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Antifungal potential of Volatile organic compounds of endophyte *Penicillium citrinum* associated with *Swertia chirayita*

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Volatile compounds are laden with various functionalities while some constitute active metabolites with antimicrobial properties. Microbial volatile organic compounds are being explored for antifungal properties against fungal phytopathogens with the possibility of substituting chemical pesticides while promoting organic farming practices. In this study, one of the fungal endophytes which was identified as *Penicillium citrinum* in the previous study was carefully assessed for the production of antifungal volatiles using a dual plate study against a species of *Fusarium, Sclerotinia, Alternaria*, and *Pestalotiopsis.* A maximum zone of inhibition was observed against *Sclerotinia* sp. followed by *Alternaria* sp. and *Fusarium* sp. However, least inhibition was observed against *Pestalotiopsis*. Crude extract obtained after fermentation of the test endophyte was analyzed using GC-MS technique wherein numerous metabolites were detected. Some of the compounds that were already identified to possess antimicrobial properties were detected in the analyte. Volatile organic compounds from endophytes could constitute a potential source of organic pesticides with suitable applications in the post-harvest management of pests.

Keywords : Endophyte, VOCs, *Swertia chirayita*, phytopathogens, *Penicilliumcitrinum*

INTRODUCTION

Phytopathogens inflict considerable loss on agricultural crops during pre-harvest and post-harvest stages. The predominant strategy for controlling the plant disease caused by these pests is the application of chemical pesticides, which exhibit high efficacy. However, this strategy also entails adverse consequences for the environment and human health. Hence, there is a demand for alternative pest control methods that are more environmentally benign and safe. One such alternative is the utilization of natural products and their derivatives, which have demonstrated promising capabilities in suppressing various phytopathogens (Jiménez-Reyes *et al.* 2019). Plants establish a mutualistic association with microorganisms in their milieu. These microorganisms can augment plant growth and fitness by producing metabolites that exert various functions.

Some of these metabolites are bioactive and can be utilized in agriculture to supplant synthetic chemicals and ameliorate crop quality. Some of the classes of bioactive metabolites that have been reported to have beneficial effects on plant health and productivity include phenolics, flavonoids, polyketides, steroids, terpenoids, alkaloids, etc. (Singh *et al.*2022).

During their metabolic activities, certain microorganisms, such as fungi and bacteria, emit Volatile Organic Compounds (VOCs). VOCs are organic molecules with high affinity for lipids, low molecular weight and low boiling point, but high vapour pressure. These properties facilitate the transport of VOCs over long and short distances through different materials. VOCs can influence plant growth and protection by altering plant physiology and biotic interactions (Chandra-sekaran *et al.*2022).

Fungal phytopathogens are a major source of biotic stress for livestock and food crops, as they can cause severe infections and spoilage that affect global food security and economy. The molecular mechanisms and evolutionary dynamics of fungal pathogenicity have been extensively studied by using various approaches. VOCs derived from microorganisms have been reported

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to exhibit decent effect against the plant pest and is gaining considerable attention in the agriculture sector (Santra and Banerjee, 2021).

Endophytic fungi are microorganisms that live inside plant tissues without causing symptoms of disease. They can produce a variety of bioactive compounds, including volatile organic compounds (VOCs), that have antimicrobial properties. During our previous studies several endophytic fungi were isolated from the plants of *Swertia chirayita* (Roxb. ex Fleming) H. Karst. Among the isolates, one of the fungal endophyte was able to secrete Indole Acetic Acid, produce siderophores as well as limit the growth of some of the selected phytopathogens during dual culture assay under invitro investigations (Sharma *et al.*2021 a,b). The endophyte which was identified as *Penicillium citrinum* is being used in this study to assess its potentiality to produce VOCs with antagonistic effects against some of the test phytopathogens and compare some of the metabolites of the endophyte and the plant sample i.e. *Swertia chirayita* using GC-MS technique.

MATERIALS AND METHODS

Test phytopathogens

Fungal pathogens used in our study include *Fusarium solani* (ITCC 7453), *Sclerotinia sclerotiorum* (ITCC 7853), *Alternaria alternata* (ITCC 7415) and *Pestalotiopsis theae* (ITCC 6599) which were obtained from Plant Pathology Division, Indian Agriculture Research Institute, New Delhi. The cultures were maintained in Potato Dextrose Agar (HiMedia, Mumbai) (PDA) slants.

Test endophyte

Fungal endophyte isolate UTCRF6 was obtained from the roots of *Swertia chirayita* collected from Uttarey, Sikkim and identified as *Penicillium citrinum* through morphological and molecular techniques in our previous study (Sharma *et al.*2021a).

Dual plate assay

The antagonistic effect of VOCs produced by the endophyte UTCRF6 was studied using Dual Plate assay technique as described by Dennis & Webster (1971)and modified accordingly. The endophyte was inoculated in PDA medium and incubated for 2 days at 28 °C. Thereafter, agar plugs containing fungal mycelium from the 5 days old culture of test pathogens were transferred to the base plate of a Petri dish containing 15 ml PDA medium. The inoculated base plates were then inverted and placed over the petri dish inoculated with the endophyte, wrapped with a parafilm seal and incubated for 5 days at 28 °C. These sets of plates were considered as test plates. Control plates containing only fungal pathogens were incubated under the same conditions.

The percentage of inhibition was calculated as follows:

Inhibition % = ((Dc - Dt)/Dc) x 100 (where Dc = diameter of the test pathogens in control plates and Dt = diameter of the test pathogens in test plates).

Culture of fungal endophyte and extraction of metabolites

A loopful of spores of endophyte UTCRF6, from 5 days old culture plate, was inoculated in 150 ml of Potato Dextrose Broth (HiMedia, Mumbai) contained in 250 ml Erlenmeyer flask and incubated at 28 °C for a period of 10 days. After incubation, the mycelium was separated from the culture broth by filtering through Whatman filter paper No 1. Metabolites from the filtrate were extracted using ethyl acetate solvent. Equal quantities of the culture filtrate and ethyl acetate were mixed vigorously in a separating funnel and allowed to stand till the organic layer separated from the aqueous layer. The top solvent layer was transferred to a round bottom flask and evaporated using a rotary evaporator in vacuo (240 millibar) at 40 °C. The crude residue obtained after evaporation of the solvent was stored at 4 °C and used for further processes (Leylaie and Zafari, 2018).

GC-MS Chromatography of the crude extracts obtained from fungal endophyte.

Analysis of the crude extracts of fungal endophyte UTCRF6 was conducted using GC-MS

(Shimadzu QP-2010 Plus with Thermal Desorption System TD 20) at Aakar Biotechnologies Pvt. Ltd., Lucknow. Analytical conditions were as follows: Column oven temperature was 60 °C, temperature for injection was 260 °C. Helium was used as carrier gas and column flow rate was set at 1.21ml/min with the split ratio of 10:1. The temperature of the oven was programmed as follows: 60 °C for 3 min, 8 °C/min to 250 °C and hold for 2 min and 15 °C/ min to 300 °C and hold for 18 min. The ion source temperature was set at 230 °C. Comparison of the data containing peaks, area and retention time, obtained from mass spectra, was done with NIST library (Bungtongdee *et al.*2019; Chen *et al.* 2020).

Statistical analysis.

All the tests were performed in triplicates and data were expressed as means and standard deviation.

RESULTS AND DISCUSSION

Dual plate assay

Growth of phytopathogens were found to be significantly reduced by volatile compounds produced by the endophyte isolate UTCRF6 after 5 days of incubation period. Highest percentage of inhibition was observed against *S. sclerotiorum* (35.55%) followed by *A. alternata* (27.15%) and *F. solani* (20.82%). However, least inhibition was observed against *P. theae* with only 10.26% (Fig 1, Fig 2).

GC-MS analysis of an extract of the endophyte UTCRF6

The chromatogram obtained from the GC-MS analysis of crude extract from the endophyte UTCRF6 was compared and interpreted through NIST database based on the retention time of the compound and peak area for the identification of the compounds present in the sample. The area and retention time of some of the important compounds are tabulated under Table.

Considerable parts of medicinal plants remain key ingredients for the preparation of medicinal concoctions popularly used by the majority of people residing in developing countries as they are conveniently accessible and cost-effective. Many bioactive constituents of allopathic drugs

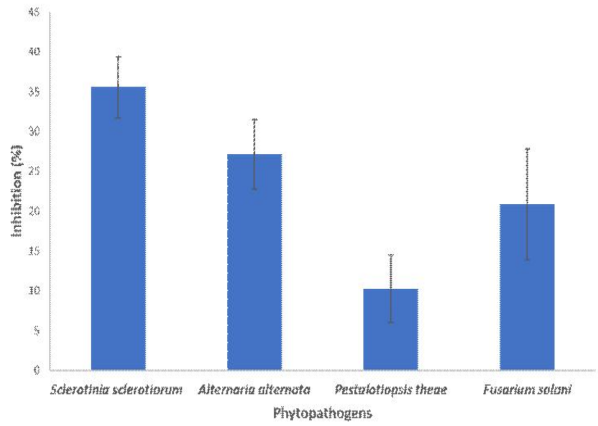

Fig.1: Inhibition of fungal phytopathogens by volatile compounds secreted by the endophyte *Penicillium citrinum* represented in percentage. Inhibition percentage = ((Dc - Dt)/Dc) x 100 (where Dc = diameter of the test pathogens in control plates and Dt = diameter of the test pathogens in test plates).

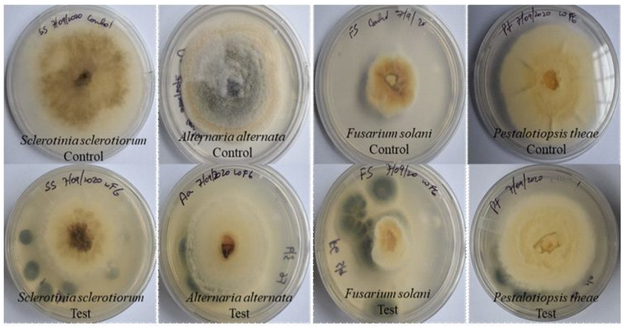

Fig. 2: Photographs exhibiting the growth of test pathogens in control set (upper row) and test set (lower row) of the experiment.The restricted growth of the pathogens in the test plates can be observed in the presence of endophyte *Penicillium citrinum*.

are obtained or derived from medicinal plants. Dependence on plant-based bioproducts could result in the overexploitation of plants and consequent decline in their population, particularly for plants that are endemic to certain regions. Numerous types of microorganisms have been identified that reside within plant tissues for most part of their life without causing adverse effects to their host plants which have been termed endophytes. Some of these endophytes are capable of secreting bioactive metabolites of plants even under *in vitro* conditions when provided with suitable culture conditions. Apart from host metabolites, endophytes are well known for the secretion of compounds with plethora of functionalities viz. antimicrobials, plant

Table.1: Chemical composition of volatile metabolites detected from the extract of endophyte *Penicillium citrinum* using GC-MS technique.

Area %	Retention time	Name	Properties/Reports
7.2	31.554	Phenol, 2,4-bis(1,1-dimethylethyl)-, phosphite (3:1)	Antioxidant and anti-enterococcal activities (Tyagi *et al.*, 2021).
6.89	34.16	D:b-friedo-b':a'-neogammacer-5-en-3-one	Reported from *Cissus quadrangularis* L (Ansarali, 2018).
2.61	29.4	Gamma-sitosterol	Reported from the extracts of *Stemphylium amaranthi,* an endophyte of *Catharanthus roseus* (Hemmati *et al.*, 2020).
2.25	30.477	Methyl commate A	Detected in the leaf extracts of Malaysian *Plectranthusamboinicus*demonstrating antibacterial and antioxidant activity (Swamy *et al.*, 2017).
1.63	12.237	Phenol, 2,4-bis(1,1-dimethylethyl)	Detected as antifungal metabolite from an endophyte *Bacillus velezensis* ZSY-1 (Gao *et al.* , 2017)
1.21	31.799	24-Norursa-3,12-diene	Reported as having high binding energy in receptor of spike and SARC -cov-2 binding domain protein complex (Kumar Paul *et al.*, 2022).
1.2	24.851	1-hexacosanol	Reported from the pulp oil of *Cassia fistula* with antifungal properties (Irshad *et al.*, 2013)
0.87	15.611	N-Hexadecanoic acid	Reported from *Sarocladium strictum* , endophyte of *Cynancum acutum*(Angel *et al.*, 2016)
0.73	13.087	2(3h)-furanone, dihydro-5-pentyl	Detected in *Trichoderma virens* 7b a part of antifungal metabolite (Angel *et al.*, 2016)
0.62	36.13	Dimethyl (bis[(4,8,8-trimethyldecahydro-1,4-methanoazulen- 9-yl)methoxy])silane	Reported from the barks of *Grewia lasiocarpa*(Akwu *et al.*, 2019).
0.43	27.948	Stigmasterol	Antifungal potential wasreported from the extract of endophyte *Colletotrichum* genus (Carvalho *et al.* , 2016).
0.31	19.008	Bis(2-ethylhexyl) phthalate	Antimicrobial properties reported from an endophyte *Epicoccum nigrum* obtained from *Ferulasumbul*(Perveen *et al.*, 2017)
0.18	16.618	Octadecanoic acid, methyl ester	Antibacterial properties reported from *Alternaria* GFAV15, an endophyte of *Tinospora cordifolia* (Yadav *et al.*, 2020)
0.07	7.344	Cyclohexene,1-methyl-4-(1-methylethenyl)	Reported from fungal endophytes known to convert agriculture waste to hydrocarbons (Strobel, 2014)

growth promoting hormones, enzymes, pharmaceuticals, etc. (Sharma *et al.* 2021b, 2021a).

Some of the endophytes have been reported to secrete volatile organic compounds with antifungal properties. An endophyte of *Swertia chirayita*, UTCRF6, was identified as *Penicillium* *citrinum* in our previous studies that exhibited various functionalities such as the production of Indole Acetic Acid, siderophores production and secretion of diffusible antifungals (Sharma *et al.* 2021a). In this study, dual plate technique was employed for preliminary investigation of antifungal capabilities of the volatile chemicals secreted by the endophyte UTCRF6. The isolate showed inhibitory effects on some of the fungal phytopathogens viz. *Fusarium solani* (ITCC 7453), *Sclerotinia sclerotiorum* (ITCC 7853), *Alternaria alternata* (ITCC 7415) and *Pestalotiopsis theae* (ITCC 6599) with maximum inhibition exhibited against *Sclerotinia sclerotiorum* and the least against *Pestalotiopsis theae*. Large number of metabolites were detected during GC-MS analysis of the extract. Some of the metabolites have been reported earlier either from plant parts viz. 1-hexacosanol, Methyl commate A,Dimethyl (bis[(4,8,8-trimethyldecahydro-1,4-methanoazulen- 9-yl)methoxy])silane and Dimethyl (bis[(4,8,8-trimethyldecahydro-1,4-methanoazulen- 9-yl)methoxy])silane, or endophytes obtained from different plants viz. Bis(2-ethylhexyl) phthalate, Cyclohexene,1-methyl-4-(1- methylethenyl), N-Hexadecanoic acid, Octadecanoic acid, methyl ester, Phenol, 2,4-bis(1,1-dimethylethyl), Stigmasterol and Gamma-sitosterol. There have been numerous reports of the metabolites indicated above having antimicrobial properties.

Similar study was conducted to assess the antifungal potential of volatiles from a strain of *Penicillium expansum* against phytopathogens such as *Colletotrichum acutatum*, *Monilinia laxa*, *Botrytis cinerea* and other isolates of *Penicillium expansum*. The isolate was able to inhibit the growth of all the test pathogens which was assessed by dual plate technique (Rouissi*et al.*2013). An endophyte isolate *Penicillium citrinum* TDPEF34 obtained from the roots of date palm has been reported to secrete volatile organic compounds with antifungal properties against *Trichoderma* sp. and *Fusarium* sp. GC-MS analysis of the volatile compounds demonstrated a remarkable toolkit of substances with biological activity that were previously documented (Ben Mefteh *et al.*2018).

In a particular study, volatile compounds derived from *Trichoderma asperellum* T1 were able to promote the accumulation of cell wall degrading enzymes such as chitinase and β-1,3-glucanase thereby inhibiting the growth of fungal pathogens *Corynespora cassiicola* and *Curvularia aeria* responsible for leaf spot disease in lettuce. The volatile compounds were also found to increase plant biomass and chlorophyll content in lettuce (Wonglom*et al.*, 2020). *Diaporthe* sp. isolated from the leaves of *Chloranthus elatior* Sw. exhibited antifungal properties against various phytopathogens (Santra and Banerjee, 2023) thereby highlighting the importance of volatile organic compounds in the control of post-harvest diseases.

The *Penicillium* genus, which includes over 200 species, is one of the largest genera of fungi, and it is particularly widely known as a source of antibiotics. Endophytic *Penicillium* have been reported to colonize ecological niches and defend their host plant from various factors demonstrating a wide range of biological capabilities that can be used in a variety of applications, including pharmaceuticals, biotechnology, and agriculture. Species of endophytes belonging to the genus *Penicillium* have been reported to produce various functionalities such as antimicrobials, anticancer compounds, antivirals, antioxidants, anti-inflammatory metabolites, antiparasitic molecules, immunosuppressant, antidiabetic, anti-obesity, antifibrotic, neuroprotective, insecticidals, and biocontrol agents. Moreover, some endophytic *Penicillium* spp. have been identified as biocatalysts, phytoremediators, plant growth promoters, and producers of important enzymes (Toghueo and Boyom, 2020).

Various microbial strains have been reported to produce an array of volatile molecules, that have the potential to be used in a variety of agricultural applications, including plant growth regulators and disease control agents. Their volatile spectra have been found to be strain-specific as well as dependent on different stages of growth, composition of media, pH, and temperature. The cost-effective and environmentally friendly nature of the volatiles have sparked curiosity in their use as biopesticides against a variety of bacterial and fungal pathogens during growing or postharvest storage conditions (Kumar *et al.* 2021).

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DECLARATION

Conflict of interest. Authors declare no conflict of interest.

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