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A REVIEW ON THE WIDESPREAD THERAPEUTIC APPLICATION OF THE TRADITIONAL HERB *DRYMARIA CORDATA*

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ABSTRACT

Drymaria cordata (family Caryophyllaceae), commonly known as Laijabori in Assamese, is a traditional herb native to tropical America with its distribution being widely extended to Northeast India. It is used as one of the ingredient in many native poly herbal formulations for its analgesic, wound healing, anti-inflammatory activity. It is also used as an antidote, appetizer, depurative, emollient, febrifuge, laxative and stimulant in both humans and animals. A number of biologically active compounds have been isolated from the leaves of this taxon including drymaritin which exhibits anti HIV properties. The present article gives an overview of *Drymaria cordata* with its economically important and extensively preferred medicinal properties. The review highlights the wide number of biological activities like analgesic and antipyretic, anti-inflammatory, anxiolytic, cytotoxic, anti-convulsant, antibacterial, antitussive activities and various other medicinal properties along with the phytochemical analysis from its leaves. The review also reveals the various biologically active constituents which have been isolated from this species and also its management and conservation for future use.

KEYWORDS: ***Drymaria cordata*; ethnopharmacology; medicinal; anti-carcinogenic; anxiolytic; anti-convulsant**

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INTRODUCTION

In different civilizations the contribution of floral biodiversity to health care has been well documented[1]. In India, several medical systems have evolved and prominent among these systems are Ayurveda, Siddha and the Unani Systems of Medicine. Because of the accelerated local, national and international interest in recent years, the demand for medicinal and aromatic plants has increased manifolds with the pharmaceutical industry perceiving plant wealth as a source of revenue. Due to easy availability, no side-effects, and sometimes only as a source of health care, the demand for medicinal plants is escalating in both developing and developed countries. The World Health Organisation (WHO) estimated that 80 % of the populations rely on time-honored medicines, mostly plant drugs, for their primary health care needs in developing countries. It has been estimated that in developed countries, plant drugs constitute as much as 25 % of the total drugs, while in fast developing countries; the contribution is as much as 80 %[2]. Considering these facts, it is important to know about the medicinal plants of the nearby areas and it becomes even more essential when the area is almost in the vicinity of the forest. The plant kingdom is a treasure house of potential drugs and in the recent years there has been an increasing responsiveness about the importance of medicinal plants. The foot hills of Northeast region of India forms an ecotone, that is bestowed with a variety of natural resources, which have been continuously exploited by mankind since time immemorial for relieving, suffering and curing ailments by trial and error. The history, religion and folklores are full of instances where the magical and curative properties of various plants have been narrated and based on speculations and superstitions the effectiveness of certain plants for different ailment was learnt[3].

Drymaria cordata is an example of such species which has enormous medicinal value and economic importance but has not been studied in detail so far. *D. cordata* (L.) Willd. Ex. Roem and Schult, a member of Caryophyllaceae, locally known as "Laijabori", a plant of North East India, has been traditionally used as one of the ingredient in many native poly herbal formulations[4,5,6] for its analgesic, wound healing, anti-inflammatory activity and is also used as an antidote, appetizer, depurative, emollient, febrifuge, laxative and stimulant in both human and animals. Its antitussive activity[7], antibacterial efficacy[8] and anti-inflammatory effects[9] making it a potential medicinal herb for drug exploration program. A number of biologically active compounds have been isolated from the leaves of this taxon including drymaritin which exhibits anti HIV properties[10, 11, 12]. This plant also commonly known as West Indian chick weed is a creeping herb and found growing in dense patches in moist shady places and also in dry sun-exposed areas, widely distributed in hilly and sub-mountain region of the country. The review outlines the recent studies carried out by various research groups, along with providing a comprehensive account of the plant its taxonomy and botanical description. The review provides a summarized account of the wide number of biological activities like analgesic and antipyretic, anti-inflammatory, anxiolytic, cytotoxic, anti-convulsant, antibacterial, antitussive activities reported from this plant.

BOTANICAL DESCRIPTION

This trailing annual herb bears numerous glandular hairs; stems often root at the nodes, stems angular, glabrous to glandular-hairy, with long simple hairs at the nodes; internodes to 5 times the length of the leaves. The glandular hairs give the plant a sticky feel and enable parts to adhere to clothing. Leaves are simple, opposite, orbicular to reniform, scarious interpetiolar stipules usually present. Leaves ovate to reniform, 6–12 mm long, 8–12 mm wide; petiole 3–7 mm long, glabrous to glandular-hairy. Pedicels 2–7 mm long, glandular-hairy. Sepals 3–5 mm long, 3-veined with scarious margins. Petals usually bifid, 2–3 mm long, white. Capsule ovoid, 1.5–2 mm long.

Bracts associated with the inflorescence, petals white, bilobed. Flowers are small, white, borne at the end of branches that a supported by a long stalk. Fruit is a dry capsule containing many rounded, compressed, roughly coated seeds. Capsules ovoid, 1.5-2.5 mm long, 3-valved; seeds reddish brown[13]. The key features of this species are the opposite, heart-shaped to circular leaves and the small white flowers with split petals that are shorter than the sepals.

ORIGIN AND DISTRIBUTION

D. cordata is native to tropical America with its distribution widely extended in the tropical regions of Asia, Africa, Central and South America[14] and in tropical and sub tropical India extending into the Himalayas up to an elevation of 2100 m. It occurs in many tropical and sub-tropical countries as a low
growing herb of predominantly moist soils[15]. It is a weed of cultivated areas which invades tea, coffee plantations as well as riverbanks, ditches and sandbars in rivers. This species is found from sea level to 1500 m, especially in shaded areas with moist soil[16]. The plant is abundantly or commonly distributed in foothill plain areas and gradually decreases in higher elevations. In Arunachal Pradesh, plants of *D. cordata* are distributed from foot hills up to 2500 m. a.s.l. range with its abundance in tropical and sub-tropical forest up to 1500 m. a.s.l. range. In Assam border it is widely distributed in paddy fields.

Classification

Kingdom	-	Plantae
Subkingdom	-	Tracheobionta
Superdivision	-	Spermatophyta
Division	-	Magnoliophyta
Class	-	Magnoliopsida
Subclass	-	Caryophyllidae
Order	-	Caryophyllales
Family	-	Caryophyllaceae
Genus	-	*Drymaria*
Species	-	*cordata*

Vernacular names and synonyms of D. cordata

English: Tropical Chickweed, Hindi: Pithpapra, Assamese: Laijabori
Manipuri: Tandal pambi, Nepali: Abhiijaani, Chinese**:** He lian dou cal
French: Mourron blanc, Petit mourron, Hawaiian: Pilipili, Pipili, Spanish: Chischina, Drimaria, Golondrina, Nervillo, Pajarera, Palitaria, Pega-pinto, Yerba de estrella

Synonyms

Stellaria adenophora, Drymaria procumbens, Alsine rotudifolia,Drymaria diandra Blume, Holosteum cordatum L

Ethno pharmacology and other uses

In different parts of North East India including Sikkim, numbers of folk-lore claims have been recorded by different workers regarding the uses of *D. cordata* (Table 1). The ethno pharmacological properties uses vary diversely from being used in skin treatment to more intrusive treatment like for dysentery etc.

Table 1
Uses of D. cordata by different ethnic groups of Northeast India

Place	Plant parts used	Uses
Assam	The plant	The plant is roasted in banana leaves and used for gastrointestinal trouble[17, 18].
Assam	The tender shoots	It is used in asthma and sinusitis[17, 18].
Assam	The plant	Young twigs when roasted with banana leaves are used for inhalation during sinusitis[19].
Sikkim (Bhutia,Lepcha and Nepalese)	Whole Plant	The plant is used in cold, cough, fever, headache and Pneumonia as well as sinusi- tis and nasal blockade. The plant is categorized under effective group of drugs[20].
Assam	Tender leaves, shoots	Tender leaves and shoots are vegetable. It is used as medicine for sinus problem, and in treatment of cuts & wounds of domesticated animal. It is herbal ingredient of preparation of rice beer[21].
West Bengal	Leaf	Used for medicinal purpose and also as fodder [22].
West Bengal (Darjeeling)	Whole plant	Used for the cure of skin diseases[23].
Arunachal Pradesh	Whole plant	Used for the cure of tooth ache[24].
Manipur	Whole plant	It is used to cure dysentery[25, 26].
Meghalaya	Whole plant	This plant is used as remedy in dysentery, in skin diseases, burns and stomach problems by war Jaintia tribes[4,27] It is used either separately or mixed with goat weed and *Gingiber officinales* rhizome or mixed with plants of Spilanthes sp, Binens beetel nut and *Gelingsoja* paraviflora[28, 29].
Nagaland	Whole Plant	This plant is used for snake bite for mouth diseases and to remove caterpillar hair from the body [30, 31, 32].

ACTIVE CONSTITUENTS

Plant containing active chemical constituents (alkaloid, glycosides, saponins, essential oils, bitter principles, tannins and mucilages) in its parts like root, stem, leaves, bark, fruit and seed, which produces a definite curing physiological response in the treatment of various ailments in humans and other animals, is regarded as medicinal plant. *D. cordata* is rich in saponins especially the pentacyclic triterpenoid types[33]. Murdiati and Stoltz 1987 detected the presence of alkaloid-like (pyrrolizidine) compounds in the plant[34]. The presence of alkaloids and saponins was also reported by[35]. The principal chemical compound found in this plant is methoxycanthin. However, it also contains starch and other compounds. The presence of succinic acid (crystal 28), alpha-spinasterol (crystal 1), and a mixture containing caproic, caprylic, capric, lauric, myristic, palmitic,stearic, oleic, linoleic and linolenic fatty acids (ether-insoluble residue) was also detected[9]. Cordatamine and the anti-leukemic substance, cordacin I have also been isolated and characterized from the plant[36]. Due to its medicinal properties, a number of biologically active compounds have been isolated from the leaves of *D. cordata* including, norditerpenes and norditerpene glycosides[37], Flavonoid glucosides[10], and Cyclopeptides[11].

PHYTOCHEMICAL ANALYSIS OF LEAVES OF D. CORDATA

This genus of sub-erect herbs has also been surveyed for phytochemical investigation[38]. Powdered forms of leaves were extracted successively with petroleum Ether (40 ºC – 60 ºC), benzene, chloroform, methanol, acetone by

using soxhlet extraction apparatus. For the identification of the phytochemicals, the solvents were completely pressed out from the marc, and were dried at room temperature. The solvents were distilled off under reduced pressure and the dried extracts thus obtained were used for further testing. The aqueous extract was prepared by maceration process using chloroform water. Venkatesan et al., 2003 have reported the presence of different phytochemicals from these extracts[38]. Venkatesan et al., 2003 have reported alkaloids and reducing sugar in chloroform, methanol, acetone and water extract[38]. Flavoniods in Petroleum ether, chloroform, methanol, acetone and water extract. Steroids in benzene, chloroform and methanol extract. Saponin in benzene, chloroform, methanol, acetone and water extract. Anthroqunone in methanol extract.

TISSUE CULTURE STUDIES IN D. CORDATA

An efficient regeneration protocol from the callus cultures is a requirement to employ any biotechnological approaches for genetic improvement of any taxa. *In vitro* micropropagation is now established as an alternate strategy for the mass multiplication of economically important plants[39]. There are efficient protocols for *in vitro* multiplication of *D. cordata* for mass propagation and also preservation of this valuable germplasm through direct organogenesis from nodal explants and leaf callus cultures[37]. Nodal cultures when raised on Murashige and Skoog (MS) medium supplemented with growth regulators like auxins and cytokinins either alone or in combination yield maximum number of shoots. Frequency of shooting response was even more (76.6 %) when nodal cultures of *D. cordata* were supplemented with only 6-Benzyl aminopurine (4.44 µM). Leaves of *D. cordata* cultured on MS basal medium supplemented with Naphthalene acetic acid (NAA) and 6-Benzyl aminopurine (BAP) produce creamish white profuse call us after three weeks of culture[37]. Shoot buds initiated from the callus after 8 weeks of culture on the solid MS medium develop roots on supplementation with auxins[37]. Another shoot regeneration in *D. cordata* was done using leaf explants cultured on Murashige and Skoog (MS) medium supplemented with a-naphthalene acetic acid (NAA) and 6-benzylaminopurine (BAP) [40]. The highest mean number of shoots per explant on MS plates was recorded as (10.65 ± 1.03) containing 3% sucrose and 0.8% agar supplemented with 0.1 mg/l NAA and 1.0 mg/l BAP. Shoot buds were stimulated in the basal parts of the leaf explants. Micropropagation technique offers an alternative method for cloning plants[41, 42].

MEDICINAL USES OF D. CORDATA

Anticarcinogenic effect of D. cordata L Willd

An anti leukemic compound (C_{17} H_{22} O_2) has been isolated from *D. cordata* which is has been reported to be effective and has an inhibitory effect on the primary cultures of human encomia cells[43]. In 2009, Sowemimo et al., studied cytotoxic activity of the ethanolic extracts of *D. cordata* using the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide) assay on the HeLa cell line[44]. The cytotoxic effect of plant extracts on HeLa (cervix adenocarcinoma) cell line was determined using a modification of the MTT assay[45]. Briefly, cells were seeded into 96-well culture plates at 6000 cells/well in RPMI1640:10 % fetal bovine serum (FBS) and left for 24 hours. Ethanolic extract of *D. cordata* was added and the cells incubated for a further 48 hrs after which the medium was replaced with 200 µl MTT. After, further 4 hr incubation at 37 ºC, the MTT was removed and the purple formazan product dissolved in DMSO and absorbance measured at 540 nm on a multi well scanning spectrophotometer. All incubation steps were carried out in a 37 ºC humidified incubator with 5 % CO_2. The assay detected over 50 % activity at 500 µg/ml.

Analgesic, anti-nociceptive and antipyretic effect of D. cordata **L Willd**

In a study, conducted to understand the analgesic and anti-nociceptive properties of the whole plant extract of *D. cordata*, various models *viz*. acetic acid induced writhing model (female mice), Eddy's hot plate (mice) and tail flick model (rat) were used for the study, while formalin-induced paw licking model (mice) was used for anti-nociceptive study[46]. *D. cordata*

(100, 200, and 400 mg/kg, p.o.) produced significant ($p<0.05$) analgesic activity in the mouse writhing, formalin (second phase), and tail clip tests. In formalin-induced paw licking model, administration of DCHE (*D. cordata* hydroethanolic extract) completely abolished the early phase at 100 and 200 mg/kg (p.o.) and in the late phase, the effect of DCHE (200 mg/kg, p.o.) was higher than indomethacin (10 mg/kg, p.o.). Akindele et al., 2012, reported the antipyretic activity of *D. cordata* in rodents by conducting the 2, 4-dinitrophenol (DNP)[47], d-amphetamine[48], and yeast-induced hyperthermia tests. *D. cordata* produced significant ($p<0.05$) dose-dependent inhibition of temperature elevation in the 2, 4-DNP and yeast-induced hyperthermia models with peak effects produced at the dose of 400 mg/kg. In the *d*-amphetamine method, *D. cordata* produced significant ($p<0.05$) dose- and time-dependent reduction of temperature elevation with peak effect produced at the dose of 200 mg/kg. Baruah et al., 2009 inferred that the aqueous whole plant extract of *D. cordata* possesses analgesic and antipyretic properties mediated through peripheral and central mechanisms[46].

Antitussive effect of D. cordata L Willd

Mukherjee et al., 1997 studied the antitussive activity of the methanol extract of *D. cordata*[7]. The study reported the effect of the methanol extract *D. cordata* on a cough model induced by sulfur dioxide gas in mice a dose dependent manner. The methanol extract *D. cordata* exhibited significant antitussive activity when compared with the control. The *D. cordata* extract (100, 200, 400 mg/kg) showed 11.6 %, 31.6 % and 51.5 % inhibition of cough with respect to the control group. The antitussive activity of the extract was reported to be comparable to that of codeine phosphate, a prototype antitussive agent.

Anxiolytic effect of hydroethanolic extract of D. cordata L Willd

The anxiolytic effect of *D. cordata*, has been reported from the hydroethanolic extracts of its leaves[49]. The hydroethanolic extract in *D. cordata* was administered at 25, 50 and 100 mg/kg (p.o.) to analyse anxiolytic effect of the extract. Different models such as hole board, Open field, Elevated plus maze and Light/dark exploration models were used in order to assess this activity. In hole board model, there was dose dependent and significant increase in the number of head pokes, in the open field test, the number of rearing and number of squares traversed increased significantly and in the remaining models, after treatment with DCHE, there were dose-dependent elevations in time spent, number of entries in open arm as those compared to the closed arm, latency period, etc. The presences of phytochemicals such as triterpines, diterpines, tannins and steroids have been implicated to be the contributor to its anxiolytic activity.

CNS depressant and anti-convulsant activity of hydroethanolic extracts of D. cordata L Willd

Barua et al., 2012 had reported the usefulness of *D. cordata* as a CNS depressant and anticonvulsant agent[50]. The hydroethanolic extract of *D. cordata* (DCHE) was administered in various behavioral models viz. spontaneous motor activity using actophotometer, anticonvulsant activity (electroconvulsion and chemoconvulsion test) and muscle relaxant activity (rotarod test). In spontaneous motor activity study, DCHE showed significant reduction in spontaneous motor activity in dose dependent manner and the maximum effect was observed at 200 mg/kg (p.o.) which was better than the standard drug. Administration of DCHE partially blocked tonic and clonic convulsions in dose dependent manner in maximal electroconvulsion and chemoshock convulsion tests in mice. But the extract was devoid of muscle relaxant activity. DCHE showed CNS depressant property as there was reduction in spontaneous motor activity. It showed anticonvulsant activity by exhibiting significant protection against electrical and chemical induced seizures but was devoid of muscle relaxant activity. DCHE showed significant reduction in spontaneous motor activity which might be closely related to sedation resulting from CNS depressant activity.

Anti-inflammatory activity of D. cordata L Willd

The anti-inflammatory activity of the aqueous extract of *D. cordata,* has been reported using the carrageenan, egg albumin, xylene induced oedema models and pleurisy test[9]. The extract (100 – 800 mg/kg) administered 1 h before induction of swelling in rat paw, by carrageenan and egg albumin injection, produced a significant ($p<0.05$) dose dependent inhibitory effect. The study showed that in the xylene test, *D. cordata* also elicited a dose dependent inhibition of ear oedema development, which reached a peak (61.39 %) at the dose of 800 mg/kg. The effect of indomethacin (10 mg/kg, p.o.) was lower in this respect, and was found to be 55.45 %. The extract (400 and 800 mg/kg) reduced the volume of pleural exudates and number of migrated leukocytes in the carrageenan induced pleurisy test. Greater inhibitory effect was observed at the dose of 400 mg/kg (53.74 % and 44.00 % decrease in exudates volume and leukocytes count, respectively). The effect of indomethacin was higher in respect of volume of exudates (65.99 %) but same in the case of leukocytes count (44.00 %). The results obtained in this study revealed that the aqueous extract of *D. cordata* possesses anti-inflammatory activity mediated possibly by the inhibition of one or a combination of mediators like histamine, serotonin, kinins and prostaglandins.

Antibacterial activity of D. cordata L Willd

The plant extract act as emollient, fibrefuge, laxative and stimulant as reported by Chopra et al., 1986[51]. The potential of *D. cordata* as an antibacterial agent has been reported from different extracts of *D. cordata* Willd (aerial parts)[52]. The different extracts of the aerial parts of the plant species were used for testing antibacterial efficacy against *Staphylococcus aureus* ATCC 29737, *Escherichia coli* ATCC 10536, *Bacillus subtilis* ATCC 6633, *Bacillus pumilis* ATCC 14884 and *Pseudomonas aeruginosa* ATCC 25619**.** The effects produced by the extracts were found to have noteworthy activities against all the organisms being tested and the effects so produced were compared with those of chloramphenicol. Earlier, the methanolic extract of *D. cordata* has been reported to be active against gram positive bacteria[53].

CONCLUSION

The efficacy of the drugs now-a-days have become more limited, hence the need for novel, better tolerated and more effectual treatments is are gaining a high score. In a way to circumvent this, herbal therapies can be considered as an alternative to complementary medicines. Recently, the search for novel therapies from medicinal plants for various illnesses has progressed significantly. This has been reflected in a large number of herbs whose potential has been assayed on a variety of animal models. *D. cordata* belongs to such group of plant species that has been blessed with quite a good number of herbal therapies for treatment of various day to day life ailments and also as folklore medicine, non-conventional vegetable food. It competes with seedlings and with low- and slow-growing crops for light and nutrients, raises the humidity around the bases of crop plants. It tolerates light to medium shade and germinates quickly after cultivation and other soil disturbance. *D. cordata* has its extreme potentiality in terms of its medicinal use as an anticarcinogenic, antibacterial, anti-inflammatory agent with a few more biological activities. In the moist and humid climatic conditions of Arunachal Pradesh, skin diseases like itching, ring worm and eczema and respiratory diseases like cold cough, asthma, sinusitis and headache etc. are very much prevalent. Since, most of the Folklore claims are strengthening for the use of *D. cordata* in skin respiratory and the stomachic diseases, and also the species is widely dispersed in the state and the other parts of the country to fulfill the required quantity for drugs on need. The existence of economically important medicinal plants is a blessing to mankind and hence, more efforts should be incorporated towards its conservation practice outstanding to the various turbulences caused to these plants.

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