

# *Trichoderma longibrachiatum*'s Secondary Metabolite-A Review on Potential Compounds for Plant Growth and Biological Control for Plant Pathogens

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## ABSTRACT

Indeed, a significant amount of agricultural production has been lost due to plant diseases that were caused by phytopathogens. Chemical pesticides are applied to protect the crops from the reduce substantial yield loss. Improved crop yields have been achieved for a long time through the use of synthetic chemical pesticides. However, the use of these pesticides may one day be limited due to their negative effects on human health and the environment. Global ecological awareness of the use of natural products and microorganisms to manage plant diseases has led to the use of beneficial antagonistic bacteria and fungi in different methods. Several microorganisms limit pathogen growth or indirectly increase plant-mediated resistance. *Trichoderma* is one of the most effective biological control agents for soil and foliar diseases. The *Trichoderma* spp., biocontrol potential depends on number of mechanisms such as antibiosis, mycoparasitism and the host induced systemic resistance. As typically recognised saprophytic fungi, *Trichoderma* species generate and exude a wide range of secondary metabolites into their environment while having little nutritional requirements. The non-ribosomal peptides (peptobiotics, siderophores, gliotoxin and gliovirin), polyketides, terpenes, pyrones and isocyanine are some of the *Trichoderma* spp., derived secondary metabolites. These metabolites are associated in different biological activities like biocontrol activities and or microbial interactions. Since, it's becoming more important to extract these molecules from safer, biodegradable antifungal solutions, which may be the next generation of biological pesticides, studies on *Trichoderma*'s antifungal active components are intensifying. This article is reviewed particularly about the major secondary metabolites that are produced by the beneficial fungus *Trichoderma longibrachiatum* and enhance the present knowledge on the potential compounds for plants.

## KEYWORDS

Secondary metabolites, *Trichoderma longibrachiatum*, bio synthesis, structural overview, volatile organic compounds, antifungal activities

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## INTRODUCTION

Phytopathogens cause major damage and losses, affecting agricultural production. Chemical fungicides, disease-resistant cultivars and other cultural practices are used to manage fungal plant diseases. Overuse of chemical fungicides directly threatens human, animal and environmental health. Because pesticides have the potential to affect the microbial communities linked with plants in the soil, it is essential to look for environmentally acceptable alternatives. Decades have passed since the invention of microbiological tools and biocontrol agents, such as bacteria and fungi as biocontrol agents that are microbial inoculants to replace insecticides. Live organisms suppress plant pathogen populations through biological control. A microbe's ability to create antibiotics or enzymes that lyse microbial cell walls, deplete iron from the nearby plant root system, develop disease resistance or compete with pathogens for niches in the rhizosphere are all examples of how they can exert biocontrol. Because they can boost crop growth and the availability and uptake of nutrients. The microbial based biocontrol agents are tools that hold great promise for the development of sustainable agriculture. Microbial biological control agents (MBCAs) are applied to crops to manage plant diseases. Products containing *Trichoderma* spp., are widely used because these fungi reduce disease and nematode population on host plants soils, mitigating abiotic stress. The *Trichoderma* sp. are being antagonistic towards *Fusarium* sp., *Pythium* sp. and *Sclerotium rolfsii*, *Rhizoctonia* sp. and also has the ability to suppress the growth of wood-rotting fungus, including *Botrytis* sp., *Verticillium* sp., *Sclerotia* sp. and *Gaeumannomyces* sp. Secondary metabolites of mycoparasitic fungi will contribute to the discovery of new antagonistic substances in the future. The most varied group of phytopathogens, fungi, have a significant impact on agriculture. The pathogenic fungus can become resistant to fungicides and infect new hosts due to their extensive genetic flexibility and broad-spectrum lifecycles. Resistance to compounds that have already been applied is a growing concern in agriculture, so there is an urgent need for the discovery of environmentally sustainable new antagonistic substances for controlling diseases. As a result, new management techniques are required to combat pathogenic fungi. Secondary metabolites from *Trichoderma* spp., have been used to protect plants from a number of phytopathogens in an efficient and effective manner. The phytopathogenic secondary metabolites from *Trichoderma longibrachiatum* were presented in this review. This article has covered a few aspects of the structural overview of secondary metabolites and the biogenesis of these molecules and also discussed overview of the secondary metabolites that are produced by *Trichoderma longibrachiatum*.

**Mycoparasitic fungi:** In order to improve their fitness and chances of survival, mycoparasitic fungi that feed on other fungi produce both volatile and non-volatile secondary metabolites. The excretion of siderophores, which result in high affinity iron chelation, is significantly upregulated in iron-limiting situations. Several antimicrobial metabolites also support in the persistence of ecological niches<sup>1,2</sup>. Due to the mycoparasitic lifestyle, there is substantial excretion of secondary metabolites and overrepresentation of genes related to secondary metabolism, which enables the fungus to access its prey and either survive in or kill the host<sup>3</sup>.

Additionally, certain fungal secondary metabolites have been shown to have positive effects on plants, including promoting root and shoot vitality and growth, enhancing the plant's resistance to abiotic stresses and activating its immune system are both outcomes of this process (induced systemic resistance, ISR) to enhance resistance and chances of being able to survive the threat of possible diseases caused by pathogens<sup>4</sup>. Evidence has recently accumulated that several secondary metabolites also function as molecules of communication across species boundaries<sup>5-6</sup>. The fungi kingdom is home to a wide variety of mycoparasitic species, particularly those belonging to the order Hypocreales<sup>7</sup>. *Trichoderma* (teleomorph hypocrea), a widespread, diversified fungus genus, is one of the most well-studied instances in this regard<sup>3</sup>. Necrotrophic mycoparasitic species of *Trichoderma* are used successfully in agriculture as biocontrol agents against agricultural plant pathogenic fungus. In addition to this, it is considered that they improve the immune systems of plants and encourage growth, vigour and resistance across the entire system. Because different species, ecological conditions and each strain of *Trichoderma* can give rise to a diverse set of chemical byproducts (Fig. 1), there is reason to be optimistic about the possibility of the discovering novel compounds<sup>1,3</sup>.

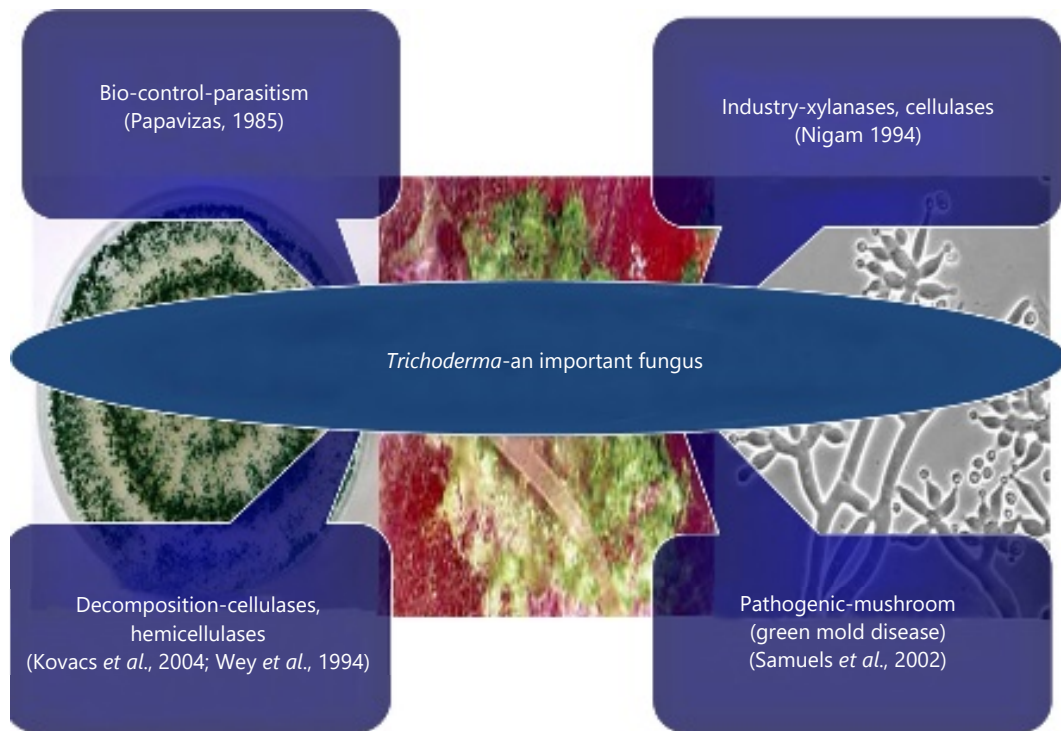


Fig. 1: Multiple activities of genus *Trichoderma* spp.

**Secondary metabolites:** Microorganism-derived secondary metabolites (SMs) may have an antifungal effect on economically significant phytopathogenic fungi<sup>8</sup>. Fungi are responsible for the production of 42% of the approximately 23,000 identified microbial secondary metabolites that serve as important sources for medicines with therapeutic applications<sup>9,10</sup>. Researchers have shown that fungus and fungal metabolites may be useful in preventing and treating plant illnesses brought on by fungal pathogens. *Trichoderma* spp., are among the fungi that have received the most attention from researchers and are now used in clinical settings due to the diverse spectrum of antimicrobial SMs that they produce<sup>11,12</sup>. *Trichoderma* species produce a multitude of metabolites that are then secreted into their environment while having very few dietary requirements. This review article recognized the value of these metabolites due to their potential use in agriculture, industry and medicine. *Trichoderma* spp., despite their low dietary demands, produce an abundance of secondary metabolites (SMs) that have antifungal effects against phytopathogenic fungi. These SMs include terpenes, pyrones, gliotoxin, gliovirin and peptaibols<sup>11,13,14</sup>. Various secondary metabolites, including viridin, harzianolide, glioviridin and growth promoting inducers (IAA, auxins, etc.), have been linked to the success of *Trichoderma* species as plant growth promoters<sup>15</sup>. Other fungus produces useful VOCs through various methods that influence biological regulation, trigger defense reactions and stimulate plant growth<sup>16</sup>.

***Trichoderma longibrachiatum*:** A member of the anamorphic genus *Trichoderma*, clade Longibrachiatum, order Sordariomycetes, family Hypocreaceae and phylum Sordariomycetes, *Trichoderma longibrachiatum* is found among the hypocrealean fungi<sup>21</sup>. There have been reports of several strains of *T. longibrachiatum* that show promise as possible biocontrol agents against plant diseases caused by fungi, bacteria and nematodes<sup>17,21-25</sup>. *T. longibrachiatum* has been used to get proteins, quinones and triterpenoids, which are all new antibiotics. This resulted in the realization that *T. longibrachiatum* could be a source of new antibiotics (Table 1)<sup>17-20,26</sup>. One of the most recent biocontrol fungi to be examined is *Trichoderma longibrachiatum*. A number of new volatile and nonvolatile metabolites, including proteins, quinones and hydrocarbons, have so far been discovered in different strains. Due to this,

Table 1: Secondary metabolites secreted by *Trichoderma* species

Compound	Source	Activity	References
Trichothecinol A, 8-deoxy-trichothecin, trichothecin B 10-cycloneren-3,5,7-triol, 10(E)-cyclonerotriol Trichodermene A	Isolated from the root of <i>Suaeda glauca</i> , a highly halophile plant	Potent antifungal activity Moderate nematocidal activity Potent antifungal activity	Du <i>et al.</i> <sup>17</sup>
Deoxytrichodermaerin	Isolated from marine red alga <i>L. okamurai</i>	Potent antimicrobial activity	Zou <i>et al.</i> <sup>18</sup>
Homodestcardin, trichomide B, homodestruxin B	Isolated from the root of <i>Suaeda glauca</i>	Moderate nematocidal activity	Du <i>et al.</i> <sup>17</sup>
Peptide-Trichokonin VI (Tk VI)		Inhibits primary root growth in <i>A. thaliana</i> (plant-microbe interactions)	Shi <i>et al.</i> <sup>19</sup>
Mycoparasitism-related metabolites Bisorbicillinoid-Bisvertinolone		Antifungal properties via inhibition of $\beta$ -(1,6)-glucan biosynthesis	Kontani <i>et al.</i> <sup>20</sup>

*T. longibrachiatum* has gained recognition as a potential source of novel antibiotics and as a helpful biocontrol agent against nematodes and bacteria that harm plants<sup>24,27</sup>. The growth of the pathogens was slowed down by these metabolites. *Trichoderma longibrachiatum*'s secondary metabolites, for instance, have been shown to be effective against *Candida albicans* and *Pyricularia oryzae*<sup>28</sup>. In addition to this, it was discovered that the secondary metabolites could stimulate protection against disease and modulate the growth of plants<sup>16</sup>.

*Trichoderma longibrachiatum* is a fungus that is typically isolated from terrestrial soil and plants. It has a wide range of potential antagonistic effects on plant pathogenic fungi, which can impede their growth. Regarding the antifungal substances obtained from *T. longibrachiatum*, they shown a strong antagonistic potential against the strains of *Botrytis cinerea* that are carbendazim-resistant, *Colletotrichum lagenarium*, *C. fragariae* and *Fusarium* spp.<sup>17,29-31</sup>.

The metabolites of *T. longibrachiatum* were recently found to have antifungal effects against two important pathogens *Sclerotium rolfii* and *Macrophomina phaseolina*. Many antifungal substances were released by *T. longibrachiatum* upon direct interactions with pathogens, (longifolene, 1-butanol 2-methyl, cedrene, caryophyllene and cuprenene). They function as intermediates in the biosynthesis of sesquiterpenoids, alkanes and the degradation of trimethylamine. Even more so, 1-pentanol, 1-hexanol, myristonyl-pantothenate, bisabolol, d-Alanine and diethyl trisulphide, attracts interest as a potentially effective antibacterial chemical with the added benefit of promoting plant growth<sup>16</sup>.

Multiple volatile organic compounds (VOCs) were detected in *T. longibrachiatum*, including monomers, esters, ketones, alkynes, esters, enzymes, carotenoids and a camphene derivative. Here, among the bioactive VOCs, epi-caryophyllene was identified as having antifungal and antioxidant activities, along with boosting seedling development & chlorophyll concentration<sup>32,33</sup>.

**Epipolythiodioxopiperazines:** Among secondary metabolites of fungi, epipolythiodioxopiperazines (ETPs) are distinguished by a diketopiperazine ring that derives from a peptide and have a high reactive potential. Since they are produced from protein hydrolysates, diketopiperazines (DKPs) are regarded as the byproduct of protein degradation and are often not desirable peptides. Epipolythiodioxopiperazines (ETPs) are toxic because they bind to proteins via disulphide bridges that generate reactive oxygen species via redox cycles, so rendering proteins inert<sup>34</sup>.

Because of their potent biological activities, scientists have focused their efforts increasingly towards DKP study in recent years. Numerous DKPs derived from microbes were identified and their biological functions investigated.

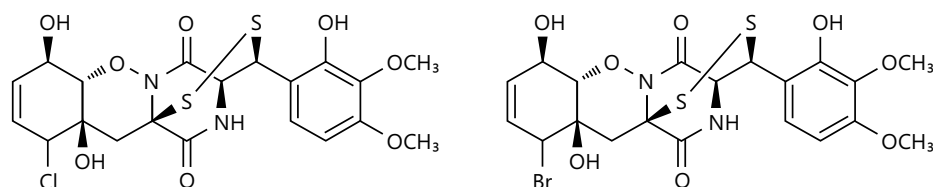


Fig. 2: Structures of gliovirin analogues derived from *Trichoderma longibrachiatum* diketopiperazines

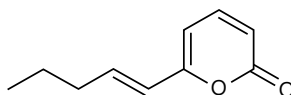


Fig. 3: Antifungal pyrone structures from the fungus *Trichoderma* spp.

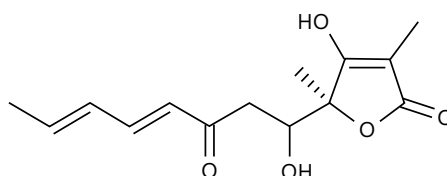


Fig. 4: Antimicrobial butenolide structures: *Trichoderma longibrachiatum* (5-hydroxyvertinolide)

The class of toxins known as epipolythiodioxopiperazines includes both gliovirin and gliotoxin, which share the characteristic disulphide bridges<sup>35</sup>.

*Trichoderma longibrachiatum* produced two gliovirin analogues (Fig. 2) which showed antifungal properties against *R. Solani*<sup>11</sup>.

**Pyrones:** The flavouring ingredient that gives coconut its distinctive aroma is called 6-pentyl-2H-pyran-2-one (6-PP) and studies have shown that it possesses antifungal and plant growth-promoting properties<sup>6</sup>. It belongs to the large class of molecules known as volatile organic compounds, which include many small molecule metabolites that have a high vapour pressure at room temperature and a low solubility in water (VOCs)<sup>36</sup>. A pyrone analogue (Fig. 3) was acquired from the fungi *Trichoderma harzianum* and *T. longibrachiatum* possess antimicrobial effects towards *Armillaria melanoma*<sup>37</sup>.

It was proposed that the synthesis of pyrones was caused by the oxidation of linoleic acid to 13-hydroperoxide-diene, followed by the formation of 5-hydroxy-2,4-decenoic acid and esterification<sup>38</sup>.

**Butenolides:** The 5-Hydroxyvertinolide (Fig. 4), an antifungal butenolide from the fungus *T. longibrachiatum*, was discovered to be antagonistic to the fungus *Mycenacitricolor*, the cause of coffee's American leaf spot disease<sup>39</sup>. Most likely, two Favorskii rearrangements of a C-14-diepoxyde are involved in the biosynthesis of these butenolides, with the two carbons that make up the lactone being driven out at the end.

**Sorbicillinoids:** A family of hexaketide fungal metabolites known as sorbicillinoids has a conventional or altered sorbyl side chain. The first found sorbicillin was in *Penicillium notatum* in 1948 as an impurity/contaminant and later in aquatic and terrestrial microbes found more than 100 sorbicillinoids (*Acremonium*, *Aspergillus*, *Clonostachys*, *Eurotiomycete*, *Penicillium*, *Phaeoacremonium*, *Phialocephala*, *Paecilomyces*, *Scytalidium*, *Trichoderma* and *Verticillium*)<sup>40-42</sup>.

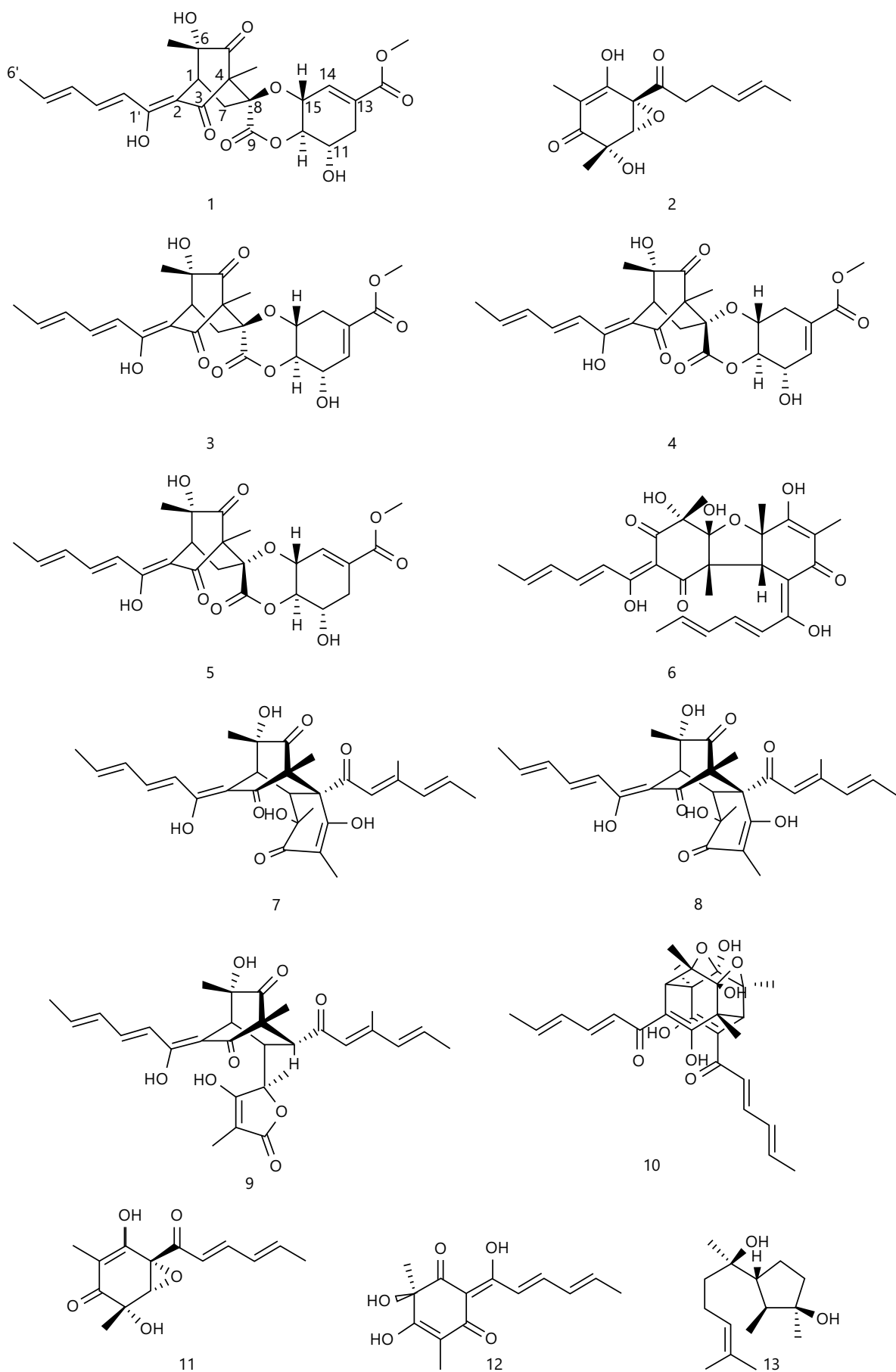


Fig. 5: Chemical compositions of compounds 1 to 13 discovered in *Trichoderma longibrachiatum* SFC100166

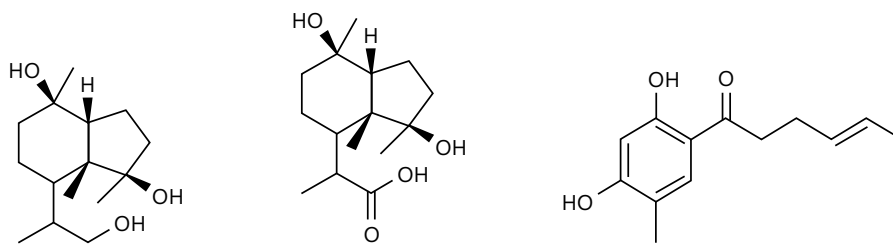


Fig. 6: 10,11-dihydrocyclonerotriol, catenioblin C and sohirnone A

The structural characteristics of different sorbicillinoids allow them to be divided into monomers, dimers, trimers and hybrids<sup>43,44</sup>.

There are 12 different sorbicillinoids in this study (Fig. 5), but they can be put into three different groups: Monomeric sorbicillinoids, dimeric sorbicillinoids and hybrid sorbicillinoids. Bisvertinolone, which is the strongest antifungal agent, is thought to be made in the body from oxosorbicillinol and sorbicillinol through a Michael-type reaction<sup>45</sup>. The investigated phytopathogenic fungi responded most favourably to the antifungal agents oxosorbicillinol, bisvertinolone and epoxysorbicillinol. Similar to this, it has been noted that bisvertinolone (6) inhibits b-1,6-glucan production in developing hyphal cells of *P. capsici*, causing morphological malformations to occur<sup>20</sup>. In this work, oxosorbicillinol (12) demonstrated a moderate antimicrobial activity against plant fungi such *Colletotrichum coccodes*, *Magnaporthe oryzae* and late blight causing fungus *Phytophthora infestans*<sup>46</sup>, with MIC values ranging from 25 to 400 g mL<sup>-1</sup>.

**Other compounds:** Three antifungal compounds were obtained from *Trichoderma longibrachiatum*, 10, 11-dihydrocyclonerotriol, catenioblin C and sohirnone A (Fig. 6), which have been demonstrated to exhibit antifungal activity against *Magnaporthe oryzae* and *C. albicans*<sup>27</sup>.

## CONCLUSION

The use of microbial antagonists for the biological management of plant pathogenic diseases is considered a potential alternative method. Potential fungal biocontrol agents against plant diseases include those belonging to the genus *Trichoderma*. There are hundreds of secondary metabolites known to be produced by useful fungi. Biocontrol fungi, including *Trichoderma* spp., secrete compounds that inhibit plant pathogens and are known to have a wide range of activities, including direct and indirect toxicity against plant diseases, activation of plant defences and stimulation of plant growth. Thus, treatment with *Trichoderma* metabolites considerably modifies the plant's expressome, transcriptome and metabolic activity by altering particular pathways involved in the generation of important hormones, biotic/abiotic stress resistance and nutrient uptake. In this study, we concentrated primarily on the compounds that were produced by *Trichoderma longibrachiatum* and that were involved in interactions with phytopathogenic agents that resulted in advantageous outcomes for agricultural production. An intriguing alternative to the use of insecticides could be the application of certain metabolites with the aim of inducing host resistance and/or improving crop productivity.

## SIGNIFICANCE STATEMENT

Among different biocontrol agents, *Trichoderma* species is well-studied and known for their ability to produce bioactive secondary metabolites such as polyketides, alkaloids, terpenoids and peptaibols against plant disease management. The secondary metabolites produced by *Trichoderma* have increased wide-ranging attention since they possess attractive chemical structures with notable biological activities. Certain species of the fungal genus *Trichoderma* are mycoparasites amongst them *T. longibrachiatum* has also been explored for use in combating fungal diseases on crops. The purpose of this review paper is to

succinctly review recent progress in the biopotential compounds of *T. longibrachiatum* and to provide a comprehensive overview with the secondary metabolites produced by *T. longibrachiatum* with emphasis on their chemistry and various bioactivities.

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