An Indigenous Medicinal plants of Himalayan altitude : *Berberis aristata* DC.

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ABSTRACT

The use of herbal medicinal plants for the treatment of several ailments is a very old traditional system. Herbal medicines are an important part of the health care system in many developing countries and the use of herbal medicines, as health promoting agents, even in developed countries has also been increased. Plants are one of the most abundant sources of compounds on the planet. Plant species have been used from ancient time in different parts of world but because of the global communication most of them are now available worldwide.

Ayurvedic Pharmacopeia of India correlates Daruharidra to Berberis aristata DC of family Berberidaceae. Daruharidra (is a Sanskrit word means 'the yellow color wood') is one of the herbs mentioned in ancient scriptures of Ayurveda. Charaka and Susruta have also mentioned its different pharmacological effects along with various indications of its use. Berberis aristata is used to treat diarrhoea, jaundice, skin diseases, syphilis, chronic rheumatism, urinary disorders as a tonic, replacement, demulcent, diaphoretic, and diuretic scientific evidence indicates that it has a wide range of biological functions that justify its traditional use in Asia. Berberis aristata comprises primarily yellow coloured isoquinolone alkaloid berberine, oxyberberine, berbamine, aromoline, a protoberberine alkaloid karachine, palmatine, oxycanthine, and taxilamine, as well as tannins, sugar, and starch, according to phytochemical studies. Berberine is the most common compound, and it has a variety of pharmacological effects. Berberis aristata has been used in traditional medicine for its variety and pharmacological properties since ancient times. Exploring this medicinal plant in greater depth is a requirement of today's medical system.

This review paper supporting the utilization of Berberis aristata plant as legends medication for the treatment of various disorders. Further examinations are expected to investigate its maximum capacity in the field of socioeconomic benefits. The current analysis focused on the phytochemical and pharmacological studies on Berberis aristata that have been published in the last two decades.

KEYWORDS: *Berberis aristata, Traditional uses, scientific use, Phytochemicals, Berberine, Oxyberberine, Berbamine, Aromoline.*

INTRODUCTION

Medicinal plants are an abundant and pure source of bioactive compounds which, in contemporary medicine, play an important role. Because of their widespread distribution, convenient Folklore medicine's availability and application, medicinal plants provide enormous possibilities for numerous biological screenings (1). Medicinal biologists are currently pursuing a high degree of interest in the pharmacological discovery of natural products, which will eventually fuel the creation of a more environmentally friendly pharmacy render a major contribution to biomedicine (2). *Berberis aristata* DC (tree turmeric) the plant species originally belonged to the Berberidaceae family, used with the analysis due to its broad medicinal properties, it is one of the most significant plant. It is commonly known as "Daru haldi or Chitra" and it has long been an important part of ayurvedic pharmaceuticals (3). The plant is indigenous to the area northern Himalayan region is broadly spread from the Sri Lanka, Bhutan, and Nepal's hilly regions are all surrounded by the Himalayas. It develops at a rapid rate an altitude of 2000-3000 m, particularly in the Himachal Pradesh area of Kumaon and Chammba. It is present in South India's Nilgiri hills as well (4). It's a spiny erect shrub widely used in the Indian medicine scheme, which is a hard, yellowish functional section. Inhabitants ingest the fruits of the species for the healing of different diseases. The entire plant also contains dye and tannin, which are used in fabric dyeing and leather tanning (5). Because of its medicinal value, It is regarded as the most important essential herbal plant in the Ayurveda, Siddha, and Unani medicinal systems. The plant's root are considered the official source of the drug (6). A number of important phytochemicals can be found in the plant such as proto-berberine alkaloids, isoquinoline, bisbenzyl-isoquinoline, and other bioactive components such as flavonoids and phenolic acids. The traditional medicinal systems of India and China reveal that there is some significant medicinal value in almost every part of this plant. Many traditional ayurvedic formulations, The roots, stem, bark, leaves, rhizomes, and fruits of Rasaut, Darvyadi kvatha, Darvyadi leha, Darvyadi taila, Rasanjana, and Dasanga lepa, among others, are used, The fruit of the plant is edible and high in vitamin C. Pharmaceuticals, neutraceuticals and cosmeceutical formulations refer to extracts derived from the herb (7). Berberine is the plant's primary alkaloid, and it can be found in the leaves, roots, rhizomes, and stem bark (8). *Berberis aristata* is composed of xyacanthine, berbamine, berberrubine, columbamine, isotetrandrine, jatrorrhizine, oxycanthine, glucoside stigmasterol, sugars, organic acids, some vitamins, polyphenolic compounds, pectin, tannin and mineral components (9).

The plant produces Oxycanthine, Berberine, Epiberberine, Palmatine, Jatrorrhizine, Dehydrocaroline and Karachine. Four alkaloids Columbamine, Pakistanine, 1-Omethylpakistanine, pseudopalmatine, 1-Omethylpakistanine Chloride and chloride with pseudo-berberine. It has functions that are hypotensive, immuno-stimulating, anti-inflammatory, antimicrobial, antiprotozoal. It also has anti-fungal, anti-helminthic and tuberculostatic effects. Berberine’s most well-known medicinal applications are inhibiting viruses, viral intestinal infections, diarrhoea, and ocular infections (10). Traditionally, the plant is used as a tonic, demulcent, diaphoretic, diuretic and alternative to treat diseases like wound healing, skin diseases, rheumatism, snakebite, menorrhagia, jaundice and eye related problems (11). The official species of India's Ayurvedic Pharmacopeia, *Berberis aristata* DC, has a niche

for pharmacological and clinical uses that have been documented. Berberine is mainly used in neurodegenerative diseases, primarily because of its powerful antioxidant effect. Several studies have demonstrated the therapeutic potential of its active phytoconstituent Berberine is used to treat Alzheimer's disease, Parkinson's disease, and Huntington's disease, among many other neurodegenerative diseases (12). Berberine has been reported to exhibit local anaesthetic, inhibitory enzymes, antipyretic and anti-amnesic action (13). In Ayurveda, it is used in the treatment of jaundice and spleen enlargement (14). Alkaloids are typically alkaline and colourless, but Berberine is naturally acidic and is known by its vivid yellow colour. It has traditionally been used as a yellow dye in a variety of nations. Pharmaceuticals, neutraceuticals and cosmeceutical preparations apply to extracts obtained from the plant. Various parts of this plant like roots, stem, bark, leaves and fruits are widely used since from the ancient times for the successful management of various ailments (15).

INTRODUCTION TO THE PLANT

Berberis aristata DC. (Family: Berberidaceae)

Daruharidra (is a Sanskrit word means ‘the yellow color wood’) has been one of the herbs mentioned in Ayurveda's ancient scriptures. Its various pharmacological effects have been mentioned by Charaka and Susruta, as well as various pharmacological effects indications of its use. Charaka has classified Daruharidra as stanyasodhana (lactode purant), kandughna (antipruritic), lekhana (a reducing herb), rasayana (rejuvenative), kandughna (antihaemorrhoidal), arsoghna (antihaemorrhoidal), svedala (promotes sweating). Susruta has given it the name ropana, which means "wound healer."

Ayurvedic Pharmacopeia of India correlates Daruharidra to *Berberis aristata* DC. of family Berberidaceae. It is a spinous, erect, deciduous shrub with obovate to elliptic, entire or toothed leaves, subacute to obtuse, Height ranges between 1.8 and 3.6 metres native at an altitude of 1000-3000 metres in the Himalayan ranges, a-nd in the Nilgiri hills in South India. Yellow flowers grow in corymbose racemes. The bright red berries are oblong-ovoid or ovoid in shape (16).

TAXONOMICAL CLASSIFICATION

Kingdom : Plantae
Division : Angiosperms
Class : Eudicots
Order : Ranunculales
Family : Berberidaceae
Genus : *Berberis*
Species : *aristata*

VERNACULAR NAMES IN DIFFERENT INDIAN LANGUAGES

English : Indian barberry, tree turmeric

Hindi : Daruhaldi, Darhald
Sanskrit : Daruharidra, darvi, kata, pitadaru, suvarnavarna
Bengali : Daruharidra
Urdu : Darhald
Tamil : Gangeti, Varatiu manjal
Telugu : Manupasupu
Gujrati : Daruharidra, Daruhuladur
Kannada : Maradarishana, Maradarishina, Daruhaladi
Malayalam : Maramannal, Maramanjal
Marathi : Daruhalad
Oriya : Daruharidra, Daruhalidi
Punjabi : Sumalu

Figure 1: PHOTOGRAPH OF STEM, LEAVES AND FLOWERS OF *BERBERIS ARISTATA* DC.

BOTANICAL DESCRIPTION

Berberis aristata is a deciduous, 3-6 m tall erect, glabrous, spinescent shrub. Obovate to elliptic in shape height, subacute to obtuse, whole or leaves with teeth, corymbose racemes of flowers are yellow, and the berries are oblong-ovoid to ovoid and bright red (17).

A) *MACROSCOPIC*

The bark is about 0.4 - 0.8 cm thick, rough, brittle, more or less hard, the xylem portion of the plant is yellowish-brown, soft, and furrowed closely and deeply, radiate with xylem rays, fracture short in bark region, splintery in xylem, pith mostly absent, when present small, yellowish-brown when dried, taste bitter.

B) *MICROSCOPIC*

Stem - Xylem rays are straight, distinct, multiseriate, consisting of radially arranged rectangular cells, each ray 30-53 cells high, 8-12 cells wide, with a few ray cells containing brown contents; xylem fibres are numerous, lignified, large, thick-walled with wide lumen, and pointed tips; xylem rays are straight, distinct, multiseriate, consisting of radially arranged rectangular. Each fibre is short, thick-walled, spindle-shaped, lignified, and has a wide lumen. Phloem fibres are arranged in tangential rows and contain 1-4 cells. Phloem rays are radially elongated parenchymatous cells that run obliquely, with the majority of phloem ray cells having single prismatic calcium oxalate crystals. Stone cells are also found in phloem ray cells in groups, rarely alone, and are mostly elongated with a few rounded edges, arranged radially, and some of which contain a single prism of calcium oxalate crystals.

C) POWDER

Yellowish, mainly consists of cork cell fragments and sieve elements, stone cells in singles or in groups, spiral thickening of xylem vessels, thick-walled, lignified xylem fibres and ray cells, yellow-colored phloem fibres, whole or in pieces, numerous prismatic calcium oxalate crystals (18).

ETHNOPHARMACOLOGICAL USE

The roots of *Berberis aristata* DC commonly known as daruharidra possess in Ayurvedic medicine significant antibacterial, antidiabetic, anticancer and anti-inflammatory activities. The drug is also mentioned as a it's a bitter tonic that's used as a cholagogue, antipyretic, stomachic, laxative, diaphoretic, and antiseptic, according to reports. External application of daruharidra treats the painful eye infections, ulcers and haemorrhoids that are not painful. Periodic neuralgia and menorrhagia can both benefit from root bark (19).

TRADITIONAL MEDICINAL USE

Berberis aristata DC is used to treat different types of uterine and vaginal disorders, wound healing, dysentery and indigestion. It's also used to treat ulcers and fevers as a tonic and as a major herb of several polyherbal formulations for treating diarrhoea (20, 21). Dental caries is treated with tender leaf buds. “Rashut” decoction prepared from root of *Berberis aristata* DC is widely used in ayurveda. A variety of *Berberis aristata* DC has been reported against a variety of ailments and diseases such as stomach disorders, skin disease, rheumatism, jaundice, diabetes, fever, and malarial fever (22). *Berberis aristata* DC roots have been used as

antiperiodic, diaphoretic and antipyretic and the bark as tonic and antiperiodic (23). *Berberis lyceum* roots, another species possess medicinal properties and used to treat chronic diarrhea, eye complaints menorrhagia, febrifuge and piles (24). Leaves are useful in jaundice and stem in the treatment of ulcers, sore eyes diabetes, wounds and broken bones. Gilani and Janbaz in 2000 reported that in different areas of India and Pakistan (25), the fruits of this plant are used as a tonic against liver and heart diseases and also possess stomachic, astringent, antihistaminic activity, antipyretic and diaphoretic (26).

Berberine from stems of *Berberis aristata* and *Cosinium fenestratum* exhibits different pharmacological effects and for the treatment of kapha, is widely used, vata, inflammations, wounds, fever and general weakness ulcers, jaundice, diabetes, dysentery, skin diseases, diseases of the eye. These are commercially used as ropes in Sri Lanka. Root and leaf extract of *Morinda umbellate*, another rich source of berberine are used as traditional medicine. Powdered leaves are used to treat dysentery, diarrhoea and also reported to possess antileukemic, antioxidant properties and the fruits are considered edible.The root and wood are rich in yellow coloured alkaloid berberine, a bitter compound, which is soluble in acids and forms salts of the alkaloid. Daruharidra has been reported to be antipyretic, diaphoretic, as Raja Nighantu, it has diaphoretic and rejuvenating properties (bitter tonic).

Some of the Daruharidra formulations used in Ayurveda are Darvyadi kavatha, Rasanjana, Dasanga lepa Darvyadi leha and Darvyadi taila. Due to several clinically effective formulations, now a days Daruharidra has got huge it has significant trade value (high volume/high value) and is a conservation concern, it becomes an endemic species. Market survey in India indicates that *Berberis asiatica*, *Cosinium fenestratum, Berberis lycium*, and *Morinda umbellata* are traded as substitutes of *Berberis aristata.* Literature survey of these plant species indicates that they possess a wide range of pharmacological activity (27).

EARLIER SCIENTIFIC WORK DONE ON *Berberis aristata* DC.

Karim *et al,* performed a comparative toxicity study of *Berberis aristata* DC using a dosage mortality curve, we tested brine shrimps (Artemia salina). In male and female mice and rats, it was reported that berberine, its bioactive phytoconstituent is although phototoxic, *Berberis aristata* extract was found to be safe in mice, with an LD50 of >5000 mg/kg body weight. In this research they also showed the LC_{50} value (28). Tiwari *et al, Berberis aristata* was subjected to a preliminary pharmacognostic and phytochemical analysis and reported that the pharmacognostical features of *Berberis aristata* have been utilized in developing standard which will be useful in the detection of its identity and authenticity. The parameters such as physicochemical analysis, preliminary phytochemical test, fluorescence analysis and HPTLC studies added to its quality control and quality assurance for proper identification (29). Tamilselvi *et al,* reviewed the endangered medicinal herb Berberis aristata and its allied species' traditional medicinal use, as well as pharmacognostical and pharmacological investigations (30).

Khan, estimated the morpho-pathological and floral genetic diversity amongst *Berberis* species from Karakoram Mountain Ranges. Genetic diversity of medicinally important *Berberis* species obtained from great mountainous heights were described. High range (0-100%) of

Genetic Distance was estimated using 31 morphological, pathological and floral characteristics which indicated the possibilities of the material using genetic selection in *Berberis* spp (31). Shigwanb *et al*. developed HPLC method validation and quantification of Berberine is derived from *Berberis aristata* and *Berberis tinctoria*, two Berberis species, Berberine was isolated from the above-mentioned plant extract using semi-preparative HPLC and separated using an isocratic mode on HPLC at a flow rate of 1 mL/min using a mixture of 0.1 percent trifloroacetic acid: acetonitrile (60:40 v/v). A plot of integrated peak area versus berberine concentration was made under these conditions was plotted which formed a straight line from 0.2 g/mL to 150 g/mL is the concentration range. The % yield of berberine in *Berberis aristata* and *Berberis tinctoria* was found to be 3.18% and 1.46% respectively (32). Rathi *et al.* was studied the comparative pharmacognostical study of *Berberis aristata* and *Berberis asiatica.* This study looks into the pharmacognostical characteristics of the root, stem, and leaf of both plant species in order to distinguish them from each other as well as other substitutes and adulterants. The two species of *Berberis* viz. *Berberis aristata* and *Berberis asiatica*, although resembling each other in most of its external features, showed differentiable characters in respect of both microscopy and quantitative microscopy including Lycopodium spore analysis (33).

Shamkuwar and Pawar, was reported that the antispasmodic and antidiarrhoeal effect of *Berberis aristata* in *in vivo* experimental models. Aqueous extract of *Berberis aristata* treated mice, significantly reduced the duration of diarrhoea, total no of stools and number of wet stools in the diarrhoea induced by magnesium sulphate. Berberis aristata had an antidiarrheal effect, according to the findings, by inhibiting, By lowering intestinal motility, it has an antispasmodic effect (34). Patel, another researcher Berberine was extracted from *Berberis aristata* using an acid dye method, and the parameters were determined. The proposed method is accurate and repeatable, according to statistical analysis (35). Ranjan *et al*., carried out standardizations and phytochemical investigations on *Berberis aristata*. In quantitative microscopy the outcomes were stomatal number-14, stomatal index-40, vein islet-09, palisade ratio -06 and vein termination-04. The phytochemical studies were positive for tannins, carbohydrates, alkaloids (36).

Gehlot *et al.*, reported that Berberine derived from *Berberis aristata* roots inhibits cataract formation in isolated goat eye lenses. *In vitro* study showed that in the berberine treated groups, glutathione, catalase and protein levels were significantly increasd ($P<0.001$). Thus isolated compound, berberine produced it can be used as an anticataract agent and has protective effects against in vitro glucose induced models (37). Ahmad *et al.,* discussed the alloxan-induced diabetic male Wistar albino rats, the anti-diabetic potential of various Berberis aristata bark extracts was investigated (150-250g). It was concluded that petroleum ether *Berberis aristata* extract (PEBA) and ethanol extract of *Berberis aristata* (EEBA) at 400 mg/kg dose possesses better antidiabetic effect when compared to diabetic rats induced by alloxan disease induced group in terms of Biochemical parameters and blood glucose levels (38). Patel *et al.,* was standardized the using traditional methods, extract *Berberis aristata* and modern HPTLC techniques. In his findings they reported that water and alcohol solubilities in water, they were found to be 81.90 percent and in 50 percent alcohol, they were found to be 84.52 percent. The drying loss was discovered to be 5.32 percent. The content of total phenol and flavonoid was

found to be 0.11 percent and 2.8 percent, respectively. Berberine content was found to be 13.47% through HPTLC method (39).

Mittal *et al.,* was evaluated that the phytochemical, cytoprotective and antidiabetic, potentiality of *Berberis aristata* DC. root extracts. In diabetic rats, an ethanol extract of Berberis aristata roots reduced STZ-induced hyperglycemia in a dose-dependent manner. When diabetic rats were compared to diabetic control rats, serum total cholesterol, triglyceride, ALT (alanine aminotransferase), AST (aspartate aminotransferase), serum creatinine, and blood urea levels were significantly reduced (40). Andola and Purohit, was interpreted in their study that *Berberis asiatica* may be in the preparation of hepatoprotective drugs, it is a good substitute for *Berberis aristata*. Commercially available berberine containing formulations include Liv-52, Livergen, Stimuliv, Livokin, Tefroliv, Octogen etc. The main component of Berberis aristata's root and stem bark was found to be an alkaloid berberine, was found responsible for hepatoprotective activity (41). Potdar *et al.,* reviewed the preliminary *Berberis aristata* has a number of phytochemical and pharmacological uses. Antipyretic, antibacterial, antimicrobial, anti-cancer, anti-oxidant, anti-hepatotoxic, anti-hyperglycaemic, and anti-lipidemic properties of the plant have been discovered. Diarrhoea, haemorrhoids, gynaecological disorders, skin diseases, HIV-AIDS, osteoporosis, jaundice, diabetes, eye and ear infections, wound healing, and malarial fever were all treated with Berberis aristata extracts and formulations (42).

Dehar *et al.,* was evaluated *Berberis aristata* induced hypnosis in rodents after being exposed to thiopental sodium. Their results indicated that the locomotor activity was unaffected by lower doses of the extract (5 mg/kg) and thiopental the higher dose of 20 mg/kg, on the other hand, significantly reduced motility and locomotor activity. When compared to the standard drug diazepam, which lasted 167.83±52.127 minutes (p=0.054), there was significant motor incoordination and the hypnosis lasted 28.67±9.812 minutes (p=0.004) (43). Kumari and Setty, described the protective *Berberis aristata's* pharmacological effect on mitomycin C and cisplatin-induced mitochondrial dysfunction. Mitomycin C and cisplatin combined therapy has been shown to be effective in the treatment of human cervical cancer, lung cancer, breast carcinoma, and anal carcinoma, among other cancers. The findings demonstrated that prior administration of *Berberis aristata* reduced the damage to mitochondrial function in cancer cells, by scavenging the free radicals and thus, prevented uncoupling of oxidative phosphorylation, generation of lipid peroxides, oxidation of phospholipids and deactivation of enzymes of electron transport chain, finally inhibited apoptosis is triggered when a signalling wave reaches the mitochondria death receptor (membrane bound cytochrome c) (44).

Sharma *et al.,* was evaluated that *Berberis aristata* DC for *in vitro* antimicrobial potentiality the pathogens that cause ear infections. The antimicrobial efficacy and the agar well diffusion method was used to test the minimum inhibitory concentration (MIC) of *Berberis aristata* and root extracts against six different ear pathogens, *Pseudomonas aeruginosa, Acinetobacter* spp, *Staphylococcus aureus, Proteus mirabilis, Escherchia coli*, and *Candida albicans.* The organic extracts of *Berberis aristata* were found to have broad spectrum antimicrobial activity in this study, suggesting that they could be used to treat ear infections (45). Akhtar *et al.,* was screened the antidiabetic in normal and alloxan-induced diabetic rabbits, activity of different fractions

of *Berberis aristata* root-bark. The test fractions of Berberis aristata root-bark caused significant hypoglycemia in normal and diabetic rabbits, according to the findings. The effect appeard to be more potent antidiabetic than even marketed drug gliclazide. It was also suggested that the active ingredients in Berberis aristata have an organotropic effect on pancreatic -cells, resulting in increased insulin release from the islets of Langerhans in rabbits (46).

Sharma *et al.,* reviewed the plant *Berberis aristata* in detailed covering its phytoconstituents and medicinal values. The edible plant fruit was found to be rich in Vitamin C. A very effective ayurvedic preparation 'Rashut' prepared by *Berberis aristata* which was used in treating aliments like ulcer, ophthalmic infections and also used as a laxative, tonic and blood purifier. Preliminary phytochemical studies showed that *Berberis aristata* contained mainly yellow colored alkaloids berberine, oxyberberine, protoberberine, aromoline, berbamine, oxycanthine and taxilamine, karachine, palmatine, tannins, sugar and starch. The plant was effective with different pharmacological properties and showed promising future prospect for further researches (45). Khan *et al.,* was screened the effect of *Berberis aristata* on lipid profile and blood coagulation parameters in albino rats. *Berberis aristata* root (25 mg/kg) reduced serum cholesterol, triglycerides, and low density lipoprotein levels significantly. There was also an increase in thrombin and fibrinogen time (47). Ray *et al.,* was reported *Berberis aristata* DC, a rare Himalayan medicinal plant, was studied using predictive distribution modelling. With the help of three different algorithms, such as Maximum entroys (MaxEnt), Genetic Algorithm for Rule-set Production (GARP), and Bioclim, the distribution model was developed using bioclimatic and topographic variables. In comparison to GARP (4.63 percent) and Bioclim, maximum entropy predicted a wider potential distribution (10.36 percent) (2.44 percent) (48). Kamal *et al.,* quantitatively analysed berberine present in fruits of With the help of three different algorithms, such as Maximum entroys (MaxEnt), Genetic Algorithm for Rule-set Production (GARP), and Bioclim, the distribution model was developed using bioclimatic and topographic variables. In comparison to GARP (4.63 percent) and Bioclim, maximum entropy predicted a wider potential distribution (10.36 percent) (2.44 percent) (49).

Balasubramani *et al.,* was *Berberis aristata* DC was differentiated from Berberis lycium Royle and Berberis asiatica Roxb. using sequence-based markers. Using universal primers, DNA markers were created by amplifying and sequencing the entire internal transcribed spacer region (ITS1, 5.8S rRNA, and ITS2) from genomic DNA. Berberis aristata, Berberis asiatica, and Berberis lycium were all successfully authenticated using the markers developed. These were useful for quality control of raw drug materials as a molecular pharmacognostic tool (50). Upwar *et al.,* was reported On normal and streptozotocin (STZ) induced diabetic rats, methanol extract of Berberis aristata DC. (MEBA) had an anti-diabetic effect. Repeated oral administration of the MEBA, effectively decreased the blood glucose level in diabetic rats ($p< 0.05$), and also showed that their was a significant reduction ($p<0.05$) in total cholesterol, triglycerides and significant increase ($p< 0.05$) in HDL cholesterol level at a dose of 250 and 500 mg/kg (51).

Wagh and Vidhale, were evaluated *Berberis aristata's* antimicrobial activity against some pathogenic bacteria and fungi isolated from humans. Amongst the Gram-positive bacteria, *Staphylococcus aureus* was found sensitive towards the decoction fraction of *Berberis aristata*. Moreover amongst the fungi, *Candida tropicalis* and *Candida albicans* were also found sensitive (52). Pareek and Suthar, were screened in streptozotocin-induced diabetic rats, researchers tested the hypoglycemic activity of a *Berberis aristata* root extract. The extract's anti-diabetic effect was more pronounced at 200mg/kg/bw, causing maximum drops in blood glucose levels of 22.9 percent ($p<0.05$) and 29.4 percent ($p<0.01$) in normal animals and 30.3 percent ($p<0.01$) and 48.4 percent ($p<0.001$) in diabetic rats, respectively.Blood glucose levels were checked after 3 hrs and 6 hrs of treatment in normal and diabetic rats respectively. The findings of the study suggested that the ethanol extract of *Berberis aristata* produced significant hypoglycemic effect in STZ induced diabetic rat when compared with standard drug metformin (53).

Gupta *et al.,* was studied the *Berberis aristata* DC stem bark has blood glucose lowering potential in alloxan-induced diabetic rats. It was screened that methanol extract of *Berberis aristata* stem bark exhibits significant antidiabetic property in a dose dependent manner, but none of its doses were better than glibenclamide. The extract was found to had significant antioxidant property to scavenge the free radicals (54). Rashmi *et al.,* quantitatively estimated Berberine was found in the roots of *Berberis aristata* DC of various provenances using the HPLC method, and their antifungal properties were investigated. (55).

Rameshwar *et al.,*was studied *Berberis aristata's* therapeutic efficacy in albino rats with type I and II diabetes mellitus (DM). There was a significant ($p<0.05$) reversal of liver glycogen depletion. The extracts had no effect on the oxidative stress brought on by streptozotocin-induced diabetes. In the Streptozotocin (STZ) and Nicotinamide induced diabetic model, however, the extracts had a greater hypoglycemic effect than glibenclamide (56). Semwal *et al.,* was evaluated in alloxan-induced diabetic rats, the root of *Berberis aristata* DC has anti-diabetic activity. When compared to a normal control group, diabetic animals had significantly higher cholesterol and triglyceride levels ($p<0.01$). The cholesterol and triglycerides levels reduced more significantly ($p<0.01$), in comparison with diabetic control group. Ethanol extract of an oral glucose tolerance test, *Berberis aristata* improved glucose tolerance (57). Gupta *et al.,* was evaluated topical application of Curcuma longa and Berberis aristata aqueous extracts had an anti-inflammatory effect on rabbits with experimental uveitis. Curcuma longa and Berberis aristata were tested for anti-inflammatory activity by scoring clinical signs, histopathologic changes, and estimating the inflammatory cell count. inflammatory cell count in the control group was 30.75, 7.33*105 cells/mL, whereas the Curcuma longa and Berberis aristata treated groups had 2.39, 0.59*105 (p 0.001 vs. control) and 11.56, 2.44*105 (p 0.001 vs. control) cells/mL, respectively. In rabbits with endotoxin-induced uveitis, topical administration of aqueous extracts of Curcuma longa and *Berberis aristata* demonstrated potent anti-inflammatory efficacy (58). Ahmad *et al.,* reviewed herbal treatment for diabetes mellitus and evaluated the mild antihyperglycaemic activity in *Berberis aristata* (59).

Singh *et al.,* was studied the antimicrobial potency of Indian *Berberis* species. The antimicrobial activity of hydroalcoholic extracts of four *Berberis* species viz. *Berberis aristata, Berberis lycium, Berberis asiatica* and *Berberis chitria* were tested against eleven bacterial and eight fungal strains. *Berberis aristata,* root extract gave low MIC values against *Staphylococcus aureus, Bacillus cereus, Escherichia coli,* and *Aspergillus flavus* while stem extract gave low MIC values against *Bacillus cereus* and *Streptococcus pneumoniae* (60). Sharma *et al.,* was studied the *in vitro* Some Himalayan medicinal plants and cultivated ornamental species have antifungal properties. *Berberis aristata* root extracts were tested for antifungal efficacy against 12 different fungal pathogens (61).

Saied *et al.,* investigated the phytochemical studies of Berberis aristata was used to isolate four alkaloids for the first time, including pakistanine (1), 1-O-methylpakistanine (2), pseudopalmatine chloride (3), and pseudoberberine chloride (4) (62). Katiyar *et al.,* (2006) isolated and characterized *Berberis aristata* DC produces lanost-5-en-3-ol heartwood. Their structural elucidated were done by IR, 1HNMR, 13CNMR, and +ve ion FAB MS were used to analyse spectral data (63).

Jian-Dong, was reported that the Berberine from *Berberis aristata* is used in Chinese medicine as a potent cholesterol-lowering agent. *Berberis aristata*, lowered cholesterol, serum LDL, and triglycerides and had a mechanism of action different from that of commercially used statins. Berberine was found to stabilize the mRNA of the LDL receptor after transcription while statins increases inhibition of the enzyme HMG-CoA reductase initiates the expression of LDL receptors in the liver during the pretranscription phase (64). Rajput *et al.,* was reported Berberis *aristata* has anti-inflammatory properties in rat pedal oedema caused by carrageenan. Aqueous and alcoholic extracts of this plant showed Significant anti-inflammatory activity on acute inflammatory processes, comparable to standard drug diclofenac sodium in terms of activity at therapeutic doses (65). Janbaz and Gilani, were Berberine was tested for its ability to prevent and treat acetaminophen and carbon tetra chloride (CCl4)-induced hepatotoxicity in rats. The use of three oral doses of berberine, 4 mg/kg every 6 hours, reduced acetaminophen-induced hepatic damage but had no effect on CCl4-induced hepatotoxicity, suggesting a selective curative mechanism against acetaminophen. Pretreatment with a single oral dose of berberine 4 mg/kg also increased strychnine (0.3 mg/kg, i.p.) induced toxicity and prolonged the pentobarbital (60 mg/kg, i.p.) induced sleeping time. Berberine's inhibitory effect on hepatic microsomal drug metabolising enzymes, cytochrome P450s CYPs, was discovered (44) (26). Gilani and Janbaz, were screened on paracetamol and CCl4 induced hepatotoxicity, *Berberis aristata* fruit extract has both preventive and curative potential. Post-treatment with three doses of *Berberis aristata* extract (500 mg/kg, 6h) reduced acetaminophen-induced hepatic damage ($p<0.01$), but did not affect CCl4-induced hepatotoxicity ($p>0.05$). *Berberis aristata* extract (500 mg/kg) significantly increased pentobarbital (75 mg/kg)-induced sleeping time and strychnine-induced lethality in mice, indicating an inhibitory effect on hepatic microsomal drug metabolising enzymes (MDME) (25).

PHYTOCHEMISTRY

Berberis aristata produces bis isoquinoline and protoberberine alkaloids (66). The main type of phytoconstituents present in Berberis *aristata* are alkaloids, flavonoids etc. Barberine, oxyberberine, berbamine, Aromoline, Karachine, Palmatine, and Oxyacanthine, as well as taxilamine, are among the compounds found in the plant (67). Four alkaloids were also isolated from *Berberis aristata*, namely pakistanine, 1-O methyl pakistanine, pseudopalmatine chloride and pseudoberberine chloride (68).

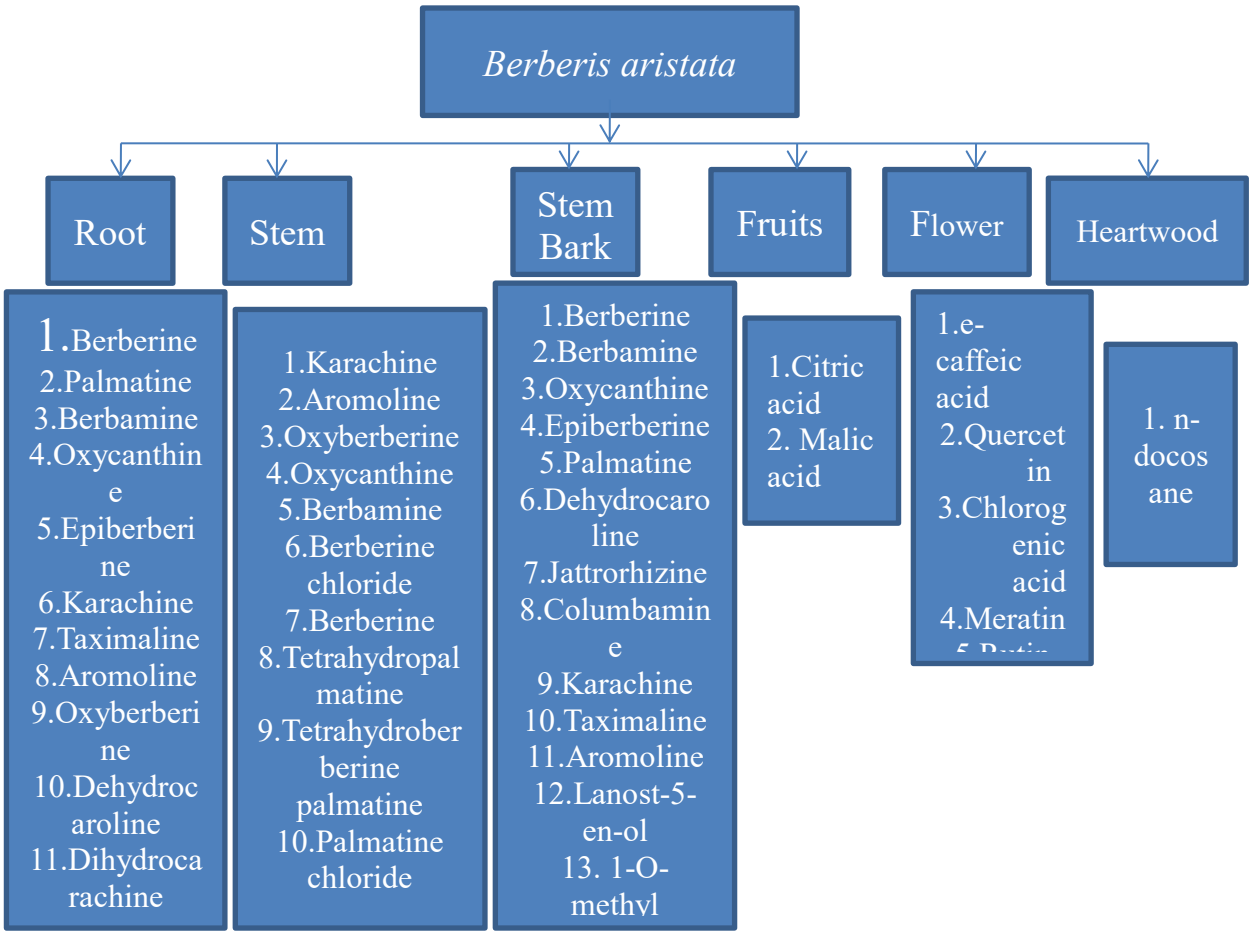


Figure 2: CHIEF PHYTOCONSTITUENTS OF *BERBERIS ARISTATA* DC.

ROOT- Berbamine, oxycanthine, epiberberine, palmatine, dehydrocaroline, jatrorrhizine, and columbamine are organic compounds found in the roots of *Berberis aristata*. Berberine, with a yield of 2.23 percent, is the most abundant bioactive found in *Berberis aristata* root, followed by palmatine (69). The root of the *Berberis aristata* also contains dihyrocarachine, karachine, taximaline, aromoline, oxyberberine (70), umballiatine and hydrastine (71).

ROOT BARK- *Berberis aristata* root bark contains karachine, a protoberberine organic compound, as well as aromoline, oxyberberine, oxyacanthine, berbamine, and berberine chloride (72). Berberine, tetrahydropalmatine, tetrahydroberberine palmatine, palmatine

chloride, and palmatine chloride or their mixtures were obtained from an alcoholic extraction of the fine bark after it had been concentrated and filtered (73).

STEM- Berberine, berbamine, oxycanthine, epiberberine, palmatine, dehydrocaroline, jatrorrhizine, columbamine, dihydrokarachine, karachine, taximaline, oxyberberine, aromaline, pakistanine, 1-o-methyl pakistanine, pseudo palmatine chloride, pseudo berberine chloride, pseudo berberine chloride, and lanost (74).

LEAVES- The main alkaloid in this plant part is berberine (8). Methanol extracts of *Berberis aristata* leaves, stalks and roots also contains the same. Active compounds like alkaloids, reducing sugars, hormones, flavonoids, terpenoids, glycosides, and saponins were discovered, but tannins were not (75).

FLOWERS- *Berberis aristata* flowers contain e-caffeic acid and chlorogenic acid (76). Quercetin, meratin, and rutin are polyphenolic flavonoids found in the flowers of *Berberis aristata* (77).

HEARTWOOD- The presence of n-docosane, a nursing open-chain organic compound, is revealed in an ethanol extract of *Berberis aristata* heartwood (78).

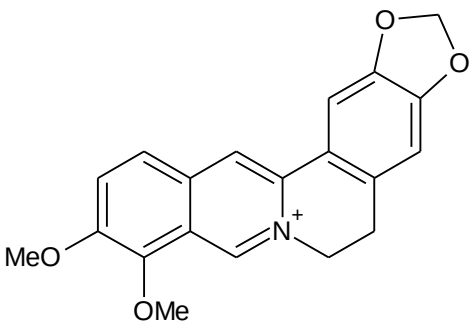
FRUITS- Citric acid, on the other hand, comes from fruit, as does malic acid (71).

RHIZOME- The plant's rhizome contains heavy metals like cadmium, lead, chromium, zinc, iron, and manganese (79).

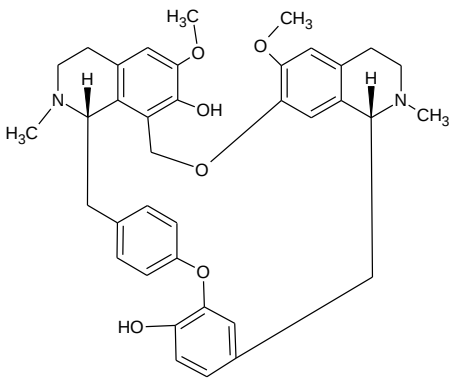
2.1.6 CHEMICAL CONSTITUENTS

Berberine, oxycanthine, berbamine, palmatine, oxyberberine, epiberberine, and jatrorrhizine are the main alkaloids found in the stem bark and root bark of *Berberis aristata* DC (80).

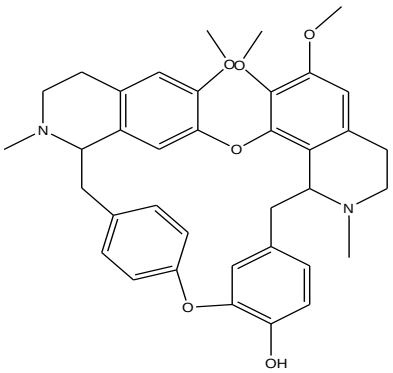
STRUCTURES OF SOME MAJOR PHYTOCONSTITUENTS OF *BERBERIS ARISTATA* DC.



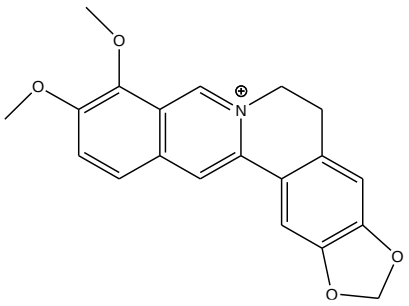
BERBERINE



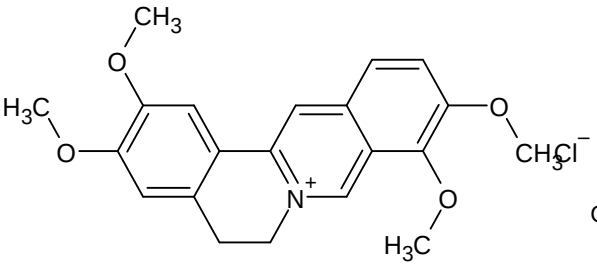
OXYCANTHINE



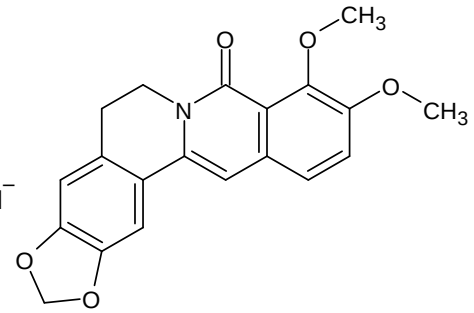
BERBAMINE



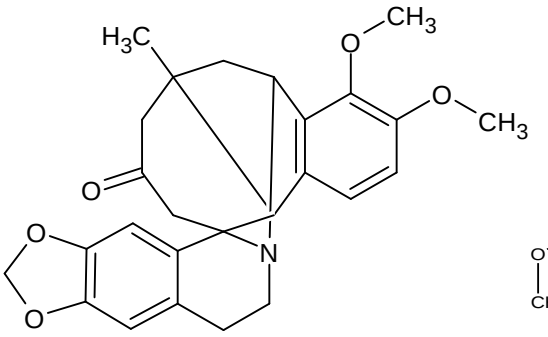
PALMATINE



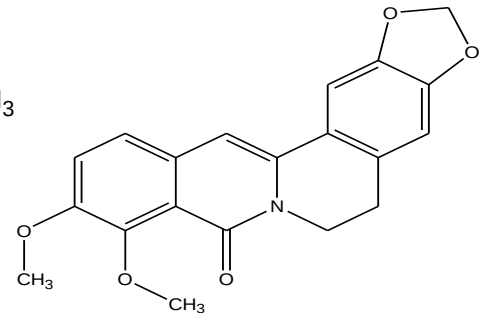
PALMATINE CHLORIDE



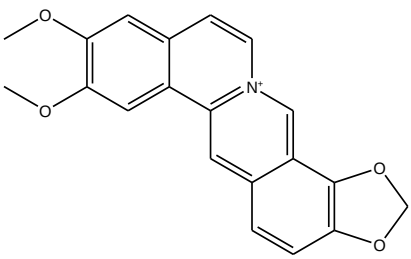
TETRAHYDROPALMATINE



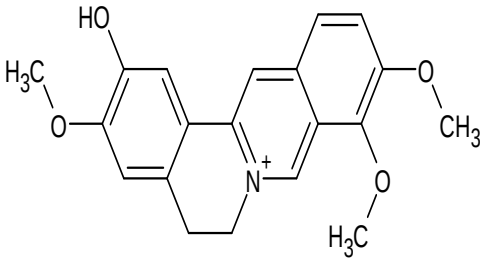
KARACHINE



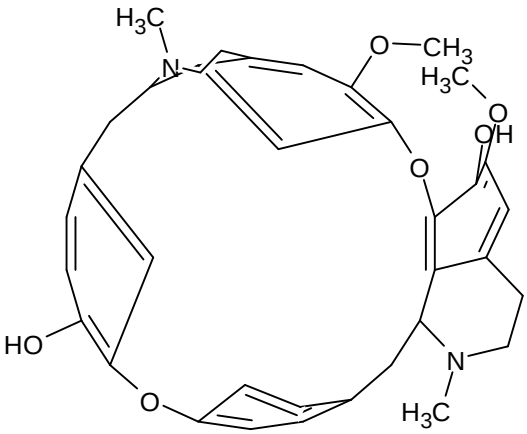
OXYBERBERINE



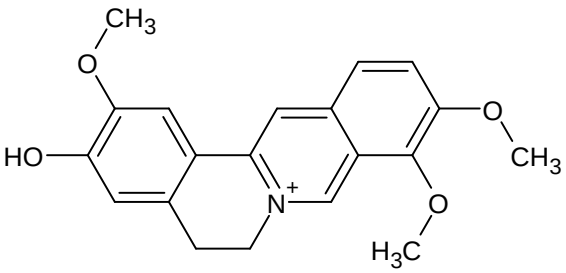
EPIBERBERINE



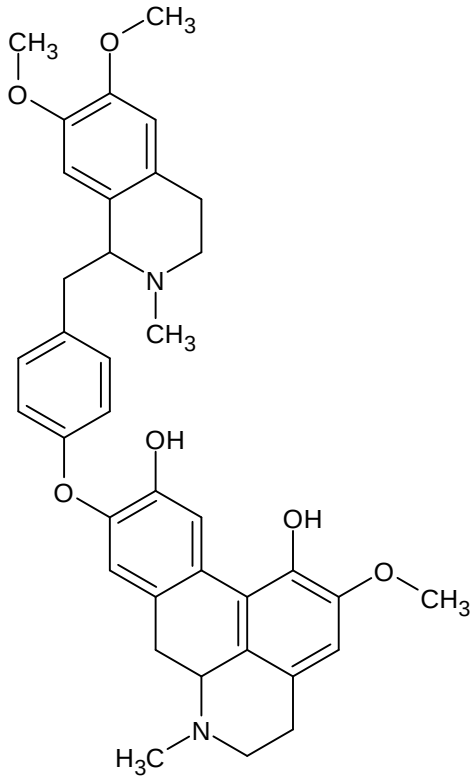
COLUMBAMINE



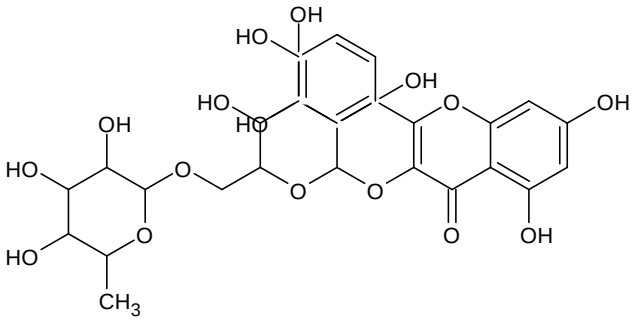
AROMOLINE



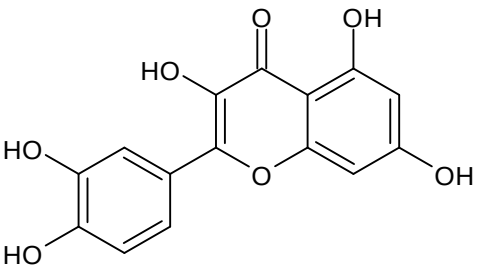
JATRORRHIZINE



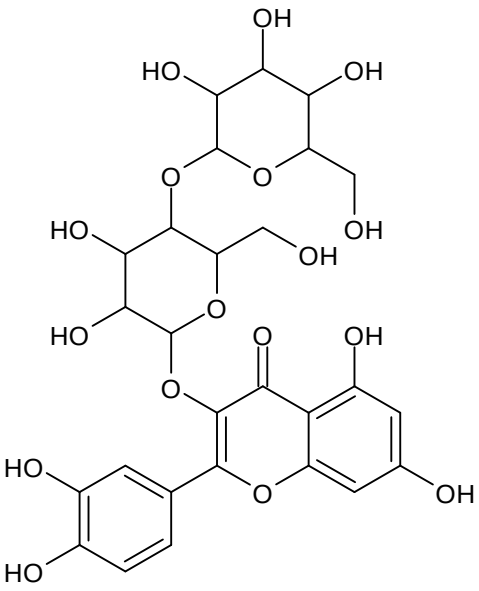
PAKISTANINE



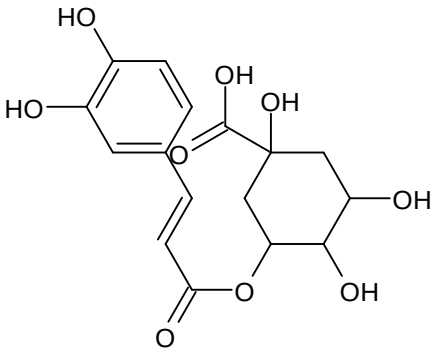
RUTIN



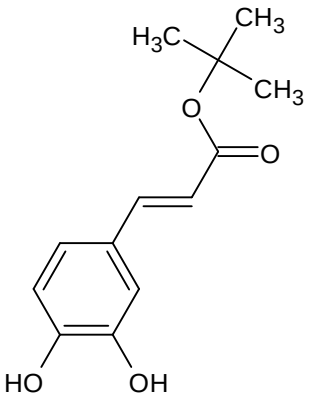
QUERCETIN



MERATIN



CHLOROGENIC ACID



E-CAFFEIC ACID

MEDICINAL PROPERTIES

The anticancer effect of *Berberis aristata* methanol extracts has been identified in some preliminary studies toward human hepatoma cells, L1210 mouse leukaemia cells and colon cancer cells that can be attributed to the inhibitory property of COX-II (81). In addition, the plant extracts exhibited important antioxidant activities (82). *Berberis aristata* aqueous-methanol extract, which has potent anti-osteoporosis efficacy and supports ethnic use in the treatment of postmenopausal osteoporosis, resulted in increased calcium and phosphorus levels in serum and a significant decrease in urine. It also has the ability to lower serum cholesterol, triglycerides, and low-density lipoprotein levels, as well as increase thrombin and fibrinogen period (83). The extract from the plant is used to treat diabetes and other ailments as an anti-hepatopathic in Sikkim and Darjeeling, India (84).

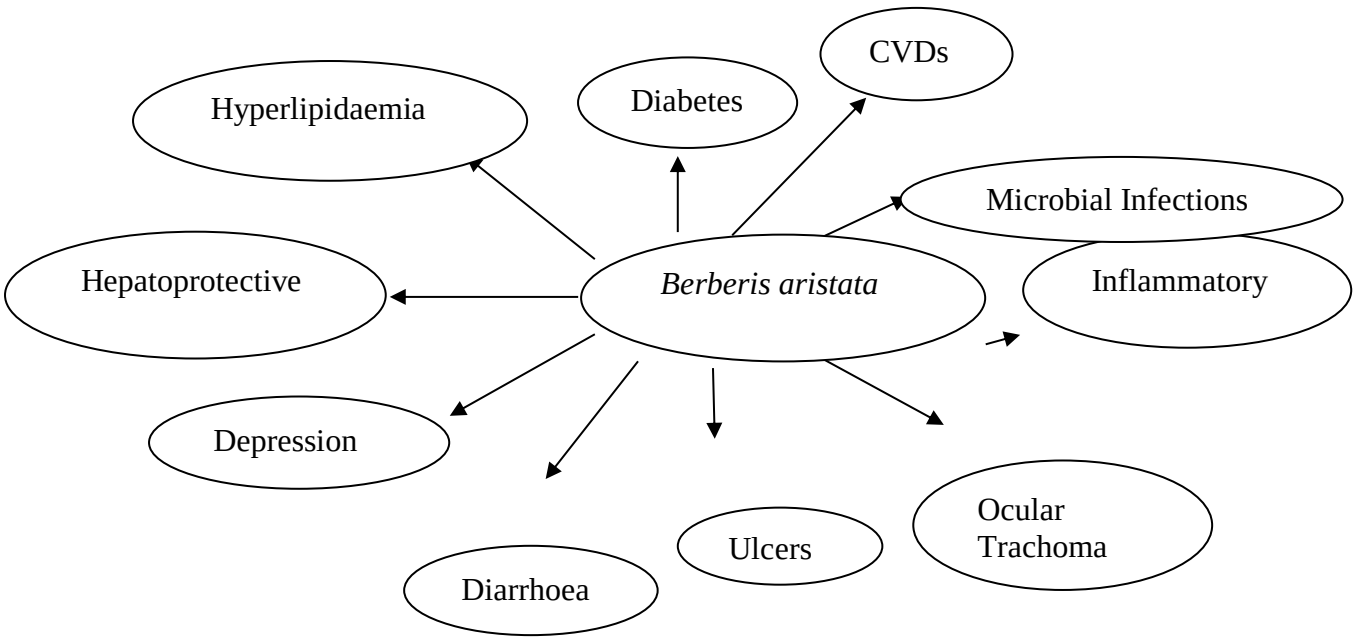


Figure 3: ROLE OF *BERBERIS ARISTATA* DC IN THE MANAGEMENT OF VARIOUS AILMENTS

ROOTS- Ethanol extract of root of *Berberis aristata* reveals antifungal activity (85). As an ophthalmic application, the roots' dry extract is used. It is also an unusual drug in the case of sun-blindness. In intermittent and remitting fevers, the bark of its root is a beneficial medication. It has no detrimental effect on the liver, intestine, brain tissues, and also on the hearing organs (86). In rabbits with endotoxin-induced uveitis, topical instillation of *Berberis aristata* aqueous extract had a good anti-inflammatory effect. In rabbits, anterior uveitis was caused by intravitreal *Escherichia coli* lipopolysaccharide injection following pretreatment with aqueous extracts (87). Berberine from the roots and barks of *Berberis aristata* inhibited the secretory reaction of heat labile enterotoxins of Vibrio cholera and Escherichia coli in the rabbit ligated intestinal loop model and infant mouse assay (88).

ROOT BARK-Antiplasmodial potency of *Berberis aristata* root bark showed significant schizontal maturation that has been found to exert inhibition of isolated *P. berghei in vitro* (89). Shri Padmavathi Mahila Viswavidyalayam Tirupati, an Indian Women's University, conducted a study to determine the efficacy of ayurvedic medicine containing *Berberis aristata*. They developed a study to provide clinical evidence for *Berberis aristata* use in the treatment of urinary problems caused by cisplatin, an anti-cancer chemotherapy medication. Cisplatin has been related to nephrotoxicity, or renal disease or dysfunction. The antioxidant properties of the decoction of *Berberis aristata* root bark reversed the side effects of cisplatin, according to the researchers (90).

STEM- *Berberis aristata* DC is also commonly prescribed to children as a cooling laxative. The stem is said to have laxative and diaphoretic properties, as well as being beneficial for rheumatism. (67). A methanol extract of the stem was found to have a significant antioxidant potential. *Berberis aristata* extracts contain a significant amount of phenols and flavonoids, both of which have strong free radical scavenging properties (91).

STEM BARK- Stem bark decoction of *Berberis aristata* plant demonstrate significant defence against nephrotoxicity caused by cisplatin (92).

LEAF- In animal models, aqueous dry extract of *Berberis aristata* leaves showed effective antidiarrheal activity (93).

FRUITS- Crude extract obtained from *Berberis aristata* (shoot and fruit) demonstrated effective defense of paracetamol and carbon tetrachloride (CCl_4) mediated liver toxicity and also suggested that the extract's hepatoprotective activity is partly attributable to inhibition of the metabolizing enzyme of the microsomal compounds (25). In earlier studies the folklore usage of this plant in hepatic harm has a clinically justified foundation, about *Berberis aristata* fruits and leaves have a blunt extract displayed hepatoprotection in the chemical induced hepatotoxicity in animal models (26). Its ripe fruits have hypochlolestrolemic activity and are used as a mild laxative in babies (94). The fruit extract of the *Berberis aristata* plant has a favorable inotropic effect (95). Several biochemical test was carried out on healthy rabbits to assess the plant's cardiovascular properties. The levels of serum cholesterol, triglycerides, and

low-density lipoprotein all fell significantly, whereas fibrinogen and thrombin levels were wincreased (95).

ANTI- *HELICOBACTOR PYLORI* ACTIVITY

Berberine isolated from the stems of *Berberis aristata* methanol extract showed strong anti *Helicobactor pylori* (*H. pylori*) activity in one of the latest research study. This anti-*H. pylori* activity may also be useful in treating ulcers caused by *H. pylori* (96).

ANTIDIABETICS ACTIVITY

Berberis aristata has significant anti-diabetic activity in alloxan-stimulated diabetic rats in a portion subordinate way. In either case, Its use as a legends drug in the treatment of diabetes was backed up by the findings (97). At different portion levels (100 and 200 mg/kg body weight), ethanol concentrates of Berberis aristata root reduced blood glucose levels in both normal and diabetic rats. The previous study's findings were promising, and they were similar to metformin, a commonly used diabetes medication. It is accounted for the hypoglycemic activity of the concentrate of home-grown plants in diabetic rats might be conceivable through insulinomimictic activity or by preventing cell death or potentially allowing recovery of partially pulverised cells or by other system, for example, stimulation of glucose take up by fringe tissue, hindrance of endogenous glucose creation or enactment of gluconeogenesis in liver and muscle cells. One of berberine's functions is to upgrade intracellular calcium. Increased intracellular calcium improves degranulation and insulin delivery from pancreatic -cells. One of the constituents, berberine, has been shown to inhibit the chemical phosphodiesterase from raising cyclic AMP (cAMP) levels. An increase in cAMP levels has also been linked to an increase in insulin secretion. The hypoglycemic/antidiabetic action of berberine may be based on these activities. More comprehensive synthetic and pharmacological studies are needed to determine the specific component of Berberis aristata root's hypoglycemic effect (98).

MISCELLANEOUS ROLE OF BERBERINE (ISOQUINOLONE ALKALOID)

The key mechanism of berberine (Bioactive phytoconstituent of *Berberis aristata* DC.) is responsible in part because of its anti-inflammatory and anti-diabetic properties. Berberine activates and inhibits the enzyme Adenosine Monophosphate Activated Protein Kinase (AMPK), Tyrosine Phosphatase 1B (PTP1B). With the successive activation of AMPK, the absorption of glucose into cells is doubled, with enhanced sensitivity to insulin, encouraging functional regeneration and glucose reduction of β-cells fabrication in the liver (99). Berberine showed that it regulates the metabolism of glucose and lipids *in vivo* and *in vitro* as well. A separate meta-analysis also showed that a comparable therapeutic effect of berberine on type 2 DM, hyperlipidaemia and metformin-negative hypertension. Berberine therapy substantially reduced triglycerides, cholesterol, LDL, elevated levels of HbA1c and increased expression of insulin receptors. Berberine, compared to metformin, demonstrated an identical effects on the regulation of the metabolism of glucose, such as HbA1c, FBG, PBG, post-prandial insulin and

fasting insulin. The berberine functions as metformin for the treatment of Polycystic Ovary Syndrome (PCOS) and resistance to insulin. However, in the lipid control berberine activity was higher than metformin metabolism (100). In obese PCOS women, berberine has enhanced several clinical, metabolic and reproductive features. The primary effects could be related to improved insulin sensitivity and a reduction in hyperandrogenemia. Changes in body composition and dyslipidaemia also seems to have greater effects (101). In preclinical studies, berberine was found to significantly inhibit 20-methylcholanthrene or N-nitrosodiethylamine-induced carcinogenesis in small animals (102).

Berberine-rich plants have also been used as an astringent to lighten skin tone. The mucous membranes of the upper respiratory tract and the gastrointestinal system also showed promising results, as well as their effects on the underlying illnesses (103). The earlier findings also indicated that berberine has significant anxiolytic properties, and that its function is linked to GABAergic neurotransmission. But the exact constituent or combination of constituents responsible for berberine's anxiolytic effect was not clearly explored and demonstrated yet (104). Berberine has contributed to reducing cardiac damage in an autoimmune myocarditis model in the lab by restricting the increase in anti-cardiac antibodies to myosin, inhibiting the differentiation of Th1 and Th2 cells, and modulating the activity of certain STATs, all of which are important in the pathogenesis of myocarditis. Experimental autoimmune neuritis is a model of the Guillain-Barre syndrome in animals that is identical to the human condition. An autoimmune damage to the peripheral nervous system characterised this neurologic condition. Berberine has shown to have potent immunomodulatory activity by inhibiting lymphocyte proliferation (especially CD4) and decreasing pro-inflammatory cytokines (IL-6 and TNF) (105).

CLINICAL STUDIES

Several clinical trials were conducted by using berberine in different studies. In one clinical trial of berberine was conducted using 356 cholera patients 264 patients were treated with chloramphenicol, and the results were compared. Berberine was found to be effective in patients who were bacteriologically positive as well as those who were bacteriologically negative. It decreased the volume and duration of diarrhoea, as well as the mortality rate, intravenous fluid intake, and convalescence time. Berberine was discovered to be superior to chloramphenicol in these areas (27).

In another trial 25 giardiasisBerberine was given at a dose of 5 mg/kg/day for six days to nine patients, and the results were compared to metronidazole given at a dose of 10 mg/kg/day for six days. For six days, 25 patients were given vitamin B complex syrup as a control group. Clinical symptoms were relieved in 12 patients who received berberine, 3 patients who received metronidazole, and 3 patients who received vitamin B complex. In 17 patients who received metronidazole and 5 patients who received B complex, the stools were giardia-free (106). Berberine was found to be effective in the treatment of gastroenteritis in 50 children in another trial. It's also an effective anti-diarrhea agent that can be given to children in the form of a palatable suspension. Berberine was not found to be toxic in any way (26).

CONCLUSION

The demand of herbal products are increasing steadily in the last three decades. Now a days herbal medicines are being used extensively in the management of different diseases like congestive heart failure, angina pectoris, diabetes, nephroprotective, diarrhoea and potential chemoprotective. The extracts from plants and herbs of various medicinal values are referred to as herbal medicinal products. Plants and their products have been used since the dawn of time for humanity and government assistance. Plants were a significant source of cures and preventions in the days when the pharmaceutical field was not properly grown.

Berberis aristata DC. is also known as daruharidra, daru haldi, For a long time, Indian barberry, tree turmeric, and chitra, a well-known plant, have been used in various medicinal systems such as Ayurveda, Homeopathy, Unani, Chinese, and Allopathy. It's a spiny, hard, yellowish herb from the Berberidaceae family. This plant possesses significant medicinal value and needs more research and studies to develop more and more herbal and ayurvedic formulations containing active phytoconstituents of *Berberis aristata* DC. Although the results from this review are quite promising for the use of *Berberis aristata* plant to treat numerous diseases and disorders. Berberine is a plant alkaloid found in the roots, rhizomes, and stem bark. As per clinical and experimental studies, the chemical constituents of the plant like berberine possess various pharmacological properties like anti-diabetic, anti-microbial, anti-cancer, antipyretic, hepatoprotective, ophthalmic and cardiotonic activity. In addition, berberine was found to have a beneficial effect in a number of clinical and preclinical studies, including metabolic, neurological, and cardiological issues. In any case, the findings of this review paper support the use of Berberis aristata plant as a legends medication for the treatment of a variety of ailments. Further investigation into its maximum capacity in terms of socioeconomic system benefits is expected.

GLOSSARY OF TERMS, ABBREVIATIONS, SYMBOLS

et al.,	and others
p	Probability
mg/kg	milligram per kilogram
MaxEnt	Maximum entroys
GARP	Genetic Algorithm for Rule-set Production
HPLC	High Performance Liquid Chromatography
%	Percentage
w/w	weight by weight
ITS	Internal Transcribed Spacer region
DNA	Deoxy Ribo Nucleic Acid
rRNA	ribosomal Ribo nucleic Acid

HDL	High Density Lipoprotein
DM	Diabetes Mellitus
STZ	Streptozotocin
TNF	Tumor Necrotic Factor
ml	mililiter
MIC	Minimum Inhibitory Concentration
IR	Infra Red
HNMR	Proton Nuclear Magnetic Resonance
CNMR	Carbon Nuclear Magnetic Resonance
FAB MS	Fast atom bombardment Mass Spectrometry
LDL	Low Density Lipoprotein
HMG-CoA	3-hydroxy-3-methylglutaryl-CoA
CCl4	Carbon Tetra Chloride
i.p.	Intra Peritoneal
h	Hour
CVDs	Cardio Vascular Disorders
COX-II	Cyclooxygenase-II
H. pylori	*Helicobacter pylori*
AMP	Adenosine Mono Phosphate
AMPK	Adenosine Monophosphate Activated Protein Kinase
HbA1c	Glycated haemoglobin
PCOS	Polycystic ovary syndrome
FBG	Fast atom bombardment
PBG	Porphobilinogen
GABA	Gamma Amino Butyric Acid
Th1	T helper type 1
Th2	T helper type 2
IL-6	Interleukin-6
TNF α	Tumor Necrosis Factor- Alpha
CD_4	Cluster of differentiation 4

DECLARATION OF COMPETING INTEREST

All authors hereby declare that there is no financial conflict of interest.

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