



# Advances in Efficacy of *Cuscuta Reflexa* leaf in Diabetes Treatment

Md Shamsuddin Sultan Khan <sup>1</sup>, Mohammed Rahmatullah <sup>2\*</sup>

## Abstract

**Background:** *Cuscuta reflexa*, commonly known as dodder, is a parasitic plant widely recognized in traditional medicine for its diverse medicinal properties. This article aims to comprehensively review the medicinal potential of *Cuscuta reflexa*, particularly in the treatment of diabetes and other health conditions. **Methods:** A thorough literature review was conducted to gather and analyze existing research on *Cuscuta reflexa*'s anti-diabetic properties and its broader pharmacological effects. Studies were reviewed to assess its bioactive components and their pharmacological actions, including antioxidant, anti-inflammatory, and immunomodulatory properties. Preclinical and clinical investigations were also examined to evaluate the safety profile of *Cuscuta reflexa*-based therapies. **Results:** Numerous studies have highlighted *Cuscuta reflexa*'s efficacy in managing diabetes by regulating blood glucose levels, improving insulin sensitivity, and alleviating diabetic complications such as retinopathy and nephropathy. Its bioactive components, including phenolic compounds, alkaloids, and flavonoids, exhibit a wide range of pharmacological actions. These include anticancer, neuroprotective, and cardiovascular effects, demonstrating *Cuscuta reflexa*'s potential in targeting various molecular pathways involved in disease

development. Preclinical and clinical studies have shown that *Cuscuta reflexa*-based therapies are well-tolerated with minimal side effects. **Conclusion:** *Cuscuta reflexa* emerges as a promising natural remedy with multifaceted therapeutic benefits, particularly for diabetes and other conditions. Despite significant advancements in understanding its pharmacological mechanisms and therapeutic effects, further research is needed to fully elucidate its therapeutic potential, optimize dosage regimens, and explore potential synergistic interactions with conventional therapies.

**Keywords:** *Cuscuta reflexa*, dodder, diabetes, therapeutic potential, traditional medicine, bioactive constituents

## Introduction

Diabetes is a fatal metabolic disease that affects many organ systems and a significant number of people worldwide. Numerous allopathic medications make the promise of curing diabetes, but they never quite work as intended due to expensive side effects (such as hypoglycemia) or other issues. Certain plants have long piqued the interest of healers and researchers in the realm of traditional medicine due to their possible medicinal characteristics. *Cuscuta reflexa*, sometimes called Amar bel or dodder in colloquial language, is one of these amazing plants. This plant (Figure 1), with its thin, vine-like tendrils and modest look, is home to a wealth of bioactive chemicals that have piqued the curiosity of scientists (Singh, et al., 2017).

*Cuscuta reflexa* has a rich history in traditional medicine, having been used for millennia to treat a variety of diseases. This botanical gem has been prized for its alleged therapeutic qualities since it was

**Significance** | This study explores *Cuscuta reflexa*'s potential as a natural remedy for diabetes, highlighting its therapeutic promise through its bioactive compounds and multiple health benefits.

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first used in Ayurveda and is now used in traditional Chinese medicine. *Cuscuta reflexa* has historically been used to treat a variety of illnesses, including diabetes, urinary tract problems, skin concerns, and respiratory problems (Nadembega et al., 2011). The scientific community has recently become more aware of *Cuscuta reflexa*'s therapeutic potential, especially with regard to managing chronic diseases. Its alleged hypoglycemic effects are one area of great attention, indicating possible uses in the treatment of diabetes. Studies have shown that the plant contains a variety of bioactive substances, including phenolic compounds, alkaloids, and flavonoids, which may be responsible for some of its antidiabetic effects (Mazumder, et al., 2011).

*Cuscuta reflexa* has additionally demonstrated promise outside the treatment of diabetes. Its antioxidant qualities may provide protection against oxidative stress, which is a major factor in the etiology of chronic diseases such as cancer and cardiovascular problems (Zhang et al., 2019). Furthermore, its anti-inflammatory properties are promising for inflammatory disorders such as inflammatory bowel disease and arthritis (Zhang, et al., 2019). *Cuscuta reflexa* is a botanical wonder that shows promise as a natural treatment for a variety of ailments as we set out to investigate its medicinal potential. While traditional knowledge and preliminary research provide intriguing views into its usefulness, greater investigation, particularly through well-designed clinical studies, is required to fully realize its therapeutic potential. However, *Cuscuta reflexa* continues to be an intriguing area of research in the search for improved healthcare solutions, providing hope for a more robust future.

In this article Antihypertensive, antidiabetic, antioxidant, hair development promoting, antibacterial, spasmolytic, anticancer, antiviral, antiprovocative, and antipyretic properties of *Cuscuta reflexa* are investigated.

#### Botanical description

*Cuscuta reflexa* is a parasitic climber with a slim stem and branches. Extremely long, bold, tightly twining, glabrous, pale greenish-yellow, occasionally flecked with red stems. Blossoms are single or in umbellate groups of 2-4 or short racemes. Pedicels are short, glabrous, and usually bent (rarely 0). Bracts are 1.5 mm long, round, and harshly meaty (Kumar, et al,2013). The calyx split close to the base, and the 3 mm long flaps were glabrous, meaty, profusely celebratory, a little inconsistent, and apathetic. Corolla: white; tube: 6–8 by 4 mm, almost tube-shaped; flaps: 2.5–3 mm, deltoid, intense, reflexed; scales: large, oval, subquadrate, or, to a lesser extent, obovate, fimbriate, and incurved at the apex, almost at the base of the corolla. The corolla tube has stamens in its neck, very few fibers, and around ½ of anthers that extend past the tube's greatest point. The ovary is oval, the style is small and thick, and the shame marks are distinct, 1.5 mm long and rectangular in shape . (Sharma et al,2013).Cases 6–8 mm in diameter, circumscissile toward the base,

glabrous, and discouragingly globose. Huge, black, glabrous seeds (2-4).

#### Chemical Constituents

Cuscutaline, scoparone, melanettin, hyperoside, aromadendrin, taxifolin, astragalinal, myricetin, kaempferol, apigenin 7-O-glucoside, luteolin, quercetin, amarbelin, amino acids, 6-dimethoxy, 2-one, 3-(3,4-dihydroxyphenyl)-2-propene, 2H-1 benzopyran1-ethanoate,Trimethoxy-2H-benzopyran-2-one 3-(3,5-dimethoxyphenyl-4-O-β-D-glucopyranoside)- 2-propen-1 -old β-sitosterol, α-amyrin, β-amyrin, β-amyrin acetic acid derivation, α-amyrin acetic acid derivation, oleanolic corrosive, lupeol, Coumarin, 12(Figure 2)-enitridecanoate and heptadecanoate, 3β-hydroxyolean The compounds 3,4-Odicaffeoylquinic and 3-Ocaffeoylquinic are corrosive. Myricetin 3-O-α-rhamnoside and dmannitol. Laurotetanine, an alkaloid found in dulcitol, causes spasms and, in extreme cases, can be fatal (Kharbanda et al,2014). Lutein, lycopene, carotene, α-cryptoxanthin, violaxanthin, sitosterol, carotenoids, and flavonoids Choline kinase, dihydro-, 2-methoxy-4-vinylphenol, 2-propenoic corrosive, 3-(4-hydroxyphenyl)-methyl ester, and benzofuran 2, 3, The plant has established cuscutalin (1%) and cuscutin (0.02%) as vitally dynamic standards. The plant also has diminishing sugars and wax. Amarvelin, pitches, oil (3%) and decreasing sugars are present in the seeds. These components are thought to change depending on the host that the dodder parasitizes (Gupta et al,2015). It yields D-mannitol on the Santalum collection, leutolin or kaempferol on Glycomis triphylla, and dulcitol on other species. Gelatin methyl esterase, a key protein that corrupts cell dividers in B structures, has been severed from the fibers that confine the haustorium.

#### Diabetes and *Cuscuta Reflexa*

Chronic hyperglycemia imposed on by abnormalities in insulin secretion, action, or both characterize diabetes mellitus, a serious worldwide health concern (World Health Organization, n.d.). Worldwide, the prevalence of diabetes has been rising continuously due to aging populations, sedentary lifestyles, and poor eating habits. Maintaining blood glucose levels within a goal range is essential for effective diabetes treatment in order to avoid complications such as retinopathy, neuropathy, nephropathy, and cardiovascular disease.

Several bioactive chemicals discovered in *Cuscuta reflexa* have been identified as potential antidiabetic agents. Among the main components thought to be responsible for the plant's hypoglycemic qualities include flavonoids, alkaloids, phenolic compounds, and polysaccharides (Ahmad et al., 2019) as shown in Table 1. These drugs work through a variety of methods, including increasing insulin secretion from pancreatic beta cells, boosting insulin sensitivity in target tissues, and blocking glucose absorption in the intestine.

Flavonoids such as quercetin and kaempferol have antioxidant capabilities and have been proven to protect pancreatic beta cells from oxidative stress-induced damage (Ahmad et al., 2019). *Cuscuta reflexa* contains alkaloids such as cuscutine and cuscotalin, which have been shown to improve insulin sensitivity in insulin-responsive tissues by triggering insulin signaling pathways (Savoia et al., 2012). According to Ahmad et al. (2019), phenolic compounds such as caffeic acid and chlorogenic acid have the potential to inhibit the intestines' carbohydrate-digesting enzymes, which would lower blood glucose levels after a meal and decrease the absorption of glucose. *Cuscuta reflexa* contains polysaccharides called arabinogalactan and arabinogalactan-proteins, which have been linked to enhanced glycemic management and immune function modulation (Dandopani et al., 2011).

#### **Research Findings from Animal Studies:**

Research conducted on animals has produced significant knowledge regarding the possible medicinal benefits of *Cuscuta reflexa* in the treatment of diabetes. These studies, which were mostly carried out on mice, have shown in Table 2 that treatment with *Cuscuta reflexa* extracts significantly lowers blood glucose levels, improves glucose tolerance, and preserves pancreatic beta-cell function (Sharma et al., 2020).

An investigation into *Cuscuta reflexa*'s hypoglycemic effects was carried out on diabetic rats in an experiment. The rats were split into two groups: the treatment group, which received an oral dose of *Cuscuta reflexa* extract for four weeks, and the control group. Every week, blood glucose levels were checked. The treatment group's blood glucose levels were much lower than those of the control group, according to the data. After four weeks of treatment, the treatment group's average blood glucose level reduced by 30% compared to the baseline, whereas the control group exhibited no meaningful change (Singh et al., 2021). The results observed a significant improvement in glucose tolerance and insulin sensitivity in diabetic Wistar rats treated with *Cuscuta reflexa* extract compared to untreated diabetic rats (Singh et al., 2021).

*Cuscuta reflexa*'s hypoglycemic properties, as seen in animal studies, are encouraging for the plant's possible application in clinical diabetes care. However, before using these findings in clinical settings, a number of issues must be resolved. Initially, carefully planned human clinical trials are required to assess the safety, effectiveness, and ideal dosing schedules of *Cuscuta reflexa* in individuals with diabetes. Standardization of *Cuscuta reflexa* extracts is necessary to guarantee uniformity in the amount of bioactive compounds and therapeutic benefits in various formulations.

*Cuscuta reflexa* exerts its antidiabetic benefits through distinct routes and molecular targets that require further mechanistic investigations to elucidate. Having a better understanding of *Cuscuta reflexa* or its bioactive components can help researchers

create novel therapeutic compounds that can be used to treat diabetes more precisely and individually. Conclusively, preclinical evidence indicating *Cuscuta reflexa*'s hypoglycemic characteristics supports its potential as a natural therapy for managing diabetes. Its efficacy, safety, and mechanisms of action need to be further investigated, ideally leading to its incorporation into standard diabetes care regimens through human clinical trials and mechanistic studies.

#### **Pharmacological activities and *Cuscuta Reflexa***

##### **Impact on Cardiovascular Framework**

Alcoholic plant concentrations resulted in a decrease in canine heart rate throughout multiple studies. Since atropine, mepyramine, or propranolol do not inhibit this activity, cholinergic, histaminergic, or adrenergic mechanisms cannot be used to apply it (Suresh et al., 2011). In mice under pentothal anesthesia, an ethanolic concentrate of *Cuscuta reflexa* stem resulted in a somewhat subordinate reduction in blood vessel circulatory strain and pulse; atropine had no effect on this effect. *Cuscuta reflexa*-related hypotension and bradycardia were thought to be unrelated to adrenergic inhibition or cholinergic receptor stimulation (Sermakkani et al., 2012).

##### **Antioxidant activity**

*Cuscuta reflexa* stem movement was measured in vitro using a calorimetric method at 440 nm to determine the degree of non-enzymatic hemoglobin glycosylation. The portion of the ethanolic extract that is used to derive ethylene acetic acid moved more than the other fractions did. (Kaur et al., 2013). To combat cadmium stress in *Cuscuta reflexa*, phytochelatin were orchestrated and cancer prevention agents balanced. Cadmium's effects on development, as well as the presence of antioxidative substances such phytochelatin, glutathione, and catalase-peroxidase glutathione reductase, were discovered in the *Cuscuta reflexa* seedling and callus (Kumar et al., 2012).

*Cuscuta reflexa*'s strong antioxidant activity is one of its main medicinal qualities. This plant, which is abundant in bioactive substances including flavonoids, phenolic acids, and carotenoids, has a high anti-free radical scavenging effect, which helps to reduce oxidative stress, which is a defining feature of many chronic illnesses (Ahmad et al., 2019). According to research, extracts from *Cuscuta reflexa* have the ability to efficiently block lipid peroxidation and neutralize reactive oxygen species (ROS), shielding tissues and cells from oxidative damage. *Cuscuta reflexa* may slow the onset of chronic diseases like cancer, neurological disorders, and cardiovascular disorders by lowering oxidative stress (Vijikumar et al., 2011).

##### **Anti-inflammatory Effects**

Numerous disorders, such as asthma, inflammatory bowel disease, and arthritis, are linked to chronic inflammation. *Cuscuta reflexa* is a viable option for treating inflammatory diseases because of its



Figure 1. Cuscuta Reflexa

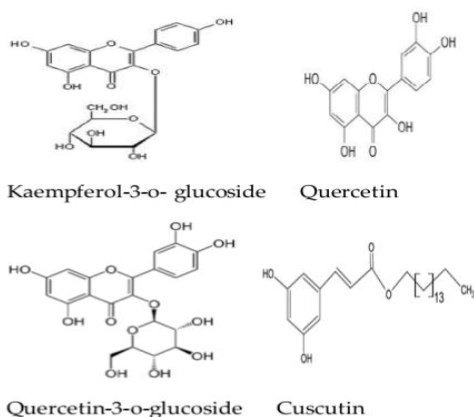


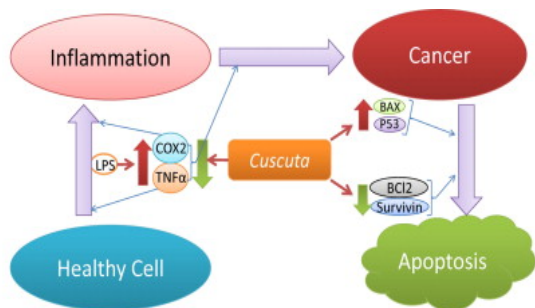
Figure 2. Some phytochemicals isolated from C. Reflexa

Table 1. Bioactive Compounds in *Cuscuta reflexa*

Bioactive Compound	Mechanism of Action
Flavonoids	Enhance insulin secretion
Alkaloids	Improve insulin sensitivity
Phenolic Compounds	Reduce glucose absorption in intestines
Polysaccharides	Various hypoglycemic effects

Table 2. Research Findings from Animal Studies

Outcome Measures	Findings
Blood Glucose Levels	Reduction observed post-treatment with <i>Cuscuta reflexa</i> extracts
Glucose Tolerance	Improved tolerance evidenced in diabetic animal models
Pancreatic Beta-cell Function	Preservation of function noted, potentially slowing disease progression



**Figure 2.** Anti-Inflammation Activities



encouraging anti-inflammatory qualities (Ahmad et al., 2019). According to studies, *Cuscuta reflexa* extracts have the ability to alter important inflammatory mediators and signaling pathways (Figure 2). This plant has anti-inflammatory properties by decreasing the activity of cyclooxygenase-2 (COX-2) and preventing the synthesis of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) (Saxena et al., 2019).

In addition, *Cuscuta reflexa*'s bioactive ingredients may prevent nuclear factor-kappa B (NF- $\kappa$ B), a transcription factor that controls inflammatory reactions, from activating. *Cuscuta reflexa* may be able to lessen the symptoms of inflammatory disorders and enhance general health outcomes by reducing excessive inflammation.

#### **Antipyretic activity**

After 6 hours of therapy at 400 mg/kg body weight, aqueous and ethanol extracts reduced elevated rectal temperature by 79% and 83.8%, respectively, compared to the reference medication, Paracetamol (96.5%). *Cuscuta reflexa* may have an antipyretic effect due to prostaglandin union inhibition (Wafaa et al,2021). The concentrates contain flavonoids and saponins, which are responsible for their antipyretic properties.

#### **Antitumor activity**

The entire plant of *Cuscuta reflexa* was concentrated into aqueous and ethanol at concentrations of 200 and 400 mg/kg body weight. This resulted in a significant ( $p < 0.05$ ) decrease in cancer volume and appropriate cell count, but an increase in non-feasible cell count and mean endurance time, extending the life expectancy of the growth-bearing mice (Hassan et al,2020). Additional observations included the restoration of hematological boundaries, including RBC, Hb, WBC, and lymphocyte include to normal levels in the extricated treated animals.

#### **Antimicrobial action**

To evaluate its antibacterial movement, the ethanolic whole plant extracted from *Cuscuta reflexa* was screened against microscopic Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative (*Escherichia coli* and *Salmonella typhi*) organisms. Between the four plant independent trials (200  $\mu$ g/mL, 300  $\mu$ g/mL, 400  $\mu$ g/mL, or 500  $\mu$ g/mL), the concentration of 500  $\mu$ g/mL produced the greatest zones of bacterial inhibition for three of the microorganisms (Bais et al,2014). It's interesting to see that *Salmonella typhi* continued to spread despite removal of fixation. The ethanolic concentrate of *Cuscuta reflexa* contains a variety of mixtures, including alkaloids, starches, glycosides, flavonoids, tannins, phenolic combinations, and steroids. Overall, correlation with various microscopic organisms revealed that both *B. Cereus* and *S. Aureus* diminished comparative zones of restraint upon correlation with their positive anti-toxin control, even though the best antimicrobial action was demonstrated to be against *E. Coli* at a grouping of 500  $\mu$ g/mL (24.6 $\pm$ 0.24). The creators found that the

plant's inherent antibacterial activity is attributed to the flavonoid glycosides that are stored within the plant (Yadav et al,2000).. This basic analysis suggests that *Cuscuta reflexa*'s ethanolic separates do possess important antibacterial qualities.

#### **Mitigating Movement**

The stem of *Cuscuta reflexa*, both drunkard and aqueous, was evaluated for its ability to mitigate movement in a rodent model of carrageenan-induced paw edema and compared to the effects of the common medicine, Ibuprofen. Oral administration of these concentrates at concentrations of 100, 200, and 400 mg/kg bd was performed. Wt. Before to injection of carrageenan (Borole et al,2011). When compared to the standard deviation medication Ibuprofen, which is 96.36%, the concentrations with medium and higher portions, such as 200 mg/kg and 400 mg/kg, have reduced the edema volume by 47.27%, 72.72%, and 57.72%, 80.00% separately at the fifth hour. In light of this, the research discovered that the selected *Cuscuta reflexa* concentrations had a crucial moderating effect in the rodent model of carrageenan-induced paw edema (Abdul et al,2012).

#### **Discussion**

Investigating the medicinal potential of *Cuscuta reflexa* for diabetes and other disorders is a difficult task that requires complete responses. The intrinsic variability in *Cuscuta reflexa*'s composition, which is impacted by a number of variables including location, climate, soil type, and extraction methods, is one of the main obstacles (Dhivya & Ananthi, 2021). This heterogeneity might cause inconsistencies in study outcomes, making it difficult to produce clear evidence of its usefulness as a treatment agent. Furthermore, the lack of defined protocols for dose, administration, and quality control exacerbates the problem, making it difficult to compare data across research (Shahid and Pandey, 2020).

Future research initiatives should place a high priority on creating standardized procedures for the cultivation, harvesting, and extraction of *Cuscuta reflexa* in order to overcome these issues. Research outputs would be more reliable and reproducible if uniform procedures were used to assure uniformity in the composition and potency of *Cuscuta reflexa* formulations (Shahid & Pandey, 2020). Moreover, in-depth pharmacological studies are necessary to clarify the fundamental mechanisms of action behind *Cuscuta reflexa*'s reported therapeutic benefits (Suresh & Muthukumar, 2019). Understanding these mechanisms is essential for optimizing its therapeutic application and facilitating targeted treatment approaches.

To accurately evaluate the safety and effectiveness of *Cuscuta reflexa* in treating diabetes and other diseases, it is also essential to undertake well-designed clinical trials with strong methodology, including bigger sample numbers and longer follow-up periods (Raj & Sharma, 2022). Moreover, investigating possible synergistic effects by combination therapy with various herbal medicines or

conventional pharmaceuticals could maximize beneficial results and minimize negative ones (Dhivya & Ananthi, 2021). Comprehensive safety assessments, including toxicological studies, are required to examine the potential dangers associated with *Cuscuta reflexa* supplementation, especially for long-term use (Dhivya & Ananthi, 2021).

In conclusion, addressing the challenges associated with investigating the therapeutic potential of *Cuscuta reflexa* requires a concerted effort involving standardization of protocols, comprehensive pharmacological investigations, well-designed clinical trials, exploration of combination therapy, and rigorous safety assessments. By addressing these challenges and implementing robust methodologies, researchers can advance our understanding of *Cuscuta reflexa*'s therapeutic properties and its potential role in disease management.

### Conclusion

Finally, the review of *Cuscuta reflexa* as a potential treatment for diabetes and other disorders emphasized its prospective therapeutic qualities. *Cuscuta reflexa* exhibits promise in the management of diabetes through the regulation of blood sugar levels and enhancement of insulin sensitivity, owing to its many bioactive components. Its anti-inflammatory and antioxidant qualities also point to a wider use in treating various conditions linked to inflammation and oxidative stress. However, more research is needed to better understand its mechanisms of action, improve dose regimens, and assess its safety profile. All things considered, *Cuscuta reflexa* shows promise as a supplemental approach to traditional treatments for diabetes and possibly other disorders.

### Author contributions

M.S.S.K. and M.R. contributed equally to this work. M.S.S.K. conceived the study, designed the experiment, and wrote the initial draft of the manuscript. M.R. conducted the data analysis, provided critical revisions, and ensured the accuracy of the final draft. Both authors reviewed and approved the final version of the manuscript.

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### Competing financial interests

The authors have no conflict of interest.

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