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Endophytes of Ayurvedic Medicinal Plants: Current Advances in *Terminalia bellerica* and *Terminalia chebula*

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Abstract:
Endophytes are microorganisms that reside within healthy plant tissues without causing disease and are increasingly recognized as valuable sources of novel bioactive compounds with significant pharmaceutical, agricultural, and industrial applications. Medicinal plants, owing to their rich phytochemical diversity, provide unique ecological niches for these microorganisms, often fostering endophytes capable of producing metabolites with remarkable biological activities. Among medicinal plants, *Terminalia bellerica* and *Terminalia chebula*, two key constituents of the traditional Ayurvedic formulation *Triphala*, have long been valued for their antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, and anticancer properties. In recent years, growing attention has been directed toward the endophytic communities associated with these species, as they represent an untapped reservoir of structurally diverse natural products and plant growth-promoting traits. This review presents a comprehensive overview of the diversity, isolation, identification, and functional significance of bacterial and fungal endophytes reported from *T. bellerica* and *T. chebula*. It summarizes the current knowledge on their ability to produce bioactive metabolites, industrial enzymes, and other value-added biomolecules with potential applications in medicine, agriculture, and environmental sustainability. The review also highlights recent advances in molecular identification, genome-based approaches, metabolomics, and microbiome research that are expanding our understanding of plant–endophyte interactions. Furthermore, existing challenges, including limited cultivability, inconsistent metabolite production, and the need for large-scale validation, are critically discussed. By integrating available evidence and identifying key research gaps, this review underscores the immense potential of endophytes associated with *Terminalia* species as sustainable resources for natural product discovery and biotechnological innovation, while providing future research directions for translating laboratory findings into practical applications.

Keywords: *Terminalia bellerica*, *Terminalia chebula*, Endophytes, Bioactive metabolites, Plant microbe interactions.

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Introduction

Medicinal plants have served as the foundation of traditional healthcare systems for centuries and continue to play an indispensable role in modern drug discovery. Their therapeutic potential is largely attributed to the diverse array of secondary metabolites they produce, including alkaloids, flavonoids, terpenoids, tannins, phenolic acids, and glycosides (Arnold, 2007). In recent years, research has revealed that the biological activities of medicinal plants are not solely determined by their own metabolic processes but are also influenced by the diverse microbial communities that inhabit their tissues. Among these microorganisms, endophytes have emerged as a promising group because of their ability to establish intimate, often mutualistic, associations with host plants without causing visible symptoms of disease. Endophytes, which include bacteria, fungi, and actinomycetes, colonize the internal tissues of roots, stems, leaves, flowers, fruits, and seeds throughout part or all of their life cycle (Mengistu, 2020). These microorganisms contribute to plant growth and survival by enhancing nutrient acquisition, producing phytohormones, improving tolerance to abiotic stresses such as drought and salinity, and protecting plants against pathogens through the production of antimicrobial compounds. In return, the host plant provides a stable habitat and a continuous supply of nutrients, creating a mutually beneficial relationship. This close interaction often influences the metabolic pathways of both partners, leading to the synthesis of unique natural products that are not commonly found in either organism alone. The growing interest in endophytes stems from their remarkable capacity to produce structurally diverse bioactive metabolites with pharmaceutical and industrial importance. Numerous endophytic microorganisms have been reported to synthesize compounds exhibiting antimicrobial, antioxidant, anticancer, antiviral, anti-inflammatory, antidiabetic, and immunomodulatory activities. Some endophytes are also capable of producing metabolites that are identical or structurally similar to those originally isolated from their host plants, highlighting their potential as sustainable alternatives for the production of valuable phytochemicals. In addition to their pharmaceutical significance, endophytes have attracted attention for their applications in agriculture as plant growth-promoting microorganisms, biological control agents, biofertilizers, and producers of industrially relevant enzymes and other high-value biomolecules (Strobel, 2003).

Among medicinal plants, *Terminalia bellerica* and *Terminalia chebula* ., members of the family Combretaceae, occupy a prominent position in traditional medicine. These species are widely distributed across tropical and subtropical regions of Asia and have been extensively used in Ayurveda, Siddha, and other indigenous healthcare systems. Together with *Phyllanthus emblica*, they constitute the renowned Ayurvedic formulation *Triphala*, which has been prescribed for centuries for the management of digestive disorders, respiratory ailments, diabetes, skin diseases, liver dysfunction, and various inflammatory conditions. Modern pharmacological investigations have validated many of these traditional uses by demonstrating the antioxidant, antimicrobial, hepatoprotective, cardioprotective, anticancer, anti-inflammatory, antidiabetic, and immunomodulatory properties of extracts obtained from these plants (Wilson, 1995). The therapeutic efficacy of *T. bellerica* and *T. chebula* is largely associated with their rich phytochemical composition. These plants contain abundant hydrolysable tannins, including chebulagic acid, chebulinic acid, gallic acid, ellagic acid, corilagin, and other polyphenolic compounds that exhibit strong antioxidant and antimicrobial activities. Such chemically diverse environments create favorable ecological niches for endophytic microorganisms, which may evolve specialized metabolic capabilities to survive

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within host tissues. Consequently, endophytes associated with these medicinal plants have become increasingly attractive as potential sources of novel natural products with enhanced biological activities and reduced environmental dependence compared with direct extraction from plant material. Over the past decade, several studies have reported the isolation of fungal and bacterial endophytes from different tissues of *T. bellerica* and *T. chebula*. These endophytes have demonstrated the ability to produce a wide range of biologically active compounds, including antimicrobial metabolites, antioxidants, extracellular enzymes, pigments, volatile organic compounds, and plant growth-promoting substances. Advances in molecular biology, high-throughput sequencing, metabolomics, and genome mining have further expanded our understanding of the diversity, functional roles, and biosynthetic potential of these microorganisms. Despite these encouraging developments, information remains fragmented, with most studies focusing on individual isolates or specific biological activities rather than providing an integrated understanding of the endophytic communities associated with these medicinal plants (Porras-Alfaro & Bayman, 2011).

This review aims to provide a comprehensive and up-to-date synthesis of the current knowledge on endophytes associated with *Terminalia bellerica* and *Terminalia chebula*. It discusses their diversity, isolation and identification methods, ecological significance, and the spectrum of bioactive metabolites produced by these microorganisms. The review also examines their potential applications in medicine, agriculture, environmental sustainability, and biotechnology, while highlighting recent advances in omics technologies and genome-based approaches that are transforming endophyte research. Finally, existing challenges, research gaps, and future perspectives are presented to facilitate the development of endophyte-based strategies for sustainable natural product discovery and innovative biotechnological applications (Backman & Sikora, 2008).

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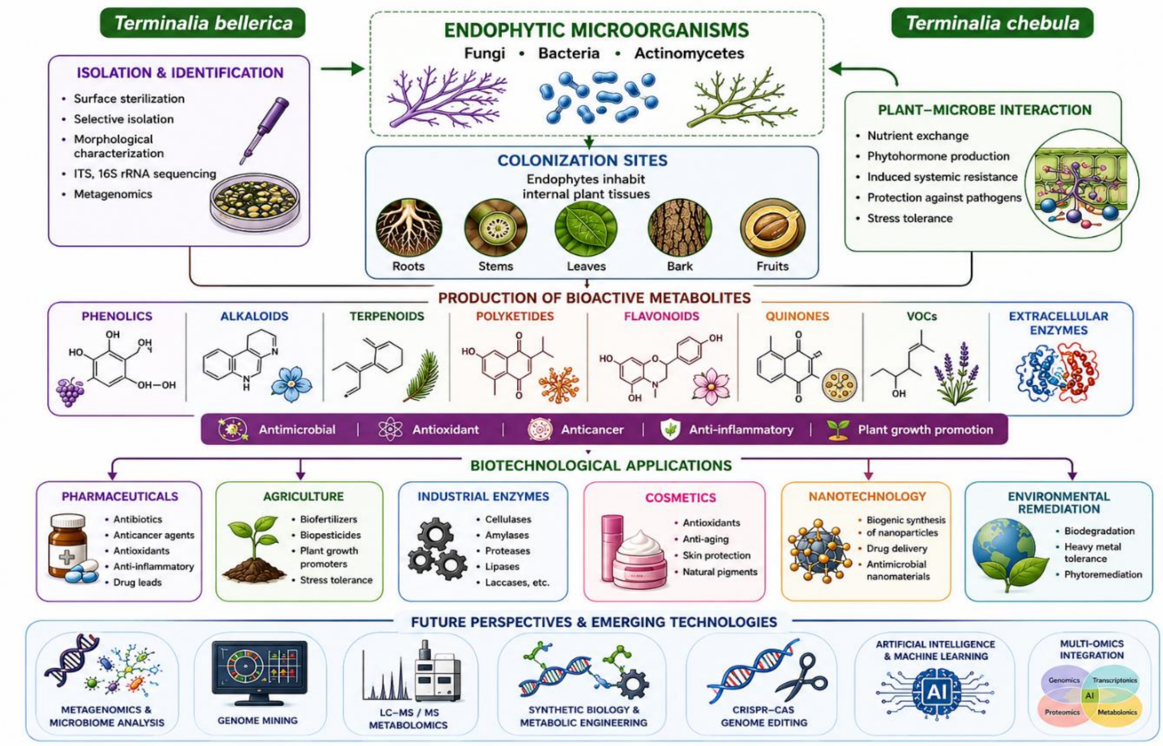

Figure 1. Graphical overview of endophytes associated with Terminalia bellerica and Terminalia chebula, illustrating their isolation, colonization of plant tissues, production of diverse bioactive metabolites, major biological activities, biotechnological applications.

Overview of *Terminalia bellerica* and *Terminalia chebula*

The genus *Terminalia* belongs to the family Combretaceae and comprises nearly 200 species of trees and shrubs distributed across tropical and subtropical regions of the world. Many members of this genus have long been recognized for their medicinal value and are widely used in traditional healthcare systems. Among them, *Terminalia bellerica* and *Terminalia chebula* are regarded as two of the most therapeutically important species because of their extensive use in Ayurveda, Siddha, Unani, and other indigenous systems of medicine. These plants are highly valued not only for their broad spectrum of pharmacological activities but also for their rich reservoir of secondary metabolites that contribute to their medicinal efficacy (Reinhold-Hurek & Hurek, 2011).

Botanical Description and Distribution

Terminalia bellerica

Terminalia bellerica, commonly known as Baheda or Bibhitaki, is a large deciduous tree that can attain a height of 20–40 m. The species is characterized by a straight trunk, grey bark, broad elliptic leaves, yellowish-green flowers, and nearly spherical, velvety fruits. It is widely distributed throughout the Indian subcontinent, including India, Nepal, Bangladesh, Sri Lanka, and Myanmar, and is also found in parts of Southeast Asia. The tree thrives in moist deciduous forests and adapts well to tropical climatic conditions with moderate to high rainfall. In India, *T. bellerica* is commonly found in central, eastern, and southern states where it naturally grows in forest ecosystems (Rosenblueth & Martínez-Romero, 2006).

Terminalia chebula

Terminalia chebula, commonly known as Haritaki, is another large deciduous tree reaching 15–30 m in height. It possesses dark brown bark, opposite or sub-opposite leaves, yellowish-white flowers arranged in spikes, and characteristic ribbed, ovoid fruits that vary in shape and size depending on the geographical region. The species is widely distributed across India, Nepal, Bhutan, Pakistan, Sri Lanka, China, Thailand, Vietnam, and other Southeast Asian countries. It prefers tropical and subtropical climates and grows well in mixed deciduous forests, particularly in regions receiving moderate annual rainfall (Fadiji & Babalola, 2020a).

Both species are ecologically significant and have adapted to diverse environmental conditions, enabling them to establish complex associations with a wide range of endophytic microorganisms. Variations in climate, altitude, soil characteristics, and host genotype influence the composition and diversity of their endophytic communities, making these plants excellent models for studying plant–microbe interactions (Fadiji & Babalola, 2020b).

Traditional and Ethnomedicinal Importance

The medicinal importance of *T. bellerica* and *T. chebula* has been documented for more than two thousand years in classical Ayurvedic literature. Along with *Phyllanthus emblica* (Amla), these two species constitute Triphala, one of the most widely prescribed polyherbal formulations in traditional Indian medicine. Triphala is traditionally used to promote digestive health, improve immunity, detoxify the body, and maintain overall well-being. In Ayurveda, *T. bellerica* is primarily recommended for the treatment of respiratory disorders, chronic cough, sore throat, digestive ailments, diarrhea, dysentery, liver disorders, hypertension, and eye diseases (Collinge & Jensen, 2022). The fruits are considered a natural rejuvenating agent and are believed to possess astringent, laxative, anti-inflammatory, and expectorant properties. Similarly, *T. chebula* has earned the title "King of Medicines" in Tibetan medicine because of its broad therapeutic applications. Different parts of the plant, especially the fruits, have traditionally been employed to manage gastrointestinal disorders, constipation, ulcers, diabetes, skin infections, urinary tract infections, wound healing, arthritis, and respiratory illnesses. Owing to its rejuvenating and adaptogenic properties, it is also regarded as a valuable component of several herbal formulations intended to improve longevity and overall health. The long history of medicinal use of these plants suggests that their therapeutic effects arise from a combination of host-derived phytochemicals and the beneficial activities of associated microbial communities, including endophytes (Ruotsalainen et al., 2022).

Phytochemical Composition

The pharmacological potential of *T. bellerica* and *T. chebula* is largely attributed to their rich and diverse phytochemical profiles. Both species are excellent sources of hydrolysable tannins, phenolic acids, flavonoids, triterpenoids, sterols, and other bioactive constituents. The fruits of *T. bellerica* are particularly rich in gallic acid, ellagic acid, ethyl gallate, β-sitosterol, lignans, tannins, and various fatty acids. These compounds exhibit potent antioxidant, antimicrobial, hepatoprotective, hypolipidemic, and anti-

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inflammatory properties. In contrast, *T. chebula* contains high concentrations of chebulagic acid, chebulinic acid, corilagin, gallic acid, ellagic acid, punicalagin, flavonoids, anthraquinones, and several glycosides. These phytochemicals contribute to its antioxidant, antimicrobial, anticancer, antiviral, antidiabetic, neuroprotective, and cardioprotective activities. The abundance of these secondary metabolites not only contributes to the medicinal properties of the host plants but also creates chemically unique microenvironments that influence the diversity and metabolic capabilities of endophytic microorganisms. Continuous exposure to these phytochemicals may drive endophytes to evolve specialized biosynthetic pathways, enabling them to produce structurally similar or entirely novel metabolites with significant biological activities (Wang & Zhang, 2023).

Pharmacological Activities

Extensive pharmacological investigations have validated many of the traditional therapeutic claims associated with *T. bellerica* and *T. chebula*. Extracts obtained from different plant parts have demonstrated remarkable biological activities in both in vitro and in vivo studies.

Major reported pharmacological properties include:

- Antioxidant activity through efficient scavenging of reactive oxygen species.
- Broad-spectrum antibacterial and antifungal effects against several human pathogens.
- Anti-inflammatory activity by regulating inflammatory mediators.
- Anticancer potential through induction of apoptosis and inhibition of tumor cell proliferation.
- Antidiabetic activity by improving glucose metabolism and inhibiting carbohydrate-hydrolyzing enzymes.
- Hepatoprotective and nephroprotective effects against chemically induced organ damage.
- Cardioprotective activity by reducing oxidative stress and improving lipid metabolism.
- Immunomodulatory effects that enhance host defense mechanisms.
- Antiviral activity against selected viral pathogens.

These diverse biological properties have generated considerable scientific interest in understanding whether associated endophytes contribute directly or indirectly to the biosynthesis of therapeutically important metabolites. Consequently, investigations into the endophytic microbiota of these plants have expanded significantly over the past decade (Yadav & Meena, 2021).

Significance of Endophyte Research in *Terminalia* Species

Medicinal plants possessing high concentrations of bioactive compounds often harbor equally diverse endophytic communities. Because endophytes inhabit the same tissues where these phytochemicals accumulate, they are continuously exposed to unique biochemical environments that shape their metabolic potential. Several studies have demonstrated that endophytes isolated from medicinal plants can synthesize compounds that are chemically identical or closely related to those produced by their hosts, making them attractive alternatives for sustainable natural product production (Adeleke and Babalola, 2021).

The growing demand for herbal medicines, coupled with increasing pressure on natural plant populations due to overharvesting, highlights the importance of identifying renewable microbial sources of valuable metabolites. Endophytes from *T. bellerica* and *T. chebula* therefore represent promising candidates for the

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discovery of new antimicrobial agents, antioxidants, anticancer compounds, industrial enzymes, and plant growth-promoting biomolecules. Furthermore, advances in genomics, metabolomics, and synthetic biology are expected to accelerate the identification and large-scale production of these metabolites, opening new opportunities for pharmaceutical development, sustainable agriculture, and environmental biotechnology (Ryan et al., 2008).

Table 1. Comparative overview of *Terminalia bellerica* and *Terminalia chebula*

Characteristics	***Terminalia bellerica* (Baheda/ Bibhitaki)**	***Terminalia chebula* (Harra)**
Family	Combretaceae	Combretaceae
Common names	Baheda, Bibhitaki, Beleric Myrobalan	Haritaki, Chebulic Myrobalan
Plant type	Large deciduous tree (20–40 m)	Large deciduous tree (15–30 m)
Native distribution	India, Nepal, Bangladesh, Sri Lanka, Myanmar, Southeast Asia	India, Nepal, Bhutan, Sri Lanka, China, Thailand, Vietnam
Medicinally important part(s)	Fruits, bark, leaves, seeds	Fruits, bark, leaves, roots, seeds
Major phytochemicals	Gallic acid, ellagic acid, β-sitosterol, lignans, tannins, ethyl gallate	Chebulagic acid, chebulinic acid, gallic acid, ellagic acid, corilagin, punicalagin, flavonoids
Traditional uses	Respiratory disorders, digestive ailments, liver diseases, diarrhea, sore throat, hypertension	Constipation, diabetes, gastric disorders, skin diseases, wound healing, respiratory infections
Major pharmacological activities	Antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, hypolipidemic, cardioprotective	Antioxidant, antimicrobial, anticancer, antidiabetic, anti-inflammatory, antiviral, neuroprotective
Role in Ayurveda	One of the three constituents of *Triphala*	One of the three constituents of *Triphala*
Reported endophytic microorganisms	Fungi, bacteria, actinomycetes	Fungi, bacteria, actinomycetes
Biotechnological significance	Source of bioactive metabolites, industrial enzymes, plant growth-promoting microorganisms	Source of antimicrobial compounds, antioxidants, enzymes, plant growth-promoting microorganisms

Endophytes: Diversity, Colonization, and Ecological Significance

Endophytes are microorganisms that inhabit the internal tissues of healthy plants for at least a part of their life cycle without causing visible symptoms of disease. They establish dynamic and often mutualistic associations with their host plants, benefiting from a protected ecological niche and a continuous supply of nutrients while enhancing plant growth, fitness, and resistance to environmental stresses. Endophytic microorganisms are now recognized as an integral component of the plant microbiome, contributing significantly to plant health, productivity, and the synthesis of biologically active compounds. The diversity of endophytes associated with medicinal plants has attracted considerable attention because these microorganisms represent an untapped source of novel metabolites with potential pharmaceutical, agricultural, and industrial applications (Rodriguez et al., 2009).

Diversity of Endophytic Microorganisms

Endophytes comprise a highly diverse group of microorganisms that include fungi, bacteria, actinomycetes, and, less frequently, archaea. Their diversity is influenced by several factors, including plant species, genotype, tissue type, geographical location, climatic conditions, soil characteristics, seasonal variations, and the developmental stage of the host plant (Zhang et al., 2006).

Fungal Endophytes

Fungi constitute the largest and most extensively studied group of endophytes. They colonize almost every plant species investigated to date and exhibit remarkable taxonomic and functional diversity. Most fungal endophytes belong to the phyla Ascomycota, Basidiomycota, and Mucoromycota, with members of Ascomycota being the most dominant in medicinal plants.

Common fungal genera frequently isolated from medicinal plants include:

- *Aspergillus*
- *Penicillium*
- *Fusarium*
- *Colletotrichum*
- *Alternaria*
- *Cladosporium*
- *Phomopsis*
- *Diaporthe*
- *Trichoderma*
- *Nigrospora*

These fungi are well known for producing diverse secondary metabolites such as alkaloids, polyketides, terpenoids, peptides, quinones, pigments, and volatile organic compounds, many of which exhibit antimicrobial, antioxidant, anticancer, and anti-inflammatory activities (Bacon and White, 2000).

Bacterial Endophytes

Bacterial endophytes are equally important components of the plant microbiome and play crucial roles in plant nutrition, stress tolerance, and disease suppression. They generally belong to the phyla Proteobacteria, Firmicutes, Actinobacteria, and Bacteroidetes.

Frequently reported bacterial genera include:

- *Bacillus*
- *Pseudomonas*
- *Enterobacter*
- *Microbacterium*
- *Streptomyces*

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- *Burkholderia*
- *Paenibacillus*
- *Rhizobium*
- *Serratia*
- *Arthrobacter*

Many bacterial endophytes possess plant growth-promoting traits such as nitrogen fixation, phosphate solubilization, siderophore production, phytohormone synthesis, and biological control against phytopathogens (Martinez-Klimova et al., 2017).

Endophytic Actinomycetes

Endophytic actinomycetes, particularly members of the genus *Streptomyces*, have gained considerable attention because of their extraordinary ability to synthesize antibiotics and industrially important enzymes. These microorganisms also produce antifungal compounds, antioxidants, anticancer metabolites, and extracellular enzymes that have significant biotechnological applications (Khare et al., 2018).

Ecological Functions of Endophytes

The ecological significance of endophytes extends far beyond their ability to inhabit plant tissues. These microorganisms contribute to numerous physiological and biochemical processes that improve plant survival under both normal and stressful environmental conditions (Chaudhary et al., 2022).

Enhancement of Plant Growth

Many endophytes stimulate plant growth through the production of phytohormones such as indole-3-acetic acid (IAA), gibberellins, and cytokinins. They also facilitate nutrient acquisition by fixing atmospheric nitrogen, solubilizing insoluble phosphate, mobilizing potassium, and producing siderophores that improve iron availability. Collectively, these mechanisms promote root development, biomass accumulation, and overall plant productivity (Liao et al., 2025).

Protection Against Plant Pathogens

Endophytes act as natural biological control agents by inhibiting the growth of pathogenic fungi, bacteria, nematodes, and viruses. They produce a wide range of antimicrobial compounds, hydrolytic enzymes, volatile organic compounds, and lipopeptides that suppress pathogen proliferation. In addition, many endophytes induce systemic resistance in host plants by activating defense-related signaling pathways, thereby enhancing the plant's innate immune response (Ameen et al., 2024).

Improvement of Abiotic Stress Tolerance

Environmental stresses such as drought, salinity, extreme temperatures, heavy metals, and oxidative stress adversely affect plant growth and productivity. Endophytes help plants cope with these stresses by producing osmoprotectants, antioxidant enzymes, exopolysaccharides, and stress-responsive metabolites. They also regulate the expression of stress-related genes and reduce the accumulation of reactive oxygen species, thereby improving plant resilience under adverse environmental conditions (Watts et al., 2023).

Contribution to Secondary Metabolism

One of the most fascinating characteristics of endophytes is their ability to influence or directly participate in the biosynthesis of secondary metabolites. Some endophytes synthesize compounds identical or structurally similar to those produced by their host plants, while others produce entirely novel metabolites with unique biological activities. This metabolic versatility is particularly important in medicinal plants, where endophytes may contribute to the overall therapeutic properties of the host (Negi et al., 2024).

Factors Influencing Endophyte Diversity

The composition of endophytic communities varies considerably among plant species and even among different tissues of the same plant. Several environmental and biological factors shape these communities.

Major factors influencing endophyte diversity include:

- Host plant genotype and species.
- Plant age and developmental stage.
- Tissue specificity (roots, stems, leaves, flowers, fruits, and seeds).
- Soil type and nutrient availability.
- Climatic conditions, including temperature and rainfall.
- Geographic location and altitude.
- Seasonal variations.
- Agricultural management practices.
- Presence of neighboring plant species.
- Environmental stress conditions.

Understanding these factors is essential for identifying endophytes with desirable functional traits and for improving their utilization in agriculture and biotechnology (Grabka et al., 2022).

Importance of Endophytes in Medicinal Plants

Medicinal plants provide chemically unique habitats enriched with secondary metabolites that influence the diversity and metabolic capabilities of their associated endophytes. Continuous exposure to compounds such as tannins, flavonoids, alkaloids, terpenoids, and phenolic acids may drive endophytes to evolve specialized biosynthetic pathways capable of producing structurally diverse natural products. Consequently, medicinal plant endophytes have become valuable resources for the discovery of novel antibiotics, antioxidants, anticancer agents, immunomodulators, enzymes, pigments, and other industrially relevant biomolecules. In recent years, increasing attention has also been directed toward their application in sustainable agriculture as biofertilizers, biocontrol agents, and stress-mitigating microorganisms (Dubey et al., 2020).

In the case of *Terminalia bellerica* and *Terminalia chebula*, their exceptionally rich phytochemical composition creates favorable ecological niches for diverse endophytic communities. Exploring these microbial populations not only enhances our understanding of plant microbe interactions but also provides opportunities to discover novel metabolites with significant pharmaceutical and biotechnological value. The following sections summarize the diversity of bacterial and fungal endophytes reported from these two medicinal plants and discuss their biological activities and potential applications (Pandey et al., 2022).

Diversity of Endophytic Microorganisms Associated with *Terminalia bellerica* and *Terminalia chebula*

Medicinal plants harbor complex and dynamic endophytic communities that contribute to plant health and serve as valuable sources of biologically active natural products. The chemical composition of medicinal plants often shapes the diversity and metabolic capabilities of their associated microorganisms. Owing to the abundance of hydrolysable tannins, phenolic acids, flavonoids, and other secondary metabolites, *Terminalia bellerica* and *Terminalia chebula* provide unique ecological niches for diverse bacterial and fungal endophytes. During the last decade, numerous investigations have reported the isolation of endophytes from different plant tissues, including leaves, stems, bark, roots, fruits, and seeds, revealing their remarkable taxonomic diversity and biotechnological potential (Kashyap et al., 2023).

Although culture-dependent techniques remain the most widely employed approach for endophyte isolation, advances in high-throughput sequencing have demonstrated that only a small fraction of the endophytic microbiome can be cultivated under laboratory conditions. Consequently, the actual microbial diversity associated with *Terminalia* species is expected to be considerably greater than currently reported.

Endophytic Diversity in *Terminalia bellerica*

Several studies have demonstrated that *T. bellerica* hosts a diverse assemblage of fungal and bacterial endophytes distributed throughout its tissues. Among these, fungal endophytes have received greater attention because of their ability to produce structurally diverse secondary metabolites with pharmaceutical importance. Members of the genera *Aspergillus*, *Penicillium*, *Fusarium*, *Colletotrichum*, *Alternaria*, *Nigrospora*, *Phomopsis*, *Diaporthe*, *Cladosporium*, and *Trichoderma* have frequently been isolated from leaves, stems, bark, and fruits of *T. bellerica*. These fungi exhibit considerable metabolic versatility and have been reported to produce phenolic compounds, flavonoids, terpenoids, alkaloids, pigments, extracellular enzymes, and volatile organic compounds. Several isolates possess strong antibacterial, antifungal, antioxidant, cytotoxic, and enzyme-producing capabilities, highlighting their potential as sources of novel bioactive metabolites (Muhammad et al., 2024).

Bacterial endophytes isolated from *T. bellerica* are comparatively less explored. Nevertheless, available studies have identified representatives of *Bacillus*, *Pseudomonas*, *Enterobacter*, *Microbacterium*, and *Streptomyces*. These bacteria exhibit plant growth-promoting characteristics such as phosphate solubilization, indole-3-acetic acid production, siderophore synthesis, and antagonistic activity against phytopathogenic microorganisms. Such functional attributes suggest that bacterial endophytes may contribute to the medicinal plant's health and resilience while also serving as promising candidates for sustainable agricultural applications. The diversity of endophytes recovered from *T. bellerica* varies depending on geographical location, environmental conditions, host tissue, and isolation methodology. Leaf tissues often exhibit the highest fungal diversity, whereas roots generally harbor bacterial communities involved in nutrient acquisition and stress adaptation (Kumar & Radhakrishnan, 2020).

Endophytic Diversity in *Terminalia chebula*

Compared with *T. bellerica*, *T. chebula* has been investigated more extensively for its endophytic microorganisms owing to its longstanding medicinal significance. Numerous fungal and bacterial endophytes have been isolated from leaves, bark, fruits, stems, roots, and seeds collected from different geographical regions.

Fungal genera commonly associated with *T. chebula* include *Aspergillus*, *Penicillium*, *Fusarium*, *Colletotrichum*, *Phomopsis*, *Alternaria*, *Curvularia*, *Cladosporium*, *Nigrospora*, *Pestalotiopsis*, and *Diaporthe*. Many of these isolates synthesize antimicrobial metabolites, antioxidants, hydrolytic enzymes, pigments, and volatile compounds with potential applications in pharmaceutical and industrial biotechnology. Certain fungal endophytes have also demonstrated the ability to inhibit multidrug-resistant bacterial pathogens and phytopathogenic fungi, indicating their value as alternative sources of antimicrobial agents (Rai et al., 2021).

Bacterial endophytes recovered from *T. chebula* belong predominantly to the genera *Bacillus*, *Pseudomonas*, *Enterobacter*, *Rhizobium*, *Paenibacillus*, *Serratia*, *Burkholderia*, and *Streptomyces*. These microorganisms contribute to nutrient cycling, phytohormone production, biological nitrogen fixation, and induction of systemic resistance. Several isolates also produce extracellular enzymes such as cellulases, amylases, proteases, and lipases that possess considerable industrial significance.

Comparative studies suggest that fungal endophytes dominate the internal microbiome of *T. chebula*, although bacterial diversity is increasingly being uncovered through molecular techniques. Differences in microbial composition have been attributed to variations in host genotype, climatic conditions, altitude, tissue specificity, and seasonal changes (Mushtaq et al., 2023).

Factors Influencing Endophytic Diversity in *Terminalia* Species

The diversity and composition of endophytic communities associated with *Terminalia* species are governed by a combination of environmental, physiological, and methodological factors. Climate, rainfall, soil characteristics, altitude, and seasonal variations influence microbial colonization by altering the surrounding microbial reservoir and host physiology. Likewise, plant age, tissue type, nutritional status, and phytochemical composition contribute significantly to microbial selection within host tissues.

Methodological differences also affect the diversity of isolated microorganisms. Surface sterilization protocols, culture media, incubation conditions, and molecular identification techniques can influence the recovery of cultivable endophytes. Recent advances in metagenomic sequencing have revealed that many unculturable microorganisms remain undetected using conventional culture-based approaches, emphasizing the need to integrate culture-independent methods for a more comprehensive understanding of the *Terminalia* endophytic microbiome.

Collectively, available studies demonstrate that *T. bellerica* and *T. chebula* harbor diverse microbial communities with considerable functional and metabolic potential. However, current knowledge remains fragmented because most investigations have focused on the isolation of individual strains or specific biological activities. Comprehensive studies integrating microbial diversity, metabolomics, genomics, and functional characterization are required to fully exploit these endophytes as sustainable sources of bioactive compounds and plant-beneficial microorganisms (Sahu et al., 2022).

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Table 2. Reported endophytic microorganisms isolated from *Terminalia bellerica* and *Terminalia chebula*.

Host plant	Plant part	Endophyte	Type	Reported activity
T. bellerica	Leaf	*Aspergillus* spp.	Fungus	Antioxidant, antimicrobial
T. bellerica	Stem	*Penicillium* spp.	Fungus	Enzyme production
T. bellerica	Bark	*Fusarium* spp.	Fungus	Antimicrobial
T. bellerica	Root	*Bacillus* spp.	Bacterium	IAA, phosphate solubilization
T. chebula	Leaf	*Pestalotiopsis* spp.	Fungus	Antioxidant
T. chebula	Bark	*Nigrospora* spp.	Fungus	Antibacterial
T. chebula	Fruit	*Cladosporium* spp.	Fungus	Phenolic metabolites
T. chebula	Root	*Streptomyces* spp.	Actinomycete	Antibiotic production
T. chebula	Leaf	*Pseudomonas* spp.	Bacterium	Plant growth promotion

Functional Characterization of Endophytes

Following identification, endophytic microorganisms are evaluated for their biological and biotechnological potential through a series of functional assays. Common screening procedures include antimicrobial assays against bacterial and fungal pathogens, antioxidant activity using DPPH, ABTS, or FRAP methods, enzyme production assays for cellulase, amylase, protease, lipase, and xylanase, and plant growth-promoting traits such as indole-3-acetic acid production, phosphate solubilization, siderophore production, nitrogen fixation, and ACC deaminase activity.

Secondary metabolites are typically extracted using organic solvents such as ethyl acetate, methanol, or chloroform and characterized through chromatographic and spectroscopic techniques, including high-performance liquid chromatography (HPLC), gas chromatography–mass spectrometry (GC–MS), liquid chromatography–mass spectrometry (LC–MS), Fourier-transform infrared spectroscopy (FTIR), and nuclear magnetic resonance (NMR) spectroscopy. These analyses enable the identification of known compounds and facilitate the discovery of novel metabolites with potential pharmaceutical and industrial applications (Eid et al., 2021).

Current Challenges and Future Directions

Despite significant methodological advances, several challenges continue to limit endophyte research. Many microorganisms remain unculturable using conventional laboratory techniques, while some isolates gradually lose their ability to produce bioactive metabolites during repeated subculturing. Variations in isolation protocols, culture media, incubation conditions, and molecular markers also hinder direct comparisons among different studies.

Future investigations should integrate culture-dependent and culture-independent approaches with metabolomics, genome mining, synthetic biology, and artificial intelligence-assisted data analysis. Such multidisciplinary strategies will provide a more comprehensive understanding of endophytic diversity and accelerate the identification of novel microorganisms and metabolites associated with *Terminalia bellerica* and *Terminalia chebula* (Verma et al., 2021).

Bioactive Metabolites Produced by Endophytes of *Terminalia bellerica* and *Terminalia chebula*

Endophytic microorganisms have emerged as an important source of structurally diverse natural products with significant pharmaceutical, agricultural, and industrial value. Living within the specialized chemical environment of medicinal plants enables these microorganisms to develop unique metabolic capabilities that often complement or resemble those of their host. In *Terminalia bellerica* and *Terminalia chebula*, the abundance of hydrolysable tannins, phenolic acids, flavonoids, and other bioactive constituents provides favorable conditions for endophytes to synthesize a wide range of secondary metabolites. Many of these compounds exhibit potent antimicrobial, antioxidant, anticancer, anti-inflammatory, and enzyme-inhibitory activities, making them attractive candidates for drug discovery and biotechnological applications.

Although investigations on endophytes associated with *Terminalia* species are still limited compared with other medicinal plants, available studies have demonstrated their remarkable biosynthetic potential. The metabolites reported from these microorganisms belong to several chemical classes, including phenolics, alkaloids, terpenoids, polyketides, peptides, quinones, flavonoids, volatile organic compounds, and extracellular enzymes (Dwibedi et al., 2022).

Phenolic Compounds

Phenolic compounds constitute one of the most important groups of metabolites produced by endophytic microorganisms. These compounds are well known for their antioxidant, antimicrobial, anti-inflammatory, and anticancer properties. Endophytes isolated from *T. bellerica* and *T. chebula* have been reported to produce various phenolic metabolites that contribute to the biological activities observed in crude extracts.

Phenolic compounds exert their biological effects primarily through free radical scavenging, inhibition of lipid peroxidation, modulation of inflammatory pathways, and protection of cellular macromolecules against oxidative damage. Some endophytes are capable of synthesizing metabolites structurally similar to those naturally occurring in their host plants, suggesting a close metabolic association between the plant and its microbiome (Zhang et al., 2022).

Alkaloids

Alkaloids represent another important class of microbial secondary metabolites characterized by diverse chemical structures and potent pharmacological activities. Endophytic fungi and bacteria isolated from medicinal plants have been shown to produce alkaloids exhibiting antimicrobial, cytotoxic, antiparasitic, antiviral, and neuroprotective properties.

Although only a limited number of alkaloids have been specifically reported from endophytes associated with *Terminalia* species, genome analyses indicate that many isolates possess biosynthetic gene clusters capable of producing novel nitrogen-containing compounds. Continued investigation of these microorganisms may therefore lead to the discovery of previously unknown alkaloids with therapeutic potential (Dudeja et al., 2021).

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Terpenoids

Terpenoids are among the largest classes of natural products synthesized by endophytic microorganisms. These compounds display a broad spectrum of biological activities, including antibacterial, antifungal, anticancer, antiviral, anti-inflammatory, and insecticidal effects.

Several endophytic fungi isolated from medicinal plants have demonstrated the ability to synthesize monoterpenes, sesquiterpenes, diterpenes, and triterpenes. The presence of terpenoid-producing endophytes in *Terminalia* species further supports their potential as renewable sources of pharmaceutically important compounds. Because terpenoid biosynthesis is often regulated by complex genetic pathways, advances in genome mining and metabolic engineering may facilitate enhanced production of these valuable metabolites (Adeleke et al., 2022).

Flavonoids and Related Metabolites

Flavonoids are widely recognized for their antioxidant and anti-inflammatory properties. While these compounds are primarily associated with plants, increasing evidence suggests that certain endophytic microorganisms possess the enzymatic machinery required for flavonoid biosynthesis or biotransformation. Endophytes isolated from medicinal plants may contribute to the accumulation of flavonoid-like metabolites through cooperative metabolic interactions with their host. Such metabolites can protect both the microorganism and the plant from oxidative stress, ultraviolet radiation, and microbial pathogens (Chaudhary et al., 2022).

Volatile Organic Compounds (VOCs)

Volatile organic compounds produced by endophytes have attracted considerable attention because of their ecological and commercial importance. These low-molecular-weight compounds participate in plant–microbe communication and often exhibit antimicrobial, insecticidal, and growth-promoting activities. Endophytic fungi belonging to genera such as *Nigrospora*, *Cladosporium*, *Phomopsis*, and *Diaporthe* have been reported to produce complex mixtures of alcohols, aldehydes, ketones, esters, terpenes, and aromatic hydrocarbons. These metabolites suppress the growth of competing microorganisms and may contribute to the natural disease resistance observed in medicinal plants (Backman & Sikora, 2008).

Extracellular Enzymes

In addition to low-molecular-weight secondary metabolites, endophytes synthesize numerous extracellular enzymes that facilitate nutrient acquisition and colonization of host tissues. These enzymes also possess considerable industrial significance.

Common enzymes produced by *Terminalia*-associated endophytes include:

- Cellulases
- Xylanases
- Pectinases
- Amylases
- Proteases
- Lipases

- Laccases

These enzymes are widely utilized in the food, textile, paper, detergent, pharmaceutical, and biofuel industries because of their high catalytic efficiency and environmental compatibility (Wang and Zhang, 2023).

Biological Activities of Endophytic Metabolites

The diverse metabolites produced by endophytes exhibit a broad spectrum of biological activities that support their pharmaceutical and biotechnological importance.

Antimicrobial Activity

Several endophytic fungi and bacteria isolated from medicinal plants produce metabolites capable of inhibiting Gram-positive and Gram-negative bacteria as well as pathogenic fungi. These antimicrobial compounds may function by disrupting microbial cell walls, interfering with protein synthesis, inhibiting nucleic acid replication, or altering membrane permeability. The increasing prevalence of antimicrobial resistance has intensified the search for novel endophytic metabolites with unique mechanisms of action (Wang & Zhang, 2023).

Antioxidant Activity

Oxidative stress plays a central role in aging and numerous chronic diseases. Phenolic compounds, flavonoids, quinones, and other metabolites produced by endophytes effectively neutralize reactive oxygen species, thereby protecting cellular components from oxidative damage. Antioxidant metabolites obtained from *Terminalia*-associated endophytes have demonstrated promising free radical scavenging activity in various in vitro assays (Porras-Alfaro & Bayman, 2011).

Anticancer Activity

Natural products continue to be an important source of anticancer drugs. Several endophytic microorganisms produce metabolites that inhibit cancer cell proliferation through apoptosis induction, cell-cycle arrest, angiogenesis inhibition, and modulation of intracellular signaling pathways. The identification of novel anticancer compounds from endophytes associated with *T. bellerica* and *T. chebula* represents an emerging area of pharmaceutical research (Wilson, 1995).

Anti-inflammatory Activity

Inflammation is closely associated with many chronic disorders, including cardiovascular disease, diabetes, arthritis, and neurodegenerative diseases. Numerous microbial metabolites suppress inflammatory responses by regulating cytokine production, cyclooxygenase activity, and oxidative stress pathways. Such compounds may contribute to the therapeutic properties traditionally attributed to *Terminalia* species.

Plant Growth-Promoting Activity

In addition to producing pharmacologically active metabolites, many endophytes synthesize compounds that enhance plant growth. These include phytohormones, siderophores, ACC deaminase, and phosphate-solubilizing metabolites that improve nutrient availability, root development, and stress tolerance. Such characteristics make these microorganisms valuable candidates for sustainable agricultural practices (Collinge & Jensen, 2022).

Future Prospects in Endophytic Metabolite Discovery

The integration of genomics, metabolomics, transcriptomics, and synthetic biology has revolutionized the discovery of microbial natural products. Genome mining has revealed numerous cryptic biosynthetic gene clusters in endophytic microorganisms that remain inactive under conventional laboratory conditions. Strategies such as co-cultivation, epigenetic modification, heterologous expression, and metabolic engineering are increasingly being employed to activate these silent pathways and enhance metabolite production (Adeleke and Babalola, 2021).

For endophytes associated with *Terminalia bellerica* and *Terminalia chebula*, future research should focus on linking biosynthetic genes with metabolite production, identifying novel compounds through advanced analytical platforms, and optimizing fermentation processes for commercial-scale production. Such multidisciplinary approaches will facilitate the development of sustainable microbial sources of high-value natural products while reducing pressure on medicinal plant resources (Rosenblueth & Martínez-Romero, 2006).

Limited Exploration of Endophytic Diversity

Although both *T. bellerica* and *T. chebula* are well-known medicinal plants, only a small proportion of their endophytic microbiota has been investigated. Most studies have focused on fungal endophytes isolated using conventional culture-based methods, whereas bacterial endophytes, actinomycetes, and unculturable microorganisms remain largely unexplored. Furthermore, investigations have been concentrated in a limited number of geographical regions, making it difficult to understand how environmental factors influence endophyte diversity and function (Khare et al., 2018).

Dependence on Culture-Based Techniques

Traditional isolation methods recover only a fraction of the microbial community present within plant tissues. Many endophytes require highly specific nutritional or environmental conditions that cannot be reproduced under standard laboratory conditions. Consequently, a substantial proportion of the endophytic microbiome remains inaccessible using conventional microbiological approaches, resulting in an incomplete understanding of microbial diversity and metabolic potential (Chaudhary et al., 2022).

Inconsistent Metabolite Production

One of the major obstacles to commercial utilization of endophytes is the instability of metabolite production during repeated laboratory cultivation. Several isolates gradually lose their biosynthetic capacity after multiple subcultures because of changes in gene expression, epigenetic regulation, or the absence of host-derived signaling molecules. This inconsistency presents a significant challenge for industrial-scale production of bioactive compounds (Watts et al., 2023).

Challenges in Commercialization

Despite promising laboratory-scale results, relatively few endophyte-derived products have reached commercial markets. Large-scale fermentation, downstream processing, quality control, regulatory approval, intellectual property protection, and economic feasibility remain significant barriers to industrial

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development. Overcoming these challenges will require close collaboration between academic institutions, industry, and regulatory agencies (Sahu et al., 2022).

Emerging Technologies and Future Opportunities

Recent technological advances offer exciting opportunities to accelerate endophyte research and overcome many of the limitations associated with conventional approaches.

Metagenomics and Microbiome Analysis

High-throughput sequencing technologies have revolutionized the study of plant-associated microbial communities by enabling the identification of both culturable and unculturable microorganisms. Metagenomic approaches provide comprehensive information regarding microbial diversity, functional genes, and biosynthetic potential without requiring laboratory cultivation. Future studies employing shotgun metagenomics combined with microbiome analysis will significantly improve our understanding of the microbial communities associated with *T. bellerica* and *T. chebula* (Mishra et al., 2022).

Genome Mining

Whole-genome sequencing has revealed that many endophytic microorganisms possess numerous cryptic biosynthetic gene clusters that remain inactive under laboratory conditions. Genome mining tools enable researchers to identify these hidden pathways and predict the classes of natural products they may produce. Combining genome mining with metabolomic profiling will facilitate the discovery of novel antibiotics, anticancer agents, antioxidants, and other valuable metabolites from *Terminalia* endophytes (Verma et al., 2021).

Metabolomics

Modern metabolomic platforms based on LC–MS/MS, GC–MS, and NMR spectroscopy allow comprehensive profiling of microbial metabolites. These technologies not only accelerate the identification of known compounds but also facilitate the discovery of previously unreported natural products. Integrating metabolomics with genomic and transcriptomic analyses will improve our understanding of metabolite biosynthesis and plant–microbe interactions (Dudeja et al., 2021).

Synthetic Biology and Metabolic Engineering

Synthetic biology provides powerful tools for improving microbial production of valuable metabolites. Genome editing technologies, including CRISPR-Cas systems, enable precise manipulation of biosynthetic pathways, while metabolic engineering allows optimization of precursor supply, regulatory networks, and fermentation performance. These approaches may eventually transform endophytes into efficient microbial cell factories capable of producing commercially important compounds in a sustainable manner (Harrison & Griffin, 2020).

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Artificial Intelligence and Machine Learning

Artificial intelligence (AI) and machine learning (ML) are increasingly being applied to natural product research. These technologies can analyze large genomic and metabolomic datasets, predict biosynthetic gene clusters, identify relationships between microbial diversity and metabolite production, and optimize fermentation conditions. AI-assisted drug discovery also enables rapid prediction of biological activities, molecular targets, toxicity, and pharmacokinetic properties of newly identified compounds, thereby accelerating the development of therapeutic candidates (Bhardwaj et al., 2023).

Multi-Omics Integration

Future research will increasingly rely on the integration of genomics, transcriptomics, proteomics, metabolomics, and microbiome analyses to obtain a systems-level understanding of endophyte biology. Such multi-omics approaches will reveal how environmental conditions, host physiology, and microbial gene regulation collectively influence metabolite production. The integration of these datasets will facilitate the identification of key regulatory pathways and support the rational design of high-yield microbial production systems (Ryan et al., 2008).

Future Perspectives

The endophytic microbiota associated with *Terminalia bellerica* and *Terminalia chebula* represents a largely untapped biological resource with immense scientific and commercial value. Future investigations should move beyond simple isolation and screening studies toward comprehensive functional analyses that integrate ecology, molecular biology, natural product chemistry, and biotechnology. Particular emphasis should be placed on discovering novel metabolites, understanding biosynthetic mechanisms, optimizing large-scale fermentation, and validating biological activities through in vivo and clinical studies. Establishing collaborative research programs involving microbiologists, pharmacologists, chemists, bioinformaticians, and industrial partners will accelerate the translation of laboratory discoveries into practical applications. As global demand for sustainable natural products continues to grow, endophytes associated with *Terminalia* species have the potential to become important microbial resources for pharmaceutical development, environmentally friendly agriculture, industrial biotechnology, and personalized medicine. Continued investment in advanced analytical technologies and interdisciplinary research will undoubtedly unlock new opportunities for harnessing these hidden microbial partners for the benefit of human health and environmental sustainability (Liao et al., 2025).

Conclusion

Endophytes associated with *Terminalia bellerica* and *Terminalia chebula* represent a promising yet underexplored source of bioactive compounds with significant pharmaceutical, agricultural, and industrial potential. Their ability to produce diverse secondary metabolites and plant growth-promoting biomolecules highlights their importance as sustainable alternatives to conventional natural product sources. Although considerable progress has been made in understanding their diversity and biological activities, many endophytic communities and their biosynthetic capabilities remain unexplored. The integration of advanced approaches such as metagenomics, metabolomics, genome mining, synthetic biology, and artificial

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intelligence will accelerate the discovery of novel metabolites and improve their commercial utilization. Future research should focus on comprehensive characterization of endophytic communities, elucidation of biosynthetic pathways, and large-scale production strategies to fully harness the biotechnological potential of endophytes associated with these medicinally important *Terminalia* species.

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