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Pharmacological and phytochemicals potential of *Cuscuta reflexa* Roxb. as parasite and its some host plants: A review

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Abstract
Cuscuta reflexa Roxb. (Dodder) is a twinning angiospermic parasite on the various types of host plants but its loves to grow on spinous trees, shrubs and herbs. Stems and seeds of this plant are reported to have very high medicinal value. *In vitro* studies showed that antimicrobial compounds of this plant are effective in the treatment of several infectious diseases due to their selective toxicity and reported to have the ability to injure or kill or suppress an invading micro-organism without harming the cells of the host plants. Several studies on phytochemistry have also confirmed the presence of various types of phytochemicals in this plant such as alkaloids, flavonoids, tannins, phenolic compounds, steroids, carbohydrates, glycosides which have pharmacological values for biological activities such as antimicrobial, antibacterial, antifungal, antiulcer, antioxidant, anti-inflammatory and anticancerous activities. It also affects the behavior of pollinators, seed vectors and diversity of host plant. This magic plant also affects the economy of farmer due to spread into the crop field and growth and yield of agricultural crops. Soil quality of the field is also affected by *Cuscuta* sps. as it decreases the aerable surface, results in loss of quantitative and qualitative crop protection and represents a vector concerning the transmission of diseases through viruses and mycoplasmas to host plant. Its impact on the diversity determines the degradation of landscapes decoration aspect. Monitoring of *Cuscuta* sps. and their spreading tendencies and their prevention and therapy generates positive and immediate protection system of cultures. In many countries this genus has been targeted to control and quarantine measures are settled without ignoring the fact that some species of *Cuscuta* may be endangered or even threatened with extinction. Since this genus has tremendous pharmacological values present in phytochemicals extracted from these elite plants, therefore, it is an urgent need to preserve this plant by adopting appropriate techniques. In this direction plant tissue culture techniques may be a suitable approach not only to preserve this wonderful plant but also to evaluate its own pharmacological values and also of host plant. Another line of futuristic research might be to know its parasitic effect on pharmacological and phytochemicals potential of host plant and on *Cuscuta* itself.

Keywords: Angiospermic parasite, *Cuscuta reflexa* Roxb, endangered, pharmacology, phytochemicals, plant tissue culture

Introduction
Cuscuta reflexa Roxb. (Dodder) is an obligate leafless and rootless angiospermic parasitic climber belonging to the morning glory family *Convolvulaceae*. Several species of this weed are found throughout India with several names such as dodder, Swaranlata, Devils guts, beggar vine, strangle weed, hair weed, love vine, field Dodder and golden dodder. It is yellowish green and thread like twinning herb and tangled mass covering several commercially important plants. The genus *Cuscuta* has about 100-170 species which attach various trees, shrubs, herbs and other plants of ethnobotanical and horticulture use have studied its host range, anatomy, biochemistry as a case study from Betla National Park, Jharkhand and identified 33 species, representing 30 genera belonging to 23 families as host plant.
Cuscuta reflexa Roxb. is a twining angiospermic parasite which makes a tangled mass covering over the host plants. This plant usually grows over every type of host found in nature but it loves to grow on spinous trees, shrubs and herbs. Stem and seeds of this plant are reported to have high medicinal value.

In India, tribes and other traditional communities use this plant as purgative, carminatives and external applications for skin disease and stem decoction is used for constipation and liver problem. *In vitro* studies on stem extract of *Cuscuta* also shown to have anti-viral and anti-cancerous properties. Since the *Cuscuta* is unpopular with several community but the traditional and tribal people are well aware in some states of India and has been adopted for their health care particularly epilepsy and jaundice and ethnoveterinary practices. Research carried out on this plant was not enough till date. More advanced research is an urgent need in this elite plant to make India healthy. The current list of parasites available in nature that come in mind are fungi, nematodes, bacteria and viruses which affected the development, growth and production of crop plants which ultimately, lead to the reduction of economy of farmer as well as country. Among the flowering plants, the *Cuscuta* genera is one of the most detrimental angiospermic parasite which grows very rapidly tangled with many economically and medicinally important plant as host, covering the whole canopy made by host plant. Most of the angiosperms, gymnosperms, bryophytes, pteridophytes are autotrophs and can synthesis their own food through photosynthetic activity. On the other hand, some examples are also found among the angiosperms which live parasitic life on other plants. For example, Indian pipe (*Monotropa*) lack chlorophyll and appear to be parasitic as mycoheterotrophs. In a host-parasite relationship, a haustorium is modified root that establishes a morphological and physiological link between the host and parasite [1] and is useful to make a distinction between the term's "parasite" and "pathogen". The species of *Cuscuta*, is commonly known as Dodder and among the obligate parasites is the best known and common parasitic angiospermic plant. The biology and control of Dodders was well reviewed [2]

Host range and distribution of *Cuscuta reflexa* Roxb. as a weed

Cuscuta reflexa Roxb. (Dodders) have a variety of host range but they prefer to feed on spinous bustry dicots as compared to monocots. As *Cuscuta* does not bear chlorophyll in its plant body thus cannot make its own food by traditional carbon assimilation process, the photosynthesis. In this way it lives as obligate parasite and draws food from other green plants of agriculture and horticulture use which may be trees, shrubs, herbs etc. The common host plants of *Cuscuta* reported so far, are *Acalypha hispida, Adathoda vasica*, *Alstonia scholaris, Annona squamosa*, *Bougainvillaea spectabilis*, *Calotropis giganta*, *Catharanthus roseus, Clerodendron viscosum, Campsis radicans, Delbergia sisso, Daheliasp, Duranta plumeiri, Euphorbia sps, Ficus glomerata, Hamelia patens, Hibiscus-rosa-sinensis, Helenium autumnale, Hevea brasiliensis, Ixora- Impatiens* species, *Jatropha curcas, Lantana camara, Linum usitatissiuym, Medicago sativa, Nerium oleander, Petunia* sps*., Phyllanthus niruri, Punica granatum, Ricinus communis, Solanum tuberosum, Vitex negundo, Zizyphus jujoba* etc. belonging to dicot families such as Euphorbiaceae, Acanthaceae, Annonaceae, Bignoniaceae, Fabaceae, Asteraceae, Moraceae, Rubiaceae, Malvaceae, Linaceae, *Balsaminaceae*, Solanaceae, Mytraceae and Rhamnaceae [3, 4, 5, 6]. As far as *Cuscuta. reflexa* Roxb. is concerned, it varies in colors of the flowers from white to pink. Flowers normally produced in the early summer and autumn. It produces large quantity of seeds which can survive in soil for many years in the search of suitable host and during this dormancy. Seeds are dependent on the food reserve present in endosperm [7].

Since ancient time Indian and Chinese people find extensive application of *Cuscuta* plant as an herbal medicine for variety of human ailments. In this connection, many species have been investigated for their phytochemical constituents as well as biological activities which are found to be beneficial medicines including *Cuscuta epithymum, C. europoea, C. lupuliformis, C. chinesis, C. japonica, C. americana, C. micrantha, C. platyloba, C. odorata, C. australis, C. pedicellata, C. gronovii, C. monogyna, C. approximata, C. tinctoria and C. californina* [8].

As far as its distribution is concerned, *Cuscuta* sps. are found in the temperate and tropical regions of the world with huge species diversity in tropical and sub-tropical regions. The various regions of India like over the Northern region of country, Bengal plains, Western ghats, Ceylon, Satara region, Himachal Pradesh, Uttar Pradesh and Uttarakhand [9]. It is also commonly found in plains of Afghanistan, Malaysia, Nepal and Thailand [5]. Although is known by several names all over the world, Dodder being the common name of it. Other names prescribed by several workers are as *Amarbel* (Immortal twine), *Akashwell* (Skytwinner), *Swarnlata, Akakhilata, Hellweed, Devils gut, Begger weed, Scald weed, Dodder of thyme, Greater dodder, lesser dodder, Devil hair, Witch's hair* and *love vine* [10, 11, 12].

***In vitro* studies of *Cuscuta reflexa* Roxb.**

Though not much literature is available on *in vitro* studies of *Cuscuta* however, more recently [9] studied the antimicrobial activity of this plant. Antimicrobial agents such as bacteria are found to be effective in the treatment of several infectious diseases due to their selective toxicity. They have the ability to injure or kill or suppress an invading micro-organism without harming the cells of the host plants. It also studied the antimicrobial activity of stem ethanolic extract of *Cuscuta reflexa* Roxb. *in vitro* by using agar cup plate technique against Gram +ve bacteria such as *Bacillus subtilis, Staphylococcus aureus* and Gram -ve bacteria such as *Escherichia coli, Pseudomonas aeroginosa* as well as some fungal forms like *Penicillium citrinum, Aspergillus niger* using Penicillin as standard [9]. In their experiments sterilized nutrient agar medium was used for bacterial growth and Sabouraud agar medium for fungal growth.

The study so performed came to the conclusion that ethanolic extract of stem of *Cuscuta reflexa* Roxb. confirmed the presence of alkaloids, carbohydrates, some amount of glycosides, flavonoids, tannins, phenolic compounds, steroids etc. Among these phytochemicals flavonoids and glycosides showed antimicrobial activity. The results also indicated that antimicrobial activity against fungi and Gram -ve bacteria was more than Gram +ve bacteria.

An attempt to screen comparative potential of different extract of *C. reflexa* obtained from two source *Acacia arabica* and *Zizyphus jujuba* for its antimicrobial activity against Gram positive and Gram negative bacteria and fungi [13]. Plant extract of *C. reflexa* was prepared using aqueous and organic solvents such as benzene, acetone, ethanol and methanol. To assess the antimicrobial potential of plant from different sources against gram positive bacteria such as

Staphylococcus aureus and *Staphylococcus epidermidis*, gram negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa* and fungus *Aspergillus niger* by using Agar well Diffusion Technique. They determined a diameter of zone of inhibition as an indicator of antimicrobial effect. The performed study showed a strong inhibitory effect of ethanol and methnol extracts of *C. reflexa* growing on the both the hosts on most of the gram-positive and gram-negative bacteria while aqueous extract of *C. reflexa* growing an *Acacia arabica* failed to show any antimicrobial activity while *C. reflexa* on *Zizyphus jujuba* showed very meager effect. At last, they concluded that *C. reflexa* as a parasite of *Zizuphus jujuba* could be considered as a potential source of natural antimicrobials. The volatile analysis and antimicrobial screening in *Cuscuta reflexa* by gas chromatography-mass spectrometry and evaluated from a total of 62 peaks, 61 compounds were identified in the oil. Accounting for 99.6% of the oil and the majority of the essential oil was dominated by the rare component cis-3-butyl-4-vinylcyclopentane (26.4%) and substantial amount of limocene (5.1%) and (*E*)-nerolidol (9.5%). On the other hand, the antimicrobial activities did not show appreciable activity against either Gram positive (*Bacillus cereus*, *Staphylococcus aureus)* or Gram negative (*Escherichia coli*, *Pseudomonas aeruginosa*) bacteria. However, marginal activity was observed against *Aspergillus niger*.

It is universal truth that the floral initiation and subsequent development in the angiospermic plant community is the essential step on which the yield of the plant depends. In some cases, external climatic factors or any abiotic stress hinders the floral development which ultimately affect the yield of the plant. In this situation to overcome the climatic influences on floral initiation and development may be helpful by conducting *in vitro* studies [14]. However, the development of seedling from larger embryos of *C. reflexa* in White's medium [15]. Floral induction of *C. reflexa* in short day period as well as dark conditions has also been studied [16, 17]. Since than more work has not been done so far. However complete tissue culture system of *Cuscuta trifolli* in liquid MS culture has been reported [18].

In vitro studies of floral induction of stem apices of *Cuscuta reflexa* Roxb. has been well discussed [16]. He cultured stem tips of *Cuscuta reflexa* on modified white's medium subjected to different light and dark conditions and observed flowered cultures when maintained either in continuous darkness or exposed to 14 hrs of daily dark period. Due to being the short day plant (SDP), the presence of 5% sucrose in the medium completely obviates the requirement for high intensity light exposers, otherwise essential for SDP. It is assumed that the bud itself shows the sensitivity towards photoperiods. There is no transportation of flower forming substance from one plant to another except the presence of natural tissue bridge formed between the host and parasite through haustorial connections. However, achieved only vegetative growth in the stem tips of *Cuscuta compestries* and obtained not more than two flower buds without attributing this to any specific light conditions [19]. Similarly, also grew shoot tips of *C. epithymum* but procured only vegetative growth [20].

The genus *Cuscuta* consisted of 100-170 species and grows as parasite on various plants of commercial, ornamental and ethnobotanical use. To explore its properties regarding pharmacological properties in relation to host plant is an urgent need through tissue culture technique for each and every species of *Cuscuta* plant except *Cuscuta campestries* and *C. epithymum.*

Mechanism of parasitism

Cuscuta plant is totally dependent on host plant for their food and nutrition. *Cuscuta reflexa* is usually found growing as parasite on several ornamental plants having thread like stem. This plant has no roots in the ground and it grow over the host body without touching the ground surface in its life span [2]. It absorbs water and inorganic nutrients through the xylem connection between the host and parasite. In fact, when *Cuscuta* choses its host and comes in contact with nourshing plant, it produces haustoria inserting themselves into the vascular system of the host. In this way, the water and inorganic nutrients are absorbed through xylem connection between the host and the parasite *Cuscuta.* While organic substances are transported from the phloem of the host to parasite via phloem connections. The *Cuscuta* epidermal cells start to elongate and enriched with cytoplasm and secrete a layer of electron dense material consisting of a mixture of non-esterified pectin and with this cement like substance the parasite is firmly fixed to host. The initial contact to the host is established by the prehaustorium or the adhesive disc followed by contacting and twinning around the host organ, either stem or petiole [21, 22, 23, 24]. More interestingly, *Cuscuta* plant has the ability not only to recognize its host for food and nutrition but also to move towards its suitable precision and efficiency. The ability to choose suitable host among many plants growing in group due to being sensitive to volatile compounds released by to be the host plant for *Cuscuta*, during normal process of transpiration [25].

An anatomical study of attachment with *Ziziphus mauritiana, Cajanus cajan* and *Ficus glomerata* as host plant of *Cuscuta reflexa* Roxb. as parasite was well described [26] and showed tremendous diversity with its host stem, indicating that *Cuscuta* haustorium can easily pen etrate in the host plant stem and penetration depends on the size of both stem as well as *Cuscuta*. The light microscopic anatomical observations revealed through transverse section of host stem shows that *Cuscuta* haustorium reached up to the secondary xylem. One of the interesting features was observed that food material is available from phloem tissue instead of the *Cuscuta* into the next phloem tissue of the host plants and this insertion shows only limited growth. Another common character was observed that the *Cuscuta* haustorium penetration has been affected by the cells of cortical tissue and this tissue tend to elongate towards the parasite therefore, stem of host plants become completely changed its structure [26]. In *Cuscuta,* haustorium apical meristem and root cap cells are absent and it develops from cortical parenchymatous cells of pericycle. It is also observed that cell elongation dominates over the cell division and therefore the number of cells of the parasitic endophytic system in the host is determined by the number of parasitic parenchymatous cells undergoing transformation during the formation of haustorium [27]. In *C. reflexa* the haustoria formation was restricted to only a sub apical region. While the *Cuscuta* easily attach itself to its host, the first difficulty was to establish connection between xylem vessels and sieve tubes of the host plants [28].

Cuscuta sps. have been a center of attraction for several researchers due to its pharmacological values for biological activities such as antimicrobial, antibacterial, antifungal,

antioxidant, antiulcer, anti-inflammatory, help to protective anti-proliferative, anti-cancerous activities. This plant contains flavonoids, glycoside, steroids and sterols, fatty acids, fixed oil, mineral and essential oils etc. The parasitism of Dodder plant has major impacts on host growth, allometry and reproduction. It also affects the behavior of pollinators, seed vectors and diversity of host plants. *Cuscuta* sps. also affect the environment and ecological balance in the nature and the economy of farmer due to spread into the crop field and growth of agricultural crops subsequently lead to very low production. Soil quality of the field is also affected by *Cuscuta*. It decreases the aerable surface, results in quantitative and qualitative crop and represents a vector concerning the transmission of diseases such as viruses and mycoplasmas to host plant and its impact on the biodiversity determines the degradation of landscapes decorative aspect. Parasitic plants such as *Cuscuta* also effect the other plant community by forming thousands of connections with many host species and may cover an area greater than 100m [29] and resulting in noticeable impacts on the plant community despite its being less than 5% of vegetation biomass [30].

It has been suggested that *Cuscuta* as a parasite not only affects the plant as hosts but many other organisms such as birds and insects herbivores, other parasites and mycorrhizal fungi may be affected directly or indirectly which lead to affect the tropic levels being a part of our biodiversity. Monitoring *Cuscuta* species and their spreading tendencies and their prevention and therapy generates positive and immediate economic and social effects by means of creating an integrated protection system of cultures. Moreover, it might also determine a qualitative and quantitative increase of agricultural production, which benefits farmer on the short, medium and long run. Further more, they will be mirror in the quantity and quality of fodders, animal health's and welfare of farmers. It is universally well known fact that the decrease in risk of disease, parasite and weeds within agricultural ecosystem would influence public health and environmental protection in positive way. The abiotic environment is also affected by parasitic plants and most significant types of ecosystems affected by *Cuscuta* species are the partologic ecosystems. However, a large number of species represent host plant for Dodder; this fact affecting the biodiversity of ecosystem at a process level as well as with regard to human society and animal health.

Plants of ethnomedicinal use are getting attention from most of the researches for the evaluation of new drugs because consuming of these drugs has polyvalent action and minimum side effect [31]. The genus *Cuscuta* has been studied for keeping five main objectives such as phytochemical, pharmacological, taxonomic, as weed and as a unique plant for plant - plant interactions. In many countries this genus has been targeted to control and quarantine measures are settled without ignoring the fact the some species of *Cuscuta* may be endangered or even threatened with extinction, [32, 33, 34, 35, 11] stated that *Cuscuta reflexa* as a parasitic weed plant has an important place in the Ayurveda and other traditional medicine systems due to its medicinal properties. Its medicinal properties depend on its host plant as it drives various nutrients from the host. Several research workers have isolated various chemicals from this miracle plant which are of therapeutic potential and show ethnomedical and pharmacological activities. However, many reviews exist about its phytochemistry, pharmacology [36, 37, 38, 39, 8] as well as parasitic management and mechanism [40, 41]. Above all the importance of *Cuscuta* in relation to host has been addressed in detail.

Though *C. reflexa* is parasitic species but it has a wide variety of natural products which greatly depend upon its host species. Its natural products expressed anti-mutagenic activity in response to familiar TA 98 and TA 100 strains of positive mutagens *Salmonella typhimurial* [42, 43]. The *C. reflexa* repressed lipopolysaccharide induced inflammatory of tumor necrosis factor-α, cyclooxygenase 2 and nuclear factor KB signaling [5]. This significant anti-tumor activity of isolates of *C. reflexa* was related to the standard 5-flurouracil in Ehrlich ascites carcinoma-affected mice [44].

Although not much attention has been given regarding pharmacological aspects of *Cuscuta* sps. However, till time several studies have been conducted to find out pharmacological properties of this plant. The medicinal potential of *Cuscuta* as identified so far are due to antineoplastic, cytotoxic, anti-nociceptive, anti-inflammatory antioxidant, antimicrobial, immunostimulatory, anti-apoptosis, antifibrotic, anti-osteoporetic, anti-obesity, anti- HIV-1, anti-depressant, antifertility, anti-epileptic properties. Moreover, in the field of ethnoveterinary, the use of Dodder plant as astringent and diaphoretic for lamb and calf; and as anti-fertility agent has also been reported [45]. *Cuscuta* has also been described as skin whitening or hair restoring treatment or for neurotrophic effect.

The seeds of *Cuscuta reflexa* Roxb. are used as carminative, analgesic and known to have detoxifying effect and its stems are known to cure bilious disorders, itchy skin, body pain and protracted fevers [5]. *Cuscuta reflexa* Roxb. is found to have usefulness towards the hair growth and its extract significantly prevents hair loss during chemotherapeutic treatment of cancer and prevents cyclophosphamide-induced damage of hair follicles. The natural product and crude extracts of *Cuscuta reflexa* have confirmed anti-HIV activity and hypoglycemic effects in glucose-loaded rats [46, 47].

The natural antimicrobial come from a wide array of sources including plants, animals and microorganisms [48]. Recently conducted researches have shown that many bacterial pathogens are becoming resistant to existing antibiotics due to their indiscriminate use in the treatment of many infectious diseases. Therefore, it is a quite urgent need to discover new and efficient antimicrobials from plants such as *Cuscuta* [49, 50].

Cuscuta as weed

Some species of this genera are considered as weed e.g., *Cuscuta pentagona (C. campestris), C. epithymum, C. europaea, C. gronovii, C. indecora, C. planiflora, C. reflexa and C. suaveolens* and are widely distributed and affect the wide range of crops such as onion, garlic, asparagus, sugar beet, pepper, cucumber, carrot, potato, alfalfa and many more. These *Cuscuta* species affect some fruit trees like citrus, pomegranate, cranberry, coffee etc. and ornamental plants like chrysanthemum, geranium, dahlia, petunia, periwinkle etc. causing a low productivity and eventually death [51, 52, 41]. For example, infestation by *C. pentagona* to tomato and carrot plants can reduce productivity by 50-75% and by 70-90% respectively [41]. Similarly, [53, 54, 52] also reported yield reductions in *Capsicum frutescens*, *Vigina mungo*, *Lens culenaris*, *Cicer arietinum*, *Medicago sativa*,

Allium cepa and Beta vulgaris by *Cuscuta* invasion as a weed. In several studies *Cuscuta* has been proved to be a bridge for viral and bacterial pathogen transmission. For instances it could transfer virus (PVYN), viroids (HSVD, CSVD), phytoplasmas (Yellow diseases, PHY P30) and bacteria (HLB) from diseased to healthy plants or trees from *Nicotiana benthamiana* [55].

Therefore, weed management is essential for agricultural production and protection. For this several strategies have been adopted for control of *Cuscuta* infestations. The methods of control of *Cuscuta* may be mechanical, chemical and biological [56]. For the suppression of *Cuscuta* under mechanical methods can be done by mechanical removal, selective pruning, deep ploughing and for chemical control herbicides can be used. Biological control is defined as the use of natural enemy or a complex of natural enemies (biological control agents) to bring about of this weed suppression. These agents can be phytophagous arthropods (insects and mites), animals (fish, birds, and sheep) or bioherbicides.

It is mentioned that according to the US Environmental Protection Agency, there are three types of biologically based herbicides [57, 58]. These are biochemical herbicides (living or dead microbes; plants pathogenic or non-pathogenic microbes mixed in or not with their metabolites) and genetically modified plants expressing herbicidal substances. Some examples of biological control studies for *Cuscuta* are the use of insects of genus Smicronyx (*Coleoptera, Curculionidae*) [59], secondary or specialized metabolite plumbagin [60], methanolic extract from *Cynodondactylon* and *Chenopodium murale* [61] or mycotoxins (Ophiobolin A, fusicoccin and derivatives, phyllostictine) [62].

The use of phytoene desaturase inhibitors, as bleaching herbicides in *Cuscuta campestris*, triggered reduction in biomass and on the development of flowers and fruits [63]. The herbicide propyzamide is sufficient for dodder control at the early stage infestations [64]. A mixture of an amino acid biosynthesis inhibitor (carfentrazone-ethyl) and a fungicide (triadimefon) was described [65]. The use of derivatives from inhibitor of the enzyme *P*-hydrox-phenylpyruvate dioxygenase in the carotenoid biosynthesis (mesotrione) or the use of an amino acid biosynthesis inhibitor halosulforon-methyl, [66] the combination of antisense nucleotide sequences for the enzyme glutamine synthase (an essential enzyme in the metabolism of nirogen), and two inhibitors of this enzyme (glufosinate-ammonium and bialaphos) [67] the use of glyphosate salts for enzyme inhibition of 5-enolpyruvylshikimate-3-phosphate synthase that participates in the aromatic amino acid biosynthesis [68] the use of mycelia and spores of a strain of *Colletotrichum* sps. [69] or the use of spores from a strain of *Fusarium tricinctum* [70]. It is essential to mention, that dodders can be tolerant to the herbicide glufusinate if they could infest glufosinate tolerant crops, which express the enzyme phosphinothricin acetyl transferase (PAT) that detoxifies this herbicide. This tolerance was due to the translocation of detoxifying enzyme from the host glufosinate tolerant crops to Dodders [71].

Phytochemistry of *Cuscuta*

Based on pharmacological activities the phytochemistry of *Cuscuta* sps. has been reported by several workers. This genus has been a reservoir of a variety of compounds as a result of both plant primary and secondary or by specialized metabolism. These secondary metabolites released from the plants have significant potential in plant defense mechanism and protect plant from microorganism, insect and other abiotic stresses. Some examples of phytochemical constituents as a result of primary metabolism are fatty acids, glycolipids, steroids, carbohydrates and phytohormones while for secondary/specialized metabolism some examples are alkaloids, coumarins, flavonoids, lignas, phenylpropanoids and terpenoids and many other. From *Cuscuta* seeds the identified phytochemicals are, 4 acidic polysaccharides, 3 alkaloids, 10 fatty acids and their derivatives, 22 flavonoids, 6 glycolipids, 1 hydroquinone, 1 lactone, 21 lignas, 12 phenolic compounds, 5 phenylpropanoids and 3 steroids. Moreover plant materials as whole plants, stems, fruits or including shoot tip cultures have also been analysed and identified: 1 alcohol, 9 aldehydes, 30 alkaloids, 3 alkanes, 2 amides, 1 benzofuran, 11 carotenoids, 3 coumarins, 1 cycloalkane, 2 diamines, 24 fatty acids and their derivatives, 32 flavonoids, 2 lactones, 9 lignas, 12 phenolic compounds, 17 phenylpropanoid's, 2 photosynthetic pigments, 1 phytohormone, 3 quinolines, 13 steroids, 2 sugars, 38 terpenoids, 3 terpenoids quinones, 2 tetrahydrofurans, 1 urea derivatives, 1 xanthonoid and 7 minerals. Some metabolites have been identified in both seeds and whole plants: such metabolites are fatty acids as oleic acid and palmitic acid, flavonoids such as astragalin, hyperoside, kaempferol, trifolin or quercelin, some lignas such as aptosimol, pinoresinol or sesamin as well as phenolic compounds such as vanillin and phenylpropanoids such as caffeic acid, coumaric acid or chlorogenic acid and derivatives. All these metabolites could be part of the primary and secondary as well as specialized metabolism of the genus *Cuscuta* as it has been mentioned on several reviews while discussing its phytochemistry and pharmacology published by many researchers [36,37,38,39,8]. The genus *Cuscuta*being a parasitic plant, absorbs metabolites from different hosts, therefore the phytochemistry of host plants may alter the phytochemistry of the Dodder as well.

The Dodder species (*Cuscuta reflexa)* which has been considered in present investigation and has been explored extensively for research purposes by several workers. They have identified a variety of chemicals constituents from these plants. Some of them are dulcitol, mannitol, sitosterol, carotenoids, flavonoids, isorhamnetin-3-*O*-neohesperidoside, apigenin-7-β-rutinoside, lycopene, 6,7-dimethoxy coumarin (scoparone), 6-hydroxy-4-(4-hydroxyphenyl)-7-methoxy-coumarin, quercetin, hyperoside [72], apigenin-7-*O*-glucoside, kalmpferol-3-*O*-α-rhamnoside, myricetin-3-o-α-rhamnoside [73], 7'-(3',4'-hydroxyphenyl)-N-N[C4-methoxyphenyl]ethyl) propionamide, 7'-(4'-hydroxy, 3'-methoxyphenyl)-N-[(4-butylphenyl)ethyl] propenamide [74], reflexin [75], Violaxanthin, lutein, lycopene, carotene, α-cryptoxanthin [76], amarbelin, cerotic, linolenic, oleic, stearic and palmitic acids, phytosterols (seeds), abscisic acid (leaves), luteolin and its glycosides [97], quercetin, cuscutin (stem) amino acids and cuscutalin [78, 79] aimed their study to disclose the potential bio-active components of *Cuscuta palaestina* through GC-MS analysis and to open future direction towards perspective application and identified 18 components in the methanolic extract of *C. palaestina* for the first time. The most appealing among them were sesamin and two other phytosterols (Campesterol

and Stigmasterol) which are scientifically proven to have anticancer activity.

Campesterol for example, has been shown to act as biomarker for cancer prevention and is reported to have potential antiangiogenic action via an inhibition of endothelial cell proliferation and capillary differentiation. Moreover, reported that stigmasterol significantly suppresses tumor promotion in two-stage carcinogenesis in mice [80]. Dodecanoic acid isooctyle ester and palmitic are the dominant compounds, demonstrating 20.9% and 10.58% decrease in tumor size, respectively [81].

Apart from above mentioned vegetative parts of *Cuscuta*, its seeds also reported to have the esters of higher aliphatic alcohol with saturated fatty acids having 26 and 28 carbon atoms among which cerotic acid has been identified. The phytochemical of this phanerogamic parasite revealed the presence of caffeic acid depsides and flavonol type flavonoids and some phenolic compounds [82]. The immobilization of *Cuscuta reflexa* starch phosphorylase carried out for production of glucose-1-phosphate by using the bioreactors [83]. The photosynthetic properties of this *Cuscuta reflexa* such as chloroplast, ultra-structure contents of chlorophyll, carotenoids and plastid proteins, photosystem and carbon dioxide fixation activities and photosynthetic genes composition [84].

Pharmacological activity of *Cuscuta*

The medicinal properties of recognized plants are due the active phytochemicals present in the plants such as alkaloids, flavonoids, glycosides, saponins, tannins, terpenoids, steroids etc. These phytoconstituents possess tremendous potential health benefits and contribute in the prevention and treatment of cardiovascular diseases, cancer, osteoporosis, antioxidant activity [11, 85, 86] concluded that polyphenols have advantageous effect on cardio-vascular system and have vital role in the prevention of neurogenerative diseases and diabetes mellitus. The natural products are proven reservoirs of new novelties in terms of therapeutic applications and play a crucial role for the advancements of scientific understanding for the designing of new drugs especially in treating cancer. Over 70% of anticancer drugs are formulated from natural products which justify the importance of the natural products as a source of anticancer drugs like podophyllotoxin from Podophyllum [87, 88]. Some other drugs such as taxol, vincristine and vinblastine are indole alkaloids based anticancer agents obtained from nature *Catharanthus roseus* (Apocynaceae).

However, *Cuscuta reflexa* has been reported to have several pharmacological activities such as hepatoprotective activity [89, 90, 91] anti-microbial activity [92], anti-tumor activity [44], wound healing activity [93, 94], anti-HIV activity [95], diuretic activity [7], anticonvulsant activity [93], anti-inflammatory and anti-cancer activities [96,44]. A systematic review an ethnopharmacology, phytochemistry and pharmacology on *Cuscuta chinensis* [38] have analyzed that this *Cuscuta*sps. contains 18 flavonoids; 13 phenoloic acids; 2 steroids; hydroquinone; 10 volatile oils, 22 lignans; a polysaccharides 2 resin glycosides; 16 fatty acids. These phytoconstituents and plants extracts show a range of pharmacological activities like hepatoprotective, renoprotective, antiosteoporatic, antioxidant, anti-aging, antimutagenic, antidepressant, improved sexual function, abortifacient effects etc.

Conclusion

Medicinally recognized vegetation are the most exclusive source of life saving drugs for majority of world's population and it is estimated that 80% of population depend upon plants to therapy themselves and among them 60% population use drugs extracted from plants having pharmacological potential to combat various diseases and 40% humans use such plants in pharmaceuticals industries, not only due to high cost of treatments in Allopathy but also having side-effects, peoples are tend to show their interest towards homeopathy and Ayurveda as these medicines system is safe and without having any side effects. Since the emergence of human civilization, people used medicinal plants for remedy of various common disorders such a toothache, pain and digestive dysfunction at household level without having the knowledge of active ingredients or phytochemicals and pharmacological activities. With the advancement of scientific application, it is now possible to know the pharmacological potential of any phytochemical present in the plant. The present review is an attempt to throw light on pharmacology and phytochemistry of *Cuscuta reflexa* Roxb.

Phytochemicals are naturally occurring primary and secondary compounds found in almost all the ethnobotanical plant parts like leaves, stems, roots, buds, seeds etc. Chlorophyll, proteins and common sugars are included in primary constituents and secondary compounds are terpenoids, alkaloids and phenolic compounds. Terpenoids exhibit anti-inflammatory, anti-cancer, anti-malarial, inhibition of cholesterol synthesis, anti-viral, anti-bacterial and other pharmacological activities. Alkaloids are used as anacothetic agents and found in several medicinal plants, whereas phlobatannins have been reported for its wound healing properties, hence they are anti-inflammatory and analgesic and anti-oxidant. Epidomylogic studies recommended that coronary heart disease is opposed by dietary flavonoids. Quantitative estimation of carbohydrate is essential when the given plants or its parts to be used as therapeutics. Lesser or zero concentration of carbohydrate in plants may be useful for herbal treatment for diabetic patients.

Hence, the phytochemical screening of plants is very important commercially as well as in pharmaceuticals industries for synthesis is and formulation of new drugs for curing various diseases. Some of the plants like *Cuscuta* have been explored extensively for its pharmacological potential on the one hand but on the other hand several strategies have been adopted for control of *Cuscuta* infestations because of its parasitic nature. Some species of *Cuscuta* are also considered as weed and affect the wide range of crops, fruits, trees and ornamental plants causing a low productivity and eventually death of infested plants. In several studies *Cuscuta* has been proved to be a bridge for viral and bacterial pathogen transmission. In many countries this genus has been targeted to control and quarantine measures are settled without ignoring the fact that some species of this genus may be endangered or even threatened with extinction. In nature most of the plants except some viruses and bacteria may not have medicinal importance, have low or high pharmacological potential, hence their existence should not under danger or at extinction and their preservation is an urgent need by applying appropriate techniques. In this direction, plant tissue culture technique may be a suitable approach not only to preserve this magic

plant but would also be helpful to evaluate its own pharmacological properties as well as when it comes in contact with its host plant. Another line of futuristic research might be to know its parasitic effect on pharmacological potential of host plant and on *Cuscuta* itself.

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