# Tree Turmeric (*Dar-e-Hald*)., A Berberine Containing Unani Medicinal Herb of Pakistan

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**Abstract: Tree turmeric (***Dar-e-hald***)** *i.e.* ***Berberis aristata*** is a fomous Greek-o-Unani herb well grown in Pakistan. Dar-e-hald is known for its anti microbial properties in eyes, ear, gastrointestinal and genitourinary infections. Medicinally, the root and root bark, stem and stem bark, berries, flowers and powdered root and stem with the bark were used. Root and stem with the bark used as a potent source of berberine, the important constituent of the plant. The yellow coloured chemical constituent, berberine, gives the powdered dry root with bark its yellow colour and is an antimicrobial, anti inflammatory agent and anti cancer agent.

**Keywords**: *Dare hald,* Medicinal plant, Hikmat, Pakistan, Berberine antimicrobial, Anti-inflammatory.

## INTRODUCTION

***Berberis aristata*** well-known medicinal herbs, is frequently use in natural medicine and are substantial part Greeko Unani (Hikmat) system of medicine. Plant belongs to family **Berberidaceae Juss.** {Genera Plantarum 286. 1789. (4 Aug 1789) (Gen. Pl.)}, consisting of 4 genera and about 500 species, mostly in North Temperate regions, tropical mountains and S. America; represented in Pakistan by 3 genera and 22 species.

In Pakistan, the plant is mostly found in W. Himalaya (Simla to Tehri and Kumaon), it was rare in Kashmir. While in India Gharwal Himalias in Uttaranchal. Also found in Nepal and Bhutan.

*Berberis glaucocarpa Stapf* and *Berberis coriaria Royle ex Lindl.* are the synonyms of the plant. In English it is known as Barberry, while in Urdu it is called as dar-e-hald, chrku, somblu. In Ayurveda it is called as daruharidra, daaru, sthirphala and parjani [1].

It is an erect spinous shrub 2-4 cm high, flowers are golden yellow, in long drooping compound racemes, penduncles and pedicels slender, leaves are obovate or oblanceolate, glossy dark green above, glossy pale green beneath. Shrub bark is pale yellowish brown, which is closely and deeply furrowed. While, berries are blue ovoid [2, 3].

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## PHARMACOLOGICAL ACTIVITIES

Dar-e-hald is known for its anti microbial properties in eyes, ear, gastrointestinal and genitourinary infections. *Berberis aristata* contains berberine which have been studied extensively and successfully being tested for many activities like antimicrobial, antiinfammatory, used in the diagnosis test of malaria, antineoplastic, trypsin and chymotrypsin inhibitor, intestial antiseptic, bitter stomachic, cardiotonic, antispasmodic, anti HIV and antiplatelets. In modern medicine, berberine is used for the treatment of diarrhoea. Its berries are antiscorbutic and laxative. Bark is used for liver problems, gastric problems including diarrhoea, cholera, dysentery, enlargement of spleen and metabolism disorders. Root bark is anticoagulant, anti-inflammatory, hypoglycemic, hypotensive, antiamoebic and antibacterial [4, 5].

### In Dentistry

The hydroalcoholic extracts of root and stem of the *Berberis aristata* DC has proven antimicrobial activity against oral pathogens [6]. Indication in periodontal diseases has been proved by the fact that Berberine hydrochloride, a major alkaloid of the plant, inhibited the expression of IL-1beta and TNF-alpha in periodontal tissues in rats periodontitis model and promoted the regeneration of the periodontal tissues. This study suggested that berberine hydrochloride may have potential clinical application [7].

### Antimicrobial Activity

*Berberis aristata* has proven antimicrobial activity against oral pathogens. The hydroalcoholic extracts of

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root and stem of the *Berberis aristata* have been effective against most of the common pathogens. It`s root extract also showed significant antifungal activity against *Aspergillus terreus* and *Aspergillus flavus. Berberis aristata* roots extracts indicated comparatively low MIC values with the concentration as low as 0.31 µg/ml. The major alkaloid berberine may be responsible for antimicrobial activity [6].

A research aiming for giving a wide look on antimicrobial activity of the crude extract of the root of *Berberis aristata* suggested remarkable antimicrobial activity especially against *V. cholera, Staphylococcus sp., Candida spp.* and *Aspergillus sp.* The research also suggested that an excellent medicine for the cholera infection can be obtained from the root of the plant. Both the aqueous and alcoholic extracts of fresh root as well as powder of dried root in water showed wide antimicrobial activity against Gram positive microorganisms. MICs were in the range of 0.003 to 0.02 mg/ml for all the microorganisms tested [8].

In addition, the activity of a preparation containing crude extract of five plants including *Berberis aristata* were studied to check its anti microbial activity against hepatic amoebiasis in experimentally produced amoebic abscess in liver of golden hamsters. The formulation showed a maximum cure rate of 73% when compared with metronidazole. In the same study it was found out that the preparation is also effective in stimulating humoral and cell mediated immunity [9]. Berberine hydrochloride was also tested for its antimicrobial activity against *Trichomonas vaginalis,* in comparison to metronidazole. The MIC values estimated invitro shows that the compound can be used in place of the reference drug and it is preferred choice as has high safety profile and can be used safely in metronidazole resistant cases. Berberine was proved to be antibacterial, antiamoebic, antifungal, antihelminthic, leishmanicidal andtuberculostatic agent [10].

**Antifungal Activities**

Hydro-alcoholic (50%v/v) and hexane ext., after soaking for 72 hrs, of *Valeriana jatamansi, Coleus barbatus, Berberis aristata, A. racemosus, A. paniculata, A. aspera, T. cordifolia, P. depressa* extracts showed differential antifungal effect against *A. niger* and *C. albicans*. The part of the plant used was not mentioned in the research article [11].

**Cardiovascular Use**

In animal isolated heart tissue, extract of *Berberis aristata* fruit shows a positive ionotrpic effect [12].

**Diabetes**

Berberine and root extract of the plant is tested for their antioxidant and glucose lowering potential on alloxan induced diabetic rats. Results showed that the sample has antidiabetic and antioxidant potential [13].

**Anti-Inflammatory Effect**

Rabbits were made to have Anterior uveitis by intravitreal injection of lippopolysaccarides from *E-coli*. Prior to this the instillation of aqueous extract of *Berberis aristata* and another herb *i.e*. *Curcuma longa* was made to observe the effect on extract to the disease condition. The results showed that the extracts had potent anti-inflammatory activity in the given condition. The parameters checked were the value of TNF-α and protein content of the aqueous humor [14]. 50% ethanolic extracts of *Berberis aristata* exhibited antioxidant and anti-inflammatory activity [15].

**Analgesic Activity**

Both the alcoholic and aqueous extract of fresh roots were tested for their analgesic activity by Eddy's hot plate with the oral dose of 50/100g.of the extract. The result showed activity for both [8].

**Antipyretic Activity**

Diphtheria-Pertussis-Tetanus (D.P.T) vaccine was injected in the ear vein of test rabbits to induce fever. Rectal temperatures were noted for the estimation of body temperature. Aqueous extract of the root showed antipyretic activity at the dose of 200mg/kg with longer duration of action while the alcoholic extract showed the same effect at the same dose with shorter duration of action [8].

**Effect of Plant on Infectious Diarrhea**

The potent compound from the plant, berberine was tested for its efficacy against cholera induced diarrhea and the compound was found effective for the prescribed condition.

The study was done on diseased rats which were given 2 and 4 g cholera toxin/kg their body weight [16].

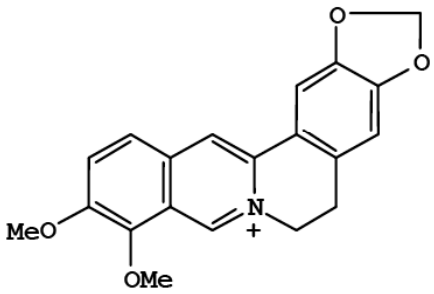


**Figure 1:** Chemical structure of Berberine.

Infection due to *Entamoeba histolytica* were also studied for antiinfective activity of a compound preparation containing *Berberis aristata*. *In vitro* antimicrobial activity was done and MICs were determined as 1000 micrograms/ml while that metronidazole has 10 micrograms/ml. in infected rats the preparation was found to be curative [17].

### Antilipidemic Effect of the Plant Extract

When a preparation composed of some herbs including the plant was tested for its effect on lipid profile on Swiss albino rats, it was estimated that the oral administration of the formulation significantly decreased the lipid profile and aids in relieving obesity [18].

### Antidepressant Activity

An isoquinoline alkaloid from *Berberis aristata*, berberine was tested for its antidepressant activity. It was found that the activity is due to the interaction of berberine chloride with the L-arginine-NO-cGMP signaling pathway. The study helps to clearify the mechanism of action of this natural product [19].

### Anticarcinogenic Activity in Liver Neoplasm

According to the research the antitumor alkaloid from the plant *i.e*. berberine chloride was found to active against the carcinogenesis produced chemically by 20-methylcholanthrene (200 microg/0.1 mL/mouse) or N-nitrosodiethylamine (NDEA; 0.02% NDEA in distilled water, 2.5 mL/animal by gavage, five days a week for 20 weeks). The study was done on small animals (experimental mice and rats) and the activity showed dose-dependent behavior. When the liver tissues were tested morphologically and the marker enzymes levels were checked, the preventive effect of berberine chloride against chemically produced cancer was further proved [20].

## PHYTOCHEMISTRY

Berberine, berberine chloride and palmatine have been isolated from the alcoholic extract of the bark of *B. aristata* [21]. Root contains 5% and stem bark 4.2 % berberine. In addition, Berbamine, karachine, oxycanthine, oxyberberine, aromoline and oxycantine were the alkaloids found in bark and root bark [22, 4].

## TOXICOLOGY

Oral acute toxicity of aqueous and ethanolic extract of *Berberis aristata* bark in mice is LD 50 of >5000mg/kg/body weight was observed [23].

## CLINICAL TRIALS

120 middle aged, menopausal women were enrolled in a single blind clinical trial where the patients were randomized to use either calcium and vitamin D or the berberine preparation (isolated from *Berberis aristata*). The berberine user group was found to have improved LDL levels and thus decreased CV risk [24].

Further, In a double blind placebo controlled clinical trial using tablets containing the extracts of *Berberis aristata* and *Silibum marianum,* on the overweight dyslipidemic patients with lower cardiovascular risk, the tablets two times a day was found effective in reducing lipid profile, improving insulin resistance and adipocytokines levels [25].

Further more, berberine lipid-lowering and insulin-resistance improving activity have been confirmed in many randomized clinical trials [26]. Additionally, the herb was proved to be hepatoprotective in a compound herbal composition in the patients receiving anti tuberculosis treatments [29].

## CONCLUSION

*Dare hald* (*Berberis aristata*) is a famous ingredient in the Greeko-Unani system of medicine (Hikmat) indicated for jaundice and enlargement of spleen. Rasut is traditional name of the root extract of the plant and the trade name is Indian barberry. Commercially it is available in the formulations indicated in the eastern herbal system of medicine as anticancer, anti inflammatory and antimicrobial agent.

The herb is emmenagogue and it is used in the treatment of jaundice. Fresh berries are used in opthalmics, especially in conjunctivitis. *Berberis aristata* showed antimicrobial activity against gram positive,

**Table 1: Phytochemicals in *Berberis spp***

| Str. # | Name | Synonym(s) | Molecular Formula |
|---|---|---|---|
| 1 | Berberine | 5,6-Dihydro-9,10-dimethoxybenzo[*g*]-1,3-benzodioxolo[5,6-*a*]quinolizinium(1+), 9CI<br>Umbellatine<br>Berbericine Natural yellow 18 C.I. 75160<br>Majarine | $C_{20}H_{18}NO_4^+$ |
| 2 | Capsanthin | 3,3'-Dihydroxy-β,κ-caroten-6'-one | $C_{40}H_{56}O_3$ |
| 3 | Columbamine *O*-methyltransferase | E.C. 2.1.1.118<br>*S*-Adenosyl-L-methionine:columbamine *O*-methyltransferase | |
| 4 | Isotetrandrine; $O^{12}$-De-Me | Berbamine<br>Berbenine | $C_{37}H_{40}N_2O_6$ |
| 5 | Obaberine; $O^{12}$-De-Me | Oxyacanthine | $C_{37}H_{40}N_2O_6$ |
| 6 | Oxyberberine | Berlambine | $C_{20}H_{17}NO_5$ |
| 7 | Palmatine | 5,6-Dihydro-2,3,9,10-tetramethoxydibenzo[*a,g*]quinolizinium(1+), 9CI<br>7,8,13,13*a*-Tetradehydro-2,3,9,10-tetrahydroxyberbinium(1+), 8CI<br>Berbericinine<br>Hindarinine<br>Gindarinine | $C_{21}H_{22}NO_4^+$ |
| 8 | Palmatine; $O^2$-De-Me | Dehydroisocorypalmine<br>Columbamine | $C_{20}H_{20}NO_4^+$ |
| 9 | Palmatine; $O^3$-De-Me | Dehydrocorypalmine<br>Jatrorrhizine<br>Jateorhizine<br>Neprotine<br>Yatrorizine | $C_{20}H_{20}NO_4^+$ |
| 10 | 3,3',4',5,7-Pentahydroxy-5'-methoxyflavylium(1+); 3-*O*-[α-L-Rhamnopyranosyl-(1→6)-β-D-glucopyranoside] | Petunidin 3-rutinoside | $C_{28}H_{33}O_{16}^+$ |
| 11 | 3,3',4',5,7-Pentahydroxy-5'-methoxyflavylium(1+);3-*O*-[β-D-Glucopyranosyl-(1→6)-β-D-glucopyranoside] | Petunidin 3-gentiobioside | $C_{28}H_{33}O_{17}^+$ |
| 12 | (*S*)-Scoulerine 9-*O*-methyltransferase | E.C. 2.1.1.117<br>*S*-Adenosyl-L-methionine:(*S*)-scoulerine 9-*O*-methyltransferase | |
| 13 | 3,4',5,7-Tetrahydroxy-3',5'-dimethoxyflavylium(1+); 3-*O*-[α-L-Rhamnopyranosyl-(1→6)-β-D-glucopyranoside] | Malvidin 3-rutinoside | $C_{29}H_{35}O_{16}^+$ |
| 14 | Karachine | | $C_{26}H_{27}NO_5$ |
| 15 | Taxilamine | (6,7-Dimethoxy-1-isoquinolinyl)(2-hydroxy-3,4-dimethoxyphenyl)methanone, 9CI<br>1-(2-Hydroxy-3,4-dimethoxybenzoyl)-6,7-dimethoxyisoquinoline | $C_{20}H_{19}NO_6$ |

gram negative species and fungal species [11, 8]. A research also suggested that an excellent medicine for the cholera infection can be obtained from the root of the plant [8]. *Berberis aristata* as one of the ingredient in formulation was checked for its anti microbial activity against hepatic amoebiasis in experimentally produced amoebic abscess in liver of golden hamsters which showed a maximum cure rate of 73% when compared with metronidazole. In the same study it was found out that the preparation is also effective in stimulating humoral and cell mediated immunity [9].

Berberine was proved to be antibacterial, antiamoebic, antifungal, antihelminthic, leishmanicidal and tuberculostatic agent [10].

Its trade name is Indian barberry. Commercially it is available in some Ayurvedic preparations and the market names of Daruhaaridraa are Daruhaldi, Rasaut and Zirisk. Dar-ehald is known for its anti microbial properties in eyes, ear, gastrointestinal and genitourinary infections. Commercial importance of this plant is in hepatic preparations such as hepatoprotective agent

**Figure 2:** *Berberis aristata* DC. : Red berries in a flowering branch, yellow flowers, blue berries.

specially used against hepatitis C, B and jaundice. It is also employed as an important ingredient in various antiobesity products [27, 8, 5, 28, 22].

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