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Cordia macleodii (Griff.) Hook. f. and Thomson (*Boraginaceae*) an ethnomedicinal tree - comprehensive review

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Abstract
Cordia macleodii (Griff.) Hook.f. and Thomson belong to the family *Boraginaceae* well known for its ethanomedicinal properties. Its perennial flowering plants. Its vernacular names are Dahiman, Dahipalash, Dadhipalash, Dahipalas, Gadhapalash, Dhengan, Gonni, Kuhman, Bohad, Daiwas, and Dahichir in the Hindi language. In core tribal areas of Gadchiroli and Gondia District it was used to make many indigenous medicines due to its phytochemical properties. Chemically, it contains varied numbers of phytochemicals such as glycosides, flavonoids, saponins, phenols, and terpenoids, traditionally used to prepare more than 150 herbal medicines. Bioactive compounds have been isolated from vegetative parts such as tree bark, stem, and leaves, which are helpful to treat many ailments such as antimicrobial, hepatoprotective, antioxidant, antivenom, analgesic activity, wound-healing, antidepressant, and antihypertensive, with great significance in pharmaceutical industries for developing new herbal drugs. Based upon its high value in ethnobotany, review data was gathered for socioeconomic benefits of society and conservation steps are recommended. Nowadays, people without knowing the ethanomedicinal properties of plants are cutting down forest areas; hence it is important to disseminate knowledge of ethanomedicinal plants and to conserve them in local habitats. It is a critically endangered plant distributed mainly in dry deciduous forests of India and used by tribal communities of different states of India for making various agricultural and household implements and treating various ailments and diseases. *Cordia macleodii* is declining fast from natural habitats due to over-exploitation and habitat degradation; hence, the present study of review was done. Consequently, arrays of biological synthesis protocols leading to the formation of nanostructures have been reported using bacteria, fungi, and plants There are many review works accomplished on silver nanoparticles stem extract of *Cordia macleodii* and its antibacterial activity against pathogenic bacteria like *Pseudomonas aeruginosa, Staphylococcus aureus, Citrobacter* sp., *E. coli*, CONS (coagulase-negative *Staphylococci*), *Acinetobacter* sp., *Enterobacter* sp., *Proteus vulgaris*, and *Klebsiella* sp. It can be concluded that this plant has potential medicinal value and is recommended for further scientific exploration to find novel bioactive compounds of pharmaceutical importance for novel drug development for the benefit of human society.

Keywords: *Cordia macleodii*, conservation, anthropogenic activities, ethanomedicinal properties, antimicrobial activity, silver nanoparticles

Introduction

Taxonomy, Distribution and Morphology

Boraginaceae family of flowering plants were well known for its ethanomedicinal importance with ranging wider diversity of trees and shrubs in cosmopolitan in distribution reportedly nearly more than 300 species adapted to warmer climatic zones [1,2]. Among them Cordia is endemic to Indian Subcontinent found to be wider present in Vidarbha region, become a part of our study more focusing on its medicinal importance and pharmaceutical importance used by tribals of Gond community dwelling in deep forest of Gadchiroli as well core region of Eastern Vidarbha [3,4]. Our manuscript illustrates in detail review of Cordia and its ethanomedicinal importance to kill or recover various ailments of human health and hygiene helpful to treat variety of disorder and diseases in human beings. There are good numbers of vernacular names of trees in Sanskrit to be called as Dadhimanth, Sitapatra, in Hindi Dahiman, Dahipalash, Dadhipalash, Dahipalas, Gadhapalash, Dhengan, Gonni, Kuhman, Bohad, Daiwas, Dahichir. In Marathi Bhoti, Dhaiwan, Daivas, Dhaim, in Tamil Palandekku and many more [5,6]. As per taxonomical nomenclature Cordia belongs to Kingdom Plantae, Phylum Streptophyta, class Equisetopsida, subclass Magnoliidae and order Boraginales with family *Boraginaceae*, genus Cordia, species macleodii (Griff.) Hook.f. and Thomson. The generic name Cordia L. commemorates Enricius Cordus (1443-1543) and his son Valerius Cordus (1515-1544), the German botanists [7]. The species name macleodii was given by William Griffith in 1843 as Hemigymnia macleodii Griff., based on a plant specimen sent to him by his friend D. Macleod from Jubbulpore (Jabalpur, Madhya Pradesh), where it was growing abundantly [8,9]. C. macleodii (Griff.) Hook.f. and Thomson J. Linn. Bot. Soc. 2: 128. 1858. C.B. Clarke Hook.f. Fl. Brit. India 4: 139.1883. Hemigymnia macleodii Griff. Calc. J. Nat. Hist. 3: 363. 1843. Lithocardium macleodii (Griff.) Kuntze Revis Ge. Pl. 2:977. 1891. Gerascanthus macleodii (Griff.) Borhidi in Acta Bot. Hung. 34: 405. 1988 [10].

C. macleodii is characterized as a moderate-sized tree reaching heights of 8-12 meters with a straight trunk and spreading crown (Fig.1) The leaves are simple, alternate, broadly ovate to elliptic, with entire margins and distinctive rough surfaces. The inflorescence appears as terminal cymes bearing white flowers that bloom during February to April, followed by drupes that ripen from May to June [4]. The species demonstrates a restricted geographical distribution, primarily found in dry deciduous forests of central Indian highlands at elevations of 300-900 meters above sea level [5]. Recent ecological surveys have categorized *C. macleodii* as

vulnerable due to habitat fragmentation, overexploitation for timber, and limited regeneration capacity in natural conditions [6]. This restricted distribution coupled with medicinal importance necessitates both conservation strategies and comprehensive scientific evaluation (fig.2,3).

Fig: 1,2,3,4

As per geographical distribution it is primarily more prominent in hilly region of Uttarakhand, North India and Central Maharashtra [11]. Among major states in India it can be found in Bihar, Chhattisgarh, Jharkhand, Gujarat, Karnataka, Kerala, Maharashtra, Madhya Pradesh, Odisha, Rajasthan, Tamil Nadu, Uttarakhand, and West Bengal [12]. C. macleodii is widely distributed in the moist and dry deciduous forests densely clouded with seasonally dry tropical biome [13].

As per morphology Cordia is a medium-sized deciduous tree with white hairy branches. Leaves alternate, broadly ovate, or orbicular, 8–18 × 7–17 cm, obtuse at apex, cordate or rounded at base, impressed rugose above, densely grey or tawny woolly tomentose beneath; petiole stout 3–5 cm long, tomentose. Flowers white, fragrant, polygamous, in terminal and axillary, dense, tomentose, paniculate cymes. Calyx 6 lobed, lobes as long as or longer than the tube, in fruits accrescent; corolla funnel-shaped; stamens 4–8, usually hairy at base. Drupe ovoid, yellowish, non-edible, supported by copular tomentose ribbed calyx [14] with reportedly blooming season of flowering and fruiting ideally in April to June.

Literature Surveyed as Methodology

All E literature were extensively surveyed through digital e-libraries by regularly studying and surfing databases of online periodicals, Google search engines, and reputed journals with the latest research manuscripts and older manuscripts from Central Government Libraries such as the Botanical Survey of India (BSI) and CSIR laboratories *viz*., NBRI, to gather and recall revision of datasets to check the potent importance of literature studied [43,44,45]. There are good number of researchers who find many more ethanomedicinal properties of Cordia by performing numerous laboratory studies to profound its pharmacological significances [28]. It is a critically endangered plant distributed mainly in dry deciduous forests of India and used by tribal communities of different states of India for making various agricultural and household implements and treating various ailments and diseases [21,22,23]. Data can be obtained by extensive literature study of various bioactive compounds with significant pharmaceutical uses [24,25,29]. There are varied techniques used to check active bio-compounds via methodologies such as HPTLC, GC/MS, FTIR, and UV–Vis to obtain good numbers of metabolites from vegetative parts of plants [27,30]. Reportedly, as active secondary metabolites, alkaloids, tannins, glycosides, and flavonoids were isolated from its vegetative parts such as leaves, bark, and stem and among reproductive whorls like flowers [31]. These bioactive compounds have immense potential against various diseases and are thus an important candidate in drug industries for developing new medicines [32,33]. Antimicrobial properties of silver nanoparticles have led to their use in different fields of medicine, industries, animal husbandry, packaging, accessories, cosmetics, health, and military [39].

Physicochemical properties of Vegetative as well Reproductive Parts

Bark

Study was carried out on pharmacognostical characters of the stem bark which includes its macroscopic and microscopic characters and preliminary phytochemistry including TLC and HPTLC. Bark shows microscopic characters like cork, cortex, medullary rays, sclerenchyma fibres, phloem, cambium, and crystals. The phytochemical tests show the presence of alkaloids, glycosides, and tannins, and the HPTLC profile shows the presence of 9 spots and 8 spots at 254 and 366 nm, respectively [34].

Physico-chemical studies of bark revealed that it contains total ash, acid insoluble ash, hexane soluble extractive, alcohol soluble extractive, water soluble extractive, sugar, starch, and tannins. The hexane and chloroform bark extract mainly contain triterpenoids; acetone, methanol, and aqueous bark extract contains reducing sugar, and aqueous bark extract also contains saponins, tannins, glycosides, and alkaloids [36]. Beside acetone, ethyl alcohol, petroleum ether and water extract also contain carbohydrate, flavonoid, and resin. Moreover, the physicochemical analysis of powdered stem bark using HPTLC reveals foreign matters, loss on drying, alcohol soluble extractive, water soluble extractive, total ash and acid in soluble ash in 2.18, 8.40, 7.01, 24.93, 17.07, and 5.86% respectively [37,38].

Unsaponifiable fraction of petrol-ether bark extract using GC/MS analysis and IR and UV characterisation yielded three compounds: Stigmasterol, Campesterol and Cholest-5-EN -3OL (3 Beta)-Carbonylchlorinated in addition with p-hydroxyphenyl acetic acid and β-sitosterol [44,45,46] UV spectrum studies of bark fraction show the presence of flavonoids. Besides, two other flavonoids apigenin and kaempferol were isolated from methanolic bark extract. The granular activated charcoal prepared from the bark at pH 11.5, 330-minute contact time, 6 mg/L initial metal concentration, 1.4 g adsorbent dose, and 650°C temperature has the potentiality in adsorbing toxic element manganese from wastewater [47, 48, 49, 50].

Antioxidant activity has also been assessed by in *vitro* method for phytochemical fraction of plant, *viz*. methanolic and butanol extracts of C. macleodii bark. The extracts were evaluated for their phenolic content and antioxidant activity.

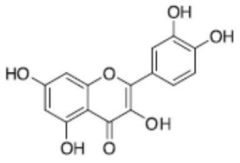
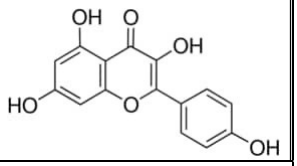
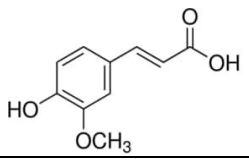
The present study revealed the *Cordia macleodii* bark has significant radical scavenging activity.

Acute Toxicity test and study was carried out at 2 g/kg oral dose. The result shows that the oral administration of the *C. macleodii* did not produce toxic effect up to 2 g/kg in oral dose. In tests, mice were given increasing doses (500–2000 mg/kg), and even at the highest level no harmful effects or death occurred, indicating a wide safety margin [51].

Leaf

Leaf physicochemical parameter average value of dry weight at 105°C 5.22%, water-soluble extractive value 12.56%, alcohol soluble extractive value 4.17%, total ash value 13.68%, acid insoluble ash value 3.12%, respectively [35]. Meanwhile, the UV spectrum analysis of a pure fraction of leaf shows the presence of phenolics and ethanolic leaf extract yielded gallic acid (3, 4-dihydroxy-5-methoxybenzoic acid) [37]. Physicochemical studies on leaves suggest that the drug moisture minimises the drying of leaves, inorganic materials in total ash content, acid insoluble ash, along with extractive values that are water and alcohol-soluble [40].

Table 2: Leaf physicochemical parameter

Leaves and Flowers	**(A) Flavonoids**	
	Quercetin	
	Kaempferol	
	(B) Phenolic and Phenolic acids	
Leaves and Flowers	Ferulic acid	

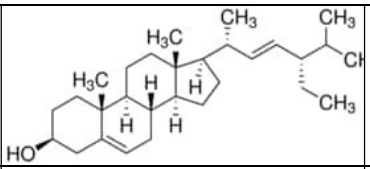
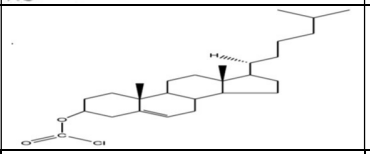
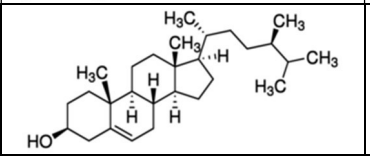
The qualitative analysis of powered, methanolic, petroleum ether and water extract of the leaf shows the presence of glycosides, alkaloids, flavonoids, tannin, fats and fixed oils, terpenoids, steroids, phenolic compounds, and resin [42]. With respect to antioxidant activity methanol leaf extract was observed to have higher antioxidant activity than other extracts. The methanol extracts showed greater antioxidant activity by DPPH scavenging the free radical with IC50 values of 7.63±0.38 µg gm-1 compared to the standard ascorbic acid.

Anti-inflammatory test the ethanolic leaf extracts demonstrated significant anti-inflammatory activity in carrageenan-induced rat paw edema models. Treated groups displayed a significant reduction in edema compared to controls. Analgesic activity was also carried out. The extracts were found to have significant analgesic activity in animal models. In a hot plate test, extracts at 400 mg/kg demonstrated pain-relieving properties comparable to Pentazocine (10 mg/kg), with effects peaking at 60–90 minutes after administration [52].

Stem

Physicochemical analysis of powdered stem bark using HPTLC reveals foreign matters, loss on drying, alcohol-soluble extractive, water-soluble extractive, total ash, and acid-insoluble ash. Macroscopically, the bark is light green externally with longitudinal striations, and reddish-brown internally, measuring 12–15 mm in thickness. Microscopic examination shows multilayered cork, cortex merging into phloem, medullary rays, sclerenchyma fibers, and abundant calcium oxalate crystals. Preliminary phytochemical screening confirms the presence of alkaloids, glycosides, phenols, flavonoids, terpenoids, and tannins [41]. Reported constituents from the leaves and bark include sterols (stigmasterol, campesterol, DHEA, cholesterol), flavonoids (quercetin, kaempferol, isorhamnetin, luteolin), alkaloids (choline, betaine, trigonelline), fatty acids (oleic, linoleic, palmitic), carotenoids (lycopene, β-carotene, zeaxanthin), triterpenoids (ursolic, oleanolic acids), and phenolics (ellagic, caffeic, chlorogenic acids), plus ascorbic acid and tocopherols (Table 3).

Table 3: Phytochemical analysis of Stem and Bark

Vegetative Parts	Phytochemicals	Chemical structure	
Bark/Stem	Steroids		
	Stigmasterol		
	Cholest-5-En-3ol (3beta)-carbonyl chlorinated		[9]
	Camphesterol		[9]

Ethnomedicinal Importance of *C. macleodii*

Being highly important ethnomedicinal tree there is urge to save jewel of forest henceforth continuous efforts were being made by first author to propagate C. macleodii in herbal garden of Arogyadham, Deendayal Research Institute, Chitrakoot and forest nursery of Forest Research and Extension Circle, Rewa with Dr. P.C. Dubey then Chief Conservator of Forest.

IUCN Red List Criteria 2000 -Version 3.1 and reported critically endangered (CR) from Vindhyan region, Central India and Chhattisgarh, and Endangered (EN) from West Bengal, Odisha, Madhya Pradesh, Chhattisgarh, Maharashtra [2] and Rajasthan.Some of the ethnomedicinal properties are highlighted with extensive survey of data,

Wound Healing Activity

Traditional use and scientific studies support wound-healing properties. Leaf pastes and formulations such as *Shikari ghrita* accelerated healing of acute and chronic wounds, preventing pus formation and supporting tissue repair.

Antivenom Activity

Ethanolic extract of *Cordia macleodii* bark significantly inhibited the Naja venom induced lethality, haemorrhagic lesion, necrotising lesion, oedema in rats. The extract also antagonised the cardiotoxic and neurotoxic effect of venom in isolated frog heart and rectus abdominus muscle of frog. The result shows that at the dose of 400 and 800 mg/kg ethanolic extract of C. macleodii bark significantly inhibited the Naja venom induced lethality, haemorrhagic lesion, necrotising lesion, and oedema in rats. The protective effect of extract of C. macleodii against Naja venom poisoning may be due to precipitation of active venom constituents

Antidepressant Activity

Antidepressant effect of this plant in rats. Injection of control did not exhibit significant effect on immobility time and swimming time in the forced swimming test compared to pre-injection status. Therefore, all experimental groups were compared with saline as the control group. The administration of fluoxetine (15 mg/kg) as a positive control, in rats significantly decreased immobility time respectively compared to the control group. While extract (100 and 500 mg/kg) significantly decreased immobility time 99.0±1.73, 63.6±5.84, 49.3±3.17 respectively. C. macleodii extract and standard drug (fluoxetine 15 mg/kg) induced significant diminution of immobility time in tail suspension test (Control, 164.33±8.37, C. macleodii 100 mg/kg and 500 mg/kg 155.6±4.6, 89.6±7.8 and fluoxetine 15 mg/kg, 96.6±6.3, compared with the control. The open field test provides simultaneous measure of locomotion, exploration, and anxiety. They concluded on their findings that the doses of C. macleodii extract (100 and 500 mg/kg) showed significant antidepressant activity.

Hepatoprotective Activity

The hepatoprotective activity of aqueous and ethanolic extract of bark in ethanol and CCl_4 induced hepatotoxicity in male Wistar rats was evaluated. In both the cases, the extract reduced level of Serum glutamic Pyruvate transaminase (SGPT) enzyme activity in liver. Further, the extract exhibited a significant reduction in the level of mitochondrial enzyme serum Glutamic Oxaloacetic Transaminase (SGOT) and Alkaline phosphatase (ALP), an enzyme obtained from hepatic parenchyma, along with maintaining liver weight.

Preparation of silver Nanoparticle and their application along with antimicrobial effect of different plant parts of C. macleodii on various microorganism

Plants provide a better platform for nanoparticle synthesis as they are free from toxic chemicals as well as provide natural capping agents. Moreover, use of plant extracts also reduces the cost of microorganism isolation and culture media enhancing the cost competitive feasibility over nanoparticle synthesis by microorganisms. Antimicrobial properties of silver nanoparticle made the use of the particles in different fields of medicine, industries, animal husbandry, packaging, accessories, cosmetics, health, and military. Consequently, arrays of biological synthesis protocols leading to the formation of nanostructures have been reported using bacteria, fungi and plants.There are so many reviews work accomplished on silver nanoparticles stem extract of *Cordia macleodii* and its antibacterial activity against pathogenic bacteria like *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Citrobacter* sp., *E. coli*, CONS (Coagulase negative *Staphylococci*), *Acinetobacter* sp., *Enterobacter* sp., *Proteus vulgaris* and *Klebsiella* sp.

Silver nanostructure exhibit interesting optical properties directly related to surface plasmon resonance (SPR), which is highly dependent on the morphology of the samples. The SPR band in nanoparticles solution remain close to 418 nm, suggesting that the nanoparticles were dispersed in the aqueous solution with no evidence for aggregation in UV-Vis absorption spectrum an ellipsoidal particle there are two peaks whereas for spherical particle there is only one peak centered at 420 nm, in the UV–VIS spectrum. The absorption spectrum of AgNPs formed in the reaction has an absorption peak at 425 nm which indicates particles are spherical in shape. The absorption peak maximum is attributed to the Mie scattering by silver metal. The optimum silver nitrate concentration 1 mM is suitable for nanoparticles synthesis. Similarly, increasing intensity indicates increasing concentration of nanoparticles. Higher concentration of silver nitrate suggests the formation of larger nanoparticles. The Scanning Electron Microscope (SEM) image of the silver nanoparticle synthesized is shown in which indicates well dispersed particles. Silver nanoparticles were synthesized using leaves extract of Acalypha indica showed the size of the control silver nitrate obtained was greater than 1000 nm, whereas synthesized Ag NPs measured 20–30 nm in size. The SEM micrographs of nanoparticle obtained in the filtrate showed that silver nanoparticles are spherical shaped well distributed without aggregation in solution with an average size of about 5–50 nm. Scanning electron microscopy has provided further insight into the morphology and size details of the synthesized nanoparticles. SEM micrographs of the synthesized silver nanoparticles using the ethanolic extract of leaves of Pisonia grandis fabricated on a glass substrate. The synthesized silver nanoparticles were well dispersed without aggregation, possessing spherical shape. The particle size was found to less than 150 nm in all three experimental conditions

Scanning Electron Microscope image of Ag nanoparticles obtained from 5 mM $AgNO_3$ and lemon extract. The results by SEM indicate that the nanoparticles consist of agglomerates of small grains with diameter approximately 75 nm

Conclusion

C. macleodii is well known for its potential therapeutic cause more utilized by tribal peoples of Vidarbha being highly endemic and endangered tree, its vegetative as well reproductive parts would be of highly importance such as leaf, stem, bark and seeds were consistently utilized by tribal peoples in core of forest thus entire tree would great resource of medicinal and pharmacological importance used to treat various ailments and disorders of physical as well physiological healing properties. It has been used as antimicrobial, antifungal, hepato protective, antihypertensiv e, antioxidant, antivenom, and antidepressant. As remedial measure there is an urge to social community to focus on protecting its natural habitat, promoting sustainable use of forest resources, and raising awareness about its ecological importance. As due anthropogenic activites in villages and urbanization *Cordia macleodii*, is facing threats due to habitat loss and degradation.

Fig 1: ***Cordia macleodii***

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