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Unveiling the Medicinal Potential of *Berberis aristata*: A Traditional Native Plant of Uttarakhand

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ABSTRACT

Since ancient times, indigenous medicinal system of India has included herbal plants as a traditional source of medicine. India is known as a rich repository of medicinal plants, and one such plant is *Berberis aristata* which belongs to the family *Berberidaceae* which grows mainly in the sub-Himalayan region and the Nilgiri Hills of Southern India. *Berberis aristata* is used as traditional medicine in various communities to treat eye disorders, piles, osteoporosis, joint pain, skin diseases, malaria, diarrhoea, dysentery, fever, allergic conditions, ophthalmia, metabolic disorders and during menopause. The plant contains various phytochemical constituents, mainly alkaloids like berberine, oxyberberine, berbamine, aromoline, karachine, palmatine, oxyacanthine, and taxilamine. Berberine, the major alkaloid, is found in roots, stem bark, rhizomes, and leaves, with the highest concentration in the roots. Various pharmacological properties of *Berberis aristata* have been reported such as immunomodulatory, anti-inflammatory, antioxidant, anti-viral, anti-cancer, anti-microbial, hepatoprotective, nephroprotective and improved reproductive health. This review aims to highlight the phytochemistry and pharmacological properties of *Berberis aristata* which will be helpful to give insights on medicinal utility of the plant. Although more elaborated clinical trials and studies at molecular level will be required to fully understand and validate these properties.

Keywords: *Berberis aristata*, Berberine, Berberidaceae, Herbal medicine, Pharmacology, Phytochemistry.

INTRODUCTION

Long before the pre-historic period different plants have been used for their medicinal properties. Evidence of using herbs or herbal plants as source of medicine exists in different cultures like by Indian vaid, Unani hakims, European people, Mediterranean people *etc.* for over 4000 years. The various reasons for shifting from the allopathic medicine towards plant material as source of medicine include side effects of different synthetic drugs, development of drug resistance strains of different microorganisms, extortionate cost of treatment, inadequate drug supply, rising population and many more. Thus, since ancient times, the indigenous medicinal system of India has included herbal plants as a traditional source of medicine as India is known as a rich repository of medicinal plants. One such plant is *Berberis aristata* which belongs to the family *Berberidaceae* which was established in the early 1789 by A.L. Jussieu [1]. It is a hard, spinous and glabrous yellowish evergreen herb which is majorly found growing in sub-Himalayan region and Nilgiri Hills of Southern India. It has a peak height of 3-5 metres and is commonly named as Indian barberry, Chitra, Daru Haldi, Daruharidra and Tree turmeric. The bark of the plant is fully carpeted with thorns and 5-8 leaf tufts with pinnate venation. The upper surface of leaves is darkish green and lower surface of leaves are mild in colour. The stem and root parts of the plant *Berberis aristata* is sold as Daruharidra in India [2]. *Berberis aristata* is used as a traditional medicine in different communities. In Bhotiya communities of Himalayan parts of India the root decoction of this plant is used to cure eye diseases [3]. Traditionally, the aqueous methanolic extract of this plant have revealed potential to treat osteoporosis, joint pain and menopause [4]. In some rural parts of India, polyherbal drugs containing *Berberis aristata* is used to cure piles [5]. In Malani tribal communities of Himachal Pradesh, it is used in the treatment of disorders such as skin diseases, jaundice, malaria and piles [6]. The plant extract has been reported to be used as anti-hepatopathic and anti-diabetic in parts of Sikkim and Darjeeling, India [7]. The leaf and fruit juices are reported to possess anti-diarrhoeal and anti-dysenteric properties and decoction of root and bark is used in the management of jaundice and fever [8]. It is reported to be used to treat allergic conditions, ophthalmia, metabolic disorders and as a laxative [9]. The plant is widely used in the treatment of urinary issues, skin disorders and pores, syphilis, rheumatism, diarrhoea and it is widely used as a tonic, demulcent, diaphoretic and diuretic [10].

The Himalayan region including Uttarakhand has a great variety of *Berberis* species (about 29 species) followed by Jammu and Kashmir (about 25 species), Himachal Pradesh (about 23 species), and Sikkim (16 species) [11]. Thus, from the wide range of the pharmacological research it is clear that the Indian barberry possess various properties such as antioxidant, anti-inflammatory, anti-coagulant, anti-diabetic, anti-microbial, anti-ulcer, anti-bacterial and anti-cancer [12]. This review provides a comprehensive overview of the medicinal significance of *Berberis aristata* as a valuable medicinal plant with a rich heritage and significant potential for treating a variety of health conditions, thereby supporting the growing interest in herbal therapy as an alternative to conventional medicine.

Phytochemical analysis of the plant

Properties of the plant *Berberis aristata* also known as *Daruharidra* are in close resemblance to those of *Curcuma longa* (Turmeric) also known as *Haridra*, thus both the plants are together mentioned as *Haridra dvaya*, meaning two *Haridras* viz. *Haridra* and *Daruharidra*. Three major types of alkaloids are present in *Berberis aristata* which includes bisbenzylisoquinoline, isoquinoline and protoberberine [13]. *Berberis aristata* is enriched with various phytochemical constituents which mainly constitute of alkaloids. The various phytochemicals present in plant of *Berberis* are berberine, oxyberberine, berbamine, aromoline, karachine, palmatine, oxyacanthine, taxilamine, protoberberine and bis isoquinoline [14]. Root of the plant contains alkaloids such as berbamine, Berberine, oxycanthine, epiberberine, palmatine, dehydrocaroline, jatrorrhizine, karachine dihydrokarachine, taximaline, oxyberberine, aromoline and columbamine [15]. Different polyphenolic alkaloids are present in the flower of the plant like meratin, rutin, quercetin and various acids like chlorogenic acid, E-caffeic acid etc. [16]. The root bark of the plant contains karachine which is a protoberberine alkaloid [17]. The major alkaloid present in *Berberis aristata* is berberine which possess very important pharmacological activities and may be present either in roots, stem bark, rhizomes or leaves followed by palamatine. Berberine (C₂₀H₁₈NO₄) or benzyl tetrahydroxy quinoline is a pale-yellow quaternary ammonium salt (5,6-dihydrodibenzo[a,g]quinolizinium derivative) which is obtained from protoberberine group of isoquinoline alkaloids extracted from *Berberis* and it is known to possess different pharmacological activities such as immunomodulatory, anti-inflammatory, anti-microbial, hepatoprotective, analgesic, antipyretic and anti-depressant activity [18]. The biosynthesis of Berberine is shown in Figure 1.

Table 1: Phytochemistry of *Berberis aristata*

Phytoconstituents	Part of plant	Reference
(Protoberberine alkaloids): Berbamine, berberine, aromoline, karachine, palmatine, oxyberberine, jatrorrhizine, oxycanthine, epiberberine, and dehydrocaroline	Roots	[72]
Berberine phenoxide, Ktoberberine benzoate A, Ktoberberine benzoate B	Methanolic extract of <i>Berberis aristata</i> stem bark	
Pakistanine, 1-O-methyl pakistanine, pseudopalmatine chloride, pseudoberberine chloride, isoquinoline and secobisbenzylisoquinoline	<i>Berberis aristata</i>	[73]
Bisbenzylisoquinoline alkaloid (Berbamine)	<i>Berberis aristata</i> roots	[74]
Oxyacanthine and Aromoline	Root and bark of <i>Berberis aristata</i> respectively	[75]
Phytosterol (sitosterolis) Stigmast-5-en-3-ol	Ethanolic extract of <i>Berberis aristata</i>	[76]
Flavonoids: E-caffeic acid, quercetin, meratin, chlorogenic acid and rutin	Flowers of <i>Berberis aristata</i>	[77]
Alkaloids, Steroids, Coumarins, Flavonoids, Terpenoids, Tanins, Glycosides, Saponins, Acids	<i>Berberis aristata</i>	[78]

Different pharmacological activities of the plant

Berberis aristata is an important medicinal plant and is officially recorded in Ayurvedic & Siddha Pharmacopoeia of India due to its

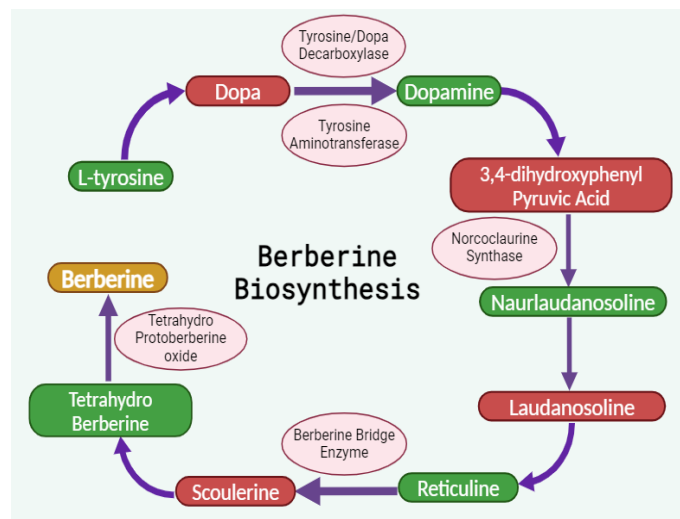


Figure 1: Berberine biosynthesis

HPTLC and spectrophotometric methods were used for detection and quantification of berberine and it was found that root part of the plant is more enriched with berberine as compared to the bark [19]. When the micronutrients of the plant were studied, it was found that rhizome of the plant is rich in different heavy metals and micronutrients such as manganese, iron, zinc, chromium, lead, cadmium etc. [20]. HPLC analysis of hydroalcoholic extract of *Berberis aristata* and total berberine content was found to be 6.7% w/w of dry extract [21]. The HPLC chromatogram indicated presence of berberine chloride as the main component and the other components were karachine, aromoline, oxyberberine, oxyacanthine and berbamine in the crude ethanolic extract of the *Berberis aristata* roots [22]. When the LCMS Fragmentation Profile of hydro-ethanolic extract of *Berberis aristata* was performed, it showed presence of different alkaloids namely, Berbamine, Berberine, Jatrorrhizine, Reticuline, Palmatine and Piperazine [23]. GCMS analysis of aril aqueous extract of *Berberis aristata* and two antioxidant compounds were extracted and recorded viz. flavone (5,7-dihydroxy-3-phenylchromen-4-one) and phytol. In detail the compounds found in the chromatogram included 2(5H)-Furanone, Lilac aldehyde C, Davana ether, 2-Propenal, Lilac alcohol B, Alpha-D-Glucopyranose, n-Hexadecanoic acid, Naphtho[2,1-b]furan-2,8-dione, Phenol,3-pentadecyl-, 5-Hepten-3-one and 1-Naphthalenemethanol [12]. The phytochemistry of *Berberis aristata* is presented in Table 1.

various pharmacological properties which are mentioned in the text below and represented in Figure 2.

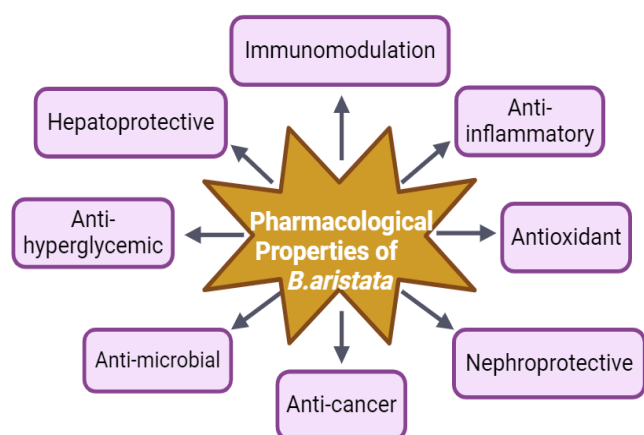


Figure 2: Pharmacological Properties of *Berberis aristata*

Immunomodulation properties

When the mitogen stimulated lymphocytes were treated with alcoholic and aqueous extract of *Berberis* species it was found that the alcoholic and aqueous extract of *Berberis* spp. suppress the proliferation of T-cells and enhance the expansion of B-cells. It is also found that the constituents present in *Berberis* spp. can also change the pattern of cytokine production in lymphocytes for e.g., it can reduce the release of IFN- γ which may contribute in suppression of T-cell expansion. There was increase in the levels of IL-4, IL-10 and TGF- β [24]. The immunomodulatory action of berberine is due to its interaction with different immune cells like macrophages, T cells, B cells, mast cells, dendritic cells, epithelial cells, keratinocytes etc. [25]. Also, evidences are available that berberine can act as an epigenetic regulator by influencing histone acetylation and methylation [26]. The constituents of the *Berberis* spp. are able to promote STAT4 degradation which leads to significant reduction in IFN- γ T cells [27]. In a study, it was found that pre-treatment with berberine was able to inhibit the LPS induced activation of NF-KB/MAPK signalling pathway and thus inhibiting the production of inflammatory factors, hence, it could be an effective product from natural plant source like *Berberis aristata* in preventing inflammatory diseases caused by LPS [28]. In another study, it was found that berberine showed anti-inflammatory activity in primary splenocytes of mouse treated with or without LPS by increasing the relative expression of IL-4/IL-2 which shifts the Th1/Th2 balance toward Th2 polarization [29]. It is also hypothesized that berberine can cause modulation of cytokine expression via transcriptional and post-transcriptional regulation in Th1 and Th2 cells [30]. In DMBA induced mouse model of tumour, pure berberine @ 30 mg/kg and *Berberis aristata* extract @ 400 mg/kg showed cytoplasmic positivity for TNF- α in the ductal epithelial cells [31].

Anti-inflammatory properties

Inflammation is one of the major types of immune response that plays a very important role in innate and acquired immune system for protection from external harmful stimulus [32]. The aqueous extract of roots of *Berberis aristata*, when tested in rats at the rate of 500-1000 mg/kg was found to possess anti-inflammatory activity [33]. When a NOD mouse model was used to study the effect of *Berberis* spp. It was found that there was a decrease in the expression ratio of Th1/Th2 cytokines and reduction in the levels of proinflammatory cytokines [34]. Berberine alkaloid which is abundant in *Berberis aristata* is known to modulate and/or suppress inflammation through suppressing the production of TNF- α , IL-6 and MCP-1, down-regulating the expression of cyclooxygenase-2 (COX-2), reducing generation of PGE2 and formation of exudates, and inhibiting the expression of MMP-2 and MMP-9 through nuclear factor-kB (NF-kB) and mitogen-activated protein kinase (MAPK) signalling cascades [35]. The spleen of an adjuvant-induced arthritis model of rats was taken and naïve T-cells were isolated and when treated with berberine it significantly reduced the differentiation and survival of Th17 cells, in

a concentration-dependent manner, through down-regulating surface marker CD196 and transcription factor ROR γ t [36]. Berberine is also able to decrease the phosphorylation of STAT3 and expression of ROR γ t transcription factor during the differentiation of Th17 cells and down-regulate phosphorylation of STAT4 and STAT1 and expression of T-bet in differentiating Th1 cells [37]. When the splenic naïve T-cells of the adjuvant-induced arthritis model of rats were treated with berberine, a shift in differentiation of naïve CD4+ T cells into CD4+ Foxp3+ Treg cells was found, instead of Th17 cells, through activating AhR/CYP1A1/Foxp3 axis and by this way berberine can directly benefit the immune system by modulating naïve CD4+ T cells differentiation [38]. In a mouse model of inflammatory bowel disease berberine was able to reduce the production of TNF- α , IL-12, IL-6 and TGF- β in the matured dendritic cells and thus decreasing the population of Th1/Th17 cells in the mesenteric lymph nodes, and thus helping in reducing the colon inflammation in colitis-induced mice model [39].

Hydroalcoholic extract of *Berberis aristata* at the rate of 200 mg/kg was found to show anti-inflammatory effect on carrageenan-induced paw edema and cotton pellet-induced granuloma in rats. There was a significant reduction in the level of serum inflammatory cytokines viz. IL-6, IL-10, IL-1 β and TNF- α as compared to the control group. There was significant downregulation in the macrophage expression of different pro-inflammatory cytokines, IL-6, IL-1 β and upregulation of anti-inflammatory cytokine IL-10. Protein expression of proinflammatory receptor and TNF-R1 was also decreased along with decreased expression of pro-inflammatory mediator COX-2 [40]. Berberine led to significant reduction of IL-1, IL-1 β , IL-6, IL-12, TNF- α and IFN- γ in 5% dextran sulfate sodium (DSS) induced ulcerative colitis rat model. Berberine pre-treatment was able to induce the mRNA expression of IL-4 and IL-10, decreased the activity of iNOS (Inducible nitric oxide synthase), MPO (myeloperoxidase) and MDA (malondialdehyde) and increased in the level of SIgA [41]. Berberine obtained from *Berberis aristata* was used as a prepared formulation of berberine-loaded invasomal gel by the thin film hydration method which showed a significant analgesic and anti-arthritic activity in rat model. There was reduction in paw diameter, proinflammatory biomarkers such as IL-6, IL-10, and TNF- α in serum were normalized at the end of day 35 which were found to be increased in disease control group, and decrease in C-reactive protein in the berberine treated group [42]. When aqueous extract of bark of *Berberis aristata* at the dose rate of 400mg/kg was used in oxazolone sensitized dermatitis mice, there was suppression of ear thickness, significant reduction in the level of TNF- α , IL-6, and IL-1 β and increase in the content of GSH and superoxide dismutase in ear tissue homogenate [43].

Antioxidant properties

Oxidative stress is considered as the main source for the initiation and development of different diseases like chronic disorders, heart diseases, neurodegenerative diseases, cancer, autoimmune disorders, cataract etc. [44]. The polyherbal ethanolic extract of *Berberis aristata*, *Nigella sativa* and *Anethum sowa* at the rate of 250 μ g/ml have shown antioxidant effects in H₂O₂ assay, FRAP assay and ABTS assay with maximum inhibition rate of 82.56%, 83.77% and 87.5% respectively [45]. The aril aqueous extract of *Berberis aristata* showed DPPH radical scavenging activity of 99.29%, superoxide (O₂⁻) radical scavenging activity of 99.94%, total antioxidant activity of 99.83% and Ferric (Fe³⁺) reducing power activity of 99.81% [12]. Methanolic extract of *Berberis aristata* showed a significant DPPH radical scavenging activity, H₂O₂ radical scavenging activity and reduce the ferric ions in a concentration dependent manner [46]. In LPS-stimulated murine macrophages it was found that berberine is able to inhibit NO production and iNOS expression in a dose-dependent manner [47]. Polyherbal preparation containing *Berberis aristata* and the hydro-alcoholic extract of *Berberis aristata* showed a significant percent scavenging of DPPH, ABTS, superoxide radical and nitric oxide (NO) [48].

Berberis spp. inhibit the production of TBARS, lowered NO levels and inhibited the oxidation of DPPH along with increase in glutathione peroxidase and superoxide dismutase activities [49]. When diabetic rats were administered the root extract of *Berberis aristata* the activity of superoxide dismutase and catalase increased by 90.32% and 41.04%, respectively along with improvement in the levels of glutathione peroxidase, glutathione reductase, improved level of reduced glutathione. There was decrease in the levels of TBARS/MDA and protein carbonyl content by 48.53% and 30.13%, respectively [50]. When the heat stressed quails were treated with the root extract of *Berberis* spp. there was a decrease in the level of MDA by 25.5% and increase in the activity of superoxide dismutase, catalase and glutathione peroxidase by 23.5%, 35.4% and 55.7 %, respectively. The expression of hepatic NF-kB and HSP70 decreased whereas hepatic Nrf2 and HO-1 increased [51]. Hydroalcoholic extract of *Berberis aristata* at a dose rate of 100 and 200 mg/kg was able to successfully manage adjuvant induced arthritis model and was able to normalize the levels of endogenous antioxidants viz. glutathione, catalase and superoxide dismutase and decreased the level of prooxidants viz. TBARS and NO [21].

Anti-viral properties

In a Haemagglutination Inhibition test, it was found that *Berberis aristata* extract (upto a dilution of 62.5µg/ml) is able to combat *Paramyxoviridae* infection by interacting with the receptors present in the erythrocytes of *Gallus gallus domesticus* (host) in the microtiter plate. Vero cell lines which were having antiviral activity for 4HA viral concentration were used to perform the cytotoxicity assay and it was found that at a concentration of 62.5µg/ml of *Berberis aristata* extract the cell viability percentage was 92.8% and the higher cell viability percentage means less threat of toxicity [52].

Anti-cancer activity

Berberine which is the main phytochemical present in *Berberis* spp. has a proven anti-cancerous activity. Berberine was able to induce apoptosis in prostate cancer cell lines LNCaP (p53 expressing) and PC-3 (p53 lacking) by arresting cell cycle at G0/G1 phase and decreasing the levels of G0/G1 regulatory proteins in p53-dependent cell growth [53]. Berberine has a cytotoxic effect on murine melanoma cell line/ B16 and human tumour cell line/ U937 [54]. Berberine has also shown a selective cytotoxic effect on mitochondria in the melanoma cell line/ K1735-M2 [55]. Methanolic extract of the stem of the *Berberis aristata* is efficient in the treatment of human breast cancer cell line (MCF-7). It was able to inhibit the proliferation of the cancer cells, inhibition of DNA synthesis and prevention of metastasis due to activation of apoptosis pathways [56]. The methanolic extract of *Berberis aristata* at the rate of 400 mg/kg is able to show a significant antitumor activity and it provides additional benefits such as increasing the haemoglobin and RBC count towards normal. Berberine is able to inhibit the tumour cell target along with good proapoptotic and cell cycle arrest properties. In DMBA induced mouse model of tumour, berberine at the rate of 30 mg/kg and *Berberis aristata* extract at the rate of 400 mg/kg shows significant improvement in tumour pathology [51]. Berberine when used @ 0.5, 2.5 and 5 mg/kg body weight was effective for significantly reducing the incidence of tumor in carcinogenesis induced (by using 20-methylcholanthren or N-nitrosodiethylamine) mouse model. Berberine extract at a concentration of 200 µg/ml showed cytotoxicity activity as high as 32.81% against HeLa cell lines and the IC₅₀ of the tested sample of the Berberine extract against HeLa cell line was 118.97 µg/ml [12]. Berberine which is a major alkaloid present in the *Berberis aristata* plant has a planar quaternary and highly aromatic structure and has the ability to intercalate with the DNA and inhibition of protein biosynthesis, which may be responsible for the observed cytotoxic effect [57]. In a study, it was found that the polyherbal formulation containing *Berberis aristata* plant as a component have a high anticancer activity when assessed by using MTT assay against MCF 7 cells in a concentration dependent manner and the IC₅₀ value

of the herbal extract was found to be 181.97 µg [45]. Thus, the plant extract containing *Berberis aristata* have a potent anticancer activity.

Anti-microbial activity

The aril aqueous extract of *Berberis aristata* plant at a concentration of 500 µg when tested for the *in vitro* antibacterial action against some gram-positive microbes like *Bacillus subtilis*, *Micrococcus luteus*, *Staphylococcus aureus* and some gram-negative microbes like *Escherichia coli*, *Shigella flexneri* expressed a zone of inhibition of 10 mm, 12 mm, 27 mm, 24 mm and 22 mm respectively which was found significantly effective as that of standard drug [12]. The aqueous extract of root and bark of *Berberis aristata* plant exhibit a broad spectrum of anti-bacterial potential and zone of inhibition ranging from 12-25 mm. The most susceptible organism was *Klebsiella pneumoniae* followed by *Staphylococcus aureus*, MRSA, *Salmonella typhimurium* 2 and *Staphylococcus epidermidis*. *Enterococcus faecalis* was found to be the least sensitive organism, whereas *Klebsiella pneumoniae* 2, *Shigella flexneri* and *Salmonella typhimurium* 1 were found completely resistant to the extract of the plant. A cytotoxic effect was found against the L20B, RD and Hep2 cell lines with IC₅₀ ranging from 245 to 473 µg/mL [58]. Berberine isolated from methanolic extract of stem of *Berberis aristata* was found to be potentially active against drug resistant *Helicobacter pylori* infection which was isolated from gastroesophageal reflux disease patients with no previous antimicrobial therapy and this extract was found to be effective at a concentration of 0.000075 µg/ml. Thus, anti-*Helicobacter pylori* activity of the berberine alkaloid may be beneficial for the treatment of ulcer mediated by *Helicobacter pylori* [59].

Anti-plasmodial activity of the aqueous extract of roots of *Berberis aristata* was checked against *Plasmodium berghei* NK-65 (lethal rodent malarial parasite) infected BALB/c mice and it was found effective at higher doses and the IC₅₀ value for *in vitro* anti-plasmodial activity was found to be 40 µg/mL. In *in vivo* studies chemosuppression was found to be variable in a dose dependent manner with higher efficacy at lower doses and a dose rate of 350 mg/kg/day was found to have a 67.1% suppressive activity and 53.9% preventive activity and the mean survival period was improved to 12.8 days in treated mice versus 7.5 days in untreated mice [60]. *Berberis aristata* showed a 91.3% anti-adhesion activity, 96.06% anti-Quorum sensing and 51.3% anti-Biofilm formation against Carbapenem Resistant *Escherichia coli* and thus attenuating its virulence [61]. The extract of *Berberis aristata* significantly inhibited H₂O₂ induced haemolysis. Significant annihilation of bacterial infectivity was seen by inhibition of binding of Carbapenem Resistant *Escherichia coli* to RBC membrane receptors thus inhibiting hemagglutination at a concentration of 25 mg/mL. It also showed bactericidal activity by damaging the bacterial cell membrane as seen in flow cytometry analysis [23]. A polyherbal preparation containing *Berberis aristata* when given at a dose rate of 800mg/kg/day was used to treat induced amoebic liver abscess in golden hamsters with a cure rate of 73% [62].

Anti-hyperglycaemic effect

In alloxan induced diabetic rats the ethanolic root extract of *Berberis aristata* plant was able to significantly lower the body weight and significant reduction of fasting blood glucose level [50]. In alloxan induced diabetic rats the ethanolic root extract of *Berberis aristata* was found to possess significant anti-diabetic effect at the rate of 50 mg/kg and 100 mg/kg body weight with 63.01% and 66.27% reduction in blood glucose level respectively when compared to diabetic control. It was also found that in plant extract treated group the level of total cholesterol and triglycerides were in control at a significant level as compared to the diabetic control. The serum level of alanine aminotransferase and aspartate aminotransferase were found to be significantly reduced in the plant extract treated group. It was also found that the levels of marker of diabetic nephropathy viz. blood urea nitrogen and serum creatinine were in control after

administration of the extract [63]. The significant antidiabetic effect of the plant extract may be due to dipeptidyl peptidase-IV (DPP-IV) inhibition [64]. In a study conducted, methanolic extract of *Berberis aristata* was found to have DPP-IV inhibition activity with an IC₅₀ value of 14.46 µg/ml as compared to the standard Diprotin A which showed an IC₅₀ value of 1.543 µg/ml [65]. The aqueous extract of *Berberis aristata* showed hypoglycemic activity in different *in vitro* assays as it showed increased glucose adsorption and inhibitory effects on movement of glucose into external solution in amylolysis kinetic experimental model and increased glucose uptake by the yeast cells [66].

Reproductive Potential

When *Berberis aristata* extract was given at the rate of 500 mg/kg for a period of 45 days in high fat diet induced obesity related reproductive changes in female wistar rats, there was a significant decrease in total cholesterol, triglycerides, insulin, leptin, visceral fat and body weight and a significant increase in the levels of estradiol when compared to the untreated rats. There was significant improvement in the levels of oxidative stress biomarkers like malondialdehyde levels, reduced glutathione levels, NO and superoxide dismutase levels after treatment with the plant extract [67].

Hepatoprotective activity

The ethanolic extract of stem bark of *Berberis aristata* when given at the rate of 100 mg/kg bwt and 300 mg/kg body weight in high dose carbon tetrachloride (CCl₄) induced hepatotoxicity model in albino wistar rats was able to reduce the levels of different liver specific parameters such as direct bilirubin, total bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase which were raised above the normal range in the positive control liver damaged group [68]. When berberine chloride was given in intraperitoneal CCl₄ induced hepatic damage model in rats, it showed preventive as well as curative hepatoprotective effects as there was a significant reduction in the level of alanine transaminase, aspartate transaminase and alkaline phosphatase in dose dependent manner [69]. In Rifampicin-Isoniazid (50mg/kg body weight each) induced hepatotoxicity model in rats, the *Berberis aristata* plant given at the rate of 50mg/kg body weight showed curative effects. In plant treated group there was significant increase in the values of total protein and reduction in elevated liver specific enzymes *viz.* aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase [70].

Nephroprotective

The decoction of root bark of *Berberis aristata* is found to be effective against cisplatin induced urinary trouble or nephrotoxicity as it was able to reverse the side effects of cisplatin due to its antioxidative properties [71]. Ethanolic root extract of *Berberis aristata* was able to down regulate the mRNA expression of antioxidant and proliferative markers *i.e., p53, p21, Cas 4, Cas 5, Cas 9, and Cyt-c* in vancomycin induced nephrotoxicity model in vero cells which were upregulated in the vancomycin group without any treatment [22].

CONCLUSION

From the above review it can be concluded that *Berberis aristata* is a valuable medicinal plant with a rich heritage and significant potential for treating various health conditions on the basis of indigenous traditional knowledge as well as scientific studies. The various phytoconstituents present in the plant make it a good source of antioxidants. Its diverse pharmacological properties and studies shows that it has good immunomodulatory, anti-inflammatory, antioxidant, anti-viral, anti-cancer, anti-microbial, anti-hyperglycaemic, hepatoprotective and nephroprotective activity. These properties make it a suitable plant for herbal therapy as an alternative to conventional medicine. Further research and clinical studies are essential to fully explore and validate the therapeutic potential of this traditional plant.

Conflict of interest

The authors declared no conflict of interest.

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