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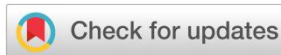
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Review Article

Unraveling the Therapeutic Potential of Miracle Plant 'Aftimoon' in Disease Prevention and Treatment: A Comprehensive Review

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Abstract



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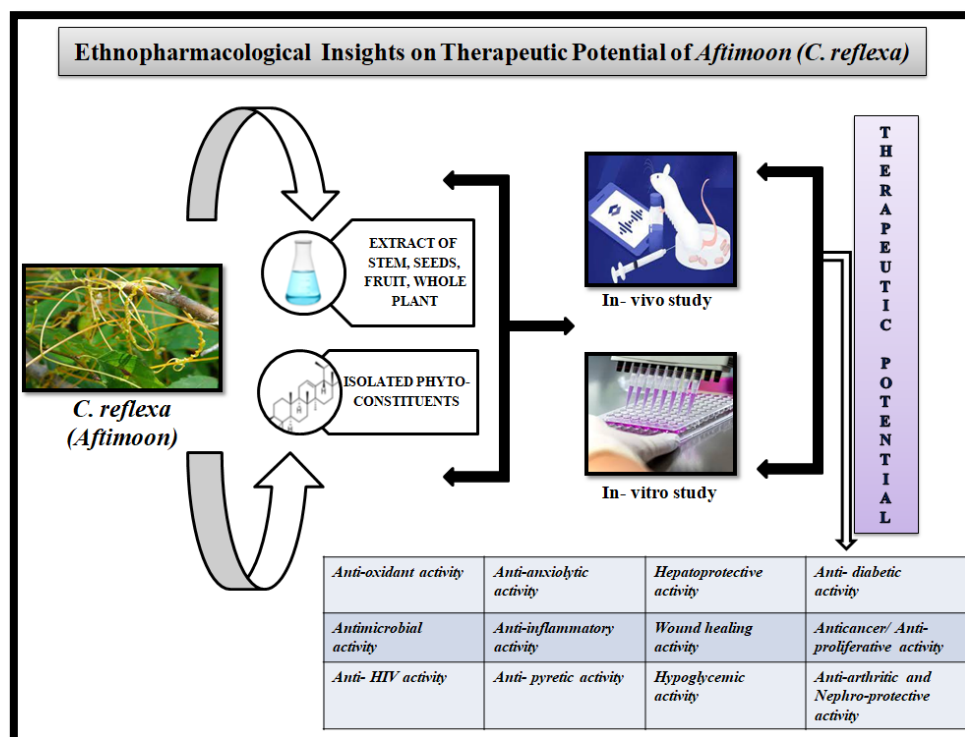
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Aftimoon (*Cuscuta reflexa*), a member of Convolvulaceae family is a miraculous parasitic plant with a rich history of utilization in traditional medicine. It has been extensively employed in the Unani treatments all over the world, particularly in the Indian subcontinent, to treat and prevent a variety of illness. Over the years, numerous research findings have documented its diverse therapeutic effects including antioxidant, anti-inflammatory, anticancer, hepatoprotective, and neuroprotective activities. It is utilized as a single medication (*mufrad*) in powder, mixture, and decoction form and as compound formulations (*murakkab*) to treat a variety of ailments, which includes hepatitis, palpitations, varicose veins, mental ailments such as epilepsy and depression as well as dermatological conditions such as vitiligo and pityriasis. A number of biologically active compounds with therapeutic potential have been recognized and isolated from this wonder plant which includes amarbelin, sterol glycosides, cuscutalin, bergenin, and others. The synergistic actions of its constituents contribute to its multifaceted healing properties. This review explores the therapeutic potential of *Aftimoon*, shedding light on its pharmacological properties, traditional uses, and emerging research. By synthesizing traditional knowledge with modern scientific insights, this review aims to illuminate the diversified healing properties of *C.reflexa* and inspire further research and foster its integration into mainstream healthcare practices.

Keywords: *Aftimoon*; *Cuscuta reflexa*; Therapeutic potential; Unani medicines

Graphical Abstract



1. Introduction

Plant-based remedies have been fundamental components of diverse cultures worldwide since ancient times. Plant products, or natural products, play a significant role in preventing and treating diseases by boosting antioxidant activity, inhibiting the bacterial growth, and modulating the genetic pathways. It is acknowledged that allopathy-based medications are costly and have harmful effects on both normal tissues and a variety of biological processes. Owing to plant's lower side effects and affordable characteristics, many plant's medicinal potential in the management of disease is being enthusiastically analyzed.^{23,81} Numerous sacred texts, notably the Bible and Quran, have also endorsed the use of herbs in various disease treatment and prevention. The Prophet Mohammed (PBUH) has advised using a variety of plants and fruits to treat ailments, and the Islamic viewpoint likewise supports the use of herbs in healthcare.⁴ The ingredients of *Aftimoon* have been widely used in the traditional Indian medical practices (Unani, Homeopathy, Ayurveda) and modern medicine for the treatment of various ailments, infections, metabolic abnormalities and malignant diseases. *Aftimoon (Cuscuta reflexa)*, is a widespread species in India, Ceylon, Bangladesh and Pakistan^{46,58,62}, indicates therapeutic implications in disease heal and treatment formulation, as it is commonly employed to address a variety of health issues. *Cuscuta reflexa* contains a complex of phytochemicals such as cuscutin, stigmaterol, kaempferol, dulcitol, myricetin, and coumarin^{7,42}, and coumarin from stems⁷⁶. Studies have shown its potential as an α -glucosidase inhibitor⁷ and its methanolic extract exhibits anti-steroidogenic, antiviral, and anticonvulsant properties²⁸. Additionally, it has been reported to possess antioxidant²⁹, anti-inflammatory³⁵, antimicrobial^{16,49,67}, antispasmodic, hemodynamic²⁷, antihypertensive activity, and act as muscle relaxant, and cardiogenic drug⁶⁸. In the Unani Medicinal system, it is regarded as an anticancer or anti-tumor agent⁴⁵. This review sums up the function of *Aftimoon* and its active constituents in the management and prevention of different diseases through the modulation of many biological pathways.

2. Habitat, Distribution and Botanical Description

TABLE 1: Taxonomic position of *Cuscuta reflexa (Aftimoon)*

Kingdom	Plantae
Sub Kingdom	Tracheobionta
Super division	Spermatophyta
Division	Angiosperms
Class	Eudicots
Subclass	Asterids
Order	Solanales
Family	Cuscutaceae
Genus	Cuscuta
Species	<i>C. reflexa</i>

C. reflexa is a parasitic, leafless and rootless, perennial climber that belongs to Cuscutaceae family. It is rampant in tropical and sub-tropical areas of the world with huge species diversity, but is rarely found in the temperate regions.^{77,79}

It is distributed throughout the plains in India,^{10,24} and climbs to an elevation of 3000 meters throughout the Himalayas¹⁰. The stem is long, slender, thread-like which appears yellow or green in color. The plant lacks chlorophyll therefore cannot produce its own food through photosynthesis. It heavily relies on host for nutrition. The medicinal properties acquired also depends on the host plant. The flower is hermaphrodite,

pentamerous, either solitary or clustered in racemes. It produces tiny, spherical capsules containing black, glabrous seeds. These seeds are dispersed via water or wind facilitating the spread of plant to new host plant, hence facilitating *Aftimoon's* development. The Taxonomical position of *C. reflexa (Aftimoon)* is mentioned in Table 1⁷⁹ and the Vernacular names in Table 2.

TABLE 2: Vernacular names of *Cuscuta reflexa (Aftimoon)*

LANGUAGE	VERNACULAR NAME	REFERENES
Arabic	<i>Shajar-ul-Zibagh, Aftimoon</i>	11,19,30,59
English	Dodder	9-12,19
Gujarati	Akaswel, Amarbel	10,11
Hindi	Amarbel, Akashbel	10,11,19,59
Marathi	Nirmuli	53
Persian	<i>Darakht-e-pechan</i>	11
Sanskrit	Amarvela, Asparsa	53
Telugu	Sitampurgonalu	10,11
Unani	<i>Aftimoon, Kashus, Kasoos</i>	9,10,12,19
Urdu	<i>Aftimoon, Aftimoon Hindi</i>	10,11

3. Active Chemical compounds of *Cuscuta reflexa (Aftimoon)*

Numerous chemical constituents isolated, have been identified to bear therapeutic potential. These include cuscutin, cuscutalin^{1,63,78,80}, benzopyrones, dulcitol, quercetin¹¹. In addition, it contains a large number of flavonoids^{1,10,80}, glucopyranoside⁶⁴, alkaloids, glycosides, resin, tannin and carbohydrate¹⁰. Stem contain the compound 5-hydroxy-7-methoxy-6-(2,3-epoxy-3-methyl butyl)-flavanone, reflexin⁷⁴ and some steroids, glycoside. Sitosterol and cuscutin, stigmaterol were isolated from the roots and have reported to display anti-inflammatory and anti-bacterial activity.

4. *Aftimoon's* Unani description and key formulations

As per the renowned Unani physician, the *Aftimoon* has hot and dry temperament (*Mizāj*) with variation in degree of its hotness and dryness.^{10,11,14,19,30,36,59}. The aerial parts of the plant, its stem and seed are used in Unani Medicine in form of drug to treat various ailments.^{10,11} The dosage prescribed by physicians vary depending upon its usage in dry form (3-5gm or 4-6gm) or fresh (14-21gm).^{10,11,15,26,36,59} It is highly toxic for people with *Safrawi Mizāj* (hot temperament)^{15,19,26}, since it results in nausea, irritability. *Aftimoon's* basic temperament (*Mizāj*) causes thirst, mouth dryness. Certain correctives (*Muslih*) are advised in order to counter the adverse effects which includes *Kateera* (gum of *Cochlospermum religiosum L.*), *Samagh-e-Arabi* (gum of *Acacia arabica*), *Kasni* (*Cichorium intybus*), *Zafran* (*Crocus sativus*), and almond oil (oil of *Prunus amygdalus*).^{14,15,18,26,30,36} The Classical Unani text throws a light on *Aftimoon's* several pharmacological properties, which includes *Mushil-i-Sawdā* (purgative of black bile)^{10,19,30,59,79}, *Mushil-i-Balgham* (purgative of phlegm)^{10,11,30,59}, *Muħallil-i-Waram* (inflammation reduction)^{10,11,30,65}, *Mudirr-i-Bawl* (Diuretic)^{11,65}, *Amrād-i-Jild* (skin disorder, anti-fungal activity)^{26,40,50,51,61}, *Muqawwi-i-Jigar* (Hepatotonic)^{11,38,39,53}, *Muħaffi-i-Dam* (Blood purifier)¹¹.

Aftimoon (C. reflexa) has long been utilized by Unani experts to cure various illness, including varicose veins^{37,43}, muscular dystrophy⁴⁴, neurological disorders notably schizophrenia, epilepsy, and melancholia¹⁹. The renowned Unani physician Hakeem Muhammad Saeed, who founded the Hamdard Foundation in Pakistan, frequently prescribed it to cure cancer.⁴¹ In Unani System of Medicine, numerous compound

formulations—which contain multiple ingredients are employed as premade formulations to treat a range of illnesses. There are variety of dosage forms accessible based on the need, the fundamentals of pharmacy, and the treatment plan. Numerous pharmacopoeia and formularies have been recognized by the Indian government to make and dispense ready-made medications in a range of dosage formats. Following are some of the Key formulations that contain *Aftimoon* as an ingredient - *Sikanjabeen-e-Aftimooni*, *Sharbat-e-Deenar*, *Itrifal-e-Aftimoon*^{10,11}, *Habbe Aftimoon*¹³, *Arq-e-MusaffiKhoon*, *Sharbat-e-Aftimoon*, *Majoon-e-Najah*, *Sharbat-e-Dinar*, *Majoon-e-Chobchini*, and *Sharbat-e-Kasoos*,etc.³³

5. Traditional Medicinal uses of various parts of *C. reflexa* (*Aftimoon*)

Due to their abundance of different phytochemicals, *Aftimoon* is widely used in traditional healthcare systems. It is used to treat illness, itching, as well as diuretic, anthelmintic, purgative, and tonic disorders. The entire plant, its stem, and its seeds are used as prescription drugs for treating ailments. Medicinal uses of various parts of *C. reflexa* (*Aftimoon*) is displayed below in (Figure 1).

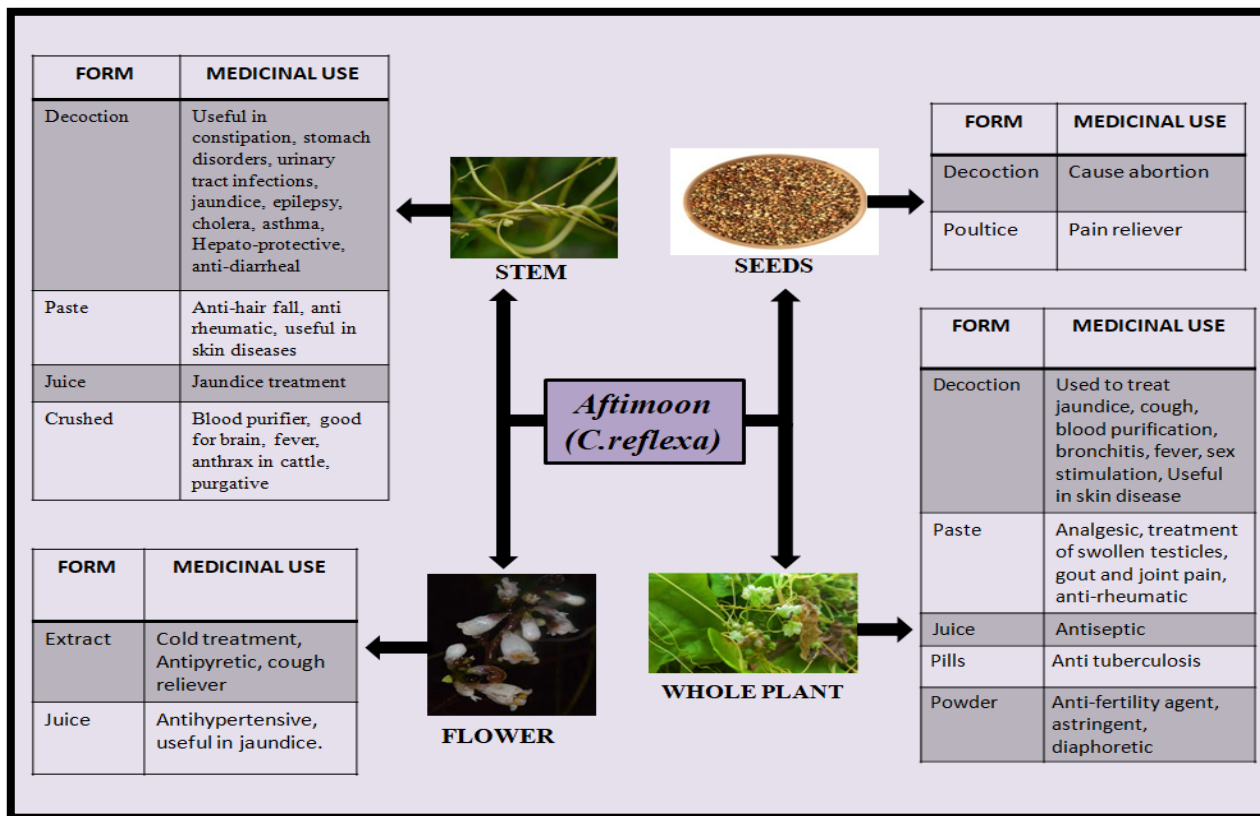


Figure1: Traditional Medicinal uses of various parts of *C. reflexa* (*Aftimoon*)

6. Therapeutic Implications of *Aftimoon* (*Cuscuta reflexa*) and Its different Ingredients in Treating Health Conditions

Research studies reveal the role of *Aftimoon's* active constituents in curing the diseases via wide range of biological activities notably the activation of the antioxidative enzyme, acting as chemoprotective by regulating the cellular pathways, etc. Pharmacological activities of *Aftimoon* is discussed as follows (Figure2).

6.1 Anti-oxidant activity - One of the primary agents responsible for the development of many ailments is the free radical or reactive oxygen species. Neutralizing free radical activity, however, is a crucial step in preventing disease. Antioxidants help to activate antioxidative enzymes, which in turn reduce the harm that reactive oxygen species and free radicals can cause. Additionally, they often neutralize and eliminate free radicals earlier than they strike sites in biological cells.⁴⁸ There have been reports of antioxidant activity in medicinal plants⁵⁴. Plants are useful in avoiding disease because of the amount of antioxidants found in their seeds, fruits, oil, foliage, bark, and roots.

Numerous researchers have used a variety of qualitative and quantitative methods to identify antioxidants in different *Cuscuta* species. The study investigated the levels of phenolics and flavonoid content in stem obtained from a variety of hosts and retrieved with multiple solvents, including water, n-hexane, 100% methanol, 80% methanol, and 100% ethanol. Their antioxidant capacity was assessed using an array of procedures, such as reducing power, DPPH scavenging action, percentage restriction of linoleic acid peroxidation, and δ -tocopherol. Antioxidant capacity and total phenolic content were shown to be closely connected.⁸

Reports have indicated that *C. reflexa* possesses antioxidant properties^{47,71}. The ability of the *C.reflexa* methanolic extract to scavenge free radicals was assessed using DPPH and reducing power assays. The IC50 value of the DPPH experiment showed that its antioxidant activity was 359.48 $\mu\text{g/ml}$, which was higher than the value of 9.22 $\mu\text{g/ml}$ for ascorbic acid, which was employed as a standard. It was discovered that the extract's reducing power was dose-dependent and rose with concentration⁶. The *C. reflexa* ethanolic extract's ethyl acetate fraction exhibited a notable antioxidant effect. Alpha tocopherol, rutin, and flavonoids—all of which were identified by preliminary phytochemical screening—may be associated with activity.³¹

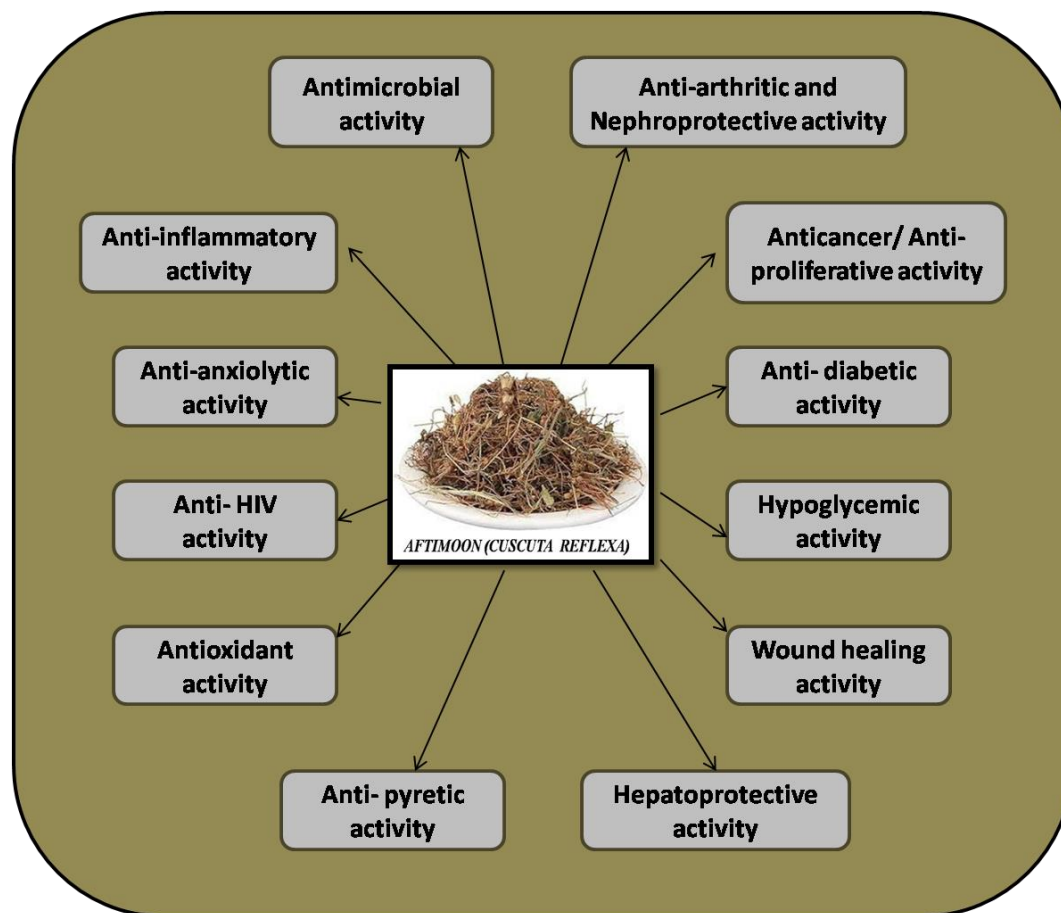


Figure 2: Pharmacological activities of *Cuscuta reflexa* (Aftimoon) in disease prevention and management by modulating various biological activities.

6.2 Hepatoprotective activity -When it comes to hepatoprotection without any negative side effects, medicinal plants and their constituents play a crucial role. The efficacy of *C. reflexa* to mitigate liver damage caused by medications such as isoniazid, ethanol, rifampicin, paracetamol, cisplatin, carbon tetrachloride, and others has been investigated by numerous researchers. Biochemical parameters including ALP, ALT, AST, and total bilirubin were determined prior to and following the administration of the *C. reflexa* extract. It improved liver function by significantly reducing serum ALT, AST, and ALP in afflicted rats that were comparable to standard. The findings are corroborated by the liver section's histopathological analysis.^{5,17,70} On Hep-3B, RAW-264.7, and HEK-293 cell lines, the chloroform abstract of *C. reflexa* has demonstrated an anti-hepatocellular carcinoma activity.⁵²

6.3 Anti-diabetic activity- Owing to a sedentary lifestyle's role in lowering physical activity levels and increasing obesity rates, the development of diabetes has evolved into a bigger risk for a significant portion of the population in almost every nation on the globe.⁶⁶ Significant hypoglycemic efficacy was shown using methanolic and chloroform extracts of the whole *C. reflexa* plant at dosages of 50, 100, and 200 mg/kg body weight. The impact on glucose-loaded Long Evans rats⁵⁵ was estimated using the oral glucose tolerance test. When mice injected with glucose were given a methanolic extract of *C. reflexa*, the results demonstrated significant drops in blood glucose and enhanced metabolic changes, supporting the traditional folkloric claims of the plant^{2,57}

6.4 Anti-inflammatory activity- Inflammatory responses are critical at various stages of the cancer pathogenesis. There is a possibility that anti-inflammatory medications cause malignant cells to undergo apoptosis and that they can serve as both a prophylactic measure and a therapeutic intervention.⁷³

In a carrageenan-induced paw swelling model in rats, the anti-inflammatory actions of ibuprofen were contrasted with the anti-inflammatory activity of alcohol and water extracts of *C. reflexa* stem. Before injecting carrageenan, these extracts were ingested orally at dosages of 100, 200, and 400 mg/kg bd. Wt. In comparison to the standard medication Ibuprofen, which reduced the swelling volume by 96.36%, the medium and higher doses of the extracts, 200 mg/kg and 400 mg/kg, respectively, reduced the swelling volume by 47.27%, 72.72%, and 57.72%, 80.00% at 5 hours. As a result, this study found that the chosen *C. reflexa* isolates significantly reduced inflammation in a rat model of carrageenan-induced paw swelling.³⁴

6.5 Anti-Cancer or Anti-proliferative activity- *C. reflexa* (Aftimoon) is the commonly prescribed antitumor medication in the Unani medicinal system, Chloroform and ethanol extract demonstrated significant antitumor effect in Ehrlich ascites carcinoma-bearing mice when combined with standard 5-fluorouracil.²¹ The anti-tumor effect of *C. reflexa* extracts in ethanol and chloroform has been indicated, and they have also been found to prolong the lives of tumor-bearing mice by inhibiting EAC cells. The host observed improvements in hematological markers and a decrease in tumor volume.^{22,75} *C. reflexa* extracts in ethanol and chloroform have demonstrated a favorable antiproliferative action in EAC-bearing mice.²¹

In colorectal cell lines HCT116, *C. reflexa* displayed mild antiproliferative properties.⁶⁰ Hep-3B cell line proliferation was shown to be dose- and time-dependently inhibited by the chloroform extract of *C.reflexa* via the intrinsic mitochondrial apoptotic mechanism.⁵²

6.6 Anti-microbial activity- Gram +ve and Gram -ve bacteria have been proven to be susceptible to the antimicrobial properties of *C. reflexa*'s ethanol extract. *E. Coli* was suppressed, at a dosage of 200 mg/mL, and at the conc. of 500

mg/mL maximum antibacterial activity was observed against *E. coli*.⁶⁹ Methanol extract of *C.reflexa* stem demonstrated broad-spectrum antibacterial activity against *S. aureus*, *P. aeruginosa*, and *E. coli* at dose ranges of 25–125 mg/ml and 50–150 mg/ml.⁴⁹

Gram -ve bacteria like *E. coli* linked to fungal strains like *Penicillium citrinum* were more effectively inhibited by the ethanolic extract of *C. reflexa*.³² Quercetin demonstrated both antiviral and antibacterial properties.⁶⁴

6.7 Anti-arthritis and Nephroprotective activity- In vitro protein denaturation methods, in vivo and in vitro formaldehyde and turpentine oil-induced arthritis models were used to assess the antiarthritic action of *C. reflexa* aqueous and methanol extracts. AMECR, at 600 mg/kg, effectively decreased acute muscle and paw swelling, peaking at 71.22% for turpentine oil at the 6th hour and 76.74% for formaldehyde on the 10th day. Furthermore, studies carried out in vitro show that, in a concentration-dependent way, protection against denaturation of both egg albumin (93.51%) and bovine serum albumin (89.30%) can be considerably enhanced at 800 g/mL. According to this study, AMECR offers defense against two medical conditions that phytoconstituents might trigger: nephrotoxicity and arthritis.³

6.8 Anti-pyretic activity-Antipyretic medications reduced body temperature in fever scenarios. It has been proven that *C. reflexa* works well as an antipyretic medication for rats that have yeast-induced pyrexia. Both the ethanolic and aqueous extracts were demonstrated to be effective and to lower rectal temperature after a three-hour treatment. Compared to the standard medication (96.5%, Paracetamol), a dose of 400 mg/kg weight reduced the elevated temperature by approximately 83.8% (ethanolic) and 79% (aqueous) after 6 hours of treatment.²⁰

6.9 Wound Healing activity- Many plants and their components are crucial to the process of wound healing in the Rat model, wounds gained recovery after being exposed to 400 mg/kg and 200 mg/kg ethanolic as well as aqueous extracts of *C. reflexa* stem.²⁵ Research analysis finds *C. reflexa* to be more effective than betadine in healing the wounds.⁵⁶

6.10 Hypoglycemic activity-At dosages of 50, 100, and 200 mg/kg body weight, respectively, both the methanol and chloroform isolates of *C. reflexa* showed hypoglycemic effect in oral glucose tolerance tests conducted in Long Evans rats and Swiss albino mice.⁷⁹ The methanol fraction of *C. reflexa* stems caused a statistically meaningful and dose-responsive drop in serum glucose levels in rats fed glucose orally.⁵⁵

6.11 Anti-HIV activity-The combination of several chemicals with distinct mechanisms of action has resulted in the Crude aqueous extract of *C. reflexa* exhibiting anti-HIV activity. Methanol fraction from *C. reflexa* showed antibacterial and free radical scavenging effects.⁴¹

6.12 Anti-anxiolytic activity- According to the study, the 400 mg/kg methanol isolate of *C. reflexa* considerably lowered the frequency of avenues into the closed arms and raised the duration of time occupied in the open arms. In both rats, the 400 mg/kg extract substantially lowered anxiety as compared to the 200 mg/kg extract. The 400 mg/kg effect was similar to the mean. As a result, the methanol isolate from *C. reflexa* has the potential to be used as an anxiolytic and to help create plant-based anxiety medications.⁷²

7. Conclusion

Natural products and their related substances are gaining immense popularity in the global fight against disease. *Aftimoon* has a wide variety of important chemical components in abundance which have been utilized

traditionally throughout history, particularly in the Indian Subcontinent, and has long been regarded as a miraculous plant with a wide range of therapeutic benefits. It is abundant in volatile oils, resin glycosides, polysaccharides, alkaloids, lignans, and flavonoid. In traditional medical systems, decoctions, extracts, pastes, powders, juices, and infusions made from various plant parts are significant herbal medicines. Clinical research has verified that *Aftimoon* is essential for preventing a wide range of illnesses. The regulation of many cell signaling pathways has been observed in tumors, indicating the function of active components as chemo-preventive agents. However, further research is warranted to explore the long-term efficacy and specific therapeutic mechanisms underlying *Aftimoon*. Additionally, efforts should be made to adapt and tailor this intervention to diverse populations and clinical settings to maximize its accessibility and effectiveness.

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