obamegine ($C_{36}H_{38}O_6N_2$) mp. 164-6 °C was isolated from the same species	Stem & Roots	Tomita and Kugo, 1956
B. koreana	• Berberine; Palmitine; Oxyacanthanine; Berbamine	Stem &Leaves	Pavel, 1965
B. tabiensis	• A bisbenzyltetrahydroisoquinoline alkaloid Tabie-nine mp. 124 -127 °C	Stems	Quevedo et al., 2008

Species	Isolated active principals	Plant parts	Reference
B. cole-tioides	• Pronuciferine N-oxide, the first naturally occurring proaporphinoid alkaloid with an N-oxide function-ality, along with the parent compound Pronu-ciferine	Roots	Fajardo et al., 2009
B. waziri-stanica	• Berberine mp.253 °C, Oxyberberine mp. 199-200 °C, Karachine mp.146 -148 °C, Corydaldine mp. 173 °C, N-Methylcorydaldine mp. 121 °C, N-methyl-6, 7-Dimethoxy-isoquinoline mp. 215 - 217 °C, Aromoline mp. 178 - 180 °C, Pakistanine mp. 154 -156 °C, Waziristanine mp. 182 °C	Root bark	Hussain, 1992

CONCLUSION AND FUTURE PROSPECTIVE

During the last few decades there has been an increase in the study of medicinal plants and their traditional use in different parts of the world. Reports of the folk medicine followed by critical scientific evaluation have given to the world newer sources as corrective, preventive and upto some extent curative measures in various diseases. *Berberis* species are among the most important traditional herbs with a vast array of pharmacological activities. The present review summarizes the taxonomic, ethno-botanical, pharmacognostic, photochemical and pharmacological claims of *Berberis* species. Literature on Phyto-chemistry reveals that the species are rich in alkaloids, of which biologically active 'Berberine' is the major and potential one.

This review is a comprehensive documentation of various species belonging to this genus and their therapeutic potentials in the present context. Previous pharmacological studies on *Berberis* and its isolated alkaloids revealed more potential towards cardio vascular, hepato-protective, antimicrobial and anticancer activities. Recent trend in research on *Berberis* species, however directed the workers to focus more towards oncology, toxicological studies and clinical trials. This review will be useful for researchers to approach the newer avenues by exploring varied pharmacological activities like anti diarrheal, antispasmodic, anti malarial, etc., which in turn will be more beneficial in developing myriads of scientifically validated herbal formulations containing naturally occurring biodynamic compounds.

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REFERENCES

Abraham Z. Ethnobotany of the Todas, the Kotas and the Rules of the Nilgiris. In: Jain SK (ed): Glimpses of Indian ethnobotany (pp 308-20). New Delhi: Oxford & IBH Publ. Co., 1981.

Ahrendt LWA. A survey of the genus *Berberis* L. in Asia. New and old species from Bhutan, Assam, South Tibet, Upper Burma and Northwest Yunan in their relation to the analytical frame work of the genus. J Botany 1941;79:1-64; 1942;79:65-80; 1942;80:81-8; 1942/43;89-96, 97-104; 1942/44;105-112; 1942/45: 113-6.

Ahrendt LWA. *Berberis* and *Mahonia:* a taxonomic revision. Bot Linn Soc. 1961;57:1-410.

Airy Shaw HK. Willi's dictionary of flowering plants and ferns. 7th ed. Cambridge: Cambridge Univ. Press, 1966.

Akhter MH, Sabir M, Bhide NK. Anti-inflammatory effect of Berberine on rats injected locally with cholera toxin. Indian J Med Res. 1977;65:133-44.

Ali MN, Khan AA. Pharmacognostic studies of *B. lycium* Royal, and its importance as a source of raw material for the manufacture of berberine in Pakistan. Pakistan J For. 1978;28:25-7.

Aliev RK, Yuzbashinskaya PA. Nature of chemical compounds of barberry leaves and the effect of a preparation made from them on the contractility of smooth muscles of the uterus. Doklady Akad Nank Azerbaldzhan SSR. 1953;9:306-7.

Anonymous. Wealth of India, Raw Material. New Delhi: PID, CSIR, 1948.

Anonymous. The alkaloid chemistry and physiology. In: Manske RHF: The alkaloids, Vol. IX (pp 43-52). New York: Academic Press, 1967.

Bashir S, Gilani AH. Antiurolithic effect of berberine is mediated through multiple pathways. Eur J Pharmacol. 2011;651:168-75.

Bentham G, Hooker JD. Genera plantarum: ad exemplaria imprimis in herbariis kewensibus servata definita. (Three volumes, 1862–1883). Vol. 1 (pp 40-5). Londini: A. Black,1862.

Bhakuni DS, Shoeb A, Popli SP. Studies in medicinal plants: Part I – Chemical constituents of *B. asiatica* Roxb. Indian J Chem. 1968;6:123.

Bhargava KS. Unusual and supplementary food plants of Kumaon. J Bot Nat History Soc. 1959;56:26-31.

Bhattacharjee S, Tiwari KC, Majumdar R, Mishra AK. Folklore medicine from district Kamrup (Assam). Bull Med Ethno Res. 1980;1:447-60.

Blasko G, Murugesan N, Freyer AJ, Shamma M. Karachine: An unusual protoberberine alkaloid. J Am Chem Soc. 1982;104:2039-41.

Carr LG, Carlos W. Surviving folktales and herbal lore among the Shinuecock Indians. J Am Folk. 1945;58:113-23.

Chamberlain DF, Hu CM. A synopsis of *Berberis* section *Wallichianae.* Notes Royal Bot Garden Edinberg. 1985;42:529-57.

Chan MY. The effect of berberine on bilirubin extraction in the rat. Comp Med East-West 1977;5:161-8.

Chandler RF, Freeman L, Hooper SN. Herbal remedies of the Maritime Indians. J Ethnopharmacol. 1979;1(1):49-68.

Chandra P, Purohit AN. Berberine contents and alkaloid profile of *Berberis* species from different attitudes. Biochem Syst Ecol. 1980;8:379-80.

Chatterjee R. Plant alkaloids. Part I- *B. Floribunda* Wal. Ex. Don. J Indian Chem Soc. 1952;28:225-8.

Chatterjee R. Studies on Indian berberidaceae from botanical, chemical and pharmacological aspects. Recent Bot Survey India. 1953;16:1-86.

Chatterjee R, Banerjee A, Barma AK, Das Gupta AK. Plant alkaloids: Part II- *B. Asiatica* roots. J Indian Chem Soc. 1954;31:84-5.

Chaudhary R, Guha HN, Chaudhary AR, Pol DC. Ethnobotanical uses of Herbaria II. J Eco Taxo Bot. 1980;1:163-8.

Chauhan NS, Uniyal MR, Sannad BN. A preliminary study of the indigenous drug used at Tibetan medical centre; Dharamshala (H.P.). Nagarjuna. 1978/79; 22:190-3.

Chen JH, Huang SM, Tan TW, Lin HY, Chen PY, Yeh WL, et al. Berberine induces heme oxygenase-1 up-regulation through phosphatidylinositol 3-kinase/AKT and NF-E2-related factor-2 signaling pathway in astrocytes. Inter Immunopharmacol. 2012;12:94-100.

Chueh WH, Lin JY. Berberine, an isoquinoline alkaloid, inhibits streptozotocin induced apoptosis in mouse pancreatic islets through down-regulating Bax/Bcl-2 gene expression ratio. Food Chem. 2012;132:252-60.

Cronquist A. The evaluation and classification of flowering plants. Boston, MA: Houghton Mufflin, 1968.

Datta SC, Nigam MC, Virmani OP, Siddiqui MS. Cold process for production of berberine hydrochloride from *Berberis* roots. Indian For. 1976;139:204.

Dobhal MP, Negi GS, Joshi BC. Chemical investigation and biological activity of *B. chitria* Han. Himalayan Chem Pharm Bull. 1988;5:41-6.

Domitrović R, Jakovac H, Blagojević G. Hepatoprotective activity of berberine is mediated by inhibition of TNF-α, COX-2, and iNOS expression in CCl_4-intoxicated mice. Toxicology. 2011;280:33-43.

Dong FC, Hong Y, Liu M, Hao YZ, Yu HS, Liu Y. Berberine attenuates cardiac dysfunction in hyperglycemic and hypercholesterolemic rats. Eur J Pharmacol. 2011;660:368-74.

Du CT, Francis FJ. Anthocyanins of contoneaster and barbery. Hortic Sci. 1974;9:40.

Fajardo V, Araya M, Cuadra P, Oyarzun A, Gallardo A, Cueto M et al. Pronuciferine N-oxide, a proaporphine N-oxide alkaloid from *Berberis coletioides*. J Nat Prod. 2009;72:1355-6.

Falco MR, De-varies JX, De-Brovetta AG, Maccio Z, Rebuffo S, Bick IRC. Two new alkaloids from *B. laurina* Billb. (1). Tetrahedron Lett. 1968;16:1953-9.

Falco MR, De-varies JX, Maccio Z, Bick IRC. Alkaloids of *B. laurina* Billb. II. Two new phenolic Biscoclaurine alkaloids. Experientia. 1969;25:1236-7.

Fang D, Zong X, Jain M, Zhoce S, Jiang M. Antifibrillatory effect of berberine. Zhongguo Yaobi Xuebao. 1986;7:321-4.

Freile ML, Giannini F, Pucci G, Sturniolo A, Rodero L, Pucci O et al. Antimicrobial activity of aqueous extracts and of berberine isolated from *Berberis heterophylla*. Fitoterapia. 2003;74:702-5.

Fukuda K, Hibiya Y, Moutoh M, Koshiji M, Akao S, Fujiwara H. Inhibition of activator protein 1 activity by berberine in human hepatoma cells. Planta Med. 1999a;65:381-3.

Fukuda K, Hibiya Y, Moutoh M, Koshiji M, Akao S, Fujiwara H. Inhibition by berberine of cycoxygenase-2 transcriptional activity in hyman colon cancer cells. J Ethnopharmacol. 1999b;66:227-33.

Gaur RD, Semwal JK, Tiwari JK. A survey to high altitude medicinal plants of Garhwal Himalayas. Bull Med Ethno Bot Res. 1976;4:102-7.

Ghosh R, Mukherjee K, Roychawdhery P, Kalayman LD. Structure of an antimalarial alkaloid, jatrorrhizine. Acta Crystallogr Sect C. Cryst Struct Commun. 1993; 49:1665-7.

Greathouse GA, Rigler NE. Isolation of the alkaloids berberine and berbamine from *Mahonia swarsii*. Plant Physiol. 1940;15:563-4.

Greathouse GA, Watkins GM. Berberine as a factor in the resistance of *Mahonia trifolioata* and *M. swasevi* to phymatotrichum root. Am J Bot. 1938;25:743-8.

Gupta RS, Dixit VP. Testicular cell population dynamics following palmitine hydroxide treatment in mole dogs. J Ethnopharmacol. 1989;25:151-7.

Habtemariam S. The therapeutic potential of *Berberis darwinii* stem-bark: quantification of berberine and in vitro evidence for Alzheimer's disease therapy. Nat Prod Comm. 2011;6:1089-90.

Han B, Lice G, Zhao S. Effects of berberine and tetra hydroberberine on α adrenoceptors. Zhongguo Yaoke Datue Xuebao. 1990;25:309-11.

Hayashi K. Chemical identification of vegetable dyes used on ancient Japanese silk. Misc Reports Res Inst Nat Res. 1950;17-18:33-42.

Hooker JD, Thomson T. Berberidaceae. In: Hooker JD (ed.): The flora of British India. Vol. I (pp 107-13). London: Reeve & Co., 1875.

Hosseinzadeh H, Ramezani M, Shafaei H, Taghiabadi E. Anticonvulsant effect of *Berberis integerrima* L. root extracts in mice. J Acupunct Meridian Stud. 2013;6:12-7.

Huang Z, Dong F, Li S, Chu M, Zhou H, Lu Z, et al. Berberine-induced inhibition of adipocyte enhancer-binding protein 1 attenuates oxidized low-density lipoprotein accumulation and foam cell formation in phorbol 12-myristate 13-acetate-induced macrophages. Eur J Pharmacol. 2012;690:164-9.

Hussain A. Studies on constituents of *Berberis waziristanica* and CD studies of chiral metal complexes. Thesis. Pakistan: University of Karachi, 1992.

Hussain FA, Shoeb A. Isoquinoline derived alkaloids from *B. chitria*. Phytochemistry. 1958;24:633.

Hussain FA, Siddiqui MI, Khan L, Frayer AJ, Guinaudean H, Shamma M. Berbamine 2'-α-N-oxide, a new bisbenzyl isoquinolive from *B. brandisiana*. J Nat Prod. 1986;49:538-9.

Hussain SF, Shamma M. Kalashine: a novel type aporphine-benzylisoquinoline alkaloid. Tetrahedron Lett. 1980;21:3315-8.

Hutchinson J. The families of flowering plants. 3rd ed.London: Oxford Univ. Press, 1959.

Ikram IM, Ensanul Huq M, Warsi SA. Alkaloids of *B. lycium*. Pakistan J Sci Ind Res. 1966;9:343-6.

Invanovska N, Philipov S. Study on the anti-inflammatory action of *Berberis vulgaris* root extract, alkaloid fraction and pure alkaloids. Int J Immunopharmacol. 1996;18:553-61.

Jafri SMH. Fasc. In: Nasir E, Ali SI (eds): Flora of West Pakistan 1975;87:1-31.

Jain N, Suri RK. Insecticidal, insect repellent and pesticidal plants of DehraDun. Nagarjuna. 1979/80;23: 177-81.

Jain SK (ed). Glimpses of Indian ethnobotany. New Delhi: Oxford & IBH Publ. Co., 1981.

Jamshidzadeh A, Niknahad H. Hepatoprotective activity of *Berberis integerrima* extract in rats treated with CCl_4: In vitro and in vivo studies. Toxicol Lett. 2006;164:S310.

Jiang Q, Liu P, Wu X, Liu W, Shen X, Lan T, et al. Berberine attenuates lipopolysaccharide-induced extracelluar matrix accumulation and inflammation in rat mesangial cells: Involvement of NF-κB signaling pathway. Mol Cell Endocrinol. 2011;331:34-40.

Ju H, Han Z. Anti-oxidant effect of berberine. Zhongguo Yaoli Xuebao. 1990;11:539-41.

Jyothilakshmi V, Thellamudhu G, Kumar A, Khurana A, Nayak D, Kalaiselvi P. Preliminary investigation on ultra high diluted *B. vulgaris* in experimental urolithiasis. Homeopathy. 2013;102:172-8.

Kim S, Han J, Lee SK, Choi MY, Kim J, Lee J, et al. Berberine suppresses the TPA-induced MMP-1 and MMP-9 expressions through the inhibition of PKC-α in breast cancer cells, J Surg Res. 2012;176:e21-9.

Kirtikar KR, Basu BD. Indian medicinal plants, Vol. I-II. Allahabad: Lalit Mohan Basu Publ., 1935.

Koetz N, Walter J. Notes on the ethnobotany of Lahul, a province of the Punjab. Quart J Crude Drug Res. 1979;17:1-56.

Krets W. *Hydrastis* and *B. laurina* hydrastinine. Tribuna Farm (Brazil). 1956;24:30-1.

Küpeli EK, Müberra Y, Erdem HK, Baer C. A comparative study on the anti inflammatory, anti nociceptive and anti pyretic effects of isoquinoline alkaloids from the roots of Turkish *Berberis* species. Life Sci. 2002;72:645-57.

Kumar V, Subramaniam B. Chromosome atlas of flowering plants of Indian subcontinent. Bot Survey India. 1986;1:89-90.

Kumazawa M. Systematic and phylogenetic consideration of Ranunculaceae and Berberidaceae. Bot Mag. 1938;52:9-15.

Lee D, Bae J, Kim YK, Gil M, Lee JY, Park CS, et al. Inhibitory effects of berberine on lipopolysaccharide-induced inducible nitric oxide synthase and the high-mobility group box 1 release in macrophages. Biochem Biophys Res Comm. 2013;431:506-11.

Leet JE, Hussain SF, Minard RD, Shamma M. Sindamine, Punjabine and Giligitine: Three new seco-bisbenzylisoquinoline alkaloids. Heterocycles. 1982; 19:2355-60.

Leet JE, Slango V, Hussain SF, Shamma M. Chenabine and Jheumine: Secobisbenzylisoquinolines or simple isoquiniline-benzylisoquinolines dimmers 7. Heterocycles. 1983;20:425-9.

Li BY, Yang BI, Zhang YC, Li WH. Hemodynamic study of berbamine and verapamil in isolated guinea pig hearts. Asia Pacific J Pharmacol. 1991;6:37-42.

Li F, Bao L, Li W. The effects of berberine on isolated guinea pig atria. Yazozue Xuebao. 1985;2:859-62.

Li J, Sui W. Influence of berberine on immune fraction in mice infected with infhcenza virous. Zhonggno Yaoli Xuebao. 1986;7:475-9.

Li N, Li W, Li Y. Effects of bereberine on isolated myocardium of guinea pays and humans. Zhongno Yaoli Xnebao. 1986;7:222-6.

Li Q, Zhang Li, Zu Y, Liu T, Zhang B, He W. Generation of reactive oxygen species by a novel berberine–bile acid analog mediates apoptosis in hepatocarcinoma SMMC-7721 cells. Biochem Biophys Res Comm. 2013;433:432-7.

Majumdar P, Saha S. 1, 4-Bis (2'-Hydroxy-5'-methylphenyl) - Butan-1, 4-Dione - a bigenetically rare type of phenolic of *B. coriaria.* Phytochemistry. 1978;17:1439-40.

Maliwichi-Nyirenda CP, Maliwichi LL, Franco M. Medicinal uses of *Berberis holstii* Engl. (Berberidaceae) in Malawi, the only African endemic barberry. J Med Plants Res. 2011;5:1367-73.

Masood M, Tiwari KP. 2-5 Bis- (2'-methaxy-5'-methylphenyl) - furan, 1 rare type of compound from *B. umbellata.* Phytochemistry. 1981;20:295-6.

Meacham CA. Phylogeny of the Berberidaceae with evaluation of classification. Syst Bot. 1980;5:149-72.

Meliani N, Dib M, Allali H, Tabti B. Hypoglycaemic effect of *Berberis vulgaris* L. innormal and streptozotocin-induced diabetic rats. Asian Pacific J Trop Biomed. 2011;1:468-71.

Miana GA. Tertiary dihydroprotoberberine alkaloids of *B. lycium.* Phytochemistry. 1973;12:1822-3.

Mittre V. Wild plants in Indian folk life - A historical perspective. In: Jain SK (ed): Glimpses of Indian ethnobotany (pp 37-58). New Delhi: Oxford & IBH Publ. Co., 1981.

Morales MA, Gallards LR, Martinez JL, Puelda RS, Hernandez DA. Effects of 7-O demethylisothalicberine, a bisbenzylisoquinoline alkaloid of *B. chitensis* on electrical activity of frog candice pacemaker cells. General Pharmacol. 1989;20:621-5.

Morales MA, Gonzalez E, Torres R, Martinez JL. Cardiodepressor effects of 7-O demethylisothalicberine, bisbenzylisoquinoline alkaloid isolated from *Berberis chilensis*. Arch Med Res. 1993;24:177-81.

Musumeci R, Speciale A, Costanzo R, Annino A, Ragusa S, Rapisarda A, et al. *Berberis aetnensis* C. Presl. extracts: antimicrobial properties and interaction with ciprofloxacin. Int J Antimicro Agents. 2003;22:48-53.

Nair PKK. Pollen grains of Western Himalayan plants. Asia Monographs India. 1965;1(5):VII, 1-102.

Neto FR. Electro pharmacological effects of berberine on canine cardiac purkinje fibers and ventricular muscle and atrial muscle of the rabbit. Brit J Pharmacol. 1993;108:534-7.

Nowicke JW, Skvarla JJ. Pollen morphology and phylogenetic relationship of the Berberidaceae. Smiths Contractors Bot. 1981;53:1-83.

Pal GD. Observations on ethnobotany of tribals of Snbansiri, Arunachal Pradesh. Bull Bot Survey India. 1984;26-37.

Pant N, Garg HS, Bhakuni K. Chemical constituents of *B. psendoambalata.* Fitoterapia. 1986;51:427-8.

Parlamarchulk AS, Bondarenko VE, Grazhevich VY, Guletskaya VN. Biochemical composition of *B. vulgaris.* Chem Abstr. 1973;79:134326 a.

Pavel P. Phytochemical investigation of *Berberis koreana*. Farmacia. 1965;13:21-8.

Potdar D, Hirwani RR, Dhulap S. Phyto-chemical and pharmacological applications of *Berberis aristata*. Fitoterapia. 2012;83:817-30.

Qadir SA, Kwon MC, Han JG, Lee HY. Normal and high-pressure extraction of bioactive compound from fruit of Korean barberry *(Berberis koreana)*. A comparison. J Biotechnol. 2008;136(Suppl):S61.

Qadir SA, Kwon MC, Han JG, Ha JH, Chung HS, Ahn J, et al. Effect of different extraction protocols on anticancer and antioxidant activities of *Berberis koreana* bark extracts. J Biosci Bioeng. 2009;107:331-8.

Quevedo R, Valderrama K, Murillo BM, Laverde M, Fajardo V. A new bisbenzyl tetrahydro isoquinoline alkaloid from *Berberis tabiensis* (Berberidaceae). Biochem Syst Ecol. 2008;36:812-4.

Rahigude AB, Kaulaskar SV, Bhutada PS. Possible therapeutic potential of berberine in diabetic osteopathy. Med Hypotheses. 2012;79:440-4.

Rajaei Z, Hajzadeh M, Shafiee S, Alavinejhad A, Samarghandian S. Effect of barberry fruit (*Berberis vulgaris*) on serum glucose and lipids in streptozotocin-diabetic rats. Clin Biochem. 2011;44:S334.

Rao RR, Hajra PK. *Berberis*. In: Sharma BD et al. (eds): Flora of India. Botanical survey of India, Kolkata, India, Vol. 1 (pp 325-404). 1993.

Sabir M, Akhter MH, Bhide NK. Further studies on pharmacology of Berberine. Indian J Physiol Pharmacol. 1978;22:9-23.

Sack BR, Frochlich LJ. Berberine inhabits internal secretary response of *Vibrio cholera* and *E. coli* enterotoxins. Infect Immunol. 1982;35:471-5.

Schneider CK. Die Gattung *Berberis* (Euberberis). Mitt Deutsch Dendrol Ges. 1942;55:1-60.

Shah NC, Joshi MC. An ethnobotanical study of the Kumaon region of India. Eco Bot. 1971;25:414-22.

Shamma M, Moniot JL, Yao SY, Miana GA, Ikram M. Pakistanine and Pakistanamine, two novel dimeric Isoquinoline alkaloids. J Am Chem Soc. 1972;94: 1381-2.

Shamma M, Foy JE, Miana GA. Baluchistanamine. A novel type dimeric isoquinoline alkaloid. J Am Chem Soc. 1974;96:7809-10.

Shamsa F, Ahmadiani A, Khosrokhava R. Antihistaminic and anticholinergic activity of barberry fruit (*Berberis vulgaris*) in the guinea-pig ileum. J Ethnopharmacol. 1999;64:161-6.

Shanbhag SM, Kulkarni HJ, Gaitonde BB. Pharmacological actions of Berberine on the central nervous system. Jap J Pharmacol. 1970;20:482-7.

Singh M, Srivastava S, Rawat AKS. Antimicrobial studies of stem of different *Berberis* species. Nat Prod Sci. 2009;15:60-5.

Singh R, Tiwari SS, Srivastava S, Rawat AKS. Pharmacognostic evaluation of roots of *Berberis umbellata* Wall. ex G. Don. Indian J Nat Prod Res. 2012;3:55-60.

Singh V, Jain DK, Sharma M. Epidermal studies in Berberidaceae and their taxonomic significance. J Indian Bot Soc. 1974;53:271-6.

Singh V, Jain DK, Sharma M. Leaf architecture in Berberidaceae and its bearing on the circumscription of the family. J Indian Bot Soc. 1978;57:272-80.

Sohni YR, Kaimal P, Bhatt RM. The antiamoebic effect of a crude drug formulation of herbal extracts against Entamoeba histolytica in vitro and vivo. J Ethnopharmacol. 1995;1:43-52.

Sohni YR, Bhatt RM. Activity of a crude extract formulation in experimental hepatic amoebiasis and in immunomodulation studies. J Ethnopharmacol. 1996; 54:119-24.

Speck FG. Medicine practices of the Northeastern Algonquians. Proceedings of the 19th International Congress of Americanists (pp 303-21). 1998.

Srivastava SK, Khatoon S, Rawat AKS, Mehrotra S, Pushpangadan P. Pharmacognostical studies of the roots of *Berberis aristata* DC. Nat Prod Sci. 2001;7: 102-6.

Srivastava S, Rawat AKS, Mehrotra S. Pharmacognostic evaluation of the root of *Berberis asiatica* Roxb. DC. Pharm Bio. 2004;42:467-73.

Srivastava S, Rawat AKS, Srivastava M, Mehrotra S. Pharmacognostic evaluation of roots of *Berberis chitria* Lindl. Nat Prod Sci. 2006;2:19-23.

Srivastava S, Rawat AKS, Mehrotra S. Pharmacognostic evaluation of the Roots of *Berberis lycium* Royle. OPEM. 2010;10:184-90.

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 Compl Altern Med. 2013;2013: 472973.

Srivastava S, Rawat AKS. Quantification of Berberine in different *Berberis* species and their commercial samples from herbal drug markets of India through HPTLC. J Adv Chem. 2014;8:1700-6.

Suau R, Rico R, Romero ML. Isoquinoline alkaloids from *Berberis vulgaris* sub. Australis. Phytochemistry. 1998;49:2545-9.

Takhtajan A. Flowering plants: origin and dispersal. Washington, DC: Smithsonian Inst. Press, 1969.

Tantaquidgeon G. Mohegan medicinal practices, weather - love and superstitions. 51–*BAE*. Annual Report. 1928;43:264-70.

Tiwari KP, Masood M. 9, 9-dimethyl tetracosane 6-one from *B. concina.*Proc Nat Acad Sci India, Sec A. 1977;48(2):76-8.

Tiwari KP, Masood M. Alkaloidal constituents of *B. concina* and *B. acanthifolium.* Chem Abstr. 1978;89: 1763334.

Tiwari KP, Masood M. Chemical constituents of *B. coriaria* Royle. J Indian Chem Soc. 1979;56:310-1.

Tomita M, Kikuchi T. Alkaloids of berberidaceous plants - IX: Alkaloids of *B. thrunbergii*. J Pharm Soc Japan. 1956;76:597-9.

Tomita M, Kugo T. Alkaloids of Berberidaceous plants - VII. Alkaloids of *B. amurensis* var. japonica from Bretschneideri-I. J Pharm Soc Japan. 1955;75: 753-5.

Tomita M, Kugo T. Alkaloids of Berberidaceous plants - XIX: Alkaloids of *B. tschonoskyana* I. Isolation of bases. Yakugak Zasshi. 1956;79:317-21.

Tomita M, Yong TH. Alkaloids of Berberidaceous plants: Alkaloids of *B. thcibergii, B. kawakamii* and *B. mingetsensis.* Yakugaku Zasshi. 1960;80:845-51.

Tsang-Hsiumg Y, Lu S. Alkaloids of *B. kawakamii* and *B. mingetsensis*. Japanese Pharm Soc. 1960;80: 847-9.

Uniyal MR. Medicinal plants of the Bhagirathi valley lying in the Uttarkashi forest division U.P. Indian For. 1964;94:407-20.

Vereskovskii VV, Sapiro DK. Chromatographic study of anthocyanin pigment in the fruits of some berbery species. Khim Prir Soedin. 1985;4:569-70.

Virjee GH, Kachroo P, Bhat GM. Ethnobotanical studies of the rural areas in District Rajouri (Jammu). J Eco Taxo Bot. 1984;5:831-8.

Wang S, Zhengui Z, Yinqi W, Yijun Y, Daifu Z, Weihu F, et al. Angiogenesis and anti-angiogenesis activity of Chinese medicinal herbal extracts. Life Sci. 2004;74:2467-78.

Wang Y, Yao X, Tan Y. Effect of berberine of physiologic properties of isolated guinea pig myocardium. Zhonggno Yaoli Xnebao. 1987;8:220-3.

Wang Y, Tan Y, Sheng B. Effect of berberine on cardiac arrhythmic following coronary artery occlusion and its mechanism. Zhongguo Yaolixne Yu Delixue Zazhi. 1993;7:108-11.

Wierzchowski Z, Budicz M. Carotenoids of the berries of *B. vulgaris.* Lublin - Polpnia Section C. 1969;14: 382-405.

Xiong C, Fang D. Effect of jatrorrhizine on isolated guinea pig atria. Zhongguo Yaolixue Yu Dulixue Zazhi. 1989;3:255-8.

Xu R, Qinghua D, Yingzi Y, Xiaoying Z, Xiaoxian G, Dong W, et al. Berbamine: A novel inhibitor of bcr/abl fusion gene with potent anti-leukemia activity. Leuk Res. 2006;30:17-23.

Yasupov MM, Karimov A, Lnlfullin KL. Alkaloids of *B. vulgaris* XII. Khim Prir Soedin. 1990;1:128-9.

Yeilada E, Küpeli E. *Berberis crataegina* DC. root exhibits potent anti-inflammatory, analgesic and febrifuge effects in mice and rats. J Ethnopharmacol. 2002;79:237-48.

Yogesh HS, Chandrashekhar VM, Katti HR, Ganpaty S, Raghavendra HL, Gowda GK, et al. Anti-osteoporotic activity of aqueous-methanol extract of *Berberis aristata* in ovariectomized rats. J Ethnopharmacol. 2011;134:334-8.

Zhou X, Zhang C, Wang X, An B, Zhang P, Zhu Z. Berberine inhibits lipopolysaccharide and polyethylene particle-induced mouse calvarial osteolysis in vivo. J Surg Res. 2012;173:e47-e52.