Abstract

*Cordia dichotoma* is a tall tree which grows in Sri Lanka, India and other warmer countries. Its medicinal properties are known since long time and it is traditionally used to cure several ailments. Its fruits are used as expectorant, astringent, coolant, emollient, purgative and anthelmintic. Anti-inflammatory, analgesic, hepatoprotective and several other pharmacological activities have also been reported from the plant. Aim of the current review was focused on the assessment of its present medicinal uses, phytochemistry and pharmacology in order to reveal its complete pharmacological and therapeutic potentials. Literature survey performed on electronic sources, scientific journals as well as books showed that this plant is of an enormous value because of its various potent pharmacological actions shown by it and several pharmacologically active principles like apigenin, arabinogalactan, quercetin which have been isolated from it. It will be certainly valuable to explore it for further research to be carried out on this medicinal plant.

Keywords - *Cordia dichotoma*, Pharmacology, Phytochemistry, Traditional uses

Introduction

*Cordia dichotoma* belonging to family Boraginaceae is a 3-4 m tall tree with 2-5 cm long petiole, 6-13x4-9 cm leaf blade ovate to elliptic, sparsely pubescent or glabrous, margin usually subundulate to undulate dentate which grows in Sri Lanka, India and other warmer countries (Fig. 1) (1). It is commonly known as Indian cherry in English and Lasora in Hindi. Its medicinal properties is known since long time and traditionally used to cure several ailments. Its fruits are used as expectorant, astringent, coolant, emollient, purgative and anthelmintic (2). Anti-inflammatory, analgesic, anticancer, hepatoprotective and several other pharmacological activities have also been reported from the plant (3, 4, 5). ‘Instant Joshanda Granules’, a polyherbal formulation, is extensively used by the people of India for the treatment of cough, sore throat, catarrh, common cold, respiratory distress, flu-like ailments and fevers of which *Cordia dichotoma* is the chief ingredient (6).

Traditional uses: Leaf paste of *Cordia dichotoma* Forst is given to the animal with water for the treatment of diarrhea in Udaipur district of Rajasthan. Leaves and fruits of the plant *Cordia dichotoma* are given to the animals suffering from leucorrhoea (7). The fruit of the plant is used as purgative, diuretic, anthelmintic and is useful in dry cough, wound purification, mouth ulcer cure and jaundice cure and to increase male potency (8, 9). Leaves of the plant are used for headaches and ulcers including decoction for sore throat (10). The bark of the plant is used in the treatment of ulcerative colitis.
and colic pain (8). 100 g powder of stem bark is taken with a glass of water to cure menstrual disorders by Korku tribe of Amravati district of Maharashtra, India (11). It is used as abortifacient in traditional or folkloric medicine (12). The pickled fruit is eaten as an appetizer in certain areas of Taiwan. The indigestible seeds and sticky pulp of the fruit can form a phytobezoar if ingested excessively (13).

**Phytochemistry:** The dry powdered seeds of *Cordia dichotoma* were found to contain glycosides, alkaloids, carbohydrates, tannins and saponins (14). Alkaloids, flavonoids, amino acids and proteins are present in the fruits of *Cordia dichotoma* (8, 9). Qualitative phytochemical tests, thin layer chromatography and TLC-bioautography of the ethanolic extract of leaves demonstrated the presence of common phytoconstituents phenols, tannins and glycosides as major active constituents (15, 16). The antinutritional factors such as phytic acid (0.2±0.1%), tannin (1.386±0.0152%) and oxalic acid (2.133±0.2081%) were found to be present in the powdered wild edible fruits of the plant. Saponin was absent (17). *Cordia dichotoma* Forst bark was identified as botanical source of Shleshmataka in Ayurvedic pharmacopoeia (18). Apigenin was isolated by column chromatography from methanolic fraction of crude methanolic extract of *C. dichotoma* bark (19). Arabinoglucan was isolated from the fruits of *Cordia dichotoma* Forst (20). The phytoconstituents arabinoglucan, D-glucose and L-arabinose were present in fruits; linolenic acid in seed; and quercetin in leaves (21). The structure and properties of the newly identified natural cellulose fabrics from the branches of the *Cordia dichotoma* indicated that they could be appropriate for blending and processing by biodegradable polymers to make green composites (22).

**Pharmacological activities**

**Analgesic, antibacterial and cytotoxic activities:** The crude ethanol extract of the leaves of *Cordia dichotoma* produced significant writhing inhibition in acetic acid induced writhing in mice at the oral dose of 500 mg/kg b wt (p<0.001) which was comparable to that of the standard drug diclofenac sodium at the dose of 25 mg/kg b wt. The extract showed significant zone of inhibition against both Gram negative and Gram positive bacteria *Streptococcus aureus, Streptococcus pyogenes, Vibrio cholerae, Streptococcus epidermis, Hafnia and Escherichia coli* in disc diffusion study which is comparable to that of Kanamycin (30 ìg/ml). The extract also showed potent toxicity against the brine shrimp *Artemia salina* (LC50: 20 ìg/ml and LC90: 180 ìg/ml) in brine shrimp lethality bioassay (3).

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**Fig. 1.** Parts of *Cordia dichotoma*. (A) Whole plant; (B) twig with leaves and fruits; and (C) twig with flowers.

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Anthelmintic activity: Five concentrations (10, 25, 50, 75 and 100 mg/ml) of ethanolic and aqueous extracts prepared from pulp obtained after separation of seeds from fruits of *Cordia dichotoma* Forst by Soxhlet extraction were studied for anthelmintic activity by using *Eudrilus euginiae* earthworms. Both ethanolic and aqueous extracts showed paralysis and death of worms in concentration dependent manner. Aqueous extract showed significant activity than ethanolic extract. The extracts also showed the presence of alkaloid, glycoside, saponin, flavonoid, triterpenoid, protein, amino acid and carbohydrate in preliminary phytochemical investigation (2).

Antibacterial activity: Antibacterial activity of alcoholic and aqueous extracts of thirty four medicinal plants including *Cordia dichotoma* were screened for potential antibacterial activity against six bacterial strains belonging to Enterobacteriaceae, viz., *Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Salmonella typhimurium*, *Proteus mirabilis* and *Proteus vulgaris* by the agar well diffusion and disc diffusion methods. The ethanol extracts were more active than aqueous extracts for all the plants studied. Aqueous extract of *Cordia dichotoma* inhibited only to *Proteus mirabilis*, while ethanolic extract inhibited to *Klebsiella pneumonia* and *Proteus mirabilis* (23).

Antibacterial activity of *Cordia dichotoma* leaves extract studied by two different methods i.e. well diffusion and disc diffusion methods against the strain of *E. coli* revealed that it possesses antibacterial activity against *E. coli*. The activity of extract is due to the flavonoid active constituent. Phytochemical analysis showed positive result for tannin, protein and flavonoid (24).

Antibacterial activity of petroleum ether, chloroform, methanol and aqueous extracts of *Cordia dichotoma* Forst ripened fruits against urinary tract pathogens such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris* and *Staphylococcus aureus* using disc diffusion method was evaluated. Results of the study showed that the methanolic extract exhibited better antibacterial activity against the bacterial strains as compared to other extracts (25).

Antioxidant activity or free radical scavenging activity: The methanolic extract of seeds and leaves of *Cordia dichotoma* demonstrated positive antioxidant activity in a concentration dependent manner during investigation of their free radical scavenging potential using *in vitro* models viz., 1,1-diphenyl-2-picrylhydrazyl (DPPH) and hydrogen peroxide (H₂O₂) models. The IC₅₀ values for the leaves were found to be 51.83 μg/ml and 55.73 μg/ml for DPPH and H₂O₂ models respectively. The IC₅₀ values for seeds were found to be 57.22 μg/ml and 48.28 μg/ml for DPPH and H₂O₂ models respectively. In both the models, the methanolic extract of the leaves exhibited low IC₅₀ values as compared to the seed’s extracts. Thus, this activity was more pronounced in leaves as compared to seeds (26).

During nitroblue tetrazolium chloride (NBT) superoxide radical scavenging assay, maximum antioxidant activity of ethanol and acetone extracts of the fruits of the plant *Cordia dichotoma* was noticed to be 54.5 and 55.5 % respectively. The inhibitory potential expressed in IC₅₀ values of acetone and ethanol extracts of *C. dichotoma* were found to be 131.0 and 149.0 μg/ml respectively (27).

The activity of peroxidase (POX), superoxide dismutase (SOD) and catalase (CAT) was determined in the fruits. The SOD and CAT activities were increased in mature fruits than ripened fruits, whereas POX activity was found to be more in ripened fruits as compared to mature fruits (28).

*C. dichotoma* contains a considerable amount of phenols. The IC₅₀ value was found to be 28 μg/ml for the methanolic extract and 36 for butanolic extract in DPPH scavenging assay. The study revealed that the bark has significant radical scavenging activity (18).

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Antidiabetic activity: Marles and Farnsworth provided information on more than 1200 species of plants reported to have been used to treat diabetes and/or investigated for antidiabetic activity, with a detailed review of representative plants and some of great diversity of plant constituents with hypoglycemic activity (29). The aerial parts of *Cordia dichotoma* administered orally were devoid of normal antidiabetic activity.

The dose of 500 and 1000 mg/kg b. wt. of aqueous extract of the leaves administered orally to alloxan induced and normoglycemic Wistar rats showed a significant (p<0.5) decrease in blood glucose levels after 4, 8 and 24 h. The dose of 1000 mg/kg b. wt. of the extract in normoglycemic rats significantly (p<0.05) decreased the blood glucose levels at 8 and 24 h (30).

The methanolic extract of the fruits of *Cordia dichotoma* reduced the blood glucose level in glucose loaded animal and alloxan induced diabetic animal models when compared to diabetic control group and exerted significant hypoglycemic and antidiabetic activities compared to standard drug metformin. The extract also reduced the rate of body weight loss in normal and alloxan induced diabetic animals (31).

Antimicrobial activity: Alcohol is found to be a better solvent for extraction of antimicrobially active substances compared to water and hexane (32). Ethanol extract of the leaves showed antimicrobial activity only against *S. aureus* (inhibition zone: 21-30 mm) and *S. dysenteriae* (inhibition zone: 10-20 mm) in the study antimicrobial activity against certain drug-resistant bacteria *Salmonella paratyphi*, *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Shigella dysenteriae* and a yeast *Candida albicans* of clinical origin. No correlation was observed between susceptibility of test strains with the extract and antibiotic resistance behavior of the microbial strains (15).

The acetone, chloroform, hexane, aqueous and ethanol extracts of the *C. dichotoma* leaves and the chloroform, aqueous and acetone extracts of the *C. dichotoma* stem bark did not show any antimicrobial activity against tested strains of bacteria and fungi determined by macrobroth dilution method on the concentration of 25 mg/ml to 0.10 mg/ml of the extracts. Only the hexane and ethanol extracts were active against only certain fungal strains (33).

The acetone and ethanol extracts of *Cordia dichotoma* fruits exhibited highest antimicrobial activity against *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans* and *Aspergillus niger*. Acetone extract showed maximum inhibitory zone of 19.1 mm whereas no inhibitory effect was observed for the aqueous extract (27).

Petroleum ether, benzene, chloroform, acetone, methanol and aqueous extracts of the plant were investigated for the antimicrobial efficacy by modified Kirby-Bauer disc diffusion method against the clinical isolates of oral cancer cases like the fungal pathogens *Aspergillus fumigates*, *Candida albicans* and bacterial pathogens *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Proteus mirabilis*. Only *S. aureus* was inhibited significantly by the petroleum ether and acetone extracts (inhibition zone: 10 and 11.33 mm respectively; MIC: 250 and 125 ìg/ml respectively), while only *S. epidermidis* by aqueous extract (inhibition zone: 10.33 mm; MIC: 125 ìg/ml). Even, other isolates were not inhibited by the remaining extracts (34).

The methanolic and butanolic extracts of the bark showed remarkable zone of inhibition of bacterial growth and fungal growth comparable with that of standard drugs against the organisms tested *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus pyogenes*, *Staphylococcus aureus*, *Aspergillus niger*, *Aspergillus clavatus*, and *Candida albicans*. The activity of the extracts increased linearly with increase in extract concentration (35).

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Antiulcer activity: Ethyl acetate, butanol and butanone fractions of ethanolic fruit extract significantly decreased the volume of gastric secretion, free acidity, total acidity and ulcer index with respect to control during the study of anti-ulcer effect of fruit extracts (300 mg/kg b wt) in Wistar rats using pyloric ligation, aspirin and indomethacin induced ulcer models (36).

The aqueous extract of fresh ripened fruits was found to be more effective than alcoholic extract as compared to ranitidine in aspirin induced gastric ulcer model (p<0.01) as well as in pylorus ligation model in rats (37).

Anti-inflammatory activity: The ethanolic and aqueous extracts of Cordia dichotoma Forst seeds at a dose of 250 mg/kg and 500 mg/kg orally showed significant activity compared with the control and diclofenac sodium (10 mg/kg as standard) in dextran-induced paw edema and carrageenan-induced paw edema models in rats on different phases of acute inflammation (14).

Apigenin (5 mg/kg b wt, po) showed significant healing and reduction in inflammatory enzymes myeloperoxidase (MPO) (from 360±0.2 U/ml due to acetic acid induction to normal 222±22.5 U/ml due to treatment) and malondialdehyde (MDA) (from 9.98±1.5 nmol/ml to 2.11±1.5 nmol/ml) when screened for ulcerative colitis induced by intrarectal administration of 150 il, 5% acetic acid (pH 2.5) 3 cm from the anal margin. It was concluded that apigenin from C. dichotoma bark may be responsible for the treatment of ulcerative colitis (19).

The methanol fraction of methanolic extract of C. dichotoma bark showed effective treatment of ulcerative colitis. It showed good healing and lower pathological scores in treated animals. It significantly reduced MDA and MPO levels in tissue and blood. It showed antioxidant potential and contains a high level of phenolics (38).

Anticerebrovascular insufficiency activity: Long term cerebral hypoperfusion in rats resulted in propensity towards listlessness and anxiety (elevated plus maze test and open field paradigm) accompanied by deficits in memory and learning (Morri’s water maze test) and tendency towards depression (Porsolt’s swim test). Gliosis, cellular edema, astrocytosis and inflammatory changes were observed in forebrain. Treatment by Cordia dichotoma (250 mg/kg po for 28 days) alleviated these cognitive, behavioral and histopathological changes suggesting that Cordia dichotoma may be useful in cerebrovascular insufficiency conditions (39).

Binding property: The mucilage isolated from the aqueous filtrate of macerated seeds, whose pulp was previously removed, possesses binding property comparable to the starch. An increase in mucilage concentration led to decrease in friability and increase in disintegration time of the tablets (40).

Angiotensin converting enzyme inhibitory activity: The ethanolic extract of bark showed high ability to inhibit the angiotensin converting enzyme (41).

Diuretic activity: Petroleum ether, solvent ether and butanol fractions of alcoholic extract of the fruits 300 mg/kg b wt were tested for diuretic activity in rats for total urine volume, urine concentration of Na+ and K+ and showed increase in cation excretion and urine volume (42).

Hepatoprotective activity: The methanolic extract of the leaves (300 mg/kg) significantly reduced the alanine aminotransferase (ALT) (p<0.001), aspartate aminotransferase (AST) (p<0.001) and thiobarbituric acid reactive substances (TBARS) levels (p<0.01); and at 500 mg/kg extract dose significantly reduced the AST (p<0.001), ALT (p<0.001), TBARS (p<0.01) and lipid peroxide levels (p<0.05) in male Wistar rats with liver damage by carbon tetrachloride treatment (4).

Antifertility activity: The reversible nature of the developed phytopharmaceutical was studied by performing pharmacological analyses followed by chronic toxicity studies. The biochemical and

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histological estimations detected the reversible contraceptive potential of the drug after withdrawal. The observations also suggested that the developed phytopharmaceutical had potential antifertility activity with safety aspects (43).

**Wound healing activity:** Petroleum ether, solvent ether, ethyl acetate, butanol and butanone successive fractions of the ethanolic extract of *Cordia dichotoma* fruits showed significant (p<0.001) wound healing activity on excision, incision and dead space wound models on Wistar albino rats (44).

**Conclusion**

Current review summarizes many important pharmacological studies, phytochemical investigations and isolated phytoconstituents of *Cordia dichotoma* which can be further assessed to find out lead molecules in the search of novel herbal drugs for the treatment of several diseases.

**References**


