



Endophytic fungi as a promising source of Antimicrobial and Anticancer Bioactive compounds: A Comprehensive Review

Muskan A. Dadlani¹*, Dr. Narendra H. Shahare², Gokul S. Bajaj³

¹Research Scholar, Department of Botany, Brijlal Biyani Science College, Amravati, Maharashtra.

²Head & Professor, Department of Botany, Brijlal Biyani Science College, Amravati, Maharashtra.

³Assistant Professor, Department of Botany, Brijlal Biyani Science College, Amravati, Maharashtra.

*E-mail: muskan.dadlani@gmail.com

ABSTRACT

Endophytes are fungal communities that flourish within the host plant tissues and synthesize a diverse array of secondary metabolites that show numerous bioactive applications. Bioactive compounds including alkaloids, phenols, terpenoids, steroids, saponins, glycosides helps the host plant to fight against plant pathogens, biotic and abiotic stress and also act as a shield against grazing animals. The present review presents an overview on the characteristics of endophytes, the isolation and identification techniques for endophytes, the bioactive compounds present in the endophytes, and the anticancer and antimicrobial potential of endophytic fungi. Endophytes are a vast field of study which is still highly unexplored for the bioactive diversity and the exploration of their therapeutic potential. The bioactive compounds synthesized by the endophytes show higher anti-microbial, anti-cancer, anti-oxidant and anti-inflammatory potential. Hence, the integrated study of endophytes in the present time and future holds vast potential; by combining both the traditional and molecular approach with the current technologies can uplift research on endophytes to a much higher level.

Keywords: Endophytes, bioactive compounds, isolation, anti-cancer.

Introduction

For centuries, plants have been recognized as a valuable source of medicinal bioactive compounds effective against a wide array of ailments (Sun and Guo, 2012). Interestingly, recent research has highlighted that microorganisms associated with plants, rather than the plants themselves, often provide materials and products with significant therapeutic potential (Aly *et al.*, 2010). Among these microorganisms, endophytes—comprising fungi, actinomycetes, and bacteria—reside within plant tissues without eliciting evident disease symptoms in their host plants (Sun and Guo, 2012). Endophytic fungi, in particular, represent a rich reservoir of naturally derived pharmaceuticals, synthesizing diverse classes of bioactive molecules such as alkaloids, flavonoids, peptides, phenolics, quinones, steroids, and terpenoids (Aly *et al.*, 2010; Beeralinga *et al.*, 2025). These compounds exhibit a broad spectrum of biological activities, including antimicrobial, antidiabetic, anticancer, anti-inflammatory, antioxidant, and immunomodulatory effects (Kuzniar *et al.*, 2025). Moreover, endophytes contribute to host plant growth and nutrient acquisition, enhance tolerance to various abiotic and biotic stresses, and bolster resistance against insects and pests. They also produce phytohormones and other bioactive substances of biotechnological relevance, including enzymes and pharmaceutical agents (Beeralinga *et al.*, 2025).

Empirical evidence suggests that every plant species examined has one or more types of endophytes (Guo, 2001). These microorganisms can colonize diverse plant tissues, including stems, roots, petioles, leaf segments, inflorescences of weeds, fruits, buds, seeds, as well as dead and hollow hyaline cells (Sun and Guo, 2012). The abundance and diversity of endophytes within a given plant species are highly variable and influenced by factors such as host species, developmental stage, inoculum density, and environmental conditions. This review article focuses on endophytes, with particular emphasis on the characteristics of endophytic fungi, methodologies for their isolation and identification, and their potential applications.

Characteristics of Endophytic Fungi

Endophytic organisms have been identified in nearly all plant species studied, with plants serving as hosts to a diverse array of endophytes that engage in various types of interactions, including symbiotic, mutualistic, commensalistic, and trophobiotic relationships (Chaudhary *et al.*, 2022). The evolutionary history of plant–endophyte interactions extends back over 400 million years, underscoring their ecological success and the essential role

endophytes play in enabling plants to thrive under challenging environmental conditions. Notably, plants possess the capacity to selectively associate with microbial endophytes from their above-ground and below-ground microbial communities that confer specific benefits (Singh and Dubey, 2018). Plant endophytes encompass a broad range of microbial taxa, including bacteria, fungi, archaea, algae, and viruses, primarily originating from the rhizosphere, phyllosphere, and seeds (Chaudhary *et al.*, 2022).

Endophytic fungi represent one of the most diverse and prevalent groups of microorganisms within numerous plant species. These fungal endophytes inhabit both the root systems and aerial parts of plants, exhibiting substantial diversity (Majhi *et al.*, 2025). Similar to bacterial colonization, fungal endophytes can systemically colonize plants up to the flowering organs. Moreover, endophytes are capable of seed transmission. For instance, many fungal endophytes, such as those belonging to the genus *Epichloa*, rely entirely on the host plant's reproductive capacity for their survival and dissemination, resulting in seed-mediated transmission (AbuTaher *et al.*, 2023). Notably, research indicates that endophytic fungi do not colonize early-stage embryos; rather, infection predominantly occurs during later stages of seed development. The initial phases of plant growth are critical for establishing the overall microbiota, and it is essential that plants utilize seed-associated microbes to maintain proper ecological functions throughout subsequent developmental stages (Andreote *et al.*, 2014; Berg *et al.*, 2014; Majhi *et al.*, 2025).

The composition of a plant's endophytic microbiome is influenced by multiple factors, including plant species, developmental stage, tissue type, soil physicochemical properties (notably pH and moisture), the plant's physiological and nutritional status, seasonal timing, and environmental conditions (Berg *et al.*, 2014). Root tissues typically harbor the greatest abundance of endophytic microorganisms, whereas aerial plant parts exhibit comparatively lower endophyte densities. Generative organs of plants are generally the least colonized by endophytic microorganisms (Bhardwaj and Agrawal, 2014; Chen *et al.*, 2021).

Endophytic fungi are categorized into three principal ecological groups: mycorrhizal fungi, balansicaceous or pasture fungal endophytes, and non-pasture fungal endophyte (Kuzniar *et al.*, 2025). Additionally, they can be classified into two groups based on taxonomy: non-clavicipitaceous endophytes (NC-endophytes) and clavicipitaceous endophytes (C-endophytes). C-endophytes, classified as Class 1, are predominantly located in plant shoots where they induce systemic intracellular infections (Bamisile *et al.*, 2018; Kuzniar *et al.*, 2025). This group is further subdivided into three types: comprising symptomatic and pathogenic species; mixed-interaction and asymptomatic endophytes; and asymptomatic endophytes. NC-endophytes are divided into Ascomycetes, represent a significant group of endophytes across various plant species; Basidiomycota and the fungal group Dikaryomycota and facultative biotrophic organisms that colonize plant roots and are characterized by the presence of melanized, dark septate hyphae, phylum Zygomycetes (Kuzniar *et al.*, 2025).

Isolation and Identification of Endophytic Fungi

The process of isolation and identification of endophytic fungi is performed by the following steps: Surface Sterilization: This preliminary procedure aims to eliminate epiphytic microorganisms from plant surfaces (Sahu *et al.*, 2022; Deepak *et al.*, 2022). Tissue Isolation Method: Sterilized plant tissues—including leaves, stems, and roots—are aseptically sectioned into small fragments (typically 0.3–0.5 cm) and placed onto appropriate culture media such as potato dextrose agar (PDA) or malt extract agar (MEA), often supplemented with antibiotics to suppress bacterial growth (Hallmann *et al.*, 2006; Mat Jalil *et al.*, 2018). Plant Tissue Maceration Method: This technique is particularly employed for isolating slow-growing or root-associated endophytes (Klahs *et al.*, 2023). Plant Intercellular Fluid Culture Method: This approach involves centrifugation to extract microorganisms residing in the intercellular (apoplastic) spaces of plant tissues, proving especially effective for root endophyte isolation (O'Leary *et al.*, 2014).

Identification Techniques using Traditional Methods:

Morphological and Cultural Characterization of Endophytic Fungi: Following initial isolation from surface-sterilized plant tissues on nutrient media, fungal colonies are purified by transferring hyphal tips or spores onto fresh agar plates to establish pure cultures (Dos Reis *et al.*, 2022; Abubtain *et al.*, 2021). Advancements in molecular biology have introduced novel methodologies for characterizing endophytic microorganisms, offering new insights into their diversity. Molecular techniques, including DNA fingerprinting and sequencing, provide effective means to circumvent the limitations inherent in cultivation-dependent methods (Blackwell, 2011). Molecular approaches, especially DNA sequence analysis of regions like the Internal Transcribed Spacer (ITS), are indispensable for the accurate identification of these sterile mycelia. Genetic sequence data enable the assignment of non-sporulating isolates to appropriate taxonomic ranks, including genus, family, or order (Sikarwar *et al.*, 2023). Molecular identification has demonstrated that morphologically similar sterile isolates may belong to phylogenetically distant taxa, underscoring the limitations of morphology-based classification. Overall, molecular methodologies substantially enhance the resolution of fungal diversity studies, particularly for sterile isolates that elude traditional identification techniques (Singh *et al.*, 2013).

Endophytic fungal communities encompass a broad spectrum of taxa from major fungal phyla such as Ascomycota, Basidiomycota, and Zygomycota, rendering morphology-based identification both challenging and labor-intensive. To address these challenges, DNA sequencing—primarily targeting the ITS region—combined with morphological data, has become a standard approach for investigating endophyte diversity. Molecular techniques facilitate the detection of diverse fungal taxa across various plant tissues and ecosystems, often revealing greater species richness than morphology alone (Suneja *et al.*, 2023). Commonly employed genetic markers include the 18S, 28S, and ITS regions, which provide taxonomic resolution ranging from broad classifications to species-level identifications. Molecular data have also led to the discovery of novel taxa and clarified phylogenetic relationships within complex fungal groups. Collectively, these molecular tools expedite and refine the understanding of fungal biodiversity in natural ecosystems, independent of the fungi's capacity to sporulate in culture (Raja *et al.*, 2017).

Traditional isolation methods for endophytic fungi frequently fail to detect many species due to slow growth rates or inability to grow on artificial media, often resulting in competitive exclusion by faster-growing fungi (Sarsaiya *et al.*, 2019; Shah *et al.*, 2019). To overcome these limitations, molecular techniques have been widely adopted to detect and analyze endophytic fungi directly from plant tissues (dos Reis *et al.*, 2022). The standard molecular detection protocol involves extracting total genomic DNA from surface-sterilized plant tissues, which contains both plant and fungal DNA, followed by PCR amplification of fungal-specific DNA regions such as the ITS, 18S, or 28S rRNA genes (Sarsaiya *et al.*, 2019).

Molecular techniques for the separation and identification of fungal taxa include methods such as Denaturing Gradient Gel Electrophoresis (DGGE), which enables differentiation of PCR-amplified products corresponding to distinct fungal groups (Michaelsen *et al.*, 2006). Representative DNA fragments obtained through these methods are often cloned and sequenced, allowing taxonomic identification by comparison with established reference databases. Phylogenetic analyses further facilitate the assignment of detected fungi to their appropriate taxonomic positions (Ohtomo *et al.*, 2019). These molecular approaches are advantageous in detecting a wider spectrum of fungal diversity, encompassing taxa that do not sporulate or are difficult to culture (de Souza *et al.*, 2004; Michaelsen *et al.*, 2006). Comparative studies have demonstrated notable discrepancies between fungal communities identified via molecular techniques and those isolated through conventional culturing, underscoring the complementary nature of molecular detection methods (Kumar *et al.*, 2016; Liang *et al.*, 2017). Nonetheless, molecular approaches present certain limitations, including challenges in achieving species-level identification when only short DNA fragments are amplified, reduced sensitivity in detecting rare species, and the necessity for more universal primers that enhance phylogenetic resolution. Additional molecular markers, such as Simple Sequence Repeat (SSR) markers, provide robust and reproducible means to further characterize fungal diversity (Mosa *et al.*, 2019; Pistone *et al.*, 2026).

High-throughput sequencing (HTS), particularly next-generation sequencing (NGS) platforms such as pyrosequencing and Illumina sequencing, has transformed the investigation of fungal endophyte diversity (Aragona *et al.*, 2022). Compared to traditional Sanger sequencing, HTS offers increased depth and resolution, enabling the detection of a greater number of fungal taxa, including rare and unculturable species. Moreover, HTS facilitates rapid and cost-effective processing of numerous samples concurrently, while reducing biases to yield a more comprehensive representation of fungal community composition (Tedersoo *et al.*, 2020; Aragona *et al.*, 2022). Applications of HTS across diverse environments have uncovered previously unrecognized fungal diversity that culture-based methods often overlook. However, challenges persist, including PCR biases related to primer selection and amplification parameters, DNA extraction biases affecting the recovery of certain taxa, limitations imposed by short read lengths on taxonomic resolution (although emerging long-read technologies such as PacBio mitigate this issue), and the need for standardized protocols in data processing, taxonomic assignment, and reporting to ensure reproducibility and comparability. Continuous advancements in sequencing technologies and bioinformatics are progressively enhancing the capacity to characterize endophytic fungi within ecological and functional frameworks (Fang *et al.*, 2015; Hariharan *et al.*, 2021; Aragona *et al.*, 2022).

DNA barcoding employs short, standardized gene regions to facilitate species identification, relying on high interspecific variability coupled with low intraspecific variation (Piombo *et al.*, 2021). While the mitochondrial cytochrome oxidase I (CO1) gene is widely utilized in animal taxa, it is unsuitable for fungi due to the presence of introns. Instead, the Internal Transcribed Spacer (ITS) region of ribosomal DNA serves as the primary barcode marker for fungi, owing to its high amplification success across diverse fungal lineages using universal primers, an appropriate length (~500–700 base pairs) for sequencing, and extensive representation in public sequence databases (Francioli *et al.*, 2021; Piombo *et al.*, 2021). The ITS region has been extensively applied in the identification of fungal species, including endophytic fungi; however, it presents certain challenges. These include variable divergence thresholds among different fungal groups that complicate universal species delimitation, limited availability of reference sequences relative to the estimated fungal diversity, the presence of misidentified sequences within databases that hinder accurate identification, and the insufficiency of ITS alone to discriminate closely related or rapidly evolving species, which may necessitate the use of additional genetic loci (Francioli *et al.*, 2021; Piombo *et al.*, 2021; Aragona *et al.*, 2022).

Bioactive Compounds Derived from Endophytic Fungi

Endophytic organisms have been documented to synthesize a diverse array of bioactive metabolites within a single host plant or microorganism, serving as a valuable reservoir for drug discovery aimed at treating various diseases (Tiwari and Bae, 2022). These metabolites also hold considerable promise for applications across agriculture, medicine, food technology, and the cosmetics industry (Harish Chandra *et al.*, 2024; Tiwari and Bae, 2022). The secondary metabolites produced by endophytes encompass multiple functional classes, including alkaloids, benzopyranones, quinones, flavonoids, phenolic acids, steroids, saponins, tannins, terpenoids, tetralones, and xanthenes, among others (Harish Chandra *et al.*, 2024; Nagib *et al.*, 2026).

Notably, Taxol (paclitaxel), a complex diterpene alkaloid synthesized by the endophytic fungus *Metarhizium anisopliae* residing in the bark of *Taxus* species, represents one of the most efficacious anticancer agents developed to date (Gouda *et al.*, 2016). Camptothecin, isolated from *Nothapodytes foetida*, exhibits both cytotoxic and antifungal properties (Wu *et al.*, 2008; Han and Rahman, 2012). Lignans extracted from the endophytic *Podophyllum hexandrum*, known for their cathartic, emetic, and cholagogue effects, have been reported to possess anticancer activity (Varghese *et al.*, 2024). Similarly, resins such as etoposide and teniposide, obtained from *Podophyllum emodi*, demonstrate potent anticancer efficacy (Ardalani *et al.*, 2017). Furthermore, compounds including oxacillin, ampicillin, catechin, gallic acid, and cefalexin are recognized for their bactericidal properties (Malczak and Gajda, 2023). Terpenoids have been identified to exert antineoplastic, antibacterial, antiviral effects, as well as gastrointestinal stimulatory actions (Masyita *et al.*, 2022). For instance, the endophytic fungus *Cytospora* sp. produces the triterpenoid helvolic acid, which exhibits strong antibacterial activity (Masyita *et al.*, 2022).

Owing to their remarkable metabolic versatility, endophytic bacteria are capable of generating a broad spectrum of secondary metabolites characterized by diverse structural features. These bioactive compounds include terpenoids, polyketides, alkaloids, phenolics, and quinones. Such metabolites are well-documented for their cytotoxic, anti-inflammatory, and antibacterial properties. Certain endophytes have been reported to synthesize hybrid terpenoids, such as meroterpenoids, which display synergistic antibacterial effects (Abu Taher *et al.*, 2023). Recent advances in understanding the metabolic diversity of endophytes have enhanced recognition of their role as precursors of valuable metabolites implicated in biotransformation processes, disease resistance, and pharmaceutical applications (Majhi *et al.*, 2025).

Applications of Endophytic Fungi in Antimicrobial and Anticancer Therapies

Endophytic microorganisms constitute a prolific and extensively studied source of bioactive secondary metabolites, with anticancer agents representing a particularly significant category of compounds (Islam *et al.*, 2025). These microorganisms produce a diverse array of molecules capable of inducing apoptosis, inhibiting cellular proliferation, and modulating cancer cell signaling pathways. For instance, the endophytic fungus *Bionectria* synthesizes Penicillinate A, a metabolite exhibiting pronounced cytotoxicity with an IC₅₀ value of 4.1 μ M. Additionally, species of the genus *Phoma* have been found to produce spiciferone F, which demonstrates potent biological activity against the MCF7 breast cancer cell line, as evidenced by its half-maximal inhibitory concentration (IC₅₀) (Hridoy *et al.*, 2022).

Camptothecin, an established anticancer agent, is derived from various plants as well as the endophytic fungus *Neurospora* sp. (Rehman *et al.*, 2008). The anticancer mechanisms of compounds derived from endophytes differ substantially from those of traditional chemotherapeutic agents. For example, paclitaxel does not disrupt DNA or RNA synthesis nor does it cause direct DNA damage in cancer cells (Zhang *et al.*, 2023). Instead, its principal mechanism involves promoting tubulin polymerization and assembly, thereby inhibiting spindle formation and inducing cell cycle arrest (Varghese *et al.*, 2024). Moreover, paclitaxel modulates the immune response by suppressing regulatory cells and tumor-associated macrophages, which enhances antitumor immunity (Kalinski *et al.*, 2025). Additionally, paclitaxel can trigger apoptosis through activation of specific intracellular signaling pathways (Zhang *et al.*, 2023).

Furthermore, the endophytic fungus *Allantophomopsis* sp. produces the α -pyrone compound allantopyrone A, which exhibits biological activity against the A549 lung carcinoma epithelial cell line and the HL-60 human leukemia cell line (Islam *et al.*, 2025). The fungal endophyte *Chaetomium* spp., associated with *Eucalyptus exserta*, synthesizes mollicellin G, a compound demonstrating cytotoxicity against HepG2 and HeLa human cancer cell lines. *Rhizopus* spp., isolated from *Nicotiana glauca*, produces Rhizoperemophilane N, which displays selective cytotoxicity against the NCI-H1650 and BGC823 tumor cell lines (Hridoy *et al.*, 2022; Islam *et al.*, 2025).

Despite the promising in vitro cytotoxicity exhibited by numerous endophyte-derived compounds, significant limitations remain to be addressed. Numerous investigations lack detailed mechanistic understanding at the molecular level, and only a limited number of compounds advance to in vivo validation stages. Therefore, future research should emphasize comprehensive pharmacological characterization, assessment of scale-up potential, and structure-activity relationship (SAR) modelling to better determine translational applicability. Moreover, rigorous in vitro and in vivo investigations are

imperative to thoroughly assess efficacy, toxicity, and molecular mechanisms of action.

Antimicrobial Activity of Endophytes

The emergence of antimicrobial resistance constitutes a critical global health concern, resulting in extended treatment durations and elevated mortality rates (Ahmed *et al.*, 2024). The pervasive resistance of pathogenic microorganisms to conventional synthetic antimicrobials has intensified efforts to explore natural compounds as alternative therapeutic agents to combat resistant strains (Salam *et al.*, 2023). Endophytes represent a natural reservoir of unique bioactive compounds exhibiting antiviral and antifungal properties of considerable medicinal relevance. These compounds have demonstrated inhibitory effects against pathogenic bacteria affecting both human and animal health (Founou *et al.*, 2017).

Bioactive metabolites derived from endophytic fungal species inhabiting *Quercus variabilis* have been shown to inhibit the growth of pathogenic bacteria such as *Escherichia coli*, *Pseudomonas fluorescens*, and *Bacillus subtilis* (Rai *et al.*, 2021). Recent studies have reported that endophytic extracts from *Anethum graveolens*, *Trichoderma* sp., and *Penicillium* sp. possess potent antibacterial activity against multidrug-resistant strains of *Salmonella typhi*, *E. coli*, *Pseudomonas aeruginosa*, and *S. aureus* (El-Zehery *et al.*, 2024). Furthermore, ethanolic extracts of fungal endophytes *Alternaria* sp. from *Withania somnifera* and *Colletotrichum* sp. from *Moringa oleifera* have demonstrated antibacterial efficacy against *S. aureus* and *E. coli* (Jahan *et al.*, 2022; Islam *et al.*, 2025). *Quercus variabilis* harbors a distinct group of endophytic fungi that synthesize bioactive metabolites capable of inhibiting the growth of other endophytic fungi (Rai *et al.*, 2021).

In a study, the endophytic fungus *Paecilomyces*, isolated from *Moringa oleifera* leaves, was cultured in potato dextrose broth to produce fungal metabolites. The antifungal potential of the *Paecilomyces* filtrate was evaluated by incorporating it into potato dextrose agar and assessing its inhibitory effect on the radial growth of *Rhizoctonia solani* (Hawar *et al.*, 2023). In a separate investigation, sixty-one endophytic fungal strains were isolated from the leaves, stems, and roots of *Tephrosia purpurea*. Among these, isolate TPL25 displayed the broadest spectrum of antifungal activity, significantly suppressing the growth of *Pythium melonis* and *Sclerotinia sclerotiorum* (Luo *et al.*, 2015). Talarergosteroid B, isolated from the fungal strain *Talaromyces* sp. SCNU-F004, exhibited potent antifungal activity against *Fusarium oxysporum* f. sp. *lycopersici*, with a minimum inhibitory concentration (MIC) of 0.78 µg/mL, surpassing that of the reference fungicide carbendazim (MIC = 1.56 µg/mL). Further analyses revealed that this compound inhibited spore germination, induced morphological abnormalities in fungal hyphae, and caused ultrastructural damage to cellular organelles (Li *et al.*, 2025).

Although numerous endophytic compounds demonstrate notable antimicrobial efficacy *in vitro*, there remains a conspicuous deficiency of *in vivo* investigations to substantiate these observations. Furthermore, an in-depth understanding of the mechanisms underlying their antimicrobial actions is essential to facilitate their advancement as new antimicrobial agents.

Future Perspectives and Challenges

Advancing research on endophytes need to focus on the molecular bases of diverse bioactivities, particularly through the application of cutting-edge technologies to identify novel bioactive compounds with improved specificity and efficacy for pharmaceutical, agricultural, and industrial uses. Additionally, there is an increasing need to explore the synergistic interactions between endophytes and their host plants to better comprehend their contributions to stress tolerance, disease resistance, and secondary metabolite biosynthesis. Sustainable biotechnological strategies, including synthetic biology and genome editing, should be leveraged to optimize endophyte-based production platforms. Expanding the exploration of endophytes from underexplored ecosystems and rare plant species may also uncover unique strains exhibiting unprecedented bioactivities. Ultimately, rigorous efforts are required to transition the most promising endophytic compounds into clinical trials to rigorously evaluate their safety and therapeutic efficacy in humans.

Conclusion

Endophytic microorganisms constitute a vast and largely untapped reservoir of chemical diversity with substantial therapeutic potential. They synthesize a wide array of secondary metabolites exhibiting anticancer, antimicrobial, antioxidant, and anti-inflammatory properties. In the agricultural domain, endophytes enhance plant resilience and contribute to disease management strategies. However, realizing this potential demands a shift from predominantly descriptive studies toward more critical, hypothesis-driven research. While classical culture-based methodologies have been instrumental, they are inherently constrained by the inability to cultivate the majority of microorganisms under standard laboratory conditions. Although contemporary molecular techniques have begun to reveal greater microbial diversity, they too possess limitations. Therefore, the future trajectory of this field relies on an integrated approach that combines the advantages of traditional and molecular methods with emerging technologies such as multi-omics and synthetic biology to surmount these challenges.

REFERENCES :

- Ababutain, I. M., Aldosary, S. K., Aljuraifani, A. A., Alghamdi, A. I., Alabdallal, A. H., Al-Khaldi, E. M., Borgio, J. F. (2021). Identification and antibacterial characterization of endophytic fungi from *Artemisia sieberi*. *International Journal of Microbiology*, 2021(1), 6651020.
- Abu Taher, M., Tong, W. Y., Leong, C. R., Ab Rashid, S., & Tan, W. N. (2023). General characteristics of endophytes and bioprospecting potential of endophytic fungi. In A. Ismail, F. Nur Zulkipli, H. S. Husin, & A. Öchsner (Eds.), *Advancements in materials science and technology led by women* (Advanced Structured Materials, Vol. 165). Springer. https://doi.org/10.1007/978-3-031-21959-7_4
- Agrawal, P. K., Agrawal, S., & Shrivastava, R. (2015). Modern molecular approaches for analyzing microbial diversity from mushroom compost ecosystem. *3 Biotech*, 5, 853–866. <https://doi.org/10.1007/s13205-015-0289-2>
- Ahmad, K. S., Hussein, S., Qurbani, K., Ibrahim, R. H., Fareeq, A., Mahmood, K. A., & Mohamed, M. G. (2024). Antimicrobial resistance: Impacts, challenges, and future prospects. *Journal of Medicine, Surgery, and Public Health*, 2, 100081.
- Aly, A. H., Debbab, A., Kjer, J., & Proksch, P. (2010). Fungal endophytes from higher plants: A prolific source of phytochemicals and other bioactive natural products. *Fungal Diversity*, 41, 1–16.
- Andreote, F. D., Gumiore, T., & Durrer, A. (2014). Exploring interactions of plant microbiomes. *Scientia Agricola*, 71, 528–539. <https://doi.org/10.1590/0103-9016-2014-0195>
- Aragona, M., Haegi, A., Valente, M. T., Riccioni, L., Orzali, L., Vitale, S., Luongo, L., & Infantino, A. (2022). New-generation sequencing technology in diagnosis of fungal plant pathogens: A dream comes true? *Journal of Fungi*, 8(7), 737. <https://doi.org/10.3390/jof8070737>
- Ardalani, H., Avan, A., & Ghayour-Mobarhan, M. (2017). Podophyllotoxin: A novel potential natural anticancer agent. *Avicenna Journal of Phytomedicine*, 7(4), 285–294.
- Beeralinga, G., Madagundi, S. D., & Habbu, P. V. (2025). Insights into endophytic fungi: Historical perspectives, isolation strategies, technological advances and future directions. *International Journal of Pharmaceutical Sciences*, 3(11), 4445–4456. <https://doi.org/10.5281/zenodo.17735983>
- Berg, G., Grube, M., Schlöter, M., & Smalla, K. (2014). Unraveling the plant microbiome: Looking back and future perspectives. *Frontiers in Microbiology*, 5, 148. <https://doi.org/10.3389/fmicb.2014.00148>
- Bhardwaj, A., & Agrawal, P. (2014). A review fungal endophytes: As a store house of bioactive compound. *World Journal of Pharmacy and Pharmaceutical Sciences*, 3, 228–237.
- Blackwell, M. (2011). The fungi: 1, 2, 3 ... 5.1 million species? *American Journal of Botany*, 98(3), 426–438. <https://doi.org/10.3732/ajb.1000298>
- Chandra, H., Yadav, A., Prasad, R., Kalra, S. J. S., Singh, A., Bhardwaj, N., & Gupta, K. K. (2024). Fungal endophytes from medicinal plants acting as natural therapeutic reservoir. *The Microbe*, 3, 100073.
- Chaudhary, P., Agri, U., Chaudhary, A., Kumar, A., & Kumar, G. (2022). Endophytes and their potential in biotic stress management and crop production. *Frontiers in Microbiology*, 13, 933017.
- Chen, Y., Hu, B., Xing, J., & Li, C. (2021). Endophytes: The novel sources for plant terpenoid biosynthesis. *Applied Microbiology and Biotechnology*, 105, 4501–4513.
- de Souza, F. A., Kowalchuk, G. A., Leeflang, P., van Veen, J. A., & Smit, E. (2004). PCR-denaturing gradient gel electrophoresis profiling of inter- and intraspecies 18S rRNA gene sequence heterogeneity is an accurate and sensitive method to assess species diversity of arbuscular mycorrhizal fungi of the genus *Gigaspora*. *Applied and Environmental Microbiology*, 70, 1413–1424. <https://doi.org/10.1128/AEM.70.3.1413-1424.2004>
- Deepak, H., & Virk, V. (2022). Optimization of surface sterilization method for the isolation of endophytic fungi associated with *Curcuma longa* L. and their antibacterial activity. *Journal of Advanced Biotechnology and Experimental Therapeutics*, 5, 334. <https://doi.org/10.5455/jabet.2022.d119>
- Dos Reis, J. B. A., Lorenzi, A. S., & do Vale, H. M. M. (2022). Methods used for the study of endophytic fungi: A review on methodologies and challenges, and associated tips. *Archives of Microbiology*, 204(11), 675. <https://doi.org/10.1007/s00203-022-03283-0>
- El-Zehery, H. R. A., Ashry, N. M., Faiesal, A. A., Attia, M. S., Abdel-Maksoud, M. A., El-Tayeb, M. A., Aufy, M., & El-DougDoug, N. K. (2024). Antibacterial and anticancer potential of bioactive compounds and secondary metabolites of endophytic fungi isolated from *Anethum graveolens*. *Frontiers in Microbiology*, 15, 1448191. <https://doi.org/10.3389/fmicb.2024.1448191>
- Fang, Y., & Ramasamy, R. P. (2015). Current and prospective methods for plant disease detection. *Biosensors*, 4, 537–561. <https://doi.org/10.3390/bios5030537>
- Founou, R. C., Founou, L. L., & Essack, S. Y. (2017). Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. *PLOS ONE*, 12, e0189621.
- Francioli, D., Lentendu, G., Lewin, S., & Kolb, S. (2021). DNA metabarcoding for the characterization of terrestrial microbiota—Pitfalls and solutions. *Microorganisms*, 9, 361. <https://doi.org/10.3390/microorganisms9020361>
- Gouda, S., Das, G., Sen, S. K., Shin, H. S., & Patra, J. K. (2016). Endophytes: A treasure house of bioactive compounds of medicinal importance. *Frontiers in Microbiology*, 7, 1538. <https://doi.org/10.3389/fmicb.2016.01538>
- Guo, L. D. (2001). Advances of endophytic fungi. *Mycosystema*, 20, 148–152.
- Hallmann, J., Berg, G., & Schulz, B. (2006). Isolation procedures for endophytic microorganisms. https://doi.org/10.1007/3-540-33526-9_17
- Han, T., and Rahman, K. (2012). Alkaloids produced by endophytic fungi: A review. *Natural Product Communications*, 7, 963–968.
- Hariharan, G., & Prasannath, K. (2021). Recent advances in molecular diagnostics of fungal plant pathogens: A mini review. *Frontiers in Cellular and Infection Microbiology*, 10, 600234. <https://doi.org/10.3389/fcimb.2020.600234>

- Hawar, S. N., Taha, Z. K., Hamied, A. S., Al-Shmgani, H. S., Sulaiman, G. M., & Elsilk, S. E. (2023). Antifungal activity of bioactive compounds produced by the endophytic fungus *Paecilomyces* sp. (JN227071.1) against *Rhizoctonia solani*. *International Journal of Biomaterials*, 2023, 2411555. <https://doi.org/10.1155/2023/2411555>
- Hridoy, M., Gorapi, M. Z. H., Noor, S., Chowdhury, N. S., Rahman, M. M., Muscari, I., Masia, F., Adorisio, S., Delfino, D. V., & Mazid, M. A. (2022). Putative anticancer compounds from plant-derived endophytic fungi: A review. *Molecules*, 27(1), 296. <https://doi.org/10.3390/molecules27010296>
- Islam, M. M., Rakib, A. R., Mahmood, M. R., Singha, A., Jahan, S., Sultana, N., Rafi, M. T. H., Islam, S., Alamin, M., Kuri, C., Jaffrin, S., & Saha, A. (2025). Bioactive metabolites from endophytes: Focus on anticancer and antimicrobial potential. *The Microbe*, 9, 100553.
- Jahan, S., Shahjahan, M., Rasna, S. S., Aktar, M., Sultana, S., Ahmed, S. M., Sabrin, F., & Nahar, S. (2022). Antibacterial effect of *Moringa (Moringa oleifera)* leaf ethanolic extract against *Staphylococcus aureus* and *Escherichia coli*. *Mymensingh Medical Journal*, 31(4), 976–982.
- Kalinski, P., Kokolus, K. M., & Gandhi, S. (2025). Paclitaxel, interferons and functional reprogramming of tumor-associated macrophages in optimized chemo-immunotherapy. *Journal for ImmunoTherapy of Cancer*, 13(5), e010960. <https://doi.org/10.1136/jitc-2024-010960>
- Klahs, P. C., McMurchie, E. K., Nikkel, J. J., & Clark, L. G. (2023). A maceration technique for soft plant tissue without hazardous chemicals. *Applications in Plant Sciences*, 11(5), e11543. <https://doi.org/10.1002/aps3.11543>
- Kumar, S., Stecher, G., & Tamura, K. (2016). MEGA7: Molecular evolutionary genetics analysis version 7.0 for bigger datasets. *Molecular Biology and Evolution*, 33, 1870–1874. <https://doi.org/10.1093/molbev/msw054>
- Kuźniar, A., Kruczyńska, A., Włodarczyk, K., Vangronsveld, J., & Wolińska, A. (2025). Endophytes as permanent or temporal inhabitants of different ecological niches in sustainable agriculture. *Applied Sciences*, 15(3), 1253. <https://doi.org/10.3390/app15031253>
- Li, J., Lin, Z., Zeng, H., Zeng, J., Ye, S., Chen, C., Jia, H., Li, K., She, Z., & Long, Y. (2025). Talarergosteroids A-C: Three unusual steroid-polyketone conjugates with antifungal activity from a *Kandelia obovata* derived fungus *Talaromyces* sp. *Journal of Agricultural and Food Chemistry*, 73(1), 595–605. <https://doi.org/10.1021/acs.jafc.4c10156>
- Liang, Z. B., Lee, D. J., Dweikat, I. M., Wedin, D. A., Yuen, G. Y., & Drijber, R. A. (2017). Molecular diversity of arbuscular mycorrhizae in roots of invasive to grasslands. *Soil Science Society of America Journal*, 81, 526–536.
- Luo, Z. P., Lin, H. Y., Ding, W. B., He, H. L., & Li, Y. Z. (2015). Phylogenetic diversity and antifungal activity of endophytic fungi associated with *Tephrosia purpurea*. *Mycobiology*, 43(4), 435–443. <https://doi.org/10.5941/MYCO.2015.43.4.435>
- Majhi, P., Pradhan, U., Toppo, A., & Shukla, A. K. (2025). Fungal endophytes: An insight into diversity, stress tolerance, biocontrol and plant growth-promoting potentials. *Current Microbiology*, 82(6), 283.
- Malczak, I., & Gajda, A. (2023). Interactions of naturally occurring compounds with antimicrobials. *Journal of Pharmaceutical Analysis*, 13(12), 1452–1470. <https://doi.org/10.1016/j.jpha.2023.09.014>
- Masyita, A., Mustika Sari, R., Dwi Astuti, A., Yasir, B., Rahma Rumata, N., Emran, T. B., Nainu, F., & Simal-Gandara, J. (2022). Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives. *Food Chemistry: X*, 13, 100217. <https://doi.org/10.1016/j.fochx.2022.100217>
- Mat Jalil, M., & Ibrahim, D. (2018). Fungal endophytes isolated from the leaves of a medicinal plant, *Ocimum sanctum* Linn and evaluation of their antimicrobial activities. *African Journal of Microbiology Research*, 12, 616–622. <https://doi.org/10.5897/AJMR2018.8812>
- Michaelsen, A., Pinzari, F., Ripka, K., Lubitz, W., & Pinar, G. (2006). Application of molecular techniques for identification of fungal communities colonising paper material. *International Biodeterioration & Biodegradation*, 58, 133–141. <https://doi.org/10.1016/j.ibiod.2006.06.019>
- Mosa, K. A., Gairola, S., Jamdade, R., El-Keblawy, A., Al Shaer, K. I., Al Harthi, E. K., Shabana, H. A., & Mahmoud, T. (2019). The promise of molecular and genomic techniques for biodiversity research and DNA barcoding of the Arabian Peninsula flora. *Frontiers in Plant Science*, 9, 1929. <https://doi.org/10.3389/fpls.2018.01929>
- Nagib, A. M., Sultan, M. H., El-Sheikh, H. H., et al. (2026). Untapped microbial factories for next-generation therapeutics: Endophytic fungi of medicinal plants. *Microbial Cell Factories*, 25, 141. <https://doi.org/10.1186/s12934-026-03036-4>
- Ohtomo, R., Oka, N., & Morimoto, S. (2019). PCR-denaturing gradient gel electrophoresis as a simple identification tool of arbuscular mycorrhizal fungal isolates. *Microbes and Environments*, 34(4), 356–362. <https://doi.org/10.1264/jsme2.ME19074>
- O'Leary, B. M., Rico, A., McCraw, S., Fones, H. N., & Preston, G. M. (2014). The infiltration-centrifugation technique for extraction of apoplastic fluid from plant leaves using *Phaseolus vulgaris* as an example. *Journal of Visualized Experiments*, (94), e52113. <https://doi.org/10.3791/52113>
- Piombo, E., Abdelfattah, A., Droby, S., Wisniewski, M., Spadaro, D., & Schena, L. (2021). Metagenomics approaches for the detection and surveillance of emerging and recurrent plant pathogens. *Microorganisms*, 9, 188. <https://doi.org/10.3390/microorganisms9010188>
- Pistone, D., Bevivino, G., Dipaola, M. G., Bandi, C., & Lombardo, F. (2026). Current and emerging molecular diagnostic approaches in the detection of human parasites. *Parasitology Research*, 125(1), 50. <https://doi.org/10.1007/s00436-026-08660-y>
- Rai, N., Kumari Keshri, P., Verma, A., Kamble, S. C., Mishra, P., Barik, S., ... Gautam, V. (2021). Plant associated fungal endophytes as a source of natural bioactive compounds. *Mycology*, 12(3), 139–159. <https://doi.org/10.1080/21501203.2020.1870579>
- Raja, H. A., Miller, A. N., Pearce, C. J., & Oberlies, N. H. (2017). Fungal identification using molecular tools: A primer for the natural products research community. *Journal of Natural Products*, 80(3), 756.
- Rehman, S., Shawl, A. S., Verma, V., Kour, A., Athar, M., Andrabi, R., Sultan, P., & Qazi, G. N. (2008). An endophytic *Neurospora* sp. from *Nothapodytes foetida* producing camptothecin. *Prikladnaia Biokhimiia i Mikrobiologiia*, 44(2), 225–231.
- Reller, L. B., Weinstein, M. P., & Petti, C. A. (2007). Detection and identification of microorganisms by gene amplification and sequencing. *Clinical Infectious Diseases*, 44(8), 1108–1114. <https://doi.org/10.1086/512818>

- Sahu, P. K., Tilgam, J., Mishra, S., Hamid, S., Gupta, A., K, J., *et al.* (2022). Surface sterilization for isolation of endophytes: Ensuring what (not) to grow. *Journal of Basic Microbiology*, 62, 647–668. <https://doi.org/10.1002/jobm.202100462>
- Salam, M. A., Al-Amin, M. Y., Salam, M. T., Pawar, J. S., Akhter, N., Rabaan, A. A., & Alqumber, M. A. A. (2023). Antimicrobial resistance: A growing serious threat for global public health. *Healthcare*, 11(13), 1946. <https://doi.org/10.3390/healthcare11131946>
- Shah, S., Shrestha, R., Maharjan, S., *et al.* (2019). Isolation and characterization of plant growth-promoting endophytic fungi from the roots of *Dendrobium moniliforme*. *Plants*, 8(5), 1–11.
- Sikarwar, V., Singh, M., & Ranawat. (2023). Endophytes: An overview. *The Pharmaceutical and Chemical Journal*, 10, 21–32.
- Simon, C., & Daniel, R. (2011). Metagenomic analyses: Past and future trends. *Applied and Environmental Microbiology*, 77, 1153–1161. <https://doi.org/10.1128/AEM.02345-10>
- Singh, P. K., Kathuria, S., Agarwal, K., Gaur, S. N., Meis, J. F., & Chowdhary, A. (2013). Clinical significance and molecular characterization of nonsporulating molds isolated from the respiratory tracts of bronchopulmonary mycosis patients with special reference to basidiomycetes. *Journal of Clinical Microbiology*, 51(10), 3331–3337. <https://doi.org/10.1128/JCM.01486-13>
- Singh, R., & Dubey, A. K. (2018). Diversity and applications of endophytic actinobacteria of plants in special and other ecological niches. *Frontiers in Microbiology*, 9, 1767.
- Sun, X., & Guo, L. D. (2012). Endophytic fungal diversity: Review of traditional and molecular techniques. *Mycology*, 3(1), 65–76. <https://doi.org/10.1080/21501203.2012.656724>
- Suneja, P., Kumar, P., Rani, S., Simran, & Dang, A. S. (2023). Identification of fungal endophytes by ITS rDNA technique. In A. Sankaranarayanan, N. Amaran, & M. K. Dwivedi (Eds.), *Endophytic microbes: Isolation, identification, and bioactive potentials* (Springer Protocols Handbooks). Humana. https://doi.org/10.1007/978-1-0716-2827-0_11
- Tedersoo, L., Anslan, S., Bahram, M., Kõljalg, U., & Abarenkov, K. (2020). Identifying the 'unidentified' fungi: A global-scale long-read third-generation sequencing approach. *Fungal Diversity*, 103, 273–293. <https://doi.org/10.1007/s13225-020-00456-4>
- Tiwari, P., & Bae, H. (2022). Endophytic fungi: Key insights, emerging prospects, and challenges in natural product drug discovery. *Microorganisms*, 10(2), 360. <https://doi.org/10.3390/microorganisms10020360>
- Varghese, S., Jisha, M. S., Rajeshkumar, K. C., Gajbhiye, V., Alrefaei, A. F., & Jeewon, R. (2024). Endophytic fungi: A future prospect for breast cancer therapeutics and drug development. *Heliyon*, 10(13), e33995. <https://doi.org/10.1016/j.heliyon.2024.e33995>
- Wu, S. F., Hsieh, P. W., Wu, C. C., Lee, C. L., Chen, S. L., Lu, C. Y., Wu, T. S., Chang, F. R., & Wu, Y. C. (2008). Camptothecinoids from the seeds of Taiwanese *Nothapodytes foetida*. *Molecules*, 13(6), 1361–1371. <https://doi.org/10.3390/molecules13061361>
- Zhang, S., Ye, T., Liu, Y., Hou, G., Wang, Q., Zhao, F., Li, F., & Meng, Q. (2023). Research advances in clinical applications, anticancer mechanism, total chemical synthesis, semi-synthesis and biosynthesis of paclitaxel. *Molecules*, 28(22), 7517. <https://doi.org/10.3390/molecules28227517>