Screening For Antimicrobials and Phytochemical and Assessing the Therapeutic Efficacy of The Extracts from The Foliage and Stem Bark of The Designated Medicinal Species Crateva Adansonii Against Multi- Drug Resistant S.Typhi

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Abstract- ***The escalating prevalence of multi-drug resistant (MDR) Salmonella typhi poses a significant threat to public health, particularly in low- and middle- income countries. In response to the dwindling effectiveness of conventional antibiotics, medicinal plants offer a promising alternative due to their rich phytochemical profiles and traditional use inethnomedicine. This review explores the antimicrobial, anti-inflammatory, and immune-modulatory properties of Crateva adansonii, focusing on its foliage and stem bark extracts. Phytochemical analysis reveals the presence of flavonoids, alkaloids, saponins, tannins, and other bioactive compounds known to disrupt bacterial cell walls, inhibit nucleic acid synthesis, and modulate inflammatory responses. Methanolic leaf extracts exhibit potent in-vitro antibacterial activity against MDR S. typhi, with significant zones of inhibition and favorable minimum inhibitory concentrations. While in-vivo and clinical data remain limited, preliminary findings suggest a potential synergistic effect with standard antibiotics and a role in mitigating inflammation-induced complications. The review underscores the therapeutic promise of C. adansonii, advocating for standardized extraction protocols, toxicological evaluations, and well-structured clinical trials to validate its efficacy and safety in typhoid fever management.***

Index Terms- Crateva adansonii, typhoid fever, multidrug-resistantSalmonellatyphi,phytochemicals, antimicrobialactivity, methanolic extract, herbal medicine, anti- inflammatory.

I. INTRODUCTION

Multi-drug resistant (MDR) bacterial pathogens are becoming more and more common, which presents a serious threat to global public health, especially in developing nations where infectious diseases continue to be the primary cause of morbidity and mortality. Salmonella typhi, the pathogen that causes typhoid fever, is one of these that has shown a remarkable capacity to develop resistance to several classes of antibiotics, making traditional treatment approaches less and less effective. This concerning pattern emphasizes how urgently alternative antimicrobial agents are needed, especially those made from natural sources that have proven ethnomedical value. Medicinal plants have long served as a reservoir of bioactive compounds with diverse pharmacological properties, including antimicrobial, anti- inflammatory, and antioxidant activities. Crateva adansonii, commonly known as the sacred garlic pear, is a medicinal species widely distributed across tropical and subtropical regions. Traditionally, various parts of this plant especially its foliage and stem bark have been used in folk medicine to treat a range of ailments, such as fever, inflammation,and gastrointestinal disorders. Recent scientific investigations have begun to validate these traditional uses, revealing the presence of potent phytochemicals with promising biological activities.

Overview of typhoid fever and current challenges

The bacterium Salmonella enterica serovar Typhi is the cause of typhoid fever, a dangerous systemic infection that is mainly spread by consuming tainted food or water. The illness is still a serious public health issue, particularly in low- and middle-income nations with limited access to sanitary facilities and clean water. Over 110,000 people die from typhoid fever each year, which is thought to afflict 9– 11 million people worldwide. Children and people living in densely populated areas are especially at risk. Typhoid can cause serious complications or even death if treatment is not received. The clinical presentation usually consists of a prolonged high fever, headache, abdominal pain, and gastrointestinal disturbances.[1][2]

The quick emergence and spread of multi-drug resistant (MDR) S. Typhi strains is one of the most urgent problems in the treatment of typhoid fever. Effective treatment options are further limited by the widespread occurrence of resistance to first-line antibiotics like ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, as well as the growing concern over resistance to fluoroquinolones and third-generation cephalosporins. In endemic areas, the disease is still spread by enduring problems like poor water, sanitation, and hygiene (WASH) infrastructure in addition to antibiotic resistance. Although vaccination is a promising preventive measure, coverage is still uneven, and underreporting and a lack of laboratory capacity frequently make it difficult to conduct accurate disease surveillance. In order to successfully control and eventually eradicate typhoid fever, these difficulties highlight the urgent need for creative solutions, such as the creation of novel antimicrobial agents and the bolstering of public health initiatives.[3]

Importance of herbal medicine in infectious diseases

The prevention and treatment of infectious diseases are greatly aided by herbal medicine, particularly in light of the growing threats posed by new pathogens and antibiotic resistance. Alkaloids, flavonoids, and saponins are among the many naturally occurring substances found in medicinal plants. These substances frequently work in concert to produce antiviral, antibacterial, and antiparasitic effects. Because of their affordability, cultural acceptance, and generally low incidence of side effects, these plant-based therapies are widely used. This makes them especially useful in primary healthcare settings and in areas where access to traditional pharmaceuticals is limited. In addition to directly fighting infections, herbal remedies also aid in balancing the body and boosting immunity, both of which are essential for healing and preventing recurrent infections. Additionally, there is potential for improving therapeutic results, lowering the risk of drug resistance, and promoting post-infection recovery when herbal medicine is combined with conventional treatments. Since multi-drug- resistant pathogens are becoming a greater threat, investigating and scientifically validating herbal remedies presents a promising path toward the creation of novel, potent antimicrobial agents and improving the management of infectious diseases worldwide.[4]

Overview of Crateva adansonii and its traditional use

A deciduous tree in the Capparaceae family, Crateva adansonii is found throughout tropical regions, particularly along riverbanks. This plant has long been valued in Asian and African ethnomedicine. A wide range of illnesses are treated with different parts of C. adansonii, such as its leaves, stem bark, flowers, and fruits. The plant is used in Cameroon and other African countries to treat ailments like constipation, asthma, snakebite, postmenopausal symptoms, and some types of cancer.[5] Crateva adansonii is a deciduous tree in the Capparaceae family that grows throughout tropical regions, especially along riverbanks. Ethnomedicine from Asia and Africa has long valued this plant. The leaves, stem bark, flowers, and fruits of C. adansonii are used to treat a variety of ailments. In Cameroon and other African nations, the plant is used to treat conditions like snakebite, constipation, asthma, postmenopausal symptoms, and certain cancers.[6] In addition to these, the plant is used in traditional medicine to treat rheumatism, diabetes, high blood pressure, bacterial infections, abscesses, and sores. Its rich phytochemical profile which includes alkaloids, flavonoids, tannins, saponins, steroids, and cardiac glycosides is responsible for its wide range of therapeutic uses. These compounds have been demonstrated to have a variety of pharmacological activities, including analgesic, hypoglycemic, antimicrobial, and anti-inflammatory effects. The extensive and diverse traditional applications of Crateva adansonii highlight its value as a medicinal resource and offer a solid basis for continued scientific research into its potential therapeutic benefits.[7]

II. PATHOPHYSIOLOGY OF TYPHOID FEVER

Causative Agent and Transmission:

Salmonella enterica serotype Typhi, a bacterium that is exclusively adapted to humans, is the cause of typhoid fever. Ingestion of food or water tainted with an infected person's feces is the main way that the disease is spread, so inadequate sanitation and restricted access to clean water are important risk factors. After entering the body, S. Typhi is taken up by phagocytic cells after passing through intestinal epithelial cells, especially over Peyer's patches in the distal ileum. Following their passage into the lymphatic system by macrophages, the bacteria spread to organs like the liver, spleen, bone marrow, and gallbladder.[8] A unique feature of S. Typhi is its Vi capsular antigen, which helps it evade immune detection by inhibiting phagocytosis and reducing neutrophil-based inflammation, facilitating systemic infection.[9]

Symptoms and Complications:

Typhoid fever usually manifests 6 to 30 days after exposure and starts with a high fever that comes on gradually and is followed by weakness, headache, constipation, mild vomiting, and abdominal pain. A distinctive rose-colored skin rash may appear in certain patients. In extreme situations, delirium and confusion may develop. Serious consequences like intestinal perforation, bleeding, encephalopathy, and, in rare instances, death may result from untreated symptoms that last for weeks or months. In order to contribute to continuous transmission, some people may develop into chronic carriers, holding the bacteria in their gallbladder and continuing to excrete it in their stool without exhibiting any symptoms.

Current Treatment Approaches and Limitations:

Antibiotic therapy is the cornerstone of typhoid fever treatment. In the past, trimethoprim-sulfamethoxazole, ampicillin, and chloramphenicol were the first-line antibiotics. However, these medications are no longer as effective due to the quick rise of multi-drug resistant (MDR) strains of S. Typhi. Another factor limiting treatment options and making disease management more difficult is the rise in resistance to more recent antibiotics, such as third-generation cephalosporins and fluoroquinolones. Supportive care is still crucial, and this includes managing complications and staying hydrated. Although vaccination is advised and accessible in high-risk areas, coverage varies and offers only partial protection. In addition to ongoing issues with water, sanitation, and hygiene infrastructure, the growing threat of antibiotic resistance highlights the urgent need for better public health interventions and new therapeutic approaches.

III. PHYTOCHEMISTRY OF CRATEVA ADANSONII

Active Compounds Identified in Crateva adansonii

The leaves and stem bark of Crateva adansonii contain a wide variety of bioactive compounds, according to phytochemical studies. Flavonoids, alkaloids, saponins, terpenoids, tannins, anthraquinones, steroids, cardiac glycosides, polyphenols, triterpenoids, coumarins, balsams, and volatile oils are the main categories of secondary metabolites that have been found.[10] Quantitative analyses have shown that leaves contain significant levels of saponins, alkaloids, tannins, phenolics, flavonoids, phlobatannins, and anthraquinones.[11] Specific compounds identified through advanced analytical techniques, such as GC-MS, include phytol,heptacosane, tetratricontane, tetratetracontane, nonacosane, and various coumarin derivatives, each contributing to the plant's antioxidant, antimicrobial, and anti-inflammatory activities.

Extraction and Analysis Methods

Phytochemicals from C. adansonii have been extracted using a variety of solvents and extraction methods. Water (aqueous), methanol, ethanol, petroleum ether, chloroform, hexane, and ethyl acetate are examples of common extraction solvents.[12] The profile and yield of extracted compounds are greatly influenced by the solvent selection; for example, anthraquinones are found in aqueous and petroleum ether extracts but not in methanolic ones, and saponins are abundant in petroleum ether extracts but absent in aqueous and methanolic ones. For initial identification, standard phytochemical screening techniques like the Salkowski test for terpenoids, the ferric chloride test for tannins, and Mayer's test for alkaloids are frequently employed. Certain phytoconstituents in various extracts are identified and quantified using sophisticated analytical techniques, such as Gas Chromatography-Mass Spectrometry (GC-MS).[13]

IV. ANTIMICROBIAL POTENTIAL OF CRATEVA ADANSONII

Mechanism of Action of Phytochemicals Against Bacterial Infections

Crateva adansonii's rich phytochemical composition, which consists of flavonoids, alkaloids, saponins, tannins, anthraquinones, and volatile oils, is responsible for its antimicrobial activity. These substances work in a number of ways:

- Cell wall disruption: Saponins and tannins can compromise bacterial cell wall integrity, leading to leakage of cellular contents and cell death.
- Inhibition of nucleic acid synthesis: Alkaloids and flavonoids may interfere with DNA and RNA synthesis, inhibiting bacterial replication.
- Enzyme inhibition: Certain phytochemicals inhibit bacterial enzymes essential for metabolism and survival.
- Antioxidant activity: The antioxidant properties of these compounds can reduce oxidative stress in host tissues, indirectly enhancing immune response and limiting bacterial proliferation.[14]

Specific Activity Against Salmonella typhi

Studies show that Crateva adansonii leaf extracts, especially those made with methanol and hexane, have strong antibacterial properties against Salmonella typhi. The strong antibacterial effects of methanolic leaf extracts are demonstrated by zones of inhibition against S. typhi that range from 10 mm to 30 mm. For S. typhi, methanol extracts usually have a minimum inhibitory concentration (MIC) of 12.5 mg/ml and a minimum bactericidal concentration (MBC) of up to 25 mg/ml. However, stem bark extracts may be effective against other bacteria, like Staphylococcus aureus, but they are typically ineffective against S. typhi.[10] The antibacterial effect is concentration-dependent, with higher concentrations (20 mg/ml) yielding maximal inhibition.[15]

Synergistic Effect with Standard Antibiotics
When used in conjunction with other plant extracts or conventional antibiotics, Crateva adansonii extracts have shown synergistic effects:
Combining extracts of Crateva adansonii with other medicinal plants (like Cryptolepis sanguinolenta) increases their antibacterial effectiveness against pathogens like Candida albicans, E. coli, and S. typhi. The two extracts worked best in ratios of 1:2 or 2:1. These combinations may help overcome resistance, increase the antimicrobial spectrum, and lower the dosage of traditional antibiotics needed.[16]

Parameter	Details
Plant Studied	Crateva adansonii (Foliage and Stem Bark)
Target Pathogen	Multi-drug resistant Salmonella typhi
Phytochemicals Identified	Flavonoids, Alkaloids, Saponins, Tannins, Terpenoids, Glycosides
Extraction Solvents	Methanol, Hexane, Aqueous, Petroleum Ether
Effective Extracts	Methanolic Leaf Extract (most potent), Hexane Extract (moderate)
Mechanisms of Action	Cell wall disruption, DNA/RNA synthesis inhibition, enzyme inhibition
Anti-inflammatory Effects	Inhibition of cytokines (IL-6, TNF- α), COX-2 modulation
In-vitro Efficacy	Zones of inhibition (10–30 mm); MIC ~12.5 mg/ml
In-vivo/Clinical Data	Limited; pre-clinical and ethnopharmacological data support efficacy
Synergistic Potential	Enhanced efficacy with combination therapies (e.g., Cryptolepis sanguinolenta)
Limitations	Lack of clinical trials, dosage standardization, bioavailability issues
Recommended Future Directions	Clinical trials, toxicological safety profiling, pharmacokinetic studies

V. ANTI-INFLAMMATORY AND IMMUNE MODULATORYPROPERTIES

Notable immune-modulatory and anti-inflammatory qualities of Crateva adansonii are highly pertinent in the context of typhoid fever. Steroids, alkaloids, terpenoids, and polyphenols (like tannins and flavonoids) are abundant in the plant's leaf extracts, and they all support its anti- inflammatory properties. Specifically, methanolic extracts exhibit powerful antioxidant properties and contain phytocompounds such as phytol and coumarin derivatives that have been demonstrated through molecular docking studies to interact with important inflammatory mediators like COX-2, TNF-α, IL-1β, and IL-6, thereby reducing inflammatory signaling.[13]

It has been demonstrated that C. adansonii extracts can modulate immune responses and reduce inflammation by reducing the expression and production of pro- inflammatory cytokines (IL-6, IL-8, and TNF-α) in infected human keratinocytes in cellular models. In cases of typhoid fever, where tissue damage and complications like intestinal perforation and hemorrhage are caused by excessive immune activation and cytokine release, this anti-inflammatory action is especially helpful. C. adansonii may help limit the severity of inflammation-associated tissue injury by lowering oxidative stress and inflammatory cytokine levels, which could lower the risk of serious complications from typhoid fever.[17]

Additionally, the plant's phytochemicals' antioxidant qualities boost immunity and mitigate the oxidative stress associated with systemic infections like typhoid. Crateva adansonii's anti-inflammatory and immune-modulatory properties support its traditional use and potential as a supplemental therapy in the management of infectious diseases by addressing the inflammatory aspect of typhoid fever and possibly offering broader protection against secondary complications.[18]

VI. PRE-CLINICAL AND CLINICAL STUDIES ON CRATEVAADANSONII FOR TYPHOID FEVER

Overview of Experimental Models Used

Ethnopharmacological surveys, in vitro tests, and, to a lesser degree, in vivo animal models have been the main methods used to investigate Crateva adansonii's anti- typhoid potential. Agar diffusion and broth dilution techniques are commonly used in in-vitro investigations to evaluate antibacterial activity against Salmonella typhi. Theuse of C. adansonii in traditional medicine for typhoid fever has been documented by ethnobotanical surveys and cross-sectional studies, which has served as a basis for laboratory research. Although they are less frequent, in-vivo research using animal models is becoming more and more advised to support conventional claims.

Summary of Efficacy Results from In-Vitro Studies

Extracts of Crateva adansonii, particularly from the leaves, have been shown to have inhibitory activity against Salmonella typhi in numerous in vitro investigations. In agar diffusion tests, methanolic and aqueous extracts have shown distinct zones of inhibition, suggesting bacteriostatic or bactericidal properties. The plant has long been used to treat typhoid fever, and the reported minimum inhibitory concentrations (MICs) fall within ranges deemed pharmacologically significant. Calls for more study into identifying active ingredients and refining extraction techniques for maximum effectiveness have been sparked by these findings.[19]

Findings from In-Vivo Animal Models

Despite the paucity of direct in-vivo research on C. adansonii for typhoid fever, the literature and ethnopharmacological evidence that is currently available point to encouraging therapeutic potential. The justification for comparable research with C. adansonii is supported by animal studies employing related medicinal plants, which have demonstrated improvements in clinical symptoms and decreases in bacterial load. Before human clinical trials can be justified, carefully planned animal model studies are required to verify the safety and effectiveness of these extracts.[20]

VII. ADVANTAGES AND LIMITATIONS OG PHYTOCHEMICAL EXTRACTSIN TYPHOID TREATMENT

Benefits Over Conventional Antibiotics

In comparison to traditional antibiotics, phytochemical extracts from therapeutic plants such as Crateva adansonii have a number of benefits. Many bioactive substances, including flavonoids, alkaloids, saponins, tannins, and polyphenols, are frequently present in these extracts. These substances can work in concert to suppress bacterial growth and regulate inflammation. One of the main drawbacks of single-compound antibiotics is the possibility of resistance development, which this multi-targeted strategy may help prevent. Moreover, extracts have shown anti-inflammatoryand antioxidant qualities that can aid in typhoid fever symptom relief and recovery.[13] Phytochemical extracts are generally more accessible and affordable, making them particularly valuable in resource-limited settings where typhoid is endemic.[20]

Adverse Effects and Contraindications

In cell-based assays, like those employing Artemia salina larvae, the majority of studies report low toxicity of Crateva adansonii extracts, indicating a favorable safety profile.[12] It is impossible to completely rule out the possibility of negative effects, particularly with high dosages or extended use. Although thorough clinical safety data are lacking, allergic reactions or interactions with other medications may result in potential contraindications. Before extensive clinical use, careful observation and additional toxicological research are required.

Challenges: Dosage Determination and Bioavailability

Clinical translation of phytochemical extracts is fraught with difficulties, despite encouraging in vitro and ethnomedicinal evidence. Because different extraction techniques, plant parts, and phytochemical compositions vary, figuring out the ideal dosage is difficult.[10] The therapeutic efficacy of many plant-derived molecules may be limited by their low bioavailability, which is the degree and rate at which active compounds are absorbed and reach target tissues. To get past these obstacles, standardization of extracts, the creation of appropriate formulations, and thorough pharmacokinetic research are necessary.

VIII. CLINICAL EVIDENCE AND FUTURE RESEARCH DIRECTION

Current Status of Clinical Trials

Clinical trials specifically assessing Crateva adansonii for the prevention or treatment of human typhoid fever are not yet published. The majority of typhoid fever clinical research and development is concentrated on vaccine approaches, such as typhoid conjugate vaccines (TCVs), which are being introduced in endemic areas after proving safe and effective in extensive trials. [21]Although Crateva adansonii has demonstrated antimicrobial and anti-inflammatory properties in vitro and is known in ethnomedicine, its application to typhoid clinical research has not been covered in the scientific literature or international clinical trial registries.

Research Gaps and Challenges

The main research gaps for Crateva adansonii in typhoid management include:

- Lack of clinical validation: Despite promising in-vitro and pre-clinical data, there is no clinical evidence for efficacy or safety in humans with typhoid fever.
- Standardization and quality control: Variability in extraction methods, phytochemical content, and dosing regimens complicate reproducibility and hinder clinical translation.
- Pharmacokinetics and bioavailability: There is limited understanding of how active compounds from C. adansonii are absorbed, distributed, metabolized, and excreted in humans.
- Toxicity and adverse effects: Comprehensive toxicological studies are needed to determine safe dosage ranges and identify potential contraindications or interactions with other medications.
- Regulatory and ethical considerations: As with all herbal medicines, rigorous regulatory oversight and ethical approval are necessary before human trials can proceed.

Future Research Directions

To advance Crateva adansonii as a potential therapeutic for typhoid fever, future research should focus on:

Establishing pharmacokinetic profiles, safety, and efficacy through carefully planned animal research. standardizing extraction procedures and figuring out the main bioactive substances that have anti-typhoid properties. launching phase I clinical trials to evaluate human safety and tolerability. investigating the potential for synergistic effects with currently available antibiotics to combat multidrug resistance. ensuring cooperation between pharmacologists, clinicians, and ethnobotanists in order to connect traditional knowledge with contemporary evidence-based medicine.

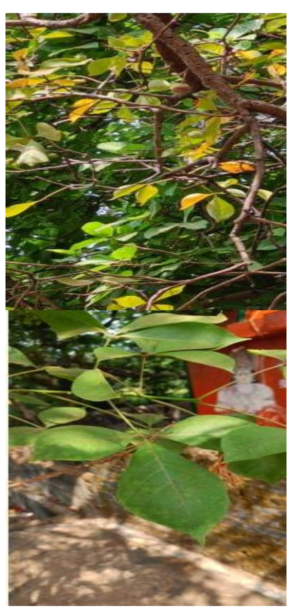
CONCLUSION

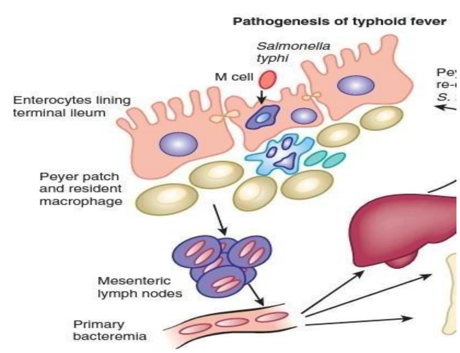
In summary, preclinical research has shown that Crateva adansonii possesses strong antimicrobial, anti- inflammatory, and immune-modulatory qualities. This is especially true of its leaf extracts, which are abundant in phytochemicals like flavonoids, alkaloids, saponins, and tannins. With mechanisms including bacterial cell wall disruption, nucleic acid synthesis inhibition, and inflammatory pathway modulation, these compounds have demonstrated notable efficacy against multi-drug resistant Salmonella typhi in vitro. Leaf extracts not only prevent bacterial growth but also lessen the inflammatory side effects of typhoid fever, whereas stem bark extracts are less effective against S. typhi. Additionally, initial research indicates that these extracts might work in concert with traditional antibiotics to improve therapeutic results and tackle the escalating problem of antibiotic resistance.

These findings have significant therapeutic implications. Extracts from the leaves of Crateva adansonii may be a useful supplement or substitute for current antibiotic regimens, particularly in areas where drug-resistant typhoid is common and access to medications is restricted. Their additional anti-inflammatory and antioxidant properties may aid in preventing complications and lessening the severity of the illness, promoting a quicker recovery and better patient outcomes. However, the absence of standardized extraction techniques, a dearth of clinical safety information, and doubts about the best dosage and bioavailability currently restrict practical application.

In the future, phytochemicals derived from medicinal plants such as Crateva adansonii hold great promise for combating infectious diseases like typhoid fever. Future research must place a high priority on conducting thorough animal studies, conducting clinical trials, and creating standardized, superior herbal formulations in order to fully realize their potential. Innovative, widely available, and successful treatments may be made possible by fusing contemporary scientific validation with traditional medical knowledge. Typhoid fever management and the larger global issue of antibiotic resistance can both be improved by utilizing the potential of phytochemicals derived from plants.

APPENDIX





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