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Exploring the Therapeutic Potential of *Cordia sinensis* Lam.: A Review of its Pharmacology and Phytochemistry

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Abstract

Cordia sinensis Lam., belonging to the Boraginaceae family, is a long-lived shrub or small tree primarily located in warm and temperate regions. This review aims to offer a thorough analysis of *Cordia sinensis*, including its botanical features, traditional medicinal applications, chemical composition, and pharmacological properties. The plant is renowned for its medicinal properties, traditionally employed in various cultures for treating ailments such as fever, respiratory disorders, gastrointestinal issues, and skin diseases. Phytochemical investigations have revealed the presence of bioactive compounds, including flavonoids, glycosides, terpenoids, and phenolic acids, which contribute to its diverse pharmacological effects. Research has indicated that *Cordia sinensis* has exhibited antimicrobial, anti-inflammatory, antioxidant, hepatoprotective, and anticancer activities. These findings underscore its potential as a valuable therapeutic agent. This review synthesizes existing knowledge on *Cordia sinensis*, highlighting its medicinal relevance and prospects for future pharmacological and clinical applications. Understanding the comprehensive profile of *Cordia sinensis* could enhance its presentation in modern medicine and promote its conservation and sustainable use.

Keywords: Boraginaceae; *Cordia sinensis Lam.;* Pharmacology; Phytoconstituents

1. Introduction

Traditional herbal medicines have played an integral role in global healthcare systems, being employed by diverse cultures throughout history. The practice of herbal medicine in India is deeply rooted in ancient cultures that include systems such as Ayurveda, Unani, Siddha, and Homeopathy, collectively constituting a vast repository of therapeutic knowledge [1-2]. Bioactive compounds sourced from plants have long served as crucial foundations for the development of new therapeutic drugs. In recent times, there has been a noticeable surge in global interest towards herbal medicines. The renewed focus on herbal medicine has spurred accelerated research into the pharmacological activities exhibited by plants traditionally used in medicine [3-5].

The *Cordia* genus, which is part of the Boraginaceae family, includes over 250-300 species of trees and shrubs found mainly in tropical and subtropical regions. The genus name honors ‘Valerius Cordus’, a German botanist who lived in the 16th century. The particular epithet "sinensis" refers to its Chinese origin. Known for its medicinal status, this genus has been widely studied for its phytochemical properties. Studies have identified a diverse array of bioactive compounds in *Cordia* species, comprising alkaloids, flavonoids, phenolic compounds, quinones, triterpenoids, lignans, saponins, steroids, phenylpropanoids, polyphenols, porphyrins, and coumarins. These compounds contribute to the genus's various therapeutic effects

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and its potential in medicinal applications [6-10].

Cordia sinensis Lam., also known by its synonyms *Cordia rothii* Roem. & Schult. and *Cordia gharaf* Ehrenb. ex Asch., is a prominent member of the *Cordia* genus. Commonly referred to as grey-leaved saucer berry or grey-leaved cordia, this plant species has been historically utilized by traditional healers for its diverse therapeutic properties. Various parts of *Cordia sinensis* are used to treat a wide range of conditions, including headaches, coughs, chronic fever, chest pain, digestive disorders, eye infections, joint ingrained inflammation, swelling, dental discomfort, parasitic infections, and as a diuretic. These traditional uses underscore the plant's significance in folk medicine [11-13]. A decoction made from the bark and roots of *Cordia sinensis* Lam. is employed to treat malaria, relieve stomachaches, and alleviate chest pain [14-15]. The bark decoction is known for its astringent qualities and is applied as a gargle [16].

Despite its extensive use in traditional medicine, scientific interest in the pharmacological properties of *Cordia sinensis* has only recently gained momentum. The objective of this paper is to contribute to the scientific literature by providing a comprehensive and up-to-date review of *Cordia sinensis*, serving as a valuable resource for researchers, herbalists, pharmacists, and healthcare practitioners. The taxonomic hierarchy [17] and vernacular names [18] of *Cordia sinensis* are outlined in **Table 1.**

Table 1: Scientific classification and Vernacular names of *Cordia sinensis*

Scientific classification	Vernacular names
Kingdom: Plantae	English: Grey-leaved cordia, Grey-leaved saucer-berry
Class: Dicotyledons	
Subclass: Gamopetalae	Sanskrit: Laghushleshmataka
Series: Bicarpellatae	Tamil: Sirunaruvuli, Nariviri, Naruvili, Sandanamamani
Order: Boraginales	
Family: Boraginaceae	Kannada: Kirichalle
Genus: *Cordia*	Hindi: Gondi, Gondni, Gundi
Species: *Cordia sinensis* Lam.	Telgu: Chinnabotuku, Chinnavirigi
	Malayalam: Veri, Verasham
	Marathi: Gondani
	Rajasthani: Gondi, Gundi
	Gujarati: Gundi, Liyargundi

Geographic distribution

Cordia sinensis thrives in dry savannas, bushlands, and along riverbanks and is mainly native to Africa, Yemen, Palestine, India, Sri Lanka, Egypt, Ethiopia, Jordan, Madagascar, Namibia, Pakistan, Tanzania, Kenya, Zimbabwe, and Sudan. In India, *Cordia sinensis* is cultivated in various regions such as Delhi, Haryana, Punjab, and South India, with a significant presence in the arid and semiarid zones of Gujarat and Rajasthan. In Ayurveda, this plant is called Laghushleshmataka, a substitute for Shleshmataka [19-20].

Morphology of *Cordia sinensis*

Cordia sinensis commonly exhibits a growth pattern as a shrub, attaining heights of up to 4 meters, or as a bushy tree, reaching heights of up to 8 meters. The bark of this species typically displays a brownish-grey hue. **Fig.1** illustrates the various parts of *Cordia sinensis.*

Fig.1. Parts of *Cordia sinensis* plant

Leaves are opposite, sub-opposite or alternate 6.3-10 x 2.3-2 cm, ovate, rounded at the apex, rough above, more or less hairy, imperceptibly pinnate below, the base narrows toward the petiole. The petioles are 1.3 cm long.

Flowers: The plant produces small, white flowers, often tetramerous, arranged in terminal or axillary cymes. These flowers have short pedicels and peduncles that are 2-2.5 cm in length. The calyx, measuring 4-5 mm, is vein-shaped and rounded when blooming, with a somewhat pubescent exterior and shiny silky hairs inside; the lobes are small and blunt. The corolla is 6 mm long, featuring four elongated, obtuse, and reflexed tubular lobes. The filaments are covered with hairs.

The **fruits** are conical, usually containing a single seed and measuring approximately 1-1.3 cm in length. When ripe, they turn orange, and upon drying, they change to yellow or reddish-brown. They have a gummy texture and are edible.

Seeds are generally rigid, abrasive, and yellowish cream in color.

Soil: The plant thrives in alluvial, sandy, red loamy, and rocky soils, particularly in moist river basin areas.

Biology: The flowering and fruiting phenology of the species exhibits a bimodal pattern. The primary flowering period occurs in the winter months, from December to February, with subsequent fruit maturation taking place in the summer, from April to June. Additionally, a secondary flowering event is observed in August, followed by fruiting in December. The fruits serve as a critical food source for various frugivores, including monkeys, giraffes, baboons, and birds, which act as the primary dispersal agents for the seeds [18, 21-23].

Nutritional information

The kernels, leaves, flowers, and tender branches of *Cordia sinensis* are edible and frequently utilized as food sources. The fruit is particularly popular during the summer and is consumed fresh when ripe, whereas unripe fruits are commonly used as vegetables and for pickling. Moreover, the leaves and flower buds are often incorporated into diets as vegetables. The leaves are notable for their high dry matter content (41.2%) and substantial crude protein content (13.8%), along with significant energy and mineral levels. The fruits of *Cordia sinensis* are characterized by their high content of protein (11.37-12.85%) and sugars (8.14-15.13%). Mineral content per 100g of *Cordia sinensis* fruits include: Calcium: 0.27-0.76 mg; Iron: 6.7-11.85 mg; Zinc: 2.0-2.7 mg; Magnesium: 60.7-86.5 mg; Manganese: 0.3-1.1 mg; Copper: 1.3-1.6 mg [24-27].

2. Photochemistry

Phytochemical analysis of *Cordia sinensis* has revealed a wide range of compounds, such as phenolics, flavonoids, free fatty acids, fatty acid esters, hydrocarbons, terpenoid quinones, terpenoid hydroquinones, phytosterols, and steroids. **Table 2** and **Table 3** provide information and structure of some phytoconstituents isolated from *Cordia sinensis* respectively.

3. Pharmacological Activities

3.1 Antioxidant Activity

The confluence of oxidative injury, inflammation, and glycation represents intertwined pathophysiological mechanisms that exert substantial influence on the progression of numerous severe diseases. The multitarget action of plant compounds and their historical use in traditional medicine provide a wide array of mechanisms help neutralize free radicals, modulate inflammatory pathways and potentially impede the formation of advanced glycation end-products [28-29].

Al-Musayeib *et al.* (2011) conducted a research wherein nine compounds were isolated from the ethyl acetate fraction of *Cordia sinensis.* Among these compounds were protocatechuic acid, rosmarinic acid, *trans*-caffeic acid, quercetin-3-O-β-D-glucopyranoside, and kaempferol-3-O-α-L-rhamnopyranosyl (1→6)-β-D glucopyranoside, all of which displayed noteworthy anti-inflammatory and antioxidant properties. The purity of these compounds was validated through high-performance liquid chromatography (HPLC) analysis. This study represented the initial isolation of compounds from the aerial parts of *Cordia sinensis*, shedding light on their considerable biological activities and enriching the knowledge of the species' phytochemistry [30].

Additionally, antioxidant activity, determined using the DPPH assay method with the methanolic extract of *Cordia sinensis* roots and stem bark, presented the highest scavenging activity at 60% [31-32].

In a separate investigation, notable antioxidant properties were found in plant extracts from *Cordia rothii* and *Viola serpens*. The IC_{50} values were 0.039 ± 0.05 mg/mL for *Cordia rothii* and 0.05 ± 0.07 mg/mL for *Viola serpens*. This antioxidative effect is likely attributed to the presence of flavonoids and phenolic compounds [33].

3.2 Antiglycation, antifungal, and insecticidal activities

The widespread use of chemical fungicides for disease control poses significant environmental risks, potential human exposure to pesticides, and concerns about residue accumulation on fruits. In response to these challenges, there is an increasing focus on exploring botanical remedies with novel applications, particularly in pest management. Plant extracts with documented antimicrobial properties are especially attractive as potential alternatives to synthetic fungicides [34].

In a research by Khan *et al.* (2021), 31 phytochemicals were identified by analysing crude extracts and fractions made from *Cordia sinensis* leaves using gas chromatography-mass spectrometry (GC-MS) and gas chromatography-flame ionisation detection (GC-FID). Significant insecticidal activity was shown by the ethyl acetate fraction against *Sitophilus oryzae*, and it also showed antifungal activities against *Microsporum canis*. Moreover, the n-hexane fraction was also evaluated for its antiglycation activity, demonstrating a significant 77.4% inhibition of advanced glycation end products (AGEs), thus highlighting its potential in this regard. These results indicated that *Cordia sinensis* leaf extracts have potential applications in the development of organic insecticides, fungicides, and agents for managing diabetes [35]

Furthermore, certain phenolic compounds isolated from the ethyl acetate fraction of the aerial parts of *Cordia sinensis* exhibited significant inhibitory effects against glycation [30].

3.3 Antibacterial and cytotoxic activities

The intricate relationship between oxidative stress and antimicrobial resistance (AMR) underscores the complexity of modern health challenges. Oxidative stress, stemming from an imbalance in reactive oxygen species (ROS) levels, inflicts cellular damage and sets the stage for DNA mutations may lead to antimicrobial resistance development. AMR, on the other hand, poses a significant global health and development threat, endangering the progress achieved in modern medicine. Remarkably, antimicrobial-resistant pathogens have the capacity to induce oxidative stress within their hosts, further intensifying the struggle against infection. The World Health Organization (WHO) emphasizes to integrate the ancient knowledge of natural remedies with traditional health practices to effectively tackle present-day health challenges [36-37].

The roots of *Cordia rothii* were processed to obtain various fractions using solvents of varying polar characteristics, namely n-hexane, chloroform, ethyl acetate, acetone, and methanol. The antimicrobial properties of the fractions were assessed using the disk diffusion method against various microorganisms. GC-MS analysis was conducted to detect the chemical components in the bioactive fractions, which revealed the presence of forty-five phytoconstituents. The study concluded that the significant antimicrobial property of *Cordia sinensis* roots could be attributed to these identified phytoconstituents [31].

In a study by Eltayeib *et al.*, the stem bark of *Cordia sinensis* was pulverized and consecutively extracted with solvents including petroleum ether, chloroform, ethyl acetate, and methanol. Initial phytochemical analysis unveiled the presence of diverse bioactive compounds in all extracts, encompassing flavonoids, tannins, glycosides, sterols, triterpenes, and alkaloids. Subsequently, the crude extracts underwent evaluation via the disc diffusion method at doses of 25 and 50 mg/mL against standard bacteria (*Bacillus subtilis, Staphylococcus aureus, Klebsiella,* and *Pseudomonas aeruginosa*) and fungi (*Candida albicans* and *Aspergillus niger*). The methanolic extract, specifically at a concentration of 50 mg/mL, exhibited substantial activity against *Klebsiella* and *P. aeruginosa*, while demonstrating moderate inhibition against *B. subtilis, S. aureus, C.albicans,* and *A. niger.* Additionally, cytotoxicity assessments were conducted using a brine shrimp lethality assay to ascertain LD_{50} values, revealing moderate toxicity across all extracts. These findings suggested that deeper examination is necessary to detect and characterize the specific active compounds responsible for the observed bioactivities, particularly in the methanolic extract of *Cordia sinensis* [32].

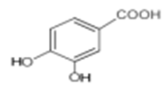
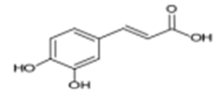
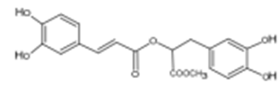
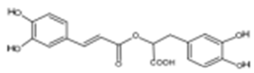
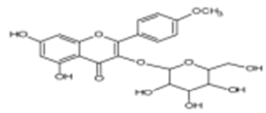
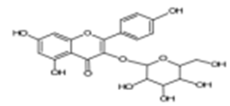
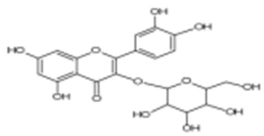
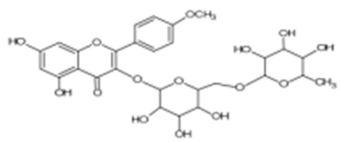
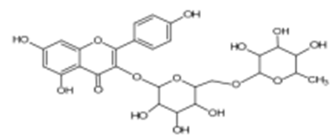
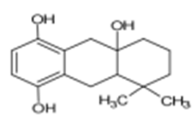
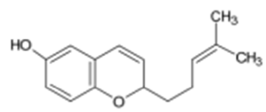
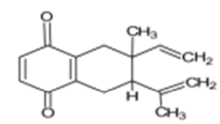
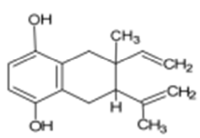
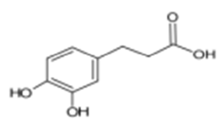
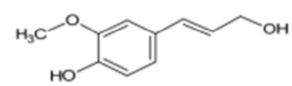
In 2009, El-Kamali and El-Karim conducted an investigation on the antimicrobial properties of several medicinal plants, including *Cordia sinensis*, which are traditionally used in Sudanese medicine for the treatment of wound infections. The researchers prepared extracts from the stem bark of *Cordia sinensis* using solvents such as ethanol, petroleum ether, ethyl acetate, methanol, and water. Following this, they assessed the antibacterial effectiveness of these extracts commonly encountered bacterial strains including *Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa*, and *Staphylococcus aureus,* employing well agar diffusion technique. The findings regarding *Cordia sinensis* revealed that the ethanol extract exhibited positive therapeutic outcomes against *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, thus validating its traditional use in managing bacterial infections [38].

Zubair *et al.* (2020) examined crude extracts from *Cordia rothii* and *Viola serpens* to determine their phytochemical composition, antioxidant potential, antibacterial, antifungal, and acute toxicity. The antimicrobial activity of the crude extracts was evaluated using the disc diffusion method, and the extracts displayed potent antibacterial effects and limited antifungal action. In vivo studies indicated that the crude extracts had a favourable safety profile with no significant acute toxicity observed at tested doses [33].

Table 2: Phytochemical constituents of *Cordia sinensis*

Part of the Plant	Phytochemical Class	Phytochemical constituents	Refs.
Aerial parts	Phenolic compounds	Rosmarinic acid, methyl rosmarinic acid, *trans*-caffeic acid, protocatechuic acid	[30]
	Flavonoid Glycosides	Quercitin-3-O-β-D- glucopyranoside, kaempferol-3-O-β-D- glucopyranoside kaempferide-3-O-β-D- glucopyranoside, kaempferol-3-O-α-L-rhamnopyranosyl (1→6) -β-D-glucopyranoside, kaempferide-3-O-α-L-rhamnopyranosyl (1→6) -β-D-glucopyranoside	
Leaves	Hydrocarbons	n- tetracosane, n- hexacosane, n-ocatcosane	[35] [40]
	Saturated and Unsaturated Fatty acids	n-tetradecanoic acid, n-pentadecanoic acid, iso-hexadecanoic acid, n-hexadecanoic acid, n-octadecanoic acid, octadec-9E-enoic acid, octadec-9Z-enoic acid	
	Fatty alcohol	1-octacosanol	
	Fatty acids methyl esters	methyl octanoate, methyl-9-oxo-nonanoate, methyl dodecanoate, methyl tetradecanoate, methyl pentadecanoate, methyl hexadec-9Z-enoate, methyl hexadecanoate, methyl heptadecanoate, methyl octadec-9Z,12Z-dienoate, methyl octadec-9Z,12Z,15Z-trienoate, methyl octadecanoate, methyl eicosanoate, methyl docosanoate, methyl tricosanoate, methyl tetracosanoate`	
	Terpenes	2,7-dimethyl-1,6-octadiene, 1,2,3,4,4a,5,6,8a-octahydro-7-methyl-4-methylene-1-(1-methylethyl)-naphtahlaene, 3,7,11,15-tetramethyl-2-hexadecen-1-ol	
	Phytosterols	β-sitosterol, stigmasta-3,5-diene, stigmast-5-en-3-*O*-*β*-D-glucoside	
	Terpenoid	6,10,14-trimethylpentadecan-2-one	
	Glycosides	Syringaresinol mono-β-D-glucoside, 6-hydroxy-3-oxo-α-ionol 9-O-β-D-glucopyranoside, Staphylionoside D, 3-(3′,5′-dimethoxy-4′-O-*β*-D-glucopyranosyl-phenyl)-prop-2E-en-1-ol	
	Glycosylated fatty acid amides	(2S,1′S,2′S,3′R,7′Z)-N-1′-(O-β-D-glucopyranosyl)methyl-2′,3′-dihydroxy-heptadec-7′-enyl-2-hydroxytetracosaneamide	
	Phenylpropanoids derivatives	Methyl 2-hydroxy-3-(4′-hydroxy)-phenylpropionate	
	Hydroxyphenyl lactic acids	(2R)-(4-hydroxyphenyl) lactic acid	
Roots	Terpenoid quinones & Hydroquinones	cordial A, cordiachromene A, cordiachrome C, cordiaquinol C	[31] [51]
	Phytosterol	stigmasta-3,5-diene,β-sitosterol, stigmasterol	
	Phenylpropanoid	coniferyl alcohol, hydrocaffeic acid	
	Triterpenoids	cycloartenol, 24-methylenecycloartanol,cycloeucalenol	
Seeds	Fatty acids	Ricinoleic acid, oleic acid, steric acid, sterculic acid	[52]
Fruits	Carbohydrates	Dextro isomers of glucose, galactose, fructose, xylose, rhamnose, galacturonic acid	[53]

Table 3 Structure of some phytoconstituents of *Cordia sinensis*

 Protocatechuic acid	 *trans*-caffeic acid	 Methyl rosmarinate
 Rosmarinic acid	 Kaempferide-3-O-β-D-glucopyranoside	 Kaempferol-3-O-β-D-glucopyranoside
 Quercetin-3-O-β-D- glucopyranoside	 Kaempferide-3-O-α-L-rhamnopyranosyl (1→6)- β-D-glucopyranoside	 Kaempferol-3-O-α-L-rhamnopyranosyl (1→6)- β-D-glucopyranoside
 Cordiol A	 Cordiachromene A	 Cordiachrome C
 Cordiaquinol C	 Hydrocaffeic acid	 Coniferyl alcohol

3.4 Hepatoprotective activity

Hepatic illness refers to any condition or disease that affects the liver, a vital organ responsible for numerous metabolic, detoxifications, and storage functions within the body. These conditions can range from mild, reversible liver inflammation to severe, life-threatening diseases like cirrhosis and liver cancer. Despite significant advancements in contemporary medicine, there remains a paucity of pharmacotherapies capable of hepatoprotection, hepatic cell regeneration, or substantial enhancement of liver function. Traditional medicine systems, like Ayurveda and Chinese medicine, have extensive experience in using various remedies for liver-related ailments, which often include herbal extracts. Even with this wealth of knowledge, effectively addressing liver disorders with a single, specific herbal remedy remains a captivating yet challenging task [39].

Iqbal *et al.* (2022) investigated the methanolic fraction derived from *Cordia rothii* for its potential antioxidant and hepatoprotective properties against liver injury induced by carbon tetrachloride (CCl_4).The study employed the DPPH assay, ferric thiocyanate (FTC) test, and HepG2 cell viability assay to evaluate the antioxidant capacity of the methanolic fraction. The findings demonstrated significant antioxidant activity in both the DPPH and FTC assays. Additionally, the methanolic fraction exhibited liver protective effects by enhancing the survival of HepG2 cells subjected to toxicity. The methanolic fraction of *Cordia rothii*, when administered to rats with liver damage, notably reduced serum levels of total bilirubin and hepatic enzymes including alkaline phosphatase, aspartate aminotransferase, and alanine transaminase. It enhanced liver antioxidant defenses, as indicated by elevated concentrations of superoxide dismutase and glutathione, coupled with reduced levels of malondialdehyde. Histopathological analysis revealed preserved hepatocyte integrity. Furthermore, this intervention restored the mRNA expressions of inflammatory biomarkers TNF-α, IL-1β, IL-10, IL-6, NF-κB, and Nrf2 to their normal levels. These findings suggest that *Cordia rothii* methanolic fraction could be a potential therapeutic agent for liver diseases, warranting further investigation to fully elucidate its molecular mechanisms and active compounds [40].

3.5 Immunomodulatory activity

The immune system plays a crucial role in the development and progression of many diseases. Researchers have explored ways to adjust immune responses for treatment. Immunomodulation seeks to boost immunity or curb unwanted reactions. Traditional medicines have been found to effectively modulate the host immune response, strengthening it when necessary and suppressing it when harmful. Plant-based natural substances are particularly intriguing for their immune-modifying abilities. They offer alternative therapies, especially beneficial when the immune system isn't functioning optimally [41].

To investigate the immunomodulatory properties of *Cordia rothii*, the leaves were initially subjected to methanol extraction. The resultant extract was subsequently fractionated using n-hexane, ethyl acetate, and butanol as solvents. This study led to the isolation and identification of ten compounds. The immune-modulating effects of the crude extract, its fractions, and pure compounds isolated from *Cordia rothii* were assessed through tests measuring oxidative burst, phytohaemagglutinin (PHA)-stimulated T-cell proliferation, and nitric oxide (NO) levels. The fraction of ethyl acetate exhibited substantial inhibition of reactive oxygen species, with an IC_{50} value of 29.4±2.8 µg/mL. The n-hexane fraction demonstrated a slowdown in PHA-stimulated T-cell proliferation, with an IC_{50} value of less than 3.12 µg/mL. Syringaresinol mono-β-D-glucoside and methyl-2-hydroxy-3-(4'-hydroxy)-phenyl propionate were recognized as potent immunomodulatory agents among the isolated compounds [42].

3.6 Cardioprotective and Hypoglycemic activities

Globally, the prevalence of long-term diseases like obesity, diabetes, cardiovascular diseases, and cancer is on the rise at an alarming rate. Cardiovascular dysfunction stands out as a particularly devastating condition in urgent need of medical advancements. While modern medications can effectively manage this ailment, they often come with unwanted side effects. Plants present a diverse array of compounds that hold promise for protecting the heart. Numerous plant-derived substances, including flavonoids, polyphenols, and antioxidants, have demonstrated positive effects on cardiovascular health [43].

Chauhan and Chavan (2009) investigated the traditional use of *Cordia rothii* bark in the Saurashtra region of Gujarat for heart ailment treatment. They utilized a bark decoction to assess its impact on isolated rat hearts using the Langendorff Perfused Heart Model, observing significant cardiotonic effects. Additionally, they found that the alcoholic extract exhibited potential in lowering blood glucose levels. These activities were attributed to the presence of a diverse range of phytochemical compounds. This research provided scientific validation for the traditional medicinal application of *Cordia rothii* bark in managing heart conditions and underscores its hypoglycemic properties [44].

3.7 Antitubercular activity

Tuberculosis (TB) remains a significant global health concern, especially in developing countries with limited access to healthcare resources. Research on anti-TB drugs is crucial for tackling the evolving challenges of TB control, such as drug resistance, treatment adherence, co-infections, and global health disparities. Many traditional medicinal plants have been utilized for centuries across various cultures to treat respiratory ailments, including TB. It's entirely reasonable to view plants as a potential source for anti-TB agents, and integrating traditional knowledge with modern scientific approaches can pave the way for the development of novel plant-based therapies for TB [45].

In 2010, Mariita *et al.* conducted a comprehensive study to investigate the antitubercular activity and phytochemical composition of methanol extracts obtained from nine medicinal plants frequently utilized within the Samburu community in Kenya, including *Cordia sinensis*. The study employed the BACTEC MGIT 960 system to evaluate the effectiveness of these methanol extracts against *mycobacterial strains: Mycobacterium tuberculosis*, *Mycobacterium kansasii, Mycobacterium fortuitum,* and *Mycobacterium smegmatis*. The findings revealed that several methanol extracts demonstrated potential as antituberculosis agents. Specifically, *Cordia sinensis* exhibited significant activity against *Mycobacterium* *tuberculosis* and *Mycobacterium kansasii*, with an inhibition (Zero Gus) observed at a concentration of 0.5 mg/mL. These results suggested that certain plant-derived methanol extracts could be promising candidates for the development of novel antituberculosis therapies [46].

3.8 Anti-inflammatory activity

Inflammation serves as a fundamental physiological response to tissue injury, infection, or noxious stimuli. It relies on coordinated interactions among cells and mediators to control essential processes like chemotaxis, migration, and proliferation. However, when inflammation persists, it can lead to the onset of various diseases such as arthritis, cardiovascular disorders, and certain types of cancer. Medicinal plants, deeply rooted in traditional medicine and increasingly supported by scientific research, offer promising avenues for developing effective treatments against inflammation [47].

The inflammation-mitigating effects of *Cordia gharaf* leaves and bark were evaluated using the carrageenan-induced paw swelling model in rats. Significant suppression of inflammation was observed at doses of 200 mg/kg and 250 mg/kg, becoming evident 5 hours post-administration. The highest suppression was noted at the 250 mg/kg dose as early as 2 hours, with further enhancement observed at the 5-hour mark. The inflammation-reducing effectiveness of the ethanolic extract of *Cordia gharaf* was found to be noteworthy and comparable to that of Indomethacin at a dose of 10 mg/kg [48].

3.9 Wound healing activity

Wound healing is a vital biological process that repairs damaged tissue and restores its structure and function. It progresses through several interconnected phases: inflammation, proliferation and remodeling. Successful wound healing is crucial as it ensures tissue integrity, prevents infections, restores function, and enhances overall well-being. Plants and their compounds provide valuable therapeutic options for wound management. Ongoing research aims to harness their potential for developing safe and effective treatments to promote wound healing and enhance patient outcomes [49].

Various extracts of *Cordia rothii* leaves were assessed for their wound healing potential using the Excision Wound Model in rats, by applying them topically at doses of 100, 200, and 400 mg/kg body weight. The study observed a significant dose-dependent enhancement in wound healing in animals analogously administered with both alcoholic and aqueous extracts in comparison to the control group. Both types of extracts showed a dose-dependent increase in the percentage of wound contraction [50]. **Fig. 2** showcases the significant secondary compounds and various uses of *Cordia sinensis*.

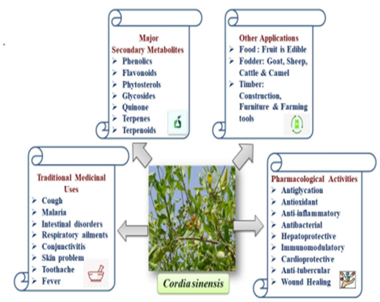


Fig.2. Major secondary metabolites and applications of *Cordia sinensis*

2. Conclusion

The use and promotion of medicinal herbs is beneficial for all current defensive strategies, as they are crucial for preventing disease. *Cordia sinensis*, a species within the Boraginaceae family, holds significant ethnopharmacological value, traditionally employed for the management of diverse medical conditions including fever, pulmonary ailments, gastrointestinal issues, and skin diseases. Extensive phytochemical research has uncovered a rich profile of flavonoids, terpenoids, phenolics, phytosterols and others, which contribute to its diverse pharmacological activities. Over centuries of traditional usage and contemporary scientific investigation, *Cordia sinensis* has emerged as a valuable medicinal plant with varied pharmacological properties. The potential of *Cordia sinensis* in developing novel therapeutic agents is considerable, offering promising avenues for modern medical applications. However, to fully harness its therapeutic potential, further detailed studies are necessary to explore its mechanisms of action, safety profile, and clinical efficacy.

In spite of the promising therapeutic potential of *Cordia sinensis*, there are several challenges that need to be addressed: *Cordia sinensis* is one of the most understudied species within the *Cordia* genus, leading to a limited understanding of its phytochemical properties and pharmacological effects. Clinical trials involving humans are notably lacking, hindering the validation of its efficacy and safety for various treatments. Additionally, there is a substantial gap in comprehensive toxicological studies, leaving potential adverse effects and long-term safety concerns unexplored, especially at higher doses. Although various pharmacological activities have been identified, the precise mechanisms of action for *Cordia sinensis* are poorly elucidated, highlighting the need for detailed mechanistic studies to develop targeted therapies. Overcoming these challenges through rigorous research, standardization efforts, and sustainable practices will be crucial for the successful integration of *Cordia sinensis* into modern medicinal applications.

3. Conflicts of interest

The authors state that there are no conflicts of interest.

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6. References

[1] Yuan, H., Ma, Q., Ye, L., & Piao, G. (2016). The traditional medicine and modern medicine from natural products. *Molecules*, *21*(5), 559. https://doi.org/10.3390/molecules21050559

[2] Jaiswal, Y. S., & Williams, L. L. (2017). A glimpse of Ayurveda -The forgotten history and principles of Indian traditional medicine. *Journal of Traditional and Complementary Medicine*, *7*(1), 50-53. https://doi.org/10.1016/j.jtcme.2016.02.002

[3] Satria, D., Sitorus, P., Dalimunthe, A., Waruwu, S. B., & Asfianti, V. (2024). Oral acute toxicity study of ethanol extract of Mobe leaves (*Artocarpus lacucha* Buch-Ham) in Wistar rats. *Pharmacia*, *71*, 1-8. https://doi.org/10.3897/pharmacia.71.e117500

[4] Tekuri, S. K., Pasupuleti, S. K., Konidala, K. K., Amuru, S. R., Bassaiahgari, P., & Pabbaraju, N. (2019). Phytochemical and pharmacological activities of *Solanum surattense* Burm. f.–A review. *Journal of Applied Pharmaceutical Science*, *9*(3), 126-136. https://dx.doi.org/10.7324/JAPS.2019.90318

[5] Suleiman, W. B., & Helal, E. E. H. (2022). Chemical constituents and potential pleiotropic activities of *Foeniculum vulgare* (Fennel) ethanolic extract; in vitro approach. *Egyptian Journal of Chemistry*, *65*(7), 617-626.+ https://dx.doi.org/10.21608/ejchem.2021.107991.4938

[6] Thirupathi, K., Kumar, S. S., Raju, V. S., Ravikumar, B., Krishna, D. R., & Mohan, G. K. (2008). A review of medicinal plants of the genus *Cordia:* Their chemistry and pharmacological uses. *Journal of Natural Remedies*, *8*(1), 1-10. https://doi.org/10.18311/jnr/2008/288

[7] Matias, E. F. F., Alves, E. F., Silva, M. K. D. N., Carvalho, V. R. D. A., Coutinho, H. D. M., & Costa, J. G. M. D. (2015). The genus *Cordia*: botanists, ethno, chemical and pharmacological aspects. *Revista Brasileira de Farmacognosia*, *25*, 542-552. https://doi.org/10.1016/j.bjp.2015.05.012

[8] Oza, M. J., & Kulkarni, Y. A. (2017). Traditional uses, phytochemistry and pharmacology of the medicinal species of the genus *Cordia* (Boraginaceae). *Journal of Pharmacy and Pharmacology*, *69*(7), 755-789. https://doi.org/10.1111/jphp.12715

[9] Hussein, H. M., Mohsen, E., Abdelmonem, A. R., Abdel Kawy, M. A., Al-Karmalawy, A. A., & El-Shiekh, R. A. (2024). New Insight into the Anticholinesterase Potential of *Cordia dichotoma* G. Forst. and *Cordia sebestena* L. Leaves, Phenolic Characterization of their Active Extracts by HPLC-DAD and Molecular Modeling. *Egyptian Journal of Chemistry*, *67*(8), 225-237. https://dx.doi.org/10.21608/ejchem.2024.256819.9007

[10] Aimey, Z., Goldson-Barnaby, A., & Bailey, D. (2020). A Review of *Cordia* Species Found in the Caribbean: *Cordia Obliqua* Willd., *Cordia Dichotoma* G. Forst. And *Cordia Collococca* L. *International Journal of Fruit Science*, *20*(sup2), S884-S893. https://doi.org/10.1080/15538362.2020.1772181

[11] Rastogi, R. P., & Mehrotra, B. N. (1990). Compendium of Indian medicinal plants. *Central Drug Research Institute, Lucknow and National Institute of Science Communication and Information Resources, New Delhi, India*, 5, 248.

[12] Ahuja, S. C., Ahuja, S., & Ahuja, U. (2020). Nutraceautical wild Fruits of India-Lasora (*Cordia*)-History, Origin and Folklore. *Scholars Academic Journal of Biosciences*, *8*, 187-209.

[13] Ghori, V. P., Gatecha, H. N., Desai, T. R., & Pandya, D. J. (2011). Pharmacognostic study of leaves of *Cordia rothii* Linn. *Pharmacognosy Journal*, *3*(22), 35-38. https://doi.org/10.5530/pj.2011.22.7

[14] Bussmann, R. W., Paniagua-Zambrana, N. Y., & Njoroge, G. N. (2020). *Cordia africana* Lam., *Cordia monoica* Roxb., *Cordia sinensis* Lam. Boraginaceae. *Ethnobotany of the Mountain Regions of Africa*, 341-350. https://doi.org/10.1007/978-3-319-77086-4_50-1

[15] Lulekal, E., Kelbessa, E., Bekele, T., & Yineger, H. (2008). An ethnobotanical study of medicinal plants in Mana Angetu District, southeastern Ethiopia. *Journal of Ethnobiology and Ethnomedicine*, *4*, 1-10. https://doi.org/10.1186/1746-4269-4-10

[16] Khare, C. P. (2008). *Indian medicinal plants: an illustrated dictionary*. Springer Science & Business Media, 173. https://doi.org/10.1007/978-0-387-70638-2

[17] Kale, B.S., & Sanap, C.S. (2022). Comparative anatomical study of two *Cordia* species (Boraginaceae) from the Northern Western Ghats, India. *International Journal of Botany Studies*, 5(7), 1-10.

[18] Kirtikar, K. R. (1935). *Indian Medicinal Plants*: Lalit Mohan Basu. Allahabad, India, 3, 1678-1679. http://asi.nic.in/asi_books/2048.pdf.

[19] Warfa, A. M. (1990). Taxonomy and distribution of *Cordia sinensis* and *C. nevillii* (Boraginaceae), a widespread species pair in Africa and Asia. *Nordic Journal of Botany*, *9*(6), 649-656. https://doi.org/10.1111/j.17561051.1990.tb00557.x

[20] Stave, J., Oba, G., Nordal, I., & Stenseth, N. C. (2007). Traditional ecological knowledge of a riverine forest in Turkana, Kenya: implications for research and management. *Biodiversity and Conservation*, *16*, 1471-1489. https://doi.org/10.1007/s10531-006-9016-y

[21] Dev, R., Dayal, D., & Sureshkumar, M. (2020). Gibberellic acid and potassium nitrate promote seed germination and growth of grey-leaved saucer-berry (*Cordia sinensis* Lam.) seedlings. *International Journal of Fruit Science*, *20*(sup2), S937-S954. https://doi.org/10.1080/15538362.2020.1774465

[22] Orwa, C. (2009). Agroforestree Database: a tree reference and selection guide, version 4.0. http://www.worldagroforestry.org/sites/treedbs/treedatabases.asp

[23] Ahmed, A., & Kordofani, M. A. (2012). Morphological and anatomical studies of *Cordia abyssinica* R. Br. and *Cordia sinensis* Lam. (Boraginaceae) in Sudan. *Journal of Chemical and Pharmaceutical Research*, *4*(10), 4582-4588.

[24] Rathore, M., & Kumar, H., (2021). *Cordia gharaf:* an important lesser known fruit tree of Rajasthan. *International Journal of Plant Sciences* (Muzaffarnagar), 16(2), 131-134. https://doi.org/10.15740/HAS/IJPS/16.2/131-134

[25] Dev, R., Sureshkumar, M., Kumar, S., Venkatesan, K., Singh, T., Tetarwal, A. S., *et al*. (2020). Collection, characterization, conservation and utilization of *Cordia sinensis* Lam.: An underexploited multipurpose fruit species of hot arid regions. *Plant Genetic Resources*, *18*(6), 427-436. https://doi.org/10.1017/S1479262120000453

[26] Kuria, SG, Wanyoike, MM, Gachuiri, CK, & Wahome, RG (2005). Nutritive value of important range forage species for camels in Marsabit district, Kenya. *Tropical and Subtropical Agroecosystems*, *5* (1), 15-24.

[27] Murray, S. S., Schoeninger, M. J., Bunn, H. T., Pickering, T. R., & Marlett, J. A. (2001). Nutritional composition of some wild plant foods and honey used by Hadza foragers of Tanzania. *Journal of Food Composition and Analysis*, *14*(1), 3-13. https://doi.org/10.1006/jfca.2000.0960

[28] Rodwattanagul, S., Nimlamool, W., & Okonogi, S. (2023). Antioxidant, antiglycation, and anti-inflammatory activities of *Caesalpinia mimosoides*. *Drug Discoveries & Therapeutics*, *17*(2), 114-123. https://doi.org/10.5582/ddt.2023.01002

[29] Youssef, H. A., Ali, S. M., Sanad, M. I., & Dawood, D. H. (2020). Chemical investigation of flavonoid, phenolic acids composition and antioxidant activity of *Tagetes erecta* flowers. *Egyptian Journal of Chemistry*, *63*(7), 2605-2615. https://dx.doi.org/10.21608/ejchem.2019.19839.2197

[30] Al-Musayeib, N., Perveen, S., Fatima, I., Nasir, M., & Hussain, A. (2011). Antioxidant, anti-glycation and anti-inflammatory activities of phenolic constituents from *Cordia sinensis. Molecules*, *16*(12), 10214-10226. https://doi.org/10.3390/molecules161210214

[31] Khan, K., Firdous, S., Ahmad, A., Fayyaz, N., Nadir, M., Rasheed, M., *et al*. (2016). GC-MS profile of antimicrobial and antioxidant fractions from *Cordia rothii* roots. *Pharmaceutical Biology*, *54*(11), 2597-2605. https://doi.org/10.3109/13880209.2016.1172320

[32] Eltayeib, A. A., & Ishag, W. (2015). Phytochemical screening, antimicrobial, antioxidant and cytotoxicity activities of bark's crude extracts of *Cordia sinensis. Advancement in Medicinal Plant Research*, *2*, 39-45.

[33] Zubair, H. M., Naveed, M., Mikrani, R., ul Hassan, N., Taleb, A., Ibrahim, M., *et al*. (2020). Phytochemical Screening, Antioxidant, Antibacterial, Antifungal Potential and in vivo Acute Toxicity of the Crude Extract of *Cordia Rothii* and *Viola Serpens*. *Research Square.* https://doi.org/10.21203/rs.3.rs-45018/v1

[34] Sales, M. D. C., Costa, H. B., Fernandes, P. M. B., Ventura, J. A., & Meira, D. D. (2016). Antifungal activity of plant extracts with potential to control plant pathogens in pineapple. *Asian Pacific Journal of Tropical Biomedicine*, *6*(1), 26-31. https://doi.org/10.1016/j.apjtb.2015.09.026

[35] Khan, K., Rasheed, M., Nadir, M., Firdous, S., & Faizi, S. (2021). GC-MS & preliminary screening profile of *Cordia sinensis* leaves–antiglycation, antifungal and insecticidal agents. *Natural Product Research*, *35*(7), 1212-1216. https://doi.org/10.1080/14786419.2019.1641809

[36] Al-Fatimi, M., Wurster, M., Schröder, G., & Lindequist, U. (2007). Antioxidant, antimicrobial and cytotoxic activities of selected medicinal plants from Yemen. *Journal of Ethnopharmacology*, *111*(3), 657-666. https://doi.org/10.1016/j.jep.2007.01.018

[37] Abdel-Aziz, A. W. A., Elwan, N. M., Shaaban, R. S., Osman, N. S., & Mohamed, M. A. (2021). High-Performance Liquid

Chromatography-Fingerprint Analyses, *In vitro* Cytotoxicity, Antimicrobial and Antioxidant Activities of the Extracts of *Ceiba speciosa* Growing in Egypt. *Egyptian Journal of Chemistry*, *64*(4), 1831-1843. https://dx.doi.org/10.21608/ejchem.2021.58716.3267

[38] El-Kamali, H. H., & El-Karim, E. M. A. (2009). Evaluation of antibacterial activity of some medicinal plants used in Sudanese traditional medicine for treatment of wound infections. *Academic Journal of Plant Sciences*, *2*(4), 246-251.

[39] Chattopadhyay, R. (2003). Possible mechanism of hepatoprotective activity of *Azadirachta indica* leaf extract: Part II. *Journal of Ethnopharmacology*, *89*(2-3), 217-219. https://doi.org/10.1016/j.jep.2003.08.006

[40] Iqbal, N., Zubair, H. M., Almutairi, M. H., Abbas, M., Akhtar, M. F., Aleya, L., *et al.* (2022). Hepatoprotective effect of *Cordia rothii* extract against CCl4-induced oxidative stress via Nrf2–NFκB pathways. *Biomedicine & Pharmacotherapy*, 156, 113840. https://doi.org/10.1016/j.biopha.2022.113840

[41] Saravanan, S., Babu, N. P., Pandikumar, P., Raj, M. K., Paulraj, M. G., & Ignacimuthu, S. (2012). Immunomodulatory potential of *Enicostema axillare* (Lam.) A. Raynal, a traditional medicinal plant. *Journal of Ethnopharmacology*, *140*(2), 239-246. https://doi.org/10.1016/j.jep.2012.01.010

[42] Firdous, S., Khan, K., Zikr-Ur-Rehman, S., Ali, Z., Soomro, S., Ahmad, V. U., *et al.* (2014). Isolation of phytochemicals from *Cordia rothii* (Boraginaceae) and evaluation of their immunomodulatory properties. *Records of Natural Products*, *8*(1), 51.

[43] Mayakrishnan, V., Kannappan, P., Abdullah, N., & Ahmed, A. B. A. (2013). Cardioprotective activity of polysaccharides derived from marine algae: An overview. *Trends in Food Science & Technology*, *30*(2), 98-104. https://doi.org/10.1016/j.tifs.2013.01.007

[44] Chauhan, M. G., & Chavan, S. S. (2009). Pharmacognosy and biological activity of *Cordia rothii* Roem. & Schult. bark. *Indian Journal of Traditional Knowledge, 8*(4), 598-601. http://nopr.niscpr.res.in/handle/123456789/6267

[45] Zhao, J., Evangelopoulos, D., Bhakta, S., Gray, A. I., & Seidel, V. (2014). Antitubercular activity of *Arctium lappa* and *Tussilago farfara* extracts and constituents. *Journal of Ethnopharmacology*, *155*(1), 796-800. https://doi.org/10.1016/j.jep.2014.06.034

[46] Mariita, R. M., Ogol, C. KPO., Oguge, N. O., & Okemo, P.O. (2010). Antitubercular and phytochemical investigation of methanol extracts of medicinal plants used by the Samburu community in Kenya. *Tropical Journal of Pharmaceutical Research*, *9*(4), 379-385. https://doi.org/10.4314/tjpr.v9i4.58935

[47] Tasneem, S., Liu, B., Li, B., Choudhary, M. I., & Wang, W. (2019). Molecular pharmacology of inflammation: Medicinal plants as anti-inflammatoryagents. *Pharmacological Research*, *139*, 126-140. https://doi.org/10.1016/j.phrs.2018.11.001

[48] Kommu, S. (2017). Evaluation of anti-inflammatory activity of *Cordia gharaf* (Forssk.) Ehrenb by carrageenan induced paw edema method. *Journal of Scientific Research in Pharmacy*, *6*(2), 9-10.

[49] Quazi, A., Patwekar, M., Patwekar, F., Mezni, A., Ahmad, I., & Islam, F. (2022). Evaluation of Wound Healing Activity (Excision Wound Model) of Ointment Prepared from Infusion Extract of Polyherbal Tea Bag Formulation in Diabetes-Induced Rats. *Evidence-Based Complementary and Alternative Medicine*, *2022*(1), 1372199. https://doi.org/10.1155/2022/1372199

[50] Hajabhai, Z. A., Pandya, S. S., & Rabari, H. A. (2012). Wound healing activity of leaf extracts of *Cordia rothii* Roem & Schult. *International Journal of Pharmacy and Life Sciences*, *3*, 2048-2054.

[51] Dongmo Zeukang, R., Kalinski, J. C., Tembeni, B., Goosen, E. D., Tembu, J., Tabopda Kuiate, T., *et al.* (2023). Quinones from *Cordia* species from 1972 to 2023: isolation, structural diversity and pharmacological activities. *Natural Products and Bioprospecting*, 13(1), 52. https://doi.org/10.1007/s13659-023-00414-y

[52] Daulatabad, C. M. J. D., Desai, V. A., & Hosamani, K. M. (1992). Unusual fatty acids of *Cordia rothii* seed oil. *Journal of the Science of Food and Agriculture*, 58(2), 285-286. https://doi.org/10.1002/jsfa.2740580219

[53] Verma, Y. S., Saxena, V. K., & Nigam, S. S. (1977). Structure of *Cordia Rothii* Roem And Schult Mucilage–Part II: Methylation And Periodate Oxidations Studies. *Planta Medica*, *32*(06), 188-194. https://doi.org10.1055/s-0028-1097582