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Study on Biosynthesis and Mechanism of Endophytic Fungi Secondary Metabolites from Tropical Medicinal Plants

Decai Dai*
Hainan Vocational University of Science and Technology, Haikou 571126, Hainan, China

**Author to whom correspondence should be addressed.*

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Abstract: Endophytic fungi from tropical medicinal plants are microbial resources with significant bioactivity. They can co-evolve with their hosts over long periods and produce compounds with novel structures. These fungi hold considerable application value in preventing and controlling agricultural plant fungal diseases and treating clinical drug-resistant bacterial infections. This study focuses on endophytic fungi from tropical medicinal plants, elucidating their chemical structure types and conducting in-depth analyses of the biosynthetic pathways, key enzyme systems, and regulatory mechanisms of gene clusters for fungicidal active products. It systematically explores the molecular mechanisms of fungicidal action and analyzes indicators such as the diameter of inhibition zones and minimum inhibitory concentrations. This research provides theoretical foundations and data references for the efficient exploration of fungicidal active substances from endophytic fungi in tropical medicinal plants, optimization of biosynthesis, and development of novel natural fungicides.

Keywords: Tropical medicinal plants; Endophytic fungi; Fungicidal secondary metabolites; Biosynthesis; Mechanism of action

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1. Introduction

Tropical regions boast a vast array of plant species, many of which have been utilized for extended periods in traditional medicine and agricultural disease prevention and control, serving as significant sources of natural active substances. Fungi that colonize within the intercellular spaces or cells of healthy plant tissues are known as endophytic fungi. These fungi do not induce disease symptoms in their hosts and instead form symbiotic or mutualistic relationships with them. A variety of secondary metabolites with diverse structural types, such as polyketides, terpenoids, and alkaloids, can be produced through the metabolism of endophytic fungi from tropical medicinal plants. Approximately 35%-60% of these metabolites exhibit fungicidal activity, demonstrating significant inhibitory effects on a wide range of plant pathogenic fungi and drug-resistant bacteria. Under the pressure of special ecological environments, endophytic fungi from tropical medicinal plants exhibit complex and diverse metabolic pathways, making them ideal candidates for discovering novel fungicidal lead compounds. Therefore, research on the biosynthesis and mechanisms of action of fungicidal secondary metabolites from endophytic fungi of tropical medicinal plants holds significant importance.

2. Resources of endophytic fungi from tropical medicinal plants and structural types of fungicidal secondary metabolites

2.1. Overview of endophytic fungi resources from tropical medicinal plants

Endophytic fungi from tropical medicinal plants are characterized by species richness, broad host range, and strong tissue specificity. Currently, reported endophytic fungi from tropical medicinal plants primarily belong to the Ascomycota and Basidiomycota phyla, with Ascomycota accounting for over 80% and serving as the main source of fungicidal active substances. Tropical and subtropical regions in China, such as Hainan and Yunnan, are the primary distribution areas. The isolation rates of endophytic fungi from tropical rainforest plants and mangrove halophytes are 45%–70% and 55%–80%, respectively, with higher isolation rates observed in typical medicinal plants like cinnamon and dragon's blood tree compared to non-medicinal plants [1]. From the perspective of tissue specificity, significant differences in the distribution of endophytic fungi are observed among leaves, stems, and roots. The isolation rate from leaves accounts for 38% of the total strains, from stems 32%, from roots 20%, and from other tissues 10%. Genera such as Penicillium and Aspergillus are dominant. 1.2 Main Structural Types of Fungicidal Secondary Metabolites The structural types of fungicidal secondary metabolites produced by endophytic fungi in tropical medicinal plants are diverse. Over 500 compounds with clear fungicidal activity have been reported, which can be classified into four categories as shown in **Table 1**.

Table 1. Main structural types and characteristics of fungicidal secondary metabolites produced by endophytic fungi from tropical medicinal plants

Compound Class	Representative Structural Types	Main Source Genera	Typical Target Organisms	Activity Range (MIC/IC50)
Polyketides	Isocoumarins, Naphthoquinones, Chromones, Anthraquinones	*Aspergillus*, *Penicillium*	*Colletotrichum*, *Fusarium* wilt pathogens, *Staphylococcus aureus*	1.5–64 μg/mL
Terpenoids	Sesquiterpenes, Diterpenes, Triterpenes	*Xylaria*, *Phomopsis*	*Rhizoctonia solani*, *Botrytis cinerea*	2.0–128 μg/mL
Alkaloids	Indole alkaloids, Pyridines, Quinolines	*Fusarium*, *Alternaria*	*Escherichia coli*, Drug-resistant *S. aureus*, *Candida albicans*	0.5–32 μg/mL
Nonribosomal Peptides & Others	Cyclic dipeptides, Lipopeptides, Phenolic acids	*Penicillium*, *Beauveria*	Phytopathogenic fungi, Clinical drug-resistant bacteria	1.0–64 μg/mL

(1) Polyketides. Polyketides, as diverse and extensive secondary metabolites, play a significant role in various fields, including medical fungicides. Their synthesis mechanism shares a high degree of similarity with the fatty acid synthesis pathway, involving the continuous condensation of simple carboxylic acid units to form a polyketide chain, which is then modified through oxidation, cyclization, etc., ultimately generating structurally complex end products. Analysis of polyketides reveals common structural types such as isocoumarins, naphthoquinones, chromones, and anthraquinones, sourced from genera like Aspergillus and Penicillium, with fungicidal targets including anthracnose fungi and blight pathogens. Polyketide compounds have novel action sites and a low probability of developing cross-resistance, making them frequently used in the development of new fungicides.

(2) Terpenoids. Terpenoids, also known as isoprenoids, are secondary metabolites with rich structural diversity in nature, and their fungicidal activity primarily originates from plants and microorganisms. Based on the number of isoprene units, terpenoids can be classified into various types such as sesquiterpenes, diterpenes, and triterpenes. Currently, sesquiterpenes and monoterpenes in some plant essential oils exhibit significant fungicidal activity by disrupting the integrity of fungal cell membranes. In terms of microbial sources, the PR toxin produced by

Penicillium belongs to the sesquiterpene class. The action mechanisms of some terpenoid fungicides interfere with fungal cell wall synthesis or affect sterol metabolism to varying degrees. Due to their complex structures and multiple chiral carbons, terpenoid compounds are difficult to synthesize. Currently, there are fewer commercially developed pure terpenoid fungicides compared to polyketides.

(3) Alkaloids. Alkaloids are basic organic compounds characterized by diverse types and complex structures, with significant physiological activity. Given their structural complexity, alkaloids can be classified into types such as indole alkaloids, pyridines, and quinolines, with fungicidal targets including Escherichia coli and drug-resistant Staphylococcus aureus. Currently, there are relatively few commercially available alkaloid-based fungicides applied directly, but they provide a rich molecular template for the development of new fungicides, especially against drug-resistant pathogens. Additionally, some alkaloids sourced from microorganisms, such as pyrroloquinoline quinone, exhibit significant antioxidant effects.

(4) Non-ribosomal peptides and others. Non-ribosomal peptides incorporate modifications such as fatty acid chains in their structures, exhibiting unique biological activities. Common structural types include lipopeptides and bacitracins. Among antibacterial agents, polymyxins exhibit strong activity. Other categories include cyclic dipeptides and phenolic acids, which, despite their diverse structures not belonging to the same class, possess unique fungicidal mechanisms. They play a crucial role in addressing the challenge of pathogen resistance and serve as indispensable lead structures in the synthesis of new fungicides, highlighting their significant role.

3. Biosynthesis of fungicidal secondary metabolites from endophytic fungi of tropical medicinal plants

3.1. Core biosynthetic pathways

The structural types of fungicidal secondary metabolites produced by endophytic fungi from tropical medicinal plants vary significantly, leading to distinct differences in their biosynthetic pathways. Therefore, it is necessary to analyze the synthetic pathways in a targeted manner based on different types.

3.1.1. Polyketide synthase (PKS)

Pathway Polyketide synthase (PKS) catalyzes the production of polyketide-based fungicidal compounds, which can be classified into types I, II, and III. Type I PKS is the predominant form in endophytic fungi. The basic reaction formula is as follows:

$$\text{n Acetyl-CoA+m Malonyl-CoA} \xrightarrow{\text{PKS}} \text{Catalyzed Polyketide Carbon Chain} + \text{Post-Modification} \rightarrow \text{Final Product}$$

PKS is composed of multiple functional domains, including ketoacyl synthase (KS), acyltransferase (AT), ketoreductase (KR), among others. The carbon chain elongation process can be approximately described using the average chain length formula:

$$L = C_0 + n \times 2 \quad (1)$$

In the above formula, L, C_0, and n represent the number of carbon atoms in the polyketide carbon chain, the number of carbon atoms in the starting unit, and the number of elongation cycles, respectively. After undergoing cyclization, oxidation, methylation, and other modifications, the polyketide backbone can form final products with fungicidal activity.

3.1.2. Terpenoid synthesis pathway (TPS)

The MVA (mevalonate) pathway and the MEP (2-C-methyl-D-erythritol 4-phosphate) pathway jointly contribute to the synthesis of precursors for terpenoid-based fungicidal compounds, generating isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP). The simplified overall reaction for precursor synthesis is:

$$\text{Acetyl-CoA} \rightarrow \text{MVA} \rightarrow \text{IPP} \rightleftharpoons \text{DMAPP}$$

Terpenoid synthase (TPS) catalyzes the chain elongation and cyclization processes:

$$\text{IPP} + \text{DMAPP} \xrightarrow{\rightarrow \text{TPS}} \text{catalyzed} \rightarrow \text{Monoterpene/Sesquiterpene/Diterpene skeleton}$$

The metabolic flux can be estimated using the precursor consumption rate, with the estimation method as follows:

$$v = \frac{d|\text{Product}|}{dt} = k|\text{IPP}|\cdot|\text{DMAPP}| \tag{2}$$

In the above formula, v represents the synthesis rate, k is the rate constant for the enzymatic reaction, and and denote the concentrations of the precursors.

3.1.3. Non-ribosomal peptide synthetase (NRPS)

Pathway Non-ribosomal peptide-based fungicidal products are catalyzed by non-ribosomal peptide synthetases (NRPSs), which do not rely on ribosomes and mRNA for assembly but directly recognize and incorporate amino acids. A typical modular catalytic process is as follows:

A-domain (adenylation domain)+ PCP (peptidyl carrier protein)+ C-domain (condensation domain) →
B-peptide chain elongation → cyclic peptide/lipopeptide

Some fungicidal products are synthesized through hybrid NRPS-PKS pathways, resulting in complex structures and enhanced activity.

3.2. Characteristics of biosynthetic gene clusters (BGCs)

Fungicidal metabolites produced by endophytic fungi exist in the form of gene clusters, which consist of core synthase genes, post-modification enzyme genes, regulatory genes, and transporter genes [2]. From endophytic fungi of tropical medicinal plants, over 120 BGCs related to fungicidal activity have been annotated, with PKS-type, NRPS-type, terpenoid-type, and others accounting for 45%, 25%, 15%, and 15%, respectively.

3.3. Strategies for activating silent gene clusters and enhancing yield

Under natural conditions, 70%-90% of BGCs in endophytic fungi remain silent. To increase the yield of fungicidal products, induction and activation strategies are required, as summarized in **Table 2**.

Table 2. Common strategies and their effects

Activation Method	Mechanism	Increase in Bactericidal Product Yield
Co-culture (Fungus–Bacterium / Fungus)	Induction by interaction signals, activating cross-pathway regulation	2–10 times
Stress Induction (Salt, pH, Oxidation)	Activation of secondary metabolic pathways by stress signals	1.5–5 times
Epigenetic Modification (5AZA, SAHA)	Inhibition of DNA methylation / Histone deacetylation	3–15 times
Heterologous Expression & Synthetic Biology	Refactoring chassis cells to eliminate host inhibition	10–100 times

The activation effect can be evaluated using the relative expression formula:

$$\text{Fold change} = \frac{\text{[Transcription/Yield] in the induced group}}{\text{[Transcription/Yield] in the control group}} \quad (3)$$

Significant activation is defined as a Fold change > 2.

4. Mechanism of action of antifungal secondary metabolites produced by endophytic fungi

4.1. Disruption of cellular structural integrity

Antifungal secondary metabolites from endophytic fungi can cause cell membrane damage and inhibit cell wall synthesis, thereby preventing the maintenance of cellular structural integrity.

4.1.1. Damage to the cell membrane

The lipid bilayer of the cell membrane can be disrupted by various terpenes and phenolic acids, increasing membrane permeability and leading to the leakage of intracellular electrolytes, proteins, and nucleic acids. The formula for calculating relative electrical conductivity is as follows:

$$\text{Relative electrical conductivity (\%)} = \frac{EC1}{EC2} \times 100\% \quad (4)$$

In the above formula: EC1 and EC2 represent the electrical conductivity of the supernatant after treatment and the electrical conductivity of the supernatant in the control, respectively.

The relative electrical conductivity of pathogenic fungi can increase by 40%–80% under the action of biologically active compounds, severely compromising cell membrane integrity.

4.1.2. Inhibition of cell wall synthesis

Chitin synthase and β-1,3-glucan synthase can be inhibited by certain polyketides and alkaloids, obstructing cell wall formation and causing an imbalance in turgor pressure in pathogenic fungi, leading to their lysis and death. The inhibition rate of fungal cell wall synthesis ranges from 50%–90%.

4.2. Interference with core physiological metabolism

4.2.1. Inhibition of energy metabolism

Blocking the mitochondrial respiratory chain can reduce ATP synthesis, with ATP levels decreasing by 30%–70%, resulting in the stagnation of pathogenic fungal growth. The relative ATP content is calculated as follows:

$$\text{ATP inhibition rate (\%)} = \left(1 - \frac{\text{[ATP]treatment}}{\text{[ATP]control}}\right) \times 100\% \quad (5)$$

4.2.2. Inhibition of nucleic acid and protein synthesis

The intercalation of DNA and inhibition of topoisomerases can reduce nucleic acid synthesis in the original fungi by 40%–80%, while also hindering protein synthesis.

4.3. Inhibition of virulence factors and biofilm formation

Inhibiting virulence factors such as extracellular cell wall-degrading enzymes and toxins produced by pathogenic fungi can reduce their pathogenicity; it can also inhibit biofilm formation and disrupt mature biofilms, with biofilm inhibition rates ranging from 40%–90%. The inhibitory effect on drug-resistant bacteria can be significantly enhanced [3]. In terms of biofilm regulation, this can enhance the bactericidal effect of compounds, delay the development of drug resistance in pathogenic fungi, and provide a basis for the development of novel antifungal agents targeting virulence factors.

4.4. Induction of defense responses in host plants

Some antifungal secondary metabolites produced by endophytic fungi from tropical medicinal plants, while directly inhibiting the original fungi, can also activate the host plant's own immune system, thereby inducing systemic disease resistance. At the enzymatic level, these metabolites can significantly increase the activity of peroxidase (POD) and superoxide dismutase (SOD) in host plants. These enzymes play a crucial role in the synthesis processes of scavenging reactive oxygen species and enhancing cell wall lignification. The synthesis and accumulation of phytoalexins and lignin in host plants can be promoted by these antifungal metabolites, thereby enhancing the mechanical strength and chemical defense capabilities of host tissues.

5. Conclusion

Endophytic fungi from tropical medicinal plants constitute an important part of the significant repository of natural products with fungicidal activity. Among them, novel scaffold compounds such as polyketides, terpenes, and alkaloids exhibit remarkable inhibitory effects against plant pathogenic fungi and clinically resistant bacteria, holding potential for the development of green fungicides and antibacterial drugs.

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Disclosure statement

The author declares no conflict of interest.

References

[1] Ruan W, 2022, Study on the Secondary Metabolites and Their Bioactivities of Endophytic Fungi from Two Medicinal Plants. Hainan University.

[2] Wang NY, Liu HX, Chen YC, et al., 2023, Study on the Secondary Metabolites of Endophytic Fungus Irpex Lacteus A878 from Pogostemon Cablin. Chinese Traditional and Herbal Drugs.

[3] Lu XX, 2022, Study on the Secondary Metabolites and Their Bioactivities of Endophytic Fungi Colletotrichum Gloeosporioides and Diaporthe Foeniculina. University of Chinese Academy of Sciences.

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