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PHYTOPHARMACOLOGICAL PROPERTIES OF *CORDIA DICHOTOMA* AS A POTENTIAL MEDICINAL TREE: AN OVERVIEW

Anjana K. Patel*, Nimish Pathak, Hardik Trivedi, Mahendra Gavania, Mihir Patel, Nitin Panchal

C.U.Shah College of Pharmacy & Research,Wadhwan.

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For Correspondence:

Anjana K.Patel

C.U.Shah College of Pharmacy & Research,Wadhwan.

E-mail:
akpatel_2312@yahoo.co.in

ABSTRACT

Cordia dichotoma L. family Boraginaceae small to moderate-sized deciduous tree with a short bole, short crooked trunk and spreading crown. *Cordia dichotoma* is a tree of tropical and subtropical regions. It grows in the sub-Himalayan tract and outer ranges, ascending up to about 1 500 m elevation. Native : India, Myanmar, Nepal. Qualitative assay, for the presence of plant phytoconstituents such as carbohydrates, alkaloids, glycosides, flavonoids, tannins and saponins. Chemical screening of both the leaves and the fruits showed the presence of pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols. Various parts of this plant such as leaves, roots, seed, bark and fruit, possess immunomodulator, antidiabetic, anthelminitic, antiulcer, antilarvicidal and hepatoprotective. The present investigation deals with the qualitative and quantitative microscopic evaluation of the leaf material. Chief microscopic characters include vascular bundles having patches of perimedullary phloem. and unicellular and multicellular covering trichome.Chief characters of powder include xylem vessels with Reticulate thickening and oxalate prisms and clusters. Various phytopharmacological evaluations have been reported in this literature for the important potential of the *Cordia dichotoma.*

INTRODUCTION

History: *Cordia dichotoma*, the fragrant manjack or the bird lime tree, is a plant species in the genus *Cordia*.It is called gunda or tenti dela in Hindi and lasura in Nepali. The fruit of the Fragrant Manjack is called phoà-pò·-chí in Taiwan where they are eaten pickled.In Burma, the Pa-O people are growing the tree (called "thanapet") for its edible leaves.It is the symbol of Phra Nakhon Si Ayutthaya Province in Thailand and can be found in the Nacunday National Park in Paraguay.The larvae of the butterfly *Arhopala micale* feed on leaves of *C. dichotoma*. It is a tree of about 15 metres high, found spanning from north India and south China to Australia and Polynesia (Kirtikar *et al*.,1935). It grows wild in the northern part of Peninsular Malaysia but is planted in the south.

Classification:

Kingdom : Plantae

Division : Magnoliophyta

Class : Dicotyledons

Subclass: Asteridae

Order : Lamiales

Family : Boraginaceae

Genus : Cordia L. – cordial

Species :*Cordia dichotoma* G. Forst.

Fragrant: Manjack

Synonym : Cordia myxa forsk, *Cordia obliqua* Willd, *Cordia myxa* Roxb.

Commoname: Bhokar,Shleshmantaka..

Vernacular name:

Malaysia	Sekendal, sekendai, petekat
English	Sebestan plum, soap berry, fragrant manjack
India	Gonda, lasora, leshora
Javanese	Kendal

Sumatran	Nunang
Thailand	Paw man

Distribution:

Cordia dichotoma is a tree of tropical and subtropical regions. It grows in the sub-Himalayan tract and outer ranges, ascending up to about 1 500 m elevation. It is found in a variety of forests ranging from the dry deciduous forests of Rajasthan to the moist deciduous forests of Western Ghats and tidal forests in Myanmar. In Maharashtra, it grows in moist monsoon forest also. It does not grow gregariously, but is found growing singly in moist shady ravines and valleys. In areas with annual rainfall less than 500 mm, it thrives along streams or depressions where moisture is available· It does not grow gregariously, but is found growing singly in moist shady ravines and valleys. In areas with annual rainfall less than 500 mm, it thrives along streams or depressions where moisture is available (Abou Shaaban et al.,1989) It is found in a variety of forests ranging from the dry deciduous forests of Rajasthan to the moist deciduous forests of Western Ghats and tidal forests in Myanmar. In Maharashtra, it grows in moist monsoon forest also. It does not grow gregariously, but is found growing singly in moist shady ravines and valleys. In areas with annual rainfall less than 500 mm, it thrives along streams or depressions where moisture is available.

Documented Species Distribution: Native : India, Myanmar, Nepal.

Local Names:

Bengali (buhal, bahubara); English (sebesten, clammy cherry,Indian cherry);
Gujarati (vadgundo, gunda); Hindi (lasura, bhokar,borla);
Javanese(kendal); Lao (Sino-Tibetan) ('man,'man khôk);
Malay (petekat, sekendai), Tamil (vidi, naruvili, kalvirusu);
Nepali (kalo bohori, bohori); Thai (mandong, manma, phakmong)
Sanskrit (bahuvarka, Shleshmatak, Shelu);

Family: Boraginaceae

Botanical Description: *Cordia dichotoma* L. family Boraginaceae small to moderate-sized deciduous tree with a short bole, short crooked trunk and spreading crown. The stem bark is greyish brown smooth or longitudinally wrinkled. leaves simple, entire and slightly dentate, elliptical-lanceolate to broad ovate with a round and cordate base.These flowers are followed by 1 in (25mm) long dull pinkish edible fruits with sticky flesh (Sharma A et al.,2007) Flowers are short-stalked, bisexual and white in colour, appear in loose corymbose cymes. The fruit is a yellow or pinkish-yellow shining globose or ovoid drupe seated in a saucer-like enlarged calyx. It turns black on ripening and the pulp gets viscid. The hard stone is 1-4 seeded. The generic name honours a 16th century German botanist, Valerius Cordus (Ilhami GO et al 2004).The specific epithet means having divisions always in pairs.

Figure 1: *Cordia dichotoma* leaf

Macroscopic characters of Leaf:

Colour & Appearance: Light green

Odour: none and pleasant

Taste: mucilageous

Botany:

A tree growing to a height of 5 to 10 meters, deciduous and smooth or nearly so. Leaves are alternate, ovate to oblong-ovate or elliptic-ovate, 6 to 10 cm long, with entire or undulate margins, pointed tip and with pointed, rounded or heart-shaped base. Flowers are stalkless, white or yellowish-white, about 7 mm long and borne in lax inflorescences 5 to 10 cm long. The calyx is ovoid. The corolla tube no longer than the calyx with spreading and reflexed lobes. Throat of the corolla and stamens are hairy. Fruit is a drupe, yellowish white or pinkish, ovoid, 10 to 13 mm long with a rather scanty pulp and a hard stone. The persistent calyx in the fruit is broadly funnel-shaped;

enlargede and about 8 mm diameter (Burkill, H.M., 1985).Flowers are bisexual. Flowering takes place from March to May with the new leaves. The old leaves are shed during winter and the trees are leafless for a short period in early summer. Fruits are formed soon after flowering, develop quickly and ripen from June to August in north India and normally before May in south India. Seed dispersal is aided by birds and monkeys which feed on the ripe fruit (Patolia MB et al., 1993)

Biophysical limits:

Altitude: 200-1 500 m

Mean annual rainfall: 250-3 000 mm

Soil type: The tree prefers deep moist sandy loam soils.

Propagation:

Germination is epigeous. 1 or 2 seedlings may appear from 1 stone. Propagation is through seed which should be sown direct into containers, beds or trays and pricked out when the first pair of true leaves have formed. Sowing is done in June-July at a depth of 2 cm in lines spaced about 20 cm apart. A seed rate of 80 g/sq. m of nursery area is adopted. Germination starts in about 3-4 weeks and is complete in 6 weeks. At lower altitudes, plantable seedlings can be obtained after 3-4 months in the nursery, but at higher altitudes, 9-12 months are needed. In India raising plants from stumps has been carried out successfully(Taton, A., 1971). The stumps should be 8-13 mm thick at the root collar, with about 4 cm stem and 20-25 cm root. Such plants should be raised in beds for 12-15 months before stumping. Shading should be for only 1 week after seedlings have been pricked out, otherwise seedlings should have full light. Frequent weeding and root pruning is necessary. Seedlings should be ready for planting in the field in about 1 year at the commencement of monsoon rains. Germination is epigeous. 1 or 2 seedlings may appear from 1 stone. Propagation is through seed which should be sown direct into containers, beds or trays and pricked out when the first pair of true leaves have formed(Rapisarda A et al.,1992).

Biophysical limits:

Altitude: 200-1 500 m

Mean annual rainfall: 250-3 000 mm

Soil type: The tree prefers deep moist sandy loam soils.

Tree management:

Young seedlings are frost tender and also suffer from exposure to hot sun. They are susceptible to browsing and fire, but recover appreciably from these injuries. The tree coppices and pollards well. On good sites the trees reach a height of 4 m in 4 years and a diameter of over 20 cm in 8-9 years. From pole stage it prefers complete overhead light, but seedlings and saplings can withstand a fair amount of shade (Nanda N et al., 1991).

Germplasm management:

Ripe fruits are collected from the trees and rubbed to remove the flesh. The healthy stones are dried in the shade and kept in tin containers. The stones can be stored for 1 year in airtight containers kept in a dry place to avoid insect attack. There are 4 000-7 000 stones/kg (Taton, A., 1971).

Pests and diseases:

A large number of insect pests are reported, defoliators being among the most important. Larvae of some insects of the families Chrysomelidae, Glyphiplerygidae, Noctuidae, Lymantreedae, Notodontidae, Pyralidae, Sphingidae and Yponomeutidae defoliate the leaves. Larvae of Gracilariidae and Lyonetiidae mine the leaves and those of Eucosmidae roll the leaves. Larvae of some insects belonging to families Eucosmidae, Curculionidae and Pyralidae bore into the fruits and shoots (Rastogi et al., 1991). Austrothrips cochinchinensis forms galls and feeds on the sap. Aceria gallae and A. pobuzii infest C. dichotoma in Taiwan and cause galls on leaves, fruits, shoots and tender stems. The weevil Barioscapus cordiae, adults attack the fruits and feed on the green pedicel, sepals and pollen grains inside the buds.

Phytochemicals Qualitative assay, for the presence of plant phytoconstituents such as carbohydrates, alkaloids, glycosides, flavonoids, tannins and saponins(Parmar, N. S et al.,1998). Chemical screening of both the leaves and the fruits showed the presence of pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols(Alarcon, D. L et al., 1994). The fruit contains about 70% pulp; the pulp contains per 100 g: water 6 g, protein 35 g, fat 37 g and carbohydrate 18 g. The seed contains per 100 g: water 32 g, fat 46 g; the principal fatty acids are: palmitic acid, stearic acid, arachidic acid, behenic acid, oleic acid and linoleic acid Srivastava SK etal.,1979).The petroleum ether and alcoholic extracts showed significant analgesic, anti-inflammatory and anti-arthritic activities in tests with rats. Four flavonoid glycosides (robinin, rutin (rutoside), datiscoside and hesperidin), a flavonoid aglycone (dihydrorobinetin), and 2 phenolic derivatives (chlorogenic acid and caffeic acid) were isolated (Yang et al., 2002). The ethanol extract of the leaves reduced acetylcholine-induced contractions of guinea-pig ileum. Ethanol extracts from fruits and leaves showed significant antioxidant activities due to the carotenoids but no antimicrobial activity against gram-positive or gram-negative bacteria. Medicine: Seeds of the species are anti-inflammatory, 2 compounds alpha-amyrin and 5-dirhamnoside have been isolated (Larson RA., 1998)

The bark is medicinal and several chemicals have been identified; Allantoin, beta -sitosterol and 3',5-dihydroxy- 4'-methoxy flavanone-7-O- alpha -L-rhamnopyranoside (Tiwari KP et al.,1979). *Cordia dichotoma* seeds have disclosed the presence of α-amyrins, betulin, octacosanol, lupeol-3- rhamnoside, β-sitosterol, β-sitosterol-3-glucoside, hentricontanol, hentricontane, taxifolin-3, 5-dirhmnoside and hesperitin-7-rhamnoside. The seed contain α-amyrin and toxifolin 3, 5, dirhamnoside, which shows significant anti-inflammatory activity by an oral dose of 1gm/kg in albino rats. The seeds of this plant reported to contain fatty acids and flavonoids (Aguilar, N.O., 2001). The chemical compounds: robinin, rutin, datiscoside, hesperidin, dehydrorobinetin, chlorogenic acid and caffeic acid isolated from *C. francisci, C.*

myxa and *C. Serratifolia.* The leaves contain 12-15% crude protein, 16-27% crude fibres, 42-53% nitrogen free extract, 2-3% ether extract, 13-17% total ash, 2-4% total calcium and \about 0.3% phosphorus.

Traditional used: The bark decoction is used to treat dyspepsia. The powdered bark is applied to mouth ulcers. The bark is also used to treat fever, abscesses and tumours. It is mixed with the pomegranate rind to treat dysentery. The extract of the bark mixed with coconut water relieves severe colic. The mucilage of the fruit treats coughs and other chest complaints. It is also used to treat uterus and urethra disorders. The kernel of the fruits in powder form is mixed with oil to heal tinea. The plant is also a diuretic and a laxative. (Ficarra, R et al., 1995)

Pharmacological properties

Acute toxicity study: This study was designed to elucidate the toxicity of the widely used plant *Cordia dichotoma* in rats (Lorke D., 1983). The methanolic, chloroform, aqueous extracts isolated from the leaves of *Cordia dichotoma* and studied their toxic effects. Acute toxicity and LD50 values were determined in experimental rats. The dead animals were obtained from primary screening studies, LD50 value determination experiments and acute studies subjected to postmortem studies. The external appearance of the dead animals, the appearance of the viscera, heart, lungs, stomach, intestine, liver, kidney, spleen and brain were carefully noted and any apparent and significant features or differences from the norm were recorded. Following the chronic administration of *Cordia dichotoma* or 14 days, the vital organs such as heart, liver, kidney, testis, spleen and brain were carefully evaluated by histopathological studies and any apparent and significant changes or differences from the norm were studied. From the acute administration of *Cordia dichotoma* the LD50 values were determined using graphical method. The hearts stopped in systolic stand-still in the acute experiments. There were no remarkable changes noticed in the histopathological studies after 50 mg/kg body wt of the extracts of *Cordia dichotoma* when administered intraperitoneally for 14 days successively. Pathologically, neither gross abnormalities nor histopathological changes were observed. After calculation of LD50 values using graphical methods, we found a broad therapeutic window and a high therapeutic index value for *Cordia dichotoma* extracts. Collectively, these data demonstrate that the extracts of the leaves of *Cordia dichotoma* have a high margin of drug safety.

Antiulcer Activity: Study yielded flavonoids in all three extracts of CD tested and showed significant anti-ulcer and cytoprotective effects against gastric ulcer in rats.

The anti-ulcer effect of extracts of *Cordia dichotoma Forst.f.* fruits (300mg/kg body weight) was studied in albino rats of Wistar strain using three different models i.e. pyloric ligation, aspirin and indomethacin induced ulcers(Wassel G et al.,1987). The extractions of *C.dichotoma Forst.f.* fruits were carried out using ethanol. This extract was fractionated using petroleum ether, solvent ether, ethyl acetate, butanol and butanone in succession. Gastric mucosal injury was produced in rats by pyloric ligation, aspirin and indomethacin induced models. Extracts of petroleum ether, solvent ether, ethyl acetate, butanol and butanone were

administered in a dose of 300 mg/kg body weight. The parameters taken to assess anti-ulcer activity were volume of gastric secretion, free acidity, total acidity and ulcer index. The results indicates that, extracts of ethyl acetate, butanol and butanone significantly ($p< 0.001$) decrease the volume of gastric secretion, free acidity, total acidity and ulcer index with respect to control. The results suggest that the extracts of *Cordia dichotomaForst.f*. fruits possess significant anti-ulcer activity.

Hepatoprotective activity: Study of the methanolic extract of *Cordia dichotoma* studied its hepatoprotective action in male Wistar rats with carbon tetrachloride induced heart damage(/ K Thirupath et al., 2007).

Protective role of *Cordia myxa L.* (CM) against liver fibrosis induced by carbon tetrachloride (CCl4) or thioacetamide (TA) was investigated. Plant was extracted in different solvents and the extracts were evaluated for their phenolic content and antioxidant activity. Phenolic content was measured using Folin-Ciocalteu reagent and was calculated as gallic acid equivalents. Antiradical activity of *C. myxa* extracts was measured by α,α-diphenyl-β-picrylhydrazyl (DPPH) assay and was compared to ascorbic acid. One milligram of the crude extract was found to be equivalent to 15µg of ascorbic acid. Protective role of *C. myxa* against carbon tetrachloride or thioacetamide induced fibrosis was assessed in serum aspartate transaminase (AST), glutamate transaminase (ALT) and alkaline phosphatase (ALP). Level of these enzymes significantly improved in rats after administration of (CCl4) + CM, or (TA) + CM as compared to rats that were treated alone with CCl4 or TA. It was found that the fresh *C. myxa* extract offered better protection against liver fibrosis induced by these chemicals.

Wound Healing activity: Study of fruit extracts of C dichotoma showed significant wound healing activity on three different models, viz. excision, incision and dead space wound models on albino rats(Kuppasta I.J et al.,2006).

The extraction of fruits of *Cordia dichotoma* Forst. f. was carried out using ethanol. This extract was further fractionated using petroleum ether (40-60%), solvent ether, ethyl acetate, butanol and butanone in succession. These fractions were screened for wound healing activity using three different models, viz. excision, incision and dead space wound models on either sex of albino rats of Wistar strain. All the fractions showed significant ($P<0.001$) activity on The fruits contain large quantities of amino acids, flavonoids, and saponins and are used as wound-healing agent in households.

Anti-Inflammatory activity: Screening showed the ethanol extract and aqueous fraction of C. dichotoma possess acute anti-inflammatory activity(Parmar, N. S et al.,1998).

The effects of *Cordia dichotoma forst f.* seeds extracts on different phases of acute inflammation were examined. Investigations were performed using different phlogistic agents-induced paw edema *viz*., Carrageenan-induced paw oedema and Dextran- induced paw oedema in rats. Various extracts (ethanol and aqueous) of *Cordia dichotoma forst* seeds at a dose of 250 mg/kg and 500 mg/kg orally were tested. Diclofenac sodium at the dose of 10mg/kg was used as standard. Both the extracts showed significant activity ($*p<0.05$ & $**p<0.01$) compared with the

control in both of these models. The dry powdered seeds were found to contain alkaloids, glycosides, saponins, tannins and carbohydrates. Thus it is revealed from the screening model used that the ethanol extract and aqueous fraction of this plant possesses acute anti inflammatory activity (Al-Awadi FM et al., 1999).

Antidiabetic activity: Antihyperglycemic effects of *Cordia dichotoma* linn in the glucose induced hyperglycemia (Kirtikar et al.1934,).

The effect of the aqueous extract of alloxan induced and normoglycemic Wister rats has been investigated. Three doses of the extract (250 mg/kg; 500 mg/kg and 1000 mg/kg) were administered orally. The 500 mg/kg extract of *Cordia dichotoma* did not show any significant change in the blood glucose levels in normoglycemic and 250 mg/kg did not show any significant change in the blood glucose levels in alloxan Induced Diabetic Wister rats, when compared to untreated control. The dose 500 & 1000 mg/kg of extract showed a significant ($p<0.5$) decrease in blood glucose levels after 4, 8 and 24 hours. In normoglycemic rats, the dose of 1000 mg/kg of the extract significantly ($p<0.05$) decrease the blood glucose levels at 8 and 24 hours. In conclusion, the doses of extract has shown both significant ($p<0.05$) hypoglycemic and antihyperglycemic effects in Wister rats (Day C.,1983).

Degenerative disorders: Role of *Cordia dichotoma* seeds and leaves extract in degenerative disorders(Sharma A et al.,2007).

A common theme which underlies etiology of several degenerative disorders is free radical induced stress. Free radicals prime the immunomodulatory response, recruit inflammatory cells and are innately bactericidal. In the body, excess production of free radicals affects lipid cell membranes to produce lipid peroxides and reactive oxygen species (ROS) which leads to decline in membrane fluidity and many biological changes, such as DNA damage, ageing, heart disease and cancer etc. Antioxidants serve as free radical scavengers, neutralizing and defending the body from a number of diseases which are born because of generation of free radicals. They offer defense against radical toxicity by antagonizing the damages caused by free radicals. The current study is therefore carried out to investigate the free radical scavenging potential of methanolic extract of seeds and leaves of *Cordia dichotoma* using *in-vitro* models viz. DPPH and hydrogen peroxide model. These models demonstrate positive antioxidant activity in a concentration dependent manner and demonstrate that highest concentration exhibits highest (100µg/ml) antioxidant activity. This activity was more pronounced in leaves as compared to seeds

Antimicrobial activity: Consequently, data pertaining only to that showed inhibitory activities against all the tested bacterial, fungal and yeast species. Extracts of *Cordia dichotoma* showed moderate activity against the tested organisms. Water extracts of the *Cordia dichotoma* plants did not show any antimicrobial activity against all the tested microorganisms (Kuppasta, I.J et al., 2003).

Miscellaneous activity: A method of treating a human body for delaying effects of ageing on skin thereof, by applying to a part of the skin in need thereof of a cosmetic or pharmaceutical composition containing an amount of an extract of *Cordia dichotoma* effective to inhibit activity of elastase in the skin, obtaining thereby the delaying of the effects of ageing on the skin and also some extend Larvecidal activity.

Microscopic evaluation of *Cordia dichotoma* leaf:

The present investigation deals with the qualitative and quantitative microscopic evaluation of the leaf material. Chief microscopic characters include vascular bundles having patches of perimedullary phloem shown in figure 3. and unicellular and multicellular covering trichomes shown in figure 4.

Figure.3 Unicellular and multicellular covering trichomes

Microscopic evaluation of *Cordia dichotoma* Powder

Chief characters of powder include xylem vessels shown in figure 4 with Reticulate thickening and oxalate prisms and clustersshown in figure.5

Figure.4 Xylem vessels

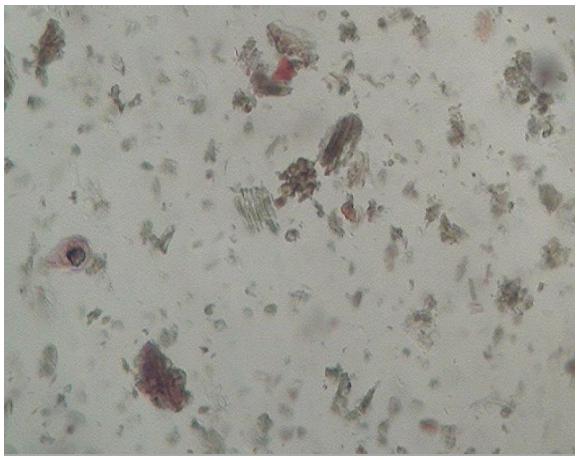

Figure.5 Calcium oxalate prisms and clusters

CONCLUSION

Numerous phytochemical and pharmacological studies have been conducted on different parts of *Cordia dichotoma.* The present literature supports the potential of *Cordia dichotoma* as a medicinal tree. In view of the nature of the plant, more research can be done to investigate the unexplored and unexploited potential of this plant.

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