Antifungal activity of metabolites from *Trichoderma spp.* against *Fusarium oxysporum*

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Abstract: The *Trichoderma* genus is well known as one of the most valuable biological control agents against several phytopathogens used in different plant species. Managing phytopathogenic fungi using the *Trichoderma* genus through various associated antifungal mechanisms is a sustainable and eco-friendly strategy that reduces the harmful presence of pathogens in soil, roots and aerial parts of plants. However, using biocontrol agents combined with chemical pesticides has evidenced further potential to reduce pathogen growth and benefit plant development. A better characterization of active metabolites secreted by *Trichoderma* and their mechanisms of action is necessary to improve its use as a biocontrol agent.

This review summarizes current evidence on *Trichoderma spp.*, used as a biocontrol against *Fusarium oxysporum*, the active secondary metabolites secreted by the former fungi, and the effect of three widely used agrochemicals to control the latter, namely Mancozeb, Chlorothalonil, and Propiconazole. A total of 155 studies were selected and used to extract information that was analyzed, resulting in more than 590 identified secondary metabolites. Fifty-four percent of these have at least one biological function. Results highlight the potential of *T. harzianum* and *T. reesei* as biological control agents to control *Fusarium oxysporum*. The antifungal activity of *T. Espirale* is associated with enzymatic reactions. Additional findings show that management of diseases caused by *F. oxysporum* can be combined by using *Trichoderma* as biological control and agrochemicals to reach: (1) higher access to the different plant tissues; (2) higher degradation of the cell wall; and (3) and activation of oxidative metabolism of *Trichoderma*.

Key words: *Trichoderma*, secondary metabolites, fungicide, mycoparasitism, biocontrol, *Fusarium oxysporum*.

Introduction

*Fusarium oxysporum* is one of the most economically important phytopathogens when referring to agriculturally important crops such as bananas and other crops. The fungus infects the host plant through the roots or stems, causing wilt, blight, rot, and cancer of many plant species leading to significant yield loss in economically important crops such as banana, onion, tomato, chilli, watermelon, cabbage, ginger, chick pea, soybean, eggplant, and ornamental plants like Chrysanthemum spp., Dianthus spp., Gerbera spp., Gladiolus spp. and Lilium spp. No curative control method is currently available against this pathogen. Current approaches to control *F. oxysporum* infestation are based on prophylactic measures and cultural practices like keeping tools, soils and substrates in good sanitary conditions, planting resistant or tolerant genotypes, paying particular attention to crop monitoring, appropriate management of irrigation and crop rotation.

Chemical fungicides have also been essential in managing *Fusarium oxysporum* wilt for decades. However, these chemical control agents often become ineffective since pathogens may develop resistance, and the chemicals may adversely affect soil fertility and accumulate in the crop. Since chemical pesticides are not selective, they can influence many beneficial non-target biotas and potentially harm the farmer’s health. Due to the harmful effects of these products, different policies that limit pesticide use have been implemented in several nations in the world.

Alternatively, biocontrol agents aim to regulate the growth of the pathogen with less harm to the plant and farmers. In this line, mycopesticides are exciting products because they use several mechanisms of action that reduce plant disease caused by phytopathogenic fungi. Biopesticides are often less toxic than chemical products and decompose quickly. This can avoid pollution problems, resistance and residue concerns. Biopesticides generally affect only the target pest and closely related organisms, thereby protecting other organisms living in the same environment. The commercial evolution of the biopesticide market is promising to be a potential tool for pathogen control with a current annual growth rate of 14.1%.

*Trichoderma* spp. comprises more than 200 validly described species distributed in soils worldwide and across various habitats and are considered a valuable resource for structurally novel natural products with diverse bioactivities, including biological control of phytopathogens. In the interest of obtaining more effective methods of pathogen control, plant growth-promoting rhizosphere microorganisms have been used as a consortium or in combination with chemical pesticides by our group and other authors. Bioassays have revealed great potential to improve current methods of managing antifungal treatments to plant culti-
vars. Yet, summarized evidence about active metabolites and the mechanism of actions of both biocontrol agents and chemical pesticides is needed to better use this possibility.

In this work, we reviewed the use of *Trichoderma* spp. as a biocontrol agent and the secondary metabolites and enzymes that have been characterized as active molecules. As additional findings, we also summarized the antifungal activity of commercial fungicides Mancozeb, Chlorothalonil, and Propiconazole, which are often used to control plant diseases caused by *F. oxysporum*.

**Narrative Findings on *Trichoderma* spp**

*Trichoderma* is a genus that belongs to the family Hypocreaceae and comprises many different fungi strains found in most diverse ecosystems[19]. *Trichoderma* strains proliferate and have a characteristic morphology, white and cottons at the beginning, then developing into yellowish green to deep green compact tufts. *Trichoderma* strains are characterized to the family Hypocreaceae and comprises many different fungi strains found in most diverse ecosystems[19]. *Trichoderma* strains proliferate and have a characteristic morphology, white and cottons at the beginning, then developing into yellowish green to deep green compact tufts. *Trichoderma* strains are characterized by the presence of active metabolites and lytic enzymes[3,31]. Myco-

Thus, current identification methods of the different functional groups within genetic tools and physiological activity are used to determine the active metabolites and enzymes. Examples have emerged as human pathogens, for example *T. longibrachiatum*, *Trichoderma* spp.

The Mechanisms of biological control by *Trichoderma* spp

*Trichoderma* act as biocontrol agents of phytopathogens and plant growth promoters[26]. They can also stimulate plant defense mechanisms against insect pests and be efficient soil bioremediation agents[27]. *Trichoderma* can also be used in waste/organic materials decomposition and polluted area detoxification[28]. Some examples have emerged as human pathogen, for example *T. longibrachiatum*. Consequently, while the studies on effective biocontrol fungal are ongoing, further research to avoid the risk for humans, plants, and other organisms contributed by *Trichoderma* spp. also need to be accomplished.

**The Mechanisms of biological control by *Trichoderma* spp**

Biological control by *Trichoderma* spp. is based on the activation of indirect and direct mechanisms. Direct and indirect mechanisms can act synergistically and depending on species and strain[29]. The indirect mechanisms are competition for space and nutrients, growth promotion, and systemic resistance induction. The mechanisms by which *Trichoderma* induces systemic resistance in plants vary depending on plant species. *Trichoderma* species, pathogen species, abiotic stress conditions, and culture methods. It has been shown that *Trichoderma* colonization of plant rhizosphere may simultaneously activate both systemic acquired resistance and induced systemic resistance mechanisms of the plant. *Trichoderma* is also found to induce the resistance of plants towards diseases by root architecture alteration during the interaction with pathogens[30].

Direct mechanisms are mycoparasitism and the production of active metabolites and lytic enzymes[31]. Mycoparasitism, the ability to parasitize on fungi, is a unique characteristic of *Trichoderma* since they can parasitize even taxonomically close species[39]. The antifungal activity of *Trichoderma* against phytopathogenic fungi is attributed to the combined action of secondary metabolites (SMs) and hydrolytic enzymes i.e., cellulases, proteases, chitinases, and xylanases[22-23]. About 500,000 secondary metabolites have been described; of these, 15,600 (47 %) are of fungal origin.

Characterization of genes involved in fungal–fungal interactions has indicated that are mainly those involved in signal transduction, fungal cell wall degradation, and production of secondary antifungal metabolites (SMs)[19].

**Secondary metabolites and enzymes produced by *Trichoderma* spp**

SMs are not essential for normal growth but are synthesized for specific environmental conditions. SMs can be either volatile or non-volatile organic compounds. Volatile SMs diffuse over a distance through systems in the soil affecting the physiology of competitor organisms[34-36]. Non-volatile SMs exert their activity through direct interactions between *Trichoderma* species and their antagonists[35].

Our search for current evidence on SMs secreted by *Trichoderma* spp. or enzymes resulted in annotating 590 unique compounds listed in the supplementary Table S1. It includes many structural classes like pyrones, butenolides, steroids, peptaibols and terpenoids[16]. Fifty-four percent of all SMs or enzymes retrieved in our search have at least one biological effect associated, described in Table S1. Even though this list of biological activities should not be considered exhaustive, it allows appreciation of the incredibly broad range of biological activities of *Trichoderma* SMs i.e., antifungal, antibacterial, antitumor, DPPH-radical-scavenging, positive effect on plant growth and development, among others (Table S1). Further investigation is required using isolated compounds to obtain a comprehensive understanding of all effects at different for the different combinations.

The list of SMs shown in supplementary Table S1 is consistent with previous papers that emphasize that the number and the number of volatile compounds detected are variable for each strain of *Trichoderma*. As example of the diversity in SMs produced by different *Trichoderma* species. A total of 115 SMs were reported for *T. reesei*, *T. harzianum* and *T. spirale* (Table S1). SM or enzymes identified for *T. reesei*, *T. harzianum* and *T. spirale* are indicated in Table 1, 2 and 3, respectively, which could be potentially used to control *Fusarium oxysporum*, due to their antifungal activity.

This result should not be understood as only *T. harzianum* secretes all these compounds. Genes encoding for proteins responsible for synthesizing these SMs are usually not expressed constitutively but due to interactions with the pathogen in the plant rhizosphere[40-41]. For example, the SM trichosetin, presumably secreted by *T. harzianum*, has only been identified in dual culture of *T. harzianum* and call of *Catharathus roseus* but not in single cultures. However, the vast diversity of SMs isolated and characterized from *T. harzianum* indicates the great potential value of this fungus as a biocontrol agent against phytopathogenic fungi.

In vitro and in vivo assays have shown *T. harzianum* isolates with higher inhibitory activity against *F. oxysporum* (F3) than other *Trichoderma* species[42]. Biocontrol potential of *T. harzianum* against *Fusarium Oxysporum* has been demonstrated in *in vivo* and *in vitro* against *F. oxysporum* in *Poplar*[43], ginger[44], *cucumber*[29-30], *lettuce*[45], *white yam*[50], *chili*[51], tomato and cucumber[52]. Nonetheless, *T. reesei* is one of the top fungal species used in industrial biotechnology and is used safely for decades in enzyme production. In contrast to *T. harzianum*, *T. reesei* is considered to have a limited production of mycotoxins[53]. Table 2 lists all SM associated with antifungal activity.

Despite the literature did not specifically listed the SMs
of *T. spirale* associated with the antifungal activity, it was worth to list the associated enzymes *Trichoderma spirale* (Table 3). This list is short but shows the potential use of *T. spirale* [A9] in the control of pathogenic fungi.

In this work, we reviewed the use of *Trichoderma spp.* as biocontrol agents, the secondary metabolites characterized as active molecules and the enzymes found in this bibliographic review which present antifungal characteristics that act directly on the phytopathogenic fungi. The following graph highlights the following strains of *Trichoderma spp.*, *T. reesei*, *T. harzianum* and *T. spirale* with the most critical metabolites and enzymes.

Additional findings on the use of *Trichoderma spp.* and 3 synthetic pesticides[A10]

The low input cost and higher crop productivity of applying biological control agents (or biopesticides) are the economic benefits observed when compared to synthetic pesticides[A10]. Thus, the use of *Trichoderma* is regarded as a sustainable approach not only ecologically but also from an economic perspective.

However, using microbial-based products as biocontrols or biostimulants has some disadvantages compared to their chemical counterparts. Microbial products have a limited shelf life and require special conditions for conser-
vation to maintain viability and efficacy44. Also, they have constraints due to dependency on the crop, geographical, and meteorological regimes and pathogens3,63.

One interesting approach that has emerged to cope with the advantages and limitations of the different methods to control crop infestation with F. oxysporum is the simultaneous application of Trichoderma as biological control with chemical pesticides and other biological control agents. For example, a combined treatment with T. polysporum LCB50 and irrigation with liquid compost applied resulted in a 100% increase in the productivity of commercial fruit64. Recent results from our group have shown a synergistic effect using T. reesei and Mancozeb, inhibiting the mycelial growth of F. oxysporum (F1)20. Also, a synergistic activity was obtained in vitro assays using T. reesei combined with Chlo.

Table 3. Enzymes associated with antifungal activity of Trichoderma spirale.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Enzymes associated with antifungal activity on Trichoderma Spirale</th>
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<tbody>
<tr>
<td>61</td>
<td>Chitinase</td>
</tr>
<tr>
<td>62</td>
<td>Endochitinase</td>
</tr>
<tr>
<td>37</td>
<td>Trichodermic acid</td>
</tr>
<tr>
<td>61</td>
<td>β-1,3-Glucanase</td>
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</table>

F. oxysporum fungus enters through the roots and disseminates throughout the plant using the vascular system. In contrast to chemical fungicides, Trichoderma fungi are part of the rhizosphere and generally grow on plant root surfaces and therefore control root diseases in particular65. Consequently, using Trichoderma as a biological control agent will provide an effective first barrier at the site of infection that will be complemented by the activity from top to bottom of chemical pesticides.

Previous work on Trichoderma spp. used as biocontrol agents have shown that cell wall degrading enzyme secreted by fungi i.e. chitinase, cellulase, protease, and β-(1-3) glucanase and peptaibols are produced concurrently during biocontrol and interact synergistically as antifungal agents66. The proposed mechanism for such an effect is based on the fact that enzymes degrade the cell wall of host fungal pathogens. This activity directly inhibits the growth of the pathogen, at the same time, facilitates the access of peptaibols to the cellular membrane. Peptaibols are small peptides of 15-20 residues characterized by non-standard amino acids in their sequences, with a special propensity for aminoisobutyric acid. The antimicrobial activity of peptaibols is related to their capacity to form pores in lipid membranes70.

The same synergistic effect has been described for the activity of cell wall degrading enzymes and other SMs targeting specific target molecules in inhibiting F. oxysporum by T. asperellum29. Table 4 summarizes SMs identified as present in extracts with potent antifungal activity against F. oxysporum; or assayed from purified preparations and with proven inhibitory activity against this phytopathogen. Yet, important differences have been reported in the activity of cell wall degrading enzymes for T. asperellum and T. harzianum29. Thus, this mechanism could not be similarly effective for all Trichoderma species.

A similar synergistic activity could explain the outcome observed by co-inoculating Trichoderma species with biocontrol capacity against F. oxysporum and Mancozeb, Chlo.

Systemic effects resulting from Trichoderma interaction with the plant would also contribute to the observed synergistic effect when used with chemical pesticides. Reactive oxygen species scavenging enzymes have been found significantly increased in plants treated with Trichoderma T-soybean, T. longibrachiatum and T. harzianum, thus improving plant resistance to oxidative stress10,11. Exposure of plants to pesticides has evidenced that most of these chemicals lead to the development of oxidative stress12. Also, root colonization by Trichoderma has been found to result in intensified levels of defense-related, including β-peroxidases
Figure 1. Secondary metabolites and enzymes associated with antifungal activity that stand out in *T. reesei*, *T. harzianum* and *T. spirale* strains identified in the literature review on using *Trichoderma* spp. as biocontrol agents against *Fusarium oxysporum*.
and hydroxide lyase of lipoxygenase-pathway of the plant. Moreover, it has been evidenced that *T. harzianum* alleviates oxidative stress by minimizing reactive oxygen species accumulation during *F. oxysporum* infection. Thus, the contribution to activating a systemic response to oxidative stress in plants could be another level of cooperative action between chemical and biological control agents to control the attack of this phytopathogenic fungus.

**Conclusions**

Deleterious effects caused by *F. oxysporum* on plant species cause significant economic losses in agriculture at domestic and industrial levels. This review presents an organized narrative of information starting with the antifungal mechanism of *Trichoderma*, listing the SMs and enzymes involved in these mechanisms and finally the potential synergy of 3 synthetic pesticides for a better control of *F. oxysporum*. Our findings suggest that there is a need to develop more effective and ecologically friendly methods of controlling *F. oxysporum*, compared to the current control methods. Both chemical and biological control agents have individually played important roles protecting crops for millennia. Also, both have advantages and disadvantages in their use. Thus, recent approaches have proposed the simultaneous use of chemical and biological pesticides and obtained promising results evidencing a synergistic activity controlling *F. oxysporum* infestation at *in vitro* and *in vivo* experiments. A better understanding of modes of action and cooperative effects of these two types of fungicide agents should let make better use of them in co-inoculation programs. The review of current knowledge on modes of action of *Trichoderma* in the control of *F. oxysporum* infection.

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Trichoderma isolate</th>
<th>Experiment</th>
<th>Reference</th>
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<tbody>
<tr>
<td>N-((tert-Butoxycarbonyl)-L-Valine*</td>
<td><em>T. asperellum</em> CCTCC-RW14</td>
<td><em>In vitro and in vivo</em> (greenhouse)</td>
<td>29</td>
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<tr>
<td>6-Dimethylamino-4-keto hexanoic acid*</td>
<td></td>
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<tr>
<td>1,3-Dioxolane-2-(3-bromo-5,5,5-trichloro-2,2-dimethylpentyl)*</td>
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<tr>
<td>1-Aminocyclopentanecarboxylic acid, N-ethoxycarbonyl-, heptyl ester*</td>
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<tr>
<td>2-[2-[2-Methoxyethoxy]ethoxy-1,3-dioxolane*</td>
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<tr>
<td>1,6-diphenylhexane-1,3,4,6-tetrone*</td>
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<tr>
<td>2-Octenoic acid*</td>
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<td>Methylmalonic acid*</td>
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<tr>
<td>Milbemycine B*</td>
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<tr>
<td>5-demethoxy-5-one-6,28-anhydro-25-ethyl-4-methyl-13-chloro-oxime*</td>
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<tr>
<td>Koninginin G</td>
<td><em>T. aureoviride</em></td>
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<tr>
<td>Cremenolide</td>
<td><em>T. cremeum</em></td>
<td><em>In vitro</em></td>
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<td>6-pentyl-α-pyrone</td>
<td><em>T. Harzianum</em>, <em>T. koningii and</em></td>
<td><em>In vitro</em></td>
<td>71,38</td>
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<tr>
<td>trichodermin</td>
<td><em>T. Harzianum</em></td>
<td><em>In vitro and in vivo</em></td>
<td>71</td>
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<td>farzianopyridone</td>
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<td>38</td>
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<td>8-dihydroxy-3-methylantraquinone</td>
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<tr>
<td>6-methyl-1,3,8-trihydroxyantraquinone</td>
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<td>6-methyl-1,3,8-trihydroxyantraquinone</td>
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<td>Koninginin B</td>
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<tr>
<td>Koninginin D</td>
<td>*T. koningiopsis, <em>T. harzianum, T. koningii, T. aureoviride</em></td>
<td><em>In vitro</em></td>
<td>71,38,67,31</td>
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<tr>
<td>Koninginin F</td>
<td><em>T. koningii, koningiopsis</em></td>
<td><em>In vitro</em></td>
<td>71,38</td>
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</table>

* denote compounds identified in extracts with antifungal activity.

Table 4. Metabolites identified in extracts, or purified, with antifungal activity against *Fusarium oxysporum*. CCTCC-RW14 is represented.
as well as the chemical fungicides Mancozeb, Chlorothalonil and Propiconazole confirms that their inhibitory activities may be compensatory and may lead to synergistic effects.

**Supplementary Materials**
Supplementary Table 1 (S1) is available under request.

**Author Contributions**
GMF, GL, VL and QG made substantial contributions conception and design, or acquisition of data, or analysis and interpretation of data. GMF and GL contributed drafting the article or revising it critically for important intellectual content. GMF and GL revised the final version of the manuscript before publication. GMF and GL ensures that any part of the work was appropriately investigated and resolved.

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Ethical review and approval were waived for this study because it does not involve humans or animals.

**Data Availability Statement**
Data is available fully in open access.

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**Conflicts of Interest**
The authors declare no conflict of interest.

**Bibliographic references**


7. Païlyzová A, Sokolová L. Metabolic profiling of Fusarium oxysporum f. sp. conglutinans race 2 in dual cultures with biocontrol agents Bacillus amyloliquefaciens, Pseudomonas aeruginosa, and Trichoderma harzianum. Published online 2019:779-787.


Trichoderma and the fate of Fusarium mycotoxins in microscales and mycotoxin treatment reveal antagonistic activities of
fungi with fungicidal metabolites suppress sclerotium disease. 178. doi:10.1016/j.aoas.2020.09.003
tomato response to rhizoctonia solani by Trichoderma harzia-
Li N, Afify A, Wang W, Nourollaì K. Volatile Compound-Medi-
ed Recognition and Inhibition Between Trichoderma Biocon-
Li MF, Li GH, Zhang KQ. Non-volatile metabolites from Trichoderma spp. Metabolites. 2019;9(3). doi:10.3390/meta-
30030100
Hu D, Yu S, Yu D, et al. Biogenic Trichoderma harzia-
num-derived selenium nanoparticles with control functional-
Manganiello G, Sacco A, Ercolano MR, et al. Modulation of tomato response to rhizoctonia solani by Trichoderma harzia-
num and its secondary metabolite harzianic acid. Front Micro-
Dini I, Marra R, Cavallo P, et al. Trichoderma strains and me-
Lombardi N, Salzano AM, Troise AD, et al. Effect of Trichoder-
ma Bioactive Metabolite Treatments on the Production, Quali-
Contreras-Corome HA, Macías-Rodríguez L, Del-Val E, Larsen J. Full Title: Ecological Functions of Trichoderma Sp. and Their Sec-
Damodaran T, Rajan S, Muthukumar M, et al. Biological Manage-
ment of Banana Fusarium Wilt Caused by Fusarium ox-
Redda ET, Mei J, Li M, Wu B, Jiang X. Biological Control of Solborne Pathogens (Fusarium oxysporum F. Sp. Cucumer-
um) of Cucumber (Cucumis sativus ) by Trichoderma sp. 2018;12:1-12. doi:10.17265/1934-7391/2018.01.001
Alamri SAM, Hashem M, Moustafa YS, Nafady NA, Abo-elyouser KM. Biological control of root rot in lettuce caused by Exserohilum rostratum and Fusarium oxysporum via induc-
Ao N, Vi G. Evaluation of Antagonistic Effect of Trichoder-
ma Harzianum against Fusarium oxysporum causal Agent of White Yam ( Dioscorearatundata pois ) Evaluation of An-
tagonistic Effect of Trichoderma Harzianum against Fusari-
Sinha A, Singh R, Verma A. Bioefcacy of Trichoderma harzia-
um and Trichoderma viride against Fusarium oxysporum f. sp. capsici causing wilt disease in chilli. ~ 965 ~ J Pharmacogn Phytochem. 2018;7(5). http://agriculture.gov.in
Frisvad JC. Safety of the fungal workhorses of industrial bio-
technology : update on the mycotoxin and secondary metab-
Frisvad JC. Safety of the fungal workhorses of industrial bio-
technology : update on the mycotoxin and secondary metab-
Persson KAM. Biological control of root rot in lettuce caused by Exserohilum rostratum and Fusarium oxysporum via induc-
Yang Z, Qiao Y, Li J, Wu FG, Lin F. A Novel Water-Soluble Photosensitizer for Photodynamic Inactivation of Gram-Posi-
tive Bacteria. doi:10.1101/2020.05.29.124768
Watts R, Daihyi J, Chaudhyi K, Tauro P. Isolation and char-
acterization of a new antifungal metabolite of Trichoderma re-
Pachauri S, Sherkanade PD, Mukherjee PK. Secondary Me-
tabolism in Trichoderma: Chemo- and Geno-Diversity BT - Microbial Diversity in Ecosystem Sustainability and Biotech-


63. Lombardi N, Salzano AM, Troise AD, et al. E ff ect of Trichoderma Bioactive Metabolite Treatments on the Production, Quality, and Protein Pro fi le of Strawberry Fruits. Published online 2020. doi:10.1021/acscjf.0c01438


69. Woo S, Fogliano V, Scala F, Lorto M. Synergism between fungal enzymes and bacterial antibiotics may enhance biocontrol. Published online 2002-353-356.


