

MYCOCHEMICAL ANALYSIS OF ENDOPHYTIC FUNGI OF *EUPHORBIA MILII* DES MOUL. WITH RESPECT TO THEIR MEDICINAL PROPERTIES

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Abstract–Euphorbiaceae is one of the largest plant family, ranging from large woody trees to simple weeds. Many of these have varied decorative, medical, industrial, and food-related characteristics. Although latex is poisonous, it is the most desirable product derived from the *Euphorbia* species and contains a variety of naturally occurring biologically active compounds. The present study focuses on mycochemical analysis of endophytic fungi from *Euphorbia milii* Des Moul., which has been reported to influence Hormonal balance and pollution-absorptive features. Endophytes can produce new lead molecules with different bioactive compounds. Fungal endophytes support the healthy life cycle of their host plants using a multitude of methods. *Alternaria* sp., *Aspergillus* sp., *Fusarium* etc. endophytic fungi were isolated from *Euphorbia milii* Des Moul.

INTRODUCTION

Globally, people are increasingly using medicinal plants and herbal products because of the intricacy of illnesses and the negative side effects of synthetic medications (Anbarasu *et al.*, 2023). Natural chemicals have been tested and proven to have pharmacological effects, including cytotoxicity, antioxidants, antidiabetic, antibacterial, and anti-inflammatory properties (Nasim *et al.*, 2022). Consequently, the identification of bioactive substances from natural sources, such as medicinal plants, has gained significant attention from the scientific community (Saleem *et al.*, 2019). The need for synthetic ingredients in the drug-making process will rise as natural plant products become progressively limited owing to the endangered status of many ethnopharmacological species.

Plants are frequently inhabited by endophytic microorganisms. These microorganisms, which include bacteria and fungi, live in plant tissues over

extended periods or at particular stages of their life cycles (Demain, 2013). Crucially, this colonization occurs without causing any harm or noticeable changes to the physical traits of the host plants. This intricate interaction has attracted attention because of its potential impact on plant growth and health (Gouda *et al.*, 2016). Nontoxic microorganisms, known as endophytes, live inside healthy plant components and shield them from diseases. Colonization, nutritional competition, antibiotic synthesis, and resistance mechanisms are some techniques used to accomplish these (Chaudhary *et al.*, 2022).

Endophytic fungi, microorganisms that live within plant tissues without causing apparent harm, have recently gained significant attention because of their diverse metabolic capabilities and potential applications in agriculture, industry, and environmental management (David *et al.*, 2022). These fungi often confer benefits such as enhanced stress tolerance and improved nutrient uptake in

host plants (Sushma *et al.*, 2021). Additionally, many endophytic fungi produce bioactive compounds and enzymes with potential biotechnological applications (Zheng *et al.*, 2016). Plant endophytic fungi are a significant and unique source of naturally occurring bioactive chemicals with potential applications (Zhao *et al.*, 2011).

The endophytic fungus *Chaetomium ovatoascomatis*, isolated from *Euphorbia milii*, shows strong antibacterial activity (Shaker *et al.*, 2022). These fungi produce bioactive compounds including coumarins, flavonoids, and terpenoids, which may play a role in plant defense mechanisms. Other endophytic fungi, such as *Fusarium sp.*, have been shown to promote plant growth and increase the production of secondary metabolites, such as terpenoids in *Euphorbia pekinensis* (Yong *et al.*, 1994). *Gymnascella thermotolerans* produces volatile organic compounds (VOCs) with notable antifungal and anticancer properties. Key metabolites include diisooctyl phthalate, which constitutes 71.99% of its VOCs and exhibits significant inhibition against pathogens such as *Fusarium solani* (El-Zayatp *et al.*, 2024). *Aspergillus sp.*, commonly isolated from *Euphorbia geniculata*, showed antagonistic activities against several plant pathogens, indicating its potential in agricultural applications (Kamel *et al.*, 2020). Metabolites from these fungi exhibit broad-spectrum antimicrobial activities and are effective against both Gram-positive and Gram-negative bacteria, as well as filamentous fungi (Shaker *et al.*, 2022).

Potential bioactive compounds have been discovered in endophytic fungi associated with *Euphorbia*. Focusing on endophytic fungi associated with *Euphorbia* revealed promising bioactive compounds. The objective of our study was to expand the literature on endophytic fungi and how they may be applied to solve environmental and agricultural problems.

MATERIALS AND METHODS

Isolation of fungal endophytes

Plant material was collected from the Baramati area using sterile polythene bags. Material samples underwent a cleaning process for thirty minutes with running tap water, followed by rinsing with double-distilled water to eliminate dust particles. The surface sterilization technique used which is proposed by Petrini *et al.* (1992). Epiphytes were

removed by dipping the tissues in 90% ethyl alcohol (1 min), followed by 4% aqueous NaOCl solution (1 min), and rinsing with 70% ethanol (0.5 min). The tissues were then rinsed with distilled water and allowed to dry under sterile conditions. After surface sterilization, the tissues were carefully cut into pieces of 0.5×0.5cm squares. Four to six small pieces of leaves were placed in separate Petri dishes containing Potato Dextrose Agar (PDA) medium supplemented with antibacterial streptomycin sulphate. To determine the efficacy of the sterilization protocol, surface-sterilized pieces were placed on separate PDA plates for two hour and then removed to leave their imprints on the PDA medium surface. All Petri plates were sealed with Parafilm and incubated in an incubation chamber. Endophytes emerging from explants showed variation in morphology (color and growth pattern) and were transferred and maintained on freshly prepared PDA plates as cultures. Morphological and microscopic identification of recovered endophytic fungi on the basis of culture characteristics, such as growth pattern, texture, color, and backside color of the colony. Under a microscope, fungal colonies were observed after being stained with lactophenol cotton blue.

Sequencing and molecular phylogenetics

By applying the forward primer ITS1 (5-TCC GTA GGT GAA CCT GCG G-3) and the reverse primer ITS4 (5-TCC TCC GCT TAT TGA TAT GC-3), the ITS1–5.8S–ITS2 genomic area was amplified from genomic DNA to perform molecular characterization by isolating 18S rDNA. Sequencing PCR products were processed for cleanup to remove unincorporated nucleotides and residual primers using Exonuclease-I and Shrimp Alkaline phosphatase enzyme (1unit/μl) followed by cycle sequencing using Big Dye® Terminator v.3.1 Cycle Sequencing Kit (Applied Biosystems, Inc.). For ITS amplicon sequencing same PCR primers were used for ITS amplicon sequencing. The thermal cycler conditions were as follows: an initial denaturation of 2 min at 96 °C and 35 cycles of 30 sec at 96 °C, 15 sec at 55 °C, and 4 min at 60 °C. Cycle sequencing was followed by sequencing cleanup by ethanol precipitation, followed by dissolving the template in HiDi formamide and bidirectionally sequencing in an ABI 3730 Genetic analyzer. Sequence alignment and assembly of PCR products were then processed for direct bi-directional sequencing using an ABI PRISM 3730 × 1 Genetic Analyzer (Applied

Biosystems, USA). The resulting DNA sequences were aligned using CLUSTALW embedded in MEGA 11, manually trimmed, and edited to obtain complete sequences. Species confirmation depends on the sequence similarity score. Homology searches were carried out using the BLASTn program against the NCBI GenBank database (<https://blast.ncbi.nlm.nih.gov/Blast.cgi>). The NJ tree was constructed using MEGA 11 with all positions containing gaps, and missing data were included in the analysis. Clade support was calculated based on 1,000 bootstrap resampling.

Production of Fermentation Medium

To produce secondary metabolites, the fungal strain was inoculated into fermentation medium. The fermentation medium was prepared using a combination of 50% potato extract and 5% carbon source, such as dextrose, along with 20% mineral sources, such as yeast extract, dipotassium hydrogen orthophosphate, magnesium sulfate with heptahydrate, sodium chloride, and ferrous sulfate. The production medium above this concentration was prepared in 200 ml of a 500 ml Erlenmeyer flask and autoclaved to maintain a sterile environment. After the production medium reached room temperature, antibiotics such as tetracycline and amoxicillin were added at a concentration of 200 mg/l. The fungal strain with spores was transferred to the prepared fermentation medium and incubated at 28 °C for 15 days (Muthukrishnan *et al.*, 2022).

Extraction of Metabolites

Extraction of secondary metabolites is the major process used to screen out the bioactive compounds produced by the endophytic fungi present in the production medium. The liquid-liquid extraction method was used to extract metabolites (intra/extracellular) from the production medium. For extracellular metabolites, the liquid broth of the production medium was collected after 20 days of

incubation. Initially, the production medium was filtered through a glass funnel and filter paper. The filtrate did not contain any mycelial or fungal cultures. This filtrate was mixed with an equal amount of ethylacetate and incubated for four hours at room temperature. The filtrate and ethyl acetate mixture were then partitioned using a separating funnel. The organic layer was collected and used for the GC-MS screening of bioactive compounds (Muthukrishnan *et al.*, 2022).

GC-MS Analysis

The identification of bioactive compounds in the extracellular and intercellular fungal extracts was conducted using GC-MS. A liquid sample without any contaminants or debris was used as the GC-MS test sample. To achieve this, the test samples were centrifuged at 3000 rpm for 5 min. The clear supernatant was used as the test sample. The sample powder was dissolved in methanol and centrifuged for the intracellular extract to obtain a clear supernatant (Elango *et al.*, 2020).

RESULTS

In this study identified one species of *Alternaria*, one species of *Fusarium*, three species of *Aspergillus*. The fungal genera identified in this study are frequently encountered across diverse ecosystems and are recognized for their significant ecological and economic impact (Dighton and White, 2017). *Alternaria* and *Fusarium* species are predominantly associated with phytopathogenic activity, inducing various diseases in agricultural crops and other plant species (Mykhalska *et al.*, 2019). *Aspergillus*, represented by three distinct species in this investigation, is a heterogeneous genus encompassing both beneficial and detrimental fungi (Uka *et al.*, 2019).

The analyzed compounds from *Aspergillus terreus* play a crucial role in agriculture, human health, and drug development. Indole-3-acetic acid supports

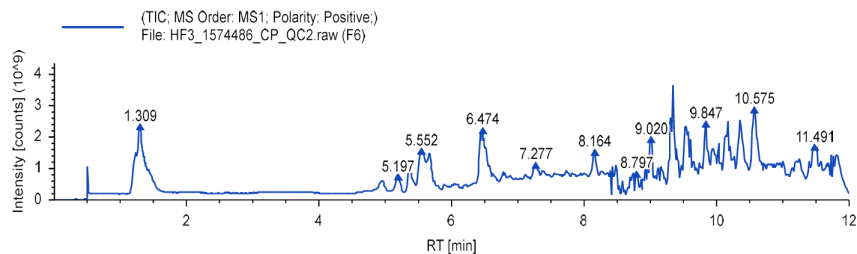
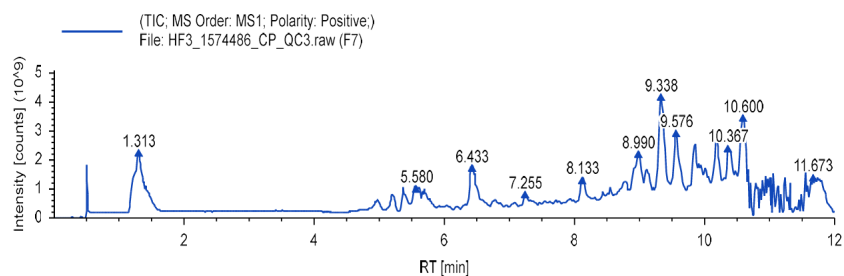


Fig. 1. GC-MS Chromatogram of *Aspergillus terreus*

Table 1. Identified compound from *Aspergillus terreus* Spectral Analysis by GC-MS

Bioactive Compound	Chemical Formula	Molecular Weight	RT (min)	Medicinal Properties
Creatinine	C ₄ H ₇ N ₃ O	316.20	6.487	Potential biomarker for kidney function
Cortisol	C ₂₁ H ₃₀ O ₅	218.10	5.241	Anti-inflammatory, immunosuppressant, stress hormone
1-Palmitoylglycerol	C ₁₉ H ₃₈ O ₄	259.18	5.486	Lipid metabolism regulator
L-Isoleucine	C ₆ H ₁₃ NO ₂	169.08	1.43	Essential amino acid, muscle recovery
Monoolein	C ₂₁ H ₄₀ O ₄	176.09	4.754	Emulsifier, drug delivery applications
Cinnamoylglycine	C ₁₁ H ₁₁ NO ₃	228.14	5.167	Antioxidant, anti-inflammatory
N,N-Dimethyldecylamine N-oxide	C ₁₂ H ₂₇ NO	135.06	4.858	Surfactant, antimicrobial
Diosgenin	C ₂₇ H ₄₂ O ₃	103.09	1.331	Precursor for steroid synthesis, anti-inflammatory
Cholecalciferol	C ₂₇ H ₄₄ O	204.08	5.216	Vitamin D3, bone health
Indirubin	C ₁₆ H ₁₀ N ₂ O ₂	113.08	5.293	Anti-cancer, anti-inflammatory
L-Pyroglutamic acid	C ₅ H ₇ NO ₃	131.06	1.354	Cognitive function, neurotransmitter precursor
Palmitoyl sphingomyelin	C ₃₉ H ₇₉ N ₂ O ₆ P	161.10	1.505	Cell membrane stability, neuroprotective
Oleoyl ethanolamide	C ₂₀ H ₃₉ NO ₂	269.30	8.148	Appetite suppressant, anti-inflammatory
L-Kynurenine	C ₁₀ H ₁₂ N ₂ O ₃	290.22	8.208	Neuroactive metabolite, immune modulator

**Fig. 2.** GC-MS Chromatogram of *A. flavus*.**Table 2.** Identified compound from *Aspergillus flavus* Spectral Analysis by GC-MS

Bioactive Compound	Chemical Formula	Molecular Weight	RT (min)	Medicinal Properties
Aflatoxin B1	C ₁₇ H ₁₂ O ₆	312.27	5.2	Carcinogenic, hepatotoxic
Aflatoxin G1	C ₁₇ H ₁₂ O ₇	328.27	6.1	Carcinogenic, mutagenic
Kojic acid	C ₆ H ₆ O ₄	142.11	4.3	Skin lightening, antibacterial
Cyclopiazonic acid	C ₁₃ H ₁₆ N ₂ O ₃	248.28	5.9	Neurotoxic, antimicrobial
Aspergillilic acid	C ₁₀ H ₈ N ₂ O ₄	220.18	5.5	Antibacterial, antifungal
Beta-nitropropionic acid	C ₃ H ₅ NO ₄	119.08	3.8	Neurotoxic, metabolic inhibitor
Fumigaclavine A	C ₁₉ H ₂₁ N ₃ O	307.39	6.7	Antimicrobial, antifungal

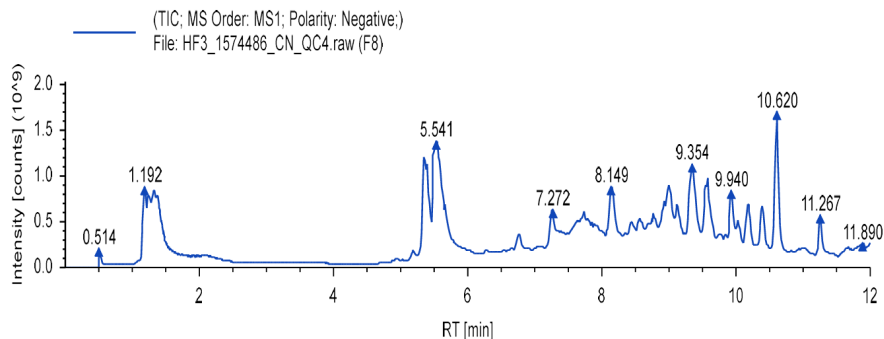
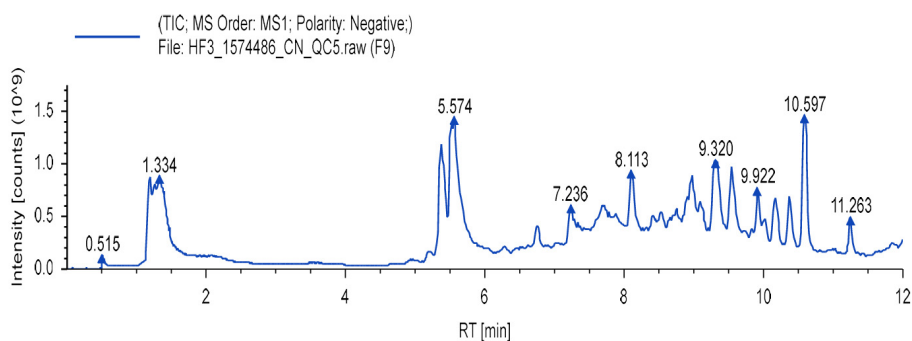
**Fig. 3.** GC-MS Chromatogram of *Aspergillus minisclerotigenes*.

Table 3. Identified compound from *Aspergillus minisclerotigenes* Spectral Analysis by GC-MS

Bioactive Compound	Chemical Formula	Molecular Weight	RT (min)	Medicinal Properties
Cortisol	C ₂₁ H ₃₀ O ₅	362.21	6.077	Anti-inflammatory, stress hormone
Diosgenin	C ₂₇ H ₄₂ O ₃	414.31	9.042	Precursor for steroid synthesis, anti-inflammatory
Cholecalciferol	C ₂₇ H ₄₄ O	384.34	9.212	Vitamin D3, bone health
Indirubin	C ₁₆ H ₁₀ N ₂ O ₂	262.07	6.614	Anti-cancer, anti-inflammatory
Oleoyl ethanolamide	C ₂₀ H ₃₉ NO ₂	325.30	9.792	Appetite suppressant, anti-inflammatory
L-Kynurenine	C ₁₀ H ₁₂ N ₂ O ₃	208.08	4.911	Neuroactive metabolite, immune modulator
DL-Glutamine	C ₅ H ₁₀ N ₂ O ₃	146.07	1.347	Supports muscle growth, immune health
5'-S-Methyl-5'-thioadenosine	C ₁₁ H ₁₅ N ₅ O ₃ S	297.09	5.178	Anti-inflammatory, neuroprotective
Riboflavin	C ₁₇ H ₂₀ N ₄ O ₆	376.14	5.363	Vitamin B2, antioxidant
5 α -Dihydrotestosterone	C ₁₉ H ₃₀ O ₂	290.22	8.208	Androgen hormone, muscle growth
Eicosapentaenoic acid	C ₂₀ H ₃₀ O ₂	302.22	9.484	Omega-3 fatty acid, anti-inflammatory
Nicotinic acid	C ₈ H ₈ N ₂ O ₃	180.05	5.251	Anti-inflammatory, potential diabetes treatment
Rifampicin	C ₄₃ H ₅₈ N ₄ O ₁₂	822.40	6.354	Antibiotic, tuberculosis treatment

**Fig. 4.** GC-MS Chromatogram of *Alternaria alternata***Table 4.** Identified compound from *Alternaria alternata* Spectral Analysis by GC-MS

Name of the Compound	Formula	Molecular Weight	RT	Medicinal Properties
D(-)-Glutamine	C ₅ H ₁₀ N ₂ O ₃	146.06922	1.316	Supports immune function, gut health, and muscle recovery
N2,N2-Dimethylguanosine	C ₁₂ H ₁₇ N ₅ O ₅	311.12228	4.974	Involved in RNA modification, potential antiviral activity
Phenylacetyl glycine	C ₁₀ H ₁₁ NO ₃	193.07406	5.658	Biomarker for metabolic disorders, potential role in neurotransmission
Rifampicin	C ₄₃ H ₅₈ N ₄ O ₁₂	822.40431	6.430	Antibiotic used to treat tuberculosis and bacterial infections
Coenzyme Q2	C ₁₉ H ₂₆ O ₄	318.18035	7.243	Antioxidant, supports mitochondrial energy production
Irganox 259	C ₄₀ H ₆₂ O ₆	660.44171	8.143	Antioxidant, used in industrial applications.
Histidyl-phenylalanyl-arginine	C ₂₁ H ₃₀ N ₈ O ₄	458.24121	9.339	Potential role in peptide-based therapies and metabolic functions
C-8 Ceramide-1-Phosphate	C ₂₆ H ₅₂ NO ₆ P	505.35406	10.598	Potential anticancer properties
1-adrenoyl-2-palmitoyl-sn-glycero-3-phosphocholine	C ₄₆ H ₈₄ NO ₈ P	810.1	11.251	Potential impact on inflammatory diseases

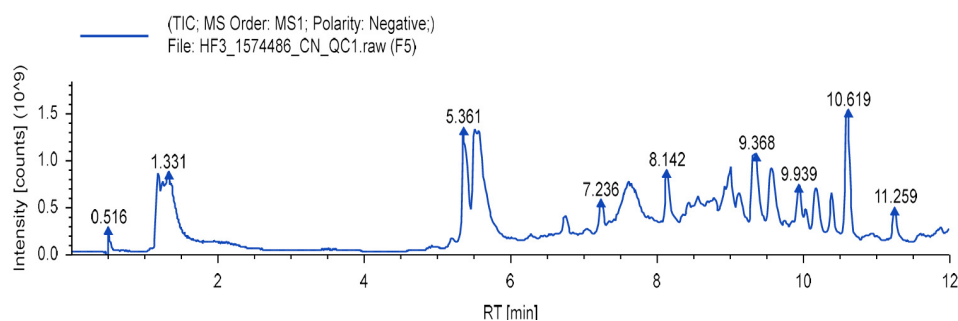


Fig. 5. GC-MS Chromatogram of *Fusarium solani*

Table 5. Identified compound from *Fusarium solani* Spectral Analysis by GC-MS

Name of the Compound	Formula	Molecular Weight	RT	Medicinal Properties
Pipecolic acid	$C_6H_{11}NO_2$	129.07914	1.331	Involved in lysine metabolism, potential role in neurological disorders
Riboflavin	$C_{17}H_{20}N_4O_6$	376.1378	5.361	Essential vitamin (B2), supports energy metabolism and antioxidant functions
Progesterone	$C_{21}H_{30}O_2$	314.2244	7.236	Hormone involved in reproductive health, used in hormone replacement therapy
Octadecanamine	$C_{18}H_{39}N$	269.30778	8.142	Used in industrial applications, limited direct medicinal use
Glycerophospho-N-palmitoyl ethanolamine	$C_{21}H_{44}NO_7P$	453.28561	9.368	Component of cell membranes, potential role in lipid metabolism
Phosphatidylcholine	$C_{48}H_{86}NO_7P$	819.61439	9.939	Supports liver health, involved in cell signaling and lipid metabolism
1-Stearoylglycerol skin hydration	$C_{21}H_{42}O_4$	358.30819	10.619	Precursor in lipid metabolism, potential role in

plant growth, while cortisol and serotonin regulate essential physiological functions in humans (Konopelski and Mogilnicka, 2022). Key pharmaceutical compounds like rifampicin and levothyroxine contribute to treating bacterial infections and thyroid disorders (Caron *et al.*, 2022). Essential biomolecules, including amino acids and vitamins, aid in metabolism and overall health.

The endophytic fungi isolated from *E. milii* revealed a diverse range of bioactive compounds with various medicinal properties. Several key metabolites, such as pipecolic acid, riboflavin, progesterone, octadecanamine, phosphatidylcholine and glycerophospho-N-palmitoyl ethanolamine, were consistently identified across multiple datasets. These compounds play essential roles in neurological functions, lipid metabolism, hormone regulation and antimicrobial activity. Additionally, other notable metabolites, including carnosine, creatinine, thymine, and ceramides, were detected, contributing to antioxidant, anti-inflammatory, and cell signaling functions. Overall, the findings indicate a rich metabolic profile with potential

applications in medicine, biotechnology and pharmacology.

CONCLUSION

The mycochemical analysis of endophytic fungi associated with *Euphorbia milii* has revealed the presence of various bioactive compounds with potential medicinal properties. The study indicates that these endophytic fungi produce secondary metabolites such as alkaloids, flavonoids, tannins, terpenoids and phenolic compounds, which are known for their antimicrobial, antioxidant, anti-inflammatory and anticancer activities.

These findings underscore the significance of endophytic fungi as a valuable source of natural bioactive compounds that could be further explored for pharmaceutical and therapeutic applications. The study also highlights the need for in-depth characterization and bioassay-guided investigations to fully harness the medicinal potential of these fungal endophytes. Future research should focus on the isolation, purification, and structural elucidation

of these compounds to develop novel drugs and bioactive agents.

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Declaration

Authors declare no conflict of interest.

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