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Therapeutics, phytochemistry and pharmacology of *Iklilul Malik (Astragalus hamosus Linn): A natural Unani Remedy*

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Abstract

Astragalus hamosus Linn is one of the most important medicinal plants traditionally used for various health needs. It is an annual herbaceous plant growing up to 30 cm of height. The fruits perfectly characterize this species as they are strongly curved. The plant is found in plains of Punjab. It is also cultivated into Afghanistan, Persia, Balochistan and Sindh. It has been in use as a pot herb from a very early period. The pods of the plant possess mohallil-e-warm (anti-inflammatory) property and have been described to be useful in various ailments. The plant has shown diverse biological and pharmacological activities. It has been used in Unani Medicine (*Tibb-e-Unani*) and other Traditional System of Medicine from time immemorial. Keeping in view the high medicinal importance of the drug in Unani Medicine, this review provides available information on traditional uses, phytochemistry and pharmacological properties of Unani drug *Iklilul Malik*.

Keywords: *Astragalus hamosus*, Iklilul Malik, Nakhuna

1. Introduction

Iklilul Malik is profusely branched weed and present in rectangular appearance. Its leaves are like those of Quince (*Cydonia vulgaris* Pers) but a little longer. It is abundant in wasteland, rugged area and hard soil [1]. National formulary of Unani medicine equated *Iklilul Malik* with three leguminosae species: *Melilotus alba*, *Trigonella uncatata*, *Astragalus hamosus* [2]. In Indian Bazaar, the dry pod of *Astragalus hamosus* is available and known as *Iklilul Maliik* or *Nakhuna* [1]. In a pharmacognostical study its identity was further confirmed as pods of *Astragalus hamosus* [3]. The *Astragalus hamosus* Linn (Family - Papilionaceae) is one of the most important medicinal plants traditionally used for various health needs.

Belonging to one of the largest angiosperm genera, *Astragalus hamosus* is an annual herbaceous plant growing up to 30 cm of height. The plant is a hard drought-tolerant legume with high seed productivity. The leaves have many leaflets and the flowers are small, white or yellow, grouped at the end of a stalk. The fruits perfectly characterize this species as they are strongly curved [4].

The pods of *Astragalus hamosus* are small, crescent or sickle shaped, greyish, yellow with a beak, slightly curved outward [1], indehiscent fleshy or oval legumes similar to some fishhooks with a 1-2 cm in diameter [4] about 2.5 cm in length, grooved on both side with a central partition divided the pod in two cell. Each cell contains a single row of seeds. The seeds are hard rhomboidal or round [1]. Each pod contains 15-20 small and rectangular shaped seeds. The pods have yellow to yellowish brown colour [4].

Iklilul Malik (Astragalus hamosus) contains seed and most of the seeds are viable can be cultivated. A cultivation trial reveals that the suitable time for sowing the seeds is 3rd week of November. The seeds take 10 days to germinate and flowering takes place in the first week of Mach. The pods appear in the month of April and mature in the month of April and May [1].

2. Distribution

The plant is found in plains of Punjab [2, 5-8]. It is distributed in Orient, Mediterranean and Canaries [8]. It is also cultivated into Afghanistan, Persia [9], Balochistan and Sindh [6]. It was distributed from North Western Africa to Asia. The plant is nowadays found in Africa: Algeria, Egypt, Libya, Morocco, Tunisia; Asia: Armenia, Azerbaijan, Gruzia, Iran, Iraq, Pakistan, Russia in Asia, Turkmenistan, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Syria, Turkey in Asia, United Arab Emirates; Australasia: Australia; Europe: Albania, Bulgaria, Corsica, Crete, former Yugoslavia, France, Great Britain, Greece, Hungary, Italy,

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Malta, Portugal, Romania, Russia, in Europe, Sardinia, Spain, Turkey in Europe, Ukraine; North America: United States [10].

3. Unani Description

In Unani literature, the morphology of the plant is described in detail by certain Unani physicians. It is an herb [11]. Its stem and branches are very thinned and green in colour, on which leaves are grown in 3-3 pairs [12]. Flowers are longer and white in colour [13]. When flowers shed off from plant it is replaced by seed pods which is known as Nakhuna or Iklilul-Malik [12]. These pods are moon shaped [14], about one inches in measurement [11] which is filled with fenugreek like small seeds [11, 13].

4. Ethnobotanical Description

The plant is an annual herb [7, 8] with much branched, diffused or erect stem of about 30-60 cm with multiple greyish white colour hairs.

4.1 Leaves: They are compound [1], paripinnate or imparipinnate, rarely unifoliolate or digitately trifoliolate [10].

4.2 Leaflets: The leaflets are grown in 8-12 pair oblong to cuneate-oblong and linear, retuse [8]. They are about 0.5 to 1.5 cm long, pale green in colour and glabrous. They are distinctly imparipinnate. The apex is round [1].

4.3 Flowers: The flowers are racemes very short, axillary in position about 4-8 in numbers [1, 8]. Flowers bracteate; bracteoles present or absent; pedicellate or sessile, violet or purple to white or pale yellow in colour [10]. Calyx are about 0.5 to 0.6 cm, teeth subulate [1].

4.4 Peduncles: These may be longer or shorter than the leaves [8].

4.5 Seed pods: The seed pods are spreading, oblong-linear, terete [8]. They are about 2.0 to 2.7 cm long and 0.8 cm in diameter, cylindrical much curved nearly semilunar in shape. The colour of immature seed pod is pale green where as that of mature greyish-yellow and present in groups of 7 to 8. A beak on lateral side is present which slightly curved outward. There are two grooves opposite to each other extending from base to apex. A central partition divides the pod in 2 cells and in each cell single row of 6 to 10 seeds are present. Seeds are flat ovate with hard, brownish-green colour testa with a deep marginal notch on one side and smells like fenugreek [1].

5. Vernaculars

The plant is known by different vernacular names in different language, areas and traditions: *Iklilul Maliik*, *Asabeaulmalik*, *Elkoren* (Arabic); *Akhilulmalik* (Bombay); Tonkin bean, Melilot, king's crown, King's clover (English); *Sainji* (Folk); *Parang*, *Purtuk*, *Nakhuna*, *Tajebadshah*, *Katila* (Hindi); *Akhile-malik* (Marathi); *Giyahqaisar*, *Naakhunaa* (Persian); *Akhilulmalik* (Punjab); *Ikli-ul-malik* (Unani); *Nakhunah* (Urdu) [2, 6-9].

6. Mizaj (Temperament)

Some Unani physicians described the temperament of '*Iklilul Maliik*' as Hot and Dry in first degree [11, 13-15], while few others described it as *murakkabul quwa* or *motadil in hararat and baroodat* [15].

7. Afaal (Action)

In classic Unani literature, various actions of the drug *Iklilul Maliik* (*Astagulus homosus* pods) have been described in

details such as *Muhallil-e-awram* [11, 12, 14-17], *Munzije-warm* [11-15], *Musakkin-alam*, *Mudir-e-bol-wa-haiz* [11, 13, 14], *Qabiz* [12], *Mulayyan* [16] and *Muqawwi-e-aza* [14].

8. Istemal (Uses)

Iklilul Maliik has been described to be useful in various ailments. Due to its *mohallile-warm* property it is useful in *warm-e-khusyatur rahem*, *awram-e-ahsha* such as *warm-e-jigar*, *warm-e-khusiya*, *warm-e-tihaal*, and also useful in *awram-e-sulbiya*. Its powder in a dose of half tea spoon along with honey is used orally to relieve the inflammatory conditions. Its decoction as *abzan* (sitz bath) is very much useful to relieve *awram-e-masaana* and *awram-e-khusiya* [17]. It is used in the form of *zimaad* (paste) to resolve the inflammation and to relieve the pain; due to this it is used in the form of paste and decoction to resolve the inflammation of liver, spleen, uterus and ovaries [11]. It is useful externally or internally in gastritis and proctitis. In *falig* (paralysis) its decoction is administered orally and applied externally. Its decoction is also used as enema to strength intestine [14].

Nutool of its decoction is beneficial in various conditions like *dard-e-sar* (headache), *dawar* (vertigo), *sadar*, *sakta*, *laqwa* (palsy) and *isterkha-e-balghami*. Local use of decoction as *nutool* also cures *Tashmnuj-e-imtilayi* and *nazla* (cold) while oral ingestion of decoction give relief in painful condition of stomach, liver and spleen [16].

Its paste along with vinegar and *roghan-e-gul* is useful in headache [16].

Juice of the fresh fruits along with *sheera-e-angoor* is good for earache [12].

Iklilul Maliik has been applied for various diseases and complications in traditional Persian medicine (TPM) and Ayurveda. Topical application of the extract of aerial parts has been reported to be effective in the control and treatment of headache, vertigo, strokes and dementia. Oral administration of its decoction has also been recommended for gastrointestinal upset, inflammations, respiratory discomfort and urinary complications [4, 18].

9. Muzir (Adverse effect)

It produces adverse effect on *unsainain* (ovaries) [11, 14, 15] and *khusiya* (testes) [13].

10. Musleh (Corrective)

Unani physicians described that *Shahed khalis* (honey) and *Anjeer* (fig) are used as corrective [13, 14].

11. Pharmacological action: (As described in ethnobotanical and traditional literature)

The drug *Astragalus hamosus* is described in detail in ethnobotanical and scientific literature and various actions have been reported to possess by it. Some pharmacological actions and therapeutic uses are as follows:

The plant is aphrodisiac, galactagogue, maturant, pectoral, antiperiodic, stomachic, wound healer [8], demulcent, laxative [5, 6, 8], emollient [5-8]. It also possesses astringent, antirheumatic and anti-inflammatory properties [2].

Decoction of beans possesses anti-inflammatory, anodyne, diuretics, emmenagogue properties [2].

Juice of the leaves is analgesic. Oil is tonic [8].

Seed pods extract shows anti-inflammatory activity. The alcoholic and aqueous extract of the pods exhibit a similar significant effect analgesic effect. Hydro-alcoholic extract of the seed pods exhibit antiproliferative, antioxidant, hepatoprotective and antimicrobial activities [4].

Fruits are tonic and have anti-inflammatory property [8].

12. Therapeutic uses

In Unani medicine, the decoction of the beans is given internally in nervous disorder; liver, kidney and spleen affection. The paste of the beans is massaged and applied externally on inflammatory areas [2, 7].

The paste of the plant with vinegar or rose water is applied for externally for headache [2, 7]. Plant is also used in catarrh affection [6]. It allays thirst, heals wound and ulcers. It is used in enlargement of liver. It also cures leucoderma. It has been used in irritation of the mucus membrane [8]. A gum like tragacanth is found in plant used externally for making gum paste [5].

The juice of the leaves is good for earache. The fruit lessens inflammation is good for intestinal troubles, headache, paralysis and bronchitis. Oil is tonic and is applied on paralytic part [8].

Iklilul Malik has been applied for various diseases and complications in traditional Persian medicine (TPM) and Ayurveda. Topical application of the extract of aerial parts has been reported to be effective in the control and treatment of headache, vertigo, strokes and dementia. Oral administration of its decoction has also been recommended for gastrointestinal upset, inflammations, respiratory discomfort and urinary complications [4, 18].

13. Phytochemistry

The callus of the plant contained amino acids, the roots contained saponins and sterols. The leaves yield 3-nitropropionic acid [2].

The pod show positive test for phenols, saponins, sterol/terpenes, and tannins. It yields 6.56% ash, 1.80% acid insoluble ash and 3.12% water soluble ash. Besides saponin, 3-nitropropionic acid after hydrolysis has been isolated. The pod sallow with the seeds has 1.84% fixed oil (RI, 1.5810; acid value, 22.54; saponification value, 188.38% and iodine value, 67.36). Fatty acid composition shows that the oil contains lauric (2.8%), myristic (2.9%), palmitoleic (31.9%), palmitic (8.2%), stearic (11.0%), oleic (18.5%) and arachidic (14.4%). The pods also contain various amino acid (ornithine, 13.8%; arginine, 14.11%; histidine, 16.35%; DL-dopa, 14.42%; alanine, 4.01%; methionine, 9.4%; norleucine, 5.61% isoleucine, 12.13%). The fructose (32.6%) and glucose (67.4%) are also been reported [1].

Physiological ash derived from the pods' tissues and non-physiological ash derived from environmental contamination such as soil or sand. Acid insoluble and water soluble ash values were determined to be 8.33±2.89 and 40.00±5.00 mg/g, respectively. Acid soluble ash value reflects silica content of the pods. Free amino acid content was 3.33±0.001 (w/w %), while soluble sugar content of the pods was 8.83±0.004 (w/w %) [4].

Polyphenols were detected in dichloromethane and ethanol fractions, visualized by FeCl₃ reagent. Several triterpenes including saponins were detected by Liebermann Burchard reagents in hexane, dichloromethane and ethanol fractions. Some glycosides and glycolipids were detected in ethanol fractions visualized by Orcinol [4].

Principal fatty acids of the pods' oil found were linoleic acid (C18: 2, 48.64%), linolenic acids (C18: 3, 25.35%), lauric acid (C12:0, 8.12%) and stearic acid (C18:0, 6.38%). Other fatty acids (1-2%) were tricosanoic acid (C23:0), 7-10-13-hexadecatrienoic acid or roughanic acid (C16:3), 9-hexadecenoic acid (C16: 1) and 13-docosenoic acid (C22:0). Cyclopropanoic acid, 2-hexyl which was detected in fixed oil (1.56%), is a cyclopropane fatty acid [4].

Fenozan acid (3-(3, 5-di-tert-butyl-4-hydroxyphenyl)-

propionic acid) was also detected in the pods' fixed oil with a concentration of 0.099%. Fenozan acid is a sterically hindered phenol which can act as a radical scavenger antioxidant [19]. It has been also reported to have antiarrhythmic and vasodilatory effects [20].

About 1.437% of the oil consists of non-fatty acids such as alkanes, alkenes or terpenoids [4].

The plant contained some flavonoids as hyperoside, isoquercitrin, astragalin and a flavanol glycosides (rhamnocitrin 4'-beta-D-galactopyranoside) has been detected in leaves of the plant. Also, some saonins have been isolated and identified from aerial parts [21, 22].

14. Pharmacological Studies

A number of studies have been carried out on pods of *Astragalus hamosus* Linn (*Iklilul Malik*) in recent years showing that it possesses diverse pharmacological effects. Some of the important pharmacological effects are as follows:

14.1 Analgesic

Analgesic effect of hydro alcoholic extract of *Astragalus hamosus* was examined by the acetic acid induced writhing response and the hot plate test. The analgesic effects of chloroform, hexane, ethyl acetate and aqueous fractions were evaluated by the hot-plate method. The hydro alcoholic extract could reduce edema in dose dependent manner. The hexane and ethyl acetate (but not the other fractions) showed significant analgesic activity when compared to morphine [23].

14.2 Anti-arrhythmic

Fenozan acid derived from pod's fixed oil has been reported to have antiarrhythmic and vasodilatory effects [20].

14.3 Anti-cancer

The anticancer activity of the isolated mixture of two saponin, derived from *Astragalus hamosus* was compared with dinaline (histone deacetylase inhibitor), decitabine (DNA methylation inhibitor), erufosine, tamoxifene (estrogen modulators) in two breast carcinoma cell lines MCF-7 estrogen receptor (ER) positive and MDA-MB 231-ER negative. The study confirmed the antineoplastic activity of the saponin mixture, derived from *Astragalus hamosus* which were previously found to be active against human leukemia cells [24].

The purified saponin mixture from *Astragalus hamosus* cytotoxicity was evaluated against a panel of human tumor cell lines. the saponin mixture demonstrated significant antiproliferative effect against a multi-drug resistant cell lines HL-60/Dox, with a collateral sensitivity phenomenon, i.e. the IC50 value was lower in the resistant subline in comparison with the chemo sensitive parent cell line HL-60 [21].

Volatile composition of this plant showed significant cytotoxic activity against human acute lymphoid leukaemia in concentration dependent manner [25].

14.4 Anti-inflammatory

The aqueous and alcoholic extract of the pod exhibit a similar significant anti-inflammatory activity in carrageenin induced rat paw oedema. It was observed that they produced inhibition of oedema after 3 hours of carrageenin injection. Their antiinflammatory activity may be by blocking prostaglandin synthesis that is mediator induced by carrageenin injection [26].

The anti-inflammatory effect of hydro-alcoholic extract of the pods was also evaluated by the rat paw oedema induced by formalin [23].

14.5 Antimigraine

In an open-label uncontrolled study, poly unsaturated fatty acids (PUFAs) were administered to 168 patients for a period of 6 months. According to the mentioned study, gamma-linolenic and alpha Linolenic acids might possess prophylactic effects on migraine headaches [27].

14.6 Antioxidant

A study was carried out to evaluate the antioxidant activity of methanolic extract of *Astragalus hamosus* [28].

14.7 Antiviral

In the evaluation of the antiviral effect of the emodin plus *Astragalus* polysaccharide (APS) in the hepatitis B virus (HBV) transgenic mice, emodin and *Astragalus hamosus* had a weak but persistent inhibitory effect on HBV replication in mice which may function as a supplementary modality in the treatment of hepatitis B infection [29].

14.8 Hepatoprotective

The hepatoprotective activity of flavanoids rhamnocitrin 4-B-D-galactopyranoside (RGP) obtained from leaves of *Astragalus hamosus* was studied against N-diethylnitrosamine (DNA) induced hepatic cancer in wistar albino rats [30].

14.9 Immunopotentiating Agent

Astragalus hamosus has a wide range of potential therapeutic applications in immunodeficiency syndrome, as an adjunct cancer treatment, and for its adaptogenic effect on the heart and kidneys. When ligusticum combined with astragalus, they have exerted a notable immunopotentiating effect [10].

14.10 Neuroprotective

The effects of rhamnocitrin 4-β-D-galacto pyranoside (RGP), isolated from *Astragalus hamosus* were evaluated on isolated rat brain synaptosomes, prepared by Percoll reagent, isolated by two-stepped collagenase perfusion. In synaptosomes, RGP had statistically significant protective effect, similar to those of silymarin, on 6-hydroxy (OH)-dopamine-induced oxidative stress [31].

14.11 In Menopausal Symptoms

Poly unsaturated fatty acids (PUFAs) have also been reported to have a role in controlling sexual hormonal balances which may be effective in menopausal disorders [32].

15. Conclusion

The pods of *Astragalus hamosus* Linn (*Iklilul Malik*) has been in use since times immemorial to treat wide range of indications. It has been subjected to quite extensive phytochemical, experimental and clinical investigations. Experimental studies have demonstrated its analgesic, antiarrhythmic, anticancer, anti-inflammatory, antimigraine, antioxidant, antiviral, hepatoprotective, immunopotentiating, neuroprotective and effect in menopausal disorders. The scientific studies have proved most of the claims of traditional medicines. However, further, detailed clinical research appears worthwhile to explore the full therapeutic potential of this plant in order to establish it as a standard drug.

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