Review Article

Phytochemical and pharmacological properties of *Cordia dichotoma* (Bhokar): A short review

Anjali Ganjare*, Nishikant Raut

Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur- 440033 (Maharashtra), India

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Abstract

Objective: Aim of present review is to explore the pharmacognostic, pharmacological and folkloric literature of *C. dichotoma.* **Methods:** Exhaustive literature survey was carried out on various search engines including but not limited to Google scholar, Science Direct, PubMed, Science hub, Research gate and Scopus. The offline literature survey was carried out at RTM Nagpur University library, University of Pune library and Pravara Rural College of Pharmacy, Ahmednagar. **Results:** *C. dichotoma* is widely used plant in traditional medicinal systems for various diseases and in many culinary preparations in many Asian countries. Its polysaccharides rich ripen fruits produce jelly-like sticky mass, mainly used for preparation of pickle in India. Its bark contains tannins, resins, saponins, diterpenes, cordifolic and cordioic acid as main chemical constituents. Unani medicinal system showed antimicrobial, antiviral and anti-tussive uses of this plant. Polyherbal formulations containing *C. dichotoma* as chief ingredients are extensively used in India for the treatment of common cold, catarrh, cough, respiratory distress and fevers. Since ancient time, leaves and stem, bark are used in the treatment of dyspepsia, fever, diarrhea, leprosy, gonorrhea and burning sensation. Leaves of the plant have been shown to have anti-helminthic, astringent, diuretic, demulcent, purgative, expectorant, properties. Present literature review has been envisaged with an intension to provide scientific information about phytochemical and pharmacological profile of *C. dichotoma*. **Conclusion:** *C. dichotoma* is highly useful plant. Traditional claims have been scientifically validated by various researchers all over the world. Extracts of various parts of this plant can be safely used for various human ailments such as common cold, catarrh, cough, respiratory distress and fevers.

***Keyword*:** *C. dichotoma,* Phyto-chemical, Pharmacology, antioxidant, ulcerative colitis

Introduction

Cordia dichotoma Forest. f. (Boragineae) is a middle sized (3-5 meters) tree grows nearly all over the Indian sub-continent and cultivated particularly in Bengal (Nadkarni, 1982). *C. dichotoma* tree has glabrous branches, soft wood which is light grey in color. Theodore Cooke (1905) in his book 'The flora of the presidency of Bombay' vol. II has described the botanical synonyms of this plant which includes *C. latifolia, C. obliqua, C. myxa , C. dichotoma*. Leaves are entire or slightly dentate, more or less rough, elliptic lanceolate to broad ovate in shape, and often with a rounded or cordate base (Nadkarni, 1982; Kiritikar and Basu, 1991). Its buds are nearly globose and flowers are small, terminal, axillary pedunculated and glabrous. Fruits are generally sweetish, demulcent, mucilaginous and contains sugar and gum. Bark contains principle allied to cathartins. Stem shows branchlets glabrous, wood soft, light gray no heartwood (Nadkarni, 1982; Kiritikar and Basu, 1991). Fruits are long yellow brown to pink in color, sweetish in taste, viscid with transparent pulp (Nadkarni, 1982; Kiritikar and Basu, 1991).

Methodology

An exhaustive literature survey was carried out through various journals, data bases and internet search engines available up to December 2018. Scientific data and published reports available offline and online journal were collected. The main source of data collection was articles both research and review published by reputed publisher like Elsevier, Springer, Taylor and Francis etc. Online databases like PubMed, Google scholar, Science hub, Research gate,

Address for Corresponding Author:
Anjali Ganjare,
Department of Pharmaceutical Sciences,
Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur – 440033 (Maharashtra), India
Email: ianjali@rediffmail.com

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Scopus and Science Direct and various books from the libraries of R.T.M, Nagpur University (Nagpur), University of Pune (Pune) and Pravara Rural College of Pharmacy (Loni, Ahmednagar) were also referred for gathering all available data on the plant. Herbarium "10003' in the Post Graduate Teaching Department of Botany, RTM Nagpur University, Nagpur, was used to collect data regarding the morphological identification characteristics of the tree and expert botanist of the same department was consulted to authenticate the identification of the plant. Indian Medicinal Plant Database and Encyclopedia on Indian Medicinal Plants were referred to explore the importance of plant in the Indian systems of medicine. The present literature review has been envisaged with an intension to provide scientific information about the phyto chemical and pharmacological profile of *C. dichotoma*. The detailed phytochemical and pharmacological review of *C. dichotoma* is as follows.

Literature was collected using Google, Scholar, PubMed and Science direct using the following keywords: *C. dichotoma*, Bhokar (Marathi name), Gunda (Hindi name), Phytoconstituents of *C. dichotoma*, pharmacological activities of *C. dichotoma*, antioxidant, anti-inflammatory, antiulcer activities of *C. dichotoma*. This review highlights the phytoconstituents of the *C. dichotoma* and also explores its pharmacological, neutraceutical and folkloric uses.

Phytochemical Studies

The Phytochemical literature revealed that the leaves and the fruits contain presence of pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols. Six flavonol glycosides and two phenolic compounds were isolated from butanol extract of the leaves of *C. dichotoma* with rosmarinic acid as a major constituent (Wang *et al*., 1996). The fatty oil content in the seeds of *C. dichotoma*

Table 1. List of phytoconstituents isolated from the various parts of *C. dichtoma* with their chemical structure and extract solvent

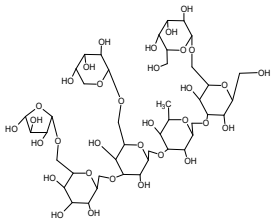
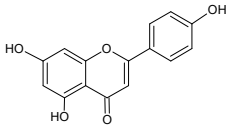
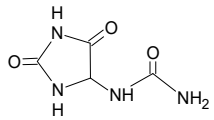
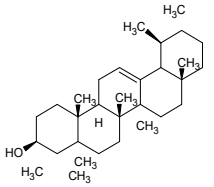
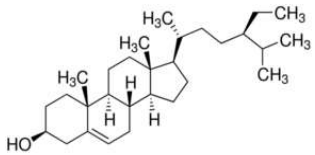
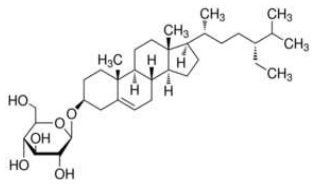
Name of Phytoconstituents	Structure	Extracts	Plant part used	References
Arabinoglucon		Water	Fruits of *C. dichotoma*	Basu et al., 1984; Basu et al., 1986
Apigenin		Methanol Ethanol	Bark Leaves	Ganjare et al., 2011; Bhattacharya and Saha, 2013
Allontoin		Not known	Bark	Jamkhande et al., 2013; Hussain and Kakoti, 2013
α-amyrin		Methanolic	Seeds	Roy et al., 2009
β sitosterol		dichloromethane extracts	Twigs	Ragasa et al., 2015
β sitosterol glycosides		dichloromethane extracts	Twigs	Ragasa et al., 2015

Table 1. Continue .....

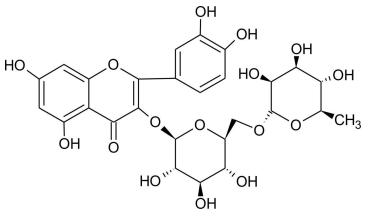
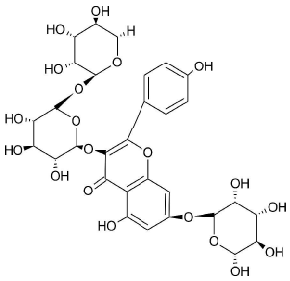
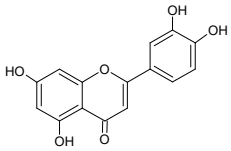
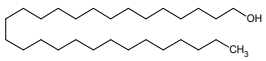
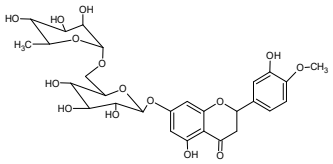
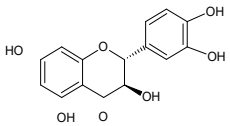
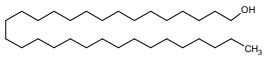
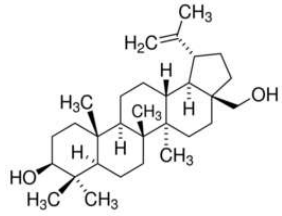
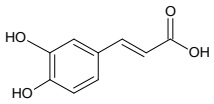
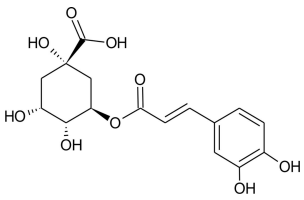
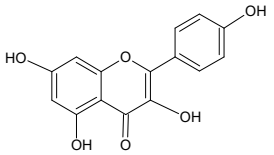
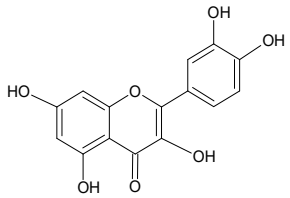
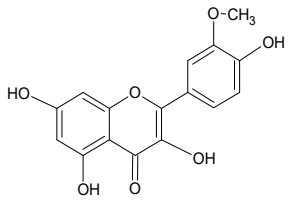
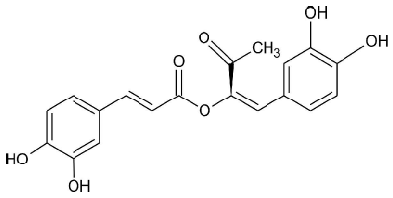
Rutin		Ethanol	Seed	Hussain and Kakoti, 2013; Fu et al., 2002
Robonine		Ethanol	Seed	Jamkhande et al., 2013; Hussain and Kakoti, 2013
Luteolin		Ethanol	Leaves	Bhattacharya and Saha, 2013
Octasanol		Ethanol	Seeds, leaves	Srivastava, 1979
Hesperidine		Methanolic	Seeds	Roy et al., 2009
Taxifolin		Methanolic	Seeds	Roy et al., 2009
Hentricontanol		Ethanol	Seeds, leaves	Srivastava and Srivastava, 1979
Betulin		Ethanol	Seeds, leaves	Srivastava and Srivastava, 1979
Caffeic acid		Ethanol	Seeds	Srivastava and Srivastava, 1979
Chlorogenic acid		Ethanol	Seeds	Srivastava, and Srivastava, 1979
Kaempferol		Butanol	Fruits	Kuppast et al., 2006

Table 1. Continue .....

Quercetin		Butanol	Fruits	Kuppast et al., 2006
Isorhamnetin		Butanol	Fruits	Kuppast et al., 2006
Rosmarinic acid		Ethanol Butanol	Seed Leaves	Tian et al., 2014; Wang et al., 1996

was found to be 7.6 % with stearic, oleic and linoleic acids as the major constituents (Dayal *et al*., 2006). Three flavonoids, kaempferol, quercetin and isorhamnetin, were isolated from the butanol fraction of fruits of *C. dichotoma* (Kuppast *et al*., 2006). Another study reported the presence of apigenin (Ganjare et al., 2011) from *C. dichotoma.* HPLC and HPTLC analysis also confirmed the presence of rutin (flavonol) in the bark of the plant (unpublished data). The seeds, leaves and fruits of the plant found to contain pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols (Jamkhande *et al*., 2013). Taxifolin from the seeds of *C. dichotoma* showed promising DPPH free radical scavenging activity at a concentration of 100 µg/mL (Mahasweta *et al*., 2014). In another work DPPH and ABTS free radical scavenging activity and Ferric reducing Antioxidant Potential **(**FRAP) of n-hexane, ethyl acetate, and methanol fractions of methanolic bark extract of *C. dichotoma* was observed (Ganjare et al., 2011). Study by Tian and coworkers (2014) on an ethanolic extract shown the presence of polyphenolic compounds (1.0%), triterpenoids (0.075%), aminoacids (1.39%) and rosmarinic acid (0.0028%).

Pharmacological Activities

Ethno medical history of *C. dichotoma* is very old and dates back to Vedic period where it has been referred as "Rajjudala*" (*https://books.google.co.in/books). Cordia gum has been found to be useful as tablet binder (due to its sticky properties) and as an emulsifier (Husain and Kakoti, 2013). The plant has got variety of uses worldwide. Rope is made from the bast and white gelatinous substance from fruit is used as glue as well as fish are cooked wrapped in leaves in Philippines. In Burma, the leaves are used for cigar wrappers (Sason and Sharma, 2015). Its importance in Ayurvedic system of medicine has been described in detail by Sason and Sharma (2015). Its ethnomedicinal uses have been scientifically validated by modern pharmacological protocols and using advance techniques. Some of these are described in the following section.

Antimicrobial/Antimicotic activity

Literature reports antibacterial and antifungal potentials of *C. dichotoma* bark (Parekh and Chanda 2007; Nariya et al., 2011) in which ethanolic and the butanolic extracts were reported to be active against *Escherichia coli*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes* and *Staphylococcus aureus* (Sharker et al., 2009). The extract was also reported to be active against pathogenic fungi *Aspergillus niger, Aspergillus clavatus* and *Candida albicans*. Rawat and coworkers (2013) have shown the comparative antimicrobial activity of various extracts of *C dichotoma.* As per their results antimicrobial activity of chloroform and methanol extracts of leaves of *C dichotoma* was found to be more active against *E coli, bacillus cereus, psedudomonas* compared to the petroleum ether leaves extracts which was found inactive against *E coli, B cereus, Pseudomonas*. Rawat and coworkers (2013) also showed that the methanolic extract of leaves of *C dichotoma* was highly active against *Candida albicans* and *Aspergillus niger* but not much effective against *Rhizopus* and *Sclorotium*.

Analgesic activity

The ethanolic extract of leaves has been explored for its analgesic properties in acetic acid induced writhing in mice

at an oral dose of 500 mg/kg by Sharker et al., (2009). At this dose extract provided 71.75% writhing inhibition in animal model which was comparable to the standard drug diclofenac sodium which showed 84.37% writhing inhibition at a dose of 25 mg/kg. Gupta and Kaur (2015) in their study reported that methanolic exctract of leaves of *C dichotoma* showed significant effect as an analgesic at a dose of 400 mg/kg as compared to lower dose. This study also showed the antipyretic potential of *C. dichotoma* plant leaves extract.

Anticancer activity

The cytotoxic activity of an ethanolic extract of *C. dichotoma* was carried on Brine shrimp lethality bioassay (Sharker et al., 2009) which suggested antitumor, antibacterial or pesticidal activity. Anticancer activity of the methanolic extract of *C. dichotoma* leaves along with apoptotic machinery has been explored against PC3 cell lines by Rahman and coworkers (2017). They also demonstrated significant cell death by MTT assay (for cytotoxicity) in PC3 cells in the presence of methanolic extract of *C. dichotoma* leaves (at IC_{50} of 74.5 µg/ml). The cell death was characterized by surface detachment, cellular shrinkage and deformation of cell bodies indicating apoptotic kind of cell death.

Hypoglycemic activity

The hypoglycemic (antidiabetic) properties of the methanolic extract of fruit pulp of *C. dichotoma* have been reported in alloxan induced diabetes study done by Mishra and co-workers (2011), on healthy male Wistar albino rats. Methanol extract of fruit pulp of *C dichotoma* significantly reduced the blood glucose level after 90 minute of administration. In alloxan induced diabetes rat *C dichotoma* methanolic extract showed a significant decrease in blood glucose level when treated for 21 days at a dose level of 200 mg/kg body weight. Day (1998) also showed significant reduction in blood glucose levels and body weight loss in glucose loaded and alloxan induced rat when treated with methanolic extract of fruit pulp.

Wound healing activity

Study of ethanolic fruit extracts of *C. dichotoma* by Kuppast and Nayak (2006) showed significant wound healing activity. Ethanolic fruit extract was further fractionated using petroleum ether (40-60%), solvent ether, ethyl acetate, butanol and butanone in succession. These fractions were tested for wound healing activity using three different models, viz. incision, excision and dead space wound models on either sex of albino rats of Wistar strain. All the fractions showed significant ($P<0.001$) activity may be due to the presence of flavonoids in fruits. A significant increase in the tensile strength of test as compared to control was also reported (Kuppast and Nayak, 2006). Results of excision, incision and granuloma wound healing models showed significant would healing property of the fruit extract of *C dichotoma*.

Antioxidant activity

Many *in vitro* and *in vivo* studies on antioxidant activity of *C. dichotoma* are available in literature. Sharma and coworkers (2009) studied the role of free radical scavenging activity of *C. dichotoma* seeds and leaves extract in degenerative disorders. Antioxidant activity was evaluated by in-vitro models using hydrogen peroxide and DPPH. Both these models demonstrate positive antioxidant activity in a concentration dependant manner and demonstrated highest antioxidant activity at higher concentrations. This activity was more pronounced in leaves as compared to seeds. Methanolic extract of seeds and leaves of *C. dichotoma* has been shown to possess free radical scavenging potential. This property of seeds and leaves extract has been explored for the management of degenerative disorders such as aging and age-associated oxidative stress related disorders by Singh and others (2009). Evaluation of the phenolic content and antioxidant potential of methanolic and butanolic extract of *C. dichotoma* bark was carried by Nariya and co-workers (2013). In this study three in vitro models were used to evaluate antioxidant activity. The first two methods employed direct measurement of radical scavenging activity and in remaining one method evaluated the reducing power. *C. dichotoma* showed strong antioxidant activity by inhibiting DPPH activity and reducing power activities when compared with standard L–ascorbic acid. In addition, both the extracts were found to contain a noticeable amount of total phenols, which play a key role in controlling oxidation. The results revealed that an extract can be used as easily available source of herbal antioxidant.

Hepatoprotective activity

The methanolic extract of the leaves of C. *dichotoma* with a dose 300 mg/kg and 500 mg/kg were tested for hepatoprotective action in male Wistar rats by Thirupathi and his team (2007). Liver damage is induced by carbon tetrachloride (CCl_4) whereas silymarin was used as standard drug against liver injury. The extract at 300 mg/kg doses showed significantly reduced activities of Aspartate Aminotransferase (AST) ($P<0.001$), Alanine Aminotransferase (ALT) ($P<0.001$) and Thibarbituric Acid Reactive Substances (TBARS) levels ($P<0.01$) and at 500 mg/kg dose significantly reduced the ALT ($P<0.001$), TBARS level ($P<0.01$), AST level ($P<0.001$). As discussed already *C. dichotoma* possess substantial antioxidant activity therefore oxidative stress induced hepatotoxicity of CCl_4 was significantly lowered. The protective activity of *C.dichotoma* was found comparable with silymarin (100mg/kg).

Anti-fertility activity

Sharma and coworkers (2015) studied an anti-fertility

activity of hydroalcoholic extract of *C. dichotoma* leaves at two dose level (200 and 400 mg/kg, p. o.) in female albino rats. The author studied the anti-implantation and estrogenic activity of extract in 10 days pregnant female rats. The hydroalcoholic leaf extract on 10 days administration showed a significant (59.39% at 200 mg and 81.22% at 400 mg/kg doses) anti-implantation activity. In addition simultaneous administration of extract along with ethinylestradiol showed significant estrogenic activity. The leaves extract further showed more significant ($P<0.01$) increase in weight of the uterus and significant change in biochemical parameters in immature rats. The results suggest that hydroalcoholic extract of *C. dichotoma* leaves possess significant anti-fertility activity, which might be due to the presence of some estrogenic chemicals in leaves that cause inhibition of implantation. The steroidal glycosides, saponins are responsible for antiestrogenic activity of the extract as these are previously reported to reduce the activity of estrogens induced enzymes in several estrogen targeted tissues.

Anti-Ulcerative Colitis activity

Wassel and others (1990) studied and showed the presence of flavonoids in extracts of *C. dichotoma* Forst. f. Fruits tested and showed significant anti-ulcer and cytoprotective effects against gastric ulcer in rats. The antiulcer activity of an extract of *C. dichotoma* fruits (300 mg/kg body weight) was studied in albino rats of Wistar strain using three different variables i.e pyloric ligation, aspirin and indomethacin induced ulcers. The extractions of *C. dichotoma* fruits were carried out using ethanol. The extract was fractionated using petroleum ether, solvent ether, ethyl acetate, butanol and butanone in succession. The 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, butane and butanone significantly ($p<0.001$) decreases the volume of gastric secretion, free acidity, total acidity and ulcer index with respect to control. These results suggest that the extracts of *C. dichotoma* Forst.f. fruits possess significant anti-ulcer activity.

The gastroprotective and antiulcer effect of aqueous and alcoholic extracts of the ripe fresh fruits of *C. dichotoma* were investigated by Shah and his fellow workers (2011) in aspirin induced gastric ulcer model and pylorus ligation model in rats. The aqueous and alcoholic extract showed a significant antiulcer activity in extract administered animals. An aqueous extract has been found to be more effective than alcoholic extract compared to standard ranitidine in both aspirin induced gastric ulcer model ($p<0.001$) as well as in pylorus ligation model. The fruits of *C. dichotoma* are edible and have got thick mucilage. This mucilage is viscous in consistency, sweet in taste and contains carbohydrates and proteins and is alkaline in nature. Due to its viscous and sticky nature it can form a protective coat in the stomach and on ulcer craters which helps to heal ulcers.

Ganjare and others (2011) have reported the anti ulcerative colitis (UC) activity of crude methanolic extract of *C. dichotoma* bark. Dried bark powder was extracted with methanol and further fractionated using various solvents. These fractions were tested for effectiveness against UC. Animals treated with methanol fraction of crude methanol extract showed lower pathological scores and good healing. In another study Ganjare and coworkers, (2011) isolated apigenin using column chromatography from methanol fraction of crude methanol extract of *C. dichotoma* bark. Apigenin from *C. dichotoma* bark may be responsible for the treatment of UC because Apigenin (5 mg/kg,p.o.) showed significant healing and reduction in inflammatory enzymes when screened for UC (Ganjare et al., 2011).

Many researchers have carried out phytochemical studies resulting in the identification of different classes of secondary metabolites, isolated from different parts (root, stem, bark, leaves and fruits) of *C. dichtoma* plant, as summarized in table 1. *C. dichotoma* is a well explored plant for its anti-inflammatory, antipyretic, anti-oxidant, anticancer, expectorant, demulcent, anti-arthritic, antidepressant, anti-ulcer, anti-fertility and cosmetic agents system of folklore medicine (Hussain and Kakoti, 2013).

Conclusion

C dichotoma is highly potent plant being used traditionally for various human ailments. Its therapeutic properties may be due to the presence of varied range of compounds isolated from this plant including but not limited to apigenin, cordioic acid, quercitin, linolenic acid, rutin, hesperidin, arabinose, caffeic acid, robinin and arabinoglucan. This plant also contains carbohydrates, proteins, tannins, saponins, amino acids, steriods, glycosides and penlolic compounds. Owing to the presence of multiple useful compounds and its multifaceted uses *C. dichotoma* attain a lot of medicinal importance.

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Conflict of Interest

Authors do not have any conflict of interest of any sort with any individual or institution.

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