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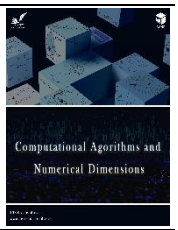

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The Pharmacognostic Profile and Pharmacological Importance of Cordia Myxa-a Review

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Abstract

This review provides an overview of the medicinal plant Cordia myxa (Boraginaceae), its pharmacognostic profile, traditional uses, and various medicinal importance in various aspects of medicinal science and recent developments in novel drug delivery. Recent trend of people shifting to natural products from synthetic ones opens up numerous ways of research in the field of natural products in drug therapeutics. This shift provides a wide range of options for designing natural product-based drugs with minimal side effects. Cordia myxa is a rich source of alkaloids, resins, terpenoids, coumarins, gums, etc., providing a wide range of activities. Cordia myxa is being investigated in various aspects other than medicinal purposes, viz. nutritional, medical dressing, supplements, etc. Cordia myxa is an ethnomedicinal plant in different world regions, including India. Traditional people utilized it for various purposes, viz. respiratory issues, making pickles, an alternative to paper glue, dyspepsia, fever, etc. Cordia myxa revealed various chemical components, proving its medicinal importance. Evaluation of pharmacological and therapeutic activities confirmed the Cordia myxa plant's hypotensive, respiratory stimulant, anti-inflammatory, antimicrobial, diuretic and immunomodulatory properties. In this review, we summarized the available published information on Cordia myxa and also discussed the enormous potential to serve as a drug candidate.

Keywords: Cordia myxa, Boraginaceae, Pharmacology, Phytochemistry, Pharmacognosy, Natural products.

1 | Introduction

Traditional medicines play a key role in preventing, treating, and mitigating many ailments. Plants have been used for decades as a source of medicines that give the present generation vast knowledge about traditional plants and their derivatives and extracts. In one of the studies by WHO, it is estimated that 80% of the developing world's population relies on conventional plant-based medications for their medical needs. India and China are the two major countries that account for 40% of global biodiversity and the availability of rare species. In the US, 25% of pharmaceutical products are plant-based [1]. Plants are the major origin of secondary metabolites used in pharmaceuticals, nutraceuticals, agrochemicals, food additives, food colors, and fragrances. This review highlights Cordia Myxa's pharmacological properties, therapeutic significance, and pharmacognostic profile.

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2 | Plant Profile

Synonyms: Bourreria glabra G. Don, Cordia ixiocarpa F. Muell., Cordia latifolia Wall.ex G. Don, Cordia myxa var. ixiocarpa (F. Muell.) Domin, Cordia officinalis Lam., Cordia paniculata Roth, Cordia paniculata Roth, Cordia petta-pelioporet B. Heyne ex Roth, Cordia scabrifolia Benth. ex Griseb., Cordia sebestena Forssk., Ehretia glabra Roth ex Roem. and Schult., Ehretia glabra Roth and Gerascanthus myxus (L.) Borhidi [2].

Table 1. Taxonomic-classification.

Taxonomic Rank	Taxon
Kingdom	Plantae
Sub kingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Lamiales
Family	Boraginaceae
Genus	Cordia L
Species	Cordia myxa L [3]

Common names: assyrian plum, Indian cherry, Lasura, Panugeri, Naruvilli, Bumber Geduri, Spistan, Gondi, Selu, Sebestan plum, Pidar, [4].

Geographical distribution: Cordia myxa is primarily grown in Asia and other regions worldwide, mostly in tropical regions. From Myanmar in the east to Lebanon and Syria in the west, it grows abundantly and spontaneously.

Habitat: its habitat ranges from 200 meters above sea level in the plains to about 1,500 meters in the hills. Cordia myxa reaches maturity when its grith reaches 1 to 1.5 m height, which takes about 50-60 years. The trunk typically grows to a height of three to four meters and is straight. It has lesser growth in unfavorable climates and may attain a crooked form; otherwise, it can be a dome-like umbrella.

Description: it bears both male and female flowers on the same tree because it is a deciduous plant. The bark is greyish-brown with vertical and longitudinal fissures, which make the species identifiable. Leaves are broad and ovate, and young leaves are somewhat hairy. The tree bears flowers of white color 5mm in diameter during March and April. The fruit is a kind of drupe, oval or spherical, 2-3.5 cm long, apiculate, light pale-brown or pink in color, and darkens when it fully ripens. The pulp is almost transparent due to the presence of viscous glue-like mucilage (*Fig. 1*). The pulp becomes sweet when the fruit is fully ripening [5]. The fruit contains 82.5% moisture, 1.8% protein, 1.0% fat, 0.3% fiber, 12% carbohydrate, 65 Kcal energy, 40 mg calcium, 60 mg phosphorus, 0.0005 mg iron, 1.66% potash, 2.13% ash, and 4.5% pectin [5].

Cultivation: the species is native to China and is extensively grown in tropical and subtropical areas. Deep clayey and sandy soil is beneficial for the plant's growth. The plant shows better growth in 100-150 cm in annual rainfall. It is also cultivated in deserted and sub-deserted zones despite numerous utilities to cultivate. It grows faster and can attain a height of 12 m; branches radiate in all directions, making it suitable for windbreak purposes in orchards. In a less favorable climate, it becomes somewhat crooked, otherwise dome-shaped. It develops longitudinally and vertically bark, making it easily identifiable [5].

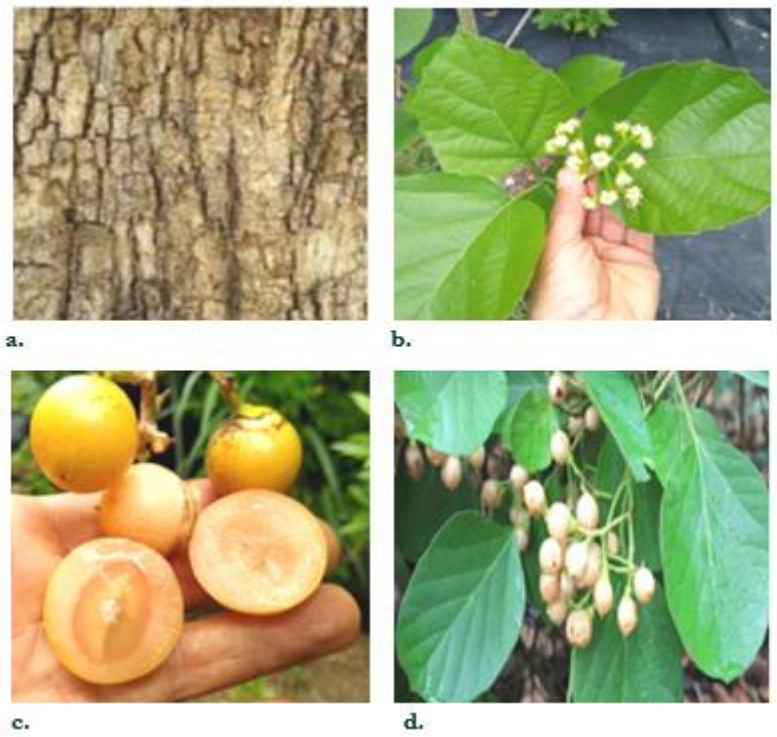

Fig. 1. a. Bark with vertical and longitudinal fissures, b. Broad ovate leaves and white flowers at an early stage, c. Full ripened fruits and d. Fruit at the half-ripened stage.

Traditional uses: every part of the tree is supposed to have its medicinal importance. Fruits were used for cough and respiratory issues as they possess a demulcent action. Immature fruits were used to make pickles and half-ripe fruits as an alternative to paper glue. Bark decoction was used to cure dyspepsia and fever. Juice of bark is useful in gripes and colic. Bark powder was also used to treat skin diseases. Powdered bark was also applied to the skin before plaster to accelerate healing in the case of broken bones. Trypanosomiasis was once treated with leaf macerate; leaf macerate in lotion form was also used to treat fly bites. Leaves were also used to apply to wounds and ulcers for better healing. Leaves have applications in curing headaches. Cordia myxa was also used to cure snakebite. During the famine, leaves were also used as livestock feed for goats and cattle. It was also used to calm rheumatic pain and also as an anthelminthic [3], [5].

Chemical constituents: phytochemical screening of Cordia myxa revealed the presence of various kinds of active phytoconstituents, for example, glycosides, alkaloids, oils, terpenoids, resins, tannins, saponins, sterols, gums, mucilage, and coumarins. Cordia myxa was identified for saturated acids using paper chromatography as only palmitic and steric acids were found to be present, along with oleic and linoleic acids in solid fractions. Cordia myxa's phenolic content was measured and calculated as gallic acid equivalents. Methanol was used to extract the soluble phenolic acids of Cordia myxa. Cordia myxa fruit had a total phenolic content of 373.91 13.93 mg/100g dry weight. Handmaceration yields a fruit extract with a high phenolic content (11.11.47% gallic acid equivalent). The fruit contains a lot of energy (281.4 kcal/100g dry weight). Mineral elements of sodium (1.62), calcium (0.46), potassium (7.83), iron (0.51), and zinc (0.35) were determined on 0.3 g fruit powder by using energy dispersive X-ray fluorescence (EXDRF) [6]–[8].

Compared with Recommended Dietary Allowances (RDA), the stem mineral content of Cordia myxa indicates that fruit might provide better supplements of nutrients like fiber, carbohydrates, and proteins [7]. This can be a good supplementary source in underdeveloped countries.

3 | Pharmacological Effects

3.1 | Analgesic and Anti-Inflammatory Effects

In the mouse model, a hydro-alcoholic fruit extract of Cordia myxa was found to be useful in treating inflammation. The hydro-alcoholic extract was prepared through the maceration process. The evaluation was carried out with the help of the formalin and acetic acid tests. A formalin test was performed. In various mice groups, normal saline (100 mg/kg), oral indomethacin (200 mg/kg), and intraperitoneal tramadol (100 mg/kg) were administered. The extent of foot licking was determined. In mice groups within 0-5 min (acute phase) and 15- 25 min (chronic phase). Within 10 minutes, the acetic acid test witherings were also examined. Hydro-alcoholic extract of Cordia myxa fruit was found to be effective in the case of the formalin test. The anti-inflammatory and analgesic activity of Cordia myxa in both the acute and the chronic phases was determined [8].

The anti-inflammatory effects of Cordia myxa on experimentally induced colitis in rats were investigated by inducing colitis in rats by administering 4% acetic acid intrarectally. After 4 days, all animals were sacrificed, and histological and myeloperoxidase activity was measured. Treatments with Cordia myxa preparation corrected the histological alterations in 50% of the animals, with only minimal inflammation appearing in 25% [9].

To reduce the adverse effects of standard medications, patients can use smaller dosages of the traditional anti-inflammatory treatment in combination with the hydro-alcoholic extract of Cordia myxa to treat inflammatory diseases [8]. In rats, Cordia myxa petroleum ether and alcoholic extract had significant analgesic and anti-inflammatory activity [10].

3.2 | Hypotensive and Respiratory Effects

Both ripe and unripe fruits' mucilages of Cordia myxa decrease rabbit atrial blood pressure without affecting the respiratory rate. Ripened Cordia myxa was found to be more potently hypotensive than other species of Cordia. The hypotensive effect was caused by parasympathetic ganglia activation and peripheral blood vessel dilation, whereas chemoreceptor activation caused respiratory stimulation [10]. The effect of Cordia myxa extract was investigated for smooth muscle relaxation in isolated tracheal smooth muscles of sheep precontracted by acetylcholine. Relaxation was seen when the muscle was exposed to Cordia myxa extract. Cordia myxa relaxes both intact epithelium and denuded trachea of sheep contracted by acetylcholine. Nitric Oxide (NO) may be responsible for the relaxation induced by Cordia myxa. Cordia myxa extract also stimulates NO synthesis [11].

3.3 | Immunomodulatory Effect

In vitro assays, immunomodulatory effects were evaluated using the activated mouse (males type BALB/c), macrophages, and lymphocytes by using lymphoproliferation and reduction of NBT strains. The result of NBT indicated the inhibition (without toxicity) [12]. The immunomodulatory effect of Cordia myxa extract was determined in mice immunized by Hydatid Cyst Fluid Antigen (HCFAg). BALB/c mice were divided into various groups immunized with HCFAg and aqueous extract of Cordia myxa. The Delayed-Type Hypersensitivity (DTH), Mitotic Index (MI), and histopathological changes were all investigated. The bone marrow and spleen MI was elevated in immunized and treated mice compared to other types. Hyperplasia of lymphoid corpuscles was shown by histopathological examination of the spleen. The aqueous extract stimulated cell-mediated immune response in mice [13]. Ethyl alcohol (70%) extract of Cordia myxa was found to elevate a few blood parameters, for example, a total count of leucocytes with an insignificant rise of lymphocytes [14].

3.4 | Antimicrobial Effect

Cordia myxa leaf extracts were tested for antibacterial efficacy against three bacterial strains (E-coli, Staphylococcus aureus, and Pseudomonas aeruginosa) and three fungal strains (Aspergillus niger, penicillium spp, and scytalidium). In the case of E-coli and then Staphylococcus aureus, Cordia myxa displayed the strongest inhibition. However, it showed no antifungal activity [15]. Another study was carried out in which leaf extract (alkaloids) were extracted with the help of various reagents. The potency of extracted alkaloids was analyzed in terms of Maximum Inhibitory Concentration (MIC), which is 150 mg/ml, and this concentration showed promised inhibition against Staphylococcus aureus, Escherichia coli, Pseudomonas aeroginosa, Proteus Sp. and klebsiella Sp. Bacteria. So, the alkaloids extracted from Cordia myxa leaves can show promising results in treating microbial infections caused by these microbes [16].

3.5 | Anti-Ulcer Effect

In rats, the impact of fruit extract on stomach ulcers brought on by indomethacin was investigated. Indomethacin injected intraperitoneally (30 mg/kg BW) was used to cause gastric ulceration. Cordia myxa fruit extract was administered orally at 125 mg/kg BW. At the same time, ranitidine served as reference medication and was administered orally at a dose of 50 mg/kg BW two weeks before indomethacin injection. There was a substantial decrease in gastric mucosa lesions, malondialdehyde (MDA), and serum Tumor Necrosis Factor (TNF) accompanied by a marked rise in the levels of the gastrointestinal mucosal enzymes catalase (CAT), NO, and Prostaglandin E2 (PGE2), as well as gastric juice mucin in pretreatment with Cordia myxa extract. A rise in mucin content, NO, and PGE2 of the same magnitude, although a preventive index of 75.9% was produced, which was not observed with ranitidine. Ranitidine substantially increased PH and decreased pepsin activity, free of gastric juice and total acidity. These findings were confirmed by histological analysis of the stomach mucosa. Cordia myxa extract can avoid indomethacin-induced gastric ulceration. It was noticed that the defense afforded by Cordia myxa extract and ranitidine co-administration was greater than that of ranitidine alone [17].

3.6 | Cardioprotective Effect

The possible protective effects of Cordia myxa methanolic extracts against cardiotoxicity induced by doxorubicin have been investigated in rats. The remarkable cardioprotective capability was demonstrated. Cordia myxa extracts exhibited strong radical scavenging and antioxidant properties in vitro. It has substantially preserved the cardiac oxidative stress markers GSH, MDA and cardiac serum markers from DOX-induced alterations. Histopathological analysis has verified the protective effect against cardiotoxicity induced by DOX [18].

3.7 | Hepatoprotective Effect

The hepatoprotective effect of Cordia myxa extract has been tested in rats. Two agents, carbon tetrachloride (CCl4) and thioacetamide, caused oxidative liver damage in rats. A rat serum measurement of aspartate transaminase, glutamate transaminase and alkaline phosphatase was evaluated for oxidative harm. Cordia myxa extracts were prepared and fed to the experimental animals over two weeks. The recovery of the liver was measured by re-measuring the liver enzymes and comparing them with the control group. CCl4 and TA caused comparative oxidative damage as assessed by hepatic enzymes. A significant liver recovery was noticed when animals were treated with CCL4/TA fed with Cordia myxa extracts [19].

3.8 | Hematological Effects

When mice were given a large dose of mefenamic acid (ponstan), the effect of Cordia myxa extract on blood images was studied. In this experiment, four classes of mice were used. Distilled water was given

to group A and acted as regulation. Group B received plant extract at 600 mg/kg of BW. Group C received ponstan at 100 mg/kg BW, and Group D received half the dose simultaneously for both treatments. To conduct histological pieces, each animal's right femur bone was taken. When the plant extract was administered alone or combined with ponstan, it improved some blood parameters. The plant extract reversed the effects of ponstan on bone marrow, causing mild degenerative changes and eliminating the negative effect [20].

3.9 | Antioxidant Effect

Cordia myxa fruits had a total phenol content of 373.91 ± 13.93 mg/100g dry weight and antioxidant activity (IC50) of 132.53 ± 5.75 µg/ml [21]. Plant extracts were assessed for their phenolic content and antioxidant activity. The phenolic content was measured and determined as gallic acid equivalents using the Folin-Ciocalteu reagent. The anti-radical potential of Cordia myxa extracts was determined by a DPPH assay and compared with ascorbic acid. One mg. of the crude Cordia extract was found to be equivalent to 15µg of ascorbic acid [22]. However, the DPPH assay was performed in another study to assess the extract's anti-radical activity and was contrasted with ascorbic acid. Its anti-radical activity, estimated as 10.0±1.24 ascorbic acid equivalent, was measured as 1634±0.81 [20].

Integrating them into the polymer matrix, such as edible coatings based on polysaccharides, enhances antioxidant efficiency. Due to its good adhering and emulsifying properties, an anionic polysaccharide gum Cordia derived from the fruit pulp may be an antioxidant carrier. The capacity of gum Cordia as a carrier of antioxidants was explored when applied to peanuts as an edible coating. For the delivery of antioxidants, Gum Cordia was compared to carboxymethyl cellulose: butylated hydroxyanisole, butylated hydroxytoluene and ascorbic acid. Uncoated and coated peanuts were stored for 126 days at 35 ° C, and the efficacy of the coating carrier was measured using chemical parameters (peroxide value and thiobarbituric acid reactive species) and sensory assessment following lipid oxidation (oxidized flavor). There were significant differences (p 0.05) between coated and uncoated samples. Gum Cordia was considered better than CMC in producing antioxidants. In combination with BHA/BHT, gum Cordia-based coating showed optimum protection (290% longer shelf life than control) based on peroxide value (40 meq. O2/kg), followed by gum Cordia plus BHT (244%), gum Cordia plus BHA (232%), CMC plus BHA/BHT (184%), CMC plus BHA (139%), CMC plus BHT (119%), gum Cordia plus AA (96%) and CMC plus AA (466%) [23].

3.10 | Wound Healing

Cordia myxa has a traditional use in accelerated wound healing. However, a non-fibrous dressing for wounds incorporated with Cordia extract is a novel approach. The fabrication of wound dressing consisting of electrospun nanofibres embedded with 5% Cordia myxa fruit extract showed higher porosity (83%), higher swelling (103.1%), and lesser in-vitro degradability (13.6%) when in contrast to the neat mat The 5% Cordia myxa fruit extract embedded mat showed enhanced human fibroblast proliferation (211.1%) after 5 days and enhanced in-vitro healing of a wound by increasing closure of the wound, reepithelization, and collagen synthesis. Due to the presence of antioxidants, the mat reduced oxidative stress on tissues.

Natural products such as Cordia myxa would benefit wound healing in novel drug delivery systems. More clinical investigation should be performed on natural products in wound care to introduce a unique set of healing enhancers [24].

3.11 | Nutrition and Free Radical Scavenging Property

The Cordia Myxa plant has great potential to enter the vegetable and pickle industry. Fruits of Cordia myxa (4 improved genotypes) were analyzed for total phenol content, nutritional importance, and radical scavenging properties. DPPH assay was performed to analyze the total phenol content and free radical scavenging property from acetone extracts of dried fruits. Fruits harvested earlier, about 20 or 30 days

before fruit set, showed higher antioxidant, radical scavenging, and nutritional properties. Cordia myxa can be a good supplement source for human health if harvesting is done properly [25].

3.12 | Uses in Pharmaceutical Preparation

A major challenge in the attempt to eliminate oral cavity infections was the fast dilution, and rapid removal of drugs applied topically because of saliva's flushing action. The use of a proper drug delivery system has a significant influence on drug delivery, and for sustained drug retention in the oral cavity, such a system should be developed. It has been tested to see if Cordia myxa mucilage can be used as a mucoadhesive material to manufacture chlorhexidine oral tablets and if it can replace synthetic polymers like HPMC. The effect of mucilage concentration on physicochemical responses (friability, hardness, dissolution, swelling, disintegration time, and muco-adhesiveness strength) was investigated and compared with mucilage swelling and HPMC. The pharmacopoeial properties of the tablets, the strength required to separate the tablets from the mucosa, and the amount of water absorbed by the tablets were all evaluated. Increasing mucilage concentration in the formulations increased disintegration time and drug dissolving rate and lowered MDT compared to HPMC. Also, the muco-adhesiveness power of oral tablets containing 20% mucilage was substantially higher than 30% HPMC. Therefore, the presence of Cordia myxa mucilage powder greatly affects the characteristics of the tablet and enhances muco-adhesiveness [26].

On the other hand, a cream containing Cordia myxa fruit was prepared using various bases and emulsifiers and tested in vitro to attain the best formulation. Cream formulations included 5% Cordia myxa fruit aqueous extract, and various quantities of lipids and surfactants were prepared using the process of fusion. Some physicochemical properties of formulations, such as pH, purity, viscosity, and physical stability, have been tested. An antimicrobial challenge test was also performed against Pseudomonas aeruginosa. All formulations were homogeneous with a Cordia extract-related odor and color, a proper consistency, a pH average of 7.175, and a viscosity average of 9010 cps. They were physically stable; no coalescence or creaming occurred after 1, 3, and 6 months of storage. During centrifugation at 2000 rpm, no sedimentation or phase separation was seen, and no microbiological growth was observed after the storage time. To summarise, Cordia myxa can be made into a topical cream. [27].

4 | Future Insights

Plant-based medicines and products are gaining favors in the modern world due to their minimal side effects, safety, and potency compared to standard drugs. Phytochemical screening of various plant products opens the way towards discovering new drugs and their pharmacological applications. Multiple studies have shown various therapeutic effects of Cordia myxa, such as analgesic, anti-inflammatory, hypotensive, cardioprotective, etc. Further research can be done on the plant to enhance its medicinal and therapeutic value. Cordia myxa as an anti-inflammatory could be an alternative to standard anti-inflammatory drugs to minimize the side effects of standard drugs. The therapeutic effect of Cordia myxa could also be mediated through increasing colonic blood flow in case of colitis. Cordia myxa fruit mucilage at various stages of maturity could be analyzed for a more potent hypotensive effect. Cordia myxa was found to be gastroprotective, and apparently, it could be used with Ranitidine for treating gastric ulcers as it could have a synergistic effect. The methanolic extract of Cordia myxa could play a vital role in cardiotoxicity (doxorubicin-induced) as it possesses some antioxidant activity. Cordia myxa powdered mucilage can be an alternative to HPMC as increased mucilage concentration could affect formulation characteristics, viz. disintegration time dissolution rate (in the case of tablets). Cordia myxa should be evaluated for its therapeutic efficacy and formulated as a topical preparation for various dermatological conditions.

5 | Conclusion

This review addressed the pharmacognostic profile and pharmacological effects of Cordia myxa as a promising herbal medication by discussing various diseases and their therapeutic benefits. Cordia myxa as an anti-inflammatory could be an alternative to standard anti-inflammatory drugs to minimize the side effects of standard drugs. Cordia myxa revealed various chemical components, proving its medicinal importance. Evaluation of pharmacological and therapeutic activities confirmed the Cordia myxa plant's hypotensive, respiratory stimulant, anti-inflammatory, antimicrobial, diuretic and immunomodulatory properties. In this review, we summarize the available published information on Cordia myxa and also discuss the enormous potential to serve as a drug candidate.

Conflict of Interest

There is no conflict of interest.

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