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Alhagi pseudalhagi: a review of its phyto-chemistry, pharmacology, folklore claims and Ayurvedic studies

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ABSTRACT
Alhagi pseudalhagi known as Yavasaka in Ayurveda and Camel thorn in English is a small thorny shrub, normally used in folk medicine as a remedy for rheumatic pains, bilharziasis and various types of gastrointestinal discomforts, urinary tract diseases and liver diseases. It is an important ingredient of many Ayurvedic formulations. As the plant is therapeutically very important, it will be worthwhile to review research on its phyto-chemistry, pharmacology, folklore claims and Ayurvedic studies to present comprehensive information on this plant. The available information on this plant is retrieved from various technical and scientific sources viz. websites, databases, books, monographs, journals, etc. and presented under different sections. The reviewed information suggests that the plant has got enormous scope for phytochemical and pharmacological studies to substantiate its therapeutic potential. The review might be helpful for scientists and researchers to find out new chemical entities responsible for its claimed traditional uses.

Keywords: *Alhagi pseudalhagi*, Yavasaka, Folk medicine, Urinary tract diseases

1. Introduction
Alhagi pseudalhagi syn. *Alhagi maurorum* is a perennial plant. It grows from a massive rhizome system which may extend to about six feet into the ground [1]. Its use as diaphoretic, diuretic, expectorant and in treatment of ulcers is well reported [2]. The plant is normally used in folk medicine as a remedy for rheumatic pains, bilharziasis, various types of gastrointestinal discomfort and in diseases of the urinary tract and liver [3]. Oil from the leaves of the plant is used for the treatment of rheumatism, while the flowers of the plant are used for the treatment of piles [4]. It is also used as laxative [5]. Conventional cough syrups have sedatives, anti-allergic nerve-soothing drugs which cause drowsiness. They are not recommended for people with cardiac problems, but a herbal cough syrup using *A. pseudalhagi* has been reported to overcome the above mentioned shortcomings of conventional cough syrups [6]. There has been a remarkable interest in this plant as evidenced by its use in traditional and folkloric systems of medicine. Therefore, we aim to compile an up to date and comprehensive review of *Alhagi pseudalhagi* that covers mainly its phytochemistry, pharmacology, folklore claims and Ayurvedic studies, which might be helpful for scientists and researchers to find out new chemical entities responsible for its claimed traditional and other medicinal uses.

2. Synonyms
Synonyms of *Alhagi pseudalhagi* (Bieb.) Desv. include *Alhagi camelorum* Fisch. Ex DC. *Alhagi maurorum* sensu Baker (non Desv.) and *Hedysarum alhagi* L. (*nom. nov.*) [1, 7-8].

3. Family
The plant belongs to family Fabaceae [9] or Leguminosae [8, 10].

4. Parts used
Leaves, stem, flower, seeds, roots, whole plant

5. Regional language name/tribal/common name
Yavasa, Yasa, Yavasaka (Sanskrit), Bhatuashak (Assamese), Persian Manna Plant (English), Javaso (Gujrati and Hindi), Bharbharra (Hindi), Turuchana gida, Javasa, Neladangara, Ballidurabi, Duralabha(Kannada), Venkatithura, Valiya Kotithuva (Malayalam), Dhamasa

(Marathi), Punaikanjuri, Kanchori (Tamil), Chinnadoolagondi, Dhanvayasamu (Telgu), Turanjabeen (Urdu), Dulal labha, Javasha (Bengali), Camel thorn Bush (South Africa), Caspian manna, Hebrew manna, Moor's Alhagi, Persian manna [1, 9, 11].

6. Geographical distribution

The plant is found in temperate and tropical Eurasia and the Middle East, Northern India, Afghanistan, Armenia, Azerbaijan, Northwest China, Cyprus, Iran, Iraq, Israel, Jordan, Kazakhstan, Kuwait, Lebanon, Mongolia, Pakistan, Syria, Tajikistan, Turkey, Turkmenistan, Uzbekistan and Russia. In China, the plant is mainly distributed in Xin Jiang Uighur Autonomous Region [12]. In India, it is mostly found in arid and dry regions of Gujarat, Punjab, Uttar Pradesh and Rajasthan [9].

7. Botanical description

Macroscopical observations indicated the roots to be stout, cylindrical, tortuous, tap root, 3 to 7 cm in length, 0.2 to 1 cm in diameter, surface rough, longitudinally irregularly striated, often shows lateral root or scars left by them, fracture outer short, inner fibrous, externally dark brown, internally pale brown. Taste is astringent. Stem with aerial branches arising from the stout basal cylindrical underground crown are rough, externally studded with nodules of stem bud, 3 to 4 cm in length and 0.1 to 1 cm in diameter, internodes are short about 0.5 to 1.5 cm in length, nodes are swollen, spiny, surface rough, longitudinally at places with globular vegetative bulk striated, axillary spines measuring 0.5 to 1.5 cm in length, fracture short, externally yellowish green to brown in colour. Leaves are simple, alternate, elliptical, 0.5 to 1.0 cm long and 0.2 to 0.5 cm broad, oblong, mucronate, subsessile, hairy, young drooping, stipulate, with silvery hue. Flower 1-8 in numbers, on spine tipped branches, red, about 7 to 9 mm long, pedicels short. Pod are 3 to 4 cm long, falcate, inequally constricted between the seeds on the lower side [13].

8. Phytochemistry

Flavonoid glycosides kaempferol, chrysoeriol, isorhamnetin, chrysoeriol-7-*O*-xylosoid, kaempferol-3-galactorhamnoside, and isorhamnetin 3-*O*-*β*-D-apio-furanosyl (1-2) *β*-D-galactopyranoside have been isolated from the ethanol extract of aerial parts [10]. Bioassay-directed separation of the chloroform extracts from the air-dried aerial part has led to the isolation of a isoflavonolignan (Pseudalhagin A), together with five isoflavones viz. pratensein, calycosin, 3′, 7-dihydroxyl-4′, 8-dimethoxylisoflavone, formonoetin, ononin [12]. Guijie et al., have isolated isorhamnetin, isorhamnetin 3-*O*-*β*-D-glucopyranoside, isorhamnetin 3-*O*-*β*-D-rutinoside, kaempferol, quercetin, rutin, ononin, 1-hexacosanol, 1-heptacosanol, octacosanol, 1-triacontanol, and triacontanoic acid methyl ester from the aerial parts by column chromatography [14]. Two oligomeric proanthocyanidin glucosides have been isolated from the aerial part and roots [15]. Seed oil is reported to contain unsaturated fatty acid 88% and a lot of microelements necessary for physiological functions [16]. Chemical studies on the stem indicated the presence of *β*-phenethylamine, N-methyl-*β*-phenethylamine, N-methyltyramine, hordenine, 3,4-dihydroxy-*β*-phenethyltrimethyl-ammonium hydroxide, 3-methoxy-4-hydroxy-*β*-phenethyltrimethylammonium hydroxide, N-methylmescaline and salsolidine. This was claimed to be first report of occurrence of 3-methoxy-4-hydroxy-*β* phenethyltrimethylammonium hydroxide in nature and of any 3, 4, 5-trioxygenated *β*-phenethylamine (like N-methylmescaline) in the family Fabaceae. Choline and traces of betaine were also obtained from the stem. The roots have essentially the same alkaloids as the stem but in poorer yields [17-18]. A flavanenol (5, 6, 7, 8, 20, 30, 50, 60-octamethoxyflavan-3-en-40-ol) has been isolated from ethyl acetate fraction of roots [19]. Three oleanane-type triterpene glycosides have been isolated from the roots and their structures have been assigned as 3*β*, 22β, 24-trihydroxy-olean-12-ene-15-oxo 3-O-*α*-L-rhamnopyranosyl-(1→2)-*β*-D-galactopyranosyl-(1→2)-*β*-D-glucuronopyranosyl 22-O-α-L-[rhamnopyranoside, 3*β*, 22*β*, 24-trihydroxy-olean-12-ene-15-oxo 22-O-*α*-L-rhamnopyranoside and 3*β*, 22*β*, 24-trihydroxy-olean-12-en 3-O-*α*-L-rhamnopyranosyl-(1→2)-*β*-D-galactopyranosyl-(1→2)-*β*-D-glucuronopyranosyl-22-O-*β*-D-glucopyranosyl-(1→2)-*α*-L-rhamnopyranoside [20]. Lupeol has been isolated in considerable quantity from the root barks [21]. Melezitose, a natural trisaccharide is found to be formed in the leaves as white secretion. This oligosaccharide possesses unique physiological activity and is used in Chinese medicines [22]. 24-alkyl sterols *viz.*, 24-methylcholest-5-en-3*β*-ol*;* 24-ethylcholest -5-en- 3 3*β*-ol*;* 24-ethylcholesta-5, 22-dien- 3 3*β*-ol*;* 24-ethylcholesta-5, 24 (28)-dien-3*β*-ol -ol; 24-ethyl-5-cholest-7-en-3*β*-ol; Δ^7-avena sterol along with cholesterol have been isolated from benzene extract of the plant [23]. Alhagitin(naringenin 5-methyl ether 4′-glucoside), alhagidin (hesperitin 7-galactosyl (1→2) [rhamnosyl (1→6)] glucoside),[24] formonoetin, 3′,7-dihydroxyl-4′-methoxylisoflavone, 3′,7-dihydroxyl-4′,8-dimethoxylisoflavone, pratensein, tamarixetin, isoquercitrin, saliylic acid, vanillic acid, β-sitosterol and daucosterol, [25] isorhamnetin-3-*O*-[-α-l-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside, 3'-*O*-methylorobol [2] and quercetin 3-O-*β*-d-glucopyranoside [26] have also been isolated from the plant.

9. Qualitative/quantitative analysis

Phytochemical screening revealed the presence of tannins, flavonoids, unsaturated sterols/triterpenes, carbohydrates, lactones, proteins/amino acids and saponins [8, 27].

9.1 Thin layer chromatography

Thin layer chromatography of the methanolic extract of plant on silica gel 60 F_{254} plate using toluene: ethyl acetate: methanol (7:3:0.5) as mobile phase shows six spots at R_f 0.28 (purple), 0.41 (faint purple), 0.63 (purple), 0.75 (purple, spot for stigmasterol), 0.82 (yellowish green) and 0.89 (blue) on spraying with anisaldehyde- sulphuric acid reagent and heating the plate, for five minutes at 105 °C [13]. The percentage of stigmasterol ranged from 0.36 to 0.44 in the various samples analyzed by HPTLC densitometric method using precoated plates of silica gel 60 F_{254} as stationary phase, toluene: ethyl acetate: methanol (7: 3: 0.5) as mobile phase and scanning at 656 nm [13]. Analysis of the mineral contents of plant collected from Ashafa, Toroba, Wahat and Wehait (Saudi Arbia) indicated that aluminum is in higher concentration (shoots and roots) followed by copper, manganese and zinc. The concentration of Zn found higher in shoots than in roots, but the concentration of Zn was less in shoots than in roots [28].

9.2 Identity, purity and strength

For dried whole plant foreign matter, total ash and acid-insoluble ash should not be more than 2.0%, 2.5%, 13.5%, respectively while alcohol-soluble extractive and water-soluble extractive should not be less than 2.0% and 10% respectively [9].

10. Pharmacological properties

In a preliminary biological screening, 50% ethanolic extract of the plant exhibited antiprotozoal activity against *Entamoeba histolytica* strain [29]. The ether extract of the shoot showed antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* [30]. The alcoholic extract of the plant was found inactive against *Escherichia coli in vitro* [31]**.** Methanol extract of stem gum has also shown promising antimicrobial activity [32]. Hexane and methanol extracts of fresh aerial parts exhibited strong antibacterial activity against gram positive and negative pathogenic bacteria; the hexane extract was found less active than the methanol extract [33]. Ethanol extracts of the leaves showed significant antibacterial activity against gram negative, gram positive bacteria, unicellular and filamentous fungi [34]. An antagonistic endobacterium (XJAS-AB-13) with strong antifungal activity to *Exserohilum turcicum* and *Bipolaris maydis* has been screened from plant and identified as *Bacillus subtilis* according to physiological and biochemical characteristics and 16S rDNA sequence features. This endobacterium (XJAS-AB-13) has found to possess important potentials in bio-controlling of *Exserohilum turcicum* and *Bipolaris maydis* [35]. Ethanolic extract of seeds demonstrated *in vitro* antifungal activity against *Alternaria alternata, Fusarium oxysporum, Phoma destructiva, Rhizoctonia solani,* and *Sclerotium rolfsii* at concentrations of 0, 3, 6, and 9% (v/v) and hence the extract may be recommended as a potent bio-fungicide [36].

Oral administration of methanolic extracts of aerial parts (400 mg/kg) exhibited antinociceptive activity in acetic acid-induced writhing and increased latency time in the tail-flick test [8]**.** Neamah (2012) has reported that aqueous extract of the plant exhibited protection against free radicals mediated inflammatory diseases [37]. Ethanolic extracts of aerial parts have shown both anti-inflammatory and anti-ulcer activity in rats [38]. The alcoholic extract (200 mg/kg, orally) of the plant exhibited anti-diarrheal activity in castor oil induced diarrhoea model and the effect was attributed to calcium channel blocking effect of the extract [27]. The total extract (300 and 400 mg/kg) and two of the isolated compounds (chrysoeriol 7-O-xylosoid and kaempferol-3-galactorhamnoside, 100 mg/kg each) showed a very promising antiulcerogenic activity [10].

Distilled product of the plant was found to be useful as a diuretic at the doses of 8 and 16 ml/kg in goats [39]. Methanol extracts of the plant also demonstrated a significant diuretic effect [40]. The flavanenol (5, 6, 7, 8, 20, 30, 50, 60-octamethoxyflavan-3-en-40-ol) isolated from ethyl acetate fraction of roots showed remarkable urease-inhibitory effect [19]. *Alhagi pseudalhagi* extract, exhibited diuretic action and was effective in reducing the urine pH and crystalurea reliably for a long period of time and hence considered to be good choice in UTI where strong diuretic along with reduction in pH is required. Ethanolic extract and 2% aqueous acetic acid extract of roots was found to possess a spasmolytic and ureter relaxing action that can enhance antiurolithiatic effect of the extracts along with relief in accompanying spastic pain. However, the extracts were devoid of stone (oxalate calculi) dissolving property [41-42]. The plant distillate was found to have a significant effect on the rate of stone expulsion and decreased the time needed for the passage of urinary stones [43]**.** Alkaloids of the plant have been found to have sympathomimetic activity. The activity was presumably, due to catecholamine release as indicated by tachyphylaxis in pressor response, intestinal relaxation, contraction of nictitating membrane and cardiostimulant effects on repeated administration of the total alkaloids. There was also some degree of stimulation of CNS. The LD_{50} of the total alkaloids in albino mice was found 296.4 mg/kg intraperitoneally [18]**.** Preliminary pharmacological studies of the total alkaloids indicated that some of the curative properties of the plant extract are due to these entities [17]. Pseudalhagin A isolated from the aerial parts possessed moderate quinone reductase inducing activity with IR value 2.3 [12]. Mice fed with the seed oil showed higher swimming endurance time in mouse swimming tests indicating antidepressant effect of the seed oil [16].

Methanolic extract of the plant has been reported to have more than 50% inhibition of acetyl-cholinesterase enzyme activity at 250 μg plant extract [44]**.** 50 % ethanolic extract of the plant has been reported to have spasmolytic activity in guinea pig ileum and anticancer activity against sarcoma 180 in mouse [29]**.** Proanthocyanidin isolated from the plant has been found to ameliorate phospholipids imbalance and decreased lipid peroxidation in experimental myocardial infarction in rabbits [45-46]**.** It also improved the metabolism and increased the work capacity of rats subjected to hypoxia [47]**.** Ethanolic extract and 2% aqueous acetic acid extract of roots showed skeletal muscle relaxant effect on rectus abdominis muscle preparation of frog [41-42].

11. Folklore claims

The plant is used as laxative, diuretic and expectorant in Rajasthan. Leaves are smoked in the treatment of asthma in Mount Abu, Rajasthan, [48] administered orally in fever [49] and applied for the treatment of haemorrhoids by indigenous people of Saurashtra region of Gujrat [50]. In Mewat, Gurgaon district, Haryana leaves are given to cure chest pain and headache [51] and in Rajasthan leaves are given for cure of rheumatism [52].Oil from leaves is used in rheumatism and flowers are used for piles.[53] Crushed flowers along with sugar are taken orally to cure bleeding piles in the Shekhawati region of Rajasthan [54]. The flowers are used to cure haemorrhoids in Rajasthan [52]. Water extract of roots is used to enlarge the ureter and to remove kidney stones [41].

In China, the plant is used for the treatment of rheumatism and cancer [12] while the secretion of aerial part of plant, called "alhagi sugar", is used as a kind of Uygur ethnomedicine to treat neurogenic headache [12]. In Palestine area of West Bank, Israel, the plant is used to cure problems of urinary systems and stones [55]. In Golan Heights and the West Bank region of Israel, the decoction of roots is consumed orally to cure kidney stones and diarrhea**.**[56] In Jordan, roots are used to cure kidney stones [57-58]. In Turkmen Sahra region of North of Iran, concentrated decoction of flowers, leaves and roots are used to treat haemorrhoids, cardiac pains and dysuria [59]. People of Kalat and Khuzdar regions of Balochistan, Pakistan use powder of flowers ground in sugar for improvement of eyesight, powder of dry flowers in stomachache and water extract of roots for liver complaints [60].

12. Medicinal properties of the plant in Ayurveda

Rasa (Madhura, tikta, kasaya), Guṇa (Laghu, sāra), Vīrya (Śīta) Vipāka (Madhura), Karma (Balakṛt, Dīpana, Kaphahara, Pittahara) [9]**.**

13. Dose
Recommended dose is 20-50 g of the drug in powder form for decoction [9].

14. Actions
Tṛṣṇānigrahaṇa, vedanasthāpana, anulomana, chardinigrahana, raktaśodhaka, mūtrajanana, vṛsya, balya [7].

15. Therapeutic indications
Therapeutics of tṛṣṇā (thirst), chardi (vomiting), kāsa (cough), jvara (fever), vātarakta (gout), raktapitta (haemorrhagic diseases), visarpa (erysipelas) [9].

16. Safety aspects
Oral administration of ethanol extract in doses 2000–4000 mg/kg body weight was found safe for human use [10].

17. Important Ayurvedic formulations
Chinnodbhavādi Kvātha Cūrṇa, Gandharvahastādi Kvātha Cūrṇa, Bhārangyādi Kvātha Cūrṇa, Arimedādi Taila [9].

18. Conclusions
The above reported information and studies clearly indicate that *Alhagi pseudoalhagi* is an important medicinal plant with diverse pharmacological uses / activities. The plant shows the presence of many chemical constituents which are responsible for varied pharmacological and medicinal properties.

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