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CUSCUTA REFLEXA ROXB.: A PHARMACOLOGICALLY MERITORIOUS HOLOPARASITIC PLANT

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ABSTRACT: Natural sources like minerals, plants, and animals were used for various diseases by the human civilization from their very initials and were called traditional medicines. The traditional system of medicine is the backbone of a new class of drugs: phytomedicine or phytopharmaceuticals. These drugs are economically very important shortly in the pharmaceutical industry. The *Cuscuta reflexa* as phytomedicine brings us many medicinal importance in many diseases. Phytomedicines are employed to the population by analyzing its safety and efficacy. The *Cuscuta reflexa* Roxb. plant products are known for its diverse traditional uses in many diseases. *C. reflexa* has many medicinal properties for effective management such as antioxidant, anti-ulcer, antispasmodic, effective in jaundice and many more. Here, we use to review for the Phytochemical investigation and pharmacological effects of the *Cuscuta reflexa* Roxb. This review will try to enlighten the very specific and predictable use of this plant following the ailment in the body as a remedy.

INTRODUCTION: About 365 plants are reported to be useful as medication in ancient times. According to WHO, about 70% to 95% of the majority of developing countries still depend on traditional medicine as their remedy for various ailments. People use plants for their various therapeutical properties against inflammation, allergies, oxidation, microbial infection, diabetes, ageing, and more. The plant as a whole is not considered a standard medicine (like in the Ayurvedic system of medicine) for getting a nearby pharmacological effect for a particular disease; we must have to become aware of the phytoconstituents present in the plants.



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By considering this, a new category of the drug came into existence called phytopharmaceutical. The phytopharmaceuticals is a balanced approach that trust everything but underlines the revalidation of the specification of the plant material or product. It is defined as a purified and standardized fraction with a defined minimum four bio-active or phytochemical compounds in the extract of a medicinal plant or its part for internal or external use by human beings or animals for diagnosis, treatment, mitigation or prevention of disease or disorder but the parenteral route of administration is discouraged by the scientists.

Phytomedicine brings new lead drug discoveries, and phytopharmaceuticals assure the people of its safe and productive use of plant-based medicinal products. Plant sources act as a new lead compound provider due to the various chemical entities present in them ¹. The plants produce Secondary metabolites, of which a total of 15000 have been isolated, which is less than 10% of the total

secondary metabolites produced by plants. These secondary metabolites act as plant's defence mechanism against various microorganisms, insects, herbivores and also effective for animals against various diseases or disorders.

Cuscuta reflexa Roxb: It is a plant used to live on other plants by climbing and curling around them like wine and sucking the necessary nutrients from the host plant via attaching a special organ called haustoria to the host. It is a parasitic plant. It is categorized as an Angiospermic plant. It belongs to the morning glory family Convolvulaceae having genus Cuscuta and species reflexa. Cuscuta comprises 100- 170 species that comes under the class Eudicots. Cuscuta is found in the temperate and mainly in tropical regions of the world, with huge species diversity in tropical and subtropical regions ². It is known to parasitize the majority of angiosperms.

Some traditional classifications placed Cuscuta in its own family, Cuscutaceae, but always allied with Convolvulaceae. With the advancement in the field of science, it is found in the molecular phylogenetic study that Cuscuta species have APG (Angiosperm Phylogeny Group) classifications which resemble the genus Ipomoea L. Data from nuclear, mitochondrial, and plastid genomes were used to show that Cuscuta was nested Convolvulaceae. Still, despite extensive analysis, its exact position in the family could not be determined. Subsequent molecular phylogenetic work has provided a robust framework for the species within the genus. In English, it is known as Dodder. It is also known as Amarbel (Immortal twine), Akashwell (Sky winner), Swarnlata, Akakhilata. Other names include Hell weed, Devils gut, Begger weed, Scald weed, Dodder of thyme, Greater dodder Lesser dodder ³.

TABLE 1: BOTANICAL CLASSIFICATION 4

Taxonomical classification		
Kingdom	Plantae	
Subkingdom	Tracheobionta	
Super division	Spermatophyta	
Division	Angiosperms	
Class	Eudicots	
Subclass	Asterids	
Order	Solanales	
Family	Convolvulaceae	
Genus	Cuscuta	
Species	reflexa Roxb.	

TABLE 2: VERNACULAR NAMES

Vernacular names	
English	Dodder Plant
Hindi	Amarabela
Sanskrit	Akasavalli, Amaravalli, Khavalli
Punjabi	Zarbut
Urdu	Akashbel
Bengali	Akashbel

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Morphological Characteristics:

Stem: It contains all the major plant parts. The stem is highly branched and vegetative during favourable conditions. It is a weak, twiner, palegreen, that develop haustoria at the point of contact with the host plant.

The main organs of the stems are vascular bundles (xylem and phloem), and meristem. The main secondary metabolites are also present, like, terpenoids, carbohydrates, fats, *etc*.

Haustoria: It is a special organ developed as a result of the evolution of plants. It has two main stages based on its maturity in the host plant body. Further developed into haustoria hairs. These are hair-like projection that ultimately enters into the host body.

Flowers: The flowers are very distinct in shape and also small as compared to the other genus of Cuscuta species.

It has 5 petals and four lobes, Bracteate, ebracteolate, hermaphrodite, actinomorphic, pentamerous, small and pale-green. Further.

Gynoecium: Style very much reduced, disc red coloured, 2 carpels, syncarpous, superior, bilocular.

Carpels: Medially placed, 2 or more ovules in each locule, axile placentation stigma bifid and hairy, a nectareous disc is present below the ovary.

Androecium: 5 stamens, epipetalous, filaments of different sizes dorsifixed, alternipetalous.

Corolla: 5 petals, united, campanulate, valvate, with 5 coronary outgrowths at the base corolla.

Calyx: 5 sepals, fused, valvate.

Seed: These are small with hard coats which helps them survive many harsh seasons and climates. The seeds are viable for a very long period of time.



FIG. 1: C. REFLEXA STEM (A) AND FLOWER (B)

Initiation of Vegetative Parts of the Cuscuta Plant:

Initiation and Development of Sepals: Initiation starts with one lateral, adaxial sepal, either to the sides of the median plane. It is followed immediately by the second lateral, adaxial sepal. All the sepals are initiated abaxially. The two sepals grows faster than the remaining three sepals. Finally, calyx aestivation is quincuncial and at a length of about 3-4 mm the calyx is pressed open by the elongating corolla-filament tubes.

Initiation and Development of Petals: Petals are pentagonal and at the angles, five petal primordia are initiated more or less simultaneously and separate from each other development of the anthers then the gynoecium is closing and at last the petals begin to grow faster and bend over these organs. The five petals are connected by bridges of the developing filaments of the stamens and a long corolla filament tube is formed.

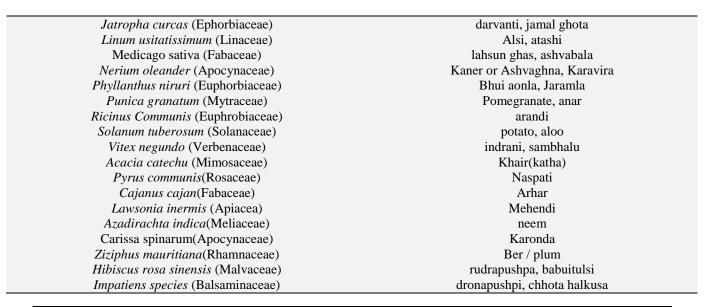
Initiation and Development of Stamen: The stamens grow along with the petals.

Initiation and Development of the Gynoecium: The gynoecium grows simultaneously with the stamens ⁵.

Geographical Distribution: Cuscuta reflexa Roxb. occurs throughout India. This species is common over the northern region of the country, Bengal plains, Western ghats, Satara region, Himachal Pradesh, Uttar Pradesh, and Uttarakhand. It is also found in the plain of Afghanistan, Malaysia, Nepal and Thailand ⁶. The Cuscuta reflexa mainly parasitizes all the angiospermic plants. The highly frequent host plants are given in the table below. The hosts include ephemeral, annual, biennial, and perennial life span; herb, shrub, climber, liana, and tree habits; and agricultural, horticultural, medicinal, weeds, forest, and economically important plants ^{7,8,9,10,11}.

TABLE 3: FAVOURABLE AND HIGHLY FREQUENT HOSTS OF THE CUSCUTA PLANT

Host plants/botanical names	Vernacular name
Justicia adhatoda (Acanthaceae)	Vasaka
Lannea coromandelica (Anacardiaceae)	Jiga
Mangifera indica (Anacardiaceae)	Aam
Calotropis gigantea (Apocynaceae)	Safed aak
Cascabela thevetia (Apocynaceae)	Karabi
Tabernaemontana divaricata (Apocynaceae)	Tagor
Alstonia scholaris (Apocynaceae)	Chhativan, satawana
Acacia nilotica (Fabaceae)	Babool
Datura metel (Solanaceae)	Dhatura
Bambusa tulda (Poaceae)	Bans
Oryza sativa (Poaceae)	Paddy/Dhaan
Aegle marmelos (Rutaceae)	Bel
Lantana camara (Verbenaceae)	Raimuniya
Annona squamosa (Annonaceae)	sitaphal
Catharanthus roseus (Apocynaceae)	shisham
Duranta plumieri (Verbenaceae)	lal dudhi
Ficus glomerata (Moraceae)	udumbra, gular, rumbal



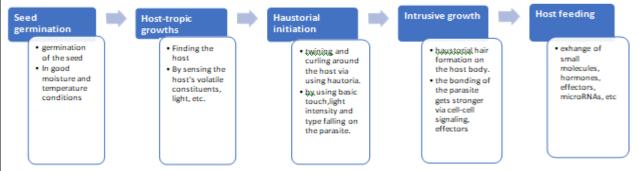


FIG. 2: LIFE CYCLE OF CUSCUTA PLANT 12:

Scientific Research:

TABLE 4: IN-VITRO STUDIES RECORDED IN CUSCUTA REFLEXA PRESENT ON THE DIFFERENT HOSTS

Host plant	Total flavonoid contents	Total phenolic content	DPPH scavenging activity
	(Mg QE/g	(Mg GAL/g	(IC ₅₀ μ/ml)***
	Extract)*	Extract)**	
D. longan	44.49±1.07c	54.09±3.26b	478.99±4.71c
S. asper	$76.88 \pm 2.18a$	$70.25 \pm 1.41a$	231.38±2.81a
Z. dongnaiensis ¹³	49.86±0.91b	57.63±1.97b	289.63±3.88b
A. indica	$82.91a\ a \pm 0.71$	$66.30 \text{ b a} \pm 2.1(80\%)$	$65.11a b \pm 2.01(80\%$
	80% methanolic)	methanolic)	methanolic)
Z. jojoba	$85.11a \ a \pm 0.93$	$71.11a \ a \pm 3.52$	79.57a a ± 1.11
M. alba	$72.03a b \pm 0.69$	$61.01c a \pm 2.18$	$44.29a d \pm 1.02$
A. arabica	$73.28a b \pm 1.29$	$51.29d \ a \pm 2.01$	$51.03a c \pm 1.02$
A. nilotica	$73.29a b \pm 1.42$	$47.02e \ a \pm 2.13$	$47.08a \pm 1.52$
E. jambulana ¹⁴	$53.11a e \pm 1.02$	$69.1 \text{ a} \pm 1.99$	$63.82a b \pm 2.11$
Coccinia grandis	114.4±0.7a	90.8±2.9a	168.7±1.0a
Ficus racemosa	79.0±1.8b	86.6±0.5b	201.6±0.5b
Samanea saman ¹⁵	67.5±2.6c	84.4±1.4b	279.7±6.0c

Values are mean (n = 3) \pm SD (standard deviation). *Values are expressed as quercetin equivalents in mg/g extract. *** Values are expressed as gallic acid equivalent in mg/g extract. *** Values are expressed as DPPH scavenged by cuscuta sample extract in IC₅₀ μ /ml.

Based on the characteristic, each type of *Cuscuta* sp. has a different phytochemical identity. Diverse types of phytocomponents have been isolated from the *Cuscuta reflexa* plant based on the host and

plant nutrition ¹⁶. Most of the phytochemicals are listed below, reported so far in the plant *Cuscuta reflexa*. They were mainly alkaloid, flavonoids, phenols, glycosides, terpenoids, *etc* ¹⁷. The various

chemical constituents are present in various extracts obtained from the plant and so the plant exhibits various pharmacological activities like

antioxidant, antibacterial, antidiabetic, anticarcinogenic, jaundice, etc ^{18, 19}. antispasmodic, effective in

	TABLE 5: PHYTOCONSTITUENTS REPORTED IN CUSCUTA REFLEXA ROXB.				
Phytochemicals	Chemical Constituents	Structure			
Flavonoids	Quercetin ²⁰ , Hyperoside, Kaempferol, Myricetin, Quercetin 3-O- neohesperidoside ²¹ , Leuteolin, Quercetin-3-O-glucoside, 3,5,7,3'-pentahydroxy flavanone (taxifolin Reflexin ²² , 5-hydroxy-7-methoxy-6- (2,3-epoxy-3- methylbutyl)-flavanone Kaempferol-3-O- glucoside ²³ , Myricetin-3-O-alpharhamnoside Apigenin-7-b-rutinoside ²⁴ 3'-methoxy-3',4',5,7-tetrahydroxy flavone, 3'-methoxy-4',5,7-trihydroxy flavone-3-glucoside ²⁵ , Myricetin-3-glucoside, 6,7,8-Trimethoxy 2H-1-benzopyran-2-one, 4,4',6-Trihydroxyauran, Chlorogenic acid ²⁶ , Azaleatin, Melanettin 3,4',5,7-Tetrahydroxy flavanone, Taxifolin 7-O- b D- glucopyranoside ²⁷ ,	Quercetin			
Alkaloids	Methylcytisine ²⁶ , Laceeroic acid Lupanine ²⁸ , Sparteine, Cuscutamine Cytisine ²⁹	Cytisine			
Glycosides	Cuscutin ²⁰ Cuscutoside-B, Arbutin, p-Coumaric acid Coumaric acid 4,5-dicaffeoylquinic acid 3,4-Di-O-caffeoylquinic acid4-oic acid-7-oxo-kaurene- 6 alpha-O- b D- glucoside ²⁶ , Cuscutoside-A ³⁰ , Caffiec acid ³¹ , 21-Hydroxy odoroside H Odoroside Cuscutin H ³² ,	Cuscutin			
Sreoids and sterols	Stigmast-5-en-3-O-b-D- glucopyranoside b Stigmast-5-en-3-yl-acetate ²³ , Campesterol Sesamin ²⁶ Gitoxigenin ³² Stigmasterol ³³	Campesterol			
Terpenoids and sesquiterpenes	Lupeol ²³ , Oleanolic acetate Alpha – Amyrin Beta – Amyrin Alpha Amyrin Acetate Beta Amyrin Acetate Hydroxyoleanane Maragenin ²⁶ , Aromandendrin ²⁷ , Ursolic acid ³² ,	Lupeol H2C H3C H3C H3C H3C H3C H3C H3C			
Carotenoids	Carotene ²¹ Lutein Lycopene ²⁴ , Violaxanthin Rubixanthin ²⁶	Lutein			

TABLE 6: TRADITIONAL USE OF CUSCUTA REFLEXA PLANT

Plant Part	Type of dosage form	Tradition use
Used whole plant	Paste	Treatment of swollen testicles, gout and joint pain, causes abortion, anti-
		rheumatic, analgesic ³⁰⁻⁴⁰ ,
	Maceration	Infection treatment ⁴¹
	Infusion	Anti-poisonous ⁴²
	Juice	Antiseptic, useful in itching skin and jaundice ^{43,44}
	Pills	Anti-tuberculosis 46
	Powder	Anti-fertility agent, astringent, diaphoretic 45
	decoction	Useful in skin disease, jaundice, cough, bronchitis, fever, sex stimulation, anti-
		diarrheal, anti-inflammatory, anti-ulcer, anti-dandruff, fracture joining 44, 46-52
stem	Decoction	Hepatoprotective, anti-diarrheal, useful in constipation, stomach disorders,
		urinary tract infections, jaundice, epilepsy, cholera, asthma ^{49, 53}
	Paste	Anti-hair fall, anti-rheumatic, useful in skin diseases ^{49,54}
	Juice	Jaundice treatment ^{49,55}
	Crushed	Blood purifier, purgative, good for brain, fever, anthrax in cattle ^{56,57}
Seeds	Decoction	Cause abortion ⁴⁹ Carminative, anthelmintic, sedative, diuretic, liver disorders
		useful in ulcer 58, 59, 60
Leaves	Poultice	Pain reliever
	Extract	Anti-hypertensive, anti-diarrheal, useful in jaundice ⁶¹⁻⁶³
Fruits	juice	Effective in scabies, eczem, Antipyretic, cough reliever ⁶⁴

Pharmacological Activities of Cuscuta reflexa: When taken internally treats the retention of urine while being applied externally for skin itches. It is also used to cure cough and diabetes, eczema abortifacient, cholinergic action, anti-steroidogenic activity, hepatoprotective activity, diuretic activity, anticonvulsant activity.

Hepatoprotective Activity: A Hydro- alcoholic extract of *C. reflexa* has hepato- protector activity in albino rats against paracetamol-induced hepatic damage and acts as a hepatoprotective agent ². The methanolic extracts of *C. reflexa* is evaluated for hepatoprotective activity on carbon tetrachloride-induced hepatotoxicity in liver histoarchitecture and alteration in certain biological parameters was observed ⁶⁵.

Antitumor Activity: The Chloroform and ethanol extracts have antitumor activity reported against Ehrlich ascites carcinoma tumour in mice at doses of 200 & 400 mg/kg body weight orally ^{66, 67}.

Antioxidant Activity: The antioxidant capacity was measured using various assays like reducing power, DPPH scavenging activity, and percent inhibition of linoleic acid peroxidation. Various extracts from treating the plant with various solvents were analyzed for the quantity of phenols and flavonoids ¹⁸. The Ethyl acetate and ethanol extract of the plant showed higher activity than other fractions, very close and identical in magnitude and comparable to the standard antioxidant agents ⁶⁸.

Antibacterial Activity: An ethanolic extract of *Cuscuta reflexa* showed antimicrobial activity against *E. coli* and *S. sonnei*. Plants collected from different seasons showed antimicrobial activity against microorganisms like *Staphylococcus epidermidis*, *Staphylococcus aureus*, *E. coli*, *Micrococcus luteus*, *Pseudomonas aeruginosa* ⁶⁹.

Antiepileptic and Anticonvulsive Activities: The significant reduction in the duration of convulsion in tonic seizure induced by pentylenetetrazol (30mg/kg Ip) in mice. The plant product reduces the convulsion induced by maximum electroshock against the tonic extension convulsion ².

Hypoglycaemic Activity: A Methanolic extract showed significant inhibition against α -Glucosidase 70, 71

Anti-HIV Activity: Water extracts of *C. reflexa* exhibited anti-HIV activity ⁷².

Effect on Blood Pressure: Alcoholic extract of *Cuscuta reflexa* has positive inotropic and cardiotonic activities on the perfuse frog heart. A Series of experiments on dogs results in a fall in blood pressure.

Cholinergic Action: The effects of the extract of C. reflexa resembled with that of an acetylcholine when tested on isolated rabbit ileum and frog rectus abdominis and heart 73 . Ethanolic extract causes a dose dependent decrease in arterial blood pressure

and heart rate in pentothal- anaesthetized rats. Four caffeoylquinic acid derivatives were isolated from the extract's active fractions and have an inhibitory effect on Angiotensin Converting Enzyme (ACE) activity. The presence of those metabolites may be responsible for the anti-hypertensive activity extract ⁷⁴.

Relaxant and Spasmolytic Action: An Aqueous and alcoholic extracts showed relaxant and spasmolytic action on small intestine of guinea pig and rabbit ²⁷.

Diuretic Activity: An Aqueous and alcoholic extracts of *C. reflexa* showed diuretic activity in Wistar rat ².

Anti-diabetic Activity: The methanol and aqueous extracts showed a significant reduction in blood glucose levels during OGTT (oral glucose tolerance test) in diabetes rats. The treatment also improved body weights, decreased HbA1c and restored lipid profile. A Methanolic extract of C. reflexa has significant antidiabetic effects and improves metabolic alterations ⁷⁵. Hair growth activity: Petroleum-ether and ethanolic extract of *C. reflexa* is given and observed in male swiss albino rats. *C. reflexa* extract is useful in the treatment of alopecia. This study showed us that it can promote follicular proliferation or prevent hair loss in cyclophosphamide-induced hair fall in *In- vivo* conditions ⁷⁶.

Anti-inflammatory and Anti-carcinogenic Activity: In different phases of the pathogenesis of cancer, inflammatory reactions play a vital role in preventing cancer from spreading. In *in-vitro* and vivo tests, aqueous and alcoholic stem extracts of *C. reflexa* and its ethyl acetate fraction showed remarkable anti-inflammatory activity. *C. reflexa* significantly suppressed inflammation by reducing edema volume in the body up to 80 percent of rats ^{77,78}

Anti-fertility Effect: Methanolic extract returns the normal oestrus cycle and decreases the ovarian and uterus weight in adult female mice79.

CONCLUSION: *Cuscuta reflexa* has enormous therapeutic potential from the early civilizations. The phytoconstituents such as flavonoids, alkaloids, glycosides, steroids, volatile oils and

important resins considered bioactive ingredients of the plant. This plant is considered a meritorious plant is having a broad spectrum of pharmacological activities. Decoction, extracts, paste, powder, juice and infusions from various parts of the plant impart therapeutic nature against numerous ailments of human beings. Limitations of this study might include that; only a fewer animal studies are employed to detect its efficacy in their pharmacological activities. Hence, this review paves the way for people to explore more for its various other therapeutic uses concerning the type of host on which it is growing. phytochemicals contain antimicrobial, anticancer, and antioxidant potentials and can be used as potential drugs to treat various diseases. C. reflexa survive as holoparasitic and depend on other host plants' nutrients, water, and carbohydrates. Cuscuta species lack roots or leaves but possess specific penetrating organs called haustoria, fully developed in 5-6 days after the first contact with the host body. The whole plant is purgative. The plant is employed in Ayurvedic medicine to treat difficulty in urinating, jaundice, muscle pain, and coughs. The juice of the plant, mixed with the juice of Saccharum officinarum or coconut water, is used to treat jaundice. C. reflexa is a parasitic weed plant that causes a huge loss to crop plants yearly. Still, C. reflexa is called a miracle medicinal plant because many chemical compounds have been isolated from this plant having medicinal properties.

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CONFLICTS OF INTEREST: Ni

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