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A REVIEW OF THE PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF *CORDIA OBLIQUA*: FROM TRADITIONAL REMEDY TO A SOURCE OF MODERN THERAPEUTICS

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Abstract

Cordia obliqua *Willd. (Boraginaceae), known as Clammy Cherry, is a staple in Ayurvedic and Unani medicine, used to treat inflammation, infections, and liver disorders. This review synthesizes and critically appraises the existing scientific literature on its phytochemistry and pharmacology. While numerous studies identify bioactive compounds—primarily fatty acids, terpenoids, and sterols via GC-MS—and demonstrate pharmacological activities like anti-inflammatory, antimicrobial, and antioxidant effects, the field is hampered by non-standardized methodologies and a lack of critical depth. A major limitation is the over-reliance on GC-MS, which overlooks many polar, thermolabile bioactive compounds. This review critically evaluates the quality of evidence, highlighting that reported activities are often based on crude extracts without dose-response comparisons to standard drugs. Furthermore, proposed mechanisms of action are frequently generic rather than being specifically demonstrated for* C. obliqua. *The conclusion underscores the stark disparity between robust traditional use and the absence of clinical validation. We recommend a paradigm shift towards standardized extraction, comprehensive phytochemical profiling using LC-MS, isolation of novel compounds, detailed toxicological studies, and well-designed clinical trials to translate this promising traditional remedy into evidence-based medicine.*

INTRODUCTION

For hundreds of years, medicinal plants have been a cornerstone of healthcare systems around the world, providing the foundation of all traditional systems of healing (Khan et al., 2025; Noreen et al., 2025). The continual relevance of these resources lies in the reservoir of bioactive compounds that remain key considerations in drug discovery and the development of new

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therapeutics (Ayim et al., 2025; Sajid et al., 2024). (Sajid et al., 2024). Their role goes beyond history, as their therapeutic potential offers a source of novel chemical structures for modern medicine. Indeed, a considerable amount of modern drugs, including aspirin, morphine, and quinine, have either had their origin from plant compounds or have been influenced by the plants themselves (Ahmad et al., 2019; Khan et al., 2020; Shabbir et al., 2023). The integration of ethnobotanical knowledge and scientific research represents a key opportunity to discover new treatments. The systematic study of medicinal plants represents not only an affirmation of traditional ethnopharmacology, but also an important frontier in the search for effective and inexpensive pharmaceuticals (Asghar et al., 2017; Khan et al., 2016).

The genus Cordia (Boraginaceae), encompassing over 300 species distributed across tropical regions, has a long history of use in traditional medicine worldwide (Thirupathi et al., 2008). Cordia obliqua Willd., commonly known as Clammy Cherry or Lasora, holds a significant place in the pharmacopoeia of Ayurveda, Unani, and various ethnomedicinal practices of the Indian subcontinent (Gupta & Gupta, 2015; Naik et al., 2022). Traditionally, various parts of the plant—including fruits, leaves, bark, and roots—have been employed to treat a diverse range of ailments such as respiratory infections, gastrointestinal disorders, inflammatory conditions, and skin diseases (Tak et al., 2024). Its use in Ayurveda for liver ailments and ulcers is particularly notable (Panda & Kar, 2006).

Pharmacological investigations into Cordia species have reported antiviral, antibacterial, anti-inflammatory, and analgesic properties, providing a scientific basis for their traditional applications (Thirupathi et al., 2008). The therapeutic potential of C. obliqua is attributed to its rich repertoire of secondary metabolites, including flavonoids, terpenoids, fatty acids, and sterols, which can be efficiently extracted using solvents like ethanol (Harborne, 1998).

Despite growing research interest, the literature on C. obliqua remains fragmented. Studies often employ disparate methodologies, particularly in extraction and phytochemical analysis, leading to data that are difficult to synthesize and compare. A critical gap exists in the standardization of these methods and the translation of promising in vitro and animal model findings into clinical applications (Tak et al., 2024). Therefore, this review aims to systematically compile and, more importantly, critically evaluate the existing knowledge on the phytochemical composition and pharmacological properties of C. obliqua. It will identify methodological inconsistencies, assess the strength of the evidence, and pinpoint crucial research gaps to guide future studies towards the development of standardized phytomedicines.

1. Phytochemical Composition: A Critical Overview

Phytochemical investigations reveal that C. obliqua contains a diverse array of bioactive compounds, which are responsible for its medicinal properties. However, the reported profile is heavily influenced by the choice of analytical technique and extraction solvent, a point that requires critical examination.

2.1. Major Compound Classes and Analytical Biases

The compounds identified in C. obliqua can be grouped into several key classes, as summarized in Table 1. A significant methodological oversight in the literature is the predominant use of Gas Chromatography-Mass Spectrometry (GC-MS). While GC-MS is excellent for profiling volatile and thermally stable compounds, it is inherently biased and poorly suited for detecting many important bioactive molecules, such as polar phenolics, most flavonoids, and thermolabile alkaloids (Holčapek et al., 2012). These compounds are better characterized by Liquid Chromatography-Mass Spectrometry (LC-MS) or HPLC, techniques that have been underutilized in studies of C. obliqua.

Fatty Acids and Esters: GC-MS studies consistently report high abundances of linoleic acid, palmitic acid, oleic acid, and their methyl esters in seed and leaf extracts (Sivakrishnan & Pradeepraj, 2019; Thirupathi et al., 2008). These lipophilic compounds are efficiently extracted with nonpolar solvents like hexane and are readily detected by GC-MS.

Terpenoids and Sterols: This class represents a major fraction of the reported bioactives.

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Common compounds include α-amyrin, β-sitosterol, lupeol, and squalene, which are associated with anti-inflammatory and antimicrobial activities [1, 6]. While these are significant, the literature largely reports common terpenoids and sterols found in many medicinal plants, with a notable lack of discovery of unique or novel compounds specific to C. obliqua.

Phenols and Flavonoids: The presence of phenolic compounds and flavonoids is often mentioned in relation to the plant's antioxidant activity (Naik et al., 2022). However, their identification via GC-MS is limited to certain derivatives. A comprehensive profiling of these polar antioxidants requires HPLC-DAD or LC-MS, suggesting the current understanding of C. obliqua's phenolic portfolio is incomplete.

Alkaloids: Conventional phytochemical screening tests suggest the presence of alkaloids (Yadav et al., 2015), but their specific identities remain largely unexplored due to the limitations of GC-MS. Targeted analysis using LC-MS is necessary to isolate and characterize these potentially important bioactive nitrogenous compounds.

Table 1 Summary of Key Bioactive Compounds in C. obliqua and Their Reported Activities

Compound Class	Example Compounds	Primary Reported biological activities	Critical Notes on Evidence
Fatty Acids & Esters	Linoleic Acid, Methyl Oleate	Anti-inflammatory, Antimicrobial	Well-detected by GC-MS; activities often inferred from compound knowledge, not robust C. obliqua-specific studies.
Terpenoids & Sterols	β-sitosterol, Lupeol, α-Amyrin	Anti-inflammatory, Antimicrobial, Analgesic	Commonly found in plants, mechanisms are generic proposals, not always directly proven with C. obliqua extracts.
Phenolic Compounds	Various Phenols, Flavonoids	Antioxidant, Radical Scavenging	Profile is likely incomplete due to reliance on GC-MS; quantification and specific compound identities are lacking.

3. Impact of Extraction Methodology on Phytochemical Yield

The solvent used for extraction is a critical variable that dramatically alters the chemical composition of the final extract, contributing significantly to the incomparability of data across different studies. A critical analysis reveals that polar solvents like ethanol and methanol yield a broader range of medium-polarity compounds, including phenolics and some terpenoids (Naik et al., 2022; Sivakrishnan & Pradeepraj, 2019). In contrast, non-polar solvents like hexane and chloroform are more efficient for isolating lipophilic components such as fatty acids, esters, and sterols (Naik et al., 2022; Sivakrishnan & Pradeepraj, 2019). This methodological diversity, without a standardized protocol, is a primary source of discrepancy in the literature. For instance, an antimicrobial study using a hexane extract would primarily test fatty acids, while a study using an ethanolic extract would test a mixture of terpenoids and phenolics, leading to different results and potencies that are difficult to correlate. The lack of standardization in parameters like extraction time, temperature, and solvent-to-material ratio further exacerbates this problem, making it impossible to establish a definitive phytochemical fingerprint for C. obliqua.

4. Pharmacological Activities and Mechanisms: A Critical Appraisal

C. obliqua extracts demonstrate a wide range of pharmacological effects. However, the evidence is

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predominantly preclinical, and many studies lack the depth required to robustly validate traditional claims or guide drug development.

4.1. Anti-Inflammatory and Analgesic Activities
The traditional use for treating inflammatory conditions is supported by animal model studies. For example, Thirupathi et al. (2008) reported that a methanol extract of C. obliqua leaves significantly reduced carrageenan-induced paw oedema in rats (Thirupathi et al., 2008). The activity is often attributed to the presence of β-sitosterol and lupeol, which are known inhibitors of prostaglandin synthesis and NF-κB signaling (Naik et al., 2022). **However, a critical gap is the lack of dose-response data and direct comparison to standard anti-inflammatory drugs (e.g., indomethacin).** Most studies report percentage inhibition at a single, often high, dose without establishing potency. Furthermore, the proposed mechanisms are often extrapolated from the known properties of the pure compounds rather than being conclusively demonstrated for the specific extract being tested.

4.2. Antimicrobial Properties
Extracts have shown activity against bacteria like Escherichia coli and Staphylococcus aureus, and fungi like Candida albicans (Thirupathi et al., 2008). The effects are generically attributed to membrane disruption by terpenoids or enzyme inhibition by flavonoids. **A significant weakness is the almost exclusive use of crude extracts.** This makes it impossible to pinpoint the specific active constituents or their synergistic relationships. Moreover, studies rarely report Minimum Inhibitory Concentration (MIC) values alongside standard antibiotics, making it difficult to assess the practical significance of the observed activity.

4.3. Antioxidant Capacity
The high antioxidant capacity of C. obliqua extracts, demonstrated in DPPH and ABTS radical scavenging assays, is one of its most consistently reported activities (Naik et al., 2022). This is logically linked to its phenolic content. While these in vitro assays are valuable, their direct relevance to in vivo therapeutic effects is limited. The link between antioxidant capacity and specific health benefits like hepatoprotection or anti-ageing needs further experimental validation in biological systems.

4.4. Other Activities and Unsubstantiated Claims
Preliminary studies suggest other potential activities:
Hepatoprotective: Some studies mention activity against CCl_4-induced hepatotoxicity (Yadav et al., 2015), but this is a severely underdeveloped area. The mechanisms and active principles remain entirely unexplored, and the claim in the abstract of the original review was not sufficiently substantiated in the text.

Antidiabetic and Anticancer: Initial in vitro reports exist (e.g., alpha-glucosidase inhibition, cytotoxicity against cell lines) (Yadav et al., 2015), but the evidence is too preliminary for any conclusive remarks. **A major omission in the original text was the mention of a "promising topical anti-inflammatory gel" in the future directions without any citation or discussion elsewhere in the article.** Such claims must be supported by evidence or removed.

5. Future Research Directions
To bridge the gap between traditional promise and modern application, future research must address several critical areas:
Standardization and Phytochemical Rigour: Implement standardized extraction and authentication protocols. Move beyond GC-MS to employ LC-MS and NMR for a comprehensive, unbiased phytochemical profile aimed at discovering novel compounds and fully characterizing polar constituents.

Mechanistic and Dose-Response Studies: Pharmacological studies must include full dose-response curves and direct comparisons to standard drugs. Research should focus on elucidating specific molecular mechanisms of action (e.g., effect on specific enzymes, cytokine levels, or gene expression) rather than relying on generic explanations.

Toxicological and Clinical Translation: Conduct thorough sub-chronic and chronic toxicological studies to establish safety profiles. The most critical step is to initiate well-designed clinical trials to validate efficacy and safety in humans for the most promising

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indications, such as inflammation or microbial infections.

Formulation Development: Research into novel drug delivery systems (e.g., nanoparticles, topical gels) should be pursued after active principles are identified and standardized, to enhance bioavailability and stability.

6. Conclusion

Cordia obliqua possesses a rich phytochemical profile that underpins a wide spectrum of pharmacological activities observed in preclinical studies, thereby providing a scientific basis for its traditional uses. However, this review identifies major weaknesses in the current body of research, including methodological inconsistencies, an over-reliance on biased analytical techniques, a lack of critical dose-response and mechanistic data, and a complete absence of clinical validation. The plant's true therapeutic potential cannot be realized without a concerted shift towards more rigorous, standardized, and translational research. By addressing these gaps, future work can transform the traditional wisdom surrounding C. obliqua into evidence-based, modern therapeutics.

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