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Phytochemical and Therapeutic Profile of *Cuscuta chinensis* in Classical and Contemporary Formulations

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Abstract

Background: *Cuscuta chinensis* Lam. is a common parasitic herb used in several Asian nations, such as China, India, and Pakistan. It is a widely consumed Traditional Chinese Medicine herb popularly known by different names, including Tu-si-zi. Historically, it has been applied in the treatment of age-associated diseases, liver and kidney dysfunctions, as well as reproductive problems. Studies show that the plant contains flavonoids, lignans, alkaloids, phenolic acids, polysaccharides, and volatile compounds. **Aim:** The present review is designed to summarise the pharmacological and biological effects of *C. chinensis* and its potential clinical utility as an herbal medicine with special emphasis on its formulation approaches. **Methods:** A literature search has been performed using scientific databases including PubMed. Experimental and review articles discussing phytochemistry, pharmacology, and newer formulations involving *C. chinensis* were considered for analysis. Special attention has been focused on those that evaluate the biological activity of various extracts as well as new formulations. **Results:** Experimental investigations have proved the plant's antioxidant, anti-inflammatory, anti-diabetic, hepatoprotective, renoprotective, neuroprotective, fertility-improving, and anti-ageing properties. Most of the pharmacological activities of *C. chinensis* are attributed to the ability of the extracts to inhibit oxidative stress markers and reduce inflammation by modulating Nrf2/HO-1 and NF-κB signalling. However, limited by poor aqueous solubility and low oral bioavailability. Recent advancements, including nanoparticle and nanoemulsion-based formulations, have shown improved stability, enhanced bioavailability, and increased therapeutic efficacy at lower doses. **Conclusion:** *C. chinensis* holds significant promise as a multifunctional therapeutic agent. Integration of advanced formulation approaches can overcome its pharmacokinetic limitations, supporting its potential role in modern drug development and integrative medicine.

Major Findings: *Cuscuta chinensis* is an herb with high flavonoid and lignan contents, which has antioxidant, anti-inflammatory, and protective properties. Its mechanisms include pathways such as Nrf2/HO-1 and NF-κB. But solubility is a limitation. Novel formulations have improved its bioavailability and therapeutic potential.

Keywords: Antioxidant Activity, *Cuscuta chinensis*, Formulations, Phytochemicals, Therapeutic Uses

Abbreviations: AI – Arthritis Index; AKT1 – Protein Kinase B; ALT – Alanine Aminotransferase; AST – Aspartate Aminotransferase; CAT – Catalase; C. chinensis (C.c) – *Cuscuta chinensis*; DPPH – 2,2-Diphenyl-1-picrylhydrazyl; ECCS – Ethanol Extract of *Cuscuta chinensis* Seeds; FBG – Fasting Blood Glucose; FRAP – Ferric Reducing Antioxidant Power; GPx – Glutathione Peroxidase; GSH – Reduced Glutathione; HO-1 – Heme Oxygenase-1; HPLC – High-Performance Liquid Chromatography; IL-1β – Interleukin-1 Beta; IL-6 – Interleukin-6; LPS – Lipopolysaccharide; MDA – Malondialdehyde; NAFLD – Non-Alcoholic Fatty Liver Disease; NF-κB – Nuclear Factor Kappa B; Nrf2 – Nuclear Factor Erythroid 2–Related Factor 2; ROS – Reactive Oxygen Species; SOD – Superoxide Dismutase; TCM – Traditional Chinese Medicine; TGF-β – Transforming Growth Factor Beta; TNF-α – Tumour Necrosis Factor Alpha; UVB – Ultraviolet B.

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1. Introduction

Cuscuta chinensis (C.c)(the Chinese dodder) is a yellow, rootless and almost leafless parasitic vine from the family of Convolvulaceae. It is a widely distributed holoparasitic plant in China,India and other Asian countries. The plant is known for its thread-like stems that wrap around host plants and extract moisture and nutrients using specialised structures called haustoria. Its seeds, called Tu-si-zi, are particularly prized in traditional medicine[1,2]. Parasites are typically smaller organisms that require a host for survival and do not survive independently and freely, but act on one or more living organisms during all or part of their life cycle to feed off the other organism, which is called their host[3]. *C. chinensis*, also called *Grammica chinensis*, Aftimun, Amarbel, Vilayati, Cabello de ángel Chinees warkruid, Devil's hair, Dodder, Kasoos, Linheiro-da-china, Shajar-ul-Sabagh, Tu-si-zi[4]. *C. chinensis* is acrid, sweet and neutral cold[5].

Dodder (*Cuscuta*) - occurring in all temperate and hot, humid areas of the world. It is not often found in colder climates; northern Europe only has four species under these conditions[6].One of the most successful and widespread obligate parasitic plants on crops and non-crops is the *Cuscuta* species. The evolutionary capacity for acceptance by multiple species suggests these plants have a diverse arsenal of host plant attachment mechanisms. In addition, the chemical composition of *Cuscuta* is determined by the type of nectar plant; thus, *Cuscuta,* which grows on medicinal plants, may achieve a more effective therapy[3]. Morphologically, the dodder stem is long, twining, branched, glabrous, pale greenish yellow or spotted with red. Ovary glabrous, curved, long ovate, oblong, obtuse, fleshy; pedicles short (1.5 mm), flowers white (or) pink. The seeds are big, black and glabrous, with 2-4 seeds[6]. *C. chinensis* has an important place in Traditional Chinese Medicine (TCM), *Ayurveda* and other folk medicine systems. Its seeds are used in TCM to nourish the liver and kidneys, improve vision, promote reproductive health and slow ageing.

The plant is also utilised as an anti-inflammatory, analgesic, aphrodisiac, and tonic in China, Korea, Pakistan, Vietnam, India, and Thailand[1,2,7]. In *Ayurvedic* and *Unani* medicine, it is used to treat conditions such as insanity, melancholy, and epilepsy[2]. *C. chinensis* is promoted by its diverse phytochemical composition, which includes flavonoids, phenolic acids, lignans, polysaccharides, and volatile oils. These phytochemicals are linked to a broad range of bioactive properties, including antioxidant, anti-ageing, liver-protective, renoprotective, anti-inflammatory, anti-osteoporotic, anticancer, and neuroprotective properties[1,2,7,8]. Despite the promising pharmacological properties, the use of *C. chinensis* in clinical settings faces setbacks. This is because many of its active phytochemicals, such as flavonoids and lignans, are poorly aqueous-soluble and have minimal oral bioavailability, which may impair their therapeutic potential. Current studies have emphasised the development of modern formulations, including nanoparticles and nanoemulsion-based gels, to improve solubility, stability, and bioavailability. These innovative delivery methods have demonstrated enhanced pharmacological effects at reduced dosages and hold promise for safer and more efficient clinical application[9,10].

2. Materials and Methods

The present review was conducted using a structured literature survey approach. Relevant scientific data on *C. chinensis* were collected from electronic databases such as PubMed, Google Scholar, and other peer-reviewed sources. The search focused on key domains including phytochemistry, pharmacological activities, traditional uses, and formulation strategies of *C. chinensis*. Keywords such as "*C. chinensis*," "phytochemicals," "pharmacological activity," "traditional formulations," and "novel drug delivery systems" were used to retrieve relevant studies. Articles describing experimental (*in vitro* and *in vivo*) studies, as well as reports on classical and modern formulations, were included. Studies lacking sufficient scientific evidence or relevance were excluded. The collected data were critically analysed and categorised into sections such as botanical description, phytochemical profile, pharmacological properties, and formulation approaches. Special emphasis was given to studies highlighting mechanisms of action and advancements in formulation technologies like nanoparticles and nanoemulsions.

3. Botanical Description and Pharmacognostic Characteristics of *C. chinensis*

Cuscuta chinensis Lam., of the family *Convolvulaceae*, is a leafless and rootless holoparasite with pale yellow to orange, thread-like stems that quickly twine around their host plants. The plant, which is chlorophyll-deficient, rootless, and leafless, relies completely on the vascular tissues of host plants for water and nutrients. When it attaches to a host, the stems produce nodular structures that give rise to haustoria, which are specialised invasive structures that invade the host tissues, establish vascular connections, and facilitate efficient resource exploitation. The haustorium is the most important anatomical feature, which is triggered by mechanical and chemical signals from the host surface. The haustorium differentiates into invasive hyphal structures and conducting cells that connect with the host xylem, increasing solute transport and often inhibiting host growth. *C. chinensis* often grows in dense mats on a variety of shrubs, ornamental plants, and herbaceous plants such as Euonymus japonicus, which indicates its wide host range and strong climbing ability[11,12].

3.1 Macroscopic Characteristics

Cuscuta chinensis twines around host plants as a thin, thread-like, yellowish vine. It depends on haustoria to draw nutrients from hosts because it lacks genuine leaves and roots. On host vegetation, filiform, smooth, yellow to orange stems frequently form dense tangles.[13,14]. The pentamerous, small, white flowers are grouped in umbel inflorescences. There are usually two to ten flowers per cluster, each with a delicate corolla[2,13]. The seeds are smooth, brownish, ovoid to globose, and have a firm testa[14,15].

3.2 Microscopic Characteristics

Cuscuta chinensis can be identified by its general shape, testa ornamentation, hairiness, and embryo exudation. Two primary forms of testa ornamentation that are stable at the subgenus level are visible using scanning electron microscopy. The thick, multilayered testa with distinctive ornamentation is visible in seeds. The embryo is coiled inside the seed, and the hilum is glabrous-shaped; exine thickness and colpus length are characteristics of pollen grains that help differentiate *C. chinensis* from related species[14,15].

4. Phytochemical Profile

At least 18 flavonoids (*e.g.*, quercetin, kaempferol, hyperoside, rutin, isorhamnetin), 13 phenolic acids (such as chlorogenic acid, caffeic acid, ferulic acid, gallic acid), 22 lignans (including pinoresinol, syringaresinol, medioresinol, cuscutoside), 9 polysaccharides (*e.g.*, galactomannan), 16 fatty acids (such as linoleic acid, oleic acid, palmitic acid), along with steroids, volatile oils, hydroquinone derivatives, and resin glycosides have been identified in *C. chinensis*, highlighting its chemically rich profile[10].

4.1 Flavonoids such as Quercetin, Kaempferol, Hyperoside, Rutin, and Isorhamnetin

These are found mainly within the seeds and are the chief active principles. They have potent free-radical scavenging, anti-inflammatory, hepatoprotective, immunostimulatory, and anti-carcinogenic properties. Flavonoids also possess the ability to enhance sexual function, protect the liver and kidneys, and aid in the healing of wounds[9,17,18].

4.2 Lignans

At least 22 lignans, like pinoresinol, syringaresinol, medioresinol, and cuscutoside, are found mainly in seeds and whole plants. Lignans have been found to have anti-inflammatory, antioxidant, and possibly anti-cancer effects. They also help in supporting healthy bones and may be used in the prevention of osteoporosis[19,20].

4.3 Alkaloids

Various alkaloids like 3-hydroxy-N-phenethyl propanamide and N-trans-feruloyltyramine have been identified, which justify the immunomodulatory and neuroprotective properties. Identified in seeds and the whole plant[21].

4.4 Polysaccharides

Complex polysaccharides like galactomannan are present in seeds, which work as prebiotics, immunomodulators, and have been found to possess

potential in treating Non-Alcoholic Fatty Liver Disease (NAFLD) and supporting gut health[22].

4.5 Volatile Oil and Resin Glycosides

These have antibacterial and antioxidant properties and are found in trace concentrations in different parts of plants[23].

5. Pharmacological Activities

5.1 Antioxidant Activity

Cuscuta chinensis has been known to possess strong antioxidant properties in various *in vitro* models like DPPH, FRAP, and lipid peroxidation assays, which are often comparable to those of synthetic antioxidants[24]. The major contributions to its antioxidant properties are made by flavonoids and phenolic acids like kaempferol, quercetin, hyperoside, and chlorogenic/cinnamic acids[9,10].The addition of polysaccharides and specific metabolites like the hydroxygallic acid derivative, zingibroside R1, sterol lipid 4 alpha formyl stigmasta 7,24 dien 3 β ol further potentiates the antioxidant and anti-ageing properties. *In vivo* and cell culture studies show that the extracts increase SOD, CAT, GPx, GSH, and decrease ROS/MDA, which protects liver, bone, and brain tissues from oxidative injury[25]. In a nanoemulsion-based gel formulation, the antioxidant-rich extract has been shown to reduce inflammation as well as enhance wound contraction in rats[9].

5.2 Anti-ageing

The anti-ageing properties of *C. chinensis* on worms (Caenorhabditis elegans) have been investigated. The maceration procedure was used to create a methanol extract from *C. chinensis* seeds. *C. elegans* was subsequently treated with these preparations. Stress resistance [heat stress] was one of the metrics that was measured. Until every worm perished, the no. of living and dead worms was routinely taken into account. It was stated that individuals who underwent therapy for *C. chinensis* had longer survival times. The pharyngeal pumping rate was measured using the pharyngeal pumping assay. While crawling on the seventh and twelfth days of adult nematodes. Increased food consumption was also noted during the study. Their fertility, physical size, and swimming habits. Calculations were made[26].

5.3 Fertility-enhancing Property

Ethanolic extracts of Semen *C. chinensis* were used in male rat models for evaluating fertility-enhancing properties. The rat model was prepared with unilateral cryptorchidism in the right testis. *C. chinensis* extract was given at 100 mg/kg and 200 mg/kg doses through intraperitoneal administration. Physiological parameters like body and reproductive organ weight, sperm count, motility, and biochemical parameters like glutathione peroxidase, catalase, and superoxide dismutase activity were elevated with extract treatment. The mechanism of action possibly involved modulation of Nrf 2 and HO 1 Signaling pathway, hampering of apoptosis, and oxidative stress[27].

5.4 Anti-rheumatoid

The activity was examined in male albino rats. Methanolic watery extracts of *C. chinensis* were administered to rats. The progression of the illness was assessed using the Arthritis Index (AI) based on the results. Within 14 days of treatment, Chinensis extracts were effective in reducing AI in the treated group. It was suggested that the pharmacology underlying its activity was the inhibition of prostaglandin synthesis and COX-2 expression. Additionally, the vascular endothelial growth factor, which is linked to angiogenesis, is decreased by *C. chinensis* extract[28]. The activity of *C. chinensis* and its potential molecular mechanism. They were shown to inhibit luteolin-IL6/VEGFA binding and quercetin-AKT1 binding, respectively[29].

5.5 Anti Diabetic Activity

In order to assess the plant's anti-diabetic properties and screen for phytochemical components using the HPLC technique, white male rats were given a hydroalcoholic extract of the *C. chinensis* plant. 200 mg/kg, 300 mg/kg, and 400 mg/kg were administered orally. The retro-orbital plexus was punctured to obtain blood samples, and the fasting blood glucose levels were measured. The anti-diabetic action was confirmed by the considerable decrease in FBG[30].

5.6 Anti-Alzheimer'sActivity

The anti-Alzheimer effects of a dry seed extract of *C. chinensis* were investigated in mice given scopolamine. The extract was taken orally at concentrations of 100 mg and 300 mg. The Morris water maze's spatial

performance test, elevated plus maze test, and passive avoidance test were all carried out. Acetylcholinesterase activity was reduced, and malondialdehyde levels were raised by *C. chinensis*. They also have lower amounts of tumour necrosis factor and interleukin-1β in the brain. These demonstrate that *C. chinensis* has anti-Alzheimer properties[31].

5.7 Anti-wrinkle Property

Cuscuta chinensis ethanol extract of seeds was evaluated for UVB-induced skin wrinkles for the purpose of wrinkle improvement. Human fibroblast cell (CCD-986sk cells) was evaluated, and biomarkers were analysed. The finding indicates that biomarkers such as melanoproteinase and procollagen were increased, thus reducing wrinkles[32].

5.8 Renoprotective

In a murine model of Lipopolysaccharide (LPS) induced acute kidney failure, the oral treatment of ethanol Extract of *C. chinensis* Seeds (ECCS) for 14 days showed significant improvement in renal injury. ECCS treatment resulted in a substantial decrease in blood urea nitrogen and serum creatinine, along with an improvement in histopathological changes in the kidneys, and a reduction in the pro-inflammatory cytokines TNF-α, IL-1β, and IL 6. This suggests a significant renoprotective and anti-inflammatory property of ECCS in LPS-induced acute kidney injury[33].

6. Classical and Marketed Formulations Containing *C. chinensis*

The traditional systems of medicine have widely used *C. chinensis* in the treatment of diseases associated with urinary tract and kidney problems. The herb is regarded as one of the vital components in the preparation of various classic medications because of its ability to act as a diuretic, antioxidant, and kidney-protective agent. Often, it is used in combination with other herbs for effective prevention and treatment of urolithiasis cases. So far, more than 80 articles concerning pharmacological and phytochemical characteristics of *C. chinensis* have been published. Besides the classical applications of the herb, there have been important breakthroughs in the creation of new formulas. At least 5-10 different innovative formulations, including nanoparticles, nanosuspensions, and nanoemulsion gel forms, have been explored experimentally. They proved to be efficient due to their high bioavailability, good stability, and greater therapeutic activity, such as elevated antioxidant enzyme levels (SOD, CAT,

Table 1. Overview of classical formulation with *C. chinensis*

S. No.	Classical formulation	System of medicine	Major ingredients	Key bioactivesfrom *Cuscuta*	Therapeutic use	References
1	Wu Zi Yan Zong Wan	Traditional Chinese Medicine (TCM)	*C. chinensis*, *Lycium barbarum*, *Schisandra chinensis*, *Rubus chingii*	Flavonoids (Quercetin, Kaempferol)	Male infertility, kidney deficiency,sperm quality,sexual dysfunction	[10]
2	Zuo Gui Wan	TCM	*C. chinensis*, *Dioscorea opposita*, *Lycium barbarum*	Phenolics, flavonoids	Yin deficiency, ageing, bone disorders	[34]
3	Er Xian Tang (modified forms)	TCM	*C. chinensis*, *Epimedium brevicornum*, *Morinda officinalis*	Flavonoids	Menopausal syndrome, osteoporosis	[35]
4	Bu Shen Yi Jing Fang	TCM	*C. chinensis*, *Astragalus membranaceus*	Quercetin, hyperoside	Improves ovarian function, fertility	[36]
5	Tusizi	TSM	*Gouqizi – Lycium barbarum*,*Cheqianzi – Plantago asiatica*,*Tusizi – C. chinensis/C. australis*	Lignans, flavonoids		[15,37]
6	Jin Suo Gu Jing Wan	TCM	*C. chinensis*, *Rosa laevigata*, *Nelumbo nucifera*	Flavanoids	Spermatorrhea, urinary disorders	[38]

Table 2. Modern pharmaceutical and novel formulations of *C. chinensis*

S. No.	Formulation	Therapeutic uses	Mechanism	Study stage	References
1	*C. chinensis*nanoparticles/ nanosuspension	Hepatoprotective	Increase antioxidant enzymes-SOD, CAT,GPx and decrease liver enzymes (ALT, AST)	Preclinical(rat model)	[39]
2	*C. chinensis*nanoemulsion-based gel	Wound healing, anti-inflammatory	Anti-inflammatory pathway (decrease IL-1β, IL-6, TNF-α) and flavonoid-mediated wound repair (TGF-β, NF-κB modulation)	Preclinical (rat wound model); potential for clinical translation	[9]
3	*C. chinensis* ethanolic extract (standardised extract formulation)	Hepatoprotective	Antioxidant mechanism reduces oxidative stress; decreases MDA, ↑ SOD, CAT, GPx	Preclinical (rat model)	[40]
4	Nanotechnology-based herbal delivery systems	Hepatoprotective, antioxidant and reproductive support	Controlled release + enhanced permeability improved pharmacokinetics of flavonoids	Translational research stage	[41]
5	*C. chinensis* nanoparticle formulation	Hepatoprotection, antioxidant therapy	-	Preclinial	[42]

Table 3. Marketed formulations of *C. chinensis*

Formulation name	Dosage form	Composition	Application	References
Wu Zi Yan Zong Wan (Chinese patent medicine)	Pills/capsules/ sachets	*C. chinensis*, *Lycium barbarum*, *Rubus chingii*, *Schisandra chinensis*, *Plantago asiatica*	Male infertility, sperm quality improvement	[43]
Wu Zi Yan Zong Wan	Pills	Same 5-herb composition with defined proportions (35:35:17:5:8) including *C. chinensis*	Clinically used for infertility	[44]
Shou Tai Wan	Pills	*C. chinensis*, *Dipsacus asper*, *Eucommia ulmoides*, *Ligustrum lucidum*	Prevention of miscarriage, reproductive support	[45]
Wu Zi Yan Zong Wan (clinical/experimental marketed form)	Pills	Contains *C. chinensis*andreproductive tonics	Antioxidant, testicular protection, anti-ageing	[46]

GPx), low expression of IL-1β and TNF-α, and better protection of the liver and acceleration of the wound healing process. Overview of classical formulation with *C. chinensis,* modern pharmaceutical and novel formulation *of C. chinensis,* and marketed formulations of *C. chinensis* described in Tables 1, 2 and 3.

7. Future prospects

Despite the significant therapeutic potential of *C. chinensis*, its clinical translation remains limited due to gaps in systematic research. Future investigations should prioritise well-designed clinical trials to establish its safety, efficacy, and optimal dosage in humans, as current evidence is largely confined to *in vitro* and animal studies. Standardisation of extracts and the identification and isolation of key bioactive constituents are essential to ensure reproducibility, quality control, and consistent therapeutic outcomes. In parallel, improving the bioavailability of poorly water-soluble compounds, particularly flavonoids and lignans, remains a critical challenge that must be addressed. Advanced drug delivery systems, including nanoparticles, nanoemulsions, and liposomes, offer promising strategies to enhance solubility, stability, and targeted delivery; however, their long-term safety, efficacy, and scalability require thorough evaluation. Additionally, comprehensive pharmacokinetic and pharmacodynamic studies, along with investigations into potential synergistic interactions among

bioactive compounds, are necessary to better understand the mechanisms underlying its therapeutic effects. Expanding research into its applications in neurodegenerative, metabolic, and reproductive disorders may further uncover novel therapeutic avenues. Furthermore, integrating traditional knowledge with modern scientific approaches—such as omics technologies and molecular docking - can accelerate the development of safe, effective, and standardised formulations of *C. chinensis*.

8. Conclusion

Cuscuta chinensis is a well-known medicinal parasitic herb used extensively in various traditional forms of medicine like TCM and *Ayurveda*. It contains several bioactive phytochemicals in its seeds, Tu-si-zi, such as flavonoids, lignans, and polysaccharides, and possesses numerous biological properties such as anti-inflammatory, hepatoprotective, antioxidant, and reproductive-enhancing actions. Various studies have indicated its potential as an alternative for treating several diseases like diabetes, neurodegenerative disorders, kidney-related diseases, and reproductive problems. Nevertheless, certain drawbacks, including poor solubility and lower bioavailability of its natural ingredients, can adversely impact its therapeutic effect. The recent progress in new drug delivery systems, especially using nanotechnology platforms, can provide some solutions for overcoming these drawbacks. More systematic investigations in this area are needed to ensure success.

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Author Contribution

Conceptualisation and design, A.M. and B.P.; methodology, A.R.; formal analysis, A.M. and A.R.; investigation, A.R.; resources, A.R.; data curation, A.R.; writing—original draft preparation, A.R.; writing—review and editing, A.R.; visualisation, A.R., A.M., and B.P.; supervision, A.R., A.M., and B.P. All authors have read and agreed to the published version of the manuscript.