UNIVERSIDADE FEDERAL DE SÃO CARLOS
CENTRO DE CIÊNCIAS BIOLÓGICAS E DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM ECOLOGIA E RECURSOS NATURAIS

VIVIANE DE CASSIA PEREIRA ABDALLA

Endophytic fungi from *Serjania lethalis* A.St-Hil leaves and their phytotoxic potential

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Tese apresentada ao Centro de Ciências Biológicas e da Saúde da Universidade Federal de São Carlos, como parte dos requisitos para obtenção do título de Doutor em Ciências, área de concentração Ecologia e Recursos Naturais

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RESUMO GERAL

Os fungos endofíticos vivem assintomaticamente no interior dos órgãos vegetais sem lhes causar prejuízo. Estes fungos vivem em associação simbionte com as plantas e seu metabolismo secundário produz compostos que são utilizados por elas como mecanismo de defesa ao ataque de predadores e patógenos. Neste trabalho foram isolados 29 fungos endofíticos de folhas sadias de *Serjania lethalis*, uma liana pertencente à família Sapindaceae de ocorrência comum no cerrado brasileiro. Estes fungos foram caracterizados macro e microscopicamente e alguns gêneros puderam ser identificados com o auxílio de técnicas de biologia molecular. Este trabalho foi pioneiro no isolamento e identificação de endófitos desta espécie vegetal. Foram selecionados dois fungos para os estudos de avaliação do potencial fitotóxico, sendo uma *Alternaria* sp. e um *Diaporthe* sp. Para estes estudos foram inicialmente preparados dois extratos de cada fungo, um extrato micelial e um extrato de meio de cultura. O primeiro foi extraído com etanol e o segundo com acetato de etila. Também foi preparado um extrato de meio de cultura estéril. Inicialmente os extratos foram testados sobre o crescimento de coleóptilos de trigo (*Triticum aestivum*) a fim de selecionar os mais ativos e verificou-se que o extrato de meio de cultura de *Alternaria* sp e o extrato micelial de *Diaporthe* sp. foram os que apresentaram maior fitotoxicidade sobre o crescimento dos coleóptilos, quando comparados com o tratamento controle negativo (solução tampão). O extrato de meio de cultura estéril não foi ativo. Com os extratos mais ativos de cada fungo foram feitos ensaios de germinação de sementes, crescimento de plântulas e crescimento de células do metaxilema com as espécies invasoras *Euphorbia heterophylla* (amendoim-bravo) e *Megathyrsus maximus* (capim-colonião). Verificou-se que o extrato de meio de cultura de *Alternaria* sp foi fitotóxico para o crescimento de plântulas de *E. heterophylla.* O extrato micelial do fungo *Diaporthe* sp. diminuiu a porcentagem de germinação de sementes e o crescimento da raiz das plântulas de *M. maximus*. Também foi fitotóxico para o crescimento das plântulas de *E. heterophylla*. Tais extratos contém metabólitos secundários produzidos pelos fungos que são responsáveis por tais atividades. A fim de se conhecer os metabólitos presentes no extrato de meio de cultura de *Alternaria* sp., este extrato foi fracionado em coluna de sílica de fase normal e as frações foram analisadas por meio de espectrometria de massas (CLAE-EM) e ressonância magnética nuclear (RMN). Assim, foram identificados o ácido indol-3-

carboxílico e as dicetopiperazinas ciclo (Pro-Leu), ciclo (Pro-Val) e ciclo (Pro-Ile). Estes compostos foram testados sobre o crescimento de coleóptilos de trigo e os resultados indicaram que apenas o ácido indol-3- carboxílico (ICA) foi fitotóxico. A atividade fitotóxica do ICA foi melhor explorada realizando-se ensaios de germinação de sementes, crescimento de plântulas e de células do metaxilema de *E. heterophylla* e *M. maximus*. Foram utilizados como controles uma solução tampão e o ácido indoleacético (IAA), um hormônio vegetal que apresenta estrutura semelhante à do ICA. Verificou-se que o ICA afetou os parâmetros da germinação das duas espécies invasoras testadas, assim como o crescimento da parte aérea e raiz de *E. heterophylla* e da raiz de *M. maximus*. Os controles não afetaram nenhum dos parâmetros estudados. Foram feitas reações de esterificação do ICA com três diferentes álcoois, o metanol, etanol e hexanol, produzindo, respectivamente, os ésteres Methyl- Indol-3- carboxylate, Ethyl- Indol-3-carboxylate e Hexyl- Indol-3-carboxylate. A atividade fitotóxica dos três ésteres foi avaliada por meio do crescimento de coleóptilos de trigo e verificou-se que o aumento da cadeia de alquil promove um aumento da fitotoxicidade. O IC_{50} e o coeficiente de lipofilia foram medidos e juntos comprovam um menor valor de IC_{50} para os ésteres de maior cadeia e um maior índice de lipofilia para os mesmos. Assim, concluímos que o ICA, um metabólito secundário produzido pelo fungo endofítico de folhas de *S. lethalis*, foi fitotóxico para as espécies invasoras testadas e é um promissor agente fitotóxico natural.

Palavras-chave: fungos endofíticos; fitotoxicidade; herbicidas naturais; *Serjania lethalis*

GENERAL ABSTRACT

Endophytic fungi live asymptomatically within plant organs without causing them any harm. These fungi live in symbiotic association with plants, and their secondary metabolism produces compounds that are used by plants as a defense mechanism to attack predators and pathogens. In this work, 29 endophytic fungi were isolated from healthy mature leaves of *Serjania lethalis*, a liana belonging to the family Sapindaceae of common occurrence in the Brazilian cerrado. These fungi were characterized macro and microscopically, and some genera could be identified with the aid of molecular biology techniques. This work was a pioneer in the isolation, and identification of endophytes in this plant species. Two fungi were selected for the studies of evaluation of the phytotoxic potential, being them an *Alternaria* sp, and a *Diaporthe* sp. For these studies two extracts of each fungus were initially prepared, a mycelial extract, and an extract of culture medium. The former was extracted with ethanol, and the second with ethyl acetate. An extract of sterile culture medium was also prepared. Initially, the extracts were tested on the growth of wheat coleoptiles (*Triticum aestivum*) in order to select the most active ones, and it was verified that the extract of culture medium of *Alternaria* sp and the mycelial extract of *Diaporthe* sp. were those that presented greater phytotoxicity on the growth of the coleoptilos, when compared with the negative control treatment. The extract of sterile culture medium was not active. The most active extracts from each fungus were seed germination, seedling growth, and metaxilema cell growth experiments with the invasive species *Euphorbia heterophylla*, and *Megathyrsus maximus*. The extract of *Alternaria* sp culture medium was found to be phytotoxic for the growth of *E. heterophylla* seedlings. The mycelial extract of the fungus *Diaporthe* sp. decreased the percentage of seed germination, and growth of the root of *M. maximus* seedlings. It was also phytotoxic for the growth of *Euphorbia heterophylla* seedlings. Such extracts contain secondary metabolites produced by the fungi that are responsible for such activities. In order to know the metabolites present in the culture medium extract of *Alternaria* sp. This extract was fractionated on a normal phase silica column, and its fractions were analyzed by mass spectrometry (HPLC-MS), and nuclear magnetic resonance (NMR) Thus, indol-3-carboxylic acid and the diketopiperazines cycle (Pro-Leu), cycle (Pro-Val), and cycle (Pro-Ile) were identified. These compounds were tested on growth of wheat coleoptiles and the results indicated that only indole-3- carboxylic acid (ICA) was phytotoxic for wheat coleoptile growth. The phytotoxic activity of ICA was better explored by carrying out tests on seed germination, seedling growth, and metaxilema cells of *Euphorbia heterophylla* and *Megathyrsus maximus*. A buffer solution and indoleacetic acid (IAA), a plant hormone with a similar structure to ICA, were used as controls. It was verified that ICA affected the parameters of the germination of the two invasive species tested, as well as the growth of the aerial part and root of *E. heterophylla*, and the root of *M. maximus*. Controls did not affect any of the parameters studied. ICA esterification reactions were performed with three different alcohols, methanol, ethanol and hexanol, producing, respectively, the methyl esters Methyl-Indole-3-carboxylate, Ethyl-Indole-3-carboxylate, and Hexyl- Indole-3-carboxylate. The phytotoxic activity of the three esters was evaluated by growth of wheat coleoptiles, and it was found by increasing the alkyl chain, it promotes an increase in phytotoxicity. The IC_{50} and the lipophilicity coefficient were measured, and together they showed a lower IC_{50} value for the higher chain esters, and a higher lipophilicity index for them. Thus, we conclude that ICA, a secondary metabolite produced by the endophytic fungus of *Serjania lethalis* leaves, was phytotoxic to the invasive species tested, and it is a promising natural phytotoxic agent.

Keywords: endophytic fungi; phytotoxicity; natural herbicides; *Serjania lethalis*

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SUMMARY

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The phytotoxic potential of indole-3-carboxylic acid produced by *Alternaria* sp, an endophytic fungus from *Serjania lethalis*, and its derivatives

INTRODUCTION

The Kingdom Fungi

The fungi kingdom consists of mushrooms, yeasts, molds, truffles, and morels. They are an independent group of plants and animals. They are heterotrophs, and can be uni, or multicellular. The general characteristics of the fungi kingdom are: eukaryotic organisms; non-vascular; typically non-mobile; heterotrophs; chitin producers; they may be saprophytes, parasites, or symbionts; produce exoenzymes for digestion; sexual, and asexual reproduction (Trabulsi et al., 2008; Madigan et al., 2010).

The fungi kingdom contains seven phyla:

- Phylum Ascomycota: It is a monophyletic group (Bruns et al., 1992), and together with Basidiomycota form the Dikarya sub-kingdom (Schaffer, 1975). They are known as sac-fungi. They produce ascospores, which are nonmotile spores. It has commercial, medical, and agronomic importance (Lutzoni et al., 2004). They may be saproba, parasites or symbionts. The most common genera of ascomycetes are *Aspergillus*; *Penicillium*; *Tuber*; *Candida* and *Saccharomyces* (Hanlin, 1998). Figure (1) below illustrates a fungus of the genus *Penicillium*.

Figure 1. *Penicillium* fungus, representative of the Ascomycota Phylum (Source: http://www.airqualityassessors.com/Blog/TabId/256/Tag/penicillium/Default.aspx)

-Phylum Basidiomycota: Together with Ascomycota it forms a monophyletic group (Bruns et al., 1992). It is formed by macroscopic fungi, with a fruiting body, mushrooms, cup fungi, coral fungi among other forms (Lutzoni et al., 2004). Figure 2 shows a mushroom belonging to the genus *Amanita*.

Figure 2. Mushroom of the genus *Amanita*, representative of the Phylum Basidiomycota (Source: http://www.mykoweb.com/CAF/photos/Amanita_muscaria(fs-03).jpg)

- Phylum Blastocladiomycota: These are aquatic environment fungi (Sharma, 2005), traditionally treated as a member of Chytridiomycota. They display alternation of sporophytic, and gametophyte generations. They are saprotrophs, as well as parasites of fungi, algae, plants, and invertebrates, and may be optionally anerobic (James et al., 2006). Figure 3 illustrates a fungus of the genus *Allomyces.*

Figure 3. Fungus of the genus *Allomyces*, representative of the Phylum Blastocladiomycota (Source: http://micol.fcien.edu.uy/atlas/Allomycesmeio.JPG)

-Phylum Chytridiomycota: Composed by about 100 species described (James et al., 2006), this phylum has already been considered part of the protista kingdom because it presents mobile spores, or zoospores (Barr, 1990). They are found in aquatic environments (James et al., 2006), and terrestrial (Barr, 2001), and are distributed from the tropics to arctic regions (Powell, 1993). They can be parasites of vascular plants, such as chytridios of the genus *Synchytrium* that parasites potatoes (Abdullahi et al., 2005), and vertebrate parasites such as *Batrachochytrium dendrobatidis* (Longcore et al., 1999). Figure 4 shows a chytridium of the genus *Synchytrium*.

Figure 4. Fungus spores of the genus *Synchytrium*, representative of the Phylum Chytridiomycota (Source: http://comenius.susqu.edu/biol/202/fungi/chytridiomycota/synchytrium.htm

-Phylum Glomeromycota: Arbuscular mycorrhizal fungi (AMFs) were found in this phylum (Stürmer and Siqueira, 2006). In this case, company is welcome, especially phosphorus (P) that are promoted by fungal hyphae (Smith and Read, 2008). Their five known AMF families are *Gigasporaceae*, *Glomeraceae*, *Acaulosporaceae*, *Paraglomaceae*, and *Archaeosporaceae* (Stürmer and Siqueira, 2006). Some of the main genera are: *Acaulospora*, *Gigaspora*, *Rizhophagus*, *Septoglomus* and *Cetraspora* (IBG, 2018). Figure 5 shows a fungus of the genus *Acaulospora*.

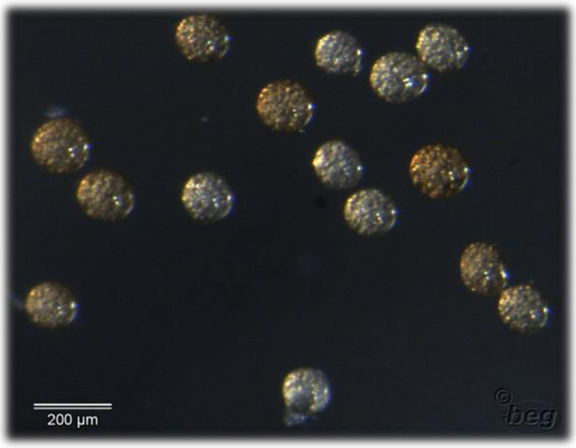


Figure 5. Spores of the fungus of the genus *Acaulospora*, representative of the Phylum Glomeromycota Source : http://www.i-beg.eu/)

-Phylum Microsporidia: This phylum owns the responsibility over intracellular parasitic fungi of animals, and they are triggers of diseases known as microsporidioses (Franzen and Müller, 1999). Some known genera are *Enterocytozoon, Encephalitozoon, Nosema, Pleistophora, Vittaforma, Trachipleistophora,* and *Brachiola.* Figure 6 shows spores of the fungus of the genus *Nosema*, which causes disease in bees.

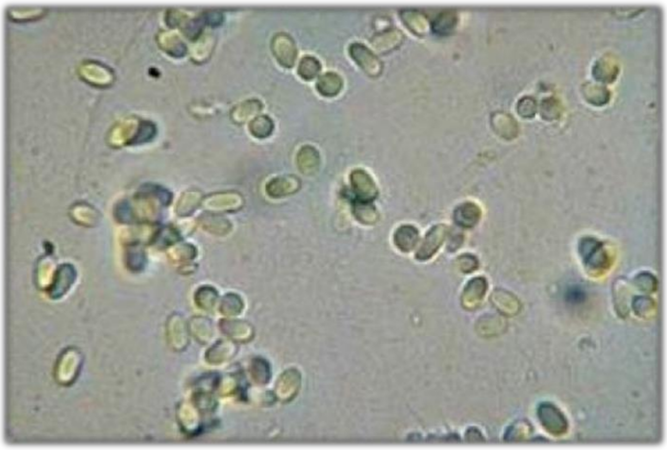


Figure 6. Spores of the fungus of the genus *Nosema* (Source: https://www.wur.nl/en/Expertise-Services/Research-Institutes/plant-research/Biointeractions-Plant-Health/Bees-1/Bee-diseases/Nosema.htm

-Phylum Neocallimastigomycota: Comprised of anaerobic fungi that live in the digestive system of ruminants. Some genera belonging to this phylum are: *Cyllamyces, Piromyces, Anaeromyces*, and *Neocallimastix* (Fliegerová et al., 2010). Figure 7 presents zoospores of the fungus of the genus *Neocallimastix.*

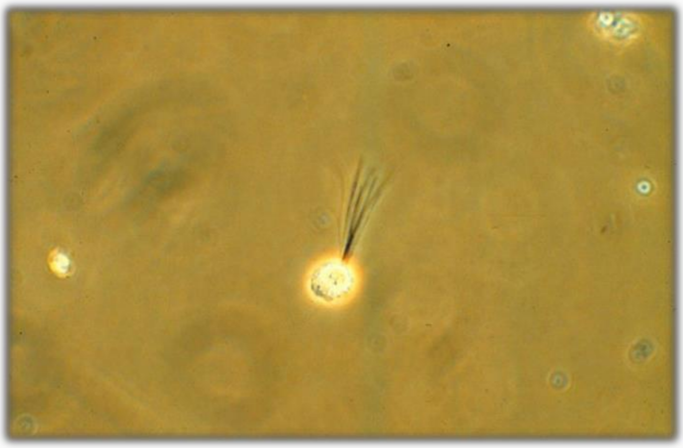


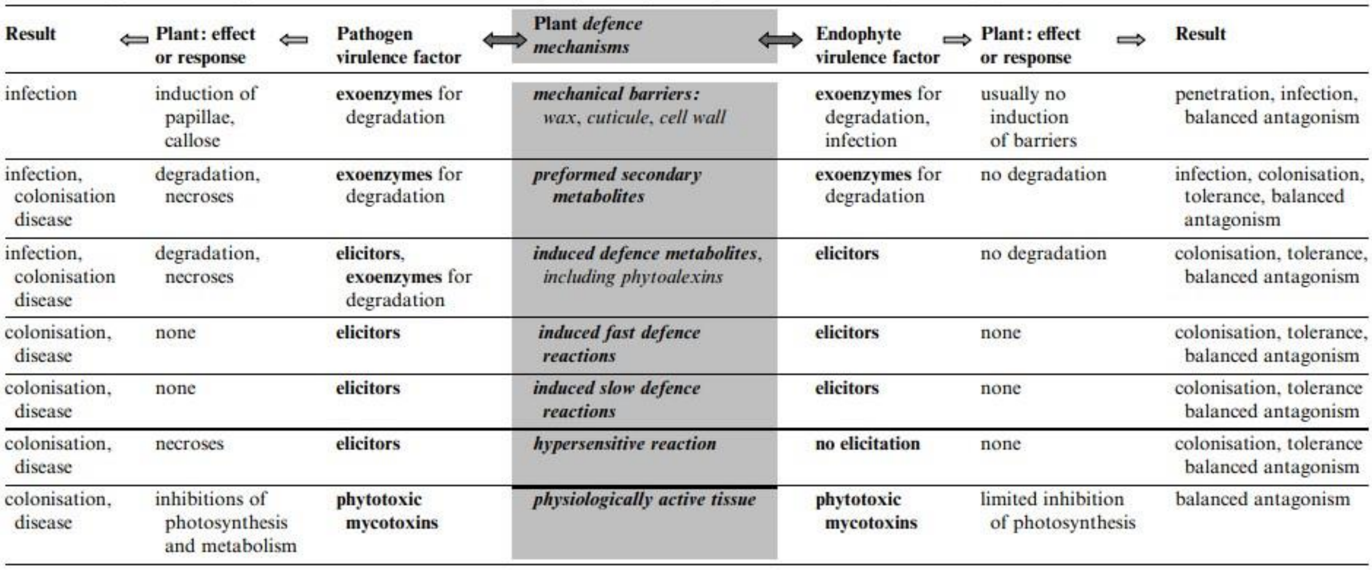
Figure 7. Zoospores of *Neocallimastix*, representative of the Phylum *Neocallimastigomycota* (Source: http://comenius.susqu.edu/biol)

Endophytic fungi

The first definition of endophytic fungi was given by De Barry in 1966, who called endophytes the fungi that live within plant tissues. In 1986, Caroll proposed a new definition, in which he considered as endophytes all the endosymbionts that cause asymptomatic reactions in host plants, being excluded from this definition mycorrhizal, and pathogenic. Petrini, in 1991, called endophytes all the microorganisms that at some point in their life cycle colonize a plant without causing damage to it. The most recent definition calls endophytes all microorganisms that have or do not have the capacity to grow in culture medium, and that colonize the interior of plants in an asymptomatic, and non-visible way, besides being unable to produce external structures such as gall (Azevedo and Araújo, 2007). These microorganisms can be transmitted to future generations through seed, or wind action (Rodriguez et al., 2009). They are considered systemic fungi, once they can be present in all parts of the plant, feeding on the nutrients present in the vegetable sap (Sherwood & Carroll, 1974; Carroll, 1988; Stone et al., 2004). Over 100 years of research suggest that virtually all plants living in natural environments live in symbiosis with mycorrhizal or, endophytic fungi (Petrini, 1986). Mycorrhizal fungi grow within the roots, and colonize only the rhizosphere, whereas endophytes can colonize all plant organs, and emerge to sporulate when the plant is senescent (Sherwood and Carroll, 1974; Carroll, 1988; Stone et al., 2004)

Asymptomatic colonization of fungi in the host plant is a result of a dynamic balance between fungus viruence, and plant immunity, i.e. plant defense responses, but host stress situations or metabolic changes that can occur both in the fungus and in the plant can alter this balance in favor of the fungus, causing it to become pathogenic (Schulz and Boyle, 2005). But after all, are fungi and plants "friends" or "enemies"? The question seems strange, since we expect to find an asymptomatic response of the plant to the fungus, but it is known that fungi can produce toxic compounds for plants (Schulz and Boyle, 2005). Table 1 presents some expected results of the interaction between fungi and plants, and the responses that they present in each situation.

Table 1. Fungus virulence vs. plant defense in a non-obligatory fungus-host interaction



Result ⇐	Plant: effect or response ⇐	Pathogen virulence factor ⇔	Plant *defence mechanisms* ⇔	Endophyte virulence factor ⇒	Plant: effect or response ⇒	Result
infection	induction of papillae, callose	**exoenzymes** for degradation	***mechanical barriers:*** *wax, cuticule, cell wall*	**exoenzymes** for degradation, infection	usually no induction of barriers	penetration, infection, balanced antagonism
infection, colonisation disease	degradation, necroses	**exoenzymes** for degradation	***preformed secondary metabolites***	**exoenzymes** for degradation	no degradation	infection, colonisation, tolerance, balanced antagonism
infection, colonisation disease	degradation, necroses	**elicitors**, **exoenzymes** for degradation	***induced defence metabolites****, including phytoalexins*	**elicitors**	no degradation	colonisation, tolerance, balanced antagonism
colonisation, disease	none	**elicitors**	***induced fast defence reactions***	**elicitors**	none	colonisation, tolerance, balanced antagonism
colonisation, disease	none	**elicitors**	***induced slow defence reactions***	**elicitors**	none	colonisation, tolerance balanced antagonism
colonisation, disease	necroses	**elicitors**	***hypersensitive reaction***	**no elicitation**	none	colonisation, tolerance balanced antagonism
colonisation, disease	inhibitions of photosynthesis and metabolism	**phytotoxic mycotoxins**	***physiologically active tissue***	**phytotoxic mycotoxins**	limited inhibition of photosynthesis	balanced antagonism

Source: Schulz and Boyle (2005)

Fungi must first cross the plant defense barriers, and cause some injury later (Schulz and Boyle, 2005). Pathogens do this with the aid of their secondary metabolites, and exoenzymes (Agrios, 1997). And these metabolites produced by the fungi both in the endophytic state and in the pathogenic state have been the target of several biological studies. It is worth noting that we call here the fungi in the "endophytic state", and "pathogenic state" because we know that the same fungus species can be present in the plant of both forms, producing different metabolites which have been studied as promising alternatives to synthetic products that are often harmful to living things and the environment.

Biological activities of secondary metabolites of endophytic fungi

From the more than 20,000 secondary metabolites produced by fungi (Owley et al., 2010), 80% are bioactive (Paranagama et al., 2007, Yang et al., 2012). Some compounds, such as Taxol ® used in cancer treatment, are produced by the fungi, and plants from which it has been isolated. Taxol® is a compound produced by the fungus *Taxomyces andreanae*, isolated from the *Taxus brevifolia* plant, which is also a source of the metabolite produced by the fungus (Stierle et al., 1994). Chapla et al. (2013) listed, and presented the biological activities of some metabolites, such as the antimicrobial activity of the compounds pestaloteol A, pestaloteol, B, pestaloteol C, pestaloteol D, cercosporamide, enfmagen, and trichodemine (Aly et al., 2012; Wang et al., 2012). Antiparasitic activity of compounds palmarumycin CP17, palmarumicin CP18;

nodulisporic acid A; tert-butyl nodulisporin, and chrysogenamide A (Aly et al., 2012; Ondeyka et al., 1997). Neuroprotective activity of chrysogenamide A (Aly et al., 2010). Antioxidant activity of the compounds isopestacin, pestacin (Jalgaonwala et al., 2011), luteolin (Zhao et al., 2014), and palmarumicin C3 (Mou et al., 2013; Aly et al., 2010). In addition, the cytotoxic activity of the cytotoxic compounds A and B (Strobel and Daisy, 2003; Guo et al., 2000). The antineoplastic activities of camptothecins and anthraquinones (Zhang et al., 2006; Sweta et al., 2010), and anticholinesterase α-hydroxy-5-N-acetylardimine (Aly et al., 2011) are also known.

As mentioned earlier, some compounds are produced by both the host plants, and their endophytes. However, some compounds are synthesized only by fungi, as it is the case of Griseofulvim polyketides, isolated from *Peniccilium* sp. and *Xylaria* sp. which has antifungal activity (Park et al., 2005), Brefeldim A produced by the fungi of the genera *Curvularia, Alternaria, Ascochyta, Phyllosticta, Penicillium*, and *Cercospora*, and which presented antifungal, antiviral and anticancer activity. Seedlings, isolated from *Aspergillus parasiticus*, an endophytic fungus of *Sequoia sempervirens*, which was active in inhibiting the growth of tumor cells in humans (Stierle, et al., 1999), and Nodulisporins, produced by fungi of the genus *Nodulisporium* sp. which are antifungal. Terpenes are also part of the classes of secondary metabolites produced by endophytic fungi. Among them, we can highlight the sesquiterpenes 5- (hydroxymethyl) -2- (20-trimethyltetrahydro-2H-pyran-2-yl) -phenol produced by the fungus *Lophodermium* sp, which has antifungal activity (Sumarah et al. 2011), and phomadecalinos 8α-acetoxyphomadecalin C, and phomadecalin E, isolated from the fungus *Microdiplodia* sp. KS 75-1 were active against the bacterium *Pseudomonas aeruginosa* ATCC 15442 (Hatakeyama et al., 2010). Other known bioactive terpenes are Xylarionas (Hu et al., 2008), Tuberculariols (Xu et al., 2009), and Peniconicins (Shin et al., 2005). A thorough review of these compounds allows us to conclude that almost all of them have antimicrobial activity. Next, we will present some compounds of fungal origin that act as controllers of the growth and development of vegetal species.

Secondary metabolites of fungi with phytotoxic activity

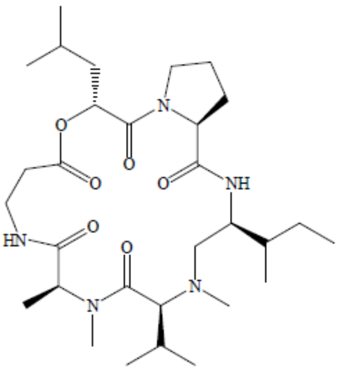
The secondary metabolites (SM) of fungi that are toxic to plants are called phytotoxins (Lou et al., 2013), and they can be classified into host-specific toxins, and host-non-specific toxins. The first refers to phytotoxins that are biologically active in a particular species of plants (Wolpert et al., 2002), while the other refers to active phytotoxins over a range of species (Berestetskiy, 2008).

The phytotoxic activity of SM from endophytic and pathogenic fungi has been studied, and proven for different compounds, such as tenuazolic acid (Stierle et al., 1988), maculosin (Liebermann et al., 1996), and tentoxin (Sanodiya et al. , 2010), all from fungi of the genus *Alternaria* sp. (Lou et al., 2013).

Fungi belonging to the class Dothideomycete, largest class of fungi of the phylum Ascomycota, produce phytotoxic SM belonging to the classes polyketides, nonribosomal peptides, alkaloids, terpenes, and mix metabolites of biosynthetic origin (Collemare and Lebrun, 2011), being the largest producers of these SM fungi from the genera *Alternaria*, and *Cochliobolus* (Stergiopoulos et al., 2012).

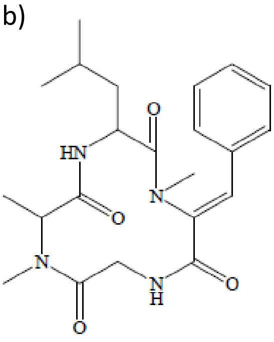
The genus *Alternaria* has been studied as a source of promising phytotoxins, such as Destruxin B (Fig. 8a), a cyclopeptide isolated from *Alternaria brassicae,* causing chlorosis, and necrosis, and is believed to be responsible for the aggressiveness of *A. brassicae* on host, and non-host plants (Buchwaldt and Green, 1992). Other known phytotoxins are tentoxin (Fig. 8b), a cyclic tetrapeptide that inhibits the development of chloroplast, and chlorosis in cucumber, and pumpkin (Halloin et al., 1970), altersolanol A (Fig. 8c), a tetrahydroanthraquinone isolated from *Alternaria solani* that inhibits the growth of *Nicotiana rustica* cells (Haraguchi et al., 1996), and bostricin (Fig. 8d), and 4- Deoxybostricin isolated from *Alternaria eichhorniae*, a pathogen of the aquatic plant *Eicchornia crassipes* (Chatudattan and Rao, 1982).

a)



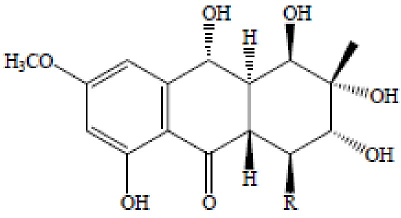
Destruxin B

b)



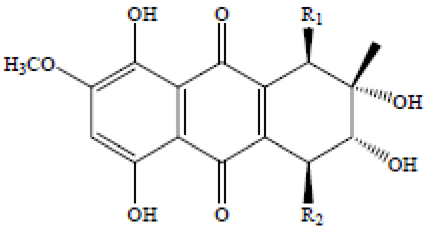
Tentoxin

c)



Altersolanol L, R = H

d)

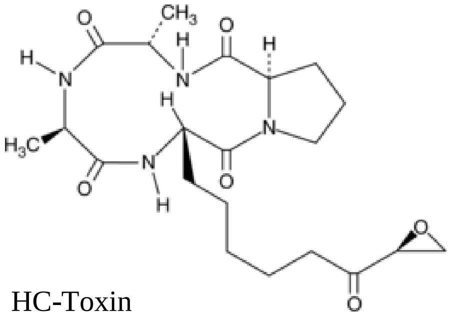


Bostrycin, R_1 = H, R_2 = OH
4-Deoxybostrycin, R_1 = H, R_2 = H

Figure 8. Some compounds isolated from fungi of the genus *Alternaria* that present phytotoxic activity. (a) Dextruxin B; (b) Tentoxin; (c) Altersolanol; (d) Bostrycin and 4-Deoxybostrycin.

The *Cochliobolus* genus produces HC-toxin (Fig. 9a), a cyclic tetrapeptide that suppresses host plant defenses (Brosch et al., 1995; Walton, 2006). It also produces T-toxin (Fig. 9b), a linear polyketide that causes disruption of plant mitochondrial activity (Walton, 1996), and Victorin (Fig. 9c), a cyclic pentapeptide that induces PCD (Meehan and Murphy, 1946; Meehan, 1947; Stergiopoulos et al., 2012).

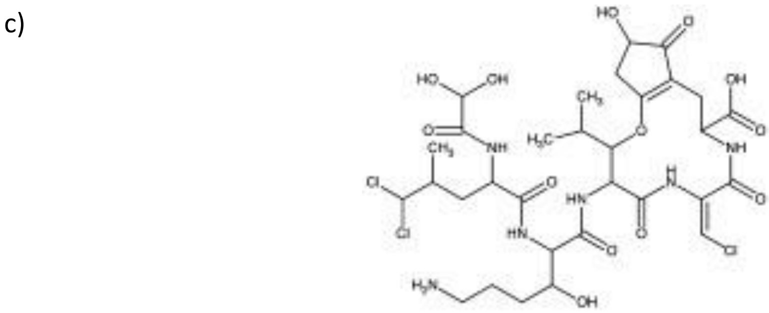
a)



HC-Toxin

b)

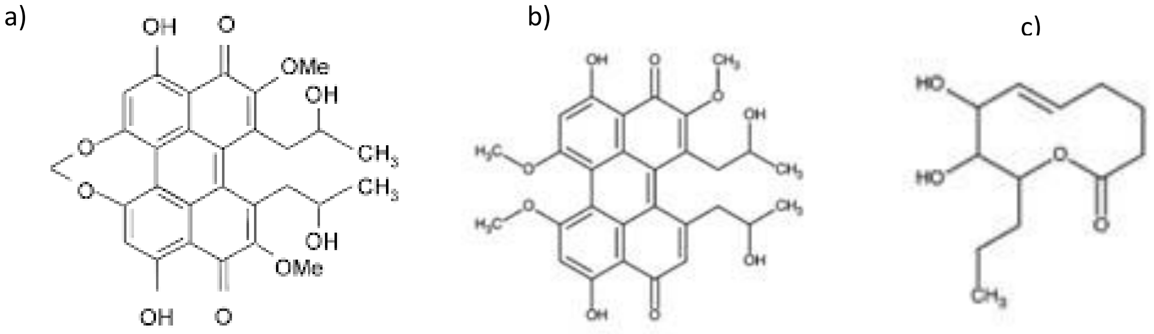
T-Toxin



Victorin

Figure 9. Some compounds isolated from fungi of the genus *Cochliobolus* that have phytotoxic activity. (a) HC-Toxin; (b) T-Toxin; (c) Victorin

Other genotypes of fungi Dothideomycetes also produce known phytotoxins, such as cercosporine (Fig 10a), produced by fungi of the genus *Cercospora*, which is phytotoxic to various plant species, among them *Nicotiana tabacum*, and *Phaseolus vulgaris* (Fajola, 1978). The phleicrome (Fig. 10b), produced by *Cladosporium phlei* that causes purple dots disease (Araki and Shimanuki, 1983), and herbarumin (Fig. 10c), produced by *Phoma herbarum*, which inhibits the germination and growth of *Amaranthus hypochondriacus* (Furstner et al., 2002).



Cercosporin

Phleicrome

Herbarumin

Figure 10. Secondary metabolites produced by fungi with phytotoxic activity. (a) cercosporin; (a) phleichrome; (c) herbarumin

The host plant *Serjania lethalis*

Serjania lethalis is a liana belonging to the family Sapindaceae, popularly known as "cipó-timbó". It occurs in the Brazilian cerrado, as well as in the states of Bahia, Ceará, Pernambuco, Amazonas, Piauí, Paraná, Rio de Janeiro, and Santa Catarina (Fernandes and Negreiros, 2001, Acevedo-Rodríguez, 1990) (Figure 11).

Figure 11. Individuals of *S. lethalis* in the cerrado reserve of UFSCar (Photo: Personal archive)

The phytotoxic activity of its leaves is known (Pereira et al., 2016) but to date no study has been done on the phytotoxic activity of the endophytic fungi of this species, as well as a survey of their endophytic community.

GENERAL CONCLUSIONS

- This work reported for the first time the endophytic fungi present in *Serjania lethalis* leaves. The species or genera found are endophytesm and plant pathogens;

- To identify the other fungi found it will be necessary to use different molecular markers because only with the primers ITS1, and ITS4 it was not possible to identify many genera.
- The extracts of culture medium of *Alternaria* sp, and mycelium of *Diaporthe* sp. have compounds that act as inhibitors of the development of invasive plants *Euphorbia heterophylla* and *Megathyrsus maximus*. Compounds responsible for such activities are present in these extracts;
- The growth of *E. heterophylla* metaxilem cells as well as their growth were affected by the culture medium extract of *Alternaria* sp.
- Mycorrhizal extract from *Diaporte* sp. affected the seed germination of *Megathyrsus maximus.*
- For having presented the best results in the tests of phytotoxicity it was decided to investigate better the compounds present in the extract of culture medium of *Alternaria* sp.
- From the culture medium extract of *Alternaria* sp. cycloproline valine, cyclo proline isoleucine and cyclo prolinaleucine, and indole-3-carboxylic acid (ICA) were isolated, being the only compound with phytotoxic activity on the growth of wheat coleoptiles (*Triticum aestivum*)
- Investigation of the phytotoxic potential of ICA showed that this compound was phytotoxic for the growth, and development of the abovementioned invasive species when tested pure, as well as for the growth of *Euphorbia heterophylla* metaxilema cells.
- The esterification reactions made with the ICA and the three different alcohols (methanol, ethanol and hexanol) showed that the esters of greater alkyl chain were the most phytotoxic for the growth of wheat coleoptiles (*Triticum aestivum*). This can also be demonstrated by means of the IC_{50}, and lipophilic index values.
- From the beginning of the work the extract of culture medium of *Alternaria* sp. was shown to be more promising in phytotoxicity assays, leading us to believe that there was a compound in it that would produce such effect. We have verified that the ICA was responsible for such activities.
- Like plants, endophytic fungi produce bioactive substances that can be used as sustainable alternatives to conventional products. This work started the search for

phytotoxic products derived from the secondary metabolism of the endophytic fungus of leaves of *Serjania lethalis, Alternaria* sp.

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