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MEDICINAL PROPERTIES, PHYTOCHEMISTRY AND PHARMACOLOGY OF *ARISTOLOCHIA ROTUNDA* LINN: A POTENT UNANI DRUG

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ABSTRACT

Aristolochia Rotunda Linn has been known as *zarawand-mudharaj* in Unani Medicine. It belongs to the family *aristolochiaceae* and commonly known as the Smearwort, snake root, European birthwort. It has been used in Unani system of medicine for various properties such as immunomodulatory, anti-inflammatory, anti-neoplastic, anti-bacterial, anti-oxidant, hepatoprotective activity. In Unani system of medicine for various therapeutic actions such as *musakkin-i-alam*, *muh'allil awrām*, *mufattih-i-sudad*, *mudir-i- hayd*, *mudir-i- baul wa hayd*, *muqawwi-e-bah*, *muqawwī*, *muharrrik*, *muqawwi-i- asab*, *muhallil*, *mulattif*, *munaffith - i- balgham*, *mushil-i-balgham*, *muqateh wa mukhrij-i-balgham*, *munaaqi e dimagh*, *munaqqie meda munaqqie qabatur ria*, *mulayyin*, *qātil-i- kirme shikam*, *mudammil qurūh*, *dāfi'-i-zaher* or *tiryāq-i-sumoom*, *jāli*, *jazib* since centuries. In Unani literature, Roots are of two type's *zarawand taveel* and *zarawand mudharaj* based on geographical distribution, some Unani scholars depicted the varieties of *zarawand mudharaj* viz. *zarawand mudharaj shami*, *zarawand mudharaj rumi* and *zarawand mudharaj maghribi*. The present article describes a detailed review of literature of this plant species including taxonomy, pharmacology, Phyto Chemical Constituents and pharmacological activities in an organized way. This review paper will surely serve as an important source for future scientific investigations on this plant.

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INTRODUCTION

The *Aristolochiaceae* family consists of seven genera and over 500 species. Members of this species can be found in the tropics and warm temperate zones. The majority of the plants are herbs or climbing bushes. Oil-secreting cells can be found all over the family, and they frequently create translucent spots on the leaves. *Aristolochia* and *asaram* are the two most important genera. Constituents of the family include alkaloids (aporphine and protoberberine), aristolochic acid, phenolic esters and ethers, volatile oils and flavonoids.¹ Historically, *Aristolochia* has played an important role in ethnobotany. The generic name is derived from the Greek *aristos*, “best”, and *lochia*, “delivery”, about its known ancient use in childbirth.^{2,3,4} In Greece it is also called *waqlasatees*. There are two major variants of *zarawand* as described by Arab doctors.²

Plant products containing aristolochic acids have been used extensively in traditional herbal medicine for various illnesses. They have been used as antirheumatics, as diuretics, in the treatment of oedema, in wound healing,^{4,5} leukocyte enhancement⁵ to facilitate childbirth, and for less common conditions such as haemorrhoids, cough and asthma, illnesses such as hepatitis, urinary tract infection, vaginitis, oral ulcer, upper respiratory tract infection, eczema, headache, dysmenorrhea, arthralgia, neuralgia, hypertension, cerebrovascular accident, bronchitis, pneumonia, heart failure and oedema have been reported to have antibacterial, antiviral, antifungal, and antitumor effects and in more recent times, have been used in conventional pharmaceuticals⁴ and as “Raiz de mato”, for the treatment of “snake bites^{3,5} and tetanum.”³ This briefly reviews the botany, phytochemistry, pharmacology, traditional knowledge and therapeutic application of *Aristolochia Rotunda* Linn. It was an attempt to compile and document information on these topics while emphasising the importance of research and development.

Botanical classification:

Taxonomic Hierarchy of *Aristolochia rotunda* L.^{2,6}

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Order: Piperales⁷

Family *Aristolochiaceae*^{4,5, 6, 8,9,10}

Genus: *Aristolochia* L.⁷

Species: *Aristolochia rotunda* L.^{5,7,9}

Vernaculars:

Urdu: *Zarawand-mudahraj*;^{2,8,9,11,12} *zarawand gard*¹³

Hindi: *Zarawand-gird*;

Arabic: *Nukhudalward*, *Zarawand-e-gird*;¹¹

English: Apple of the Earth, Mercury goosefoot,^{9,11} Round-leaved birthworts, Smearwort,^{9,10,23,11} snake root⁹, European birthwort^{6,9} round *Aristolochia*^{6,13}

Persian: *Zārāwand-gird*, *Zārāwand-mudahraj*;^{11,12,14,15}

European: Birthworth, round *Aristolochia*⁶

French: *Aristolochie à feuilles rondes*, *Aristolochie arrondie*, *Aristolochie ronde*;¹⁶

German: Knollige osterluzei, Rundblättrige osterluzei, Runde osterluzei, Rundknollige osterluzei;

Italian: *Aristolochia rotunda*;

Spanish: *Aristolochia redonda*;

Turkey: *Zeravent otu*;^{11,16}

THE ETHANO BOTANICAL DESCRIPTION:

A small plant with slender stems and almost sessile, obtusely cordiform leaves; flowers are solitary in the axils of the leaves, tubular, yellow outside and orange-brown within. The whole plant is acrid, aromatic and bitter.⁸ The root is about 5-25 cm long, hard, horny, tuberous, placentiform.^{11,16} and heavy when dry; more or less mammillated on the undersurface, of a reddish-brown colour; the remains of many stems or small pits can be seen on the upper surface, indicating where they were attached. One central scar marks the connection of the rootlets on the underside. It has a bitterish, fragrant, and camphoraceous flavour, as well as a camphoraceous⁸ odor.^{8,11,17}

Habitat and distribution:

Aristolochia were widely distributed in tropical, subtropical and temperate regions of the world.¹⁸ Indigenous in southern Europe.⁶ It is the female of *A. longa* that grows throughout the Mediterranean, southern Europe, Central Asia, and Kashmir; both *A. longa* and *A. rotunda* can also be found in Iran and Iraq.¹¹

Macroscopic characters:

The sample comprises rounded, flattened, disc-like tuberous pieces which are very hard, smooth, yellowish-brown to light brown. The surface is marked with thin, light stripes all around. It has a centrally situated pit both on upper and lower surfaces. The tubers are 2-3 cm in diameter. The pieces are tough and do not break by hands or under teeth.¹¹

Plant type: is a shrub or perennial herb, prostrate or twinning and belongs to the family Aristolochiaceae.¹³

Odour and taste: aromatic bitter¹⁹ slightly spicy odour^{2,6} mild fragrance²⁰ taste: acrid and slightly bitter^{6,21} slightly warm and sweet.²⁰

Microscopic:

The cross-section of tubers shows that it has all the features of a monocot tuberous stem rather than that of a dicot root. It has a very large zone of ground cells having vascular bundles scattered irregularly. The outermost layer is an epidermis which also has some depositions at places on the outer surface. The epidermal layer is followed by 2-3 rows of rectangular, comparatively smaller parenchymatous cells, following this is a broad region, occupying the whole area up to the center, of parenchymatous ground cells, rounded to polygonal in shape and filled with starch, granular in appearance. The phloem elements not being elaborate. The cells surrounding these vascular areas become compact, much smaller in size and elongated, forming a ring or sheath of radiating cells around the vascular areas. The cells of ground tissue are closely packed and also have needles or prisms of calcium oxalate.⁶

Plant description in Unani (Māhiyyat):

It is a round root that looks like a beetle nut and also resembles *Reetha* (Indian soapberry) but maybe slightly smaller, larger and wider in size.^{12,14,15,22} It's flattened, color is yellowish on the outer side and reddish on the inner side. The fresh and unripe root is best; its strength lasts for two years.²² Dioscorides (40-90 AD) has described its three varieties: (i) *Zarawand Taveel*, where the root is long and possesses male characteristic features; (ii) *Zarawand Mudharaj* whose root is round in shape and considered as a female plant; (iii) The root of third variety is similar to grape wood (*Chob-i-Angoor*).^{23,16} This plant has many branches that come from a root. Taller than 1ft. the leaves are similar to *zarawande taveel* but smaller, aromatic, slightly spicy taste and softer. The flowers are white, red on the inner side, with a bad odour resembling a Cap.^{24,20} Moreover, based on geographical distribution, some Unani scholars depicted the varieties of *Zarawand Mudharaj* viz. (i). *Zarawand Mudharaj Shami*: A variety of Syria whose root is round and slightly conical in shape and one edge is saffron-reddish; (ii). *Zarawand Mudharaj Rumi*: This type is indigenous to Rome whose root is not round and its edge is saffron in colour; (iii). *Zarawand Mudharaj Maghribi*: This is indigenous to Europe and is conical in shape.^{2,16}

PHYTO CHEMICAL CONSTITUENTS:

Organic: Phenolics tannins, starch, steroids and terpenoids.

Inorganic: Bismuth, calcium, iron, magnesium, potassium and zinc.⁶

The secondary metabolites from *Aristolochia* species cover 16 major groups classified by their chemical structures, including aristolochic acids and esters, aristolactams, aporphines, protoberberines, isoquinolines, benzyloquinolines, amides, flavonoids, lignans, biphenyl ethers, coumarins, tetralones, terpenoids, benzenoids, steroids, and others. The aristolochic acids were a host of phenanthrene derived metabolites in which the aristolactams also possessed a similar skeleton.¹⁸

The structures of two novel sesquiterpene hydrocarbons, ishwarane and aristolochene, and a tetracyclic sesquiterpene, ishwarone, were discovered in roots. A new sesquiterpene hydrocarbon (I) is isolated and characterized as 5 β -H, 7 β , 10 α -selina-4(14) and II-dien. Five new phenanthrene derivatives (II–VI) are isolated and characterized in addition to isolation of stigmast-4-en-3-one, sitosterol and two uncharacterized isomeric sesquiterpene alcohol M.P 1030 C and 1500 C.¹³

Hişā-i-Musta'mala (Part used): root^{6,13,21,25}

Part studied: root⁶

Mizāj (Temperament): 2° Hot and 3° Dry^{23,26} Hot and Dry^{22,27} Hot and Dry 2°^{2,6,24,12,14,15,20} Hot and Dry 3°²¹

Miqdār-ikhūrāk (Therapeutic Dosage): 6gm,²² 4.5 to 7 gm,^{6,20} 3-4 gm,^{24,27} 3-5 gm,^{12,14} 4-7 gm.²

Shelf life: 3yrs,²² 2 yrs²⁰

Nisbat sitara: Neer Azam Shams¹⁵

Nafah Khas (Important action): *Mushile Balgham*,¹⁴ antidote to poisons and brain tonic.¹⁵

AF'ĀL (PHARMACOLOGICAL ACTION):

- *Musakkin-i-alam*: Analgesic^{13,12,14,24}
- *Muh'allil awrām*: Anti-inflammatory¹³
- *Mufattih-i-sudad*: Deobstruent^{6,13,20, 23,24}
- *Mudir-i- hayḍ*: Emmenagogue^{6,12,14,23,27,28}
- *Mudir-i- baul wa hayḍ*: Diuretic and Emmenagogue^{18,114,122,124,126}
- *Muqawwi-e-bah*: Aphrodisiac^{2,12,13,14,24}
- *Muqawwī*: Tonic^{6,29}
- *Muharrrik*: Stimulant^{6,22,29}
- *Muqawwi-i- asab*: Nervine tonic²²
- *Muhallil*: Resolvent^{6,12,14,20,24}
- *Mulattif*: Demulcent^{20,23,24}
- *Munaffith -i- balgham*: Expectorant^{13,24,27}
- *Mushil-i-balgham*: Purgative for phlegm^{14,24,27}
- *Muqateh wa mukhrij-i-balgham*: Expectorant.^{12,14}
- *Munaaqi e dimagh, munaqqie meda munaqqie qabatur ria*.²⁰
- *Mulayyin*: Laxative
- *Qātil-i- kirme shikam*: Vermicidal¹³
- *Mudammil qurūh*: Cicatrizant /healing agent^{23,22}
- *Dāfi 'i-zaher or tiryāq-i-sumoom*: Antidote^{6,22,23}
- *Jāli* : Detergent^{12,14,24}
- *Jazib* : absorbent²³

ISTI'MĀLĀT (THERAPEUTIC USES):

Used in *Dard-i- raḥim* (Dysmenorrhea),³⁰ *idrar-i- hayḍ*^{12,24,27} *ikhtināq al- raḥim* (hysteria).²² *du'f al-aam* (general debility), *ihtibās bawl* (amenorrhea).^{6,24,27} *dypnea, waram salabat ' al -tihal wa jiga'*,²⁴ *larza and dard-i-pahlu* (chest ailment).²⁰ as hemoptysis and for *tanqiya-i- raḥim*,^{20,27} *joshānda* (decoction) (internally) and *ḍimād* (externally) used in case of *ihtibā al-bawl* (retention of urine),²⁷ *surfa muzmin* (chronic cough),^{23,27} *rabw* (asthma),^{23,15,27} *waja' al -mafāsīl* (arthritis), *muzmin waja'* (chronic pain), *dhāt al-janb* (pleurisy),²⁷ *dhāt al- ri'a*,^{14,27} *irq al-nasā* (sciatica),^{12,13,14,15,20,24} *waram al-kabid, waja' al-zahr, waram ' al -tīhāl*,^{12,13,14,20,24} *niqris* (gout).^{12,13,15,20,24} Used as syrup and decoction and also applied externally in chronic inflammations of the spleen and liver.^{24,13}

As *ḍimād* it is used to remove, thorns, arrows and bones.²⁰ The paste prepared with honey is useful in hepatosplenomegaly. *Zarawand mudaharaj* along with *filfil* (piper) is useful to evacuate morbid humour from the brain and is beneficial in the treatment of epilepsy and strengthening gums.^{2,16}

Sharab and *majun* prepared from *zarawande mudaharaj* is more invigorating enhances sexual desire and increase libido.^{13,20}

Cleans the teeth and brightens face.²³ In combination with *gil-i-armani* (armenian bole) and *babool* (acacia arabica wild.) to enhance its astringent property.^{2,16}

When used along with black pepper and *murmakki* orally or as *humool* is prescribed to eliminate morbid humour from the uterus.^{20,22,27}

Zarawand mudaharaj along with *sikanjbeen* (a formulation prepared with vinegar and honey) helps to remove morbid humour from the body.^{2,22}

The pills or tablets prepared with the powder of *Zarawand Mudaharaj* and ghee (3.5 g) relieve breathlessness when its smoke is inhaled.^{2,16,20}

Zarawand mudaharaj and honey rubbed together in white leprosy, also useful in dropsy paralysis and increase radiance in the skin.^{20,29}

Zarawand mudaharaj macerated with black pepper given in cases of cholera and diarrhoea, and with ginger, it acts like carminative and is used in bowel complaints.²⁹

Powder of 4.5g with water helps in *fawq*.^{15,20,21}

Zarawand with honey is used to treat *safravi* and *balghamī yaraqān*.²⁰

Joshānda of *zarawand mudaharaj* when put into ears as drops, removes dirt clears them and increases hearing function.^{20,23}

Zarawand mudaharaj, sosan aasman jooni and honey internally and Externally when wounds are washed and powder sprinkled disinfects and heals deep wounds.^{6,11,20,26}

For chronic ulcers (*qurūh qabisa*) it is used in the form of ointments.^{13,21,24} also used in uterine wounds, when given along with *filfil* it detoxifies the brain.²¹

A valuable antidote to snakebite and bites of poisonous insects as scorpion it is used internally and externally, it makes the part bitten insensible to the ill effects of the poison.⁶

Zarawand mudaharaj, irsa and honey remove ulcers from wound, and cleans the wound.^{11,20}

Other Uses:

As decoction can be used externally on ulcers and sacral fistula, in a hip bath. And used in eczema and other skin complaints.¹⁰ To prevent arthritis, as a stimulant and an emmenagogue. It's used to treat digestive problems like raising appetite and toning the digestive organs. Other uses include stimulant, tonic, diaphoretic, and diuretic. In Amenorrhoea to induce menstruation, used for its purgative action and also to induce abortion.²⁵

It is used as carminative and anti-inflammatory, beneficial in headaches, migraine, epilepsy, melancholy, hiccup and jaundice; and also as an antidote to plant and animal poisons.¹¹

Antitumour, antifertility, immunomodulating, mutagenic.⁸

Useful in headache migraines and epilepsy.¹⁵

Due to good fragrance used as an ingredient in fragrant oils.²¹

Badal (Substitute):

*Revand chini*²²

Zarawand e taveel and revand cheeni^{12,14,24}

Zarawand e taveel and 1/2 part revand chini^{15,20}

*Zarawand taveel and narkachur*⁶

*1 1/2 Zarawand e taveel*²¹

*1 1/2 Zarawand e taveel or rasan*²⁰

*Zarawand e taveel and 1/3 part jawetri*²⁶

*Equal quantity zaraband and 1/3 part bisbasa and 1/2 qust shirin*²³

*Equal quantity zaraband and 1/2 anzaroot*²¹

*Equal quantity of sheetraj or zarandbad*²⁰

*Zaranbad and qust*³¹

Adverse Effects (Muzir): Toxic to *tiḥāl* by producing its dryness,^{14,15,20} *Aṣab* by producing its coolness and dryness^{12,14,15,24} and liver³¹

Mušliḥ(Corrective): for spleen- *zarishk* (berberry) or honey^{2,6,12,14,15,18,20}, for general dryness- *roghan-e-kaddu* and *roughan-e-banafsha*

EVIDENCED-BASED PHARMACOLOGICAL ACTIVITIES:**Immunomodulatory Activity:**

Immuno modulation is the altering of the immune response as a result of foreign substances entering the body. A vast range of herbal medications is recommended in traditional Indian treatments, in addition to the existing drugs, for their immunomodulating potential (Yadav *et al.*, 2010).

Aristolochic acid has been demonstrated to attach to lymphocyte surface receptors, influencing immunological response. An immuno-stimulating action was reported in a human study that measured increased phagocytic activity after 3 days of treatment (Kluthe *et al.*, 1982).³²

Anti-inflammatory activity:

Aristolochic acid also played a regulatory role in prostaglandin synthesis. It inhibited inflammation by both immunological and non-immunological agents. One mechanism of activity was thought to be a direct inhibitor of phospholipase A2, decreasing the generation of eicosanoids and platelet-activating factors (Achari *et al.*, 1981). Another anti-inflammatory mechanism may be the effect on arachidonic acid mobilization in human neutrophils. The active fractions of *Aristolochia indica* were found to neutralize rattlesnake venom actions (Samy *et al.*, 2008).³² The studies carried out on different bioactive compounds isolated from *Aristolochia* species such as aristolochic acid I, aristolochic acid IVa, aristolochic acid IIIa and aristolamide II showed significant anti-inflammatory effects.¹⁶

Anti-neoplastic activity:

The plant was reported as an anti-neoplastic agent against Ehrlich ascites carcinoma in mice by Masud Rana and Khanam (2002). Additionally, Kupchan and Doskotch (1962) demonstrated the anti-tumor activity of *Aristolochia* species in bio screening studies. Aristolochic acids have been shown to bind to adenine in codon 61 in the H-ras mouse oncogene and to purines in the human p53 gene. Mutations identified in tumors of rodents exposed to aristolochic acids include A:T to T:A transversions in codon 61 of the c-H-ras gene in forestomach tumours (from rats and mice), lung tumours (from rats and mice), and ear-duct tumours (from rats). No mutations were identified in tissues from rats with chronic renal failure that had not been exposed to aristolochic acids (Schmeiser *et al.*, 1991).

Anti-bacterial Activity:

They showed that the root extracts were effective against gram-positive bacteria. Aristolochic acid was shown to possess anti-microbial activity against *Bacillus subtilis* and *E. coli* by Angalapameswari *et al.* (2012).

Anti-oxidant Activity:

Anti-oxidant properties and DPPH free radical scavenging activity of *Aristolochia* species was studied by Thirugnasampandan *et al.* (2007).³²

Hepatoprotective activity:

A study has reported that the hydro-alcoholic extract of rhizome of *Aristolochia rotunda* L. at the dose level of 89.64 mg/kg b. w. significantly reduces serum bilirubin, SGOT, SGPT and ALP levels in CCl₄ induced liver toxicity in albino Wistar rats.

Studies on reducing toxic effects of other drugs:

The in vitro study has reported that aristolochic acid reduces the toxic effects of prednisolone, chloramphenicol and tetracycline.¹⁶

CONCLUSION

Above research findings proves that *Zarawand mudaharaj* has immunomodulatory, anti-inflammatory, anti-neoplastic, anti-bacterial, anti-oxidant, hepatoprotective activity. Moreover it safe for human consumption. In view of the above findings it may be concluded that potential claims of Unani literature regarding *Zarawand mudaharaj* can be helpful in finding solution for various health problems i.e. Allergic disorders, dysmenorrhoea, Asthma, chest ailment, retention of urine, hysteria, hemoptysis, pleurisy, cholera, epilepsy, sciatica, gout, chronic inflammations of the spleen and liver and as disinfectant etc. through extensive research on it.

Despite its economic and medicinal importance, it has not gained widespread acceptance due to its high perish ability. The goal of this review was to compile all of the available literature on medicinal plants that described the relationship between the plant's physiology, biochemistry, and nutritional characteristics. As a result, we will be able to provide gathered data for further research purposes, as this plant has enormous potential to improve health quality and marketing opportunities.

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CONFLICT OF INTEREST

The authors have no conflicts of interests to declare pertaining to this article.

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