An updated review on the parasitic herb of *Cuscuta reflexa* Roxb.

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**ABSTRACT:** *Cuscuta reflexa* Roxb. is a golden yellow, leafless, perennial, parasitic herb of the family Convolvulaceae. *C. reflexa* has been investigated for antispasmodic, hemodynamic, anticonvulsant, antisteroidogenic, antihypertensive, muscle relaxant, cardiotoxic, antiviral, antibacterial, antioxidant, cholergic, diuretic and hair growth activities. Many chemical constituents have been isolated from *C. reflexa* such as cuscutin, amarbelin, $\beta$-sitosterol, stigmasterol, kaempferol, dulcitol, myricetin, quercetin, coumarin and oleanolic acid. This review presents a detailed survey of the literature on pharmacognosy, phytochemistry and traditional and biological medicinal uses of *C. reflexa*.

**KEYWORDS:** *Cuscuta*, Convolvulaceae, plants, medicinal, flavonoids, review

Angiosperm parasites in primary habitats are an integral part of ecosystem. They behave as "prudent predators" and adapt to the life cycle through their principal hosts. Approximately 3,900 species of parasitic plants have been recorded\(^1\). These parasitic angiosperms belong to 22 families and they have been recognized as an entity for over 2,000 years. Almost half of the parasitic plants belong to the family Scrophulariaceae. On the basis of the extent of autophism, plant parasites can be classified as holoparasites and hemiparasites. While, on the basis of the selection of host, plant parasites are respectively divided into specialist and generalist plant parasites. Generalist plant parasite like *Cuscuta reflexa* Roxb. can attack several host species simultaneously\(^2\). Interaction between the host and the parasite occurs at the haustorium interface. The foreign parasite tissue grows into the host and forms a connection with the vascular system.

1 *General introduction*

*C. reflexa* is a perennial, parasitic herb of the Convolvulaceae family. It is also known as Tukhm-e-Kasools (dodder), Aftimoon or Kasools in Unani Tibbi, Akashabela or Amarabela in Hindi, Swarnalata in Bengali and Akakhilata in Assamese. It is usually found in India and Ceylon up to an altitude of 2,348 m, sometimes completely covering bushes and trees. It is also found in plains of Afghanistan, Malaysia, Nepal and Thailand.

*C. reflexa* is also an extensive climber. The
parasitism of *C. reflexa* is by wrapping itself around the host plant after attaching to it. If the host contains food beneficial to *C. reflexa*, it will produce the haustoria inserting themselves into the vascular system of the host. The initial contact to the host is established by the prehaustorium or the adhesive disk. Following contacting and twinning around a host organ, namely, a stem or a petiole, the *C. reflexa* epidermis cells start to elongate and become enriched with cytoplasm. Eventually, they secrete a layer of electron dense material consisting of a mixture of nonesterified pectin. With these cement-like substances, the parasite is closely fixed to the host. Haustorial development is initiated inside the *C. reflexa* stem cortex by tangential and radial cell divisions, and the original root of the parasite in the soil then dies. In tropical area, it grows more or less continuously, and may reach high into the canopy of shrubs and trees; while in temperate regions, it is an annual plant restricted to the relative low vegetation that can be reached by new seedlings in each spring. *C. reflexa* is parasitic on a very wide variety of plants including a number of agricultural and horticultural crop species such as alfalfa, lespedeza, flax, clover, potatoes, chrysanthemum, dahlias, helenium, trumpet vine, ivy and petunias. Among others, it ranges in severity based on its species, the species of the host, the time of attaching and whether any viruses present in the host plant. By debilitating the host plant, *C. reflexa* decreases the ability of host plants’ resisting viruses, and spreads the plant diseases from one host to another when it attaches to more than one host plant.

The host searching of *C. reflexa* is by using airborne (volatile) chemical cues. Seedlings of these plants exhibit growth responses to volatiles released by tomato and other species of host plants. When given a choice between volatiles released by the preferred host tomato and the non-host wheat, this parasitic herb exhibited the preferential growth towards the former. Further experiments demonstrated the attraction to a number of individual compound released by host plants and the repellence of one compound released by wheat. These results do not rule out the possibility that other cues such as light may also play a role in host location.

It was found that species of genus *Cuscuta* are widespread phanerogamic stem holoparasites. They are able to grow on a plethora of different host plants including economically important crops. The distributions of the parasitic herb on these hosts were well thought-out as the supplementary host-parasite relationship reported from northeastern part of India. Based on this investigation, *C. reflexa* has no host specified and it may even thrive well by absorbing least amount of water and nutrient from the host due to containing the special glandular cells facilitating adhesion of the parasite to the host. Various hosts attacked by *C. reflexa* are show in Table 1.

<table>
<thead>
<tr>
<th>No.</th>
<th>Host plant species</th>
<th>Family</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Argyreia argentea var. venusta</em> (Choisy) C. B. Clarke.</td>
<td>Convolvulaceae</td>
</tr>
<tr>
<td>2</td>
<td><em>Bougainvillea spectabilis</em> Willd.</td>
<td>Nyctaginaceae</td>
</tr>
<tr>
<td>3</td>
<td><em>Clerodendrum viscosum</em> Vent.</td>
<td>Verbenaceae</td>
</tr>
<tr>
<td>4</td>
<td><em>Jatropha curcas</em> L.</td>
<td>Euphorbiaceae</td>
</tr>
<tr>
<td>5</td>
<td><em>Lantana Camera</em> L.</td>
<td>Verbenaceae</td>
</tr>
<tr>
<td>6</td>
<td><em>Mikania micrantha</em> (L.) Kunth.</td>
<td>Asteraceae</td>
</tr>
<tr>
<td>7</td>
<td><em>Ricinus communis</em> L.</td>
<td>Euphorbiaceae</td>
</tr>
<tr>
<td>8</td>
<td><em>Syzgium cumini</em> (L.) Skeels.</td>
<td>Myrtaceae</td>
</tr>
<tr>
<td>9</td>
<td><em>Vitex negundo</em> L.</td>
<td>Verbenaceae</td>
</tr>
<tr>
<td>10</td>
<td><em>Ziziphus mauritiana</em> Lamk.</td>
<td>Rhamnaceae</td>
</tr>
</tbody>
</table>

2 Phytochemistry of *C. reflexa*

As *C. reflexa* is a parasitic plant, its phytoconstituents are varied on the type of hosts. Various phytoconstituents have been isolated from their different hosts. The chemical constituents of *C. reflexa* are dulcitol, mannitol, sitosterol, carotenoids, flavonoids, isorhamnetin-3-O-neohesperidoside, apigenin-7-β-rutinoside, lycopene, 6,7-dimethoxy coumarin (scoparone), 6-hydroxy-4-(4-hydroxyphenyl)-7-methoxy-coumarin, quercetin, hyperoside, apigenin-7-O-glucoside, kaempferol-3-O-a-rhamnoside, myricetin-3-O-a-rhamnoside.

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7’-(3’, 4’-hydroxyphenyl)-N-{[(4-methoxyphenyl) ethyl] propionamide, 7’-(4-hydroxy, 3’-methoxyphenyl)N-{[(4-butylphenyl)ethyl] propenamide, reflexin, violaxanthin, lutein, lycopene, carotene, α-cryptoxanthin, amarbelin (pigment), cerotic, linolenic, oleic, stearic, and palmitic acids, phytoferols (seeds), abscisic acid (leaves), leuteolin and its glycosides, quercetin, cuscutin (stem), amino acids and cuscutalin. Seeds of *C. reflexa* also contain the esters of higher aliphatic alcohol with the saturated fatty acids respectively containing 26 and 28 carbon atoms among which cerotic acid has been identified. And seeds yield a transparent greenish yellow semi drying oil.

Phytochemical analysis of phanerogamic parasite *C. reflexa* showed that it mainly contained caffeic acid depsides and flavonol type flavonoids. Some phenolic constituents were also reported. The immobilization of *C. reflexa* starch phosphorylase was carried out for production of glucose-1-phosphate by using the bioreactors. Choudhury *et al.* reviewed photosynthetic properties of *Cuscuta* species such as chloroplast, ultra structure contents of chlorophyll, carotenoids and plastid proteins, photo system and carbon dioxide fixation activities and photosynthetic genes composition. Protoplasts isolated from *C. reflexa* exhibited a higher rate of exogenous nicotinamide adenine dinucleotide oxide as compared to nicotinamide adenine dinucleotide phosphate in dark.

The various phytoconstituents isolated from *C. reflexa* along with their structures are shown in Figure 1.
3 Ethnomedical uses of *C. reflexa*

In India, the plant is traditionally used for various medicinal purposes. The rural people of India use the juice of this plant as inhalant for treating jaundice and its warm paste is applied in rheumatism, gout and other affected parts of the body, and the paste of whole plant is applied for relieving headache\(^{[21]}\). The juice of the plant mixed with the juice of *Saccharum officinarum* is used in the treatment of jaundice. The plant juice is given in combination with other purgative decoction. It internally treats the retention of urine while being applied externally for skin itching\(^{[22]}\). The stem is used in the treatment of bilious disorders, internally in treating protracted fevers and externally in the treatment of body pain and itchy skin. Stems of *C. reflexa* are also used in constipation, flatulence, liver complaints and bilious affections. *C. reflexa* is also applied as a hair growth promoter\(^{[23]}\). The fruits are used in treating fever and cough. The seeds are used as sedative, emmenagogue, alterative, anthelmintic, carminative and diuretic in liver and spleen diseases, chronic fevers, gripping and hiccup\(^{[24]}\). Seeds are said to be tonic, diaphoretic and demulcent and are used to purify the blood. The cold infusion of seeds is given as a depurative and carminative in pains and stomach ache\(^{[24]}\). As being a purge, the whole plant of *C. reflexa* is also useful in curing the diseases of bile as well as mental diseases such as melancholy and insanity. Besides, the decoction of this plant can be used as a wash for sores.

In traditional Chinese medicine, the seeds of *C. reflexa* called Tusizi, have been used for thousands of years. According to traditional Chinese medicine practitioners, seeds of Tusizi have a neutral nature, pungent and sweet taste. Their ethnomedical uses are associated with the treatment of liver and kidney diseases and yin and yang deficiencies. It was considered as both the aphrodisiac and longevity herb for slowing down the loss of fluids from the body. Contemporary Chinese herbalists use *C. reflexa* in formulas to treat a range of conditions including impotence, premature ejaculation, frequent urination, ringing in the ears, lower back pain, white discharge from the vagina (leucorrhoea), dry eyes, blurred vision and tired eyes.

4 Pharmacological activities

4.1 Relaxant and spasmyolytic action  Aqueous and alcoholic extracts of *C. reflexa* stem have got a relaxant and spasmyolytic action on small intestine of guinea pig and rabbit. Also the extracts exhibited acetylcholine-like action\(^{[25]}\).

4.2 Effect on blood pressure  The alcoholic extract of this plant has positive inotropic and cardiotonic activities on the perfuse frog heart. In a series of experiments on dog blood pressure, it caused a fall in blood pressure. This depressor action was not blocked by atropine, mepryamine or propranolol, thus it could not be exerted through cholinergic, histaminergic or adrenergic mechanisms. Although the site of action remains to be elucidated, the possibility of action on the ganglia cannot be excluded\(^{[26]}\). An ethanolic extract of the stem of *C. reflexa* caused a dose-dependent decrease in arterial blood pressure and heart rate in pentothal-anaesthetized rats, and these effects were not blocked by atropine. Hypotensive and bradycardic effects of *C. reflexa* were found to be independent of cholinergic receptor stimulation or adrenergic blockade\(^{[27]}\).

4.3 Cholinergic action  The effects of the stem extract of *C. reflexa* resembled acetylcholine when tested on isolated rabbit ileum and frog rectus abdominis and heart. These effects were blocked by atropine. Effect of the extract on isolated frog rectus abdominis muscle was blocked by pancuronium and potentiated by neostigmine\(^{[28]}\).

4.4 Anti-HIV activity  The crude water extracts of *C. reflexa* exhibited anti-HIV activity that could be due to combinatory effects with compounds of different modes of action\(^{[29]}\).

4.5 Antioxidant activity  *In vitro* antioxidant activity of *C. reflexa* stem extract by estimating degree of non-enzymatic haemoglobin glycosylation was measured calorimetrically at 440 nm. Ethyl acetate fraction of ethanolic extract showed higher activity than other fractions\(^{[31]}\). Srivastava et al\(^{[30]}\) synthesized phytochelatins and carried out modulation of antioxidants in response to cadmium stress in *C. reflexa*. The effects of cadmium on growth, the antioxidative enzymes, namely, catalase, peroxidase glutathione reductase, glutathione and phytochelatins were investigated in callus and seedling of *C. reflexa*.

4.6 Toxicological evaluation  Methanol extract of *C. reflexa* stem (MECR) contains flavonoids (0.2%). The effects of multiple weekly doses of MECR (25, 50 and 75 mg/kg, intraperitoneally) on liver and kidney functions and haematological parameters in mice were studied for chemical and toxicological evaluations. There were no significant alterations of red blood cell count or haemoglobin content observed in all dose levels of treatment in MECR-treated mice whereas a significant increase of clotting time was seen in moderate and high doses. MECR caused a significant increase in white blood cell count only in high dose level of treatment. The medium and high dose levels significantly increased serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), non-protein nitrogen and plasma cholesterol. Serum alkaline phosphatase (ALP) and total bilirubin were also increased by moderate and high doses. High dose level of MECR significantly increased creatinine level. The elevated levels of
AST, ALT and serum ALP activity in moderate and high dose levels of weekly treated mice may be due to improper liver function following the treatment. Increased urea, non-protein nitrogen and creatinine contents in blood have been observed with impaired renal function. However, low dose of MECR did not exhibit any remarkable changes on liver and kidney functions and haematological parameters.[33]

4.7 Antisteriodogenic activity Effects of multiple intraperitoneal doses of methanol extract of C. reflexa stem and Corchorus olitorius seed on the activity of carbonic anhydrase in mice uterus were investigated. These methanol extracts caused a significant increase in carbonic anhydrase activity in the uterus of mice. The increased rate of enzymatic activity might be associated with elevated level of progesterone induced by these methanol extracts. This established the antisterility nature of the methanol extract of C. reflexa stem.[34]

4.8 Antibacterial activity The methanol fraction of C. reflexa stem at the concentrations of 25 to 125 μg/mL exhibited a broad spectrum of anti- bacterial activity against all the tested strains, while the other fractions (petroleum ether or chloroform) had no such activity. The antibacterial efficacy was concentratedly dependent against all the tested strains. Methanol fraction at the dose of 125 μg/mL showed significant antibacterial activity against Staphylococcus aureus, Shigella boydii, Pseudomonas aeruginosa, Shigella dysenteries and Escherichia coli with a zone of inhibition ranging 16 to 24 mm when compared to that of chloramphenicol (10 μg/mL).[35] The methanol extract of C. reflexa exhibited antibacterial and free radical scavenging activities.[34]

4.9 Hair growth activity The petroleum ether extract of C. reflexa and its isolate were useful in treatment of androgen-induced alopecia by inhibiting the enzyme 5a-reductase.[36]

4.10 Hepatoprotective activity The methanol extract of C. reflexa improved the liver function by decreasing the serum ALT, AST and ALP levels in hepatotoxic rats. Although there would be an increasing of ALT and AST in heart and liver diseases, the increase of AST was higher in heart disease while the increase of ALT was higher in liver disease.[35]

4.11 Hypoglycaemic effect The hypoglycaemic effects of methanol and chloroform extracts of the whole plants of C. reflexa were investigated in oral glucose tolerance tests in Long Evans rats. Both methanol and chloroform extracts of C. reflexa whole plant demonstrated a significant oral hypo- glycaemic activity in glucose-loaded rats at doses of 50, 100 and 200 mg/kg body weight.[39]

4.12 Diuretic activity The aqueous and alcoholic extracts of C. reflexa have diuretic activities in Wistar rats.[31]

4.13 Anticonvulsant activity The ethanolic extract has anticonvulsant property and may probably affect both the gamma amino butyric acid (GABA) aminergic- and glycine-inhibitory mechanism. The main active chemical constituent is flavonoid which is responsible for depressant activity.[38] The methanol extract of both C. reflexa stem and Corchorus olitorius seed showed marked protection against convulsion induced by chemo- convulsive agents in mice. The catecholamine contained in the extracts was significantly increased in the processed extract-treated mice. The amount of GABA, which is most likely to be involved in seizure activity, was increased significantly in mice brain after a six-week treatment. The processed extracts showed a significant anticonvulsant property by altering the levels of catecholamine and brain amino acids in mice.[39]

4.14 Anti-inflammatory and anticancer activities C. reflexa inhibited lipopolysaccharide-induced inflammatory responses in RAW264.7 cells (mouse macrophage cell) through interplay of tumour necrosis factor-α, cyclooxygenase 2 and nuclear factor κB signalling. It induced apoptosis in Hep3B cells (human hepatoma cell) through the up-regulation of p53, B-cell lymphoma 2 (Bcl-2)-associated X protein and down regulation of Bcl-2 and survivin[40]. The chloroform and ethanol extracts of C. reflexa exhibited a significant antitumor activity in Ehrlich ascites carcinoma-bearing mice that is comparable to that of the reference standard, 5-fluorouracil[41].

5 Random amplified polymorphic DNA markers for authentication of C. reflexa

The randomly amplified polymorphic DNA (RAPD) technique was employed for authentication of C. reflexa and its adulterant C. chinensis. Thirty-two decamer oligonucleotide primers were used to amplify the genomic DNA isolated from the dried stems as well as the seeds of both plants. Out of the 32 primers used, 14 did not amplify, 11 gave faint and non-reproducible, while seven gave species-specific reproducible unique bands. The unique bands obtained in polymerase chain reaction amplification clearly discriminated that these two plants have similar morphology and thus, RAPD may serve as a complementary tool for quality control[45].

6 Conclusion

The various pharmacological activities of C. reflexa are antispasmodic, hemodynamic, anticonvulsant, antisteroidogenic, antihypertensive, muscle relaxant, cardiotonic, psychopharmacological, antiviral, antibacterial, antioxidant, cholinergic, diuretic and hair growth-promotion. As evident by a number of studies cited above, C. reflexa is a very promising drug of plant origin. It may have superior polyherbal formulation in the near future for hair growth and other diseases. There are many works
on this plan remaining to be explored.

7 Competing interests

The authors declare that they have no competing interests.

REFERENCES


寄生草本植物大花菟丝子的生药研究综述

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**摘要**：大花菟丝子是一种金黄色、无叶、多年生寄生草本植物，它隶属于旋花科，俗称发菜、鬼肠等。经研究，大花菟丝子具有止咳、抗炎、抗类固醇生成、降血压、助肌肉松弛、强心、利尿、抗病毒、抗菌、抗氧化以及助毛发生长等一系列药用作用。目前从大花菟丝子中提取的有效化学成分有岩白菜素、阿马利林、β-谷甾醇、豆甾醇、山奈酚、半乳糖酵、杨梅醇、积皮素、香豆素和齐墩果酸等。本文概述了生药学和植物化学文獻有关大花菟丝子的研究结果，并从传统医学和生物学角度评价了它的医药用途。

**关键词**：菟丝子属；旋花科；植物；药用；类黄酮物质；综述