
Berberis aristata DC. An updated review of its botany, phytochemistry and pharmacology along with its ethnomedicinal uses

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Abstract:

Berberis aristata (family Berberidaceae), commonly known as Daruhaldi is widely distributed from Himalayas to Sri Lanka, Bhutan and hilly areas of Nepal and used in folk medicine. A wide range of medicinally and nutritionally important phytochemical constituents have been isolated from plant such as yellow colored alkaloids Berberine, oxyberberine, berbamine, aromoline, a protoberberine alkaloid karachine, palmatine, oxycanthine and taxilamine and tannins, sugar, starch. Plant possesses minerals such as Sodium, Sulphur, Iron, Zinc, Lead, Magnesium, Potassium and Phosphorus, which contribute to broad variety of biological processes and are valuable in the treatment of various disorders. Traditionally used in Indian system of medicine, the plant has been used against as a tonic, alternative, antimicrobial, anti-cancerous, anticoagulants, antipyretic, hepatoprotective hypoglycemic, demulcent, CNS depressant, diaphoretic, and diuretic, in the treatment of diarrhea, jaundice and skin diseases, syphilis,

chronic rheumatism and urinary disorders. In this updated review, a comprehensive account of the botany, phytochemical constituents and pharmacological activities is presented along with ethnomedicinal/traditional uses in a view of many recent findings and its potential for future research.

Key words: Antidiabetic, antimicrobial, anticancer, *Berberis aristata*, hepatoprotective.

Introduction:

Berberis belongs to family Berberidaceae, represented by around 12 genera and 600 species of which *Berberis* L. is the major group with around 500 species (1) widely distributed in temperate and sub-tropical regions of Northern hemisphere and temperate South-America (2). These plants are known to have various medicinal components especially alkaloids having different pharmacological activities (3). Apart from its medicinal uses, some species are also used as a source of natural dye (4-5). Fruits of *Berberis* are commonly used in Persian and Georgian cuisines (6). Kirtikar and Basu (7)

clustered this genus into three groups on the basis of their medicinal value viz. The Rocky Mountain group (*B. aquifolium* Pursh), the Asiatic group (*B. aristata* DC) and European group (*B. vulgaris* L).

Berberis aristata DC. commonly called ‘daruharidra’ is critically endangered species of Indian Himalaya because of its extensive collection for roots to extract Berberine alkaloid (8). *B. aristata* is the most important species and

Table 1: Vernacular names of *Berberis aristata*

Region/Language	Vernacular name
English	Indian Barberry, Tree Turmeric
Bengal	Darhaldi, Daruharidra
Gujarat	Daruharidra, Daruhuladur
Himachal Pradesh	Rasont, Kashmal
Hindi	Chitra, Dar-Hald, Rasaut, Kashmal
Sanskrit	Katamkateri, Dirvi
Kerala	Maradarisina, Maramanjala,
Maharashtra	Daruhald
Nepal	Chitra, Chutro
Punjab	Chitra, Kasmal. Simlu, Sumlu
Tamil Nadu	Mullukala, Usikkala
Sanskrit	Daruharidra, Darvi, Kata, Pitadaru, Suvarnavarna

Distribution:

B. aristata is found growing wild, in small patches on the hill slopes (19), distributed throughout the Himalayas, from Bhutan to Kunawar (altitude 6-10,000 ft), Nilgiri hills (altitude 6-7,000 ft) and Sri Lanka (altitude 6-7,000 ft) (20-21).

A. Botany:

used as raw drug and in different ayurvedic and homeopathic formulations (9-10). It is commonly used in Indian system of medicine as antichlamydial, antimicrobial, hepato-protective, anti-diarrhea, hypoglycemic, anti-cancer, gastro-irritant, anticoagulants, antipyretic, hypotensive, CNS depressant and diaphoretic (7, 12-15). Due to its over exploitation by the herbal industries, *B. aristata* is substituted with *B. asiatica* Roxb, *B. chitria* Ahrendt and *B. lycium* Royle (16-18).

The plant is an erect glabrous spinescent shrub, ranging between 3-6 m in height with 10-20 cm stem diameter with hard and yellow wood (8).

Roots are thick, woody, yellowish brown in color, cylindrical in outline, knotty and covered with a thin brittle yellowish brown bark. Internally surface of bark is bright yellow, rough,

fibrous with small fine ridges, odorless and bitter in taste (22-23)

Leaves (3.8-10 × 1.5-3.3 cm long) are simple, in tufts of 5-8, obovate to elliptic in shape, subacute to obtuse apex, entire or toothed margins, verticillate phyllotaxy, leathery, with reticulate pinnate venation, glossy deep green on the dorsal surface and light green on the ventral surface (8, 24).

Flowers numerous, stalked, complete, hermaphrodite, cyclic, actinomorphic, perigynous, pedicellate (4-6 mm long) and yellow in color with the average diameter of a fully opened flower being 12.5 mm. Inflorescence a simple corymbose raceme (2.5-7.5 cm long), and dense-flowered (11-16 flowers per cluster) (8, 20-21).

Polysepalous: 6 sepals (3 small, 3 large), yellow, actinomorphic caducous, 4 to 5 mm long; **Corolla, polypetalous:** 6 petals, yellow, actinomorphic, 4 to 5 mm long; **androecium,** polyandrous, with 6 stamens, adnate, 5 to 6 mm long; **gynoecium,** one, 4 to 5 mm long, with a short style and a broad stigma (24).

Fruit is a small berry (7-10×4 mm in size), globose to ovoid in shape, bluish black or bright red in color and covered with a thick pale or bluish white bloom with persistent style and stigma and are born in pendulous clusters. Seeds

are 2-5 in number, varying in colour from yellow to pink (8, 20-21, 24).

Flowering in *B. aristata* starts from the first fortnight of March and remains in progress up to the end of April and the fruiting starts from the second week of May and continues throughout June. The fruiting season, therefore, ends abruptly with the commencement of the rainy season (24).

B. Nutritional attributes:

Andola *et al.* (25) carried out comparative studies on the nutritive and anti-nutritive properties of fruits in selected *Berberis* species of West Himalayas. In seed samples of *B. aristata* various nutritionally important components present were Zinc (1.35), Iron (23.4 mg/100 g), Magnesium (8.4mg/100g), Sodium (239.8 mg/100 g), Potassium (526.4 mg/100 g) and Lithium (7.4mg/100g). As far as nutritional value of its fruit pulp is concerned, these also have got Zinc (11.2 mg/100 g), Iron (180.8 mg/100 g), Magnesium 5.8 mg/100 g, Cobalt (3.5 mg/100g), Sodium (72.6 mg/100 g), Calcium (872 mg/100 g) and Lithium (8.5 mg/100 g).

C. Ethnobotanical studies:

Tincture made from *B. aristata* leaves is used as a bitter tonic and alterative, in cases of remittent as well as intermittent fevers and also in debility, hepatotoxicity, periodic neuralgia and

menstrual disorders (26-27). While, Chauhan (28) reported the use of root decoction against piles and gastric disorders by local people of Tibet, Shah (29) reported the tribal people of Kumaum region using its root decoction for treating eye-infections and boils. Bently (30) reported the plant being used in intermittent and remittent fevers and in debility, diarrhea and dyspepsia. Traditionally, the decoction of root bark, mixed with an equal quantity of milk, is used to cure piles (31). Leaf extract are used for preventing acetaminophen-induced liver damage (10), however, Chatterjee (32) reported the use of root powder mixed with butter to cure bleeding piles. While, ripe fruits of this plant species are used as mild laxative for children and exhibits hypochlolestromic activity, cambium paste is used for treating rheumatism (33-35).

Berberine is the active constituent of *B. aristata*, which is chiefly found in outer barks of stem and root of the plant having wide range of pharmacological effects (36). Root-bark extract commonly known as 'Rasot' contains berberine chloride, palmatine chloride and is used as a wash for infected wounds and ulcers, and is anthelmintic, antimalarial, treats different types of skin diseases, menorrhagia, diarrhea, malaria, jaundice, and eye troubles (10, 20-21, 37-40). Alcoholic (aqueous) root extract of this species is anti-diabetic, anti-cancerous and used as

contraceptive in combination with the extracts of *Iris germanica* and *Terminalia chebula* (41-42). However, Chhetri et al. (43) reported the tribal people of Sikkim and Darjeeling using root bark extract of *B. aristata* (5–10ml) twice a day for 1–2 weeks to treat diabetes. Daruharidra is also used traditionally to cure ophthalmic and other eye diseases (19).

D. Phytochemical composition:

Rastogi and Mehrotra (44) reported constituents are berberine, berbamine, aromoline, karachine, palmatine, oxyacanthine and oxyberberine in *B. aristata*. Later, Sivakumar and Nair (45) reported various polyphenolic flavonoids like (E)-caffeic acid, quercetin, chlorogenic acid, meratin and rutin from the flower extract of *B. aristata*. While, Andola *et al.* (46) has reported higher berberine content in *B. asiatica* (4.3 %) in comparison to *B. lycium* (4.0 %) and *B. aristata* DC (3.8 %); Srivastava et al. (18) noticed these values higher in *B. aristata* (2.8 %) as compared to *B. asiatica* (2.4 %). Same results (Berberine=1.86 %) were noticed by Rashmi et al. (47) in the roots of *B. aristata* (winter samples) using High Performance Liquid Chromatography (HPLC). For identification and authentication of *Berberis* raw material and formulations, HPTLC fingerprinting is the most popular choice till date due to its simplicity (48-

51). Kamal et al. (52) used this technique for the quantification of Berberine in *B. aristata* fruits.

B. aristata contains protoberberine and bis isoquinoline type of alkaloid. Ray and Roy (53) reported the major alkaloid found in *B. aristata* as Berberine having yield of 2.23% followed by palamatine. Various other phytochemicals from the roots of this plant viz. berbamine, Berberine, oxycanthine, epiberberine, palmatine, dehydrocaroline, jatrorhizine and columbamine, karachine, dihyrokarachine, taximaline, oxyberberine, aromoline, pakistanine, 1-O methyl pakistanine, pseudopalmatine chloride, pseudoberberine chloride and a secobisbenzisoquinoline or simple isoquinoline alkaloid have been reported from time to time by different workers (26, 54-60).

Rout *et al.* (49) analyzed berberine in marketed Ayurvedic formulations containing *B. aristata* by developing a sensitive, simple, rapid and efficient high performance thin-layer chromatographic (HPTLC) method. Later, Upwar *et al.* (61) carried out preliminary phytochemical screening of the methanolic extract of *B. aristata* and confirmed the presence of alkaloids, glycosides, carbohydrates, bitter principles and saponins. Basanta Lamichhane *et al.* (62), however, using HPTLC densitometric method performed phytochemical screening of methanolic extract of *B. aristata* and revealed

high amount of alkaloid (2.45%), active constituents' berberine (3.55%) and tannin (0.935%) in addition to other phytochemicals like steroids, flavonoids, coumarin and terpenoids that were also present in trace amount.

E. Pharmacology:

The chief constituent of *B. aristata* is barberine, which is a bitter alkaloid. A very effective preparation known as rasaut is formulated from the root-bark and lower part of stem of this plant by boiling them in water, followed by straining and evaporation till a semi-solid mass (rasaut) is obtained. Rasaut mixed with butter and alum, or with opium and lime-juice is applied externally to the eyelids to cure ophthalmic and other eye diseases (63). Reported to be a mild laxative and tonic, it is also useful in curing ulcers and fevers. A watery solution of this preparation is also used for washing piles, oriental sores and glandular swellings (63). As per Singh *et al.* (64) the most important clinical use of *B. aristata* includes treatment of diarrhea due to microbial infections caused by bacteria, fungi, virus and protozoa. Shahid *et al.* (65) reported drugs prepared from extracts of *B. aristata* can be excellent for treating cholera.

1. Anti-microbial activity

Pharmacological studies reported berberine to be effective in reducing mortality rate, volume and duration of diarrhea (66). Root extracts of this

plant also showed significant antifungal activity against *Aspergillus terreus* and *Aspergillus flavus* and these workers suggested alkaloid berberine responsible for antimicrobial activity. *B. aristata* stem-bark extract is reported to be useful in curing bacillary dysentery and diarrhea (67). Evidence indicates that it also has multiple pharmacological effects such as immunomodulatory, anti-inflammatory, antidiarrheal (68-69).

Singh et al. (64) demonstrated the antimicrobial activity of hydro alcohol extract of four *Berberis* species including *Berberis aristata* against 11 bacterial and eight fungal strains excluding *Shigella*. Joshi et al., (70), however, examined the antimicrobial profile of bark extracts of *B. aristata* and compared it with standard drugs against four strains of *Shigella*. These extracts showed antibacterial activity against all four strains of *Shigella* and were effective than the standard drugs with zones of inhibition ranging between 8 and 23 mm. Experimental observation of Basanta Lamichhane et al. (62) reported the plant extract of *B. aristata* were sensitive against *C. albicans*, *S. typhii*, *P. aeruginosa* and *E. coli*, while it didn't show any activity against *K. pneumonia* and *S. aureus*. Later, Saravanakumar et al. (71) studied the methanol stem extracts of *B. aristata*, its substitutes and market samples and noticed

antimicrobial activity against *Nocardia*, *S. pneumonia* and *E. coli*.

2. Anti-diabetic activity:

Root extract of *B. aristata* has strong potential to regulate glucose homeostasis through decreased gluconeogenesis and oxidative stress (72). Semwal et al. (73) examined the antihyperglycemic activity of ethanol extract of root of *B. aristata* and reported that it possess anti-diabetic activity in alloxan induced diabetic rats. Gupta et al. (74) studied the methanol extract of the stem bark of *B. aristata* for antidiabetic properties and noticed that daily administration of 250 mg/kg and 500 mg/kg of methanol extract led to a dose-dependent reduction in blood sugar levels.

Chakrabarti et al. (75), however, carried out DPP-IV assay of *B. aristata*. From 500µg/ml crude extract (10mg dissolved in 20ml of dH₂O) different working concentrations (12.5, 50, 200, 400µg/ml) were prepared. 20µl of each of above stock concentrations was made to 35µl using Tris-HCl Buffer (50mM, pH 7.5) to obtain final inhibitory concentrations of 2.5, 10, 40, 80µg/ml respectively in a total well volume of 100µl. The results obtained from DPP-IV enzyme inhibition assay (*in vitro*) explained the effectiveness of *B. aristata* in regulating diabetes. Besides, Upwar et al. (61) reported the maximum reduction in serum glucose levels in methanol extract of *B.*

aristata at the dose of 500 mg/kg and concluded that methanolic extract of *Berberis aristata* DC had a beneficial effect on carbohydrate metabolism in diabetic rats. Later, Ahmad et al. (76) studies on petroleum ether and ethanol extracts (400 mg/kg) of *B. aristata* bark revealed that it has significant anti-diabetic activity in alloxan induced diabetic rats in a dose dependent manner. However, Mittal et al. (77) reported the use of ethanol extracts (50mg and 100mg/kg b. wt.) of *B. aristata* roots in diabetic rats showing dose dependent and statistically significant reduction in hyperglycemia. These workers noticed 63.01 % and 66.27% reduction in blood glucose level at 50 and 100 mg/kg b. wt. in contrary to diabetic control.

3. Anti-diarrheal activity

Jia et al. (78) examined the bark extracts of *B. aristata* and noticed berberine, isoquinoline alkaloid, in it that has been used as a standard anti-diarrheal drug in many pharmacological experiments. Later on studies carried out by Joshi et al. (70) provides a qualitative and quantitative chemical profiling of a potent plant species used as anti-dysentery.

4. Hepatoprotective activity

B. aristata is known for its hepatoprotective activity (79). Leaves and fruits of this plant are known to exhibit hepato-protection possibly through inhibitory action on hepatic drug

metabolizing enzymes (80-81). Besides, Rathi et al. (82) performed serum biochemical analysis and compared standard drug Silymarin 100 mg/kg with the ethanolic extract stem bark of *Berberis aristata*. These workers found significance results against CCl₄ induced alteration in the serum enzyme levels suggesting that the use of ethanolic extract of *Berberis aristata* exhibit significant protective effect from hepatic damage in CCl₄ induced hepatotoxicity model.

5. Anti-inflammatory activity

Akhter *et al.* (83) have reported berberine sulphate present in *B. aristata* showing anti-inflammatory properties.

6. Anti-cancer activity

Das *et al.*, (84) while carrying photochemical screening of *B. aristata* reported the presence of alkaloids in the methanol stem extract of this plant having anti-cancer activity. This plant species is very effective against breast and colon cancers (85-86). Similarly, Serasanambati et al. (87) while studying methanol extracts of *B. aristata* of different concentrations noticed anticancer activity significantly in MCF-7 breast cancer cell lines considered as a prognostic anticancer activity indicator with IC₅₀ value being 220 µg. Basanta Lamichhane *et al.* (62) carried out Cell viability assay; MTT that showed a significant cytotoxicity to MDA-MB-

231 and U-87 MG human cancer cell line compared to NIH/3T3 standard embryonic fibroblast cell lines of mouse

7. Anti-oxidant

Basanta Lamichhane et al. (62) reported that *B. aristata* have an effective H₂O₂ scavenging activity with percentage scavenging activity on H₂O₂ radical being 81.8% of extract at 100 µg/mL.

8. Anti-depressant

Das et al. (84) have demonstrated that berberine possesses central nervous system activities, particularly the ability to inhibit monoamine oxidase-A, an enzyme involved in the degradation of norepinephrine and serotonin (5-HT) berberine exerted antidepressant-like effect in various behavioural paradigms of despair possibly by modulating brain biogenic amines (norepinephrine, serotonin and dopamine).

Conclusion:

From the above review, it can be dissolved that *Berberis aristata* DC. is used traditionally since many years as communicated in various literature. From medicinal point of view this rare plant possesses important pharmacological properties such as antidiabetic, anti-oxidant, anti-inflammatory, hepatoprotective, antibacterial, antifungal, antimutagenic and wound healing properties. However, after the identification and verification

of different brand new medicinal components and their traditional uses, *B. aristata* is now gaining attraction by various researchers to develop some more new search for the future development by understanding the gene level study. Therefore, taking into attention of these versatile medicinal uses, there is plenty of scope for future research on *B. aristata* and hence further pharmacological investigations are needed. In this review, we tried to compile all the available information till date from both traditional and published scientific literatures regarding the medicinal use and pharmacological activities of *B. aristata* which will be beneficial for researchers to get the information in a nut shell.

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