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A comprehensive review on Aftimoon (Cuscuta reflexa Roxb) in context of unani system of medicine

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Abstract

Traditional system of medicines relies on the plant products for the treatment of various disorders. *Cuscuta reflexa* Roxb plant belongs to the genus Cuscuta and the Cuscutaceae family and in Unani medicine it is known as Aftimoon. It is a parasitic plant that can be found growing abundantly on various host plants in India up to 3000 meters in altitude during the rainy season. In the Unani system of medicine, it has been used for years to cure a variety of illnesses, including psychiatric illnesses like melancholia, schizophrenia, epilepsy and various skin disorders. It is used as mufrad (single drug) in the form of powder, concoction, decoction, etc., and in the murakkab (compound formulations) form in the Unani system of medicine. Various chemicals have been isolated from this plant having therapeutic potential and possessing ethnomedical and pharmacological activities. This review represents a detailed study of *Cuscuta reflexa* in the context of Unani medicine, its chemical constitution, ethnomedical uses and pharmacological activities.

Keywords: Aftimoon, Kasoos, Cuscuta reflexa, Amarbel, Unani system of medicine

1. Introduction

Cuscuta reflexa is a perennial parasitic climber on other plants, golden yellow, without root and leaves, therefore called "Akashbel" (sky twiner) [1]. It is also known as devil's gut, strangle tare, beggar weed, hell weed, and scald weed [2]. Since ancient times, it has been utilized by Unani doctors to treat a variety of illnesses, including neurological disorders including melancholia, schizophrenia, and epilepsy. It is also used to treat a number of other conditions, including hepatitis, skin conditions, and palpitations [3]. The parasites in the genus Cuscuta are occasionally classified under the Cuscutaceae, a distinct family. Certain dodder species parasitize flax and clover. The Indian subcontinent's Cuscuta reflexa is utilized in many traditional medicines; an alcoholic extract of the plant possesses bradycardiac and hypotensive properties [4]. The medicine Aftimoon is prepared from the dried stems and fruits of *Cuscuta* reflexa Roxb. It is found as a full parasite in India, Afghanistan, Thailand, Nepal, Pakistan, Malaysia, and Sri Lanka. It grows profusely on a variety of host plants throughout India's plains (particularly abundant in Bengal) during the rainy season [5]. It has no roots in the ground and only grows as a parasitic twiner on other plants, earning it the names akaswel (sky twiner) and Amarwel (immortal twiner) because it only grows in the rainy season and on the same plant year after year [1]. Alkaloids and other active metabolites from the plant it hosts are accumulated by cuscuta. Amarbelin and kaempferolare among the active substances it contains; the stem includes cuscutin, cuscutalin, bergenin, beta sitosterol, luteolin, and kaempferol [3]. Aftimoon is said to have several pharmacological action in the classical Unani literature, including Mushil i Sawda (purgative of black bile), Mushil i Balgham (purgative of phlegm), Mudir i Bawl (diuretic), and Muhallil i Waram (anti inflammatory) [5].

2. Botanical description

2.1 Morphology

It is a parasitic, leafless plant and has a tall, robust, densely twining and branching pale yellowish green stem with red flecks. The brownish black mature seeds are snoot, extricate, and about 0.4 0.6 mm in diameter, convex on one side and concave on the other. The seeds have no smell, but they have a strong bitter taste. The albuminous seeds have a coiled embryo that is 3 4 mm long but no fleshy cotyledons. Black or white on immature fruits, white or pinkish corolla with scales that are detached from the filament (capsule) [12].

1.2 Taxonomical Classification U.S. Department of Agriculture (USDA) [6]

Kingdom:	Plantae
Subkingdom:	Tracheobionta
Superdivision:	Spermatophyta
Division:	Magnoliophyta
Class:	Magnoliopsida
Subclass:	Asteridae
Order:	Solanales
Family:	Cuscutaceae
Genus:	Cuscuta L.
Species:	Cuscuta reflexa Roxb.

1.3 Vernacular names [5]

Arabic:	Aftimoon, Shajru's sabagh [7], Sab us Sha'eer [8].
Urdu:	Aftimoon.
Hindi:	Amar bel, Akashbel, Amar lata.
Unani:	Aftimoon.
English:	Dodder, Cuscuta [9]. Ari Creeper [10].
Persian:	Darakht e pechan [10]. Tukhm e kasus [1].
Assam:	Amarlati, Rabonor Nari, Akashi lata, Halaodhiya lata,
	Honboronia lata.
Malayalam:	Moodillathali, Nirmuli.
Sanskrit:	Amaravela, Khavalli, Akashvalli. Asparsa [11].
Telugu:	Sitamma Pogunalu, Nulutega, Erumaikkottan.
Tamil:	Kodiyagundal, Varillakothan, Akashvalli, Kotana.
Sindhi:	Be paadi desi.
Marathi:	Nirmali, Akasavela, Amaravela, bel, Antar vela.
Punjabi:	Nilathari, Viaradhar, Amil, Akasbel, Niradhara.
Gujarat:	Amarabel, Akaswel.
Bengali:	Sawarna lata, Algusi, Haldi algusilata, Aloka lata,
	Akashbel.

2.2 Habitat

It is occurs throughout the plains of India, and ascend the Himalayas to about 3000 meters.

2.3 Macroscopic Character

The plant has leafless, slender, pale green stems that are long, branched, closely twining, and glabrous. Few stomata are present in mature plants. The stem surface exhibits simple epidermal outgrowths. Fresh material has a characteristic odour and a slightly bitter taste [13].

2.4 Microscopic Character

The T.S stem shows the transverse section is circular with irregular outlines. It is with unicellular epidermis with very thin cuticle and isolated stomata. Beneath it, 3-4 layers of parenchymatous cortex with brown material are found. The Endodermis is a complete ring of tangentially elongate cells, with starch grains and calcium oxalate crystals.

There are 15-20 collateral, conjoint to the vascular bundles in a ring. A complete ring of xylem forms in the mature stem; external to the xylem is a region of phloem, being the food conducting part of the stalk, consisting of sieve tubes with groups of companion cells, fibres, and phloem parenchyma. Some bundles have visible cambium. The vessels, trachecides, and parenchyma form the same xylem. The schizogenous canals develop in the cortex and the xylem phloem interface. There is only a large pith, formed of soft, unlignified [13].

3. Hissa e Mustamila (Parts Use)

Stem and Seeds [1, 8, 14].

4. Mizaj (Temperament)

Hot3° & Dry2° [10,14].

5. Nafa'e khas (Main action)

Mus'hil (Purgative) for Melanic and phlegmatic humours, Muhallil (Subsident) [5].

5.1 *Diger Afa'al* (Other Actions) [15 19]

Mus'hil wa mukhrij i Sawda' (Melanagogue), Mushil wa mukhrij i Balgham (Phlegmagogue) [20, 21, 23, 24]. Mushil wa mukhrij i Safra' (Purgative of bile) [22, 23]. Mus'hil (Purgative) [13, 20]. Muwallid i Mani, Mutawwil i Sha'r (Hair longator), Mudammil i Qurüh (Healing agent) [21], Musaffi e dam (Blood purifier) [1,21,14]. Mulattif (Demulcent) [21,22,23,25]. Kasir Riyahh (Carminative), Mufattih Suda''d (Deobstruent) [26], Qatil Didan Ama (Anti helminthic) [8,15,21]. Mudirr i Baul (Diuretic), Mudirr i Hayd (Emmenogogue) [26]. Munaqqi i dimagh (Sporific) [8], Musakhkhin (Calorific), Mujaffif (Desiccant) [14].

5.2 *Iste'maal* (Therapeutic uses)

Malinkholia (Melancholia) [25 27], Kabus (Nightmare), Junoon (Insanity) [8, 26], Khafqan Sawdawi (Palpitation) [14], Dimagh i Amrad (Brain disorders) [14, 24], Wahshat [8, 21, 25], Sawda'w i amrad (Ailments due to excessive black bile) [25, 27], Didan i Am'a' (Intestinal worm) [1,8,25], Humma (Fever) [27], Laqwa (Facial paralysis), Khadar (Insensibility) [28], Tashannuj (spasm) [29], Falij (Paralysis) [30], Saudaw i Waswasa [20], Sara (Epilepsy) [23] Muqawwi i Bah (Aphrodiasac) [14, 30] Imtila' [23], Hikka (latching) [1] Du'f al Kabid (Weakness of Liver) Du'f al Mi'da (Weaknes of stomach), Du'f al Tihal (Weakness of spleen) [21, 22, 26] Intishar al Sha'r (Alopacia) [21, 28] Kalaf (Malasma) [29] Sartaan (Cancer) [14, 23, 29] Waja'al 'Adalat wa Mafaşil (Pain in muscles & joints) [23, 25] Amrad al Jild (Skin disorders) [14,21] Nafkh al Mida (Flatulence) [1, 8, 14, 20, 23] Amrād al Kabid wa Marara (Liver & bilious disorder) [1, 10, 17] Suda' (Headache) [8,23] Yaraqan (Jaundice). [10,21]

6. Muzir Atharāt (Side effects)

It is defined as harmful to the lungs in large doses or if used for an extended period $^{[8,10,14]}$. In certain cases, it can cause nausea, restlessness, thrust and dryness in a bilious temperament person (Mahroorin) $^{[8,14]}$.

7. Musl'eh (Corrective)

Zafran (*Crocus sativa*), Raughan Badam (*Almond oil*). Samagh Arbi (*Acacia arabica*) for lungs, Apple (*Malus domestica*), Anar (*Punica Granatum*), Sharbat e sandal, ^[8, 14] Kateera (*Astragalus gummifer*), Lajward (*Lapis lazuli*), ^[25] Kasni (*Cichorium Intybus*), sikanjbeen, ^[15], Usţūkhūdūs (*Levandula stoechas*), Gul e banafsha (*Viola odorata* L). ^[8,24]

8. Badal (substitute)

Turbud (*Ipomoea turpethum*) in equal weight. Hasha (*Thymus serpyllum* Linn.) [22,29],Bisfaij (*Polypodium vulgare*) [8, 14], Afsantin (*Artemisia absinthium*) [10].

9. Miqdar e khurāk (Dose)

Sufoof: 3 7 Grams, as Decoction: 15g 25g. [31].

10. Mash hoor Murakkabat (Compound formulation)

Habb e Aftimoon, Sharbat i Aftimoon, Sikanjibeen Aftimooni, Sharbat i Ahmad Shahi, Sharbat Dinar, Sharbat i Kasūs, Itrifal Aftimoon, Majun i Sana, Itrifal didan, Itrifal Mus'hil, Itrifal Ustakhūdas, Majun Ustukhudus, Arq Musaff e khoon, Sharbat i Mulayyin, Majun Najah, Majūn e Talkh,

Majūn e ChobChini, Ma'jūn e Ushba, Sufūf Chobchini. Itrifal Ghudadi, Jawarish Shehryaran, Majun e Dabidulwarad, Mufarrih Mo'tadil, Mufarrih Kabir, Sufuf Namak e Sulaimani, Sharbat i Bazoori Harr, [5, 13, 21, 26]

11. Chemical constituents

As a parasitic plant, the phytoconstituents of Cuscuta reflexa vary depending on the type of host. From their various hosts, various phytoconstituents have been isolated. Dulcitol, mannitol, sitosterol, carotenoids, and flavonoids are chemical components of Cuscuta reflexa. lycopene, quercetin, hyperoside. propenamide, reflexin, violaxanthin, lutein, lycopene, carotene, acryptoxanthin, Amarbelin (pigment), cerotic, linolenic, oleic, stearic, and palmitic acids, phytosterols (seeds), abscisic acid (leaves), leuteolin and its glycosides quercetin, cuscutin (stem), amino acids and cuscutalin. Cuscuta reflexa seeds also contain esters of the higher aliphatic alcohol and saturated fatty acids with 26 and 28 carbon atoms, respectively, among which cerotic acid has been discovered. Seeds produce a semi drying clear greenish yellow oil [13, 32, 33]. The phanerogamic parasite Cuscuta reflexa contains mostly caffeic acid depsides and flavonol type flavonoids, according to phytochemical research. There were also some phenolic components found [34]. The bioreactors were used to immobilize Cuscuta reflexa starch phosphorylase for the synthesis of glucose 1 phosphate [35]. Choudhury et al. looked studied the chloroplast, ultra structure contents of chlorophyll, carotenoids and plastid proteins, photosystem and carbon dioxide fixation activities, and photosynthetic gene composition in Cuscuta species in the dark [36]. Protoplasts obtained from C. reflexa showed a greater rate of exogenous nicotinamide adenine dinucleotide oxide than nicotinamide adenine dinucleotide phosphate.

12. Recent Pharmacological Activities of Aftimoon (Cuscuta reflexa Roxb.)

12.1 Cholinergic Action

The stem extract of *C. reflexa* resembled acetylcholine when tested on isolated rabbit ileum and frog rectus abdominis and heart. On isolated frog rectus abdominis muscle, pancuronium inhibited and neostigmine potentiated the extract's action [37].

12.2 Effect on Blood Pressure

An ethanolic extract of the stem of *C. reflexa* caused a dose dependent drop in arterial blood pressure and heart rate in pentothal anesthetized rats, which was not blocked by atropine. Cholinergic receptor activation or adrenergic inhibition had no influence on the hypotensive and bradycardic effects of *Cuscuta reflexa* [38].

12.3 Anti inflammatory and anti cancer activities

Cuscuta reflexa inhibited lipopolysaccharide induced inflammatory responses in RAW 264.7cells by interacting with tumor necrosis factor α , cyclooxygenase 2, and nuclear factor KB signaling (mouse macrophage cells). By upregulating p53, B cell lymphoma 2 (Bcl 2) associated X protein and down regulating Bcl 2, it produced apoptosis in Hep3B cells (human hepatoma cells) while allowing the cells to survive. Chloroform and ethanol extracts of *Cuscuta reflexa* demonstrated anti tumor activity comparable to 5 fluorouracil in Ehrlich ascites carcinoma bearing mice [39].

12.4 Anti convulsant activity

The ethanolic extract has anticonvulsant characteristics and is hypothesized to impact gamma amino butyric acid's

aminergic and glycine inhibitory systems (GABA). The primary active chemical component, flavonoid, has depressive effects [40]. A methanol extract of *Cuscuta reflexa* stem and *Corchorus olitorius* seed provided considerable protection against chemo convulsive agent induced convulsions in mice. The catecholamine level of the extracts was somewhat higher in the refined extract treated animals. The volume of GABA in mice brains increased dramatically after a six week therapy, which is mostl ikely linked to seizure activity. The processed extracts exhibited a significant anticonvulsant impact in mice by altering catecholamine and amino acid levels in the brain [41]

12.5 Diuretic activity

Cuscuta reflexa extracts, both aqueous and alcoholic in the wistar rat, has diuretic properties ^[42].

12.6 Spasmolytic and relaxant effects

Cuscuta reflexa stem extracts, both aqueous and alcoholic, showed a relaxing and spasmolytic action on the small intestine of guinea pigs and rabbits. In addition, the extracts showed acetylcholine like action [43].

12.7 Hypoglycemic effect

The hypoglycemic effects of methanol and chloroform extracts of whole *Cuscuta reflexa* plants were investigated in oral glucose tolerance trials in Long Evans rats. Methanol and chloroform extracts of *Cuscuta reflexa* whole plant revealed significant oral hypoglycemic action in glucose loaded rats at doses of 50,100, and 200 mg/kg body weight [44].

12.8 Anti oxidant activity

In response to cadmium exposure, Srivastava *et al.* synthesized phytochelatins and investigated anti oxidant modulation in *Cuscuta reflexa*. The effects of cadmium on the development of anti oxidative enzymes such as catalase, peroxidase, glutathione reductase, glutathione, and phytochelatins in *Cuscuta reflexa* callus and seedlings were examined ^[45].

12.9 Anti bacterial activity

At concentrations of 25 to 125 ug/ml, the methanol fraction of *Cuscuta reflexa* stem displayed wide anti bacterial activity against all of the tested strains, but the other fractions (petroleum ether or chloroform) had none. The antibacterial activity was greatly reliant on the strain against which it was tested. The methanol fraction of *C. reflexa* showed excellent anti bacterial activity against *Staphylococcus aureus*, *Shigella boydii Pseudomonas aeruginosa*, *Shigella dysenteries*, and *Escherichia coli* with a zone of inhibition spanning 16 to 24 mm when compared to chloram phenicol (10pg/ml) [46].

12.10 Anti steroidogenic activity

After multiple intraperitoneal doses of methanol extract of *Cuscuta reflexa* stem and *Corchorus olitorius* seed, the activity of carbonic anhydrase in the uterus of mice was investigated. These methanol extracts significantly increased carbonic anhydrase activity in the uterus of mice. The enhanced rate of enzymatic activity may be connected to the greater quantity of progesterone generated by these methanol extracts. The methanol extract of *C. reflexa* stem was found to be anti fertility [47].

12.11 Hepato protective activity

The methanol extract of C. reflexa improved liver function in

hepatotoxic rats by reducing serum ALT, AST, and ALP levels. While both AST and ALT levels increased in heart and liver disorders, AST increased more in heart disease and ALT increased more in liver disease [48].

12.12 Toxicological evaluation

Flavonoids are present in a methanol extract of C. reflexa stem (MECR). For chemical and toxicological evaluations, the effects of several weekly doses of MECR on liver and kidney functions and haematological parameters in mice were observed. In MECR treated mice, there were no major changes in red blood cell count or haemoglobin content at any dose range, although there was a significant improvement in clotting time at low and high doses. Only the high dose level of MECR therapy resulted in a substantial improvement in white blood cell count. The serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), non protein nitrogen, and plasma cholesterol all increased dramatically at the medium and high dose levels. Moderate to high doses have boosted serum alkaline phosphatase (ALP) and overall bilirubin. The use of a high dose of NIECR resulted in a substantial rise in creatinine levels. The increased levels of AST, ALT, and serum ALP production in weekly treated mice at moderate and high dose levels may be attributed to poor liver function during the procedure. With reduced kidney activity, blood levels of urea, non protein nitrogen, and creatinine are higher. Low doses of MECR, on the other hand, have no discernible effects on liver and kidney functions, as well as haematological parameters [48].

12.13 Hair growth activity

The petroleum ether extract of C. reflexa and its isolate is useful in the treatment of androgen induced baldness by blocking the enzyme 5 a reductase [^{49]}.

12.14 Anti arthritic and Nephroprotective Effect

The anti arthritic effectiveness of *Cuscuta reflexa* aqueous and methanol extracts was evaluated using *in vitro* protein denaturation techniques, *in vivo* formaldehyde and turpentine oil induced arthritis models, and *in vitro* formaldehyde and turpentine oil induced arthritis models. With a maximum inhibition of 76.74% on the tenth day for formaldehyde and 71.22% on the sixth hour for turpentine oil, AMECR at 600 mg/kg successfully decreased paw and joint edema. Furthermore, *in vitro* research demonstrates a significant concentration dependent enhancement in defense against denaturation of bovine serum albumin (89.30%) and egg albumin (93.51%) at 800 g/mL. This research shows that AMECR provides protection against nephrotoxicity and arthritis, which can be caused by phytoconstituents [50].

12.15 Antiemetic activity

C. reflexa extract in pigeons, both aqueous and methanolic. Each pigeon received varying intramuscular dosages of aqueous and methanolic extract (50, 100, and 200 mg/kg). According to the study, *C. reflexa* aqueous and methanolic extracts show strong antiemetic properties and contain one or more pharmacologically active constituents that work by irritating the gastrointestinal tract and stimulating the 5 HT3 receptor to block the action of emetic mediators ^[51].

12.16 Neuro protective activity

Cuscuta reflexa hydroalcoholic extract is used in both in vitro and in vivo to reduce the neurodegenerative effects of aluminum chloride. Cuscuta reflexa extract significantly

decreased aluminum chloride induced cytotoxicity in PC12 cells, according to the *in vitro* investigation. According to the open field test and Morris water maze test, the *in vivo* investigation employing the aluminum chloride induced Alzheimer's disease rat model demonstrated that the extracts of *Cuscuta reflexa* treatment enhanced learning and memory [52]

12.17 Anti HIV activity

According to Mahmood N *et al.*, anti HIV activity was found in crude water extracts of *Cuscuta reflexa*, which could be ascribed to the combinatory effects of chemicals with different modes of action. The methanol extract of *Cuscuta reflexa* was antibacterial and free radical scavenging ^[53].

12.18 Anti diabetic activity

The study found that *Cuscuta reflexa* has strong anti diabetic effects. With an IC₅₀ value of 11.25/ug/ml, which is comparable to the reference drug tocopherol, the ethanolic extract prevented a significant rise in glycosylated hemoglobin *in vitro*. The extract's effects are similar to those of the drug Glibenclamide, and in the single dose study, it dramatically lowered blood glucose levels in rats with alloxan induced hyperglycemia as compared to the control ^[54].

13. Conclusion

This review work shows the ethnobotanical value of *Cuscuta reflexa* as a miraculous medicinal plant. This article carefully reviewed the research on Aftimoon's pharmacological properties and historical uses to better understand its effectiveness and usefulness. Nevertheless, regarding scientific inquiries grounded in evidence, published data and clinical evidence in the domain of Unani medicine remain unacquired. The Traditional medicine systems like Unani medicine have used this plant as medicine in both single and compound forms for a long time. The established literature and the experiences of many well known Unani scholars support this use, which suggests that the plant works.

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