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***Derleme* (*Review*)**

The role of fungal volatile organic compounds (FVOCs) in biological control

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Biyolojik mücadelede fungal uçucu organik bileşiklerin (FVOCs) rolü

Öz: Tarımsal üretimde bakteri, fungus, virüs ve nematod gibi organizmalar verim ve kalite kaybına neden olur. Özellikle fungal patojenlerin kontrolü zordur. Bu patojenlerin kontrolünde kullanılan sentetik pestisitlerin çevre dostu olmaması, biyopestisit kullanımı gibi alternatif yöntemlerin önemini artırmaktadır. İnsan sağlığına ve çevreye göreceli olarak zararlı olmayan biyopestisitler genellikle bitkilerden, virüslerden, bakterilerden ve funguslardan elde edilen ikincil metabolitlerdir. Funguslar, çeşitli uçucu organik bileşiklerin (VOC'ler) karışımlarını üretir. Aldehitler, alkoller, benzen türevleri, fenoller, heterosikler, hidrokarbonlar, ketonlar, sikloheksanlar, tiyoesterler ve tiyoalkollere ait 300'den fazla farklı fungus VOC'si tanımlanmıştır. Fungal VOC'ler ile bitki patojenleri arasındaki etkileşim, kimyasal pestisitlere çevre dostu bir alternatif oluşturmaktadır. Araştırmalar, fungus uçucu organik bileşiklerin bitki patojenlerine ve böcek zararlılarına karşı önleyici veya kovucu yönleriyle biyopestisit olarak etkili bir şekilde kullanılabileceğini göstermiştir. Bu derlemede, biyolojik mücadele kapsamında kimyasal pestisitlere alternatif olarak farklı bitki hastalık ve zararlılarına karşı fungal uçucu organik bileşiklerin kullanılma olanakları özetlenmiştir.

Anahtar kelimeler: Uçucu organik bileşikler, biyolojik mücadele, biyopestisitler

Abstract: Organisms such as bacteria, fungi, viruses and nematodes cause yield and quality loss in agricultural production. The control of fungal pathogens is especially challenging. The chemical pesticides used in the control of these pathogens are not environmentally friendly, which increases the importance of alternative methods such as the use of biopesticides. Biopesticides, which in relative terms are not harmful to human health and the environment, are generally secondary metabolites from plants, viruses, bacteria and fungi. Fungi produce various mixtures of volatile organic compounds (VOCs). More than 300 different fungal VOCs, including aldehydes, alcohols, benzene derivatives, phenols, heterocycles, hydrocarbons, ketones, cyclohexanes, thioesters and thioalcohols, have been described. The use of fungal VOCs against plant pathogens potentially provides an ecofriendly alternative to the use of chemical pesticides. Research has shown that fungal VOCs can be used effectively as inhibitory or repellent biopesticides against plant

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pathogens and insect pests. In this review, the potential uses of fungal VOCs against different plant diseases and pests as substitutes for chemical pesticides within the scope of biological control, are summarized.

Keywords: Volatile organic compounds, biological control, biopesticides

Introduction

Some pathogenic microorganisms that cause loss of yield and quality in agricultural production are fungi, viruses, bacteria and nematodes. Among these pathogens, fungi are the main causal agent of many plant diseases (Oka et al. 2015). To reduce the damaging effects of phytopathogenic microorganisms, chemical pesticides have been used in agriculture, significantly enhancing crop yield and quality (Macías-Rubalcava et al. 2018). However, this is not an ecofriendly approach (Naher et al. 2014). The prolonged and excessive use of chemical pesticides can contaminate water resources, cause air pollution, affect human health adversely and leave harmful residues that can result in the occurrence of pesticide-resistant pathogens (Naher et al. 2014; Oka et al. 2015; Macías-Rubalcava et al. 2018).

To overcome these problems, many researchers have been looking for alternatives to synthetic chemicals, such as the use of biopesticides (Naher et al. 2014; Medina-Romero et al. 2017). The use of biopesticides is an appropriate option for protecting commercially valuable products from pathogenic microorganisms (Medina-Romero et al. 2017). Biopesticides, which are comparatively non-harmful and environmentally friendly (Mercier & Jiménez, 2004; Medina-Romero et al. 2017), are mostly secondary metabolites of plants, fungi, viruses and bacteria (Medina-Romero et al. 2017).

Volatile Organic Compounds (VOCs) are mixtures of a carbon-based combination derived from primary (DNA, amino acid and fatty acid synthesis) or secondary metabolism (primary metabolism intermediates) (Korpi et al. 2009; Li et al. 2015). The molecular weight of VOCs is low, which means they can travel over a long distance (Reino et al. 2008; Schalchli et al. 2015) and disperse in the air and soils because of their small size (Morath et al. 2012).

Fungi produce various mixtures of FVOCs (Morath et al. 2012). Over 300 different FVOCs have been described, including alcohols, aldehydes, benzene derivatives, cyclohexanes, heterocycles, hydrocarbons, ketones, phenols, thioesters and thioalcohols (Morath et al. 2012; Zhang et al. 2015; Wang et al. 2018). Many ecological interactions between living organisms take place through VOCs (Morath et al. 2012). Compounds such as VOCs involved in these interactions are called "infochemicals" (Wheatley, 2002). Within the scope of biological control, the negative interactions between FVOCs and plant pathogens represent an ecofriendly alternative to chemical pesticides. Some researchers have shown that FVOCs can be used effectively, through their inhibitory or repellent activities against phytopathogens and insect pests (Lacey & Neven, 2006; Riga et al. 2008; Morath et al. 2012; Schalchli et al. 2015; Liarzi et al. 2016a; Terra et al. 2018).

Research on the secondary metabolites of organisms such as fungi, bacteria, viruses and plants has increased in recent times and important studies have been carried out in the use of VOCs as biopesticides against plant diseases and pests. These studies have revealed that the FVOCs of fungi are an effective group of biopesticides. In this review, comprehensive information on the use of FVOCs against different plant diseases and pests is provided, and expectations of their more widespread use as eco-friendly biological pesticides are discussed.

Fungal volatile organic compounds (FVOCs) and endophytic fungi

VOCs are a broad group of carbon-based, primary or secondary metabolites of living organisms that have low molecular weight (lower than 300 g/mol) (Zhang et al. 2015) and high vapour pressure (between 3.03 and 7.46 mg/m^3) (Korpi et al. 2009; Bennett &Inamdar, 2015; Naik, 2018). VOCs, contain up to 20 carbon atoms, and are lipophilic (Effmert et al. 2012; Terra et al. 2018). VOCs are normally gaesous at room temperature because they have low vapour pressure (Medina-Romero et al. 2017). Their physical characteristics make them important as 'infochemicals' or 'semiochemicals' for inter-species contact, and they can move long distances under and above ground, especially in non-aqueous environments (Rasmann et al. 2005; Hung et al. 2013; Schmidt et al. 2016). The known VOCs are mainly alcohols (3-methyl1-butanol, ethanol, 2-phenyl ethanol, 2-methyl-1-butanol), aldehydes (2-methyl-2-hexenal and 2-isopropyl-5-methyl-2-hexenal) (Buzzini et al. 2003) and esters (ethyl octanoate, ethyl acetate) (Francesco et al. 2015). Fungi are a very rich resource in terms of VOCs and more than 300 different FVOCs have been identified (Korpi et al. 2009; Effmert et al., 2012; Lemfack et al., 2014). FVOCs are not only involved in communication among living things but they also have the ability to restrict the activities of rival organisms to their producers (Wang et al. 2018).

The definition of endophytic fungus varies but the definition of Petrini (1991) is the most widely used: “All organisms that can colonize internal plant tissues at any time in their lifecycle without causing obvious harm to the host plant.” Endophytic fungi produce active, anti-fungal, volatile organic compounds with possible uses in medicine, industry and agriculture. Studies on the VOCs of endophytic fungi began in the 1970s (Effmert et al. 2012). Recent research carried out on endophytic fungi has demonstrated that they are potentially of great significance as a source of volatile compounds. FVOCs can be utilized as biologically-based fumigants in integrated pest management to defend crops from fungal phytopathogens (Sánchez-Fernández et al. 2016). Biocontrol agents, which are seen as an alternative to agrochemicals whic cause severe health and environmental problems, are promising and environmentally friendly substances in the control of plant diseases (Chen et al. 2016).

In recent times, the VOCs of various endophytic fungi and their efficacy against phytopathogens and pests have been studied by many researchers. Standing out as the most important source of VOCs among fungi, *Muscodor albus* was first isolated from extracts from the cinnamon tree in Honduras, and then from different tree species in various parts of the world (Liarzi et al. 2016b). Some other recent examples of VOC-emitting endophytic fungi which have efficacy as biocontrol agents are: *Hypoxylon* and its anamorph, *Nodulisporium* sp. (Sánchez-Fernández et al. 2016; Medina-Romero et al. 2017; Macías-Rubalcava et al. 2018); *Trichoderma gamsii* (Chen et al. 2016); *Trichoderma harzianum* (Coppola et al. 2017); *Aureobasidium pullulans* (Francesco et al. 2015); *Daldinia cf. concentrica* (Liarzi et al. 2016b); and *Muscodor vitigenus* (Daisy et al. 2002).

FVOCs extraction and identification

The gas chromatography (GC) method is the one mostly commonly used to identify FVOCs (Stoppacher et al. 2010). Initially, fungi are cultivated on solid growth medium (Nemčovič et al. 2008) or in liquid growth medium (Pinches & Apps, 2007). The FVOCs excreted from the fungi can be extracted by headspace-solid phase microextraction (HS-SPME) and identified by gas chromatography (GC) combined with mass spectrometry (MS). However, many other methods can be used to extract and identify FVOCs (Stoppacher et al. 2010). Some methods such as on-line gas enrichment with adsorption tubes (Wheatley et al. 1997), solid-phase extraction with C18 or silica gel columns (Keszler et al. 2000), closed-loop stripping analysis (Meruva et al. 2004), organic solvents (Reithner et al. 2005) and dynamic headspace (Deetae et al. 2007) can be used for the extraction of FVOCs. Additionally, after extraction and GC separation, the components of complex mixtures of FVOCs can be identified through flame ionization detection (FID) (Elke et al. 1999) instead of MS (Hynes et al. 2007), which is most frequently used nowadays (Stoppacher et al. 2010).

In addition to the GC method, the electronic nose (E-nose) can also be used to identify FVOCs. E-nose is a modern technology used to detect volatile metabolites with a variety of chemical sensors (Wang et al. 2016). Commercially, various non-specific sensors, including metal oxide, conductive polymer, quartz crystal microbalance sensors, surface acoustic wave and mass spectrometry, have been utilised (Wang et al. 2016). The E-nose technique is very promising for the quick and cost-efficient detection of fungi, especially in confined places such as warehouses, as they secrete specific VOCs; E-noses can differentiate between mouldy and non-mouldy samples, and also identify some fungal species (Kuske et al. 2005).

Insecticidal aspects of FVOCs

FVOCs can be attractive or repellent to agricultural pests as biological control agents and are environmentally friendly (Li et al. 2015). For example, naphthalene secreted by *M. vitigenus* was found to be repellent to the wheat stem sawfly, *Cephus cinctus*, at the adult stage (Daisy et al. 2002), and the VOCs of *M. albus* have an insecticidal effect on the potato tuber moth (Lacey & Neven, 2006). In addition, Hussain et al. (2010) investigated the pathogenicity of the VOCs secreted from *Isaria fumosorosea*, *Beauveria bassiana* and *Metarhizium anisopliae* to the subterranean termite, *Coptotermes formosanus*. The termites were found to regulate their responses to the entomopathogenic fungi in keeping with the profile of the FVOCs. In particular, the FVOCs emitted by *M. anisopliae* repelled termites. This may therefore be an effective method of protecting trees from termite infestation.

FVOCs can also be involved indirectly in biological control. For example, *Trichoderma*, the symbiote of plant roots, is known for its enhancement of the defence against phytopathogens by triggering plant resistance mechanisms. Similarly, Coppola et al. (2017) reported that the FVOCs secreted by *T. harzianum* attracted the parasitoid, *Aphidius ervi*, of the aphid, *Macrosiphum euphorbiae*, which damages the tomato plant.

Antifungal and antibacterial effects of the FVOCs

A number of fungi, mainly endophytes. have been tested for their ability to generate a broad variety of volatile compounds that can be utilized in biological control. The genera most investigated for biocontrol purposes are *Muscodor* and *Trichoderma* species (Schalchli et al. 2015). *Muscodor albus*, isolated from *Cinnamomum zeylanicum* (cinnamon tree), is a highly studied endophytic fungus. It produces a VOC mixture that includes alcohol, ester, ketone, acid and lipid compounds, and kills a wide range species of bacteria and fungi that are pathogenic to plants and humans. It has been demonstrated that when used as a biofumigant, *M. albus* is effective for controlling soil-borne plant diseases and smut disease on cereals, as well as controlling post-harvest diseases (Lacey & Neven, 2006). Genetic screening and biochemical assay were used by Alpha Cambria et al. (2015) to investigate the mode of action of *M. albus* VOCs and they discovered that *M. albus* causes the death of *Escherichia coli* by damaging its DNA. The DNA damage evidence indicated that if not repaired properly, it can cause breaks in DNA replication and transcription. In addition, the cytotoxicity profile showed that *E. coli* was filamentous and that there was a rise in cell membrane permeability during VOC exposure. Beside *M. albus*, other *Muscodor* species, *Muscodor sutura* (Kudalkar et al. 2012), *Muscodor crispans* (Krajaejun et al. 2012), *Muscodor kashayum* (Meshram et al. 2013) and *Muscodor yucatanensis* (Macías-Rubalcava et al. 2018), have been studied for their biocidal capacity and it has been demonstrated that *Muscodor* species have major effects on some fungi and bacteria.

Another well-known genus of endophytic fungi is *Trichoderma*, which in root, soil and foliar environments, are highly interactive. They have been recognized for many years for parasitizing other fungi by developing a broad variety of antibiotic substances and inhibiting other microorganisms by competing for space and/or nutrients (Harman et al. 2004). The VOCs of most *Trichoderma* spp. have antifungal effects at varying levels on fungal plant pathogens. In a recent study, Amin et al. (2010) demonstrated that the volatiles of *T. harzianum* (Th-1), *T. harzianum* (Th-2), *Trichoderma virens* (Ts-1), *T. viride* (Tv-1), *T. viride* (Tv-2) and *T. viride* (Tv-3) reduce the mycelial growth and sclerotial production of *Alternaria brassicicola, Colletotrichum capsici, Fusarium oxysporum, Helminthosporium oryzae, Rhizoctonia solani, Sclerotium rolfsii* and *Sclerotinia sclerotiorum.* In similar studies, it was demonstrated that *Trichoderma* species such as *T. album, T. aureoviride, T. hamatum, T. harzianum* and *T. viride* reduced the mycelial growth of *Alternaria alternata, Alternaria brassicae, Alternaria solani, Botrytis fabae*, *F. oxysporum* and *Fusarium solani* at an acceptable level through the production of volatile and non-volatile organic metabolites. Moreover, *Trichoderma* species also inhibited plant pathogenic bacteria through their non-volatile and volatile organic compounds (Barakat et al. 2014; Meena et al. 2017). In addition, Gangwar and Sinha (2010) demonstrated that *T. harzianum, T. hamatum,* and *T. virens* have high biocontrol activity against *Xanthomonas oryzae pv. oryzae* which induces leaf blight on rice.

In recent years, some research has been carried out on the biocontrol activity of many fungi species, other than *Muscodor* and *Trichoderma* species, against bacteria and other fungal species, and promising results have been obtained. For example, Naznin et al. (2014) extracted and described the VOCs of the plant growth-promoting fungi, *Ampelomyces* sp., *Cladosporium* sp. and *Phoma* sp., and showed that of three VOCs extracted, two emitted from *Ampelomyces* sp., and one from *Cladosporium* sp., substantially decreased the severity of disease caused by *Pseudomonas syringae* pv. *tomato* DC3000 in *Arabidopsis* plants. In addition, Schalchli et al. (2015) used the double- compartmented Petri dish method for the investigation of the effects of eight, white-rot fungal strains on the mycelial growth of *Botrytis cinerea, F. oxysporum* and *Mucor miehei*. Among the fungi examined, *Anthracophyllum discolor. sp4* had a highly inhibitory effect on *B. cinerea* and *M. miehei*, at approximately 76% and 20%, respectively. However, it had less inhibitory activity against *F. oxysporum* (approximately 10%) through the emission of various volatiles. Separately, Liarzi et al. (2016b) characterized a VOC-emitting endophytic fungus that had been extracted from *Olea europaea* L. (olive tree) grown in Israel; the fungus was described as *Daldinia cf. concentrica*. The authors indicated that the VOCs emitted by *D.cf. concentrica* prevented the growth of moulds on dried organic fruits and suppressed the infection of peanuts by

Aspergillus niger. In another study, two different inhibition bioassays were used for the investigation of the antifungal activity of some fungi, including *Schizophyllum commune, T. viride* and *Trametes versicolor,* against the fungal phytopathogens, *B. cinerea* and *F. oxysporum,* and the saprotrophic mould, *M. miehei*. It was demonstrated that *B. cinerea* and *M. miehei* were the ones most inhibited by an isolate of *S. commune,* at 86.0 ± 5.4% and 99.5 ± 0.5%, respectively (Schalchli et al. 2011).

Nematicidal activity of FVOCs

Plant-parasitic nematodes (PPNs) are among the most important pests that cause damage to plants, causing an estimated 10% agricultural production loss worldwide (McCarter, 2008). The most destructive and widely dispersed species belong to the genus *Meloidogyne*; *M. incognita,* which is extremely polyphagous, can parasitize over 2000 plant species (Sasser, 1980). Nowadays, various synthetic chemical nematicides are used commercially to control PPNs. However, due to their harmful effects on the environment, they are increasingly facing restrictive regulations (Noling, 2002; Yang et al. 2012).

Muscodor albus, an endophytic fungus, can prevent the growth of some species of nematodes and arthropods, as well as a wide variety of pathogenic fungi and bacteria (Alpha Cambria et al. 2015). The VOCs produced by *M. albus* were tested for their nematicide potential against four PPNs, namely *Meloidogyne chitwoodi*, *Meloidogyne hapla*, *Paratrichodorus allius* and *Pratylenchus penetrans* (Riga et al. 2008). After 72 hours of exposure to the FVOCs of *M. albus*, the mortalities of *P. allius, P. penetrans and M. chitwoodi* were 82.7%, 82.1% and 95%, respectively. Grimme et al. (2007) reported that a volatile mixture of *M. albus*’s VOCs can protect tomato plant roots from *M. incognita*, the root-knot nematode. Also, the VOCs of *Fusarium oxysporum* are lethal to *M. incognita* (Zhang et al. 2015), and Freire et al. (2012) reported that the VOCs from *F. oxysporum* caused 88% to 96% lethality to the root-knot nematode, *M. incognita,* in the second juvenile stage. Similar research by Terra et al. (2018) supported these data; they further reported that the proportion of egg hatching was decreased by 43% when *M. incognita* eggs were exposed to VOCs from *F. oxysporum* for 72 hours. Liarzi et al. (2016a) showed that *D.* cf. *concentrica* contains FVOCs that have biological activity and then investigated their capability to suppress *Meloidogyne javanica* in both lab and glasshouse experiments. They stated that the VOCs of *D.* cf. *concentrica* had nematicidal activity against juveniles of *M. javanica* whose viability was reduced by 67%. Furthermore, the fungal genus *Trichoderma* produces inhibitory metabolites against PPNs. More specifically, Yang et al. (2012) showed that the volatile organic compound, 6-pentyl-2H-pyran-2-1, from *Trichoderma* sp., is nematicidal, killing over 85% of *Caenorhabditis elegans*, *Bursaphelenchus xylophilus* and *Panagrellus redivivus*.

The role of FVOCs in post-harvest and stored products

Economic losses may occur in stored products due to fungal and insect pathogens that reduce quality (Herrera et al. 2015). For the biofumigation, including micofumigation, control of pests, many researchers have used fungal VOCs as alternatives to synthetic chemicals, especially in stored agricultural products (Strobel et al. 2001; Stinson et al. 2003; Mercier & Jimenez, 2004; Mercier & Manker, 2005; Park et al. 2010; Alpha Cambria et al. 2015). Various FVOCs released by *Ceratocystis fimbriata* have strong bioactivity against many fungal varieties, oomycetes and bacteria. Fungal germination and bacterial colony formation were substantially reducedfollowing exposure to *C. fimbriata* cultures (Li et al. 2015). In many potato-producing countries, *Phthorimaea operculella*, the potato tuber moth (PTM), is a serious problem in stored potatoes. In 2006, Lacey and Neven tested FVOCs secreted from *M. albus* against PTM to determine their insecticidal activity. They found that the pupal development period of PTM exposed to a culture of *M. albus* decreased by more than 60% compared to the controls.

Sitophilus zeamais Motschulsky (Coleoptera: Curculionidae) is an important pest of stored maize. Three FVOCs, 1-octen-3-ol, 3-octanol and 3-octanone, were tested by Herrera et al. (2015) for their biopesticidal potential. The most effective FVOC against *S. zeamais* was 1-octen-3-ol with an LD50 value of 27.7 (mL/L air), followed by 3-octanone and 3-octanol with LD50 values of 219.7 (mL/L air) and 43.2 (mL/L air), repectively. Additionally, in vitro and in vivo experiments carried out by Francesco et al. (2015) showed that the FVOCs, 2-methyl-1-butanol, 3-methyl-1-butanol, 2-methyl-1-butanol, phenethyl alcohol and 2-methyl-1-propano, produced by *A. pullulans*, are active against *B. cinerea*, *C. acutatum* and *Penicillium* spp.

FVOCs emitted by fungi such as *M. albus* and *Penicillium expansum* were very effective against some post-harvest fungal diseases and their application was promising (Rouissi et al. 2013). The FVOCs of two *A. pullulans* strains that were known to have inhibitory effects on some post-harvest pathogens were applied against five pathogens, *B. cinerea*, *Colletotrichum acutatum*, *P. expansum*, *Penicillium digitatum* and *Penicillium italicum*; the FVOCs produced by *A. pullulans* substantially limited conidia formation by all five pathogens, especially the *Penicillium* species (Francesco et al. 2015). In post-harvest experiments by Liarzi et al. (2016b), FVOCs of *D.* cf. *concentrica* prevented mold growth on organic dried fruits and exterminated *A. niger* infection in peanuts. Ascencio-Álvarez et al. (2008) reported that *F. oxysporum*, a phytopathogenic fungus, was responsible for about 60% of production losses of tomatoes, and significantly reduced fruit quality after harvest. For controlling *F. oxysporum*'s undesirable effects on cherry tomatoes, Medina-Romero et al. (2017) successfully utilised the synergic effects of six FVOCs, namely terpinolene, phenyl ethyl alcohol, ocimene, 2-methyl-1-butanol, eucalyptol and 3-methyl-1-butanol. The effectiveness of all of the FVOCs varied, depending on the dosage, which ranged from 12.5 to 1000 μg/mL. Similarly, while a high dose (over 0.53 mM) of 1-octen-3-ol inhibited the development of *Fusarium verticillioides*, low doses (under 0.13 mM) of 1-octen-3-ol stimulated its growth (Herrera et al. 2015).

Factors affecting FVOC type and density

The main factors affecting the type of FVOC are species (Schalchli et al. 2011; Strobel, 2011), culture medium (Wheatley et al. 1997) and fungus age (Lee et al. 2015). When *Trichoderma* isolates were grown on malt agar rather than nutrient agar, their VOCs were found to be more effective against *Postia placenta* and *T. versicolor*; *Trichoderma* isolates grown on nutrient agar had no inhibitory effect on *P. placenta* or *T. versicolor* (Wheatley et al. 1997). The number and concentration of FVOCs varied depending on the substrate type (Fiedler et al. 2001). Change in the FVOC types with environmental conditions is a challenging factor to work in this field (Herrmann, 2010; Bitas et al., 2013). In addition, Lee et al. (2015) compared FVOCs emitted by *Trichoderma atroviride* after 5 days and 14 days by using GC - MS. They determined that some FVOCs were no longer secreted as the fungus aged. However, 24 new FVOC compounds began to be secreted.

Conclusions and a perspective on the future

Due to the negative effects of agrochemicals on human health and the environment through residue problems, and the increase in pathogen resistance over time, the importance of the use of biological control methods as an alternative to synthetic chemicals has increased significantly in recent years. The most striking trend associated with this purpose worldwide is the development of biocontrol products, with numerous studies having been conducted on the use of biological control agents in the fight against diseases and pests in crop production in recent years. In this context, the organic compounds emitted by endophytic fungi is one of the most studied topics and results have showed promise of high biocontrol potential. Therefore, the VOCs emitted by the endophytic fungi, which may be able to replace agrochemicals and eliminate their undesirable effects on health and environment, have been reviewed in this article.

Much research in this field has demonstrated that the VOCs released by some endophytic fungal species of genera such as *Muscodor, Trichoderma, Schizophyllum* and *Anthracophyllum* are effective for the control of various fungi, bacteria, nematodes and insects. Of the studies carried out, the prevention of diseases, especially in the postharvest period, with the VOCs produced by endophytic fungi, is very promising in terms of decreasing synthetic pesticide residues. However, a large amount of work needs to be done to realize the widespread use of fungal VOCs as biological control agents both in the cultivation and the postharvest period for the control of phytopathogens and pests.

Nowadays, standard devices, such as GC, HS-SPME, MSFID, are widely used for the detection of FVOCs. However, these devices do not achieve fast and low-cost detection of FVOCs but a new and promising device called E-nose will be widely used in the future to detect FVOCs quickly and affordably and will make an important contribution to the production of fungal VOCs.

The inhibitory effect of VOCs secreted by various endophytic fungi on plant diseases and pests has been confirmed, as can be seen from the many studies cited in this review. The most important problem that must be overcome is the mass production of the FVOCs of endophytic fungi that have inhibitory effects on target organisms. For eco-friendly fungal VOCs to be used as biocontrol agents during cultivation and the postharvest period, future studies in this field should be aimed at commercializing these compounds through the production of large quantities at low cost. In this way, fungal VOCs could contribute greatly to sustainable agriculture.

References

Alpha Cambria J., M. Campos, C. Jacobs-Wagner & S.A. Strobela, 2015. Mycofumigation by the volatile organic compound-producing fungus *Muscodor albus* induces bacterial cell death through DNA damage. *Applied and Environmental Microbiology*, 81 (3): 1147-1156.

Amin F., V.K. Razdan, F.A. Mohiddin, K.A. Bhat & P.A. Sheikh, 2010. Effect of volatile metabolites of *Trichoderma* species against seven fungal plant pathogens in-vitro. *Journal of Phytology*, 2 (10): 34-37.

Ascencio-Álvarez A., A. López-Benítez, F. Borrego-Escalante, S.A. Rodríguez Herrera, A. Flores-Olivas, F. Jiménez-Díaz & A.J. Gámez-Vázquez, 2008. Marchitez vascular del tomate: I. Presencia de razas de *Fusarium oxysporum f. sp. lycopersici* (Sacc.) Snyder y Hansen en Culiacán, Sinaloa, México. *Revista Mexicana de Fitopatología*, 26: 114-120.

Barakat F. M., K.A. Abada, N.M. Abou-Zeid & Y.H.E. El-Gammal, 2014. Effect of volatile and non-volatile compounds of *Trichoderma* spp. on *Botrytis fabae* the causative agent of faba bean chocolate spot. *American Journal of Life Sciences*, 2 (6): 11-18.

Bennett J.W. & A.A. Inamdar, 2015. Are some fungal volatile organic compounds (VOCs) mycotoxins? *Toxins*, 7(9): 3785-3804.

Bitas V., H.S. Kim, J.W. Bennett & S. Kang, 2013.Sniffing on microbes: diverse roles of microbial volatile organic compounds in plant health. *Molecular Plant-Microbe Interactions*, 26: 835-843.

Buzzini P., A. Martini, F. Cappelli, U.M. Pagnoni & P. Davol, 2003. A study on volatile organic compounds (VOCs) produced by tropical ascomycetous yeasts. *Antonie Van Leeuwenhoek*, 84: 301-311.

Chen J.L., S.Z. Sun, C.P. Miao, K. Wu, Y.W. Chen, L.H. Xu & L.X. Zhao, 2016. Endophytic *Trichoderma gamsii* YIM PH30019: a promising biocontrol agent with hyperosmolar, mycoparasitism, and antagonistic activities of induced volatile organic compounds on root-rot pathogenic fungi of Panax notoginseng. *Journal of Ginseng Research*, 40 (4): 315-324.

Coppola M., P. Cascone, M.L. Chiusano, C. Colantuono, M. Lorito, F. Pennacchio & M.C. Digilio, 2017. *Trichoderma harzianum* enhances tomato indirect defense against aphids. *Insect Science*, 24 (6): 1025-1033.

Daisy B.H., G.A. Strobel, U. Castillo, D. Ezra, J. Sears, D.K. Weaver & J.B. Runyon, 2002. Naphthalene, an insect repellent, is produced by *Muscodor vitigenus*, a novel endophytic fungus. *Microbiology*, 148 (11): 3737-3741.

Deetae P., P. Bonnarme, H.E. Spinnler & S. Helinck, 2007. Production of volatile aroma compounds by bacterial strains isolated from different surface-ripened French cheeses. *Applied Microbiology and Biotechnology*, 76: 1161-1171.

Effmert U., J. Kalderás, R. Warnke & B. Piechulla, 2012. Volatile mediated interactions between bacteria and fungi in the soil. *Journal of Chemical Ecology*, 38(6): 665-703.

Elke K., J. Begerow, H. Oppermann, U. Krämer, E. Jermann & L. Dunemann, 1999. Determination of selected microbial volatile organic compounds by diffusive sampling and dual-column capillary GC-FID-a new feasible approach for the detection of an exposure to indoor mould fungi? *Journal of Environmental Monitoring*, 1: 445-452.

Fiedler K., E. Schütz & S. Geh, 2001. Detection of microbial volatile organic compounds (MVOCs) produced by moulds on various materials. *International Journal of Hygiene and Environmental Health*, 204 (2-3): 111-121.

Francesco A.D., L. Ugolini, L. Lazzeri & M. Mari, 2015. Production of volatile organic compounds by *Aureobasidium pullulans* as a potential mechanism of action against postharvest fruit pathogens. *Biological Control*, 81: 8-14.

Freire E.S., V.P. Campos, D.F. Oliveira, A.M. Pohlit, N.P. Norberto & M.R. Faria, 2012. Volatile substances on the antagonism between fungi, bacteria and *Meloidogyne incognita* and potentially fungi for nematode control. *Journal of Nematology*, 44: 321-328.

Gangwar G.P. & A.P. Sinha, 2010. Comparative antagonistic potential of *Trichoderma* spp. against *Xanthomonas oryzae pv. oryzae*. *Annals of Plant Protection Sciences*, 18(2): 458-463.

Grimme E., N.K. Zidack, R.A. Sikora, G.A. Strobel & B.J. Jacobsen, 2007. Comparison of *Muscodor albus* volatiles with a biorational mixture for control of seedlings diseases of sugar beet and root-knot nematode on tomato. *Plant Disease* 91: 220-224.

Harman G.E., C.R. Howell, A. Viterbo, I. Chet & M. Lorito, 2004. *Trichoderma* species-opportunistic, avirulent plant symbionts. *Nature Reviews Microbiology*, 2 (1): 43-56.

Herrera, J.M., R.P. Pizzolitto, M.P. Zunino, J.S. Dambolena & J.A. Zygadlo, 2015. Effect of fungal volatile organic compounds on a fungus and an insect that damage stored maize. *Journal of Stored Products Research*, 62: 74-80.

Herrmann A, 2010. The Chemistry and Biology of Volatiles. John Wiley & Sons, Chichester, U.K. 422 pp.

Hung R., S. Lee & J.W. Bennett, 2013. *Arabidopsis thaliana* as a model system for testing the effect of *Trichoderma* volatile organic compounds. *Fungal Ecology*, 6: 19-26.

Hussain A., M.Y. Tian, Y.R. He, J.M. Bland & W.X. Gu, 2010. Behavioral and electrophysiological responses of *Coptotermes formosanus* Shiraki towards entomopathogenic fungal volatiles. *Biological Control*, 55 (3): 166-173.

Hynes J., C.T. Müller, T.H. Jones & L. Boddy, 2007. Changes in volatile production during the course of fungal mycelial interactions between *Hypholoma fasciculare* and *Resinicium bicolor*. *Journal of Chemical Ecology*, 33: 43-57.

Keszler Á., E. Forgács, L. Kótai, J.A. Vizcaíno, E. Monte & I. García-Acha, 2000. Separation and identification of volatile components in the fermentation broth of *Trichoderma atroviride* by solid phase extraction and gas chromatography-mass spectrometry. *Journal of Chromatographic Science*, 38: 421-424.

Korpi A., J. Järnberg & A.L. Pasanen, 2009. Microbial volatile organic compounds. *Critical Reviews in Toxicology*, 39 (2): 139-193.

Krajaejun T., T. Lowhnoo, T. Rujirawat, W. Yingyong, S. Fucharoen & G.A. Strobel, 2012. In vitro antimicrobial effect of the volatile organic compounds from *Muscodor crispans* against the human pathogenic oomycete-*Pythium insidiosum*. *Southeast Asian Journal of Tropical Medicine and Public Health*, 43 (6): 1474-1483.

Kudalkar P., G. Strobel, S. Riyaz-Ul-Hassan, B. Geary & J. Sears, 2012. *Muscodor sutura*, a novel endophytic fungus with volatile antibiotic activities. *Mycoscience*, 53 (4): 319-325.

Kuske M., A.C. Romain & J. Nicolas, 2005. Microbial volatile organic compounds as indicators of fungi. Can an electronic nose detect fungi in indoor environments? *Building and Environment*, 40 (6): 824-831.

Lacey L.A. & L.G. Neven, 2006. The potential of the fungus, *Muscodor albus*, as a microbial control agent of potato tuber moth (Lepidoptera: Gelechiidae) in stored potatoes. *Journal of Invertebrate Pathology*, 91: 195-198.

Lee S., R. Hung, M. Yap, & J.W. Bennett, 2015. Age matters: the effects of volatile organic compounds emitted by *Trichoderma atroviride* on plant growth. *Archives of Microbiology*, 197 (5): 723-727.

Lemfack M.C., J. Nickel, M. Dunkel, R. Preissner & B. Piechulla, 2014. mVOC: a database of microbial volatiles. *Nucleic Acid Research,* 42: 744-748.

Li Q., L. Wu, J. Hao, L. Luo, Y. Cao & J. Li, 2015. Biofumigation on post-harvest diseases of fruits using a new volatile-producing fungus of *Ceratocystis fimbriata*. *PlosOne*, 10 (7): 1-16.

Liarzi O., P. Bucki, S. Braun Miyara & D. Ezra, 2016a. Bioactive volatiles from an endophytic *Daldinia* cf. *concentrica* isolate affect the viability of the plant parasitic nematode *Meloidogyne javanica*. *PlosOne*, 11 (12): 1-17.

Liarzi O., E. Bar, E. Lewinsohn & D. Ezra, 2016b. Use of the endophytic fungus *Daldinia cf. concentrica* and its volatiles as bio-control agents. *PlosOne*, 11 (12): 1-18.

Macías-Rubalcava M.L., R.E. Sánchez-Fernández, G. Roque-Flore, S. Lappe-Oliveras & Y.M. Medina-Romero, 2018. Volatile organic compounds from *Hypoxylon anthochroum* endophytic strains as postharvest mycofumigation alternative for cherry tomatoes. *Food Microbiology*, 76: 363-373.

McCarter J.P., 2008. Molecular approaches toward resistance to plant-parasitic nematodes (Editors: Berg, R.H., Taylor, C.G., Cell Biology of Plant Nematode Parasitic, Plant Cell Monographs), Springer, 239-267.

Medina-Romero Y.M., G. Roque-Flores & M.L. Macías-Rubalcava, 2017. Volatile organic compounds from endophytic fungi as innovative postharvest control of *Fusarium oxysporum* in cherry tomato fruits. *Applied Microbiology and Biotechnology*, 101: 8209-8222.

Meena M., P. Swapnil, A. Zehra, M.K. Dubey & R.S. Upadhyay, 2017. Antagonistic assessment of *Trichoderma* spp. by producing volatile and non-volatile compounds against different fungal pathogens. *Archives of Phytopathology and Plant Protection*, 50 (13-14): 629-648.

Mercier J. & J.I. Jiménez, 2004. Control of fungal decay of apples and peaches by the biofumigant fungus *Muscodor albus. Postharvest Biology and Technology*, 31: 1-8.

Mercier J. & D.C. Manker, 2005. Biocontrol of soil-borne diseases and plant growth enhancement in greenhouse soilless mix by the volatile-producing fungus *Muscodor albus*. *Crop Protection*, 24: 355-362.

Meruva N.K., J.M. Penn & D.E. Farthing, 2004. Rapid identification of microbial VOCs from tobacco molds using closed-loop stripping and gas chromatography/time-offlight mass spectrometry. *Journal of Industrial Microbiology & Biotechnology*, 31: 482-488.

Meshram V., N. Kapoor & S. Saxena, 2013. *Muscodor kashayumsp. nov*.–a new volatile anti-microbial producing endophytic fungus. *Mycology*, 4 (4): 196-204.

Morath S.U., R. Hung & J.W. Bennett, 2012. Fungal volatile organic compounds: A review with emphasis on their biotechnological potential. *Fungal Biology Reviews*, 26: 73-83.

Naher L., U.K. Yusuf, A. Ismail & K. Hossain, 2014. *Trichoderma* spp.: A biocontrol agent for sustainable management of plant diseases. *Pakistan Journal of Botany*, 46 (4): 1489-1493.

Naik B. S., 2018. Volatile hydrocarbons from endophytic fungi and their efficacy in fuel production and disease control. *Egyptian Journal of Biological Pest Control*, 28: 1-9.

Naznin H.A., D. Kiyohara, M. Kimura, M. Miyazawa & M Shimizu, 2014. Systemic Resistance Induced by Volatile Organic Compounds Emitted by Plant Growth Promoting Fungi in *Arabidopsis thaliana*. *PlosOne*, 9 (1): 1-10.

Nemčovič M., L. Jakubíková, I. Víden & F. Vladimír, 2008. Induction of conidiation by endogenousvolatile compounds in *Trichoderma* spp. *FEMS Microbiology Letters*, 284: 231-236.

Noling J.W., 2002. The practical realities of alternatives to methyl bromide: concluding remarks. *Phytopathology*, 92: 1373-1375.

Oka K., A. Ishihara, N. Sakaguchi, S. Nishino, R.Y. Parada, A. Nakagiri & H. Otani, 2015. Antifungal activity of volatile compounds produced by an edible mushroom *Hypsizygus marmoreus* against phytopathogenic fungi. *Journal of Phytopathology*, 163: 987-996.

Park M.S., J. Ahn, G.J. Choi, Y.H. Choi, K.S. Jang & J.C. Kim, 2010. Potential of the volatile-producing fungus *Nodulisporium* sp. CF016 for the control of postharvest diseases of apple. *The Plant Pathology Journal*, 26: 253-259.

Pinches S.E. & P. Apps, 2007. Production in food of 1, 3-pentadiene and styrene by Trichoderma species. *International Journal of Food Microbiology*, 116: 182-185.

Petrini O., 1991. Fungal endophytes of tree leaves (Editors: Andrews, J.H. and S.S. Hirano, Microbial Ecology of Leaves), Springer-Verlag, New York, USA,179-197.

Rasmann S., T.G. Köllner, J. Degenhardt, I. Hiltpold, S. Toepfer, U. Kuhlmann, J. Gershenzon & T.C.J. Turlings, 2005. Recruitment of entomopathogenic nematodes by insect-damaged maize roots. *Nature*, 434: 732-737.

Reino J.L., R.F. Guerrero, R. Hernández-Galán & I.G. Collado, 2008. Secondary metabolites from species of the biocontrol agent *Trichoderma*. *Phytochemistry Reviews*, 7 (1): 89-123.

Reithner B., K. Brunner, R. Schuhmacher, P. Peissl, V. Seidl, R. Krska & S. Zeilinger, 2005. The G protein α subunit Tga1 of *Trichoderma atroviride* is involved in chitinase formation and differential production of antifungal metabolites. *Fungal Genetic Biology*, 42: 749-760.

Riga E., L.A. Lacey & N. Guerra, 2008. *Muscodor albus*, a potential biocontrol agent against plant-parasitic nematodes of economically important vegetable crops in Washington State, USA. *Biological Control*, 45 (3): 380-385.

Rouissi W., L. Ugolini, C. Martini, L. Lazzeri & M. Mari, 2013. Control of postharvest fungal pathogens by antifungal compounds from *Penicillium expansum*. *Journal of Food Protection*, 11: 1879-1993.

Sánchez-Fernández R.E., D. Diaz, G. Duarte, P. Lappe-Oliveras, S. Sánchez, & M.L. Macías-Rubalcava, 2016. Antifungal volatile organic compounds from the endophyte

Nodulisporium sp. strain GS4d2II1a: a qualitative change in the intraspecific and interspecific interactions with *Pythium aphanidermatum*. *Microbial Ecology*, 71 (2): 347-364.

Sasser J.N., 1980. Root-knot nematodes Meloidogyne: a global menace to crop production [Includes activities and principal research findings of the International Meloidogyne Project (IMP)]. *Plant Disease*, 64: 36-41.

Schalchli H., E. Hormazabal, J. Becerra, M. Birkett, M. Alvear, J. Vidal, & A. Quiroz, 2011. Antifungal activity of volatile metabolites emitted by mycelial cultures of saprophytic fungi. *Chemistry and Ecology*, 27 (6): 503-513.

Schalchli H., E. Hormazábal, J. Becerra, G. Briceño, V. Hernández, O. Rubilar & M.C. Diez, 2015. Volatiles from white-rot fungi for controlling plant pathogenic fungi. *Chemistry and Ecology*, 31 (8): 754–763.

Schmidt R., D.W. Etalo, V. de Jager, S. Gerards, H. Zweers, W. de Boer & P. Garbeva, 2016. Microbial small talk: Volatiles in fungal–bacterial interactions. *Frontiers in Microbiology*, 6: 1-11.

Stinson A.M., N.K. Zidack, G.A. Strobel & B.J. Jacobsen, 2003. Mycofumigation with *Muscodor albus* and *Muscodor roseus* for control of seedling diseases of sugar beet and Verticillium wilt of eggplant. *Plant Disease*, 87: 1349-1354.

Stoppacher N., B. Kluger, S. Zeilinger, R. Krska & R. Schuhmacher, 2010. Identification and profiling of volatile metabolites of the biocontrol fungus *Trichoderma atroviride* by HS-SPME-GC-MS. *Journal of Microbiological Methods*, 81 (2): 187-193.

Strobel G.A., E. Dirkse, J. Sears & C. Markworth, 2001. Volatile antimicrobials from *Muscodor albus*, a novel endophytic fungus. *Microbiology*, 147 (11): 2943-2950.

Strobel G, 2011. *Muscodor* species-endophytes with biological promise. *Phytochemistry Reviews*, 10 (2): 165-172.

Terra W.C., V. P. Campos, S.J. Martins, L.S.A. S. Costa, J.C. Pereira da Silva, A.F. Barros, L.E. Lopez, T.C.N. Santos, G. Smant & D.F. Oliveira, 2018. Volatile organic molecules from *Fusarium oxysporum* strain 21 with nematicidal activity against *Meloidogyne incognita*. *Crop Protection*, 106: 125-131.

Wang A., M. Haapalainen, S. Latvala, M. Edelenbos & A. Johansen, 2018. Discriminant analysis of volatile organic compounds of *Fusarium oxysporum* f. sp. *cepae* and *Fusarium proliferatum* isolates from onions as indicators of fungal growth. *Fungal Biology*, 122: 1013-1022.

Wang Y., Y. Li, J. Yang, J. Ruan & C. Sun, 2016. Microbial volatile organic compounds and their application in microorganism identification in foodstuff. *Trends in Analytical Chemistry*, 78: 1-16.

Wheatley R.E, C. Hackett, A. Bruce & A. Kundzewicz, 1997. Effect of substrate composition on production of volatile organic compounds from *Trichoderma* spp. Inhibitory to wood decay fungi. *International Biodeterioration and Biodegredation*, 39: 199-205.

Wheatley R.E., 2002. The consequences of volatile organic compound mediated bacterial and fungal interactions. *Antonie van Leeuwenhoek*, 81: 357-364.

Yang Z., Z. Yu, L. Lei, Z. Xia, L. Shao, K. Zhang & G. Li, 2012. Nematicidal effect of volatiles produced by *Trichoderma* sp. *Journal of Asia-Pacific Entomology*, 15 (4): 647-650.

Zhang Q., L. Yang, J. Zhang, M. Wu, W. Chen, D. Jiang & G. Li, 2015. Production of anti-fungal volatiles by non-pathogenic *Fusarium oxysporum* and its efficacy in suppression of *Verticillium* wilt of cotton. *Plant Soil*, 392: 101-114.