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MEDICINAL POTENTIAL OF BERBERIS ARISTATA: A REVIEW

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Abstract:

Plant and their products are used from ancient time to mankind and human welfare. In old days when pharmaceutical field was not properly developed then plants were major source to cure and prevent illness. Herbal markets are globally increased due to safe drug delivery with fewer side effect compared to synthetic drugs. Cost of herbal drugs is much less than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs. ***Berberis aristata****, also known as* ***Indian barberry****, "chutro" or* ***tree turmeric****, is a shrub belonging to the family Berberidaceae and the genus Berberis. The plant of Berberis genus contains barberine, oxyberberine, berbamine, aromoline, karachine, palmatine, oxyacanthine and taxilamine. From different research Berberis aristata have found to be different pharmacological activities like Anti-depressant activity, Immunomodulatory activity, Antidiabetic effects, Activity against cardiovascular diseases, Antidiarrhoeal activity, Antioxidants, Anticancer, Antimicrobial, Hepatoprotective, Antipyretic activity etc.*

Keywords: *Berberis aristata, Darhaldi, Kashmal, Barberine, Oxyberberin*

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INTRODUCTION:

The traditional life science has taken care of humankind for hundreds of years. Many people assume that medicinal plants were hard to find and a lot of effort has to be put in to find them in the forest regions. The plants provided food, clothing, shelter and medicine. Much of the medicinal use of plants seems to have been developed through observations of wild animals and by trial and error. As time went on, each tribe added the medicinal power of herbs in their area to its knowledge base. Herbal medicinal products are defined as any medicinal product, exclusively containing one or more active substances. Herbs had been used by all cultures throughout history. It was an integral part of the development of modern civilization. Herbal markets are globally increased due to safe drug delivery with fewer side effect compared to synthetic drugs. [1]

Advantages of herbal medicines:

1. Mostly herbal drugs are well tolerated by the patient, having fewer unintended consequences and fewer side effects than traditional medicine, and may be safer to use.
2. Herbal drugs are more effective for long-standing health complaints that don't respond well to traditional medicine.
3. Cost of herbal drugs is much less than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.
4. Herbs are available without a prescription. Simple herbs, such as peppermint and chamomile, can be cultivated at home. [2]

Berberis aristata, also known as **Indian barberry**, "chutro" or **tree turmeric**, is a shrub belonging to the family Berberidaceae and the genus *Berberis*. The genus comprises approximately 450-500 species of deciduous evergreen shrubs and is found in the temperate and sub-tropical regions of Asia, Europe, and America. *B. aristata* is native to the Himalayas in India and in Nepal. It is also naturally found in the wet zone of Sri Lanka.

English names: Indian barberry, tree turmeric. Indian names: darhaldi (Bengal), kashmoi (Garhwal), rasont, kashmal (Himachal Pradesh), chitra, dar-hald, rasaut, kashmal (Hindi), maradarisina, maramanjal, (Kerala), daruhald (Maharashtra), chitra, chutro (Nepal),chitra, kasmal. simlu, sumlu (Punjab) mullukala, usikkala (Tamil Nadu), daruharidra, darvi, kata, pitadaru, suvarnavarna (Sanskrit). There are 12 – 13 varieties like *Berberis asiatica, Berberis lycium, Berberis vulgaris, Berberis nepalensis* etc. [3]

Taxonomy of *Berberis aristata* [4]

Kingdome: Plante
Clade : Angiosperms
Order : Ranuculases
Family : Berberidaceae
Genus : *Berberis*
Species : *B. aristata, B. vulgaris, B. lyceum, B. nepalensis etc.*

Pharmacognosy:

Macroscopy: Stem pieces are nearly cylindrical, variable in length and thickness about 15 to 20 mm., bark about 0.4-0.8 cm thick, pale yellowish brown, soft, closely and deeply furrowed, surface rough, brittle, wood portion yellow, more or hard radiate with xylem rays. Pith present very small. Stems also branched; bark thin, fracture surface short and gets period off at places exposing the inner dark yellow wood.

a) Leaf

b) Fruit

c) Flower d) Root

Figure 1: *Berberis aristata* a) Leaf, b) Fruit, c) Flower, d) Root

Microscopy: Stem is circular in outline with outer well developed cork, narrow pericycle traversed by stone cells, central narrow pith surrounded by xylem and medullary rays pith surrounded by xylem and medullary rays are present occupying 60% area of the selection. T.S. of stem shows multilayered cork consisting of 3-45 rectangular to squarish radically arranged suberized cells, yellow coloured and thin walled arranged radially. Cortex is narrow, composed of tangentially elongated parenchymatous tissue containing stone cell are isolated or in-group and starch grains. Pericycle characterized by discontinuous band of isolated or group of 2 to 5, lignified fibers. Sieve elements are irregular in shape, thin walled a few cells containing yellowish-brown contents; Phloem fiber are arranged in tangential rows, consisting of 2-4 cells, each fibre short, thick-walled and spindle shaped and lignified. Medullary ray in continuation with xylem and containing calcium oxalate crystal, cambium distinct. Xylem consists of vessels, tracheids, fibers and parenchyma. Xylem vessels are numerous, small to medium sized, in single or in groups arranged radially. Centrally located parenchymatous pith is found. Simple starch grains and prismatic crystals of calcium oxalate are present throughout parenchymatous cell section. Occasionally dark brownish content found in ray cell [5]

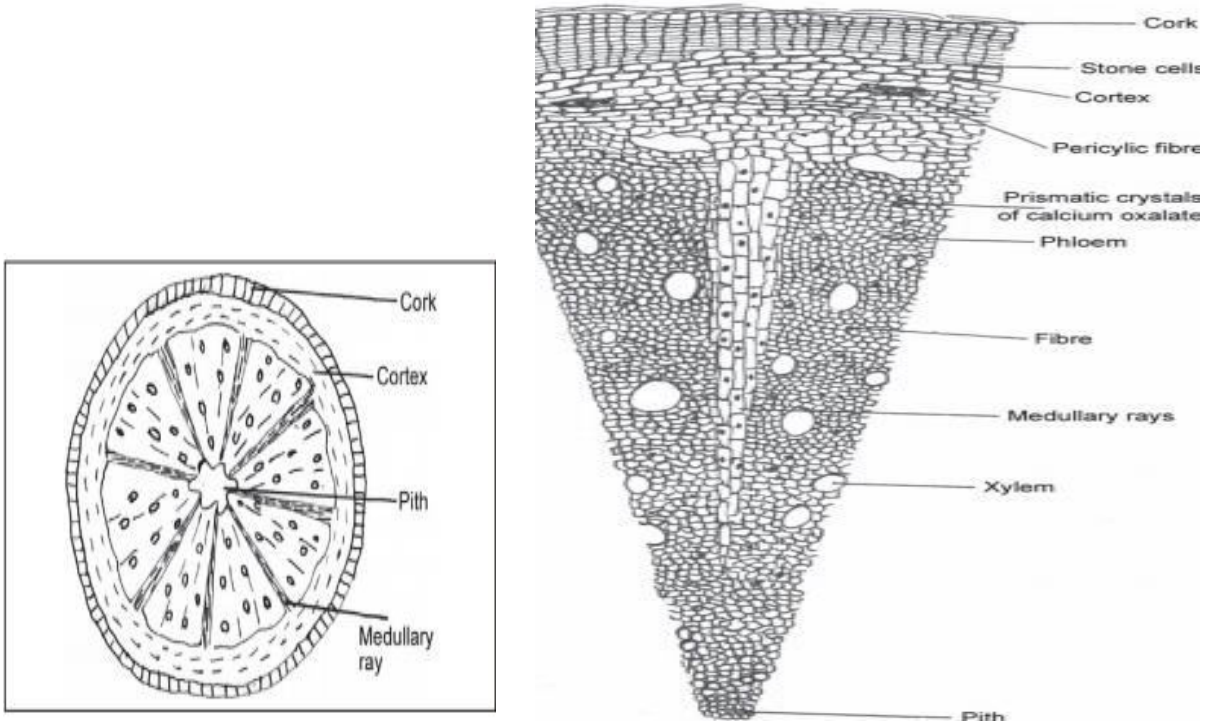
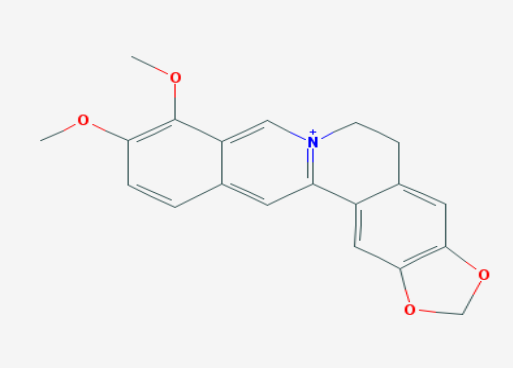
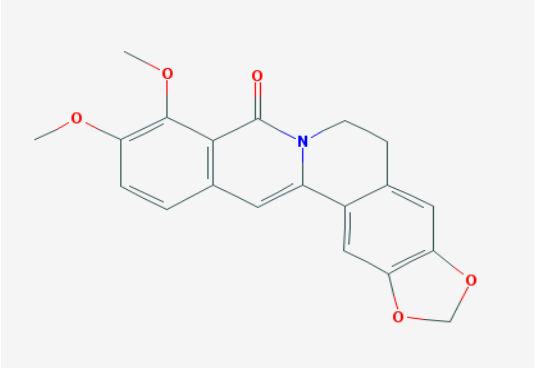


Figure 2: T.S. of *Berberis aristata* DC stem

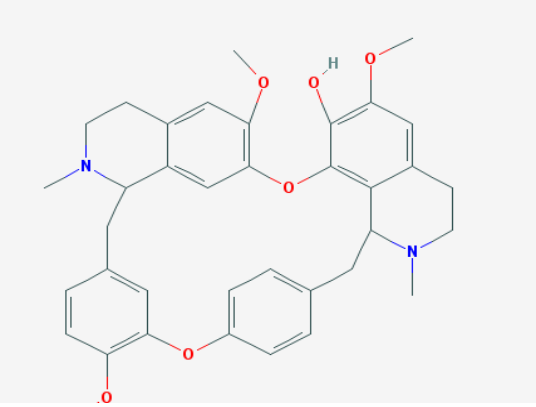
Phytochemistry: The plant contains barberine, oxyberberine, berbamine, aromoline, karachine, palmatine, oxyacanthine and taxilamine [6]. *Berberis aristata* contains protoberberine and bis isoquinoline type of alkaloid. Root of plant *Berberis aristata* contains alkaloid which are berbamine, Berberine, oxycanthine, epiberberine, palmatine, dehydrocaroline, jatrorhizine and columbamine [,7,8] karachine,dihyrokarachine, taximaline, [9] oxyberberine, aromoline [10]. Four alkaloids, pakistanine, 1-O methyl pakistanine, pseudopalmatine chloride and pseudoberberine chloride were also isolated from *Berberis aristata* [11,12]. A secobisbenzlisoquinoline or simple isoquinoline alkaloid was isolated from *Berberis aristata*.[13] The major alkaloid found in *Berberis aristata* is Berberine having yield of 2.23% followed by palamatine [14]. Variation of Berberine content in root and stem of *Berberis aristata* with altitude was determined. It was found that plants growing at lower altitude have more Berberine content. Berberine content in plant is also influenced by potassium and moisture content of soil [15]. HPTLC fingerprinting of Berberine in *Berberis aristata* was done to quantify the amount of Berberine. Total alkaloidal content of *Berberis aristata* was also done.



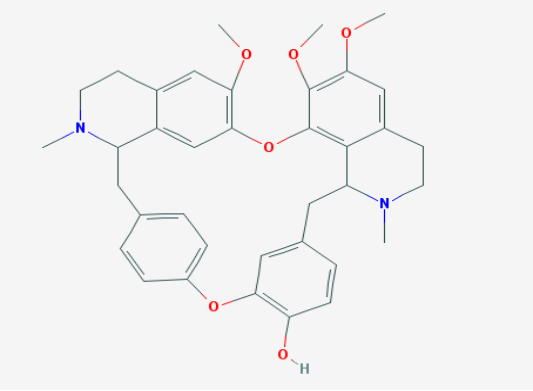
a) Berberin



b) Oxyberberin



c) Aromoline



d) Berbamine

Figure 3: Structure a) Berberin, b) Oxyberberin, c) Aromoline, d) Berbamine

Pharmacological importance of *Berberis aristat:*

Anti-depressant activity: Berberine, an alkaloid isolated from *Berberis aristata* Linn. has been used in the Indian system of medicines as a stomachic, bitter tonic, antiamoebic and also in the treatment of oriental sores. Evidences have demonstrated that berberine possesses central nervous system activit ies, particularly the ability to inhibit monoamine oxidase-A, an enzyme involved in the degradation of norepinephrine and serotonin (5-HT). With this background, the present study was carried out to elucidate the antidepressant-like effect of berberine chloride in different behavioural paradigms of despair. Berberine (5, 10, 20 mg/kg, i.p.) inhibited the immobility period in mice in both forced swim and tail-suspension test, however, the effect was not dosedependent. Berberine (5 and 10 mg/kg, i.p.) also reversed the reserpine-induced behavioral despair. [16]

Immunomodulatory activity: The activity of a crude extract formulation was evaluated in experimental immunomodulation studies. The formulat ion comprises the following five plants - *Boerhavia diffusa, Tinospora cordifolia, Berberis aristata, Terminalia chebula* and *Zingiber officinale.* In immunomodulation studies humoral immunity was enhanced as evidenced by the haemagglutination

titre. The T-cell counts remained unaffected in the animals treated with the formulation but cell-mediated immune response was stimulated as observed in the leukocyte migrat ion inhibit ion (LMI) tests.[17]

Hypoglycemic effect and Anti diabetic activity: The anti-diabetic activity of stem bark of *B.aristata* in alloxan induced diabetic rats was evaluated and reported the ethanolic extract to reduce blood glucose level in diabetic rats [18]. The analysis of serum urea, protein, blood cholesterol, total lipids, SGOT and SGPT, body weight and liver glycogen showed reduced levels than standard levels. B.aristata root extract was found to possess anti hyperglycemic and strong anti oxidative properties by reducing blood glucose level in alloxan induced diabetic rats, restoring antioxidant status, reducing oxidative stress and modulating enzymes for glucose metabolis [19]. The extract of the root of *B. aristata* was reported to have strong potential to regulate glucose homeostasis through decreased gluconeogenesis and oxidative stress.The methanolic extract of *B.aristata* stem bark was reported to possess blood glucose lowering potential and in vitro antioxidant property [20]. Ethanolic, acidifiedbasified and chloroform: methanol fractions isolated from the root bark of *B.aristata* and treated with alloxan induced diabetic rabbits found a significant decrease in the blood glucose level at 2, 4, 8 and12 hrs of observation for both normal and alloxan induced rabbits, which was higher than gliclazide confirming the roots bark of *B.aristata* possess hypoglycemic activity for all the above mentioned fractions [21]. Comparative study of the effects of the crude extract of *B.lycium* with pure berberine and as an attempt to validate its use as a therapeutic agent, demonstrated Berberis extract and berberine had similar effects on all parameters viz., glucose tolerance, glycosylated haemoglobin, serum lipid profiles and body weight of experimental animals measured and the extract was comparable in efficacy to berberine. Antihyperglycemic effect of the ethanolic extract of root samples of *B.lycium*, when studied using alloxon induced diabetic rats, indicated significant hypoglycemic activity. Similarly, antidiabetic claim of *B.lycium* suggested the possible use of water extract as an adjunct to insulin. [22, 23]

Antidiarrhoeal activity: Study with berberine from the roots and barks of *B.aristata* reported the inhibition of secretary response of heat labile enterotoxins of Vibrio cholerae and Escherichia coli in rabbit ligated intestinal loop model and infant mouse assay and possible clinical effectiveness in treating acute diarrheal disease.[24] The effectiveness of alcoholic extract of the stem of *B.aristata* against castor oil induced diarrhoea was analysed in rats indicating the antienteropooling activity (prevention of induced intestinal fluid accumulation) of the extract. The leaf powder of *M. umbellata* has been used in treating diarrhoea and dysentery. [25]

Hepatoprotective: B. aristata roots have been used in treatment of jaundice in Ayurveda. Hepatoprotective and antioxidant activity of dried aerial part of *B. aristata* was investigated in aqueous and methanolic extract and berberine, against CCl_4 induced liver injury. Results obtained were comparable to standard drug silymarine. [26] Crude extract of *B. aristata* (Shoot and fruit) shows Paracetamol and CCl_4 protection against induced liver toxicity and it also indicates that hepatoprotective action of extract is partially through inhibition of microsomal drug metabolizing enzyme. [27, 28]

Antioxidant: Antioxidant potential of 50% aqueous ethanolic root extract of *Berberis aristata* was studied. Effect of extract on antioxidant enzymes of liver was studied in diabetic rats along with its safety parameters. The extract of *Berberis aristata* (root) has strong potential to decrease oxidative stress. [29] Antioxidant potential of dried aerial part of B. aristata was investigated in aqueous and methanolic extract and berberine, against CCl_4 induced liver injury. The result was found significant. [30]

Anticancer: In vitro cytotoxic activity against MCF-7 cell line at different concentrations of methanolic extracts of *B. aristata* was evaluated. Cytotoxic effect against the breast cancer cell line is considered as a prognostic anticancer activity indicator and IC_{50} value calculated for *B. aristata* methanolic extract is 220mcg, which indicates potentially presence of cytotoxic activity and should be evaluated against primary cell lines to examine the selectivity of their effects. The exhibited cytotoxic activity in MCF-7 cell lines may be due to the presence of alkaloids in the methanolic extract of *B. aristata* stems which was investigated earlier in photochemical screening of the extract. *B. aristata* has been used for medicinal applications traditionally in India and its therapeutic investigations needed to provide some additional insight for using as curative agent for breast cancer. Recently, anti-cancer properties of berberine, a major compound in this plant, that has shown the inhibition of cancer cell proliferation, metastasis, angiogenesis, activation of apoptosis, DNA binding and inhibition of telomerase. Previous studies revealed the anti-proliferation activity of berberine through influencing the mitochondrial trans-membrane potential, matrix

metalloproteinase (MMP) regulation, p53 activation, nucleated factor kappa B (NF-kB) signal activation and dose-dependent reduction in cancer cell growth assessed by increased DNA content in G2/M and S phases and targeted AMP activated protein kinase, which regulates tumor progression and metastasis . Further, the 48 h exposure of methanolic extracts of *B. aristata* to MCF-7 cell lines in present study exhibited a suppressive effect significantly ($p \leq 0.001$) on anchorage dependent growth measured by soft agar assay and cell migration as well as increased apoptotic cells. Such an antineoplastic and anti-metastatic effect of berberine and siRNA synergistically was previously reported in bladder cancer cells through attenuating the migration and invasion of bladder cancer cells. It also suppress tissue plasminogen activator induced PKC-α phosphorylation which leads to inhibition of MMP-1 and MMP-9 expression and also via Akt / NK-kB and AP-1 signaling pathway in breast cancer cells. In addition, berberine exhibited p53- dependent apoptotic death in human neuroblastoma and prostate cancer cells and inhibition of telomerase activity in nasopharyngeal carcinoma cells. In present study the metholoic extracts of *B. aristata* resulted anticancer activity significantly in MCF-7 breast cancer cell lines, it may be postulated that the plant extract would be helpful in pharmacological applications in treatment of breast cancer. However, the present study would be helpful to investigate further in elucidating the mechanism involved by active components such as berberine in anticancer activity. [31]

Antipyretic activity: The antipyretic activity test was carried out by using the Diphtheria-Pertussis-Tetanus (D.P.T.) vaccine as the pyrexia-inducing agent. Rabbits, weighing 1.0 – 1.5 kg, were divided into three groups containing five animals in each group. Two groups served as test groups and one group as the control group. The initial temperature of each animal was recorded using a clinical thermometer, inserted half inch deep into the rectum. Alcoholic and aqueous extracts were administered at a dose of 200 mg/kg orally to the respective test groups, and the control group was administered water in the usual manner. The D.P.T. vaccine (Central Research Institute, Kasauli, Himachal Pradesh, India) was injected intravenously in the ear vein at a dose of 0.5 ml/kg. Rectal temperature of the test and control groups was recorded after vaccine injections at 30-min intervals for a period of three hours. The mean rectal temperature of the test group was compared with that of the mean rectal temperature of the control group at corresponding intervals and analyzed statistically by using test of variance (ANOVA).[32]

Activity on cardiovascular diseases: Recent studies show that berberin has useful cardiovascular effects such as positive inotropic effect (tested in a separated atrium of guinea pigs), negative chronotropic effect, anti-arrhythmic effect and anti-high blood pressure effects and it reduces vascular resistance. Several therapeutic effects have been described for *Berberis vulgaris*. In present study, the effects of ethanolic extract from *Berberis vulgaris* on isolated heart were examined. The heart mounted on a Langendorff aparatus and perfused through aorta. Heart contractility were determined on the presence of four concentrations of ethanolic extract (0.5, 1, 2 and 5 g %) and diltiazem, (0.1, 1, 10 and 100 µM). [33]

Table 1: List of different pharmacological activities done on *B. aristata*

Pharmacological activity	Berberis spercies	Part of plant	Year	Reference
Anticancer	*B. aristata*	Fruit	2012	34
	B. aristata	Stem	2009	35
	B. vulgaris	Fruit	2012	36
	B. libanotias	Root	2014	37
	B. lycium	Root	2010	38
	B. vulgaris	Fruit	2008	39
Antihistaminic	*B. vulgaris*	Fruit	1999	40
	B. vulgaris	Fruit	2005	41
Cardiovascular/ hypertension	*B. orthobotrys*	Root	2013	42
	B. integerrima	Root	2015	43
	B. vulgaris	Fruit	2005	44
	B. crataegina	Root	2002	45
Gastrointestinal disease	*B. aristata*	Bark	2011	46
	B. aristata	Stem	2013	47
Antiepileptic	*B. integerrima*	Root	2013	48
	B. vulgaris	Root	2010	49
	B. aristata	Root and stem	2007	50
Lipid profile	*B. lycium*	Root	2009	51
	B. lycium	Root	2011	52

Antihyperglycemic	*B. vulgaris*	Bark	2011	53
	B. aristata	Root	2009	54
	B. lycium	Root	2008	55
	B. integerrima	Root	2012.2013,2013	56,57,58

Table 2: List of Patents on *Berberis aristata* [59]

Patent no.	Year	Title	Pharmacological Activities
KR2011051820	18-05-2011	Composition containing lacquer tree used as feed additive for livestock.	Immunostimulant
IN2009DEL01056	26-11-2010	Herbal ophthalmic composition for common eye ailments.	Anti-microbial
US20100239603	23-09-2010	Combinations of botanical extracts for promoting cardiovascular health.	Cardiotonic
JP2010202634	16-09-2010	Crude drug containing composition used for improving metabolic syndrome, obesity and liver function, comprises Garcinia, Terminalia beleria, Commiphora mukul, Gymnema sylvestre, Boswellia serrata and Salacia reticulata.	Anti-lipidemic
WO2010104595	16-09-2010	Methods and compositions for the treatment of metabolic and cardiovascular disorders.	Anti-lipidemic, anti-diabetic, cardiotonic
JP2010195731	09-09-2010	Agent useful for whitening skin and preventing and suppressing pigmentation and liver spots by inhibiting Dopa oxidase activity, contains extract of plant e.g. Berberis vulgaris and Berberis aristata.	Dermatological (Dopa oxidase inhibitor activity)
US7771757	10-08-2010	Nasal irrigation solutions and methods of using the same.	Anti-microbial, anti-inflammatory
KR2010084909	28-07-2010	Feed additive containing medicinal herb composition.	mmunostimulant
US20100178367	15-07-2010	Herbal formulation for wound healing.	Anti-microbial, anti-fungal, wound healing
US20100143510	10-06-2010	Intramammary teat sealant	Anti-infective, anti-bacterial, anti-fungal
WO2010032267	25-03-2010	Herbal formulation for prevention and treatment of diabetes and associated complications.	Anti-diabetic
WO2010029562	18-03-2010	Bioactive composition for the treatment of the HIV/AIDS and method for manufacturing and using the same.	Anti-HIV
US7658954	09-02-2010	Synergistic anti-pyretic formulation.	Anti-pyretic
EP2149377	03-02-2010	Compositions containing berberine and/or analogues thereof or extracts containing it, for the prevention and treatment of alterations of the lipid and carbohydrate balance.	Anti-lipidemic
IN2009DEL01212	01-01-2010	Broad spectrum polyherbal formulation for treatment of alopecia and chronic skin disorders.	Dermatological-anti-microbial
IN2009KOL01123	27-11-2009	Herb-based nutritional composition for correction of metabolic disorders.	Anti-cancer
IN2008CHE00849	09-10-2009	Berberis aristata plant extract comprises extract or concentrate of plants belonging to Berberis, which includes Berberis aristata or their mixtures, and extracts, which are isolated from different parts of Berberis aristata plant.	Cardiotonic
IN2005DEL02645	02-10-2009	Herbo-mineral compound formulation for management of maturity onset diabetes mellitus.	Anti-diabetic

EP2090315	19-08-2009	Method and system for producing medicinal alcohol as a prophylactic or remedy for cancer, HIV, AIDS and autoimmune diseases.	Anti-inflammatory
IN2004DEL01330	19-06-2009	Herbal composition for treatment of HIV and process of preparing the same.	Anti-HIV
US20090136469	28-05-2009	Formulation for oral administration with beneficial effects on the cardiovascular system.	Cardiotonic
DE102007040798	02-04-2009	Herb mixture, useful e.g. to slow the ageing process, comprises e.g. Crocus sativus, Elettaria cardamomum, Cinnamomum zeylanicum, Hedychium spicatum, Terminalia chebula, Trichosanthes dioica, Coleus forskolin and Berberis aristata	Anti-ageing
KR20090032617	01-04-2009	An anti-cancer medicine including berberine.	Anti-cancer
WO2008126088	23-10-2008	Anti-pyretic vasodilators.	Anti-pyretic
US20080081781	03-04-2008	Methods and compositions for the treatment of metabolic syndrome.	Anti-lipidemic, Cardiotonic
WO2008007215	17-01-2008	Berberis aristata plants extracts for treating osteoporosis and the extraction process thereof.	Osteopathic, cytostatic, anti-arthritic
EP1411951	26-09-2007	Enteral compositions for the prevention and/or treatment of Sepsis.	Anti-microbial, anti-bacterial
IT2007MI0988	16-08-2007	Potentiation of antitumor chemotherapy and (or) radiotherapy by using a plant-derived food supplement.	Anti-cancer
US20070098649	03-05-2007	Method and composition for controlling oral pathogens.	Anti-inflammatory, anti-bacterial, antimicrobial
US20070065394	22-03-2007	Compositions effective in altering the perception of malodor.	-
US20070027176	01-02-2007	Compositions for veterinary and medical applications.	Anti-microbial
US20060223838	05-10-2006	Methods and compositions for the treatment of hyperlipidemia.	Anti-hyperlipidemic
IN2004CHE0679	02-06-2006	Side effect-less curing medicine for diabetes mellitus by immunopathy.	Anti-diabetic
IN218675	24-03-2006	Herbal composition for controlling blood sugar level comprises e.g., Melia azadirachta (Neem Bark) and Syzygium cumini (Jamun or Black Berry).	Anti-diabetic
WO2005030232	02-03-2006	Herbal compositions for effective treatment of AIDS, preparation thereof and method for treatment of AIDS patients.	Anti-HIV
JP2005325025	24-11-2005	Composition for treating and preventing diabetes comprises crude drug component of Guggul, Licorice, Balsam Pear, Gymnema sylvestre,	Anti-diabetic

Nutrition facts of *B. vulgaris* fruit

B. vulgaris fruit is sour and contains different nutrients including dextrose, fructose, malic acid, tartaric acid, citric acid, pectin, and resin. It is also rich in vitamins C and A, calcium, iron, and potassium (60, 61). In *B. vulgaris* fruit, the concentrations of iron, zinc, copper, and manganese are estimated 2650 mg/kg, 27.5 mg/kg, 33.7 mg/kg, and 58.6 mg/kg, respectively (62). Decomposition of *B. vulgaris* fruit shows that this fruit contains 79.6% humidity, 1.16% fat, 2% protein, 16.24% carbohydrate, and 0.99% ash. The amount of anthocyanin is estimated 281 mg/l (63).

In Iran, dried *B. vulgaris* fruit is used in many foods. As well, the fruit or its derivatives are used to produce certain products such as sauce, jelly, juice, jam, marmalade, and carbonated drinks. Besides that, *B. vulgaris,* considered of nature-based and useful substance, is used to season, flavor, and garnish foods to satisfy different sapors (64, 65). This fruit is also used in industries. For example, the anthocyanin found in *B. vulgaris* fruit is used as a nature-based color (66).

CONCLUSION:

As per the present review- B. aristata found in the temperate and sub-tropical regions of Asia, Europe, and America and is native to the Himalayas in India and in Nepal. It is a traditional medicinal plant used in Ayurvedic, Chinese and other medicinal systems in the world for a long time. Every part of this plant has gained importance for its different pharmaceutical activities. The plant contains chemical constituents like barberine, oxyberberine, berbamine, aromoline, karachine, palmatine, oxyacanthine and taxilamine. The most important pharmaceutical properties of this plant include anti-diabetic, anti-depressant, immunomodulatory, anti-pyretic, anti-PAF, anti-diarrheal, gynaecological, hepatoprotective, ophthalmic, dermatological and cardiotonic activity. However much information is not there to prove that, this plant is for anti-neoplastic, anti-fertility, anti-leprotic etc. This plant is becoming potent medicinal herb to cure different diseases.

Future directions

A lot of medicinal value is reported for *B. aristata* in literature but for future use there is needed a lot of work for the confirmation of all the activities.

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