

HEPATOPROTECTIVE POTENTIAL AND NUMEROUS PHARMACOLOGICAL PROPERTIES OF AFTIMOON (CUSCUTA REFLEXA ROXB) A MIRACLES DRUG IN UNANI MEDICINE. A COMPREHENSIVE REVIEW

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Abstract

Liver is the most essential organ in the body. It regulates many physiological processes, including metabolism, secretion and storage. Liver illnesses continue to be a major hazard to public health and a global problem. Several herbal plants have been traditionally utilised to treat liver diseases in conventional medical practises. *Cuscuta reflexa* Roxb is one of these herbs known as Aftimoon. It belong to the family Convolvulaceae commonly found in Ceylon, Pakistan, Bangladesh, western Bengal plains of India and throughout Thailand. Approximately 170 or more species known to exist. It has no underground roots and grows as new parasite on the host plant hence the name "Akashbel" (sky-twiner). It contains variety of alkaloids, glycosides, flavonoids and active compounds such as amarbelin, kaempferol, dulcitol, myricetin, cuscutin and kaempferol. In the Unani system of medicine (USM) this plant is used to treat diseases such as zof-e-kabid (liver debility), Waram-e-kabid (Hepatitis), sartan (cancer), Amraz-e-Dimaghi wa Asabi (diseases of nervous system), Amraz-e-Sawdawi wa Balghami (diseases of black bile and phlegm), Junoon (Mania), Malikholia (melancholia), Sara (Epilepsy), Amraz-e-jild (skin diseases), Auram (inflammation) etc. It is considered as an anticancer or anti-tumor drug in USM. Pharmacological properties of this plant have been reported as hepatoprotective anticancer, antioxidant, anticonvulsant, anti-inflammatory, antimicrobial activities. Various Unani compound formulations such as Sharbat-e-Deenar, Majun-e-Najaah, Itrifal-e-Aftimoon, Majun-e-Chobchini, Sikanjbeen-e-Aftimooni, Habb-e-Aftimoon, Sharbat-e-Kasoos, Sharbat-e-Aftimoon etc. Throughout information about *Cuscuta reflexa* with a focus on Unani medicine provided in this review, it will also validate the plant's numerous effects using pharmacological research that has already been done.

Keywords: Aftimoon, hepatoprotective, Anticancer, *Cuscuta reflexa*, Unani.

Introduction:

The liver is the most essential organ in the body. It regulates many physiological processes in the body, including metabolism, secretion and storage. It has a high capacity to detoxicate harmful chemicals and synthesize useful substances [1,2]. It helps in internally preservation, performance and homeostasis regulation. It is involved in practically all metabolic pathways that lead to growth, disease resistance, nutrition transportation, energy provision and reproduction. It also helps in glucose, protein, fat metabolism, detoxification, bile secretion and vitamin storage [3]. Liver damage is frequently associated with the impairment of several of these functions because the portal vein provides blood to the liver following intestinal absorption, it is constantly exposed to hazardous substances [1,2]. Liver illnesses continue to be a major hazard to public health and a global problem [4]. They are primarily caused by substances such as paracetamol (in higher dosages), excessive alcohol intake, infections and autoimmune disorders. The majority of hepatotoxic substances harm liver cells by generating lipid peroxidation and other oxidative damage [5–7]. Liver disorders have become a global concern and

mortality from liver diseases are increasing at a rapid pace each year. World Health Organisation (WHO) has forecast it to be the eleventh most important cause of death in the world by 2030 [8]. Plants have been employed in the treatment of liver illnesses since ancient times and several studies have demonstrated the preventative and therapeutic efficacy of plants as a hepatoprotective agent. [9] Several herbal medicinal plants have long been used in traditional medicine to treat liver disorders [10–12].

Cuscuta reflexa Roxb is one of the herbal medicinal plants known as Aftimoon [13]. It is an epiphytic parasitic plant belonging to the family Convolvulaceae and also recognised as giant dodder. It is commonly found in Pakistan, Ceylon, Bangladesh, western Bengal plains of India and throughout Thailand [14–18]. It is a perennial parasitic climber on other plants that is golden yellowish in colour. It is harmful and destroy the plants on which it inhabitant, but it has excellent medicinal properties. It has no underground roots and no leaves, it grows as a new parasite on the host plant during the rainy season, hence the name "Akashbel" (sky-twiner) [19–24]. It lacks chlorophyll and therefore cannot produce food through photosynthesis. [24–26] It is also known as beggar weed, hell weed, devil's gut, strangle tare and scald weed [27]. The various *Cuscuta* species are widely distributed throughout the world with approximately 170 or more species known to exist [28]. In the Unani System of medicine, *Cuscuta reflexa* Roxb is known as Aftimoon or Kasoos and Tukhm-e Kasoos refers to the seeds. In Unani medicine, the thinness and red color of Aftimoon is considered to be the highest quality, as the aerial parts of the plant are typically used in a dried form, fragrant, reddish and thin stemmed [29,30]. It contains a variety of alkaloids, glycosides, flavonoids and other compounds. It contains active compounds such as amarbelin, kaempferol, dulcitol and myricetin; the stem contains cuscutin, cuscotalin, bergenin, beta-sitosterol, luteolin tetrahydrofuran derivatives, coumarin and kaempferol [28, 31–33]. This plant yielded a number of -glucosidase inhibitory compounds [32]. It has also been studied for a new flavanone-reflexin [34]. The plant is widely used in various traditional medicine for various diseases such as liver diseases, melancholy, depression, mental disorders, skin diseases, fever, coughs, muscular pain, urinary disorders and more. The entire plant is used to treat the most of bilious disorders [23,24].

It has been recommended by renowned Unani physicians for a variety of ailments since ancient times. In the Unani system of medicine, this plant is used to treat diseases such as zof-e kabid (liver debility), Waram-e kabid (Hepatitis), sartan (cancer), Amraz-e Dimaghi wa Asabi (diseases of nervous system), Amraz-e Sawdawi wa Balghami (diseases of black bile and phlegm), Junoon (Mania), Malikholia (melancholia), Sara (Epilepsy), Amraz-e jild (skin diseases), and other conditions such as Deedan-e Ama (Intestinal Worms), Tap-e kohna (chronic fever), Ashob-e Chashm (conjunctivitis), khafqan (Palpitation), Nafakh (flatulence), Tasannuj (spasm), Auram (inflammation), Wajaul mafasil (arthralgia) also it is specially mentioned useful for geriatric and debilitate people [29,30,35–37]. In folk medicine, *C. reflexa* is used as a fever, cough, carminative, anthelmintic and to treat liver disorders [3]. It is also applied topically to relieve itching [38]. *C. reflexa* is taken orally to treat rheumatism, sexual problems and diabetes, it is also applied topically to treat toothache [39,40]. It is considered as an anticancer or anti-tumor drug in the Unani system of medicine [29,41].

Pharmacological properties of this plant have been reported as hepatoprotective, anticancer antioxidant, antibacterial, antiviral as well as antidiabetic activities [17,42–46]. Methanolic extract has anticonvulsant and anti-steroidogenic properties [47]. It has also been reported to be an anti-inflammatory [48], antimicrobial [25,26,49], antispasmodic, hemodynamic [20], antihypertensive, muscle relaxant and cardiogenic drug [20,50]. Aftimoon is a single drug that is used as a important ingredients to make various Unani compound formulations such as Sharbat Deenar, Majun Najaah, Itrifal Aftimoon, Majun Chobchini, Sikanjbeen Aftimooni, Arq e Musaffi [37,51,52], Habbe Aftimoon[53], Sharbat-e-Kasoos, Sharbat-e-Aftimoon etc [50].



Fig. 1 & 2 Original Photograph of Aftimoon (*Cuscuta reflexa* Roxb)

Table 1: Vernacular Names & Scientific Classification

Vernacular Names:		Scientific Classification:[43,54]	
Arabic	Shajar-ul-Zibagh, Aftimoon [29,37,55,56].	Kingdom	Plantae
English	Dodder [29,37,51,57,52].	Subkingdom	Tracheobionta
Gujarati	Akaswel, Amar bel [37,51].	Superdivision	Spermatophyta
Hindi	Amarbel, Akashbel [29,37,55,51].	Division	Angiosperms
Marathi	Nirmuli [58].	Class	Eudicots
Persian	Darakht-e-pechan [37], Aftimoon, Tukhm-e-kasus [23,24].	Subclass	Asterids
Sanskri	Amarvela, Asparsa [58], akashavalli, Amaravallari [23,24].	Order	Solanales
Telugu	Sitamapurgonalu [37,51], Savarapukada [23,24].	Family	Cuscutaceae
Unani	Aftimoon [29,52], Kashus [51], Kasoos [57].	Genus	Cuscuta
Urdu	Aftimoon [37], Aftimoon Hindi [51].	Species	Reflexa
Punjabi	Nilathari [23,24,37].	Botanical Name	Cuscuta reflexa

Habitat & distribution:

Aftimoon (*Cuscuta reflexa*) is found in tropical and subtropical areas of the world and it is primarily found on the plains of Malaysia, Thailand, Afghanistan and Nepal [51]. Aftimoon can also be found in the plains of India, primarily in Bengal, Ceylon and Malaya, It can also be found ascending the Himalayas to altitudes of thousands of feet [23,24]. It is present throughout the year, but flowering occurs from late October to March [51].

Macroscopic:

Aftimoon (*Cuscuta reflexa*) is a rootless, leafless, perennial herb which is an extensive climber. The plant is acrid and tastes bitter and sharp. It grows as homoparasite and it has very low level of chlorophyll and photosynthesis activity, completely depends over the host plant for its survival. The dried stems are like thread, long, narrowly twined, branched, glabrous, brown or pale greenish-yellow in colour, often dotted with red about 0.8 mm in thickness; fruits capsule, small, globose or ovoid, seeds dark in colour, spherical to ellipsoidal, less than 1 mm in thickness, no specific odour or taste [24,37,51].

Microscopic:

Transverse section shows outline of stem circular or slightly wavy, epidermal cells oblong, thin walled; cortex wide, parenchymatous; vascular system reduced to a central core of a few collateral, 4 or 5 bundles, around a central small pith region. The epidermis is accompanied by 3 - 4 layers of cells consisting of various sizes and shapes of thin walled parenchymatous cells. Endodermis is formed by tangentially elongated cells; a complete ring is often formed. The vascular bundles are simple, conjoint, collateral, 15 - 20 in numbers and arranged in a ring. The xylem lies on the outer side, surrounded by phloem in old stem. It is made up of vessels, parenchyma xylem and tracheids. Phloem is found in prominent patches on the outermost strands of each xylem strand. Also, few cells of cambium are found in some of the vascular bundles [37,51].

Fruit:

The fruit's pericarp is thin and membranous, with an outer layer of tangential and narrowly oblong parenchymal cells with thin walls. at certain places the parenchyma cells exhibit periclinal division: the inner layer consists of a large, barrel-shaped cell with very thick inner tangential and radial walls. In cross-section, the thickened portion appears to be "U" shaped [37].

Seeds:

Transverse section of seeds triangular or rectangular; testa thick and brittle; a thick echinate cuticle present followed by a narrow zone of epidermis consisting of radially elongated cells with thick walls; inner to epidermis a broad compact, thin walled radially elongated palisade like layer of cells present. Mesophyll tissue has shrunken and collapsed, forming a membranous zone, adhering to the inner layer in some places but occasionally becoming detached; embryo is minute, embedded in a mass of crushed or shrunken cotyledons [37].

Table 2: Standardisation profile of Aftimoon (*Cuscuta reflexa* Roxb) [37].

Identity, Purity, and strength	
Foreign Matter	Not more than 2%
Total Ash	Not more than 10%
Acid insoluble Ash	Not more than 9%
Alcohol soluble extractives	Not less than 9%
Water soluble extractives	Not less than 16%

Unani Description of drug according to USM:

Ajza-e mustamila (Part used):

Whole plant [23,29,30,35–37], Stem and seeds [59].

Mizaj (Temperament):

According to renowned Unani physicians it is Ḥarr & Yabis (Hot and dry) with a variation in the degree of hotness and dryness. (1)Ḥarr³ & Yabis³ (Hot 3o Dry 3o) According to most Unani physician [29,35,55,56,60], (2)Ḥarr³ & Yabis² (Hot 3o Dry 2o) [51], (3)Ḥarr³ & Yabis¹ (Hot 3o Dry 1o) [61], (4)Ḥarr² & Yabis² (Hot 2o Dry 2o) [30,37].

Nafa Kahas (Main Function)

Useful as a Mukhrij-e-Sauda (excretion of black bile) [36].

Miqdar Khoraq (Dosage):

The different dosage of Aftimoon as dry and fresh for internal use is prescribed by unani physician as follow.

Dose of Dry Drug 3-5g [37], 3.5-7g [29], 4-6g, [37] 7-14g [30].

Dose of Fresh Drug 14-21 gm. [35,55,60]

Muzir (Toxicity):

The basic temperament of Aftimoon causes dryness of mouth, irritability and thirst. Syncope is one of its side effects. It is also Muzir (harmful) for lungs and it is harmful to a person with Safrawi Mizaj. It is also harmful for people of hot temperament as it may cause irritability, nausea and vomiting [29,30,35,60].

Musleh (Correctives):

To neutralise negative effects of Aftimoon, different drugs are used as a Muslih (corrective) which includes (1) Samagh-e-Arabi (gum of Acacia arabica), (2) Kateera (gum of Cochlospermum religiosum L.), (3) Zafran (Crocus sativus), (4) Roghan badam /almond oil (oil of Prunus amygdalus), (5) Kasni (Cichorium intybus) [30,35,36,56,60].

Badal (Substitute):

According to unani literature, Aftimoon substitutes include Turbud (Ipomoea turpethum) [29,51], Ustukhuddus (Lavandula stoechas L.) [30] Hashaa (Mentha polijgonum) [29,51], Bisfajj (Polypodium vulgare L.) [30], Lajward (lapis lazuli) [30,55], Afsanteen (Artemisia absinthium) [35,36] and Gil-e-Armani (Aluminium Silicate) [30,56].

Afaal (Pharmacological Actions):

Accordin to USM Aftimoon Act as Muhallil-e-Warm (Anti-inflammatory) [51], Mulattif (Demulcent) [62], Mushil-e-Balgham (Purgative of phlegm) [51,62], Mushil-e-Sauda (Purgative of black bile) [51,62], Mudir-e-Baul (Diuretic) [24,29,30,37,51,61], Mudir-e-Tams (Emmenagogue) [24], Musaffi Dam (Blood purifier) [24], Qatil-e-Deedan (Anthelminthic) [24], Munavim (Sedative) [24], Muqawwi Bah (Aphrodisiac) [24], Mufatteh Sudad (Deobstruent) [51], Muqawwi (Tonic) [62], Munaffis (Expectorant) [24] and Kasir-e-Riyah (Carminative) [24].

Istematat (Therapeutic Uses):

It utilized as a single drug in variety of illness like Junoon (Schizophrenia) [51], Malikhuliya (Melancholia) [29,51,61], Kaboos (Nightmare) [51], Saudavi Amraz (Ailments due to excessive black bile) [51], Sara (Epilepsy) [29,61], Dimaghi Amraz (Brain disorders) [30], Faalij (Paralysis) [30], Laqwa (Facial paralysis) [30], Warm-e-Kabid (Hepatitis) [37,62], Zof-e-Kabid (hepatic insufficiency) [51], Yaraqan (Jaundice) [24], Warm-e-Tehal (Spleenomegaly) [30], Nafakh-e-Shikam (Flatulence) [29,62], Deedan-e-Ama (Intestinal worms) [51], Waja-ul-Azlaat wa Mafasil (Pain in muscles & joints) [24], Sartan (Cancer) [30], Khadar (Numbness) [30], Khafaqan (Palpitation) [30] and Amraz-e-Jild (Skin diseases) [30].

Mashhoor Murakkabat (Commonly used Compound Unani formulations):

Many readymade compound formulations with more than one ingredient are used in USM to treat a variety of diseases. Some formulations containing Aftimoon are mentioned as Sharbat Deenar, Majun Najaah, Itrifal Aftimoon, Majun Chobchini, Sikanjbeen Aftimooni, Arq e Musaffi [37,51,52], Habbe Aftimoon [53], Sharbat-e-Kasoos and Sharbat-e-Aftimoon [36]

Table 3: Compound Unani formulations of Aftimoon, there dosage forms, actions, indications and doses.

Name of the unani formulation	Dosage forms	Actions	Indications	Doses
Habb-e-Aftimoon [63].	Jamid (Solid) Pills	Munaqqi-e-Dimagh (Brain Tonic), Mulaiyin (Lexative).	Malikhuliya, (Melancholia), Waswas (insanity).	5 to 10 g.
Majun Najaah [64].	Neem Jamid (Semi Solid) Qiwam based	Musaffi-e-Dam, (Blood purifier) Muqawwi-e-	Malikhulia, (Melancholia), Qulanj	5 to 10 g.

		Asab (nervine tonic).	(colic), Ikhtinaq-ur-Rahem (hysteria).	
Majun Musaffi Khas [65].	Neem Jamid (Semi Solid) Qiwwam based	Musaffi-e-Khoon (Blood purifier)	Fasad-e-khoon (Putrefaction of blood), Kharish (Pruritis), Aatishak (Syphilis), Suzak (Gonorrhoea).	5 g.
Majoon Boolis [63].	Neem Jamid (Semi Solid) Qiwwam based	Muqawwi-e-Dimagh (Brain Tonic).	Zof-e-Dimagh (Weakness of brain), Nisyan (amnesia).	5 to 10 g.
Itrifal-e-Mushil [63].	Neem Jamid (Semi Solid) Qiwwam based	Musaffi-e-Dam (Brain Tonic), Jali (detergent).	Baheq (pityriasis), Bars (vitiligo), Juzam (leprosy), Da-ul-Feel (Elephantiasis).	15 to 25 g.
Jawarish Kamooni Mushi [63].	Neem Jamid (Semi Solid) Qiwwam based	Munaqqi (tonic).	Sailan-e-Loab-e-Dahan, (Excessive salivary secretion), Bakhr-ul-Fam (Halitosis)	5.to 10g.
Khamira Marwareed Banuskha-e-Kalan [65].	Neem Jamid (Semi Solid) Qiwwam based	Muqawwi-e-Qalb Heart Tonic), Mufarreh (Exhilarant),	Khafaqan (palpitation), Zof-e-Qalb (Weakness of cardiac muscles), Zof-e-Aam (General weakness)	3-5 g
Mufarreh Motadil [64].	Neem Jamid (Semi Solid) Qiwwam based	Musakkin (sedative), Muqawwi-e qalb, Kasir-e riyah (Carminative).	Nafkh-e Shikam, (Flatulance), Zof-e Qalb (Weakness of cardiac muscles),	5-10g
Sharbat Deenar [64].	Sayyal (Liquid) Syrup	Mudirr-e-Baul (Diuretic), Mufatteh Sudad (Deobstruent).	Waram-e-Kabid (Hepatitis), Waram-e-Rahem (Metritis), Yarqan-e-Suddi (Obstructive jaundice), Istisqa (Ascites), Zatul Junb (Pleurisy), Qabz (Constipation).	20-40ml.
Sharbat-e Kasoos [66].	Sayyal (Liquid) Syrup	Muqawwi-e-meda (stomachic), Muqawwi-e-jigar (liver tonic),	Zof-e-meda (Weakness of stomach), Zof-e-jigar (hepatic insufficiency).	50 ml with arq badiyan 125 ml
Sufoof-e chobchini [64].	Jamid (Solid) Powder	Munaffis-e-Balgam (Expectorant) Daf-e Safra (Antibilious), Musaffi-e Dam (Blood Purifier)	Waj-ul-mafasil (Polyarthritis), Niqras (gout), Aatishak (Syphilis), Irq-un-Nisa (Sciatica), Fasad-ud-Dam (Putrefaction of blood).	5-10g
Sufoof-e-Lajward [64].	Jamid (Solid) Powder	Munaqqi, (Hypotonic),	Malikhuliya (Melancholia).	5-10g

		Mufarreh (Exhilarant), Mulayyan (Lexative).		
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Phytochemicals from *Cuscuta reflexa*: Various chemical compounds were isolated from *C. reflexa*, such as astragalinal kaempferol-3-O-glucoside [67], cuscutalin, cuscutin (colouring matter) [68–71], dulcitol, quercetin, luteolin [37]. Moreover, it also contains alkaloids, protein, resin, tannin, glycosides, carbohydrates [51], a large number of glucopyranoside [72] and flavonoids [51,73,68]. Some minerals like sodium, potassium, aluminium, iron and calcium were also isolated [51]. The quercetin, quercetin-3-O-glucoside β - sitosterol, and bergenin were also isolated from the *C. Reflexa* [71]. The corticosteroids, essential oils, anthraquinones, phenolic compounds, alkaloids and flavonoids were also detected [74]. The flavonoid glycosides such as kaempferol and quercetin were also extracted [75]. Moreover, (3'-methoxy-4',5,7-trihydroxy flavone-3glucoside) and (3'-methoxy-3,4',5,7-tetrahydroxy flavones) were also isolated from *C. Reflexa* [76]. The stems of *C. Reflexa* contain reflexin, 5-hydroxy-7-methoxy-6-(2, 3-epoxy-3-methyl butyl)-flavanone [34]. It also contained some steroids and glycoside. A high molecular weight carboxymethylcellulose was also obtained from it [77]. The HPTLC confirms quercetin, sitosterol, gallic acid and stigmasterol [78].

Table 4: Evidence based Pharmacological activities of *Cuscuta reflexa*:

Activity	Extract Used	Conclusion of the Studies
Hepatoprotective Activity:	Hydroalcoholic extract	The hydroalcoholic extract of <i>Cuscuta reflexa</i> Roxb was observed to have hepatoprotective activity against paracetamol-induced hepatic damage in albino rats. The results has shown positive response against paracetamol-induced liver damage [46].
	Methanol extract	The hepatotoxic rats induced by Isoniazid and Rifambicin, the methanol extract of <i>Cuscuta reflexa</i> improved liver function by decreasing serum AST, ALT, ALP and total bilirubin levels, indicating that it protects the liver and improves its functional efficiency [79].
	Ethanollic extract	<i>C. reflexa</i> extracts shown potential anti-cancer activity as well as hepatic cell protection, suggesting that they could be used to treat colon or colorectal cancer as well as hepatic impairments [80].
	Aqueous extract	<i>Cuscuta reflexa</i> whole plant extract was tested in vivo for hepatoprotective efficacy in carbon tetrachloride, ethanol and paracetamol-induced hepatotoxic rat models and compared to silymarin (20 mg/kg) as a standard drug. A two-way analysis of variance examination of the estimated biochemical parameters, such as aspartate aminotransferase, alanine amino transferase, and alkaline phosphatase, revealed a significant difference (p-value < 0.001) between the three treatment groups [81].
	Aqueous and Alcoholic extracts	The aqueous (AQESCR) and alcoholic (AESCR) extracts of stem of <i>C. reflexa</i> were studied for hepatoprotective effect against thioacetamide-induced hepatotoxicity in rats. The levels of ALT, AST, ALP, total bilirubin, direct bilirubin, albumin, total proteins and histological changes in the livers were also measured. Both extracts significantly decreased the thioacetamide-induced elevations of the serum levels of ALT, AST, ALP, BILT and BILD while increased the levels of ALB and PRO. In histological changes significant hepatoprotective effects were observed. When compared to the standard medicine silymarin (25 mg/kg p.o.)

		treated group, the medium and high doses of AESCR and AQESCR (200 and 400 mg/kg) demonstrated better hepatoprotective effect [48].
Anticancer Activity/Anti proliferative Activity	Ethanol and Chloroform extracts	The ethanol and chloroform extracts of <i>Cuscuta reflexa</i> was evaluated for antitumor activity against Ehrlich ascites carcinoma (EAC) tumor in mice at doses of 200 and 400 mg/kg body weight orally. The results exhibit significant antitumor activity in EAC-bearing mice. The standard antitumor was used 5-fluorouracil [82].
	Chloroform extract	The anti-hepatocellular carcinoma (HCC) activity of <i>Cuscuta reflexa</i> chloroform extract (CRCE) was tested in Hep 3B cells. The results showed that CRCE can induce apoptosis in Hep 3B cells in a dose and time dependent manner by the intrinsic mitochondrial apoptotic pathway [78].
	Ethanol extract	Anticancer effects of extracts of <i>Cuscuta reflexa</i> on 1,2-Dimethyl hydrazine (DMH)-induced animals were investigated. The findings suggested that <i>C. reflexa</i> extracts have potential anti-cancer activity as well as hepatic cell protection, therefore might be used in the treatment of colon or colorectal cancer as well as hepatic impairments [80].
Antioxidant activity:	Alcoholic extracts	The anti-oxidant activity of alcoholic extracts of <i>Cuscuta reflexa</i> and <i>Cassipoupa filiformis</i> was investigated for free radical-scavenging activity using the (1,1-diphenyl-2-picrylhydrazyl) DPPH radical, as well as inhibition of lipid peroxidation induced by FeSO ₄ in egg yolk. As a standard Ascorbic acid was used. The results indicated that the <i>Cuscuta reflexa</i> plant had higher in vitro antioxidant activity [83].
	Ethanol extract	<i>Cuscuta reflexa</i> stem extract was tested for in vitro antioxidant activity by assessing the degree of non-enzymatic haemoglobin glycosylation at 440 nm. The ethanol extract's ethyl acetate fraction had greater activity than the other fractions. When compared to commonly used standard antioxidant chemicals, extracts' antioxidant activity is quite similar, identical in magnitude and equivalent [68].
	Methanolic extract	The DPPH radical scavenging method was applied to determine in vitro antioxidant activity. This method revealed that the ethyl acetate fraction (15.70 1.82 g/ml) had the maximum radical scavenging. This study's findings highlighted the importance of <i>C. reflexa</i> as a source of bioactive compounds with antibacterial and antioxidant activities [84].
Anticonvulsant activity:	Ethanol extract	The anticonvulsant action of <i>Cuscuta reflexa</i> Roxb was analysed. The findings suggest that it has anticonvulsant effects and is probably going to have an impact on both the GABA aminergic and the glycine inhibitory processes [85].
	Methanolic extract	Methanolic <i>Cuscuta reflexa</i> significantly increased catecholamine levels in the brains of mice after a 6-week treatment in a dose-dependent manner. When compared to the control groups, the extract significantly increased GABA, glutamine and glutamate levels. The research discovered that <i>Cuscuta reflexa</i> extract has anticonvulsant activity [45].
Anthelmintic activity:	Petroleum ether,	<i>Cuscuta reflexa</i> extracts inhibited the spontaneous motility (Paralysis) of earthworms in a dose-dependent manner. All

	Chloroform, and Methanol extracts	petroleum ether, chloroform and methanol extracts were found to have anthelmintic activity when compared to albendazole as the reference drug [86].
	Methanolic extract	The anthelmintic activity was tested on adult Indian earthworm <i>Pheritima posthuma</i> using standard procedures. Methanolic extracts of aerial portions of <i>Cuscuta reflexa</i> Roxb (MECR) demonstrated significant effects on anthelmintic activity at the doses of 25, 50 and 100 mg/kg [87].
	Methanolic extract	Anthelmintic potential of <i>Cuscuta reflexa</i> Roxb stem and flower methanolic extracts were examined. <i>Pheretima posthuma</i> , an Indian earthworm, was subjected to tests at 5 different concentrations (ranging from 2% to 10%) with albendazole serving as the standard reference. The anthelmintic activity test results showed that both stem and flower extracts reduced the duration of time required for paralysis and death in all test groups of the study. It was discovered that among them, stem extract was more effective than the flower extract [88].
Anti-inflammatory activity:	Alcoholic and Aqueous extract	Alcoholic and aqueous extracts of <i>Cuscuta reflexa</i> stem were tested for anti-inflammatory action in a carrageenan-induced paw oedema model in rats and their activity was compared to the effect of the reference medicine, Ibuprofen. Before carrageenan injection, these extracts were administered orally at concentrations of 100, 200 and 400 mg/kg bd.wt. At the 5th hour, both extracts with medium and higher doses reduced oedema volume by 47.27%, 72.72% and 57.72%, 80.00%, respectively, when compared to the standard drug Ibuprofen, which reduced it by 96.36%. Thus, the current investigation found that the <i>C. reflexa</i> extracts significantly reduced inflammation in a rat model of paw oedema caused by carrageenan [89].
	Methanolic extract	It is also reported that the Methanolic extract of <i>Cuscuta reflexa</i> (MECR) and its ethyl acetate soluble fraction (EAMECR) show significant antiinflammatory activities which may be due to the presence of phenols, polyphenols and flavonoids [86].
Anti-HIV activity:	Aqueous extract	The anti-HIV activity of the crude water extracts of <i>Cuscuta reflexa</i> may have resulted from combinations with substances with various mechanisms of action [90].
Antibacterial activity	Methanol Extract	The methanol fraction of <i>C. reflexa</i> stem (MECR) displayed wide range of antibacterial activity against all tested microorganisms at concentrations ranging from 25 to 125 g/ml. MECR, at 125 g/ml concentrations, had significant antibacterial activity against <i>S. aureus</i> , <i>S. boydii</i> , <i>P. aeruginosa</i> , <i>S. dysenteriae</i> and <i>E. coli</i> , with zones of inhibition ranging from 16 to 24 mm [48].
	Dichloromethane and Petroleum ether extracts	The antibacterial potency of <i>C. reflexa</i> plant extracts has been tested against <i>Bacillus subtilis</i> , <i>Sarcina lutea</i> , <i>Xanthomonas campestris</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus vulgaris</i> and <i>Pseudomonas denitrificans</i> by disc diffusion assay. All examined bacteria were very susceptible to the antibacterial effects of <i>C. reflexa</i> extracts in dichloromethane and petroleum ether. Minimum inhibitory concentration values of various extracts ranged from 16 to 512 µg/mL [91].
Antimicrobial activity:	Ethanollic extracts	Ethanollic extracts of the whole plant of <i>Cuscuta reflexa</i> Roxb were tested for antimicrobial activity against Gram positive

		(Bacillus subtilis and Staphylococcus aureus) and Gram negative (Escherichia coli and Salmonella typhi) bacteria. There were four concentrations (200 µg/mL, 300 µg/mL, 400 µg/mL or 500 µg/mL) of plant extract were tested. Only the growth of E. coli was inhibited at 200 µg/mL. Despite the fact that the greatest antimicrobial activity was demonstrated at a concentration of 500 µg/mL, against E. coli [92].
	Methanolic extracts	Cuscuta reflexa was collected over different plants exhibited considerable antimicrobial activity. The methanolic extracts exhibited good biological activities as compared to n-hexane extracts [93].
Diuretic activity:	Aqueous and Alcoholic extract	Cuscuta reflexa aqueous and alcoholic extract was tested for diuretic efficacy in Wister rats at a dose of 300 mg/kg given orally. Frusemide (20mg/kg) was used as standard drug. Both extract exhibited significant diuretic activity and caused marked increase in Na ⁺ and K ⁺ excretion, when compared to saline treated controls [94].
Hypoglycemic activity:	Methanol and chloroform extracts	The hypoglycemic effects of methanol and chloroform extracts of whole plants of Cuscuta reflexa, were investigated in oral glucose tolerance tests in Long Evans rats and Swiss albino mice, respectively. Cuscuta reflexa whole plant extracts revealed considerable oral hypoglycemic efficacy in glucose-loaded rats at dosages of 50, 100 and 200 mg/kg body weight [95].
	Methanol extract	Other study revealed that Significant inhibition against α - Glucosidase was seen in the methanol extract of C. reflexa Roxb. & its subsequent ethyl acetate fraction. It is a membrane bound enzyme found in the small intestine epithelium. This enzyme's inhibition increases the time it takes for glucose to be absorbed in the blood after a meal [32].
	Ethanolic extract	The anti-diabetic effect of several extracts of Cuscuta reflexa bark was investigated in alloxan-induced diabetic rats and through glucose tolerance tests in normal rats. The extract produced a significant decrease in blood glucose levels when compared to controls in alloxan-induced hyperglycemic rats in the single dose experiment at the tested dose level and is comparable to the standard drug glibenclamide. This study demonstrated that the ethanolic extract prevented significant elevation of glycosylated haemoglobin in vitro, with an IC ₅₀ value of 11.25 g/ml, which is comparable to the reference drug – tocopherol [96].
Anti-ulcer activity:	Alcoholic and Aqueous extracts	The anti-ulcer activity of alcoholic and aqueous extracts of Cuscuta reflexa was investigated in rats using a pyloric ligation model of experimentally induced gastric ulcer. In pylorus ligation-induced peptic ulcerated rats, oral administration of alcoholic and aqueous extracts of Cuscuta reflexa gave dose-dependent significant protection [97].
Toxicological studies:	Alcoholic and Aqueous extracts	According to LD ₅₀ studies, for both alcoholic and aqueous extracts of Cuscuta reflexa up to a maximum dose level of 2000 mg/kg did not cause any animal deaths, indicating that they are basically harmless and nontoxic in nature [97].
Gastroprotective activity:	Aqueous Methanolic crude extract	Cuscuta reflexa crude extract has in-vivo gastroprotective activity and antiulcer potential. Oral administration of Cuscuta reflexa crude extract (Cs.Cr) exhibited dose-dependent (30-300 mg/kg)

		significant protection ($p < 0.05$) in Aspirin-induced peptic ulcerated animals. The study's findings clearly demonstrated that Cs.Cr has gastroprotective potential [98].
Antipyretic activity:	Aqueous and Ethanol extracts	The antipyretic activity of <i>Cuscuta reflexa</i> Roxb was tested aqueous and ethanol extracts in rats using Brewer's yeast induced pyrexia. The extracts at 200 and 400 mg/kg body weight doses reduced the increased rectal temperature significantly ($p < 0.05$). The ethanol extract was slightly more potent than the aqueous extract and the results are comparable to the reference antipyretic medication (paracetamol) [99].
Anxiolytic activity:	Methanol extract	The anxiolytic effect of a methanol extract of the whole plant of <i>Cuscuta reflexa</i> at doses of 200 and 400 mg/kg was assessed using an elevated plus maze and a light and dark chamber In mice. In both models, the extract 400 mg/kg had a significant anxiolytic effect when compared to the extract 200 mg/kg. The 400 mg/kg effect was comparable to the diazepam 5 mg/kg as standard drug [100].
Antidiarrheal activity:	Aqueous and methanol extract	The antidiarrheal effect of <i>C. reflexa</i> was evaluated in pigeons. Castor oil (6 mL/kg, PO), magnesium sulphate (2 gm/kg, PO), ampicillin (250 mg/kg, IP) and cisplatin (6 mg/kg, IV) were used to induce diarrhoea. As a positive control, loperamide (2 mg/kg, IM) was used in these investigations. whereas, each pigeon in the test groups received intramuscular injections of juice (JCR) 1 mL/kg 1% and 2%, aqueous (CRAE) at dosages of 50, 100 and 200 mg/kg and methanol (CRME) at doses of 50, 100 and 200 mg/kg. All paradigms evaluated produced significant results ($P < 0.01$) in addition to cisplatin-induced diarrhea [101].

Conclusion:

Herbal drugs are used by more than 80% of the population and these drugs are becoming more popular in developing countries. Due to their safety and efficacy in a variety of disease conditions, herbal drugs are becoming increasingly popular in developed countries. According to USM, *C. reflexa* has multiple actions and uses in treating many disorders relating with the liver, brain and nerves such as Zof-e kabid (liver debility), Waram-e kabid (Hepatitis), Sartan (cancer), Malankhuliya (melancholia), Şara (epilepsy), Junun (insanity) Laqwa (facial palsy), Faliş (paralysis) and schizophrenia. and used in Sartan (cancer) management by some renowned Unani physicians. The drug has several pharmacological properties and several studies, including USM, have been conducted to validate its uses like Hepatoprotective [46,79], anticancer [78,82], antiproliferative [29], Antioxidant [68,83], anticonvulsant [85], diuretic [94], anti-HIV [90], Anti-ulcer activities[97] etc. Several pharmacological studies have demonstrated its promising results. The outcomes confirm its significance and value in the management of illness such as cancer and other diseases. The literature currently available and recent investigations on *C. reflexa* have demonstrated its significance as a Potential medication of USM that may be thoroughly investigated for the treatment of hepatic diseases, cancer and other therapeutic illnesses. Clinical trials to investigate its anticancer activity may be conducted in order to validate the Unani claim for this action.

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Conflict of Interest:

The authors declare that they have no conflict of interest.

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