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REVIEW ARTICLE

Stemphylium and *Ulocladium* between Benefit and Harmful

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ABSTRACT

Background: Emerging of microbial resistance, spread of life-threatening diseases, and biological control of pathogens destroying economically important crops, are serious problems that encourage scientists to search for unusual sources for novel compounds with biological activities. Fungi are promising sources for such compounds due to their ability to produce variety of secondary metabolites that could be, if truly investigated, the solution for currently serious problems.

Aim: The aim of this review is to highlight the diversity of compounds produced by endophytic *Stemphylium* and *Ulocladium* and represents their ability to produce biologically diverse metabolites.

Materials and methods: This was a narrative review. A comprehensive literature search was done using PubMed, Google Scholar, Scopus, and EMBASE using the keywords, *Stemphylium*; *Ulocladium*; Secondary metabolites; biological activities.

Results: Many studies reported that the endophytic *Ulocladium* especially, *Ulocladium* **atrum Preuss**, showed promising biocontrol activity against *Botrytis cinerea* on crops cultivated in the greenhouse and the field. The endophytic fungus *Stemphylium* especially, *Stemphylium globuliferum* was isolated from stem tissues of the Moroccan medicinal plant *Mentha pulegium*. Extracts of the fungus exhibited significant cytotoxicity when tested in vitro against L5178Y cells.

Conclusion: Endophytic fungi are a noble and consistent source of unique natural mixtures with a high level of biodiversity and may also yield several compounds of pharmaceutical significance, which is currently attracting scientific surveys worldwide. Every study conducted on *Stemphylium* and *Ulocladium* resulted in discovery of new metabolites or pointing to a possible application, which made *Stemphylium* and *Ulocladium* species potential source of pharmaceuticals and attracted attention for further investigations of their biological control.

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INTRODUCTION

Endophytic fungi regarded as fascinating group of organisms colonize the living internal tissues of their host usually higher plants. Endophytes do not cause any symptoms of disease in the host cells and produce natural bioactive compounds considered as an elicitor for plant secondary metabolites production [1,2]. The ability of endophytic fungi is to produce new and interesting bioactive secondary metabolites, which are of pharmaceutical, industrial and agricultural importance [3-7]. The various natural products produced by endophytic fungi possess unique structures and bioactivities against various diseases [5,7-11]. Secondary metabolites are chemically different natural compounds of relatively low molecular weight that are mainly produced by microorganisms and plants, and typically associated to individual genera, species or strains. They are biosynthesized along specialized pathways from primary metabolites, exhibit a wide range of biological activities and play an important role in regulating interactions between organisms [12].

Included in this group are antibiotics, which are natural products capable of inhibiting or killing microbial competitors [13,14]. Fungi are among the most abundant and frequently isolated endophytic residents of plants. Some genera of endophytic fungi include **Aspergillus, Bipolaris, Chaetomium, Cladosporium,**

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Diaporthe, Fusarium, Alternaria, Mucor, Nigrospora, Paecilomyces, Penicillium, Piriformospora, Porostereum, Phoma, Trichoderma, *Ulocladium*, **and** *Stemphylium.* Some of these genera contain both opportunistic pathogens and beneficial organisms. For example, the genus **Trichoderma** is composed of species with endophytic capacity [15].

Stemphylium and *Ulocladium,* description and ecology

Stemphylium belonging to Ascomycota, Class: Dothideomycetes; Order: Pleosporales; Family: Pleosporaceae. *Stemphylium* is a dematiaceous filamentous fungus that is widely distributed on decaying vegetation and in the soil. It is commonly considered as a contaminant. *Pleospora* is the telemorph of *Stemphylium*. Colonies of *Stemphylium* grow rapidly and mature in 5 days. At 25˚C and on potato dextrose agar, they are velvety to cottony in texture. From the front, the color is gray, brown, or brownish-black. Reverse is black. Septate hyphae, conidiophores, and conidia are visualized. The hyphae are pale brown to brown in color. Conidiophores are dematiaceous and may be simple or branched. They bear a number of vesicular swellings or nodes. These knobby structures are more readily produced by aging. Conidiogenous cells are terminally located and percurrent (the proliferation which grows through the tip of the conidiogenous cell). Conidia (12-20 x 15-30 µm) are solitary, light brown to black in color, and rough- or smooth-walled. They are oblong or subspherical and rounded at the tips. These conidia have transverse and vertical septations (Muriform conidia) and there is a typical constriction at the central septum. And they have thickened scars) at their base [16,17]. *Stemphylium* is differentiated from *Ulocladium* by producing percurrent conidiophores (Figure 1). Most common *Stemphylium* species is *Stemphylium vesicarium*, *Stemphylium herbarum* (Teleomorph: *Pleospora allii*, *Pleospora herbarum*), *Stemphylium botryosum* (Teleomorph: *Pleospora tarda*), *Stemphylium alfalfae* (Teleomorph: *Pleospora alfalfae*), *Stemphylium solani* (Teleomorph: *P. solanum*) [16,17].

Ulocladium belonging to Ascomycota, Class: Euascomycetes; Order: Pleosporales; Family: Pleosporaceae. *Ulocladium* is a dematiaceous filamentous fungus that inhabits the soil and decaying herbaceous plants. It is widely distributed in nature and may be isolated from paper, textiles, and wood as well. *Ulocladium* is commonly considered as a contaminant. The genus *Ulocladium* has two most common and active species; *Ulocladium chartarum* and *Ulocladium botrytis*. The morphological features of the conidiophores and the conidia aid in differentiation and identification of the two species. Colonies of *Ulocladium* grow moderately rapidly. At 25˚C and on potato dextrose agar, the colonies are woolly to cottony. From the front and the reverse, the color is olive brown to black. Microscopic Features: Septate brown hyphae, brown conidiophores, and conidia are visualized.

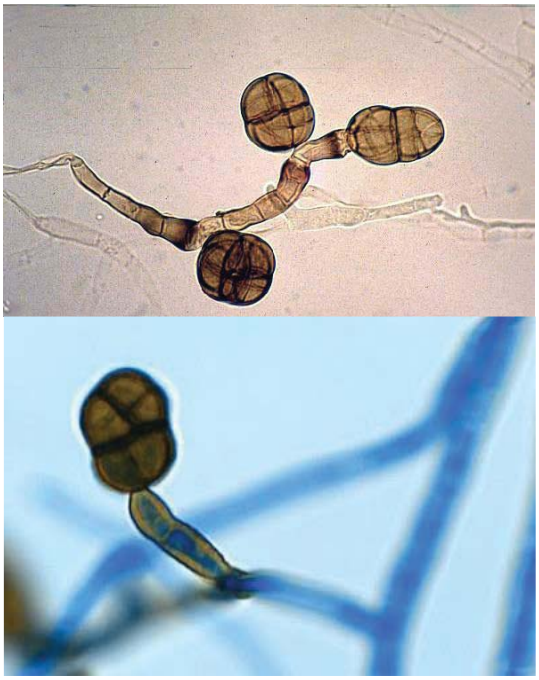

Figure 1 *Stemphylium* spp., different species, hosted by https://drfungus.orgknowledge-basestemphylium-species and http://thunderhouse4-yuri.blogspot.com201507/stemphylium-species.html).

Conidiophores are simple or branched, smooth, strongly geniculate (bent at the points where the conidia are produced, leading to a zigzag appearance, and bear the conidia. Conidia (13-30 x 6-19 µm) are brown to black, round to oval in shape, smooth or rough and verrucous. They are usually egg-shaped and have a narrower base compared to its apex. These conidia are typically muriform and have transverse and longitudinal septations. They are solitary like *Ulocladium botrytis* or may form short chains like *Ulocladium chartarum*. When chains are produced, a tubular, short outgrowth is formed on the conidia at the point of secondary conidium formation. Pale pigmented ellipsoidal structures may be observed [16,17]. *Ulocladium* differs from *Alternaria* by its strongly geniculate conidiophores, and the absence of beak-like tapered apex of conidia. It differs from *Bipolaris*, *Curvularia*, and *Drechslera* by producing muriform conidia. *Ulocladium* is differentiated from *Stemphylium* by having geniculate, sympodial conidiophores (Figure 2). Most common *Ulocladium* species is *Ulocladium* chartarum species which is most commonly found and *Ulocladium botrytis* [16,17].

Stemphylium and *Ulocladium* as source of biologically active compounds

Plant diseases are major threat for the cultivation of crops in intensive agriculture, where plant protection measures are important to control diseases which include frequent application of pesticides. The disadvantages of chemical pesticides usage in control of plant diseases are many (Development of resistance to pesticides and side-effects on beneficial organisms and the environment), which force

Figure 2 *Ulocladium* spp., different species, hosted by https://alchetron.com/Ulocladium and https://www.etsy.com/it/listing/711900159/ulocladium).

us for new management strategies for crop protection [18]. The biological control is one of the strategic crop protection method to replace chemicals and this can be combined with organic crop protection measures to increase the spectrum of biological control in disease management. Farmers have to select combined improved method of control to reduce or avoid chemical inputs into the food and environment to manage the crop diseases [18,19].

Ulocladium, which is phylogenetically related to *Alternaria*, contains species that are food spoilers and plant pathogens, but also species that have potential as enzyme producers and bio-control agents. *Ulocladium* spp. are often found on dead vegetation, in soil, air and dust, but also on feedstuffs and on water-damaged building materials [20]. In this review attempts have been made to highlight the *Ulocladium* genus, especially *Ulocladium atrum* as potential biological control agent. The genus *Ulocladium* is an anamorphic fungus which belongs to phylum - Ascomycota, sub-phylum - Pezizomycotina, mostly found on plant materials and in soil as common saprobes. *Ulocladium* **atrum Preuss**, showed promising biocontrol activity against Botrytis cinerea on crops cultivated in the greenhouse and the field. *Ulocladium* **atrum Preuss** produce a cyclopeptolide characterized by an abundance of N-methylated amino acids and showed potent antifungal activity against **Botrytis cinerea** and moderate activity against Alternaria alternata and Magnaporthe **grisea [21].** Biological control involves the use of antagonistic microorganisms such as bacteria, yeast, and fungus. Botrytis blight caused by Botrytis cinerea is a difficult disease to control in many ornamental crops. The competitive saprophytes *Ulocladium* **atrum** has been evaluated with some success for suppression of Botrytis **cinerea** on cyclamen, geranium, and rose [22]. Biological control of **Botrytis** in cyclamen is possible by treatments of leaves with a conidial suspension of the saprophytic fungi *Ulocladium* **atrum** under commercial growing conditions was as effective as the standard chemical fungicide program. This work was continued in roses, where it was shown also that *Ulocladium* **atrum** had a strong reducing effect on Botrytis sp. [23].

Ulocladium, which is phylogenetically related to *Alternaria*, contains species that are food spoilers and plant pathogens, but also species that have potential as enzyme producers and bio-control agents. *Ulocladium* spp. are often found on dead vegetation, in soil, air and dust, but also on food and feedstuffs and on water-damaged building materials. Andersen and Hollensted [20], reported that, Cultures of 52 *Ulocladium* strains were identified morphologically, and then extracted and analyzed using automated Chemical Image Analysis. Production of individual metabolites was correlated to species identity and source of isolation. Chemical analyses verified the morphological identifications and showed the existence of several species species-specific metabolites, of which most were known compounds. The production of curvularins was specific to *Ulocladium atrum*, while most species produced infectopyrones and derivatives of altertoxin I. None of the 52 *Ulocladium* strains produced alternariols, tenuazonic acid, altersolanols or macrosporin, which are common in species of *Alternaria* [20].

The endophytic fungus *Stemphylium globuliferum* was isolated from stem tissues of the Moroccan medicinal plant *Mentha pulegium*. Extracts of the fungus, which was grown on solid rice medium, exhibited considerable cytotoxicity when tested in vitro against L5178Y cells. Chemical investigation yielded five new secondary metabolites, alterporriol G and its atropisomer alterporriol H, altersolanol K, altersolanol L, stemphypyrone, and the known compounds 6-O-methylalaternin, macrosporin, altersolanol A, alterporriol E, alterporriol D, alterporriol A, alterporriol B, and altersolanol J [24].

Harmful Sides of *Stemphylium* and *Ulocladium*

Non endophytic *Stemphylium* and *Ulocladium* species are well-known plant pathogens found on a wide range of vegetables, including beans, lettuce, pea and tomato [25,26]. Some species are plant pathogens that cause leaf spot diseases, e.g. *Stemphylium* leaf blight, caused by *Stemphylium vesicarium*, which typically infects leaf tips of onion [27]. The fungus *Stemphylium solani* causes leaf blight of tomato (*Lycopersicon esculentum*) in Brazil [28]. *Stemphylium* species are also capable of causing similar allergies. It is documented that *Stemphylium* induces rhinitis and asthma in children, and also angioedema, conjunctivitis, allergic sinusitis, and bronchopulmonary mycosis in sensitive individuals [29].

Apart from health effects on human bodies and environment, the genus *Ulocladium* can cause a lot of damage to human home. *Ulocladium* destroys wood and surfaces like walls and doors. Peoples spending a lot of money to remove them and the surfaces may sometimes need repair. In more severe cases, the items end up being replaced since the mold eats them up. Structural damage is the most common side effect that this mold causes. The worst situation happens when the *Ulocladium* mold is growing in the house together with other types of molds like Bipolaris. The fungus also discolors the surfaces it has invaded. In this case, surfaces that were once clear from dirt usually turn into brown, green or black patches [30-32].

CONCLUSION

Stemphylium and *Ulocladium* is an endophytic fungus. Moreover, *Stemphylium* and *Ulocladium* Sp. are known for their capability of producing various biologically active compounds with medical applications as, antimicrobial, and anticancer agents. The aim of this review is to highlight the diversity of compounds produced by endophytic *Stemphylium* and *Ulocladium* and pointing out their medical and bio-control against some fungal plant pathology. Besides, describing the unique chemical diversity of these fungal genera involved in medical, pharmaceutical, agricultural applications. Many researches performed on endophytic *Stemphylium* and *Ulocladium* resulted in discovery of new metabolites or pointing to a possible application, which made *Stemphylium* and *Ulocladium* species potential source of pharmaceuticals and attracted attention for further investigations of their biological control.

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