



## Professional article

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## ***CLADOSPORIUM SPP.* - CAUSE OF OPPORTUNISTIC MYCOSES**

### SUMMARY

*Cladosporium spp.* have a world-wide distribution and are among the most common air-borne fungi. Some species are frequently isolated contaminants, however, some species are pathogenic and toxigenic to humans. *Cladosporium spp.* are known to be the cause of cerebral and cutaneous phaeophycomycoses. In addition, *Cladosporium spp.* are strong aero-allergens and cause serious allergic diseases of the respiratory tract, as well as intrabronchial lesions.

Identification of *Cladosporium spp.* as well as differentiation of species of this genus is possible only on the basis of morphologic and morphometric characteristics after standard procedure of cultivation and isolation of these strains in a laboratory for mycology. The procedure of isolation of these species is conducted in biologically safe cabinets, with obligatory taking all preventive measures. There is a few information in the literature about sensitivity of *Cladosporium spp.* to antimicrotics.

**Key words:** *Cladosporium spp.*, opportunistic mycoses

### INTRODUCTION

Phaeohyphomycosis is a fungal infection caused by fungi from the group dematiaceae (pigmented moulds). The cause of this infection is also *Cladosporium spp.* (1,2).

*Cladosporium spp.* are pigmented moulds (dematiaceae) widely distributed in the air as well as decayed organic matter, and very often they are food contaminants. Some species are most widely distributed in the tropics and subtropics (3,4). Also, some species of this genus are associated with fish diseases (5). They stand for the most isolated fungi in nature, however, their number decreases in their natural habitats during winter months.

Home species of *Cladosporium spp.* differ from those living in nature (6). It is interesting that they develop on the surface of glass fibers, inside the

water pipes (7,8). Different species of plants are the food source to these fungi, so that *Cladosporium spp.* can be found on dead plants, wood plants, food, straw, soil, colors, and textile. They contain more than 10 antigens.

### CLASSIFICATION

*Cladosporium spp.* comprise fungi which are not characterized by sexual phase of multiplication, and, therefore, belong to the group *Fungi imperfecti*. This genus comprises more than 30 species. The most isolated species are *Cladosporium elatum*, *Cladosporium harbarum*, *Cladosporium sphaerospermum* and *Cladosporium cladosporioides* (1,2). Table 1 presents species of *Cladosporium spp.*, their latest and former names.

Table 1. The latest and former names of *Cladosporium* spp.

The latest name of the species	The former name of the species	The oldest name of the species
<i>Cladophialophora bantiana</i>	<i>Cladosporium bantianum</i> <i>Cladosporium trichoides</i> <i>Cladosporium trichoides</i> var. <i>chlamydosporum</i>	<i>Xylohypha bantiana</i> <i>Xylohypha emmonsii</i>
<i>Cladophialophora carrionii</i>	<i>Cladosporium carrionii</i>	<i>Cladophialophora ajelloi</i>
<i>Stenella araguata</i>	<i>Cladosporium castellanii</i>	-
<i>Hyphopichia burtonii</i>	<i>Cladosporium chodatii</i>	<i>Cladosporium fermentans</i>
<i>Cladosporium cladosporioides</i>	<i>Cladosporium hypophyllum</i>	<i>Penicillium cladosporioides</i> <i>Hormodendrum</i> <i>cladosporioides</i>
<i>Cladophialophora devriesii</i>	<i>Cladosporium devriesii</i>	
<i>Cladosporium herbarum</i>	<i>Cladosporium epiphyllum</i> <i>Cladosporium graminum</i>	<i>Dematium herbarum</i> <i>Mycosphaerella tassiana</i> Sexually reproductive stage of the species
<i>Exophiala castellanii</i>	<i>Cladosporium mansonii</i>	<i>Dematium mansonii</i>
<i>Cladosporium oxysporum</i>		
<i>Cladosporium sphaerospermum</i>		

According to general characteristics, fungi of this genus are classified in the group of dermatiaceae, where other fungi containing melanin in the cellular wall of conidia, hyphae, or/and one of both belong, which gives a characteristic color to colonies, ranging from olive-grey to black color (1,2,9,10).

#### Microscopic morphological characteristics

In the saprophytic phase, *Cladosporium* spp. form pigmented, septate hyphae ending with conidiophore (spore carrier) along which come, in shorter or longer chains, conidioconidia (conidiospores). Conidia (spores) are darkly pigmented, ellipsoid to cylindrical in shape, with flat walls on which scarves can be noticed. (9,10).

In the parasitic phase, feoid (brown-pigmented) hyphae can be observed in the tissue. One should bear in mind the fact that these fungi in the tissue can vary as far as their structure is concerned, ranging from yeast-like to that of long hyphae, or the combination of these may be seen (1,2).

Based on the morphological characteristics, it is also possible to identify species inside the genus. Therefore, in *Cladosporium cladosporioides* and *Cladosporium sphaerospermum*, there are no knee-like joints of conidiophores. *Cladosporium herbarum*, besides knee-like joints of conidiophores, is characterized by terminal and intercalary thickenings. *Cladosporium cladosporioides* produces one-celled conidia (spores), while conidia

of *Cladosporium herbarum* are one- to four-celled. *Cladosporium sphaerospermum* forms long and septate conidia, known as ramoconidia (11,12).

#### Cultivation

Fungi of *Cladosporium* spp. grow fast on agars (Sabouraud-agar with or without addition of antibiotics, without actidione, etc.) forming darkly pigmented (pigmented moulds), olive-green to darkly brown colonies of powder-like structure. The vegetative mycelium is usually dark-colored. The colonies are formed after five days. The identification and differentiation of species is possible after cultivation on potato-dextrose agar at the temperature of 25° C. The greatest number of *Cladosporium* spp. do not multiply at the temperature of 25° C (4,11,12).

#### Identification and differentiation of fungal species inside genus *Cladosporium*

*Cladophialophora* spp. differ from *Cladosporium* spp. on the basis of dark scarves' appearance at the end of conidia. *Cladophialophora bantiana* grows at the temperature of 42-43° C, while *Cladophialophora carrionii*, as well as a great number of *Cladosporium* spp., does not grow at the temperature above 35° C.

*Cladosporium cladosporioides* is characterized by colonies of 3cm in diameter. After seven days, they grow on potato-maltose agar. The colonies are olive-green pigmented or they are brown pig-

mented, while the basal sides are darkly pigmented. Conidiophores branch widely and produce a great number conidioconidia in branched chains, with greater number of conidia at the beginning of chain and conidia of smaller dimensions at the top, that is the end of the chain. Conidia are one-celled, rarely two-celled, usually flat-walled or of a little bit rougher structure, with bifurcations on the top if two or three daughter cells or chains of conidioconidia grow. Conidioconidia are ellipsoid or lemon-like in shape, measuring 3-7 (also 11)  $\mu\text{m}$  x 2-4 (also 5)  $\mu\text{m}$ , on which scarves (appearing darkly) can be seen, slightly elevated at the site of junction with conidiophore or another conidioconidium (3,4,13).

*Cladosporium sphaerospermum* is similar to the previous species, however, conidioconidia, especially those in the chain, which are closer to its end, are ball-like in shape, measuring 3-4 (also 7)  $\mu\text{m}$ . The walls of conidioconidia are of rougher structure, but also flat-walled strains of this species can be isolated, which is the case with *Cladosporium cladosporioides* (14,15).

*Cladosporium herbarum* is also similar to *Cladosporium cladosporioides*, except for the existence of knee-like joints, that is conidiophores grow slightly bented making a junction similar to that of the knee joint. Therefore, in this species, long, mature conidiophores can be seen, which can have a great number of knee-like junctions along all its length. Conidioconidia are much larger than those in the aforementioned species, and they are usually two-celled, measuring 5,5-13 x 3,5-6  $\mu\text{m}$ , and also are characterized by rougher structure of cellular walls. This species has reproductive stage *Mycosphaerella tassiana* (3,4,12).

Identification of these moulds is possible only on the basis of morphological and physiological characteristics. There are commercial agglutination tests for detection of galactomannan antigens of *Cladosporium herbarum* in the patient's serum, but also the cross-reactions with antigens of fungi of *Aspergillus spp.* are possible (16).

When suspecting of infection caused by *Cladosporium spp.*, it is essential to provide proper conditions, which means that the procedure presupposes biologically safe cabinets. As the spores of fungi of *Cladosporium spp.* are frequent air contaminants, it is necessary to take all hygienic-epidemiologic measures in the working laboratories so as to prevent possible contaminations of air, surrounding, and even the staff.

So far, there has been little data on sensibility of these fungi as the cause of opportunistic mycoses to antimycotics.

#### Pathogenicity and toxicity of *Cladosporium spp.*

In the routine laboratory work, *Cladosporium spp.* are frequently isolated as contaminants, but this species can, though rarely, be pathogenic and toxic to humans. Insofar, we could have found in the referent literature data on cases of cerebral phaeohyphomycosis, cutaneous infections, onychomycosis, sinusitis and pulmonary infections caused by *Cladosporium spp.* (11,12,17).

*Cladosporium spp.* are well-known and frequent aeroallergens inhabiting plants, wooden and leather objects. Conidia (spores) easily spread along the airways, so that they can be the cause of allergic reactions on the respiratory tract mucosa or asthma which is followed by edema and bronchospasm in the acute phase, while in chronic asthma, pulmonary emphysema can develop (3).

It is interesting that *Cladosporium spp.* can be isolated from the indoor air environment of asthmatics and non-asthmatics, which was confirmed in 26,3% of the cases investigated (18). There is little data on the available literature on the association between the infection caused by *Cladosporium spp.* and findings of specific antibodies to antigens of these fungi. One of the studies done in the recent years has determined that sinusitis caused by moulds are followed by an increase in specific antibodies of IgG class, while bronchitis as a complication is followed by decrease of specific, most probably protective antibodies (15).

Patients on peritoneal dialysis stand for a high-risk group to develop fungal peritonitis caused by filamentous fungi, moulds. This is confirmed by the case of a patient on peritoneal dialysis, hospitalized at the Clinic of Nephrology in Nis, who got peritonitis caused by *Cladosporium spp.* (19).

The latest data point that these fungi, besides causing allergic reactions, can also cause invasive fungal infections of the respiratory tract. There has been a case with intrabronchial lesion caused by *Cladosporium sphaerospermum* in a non-asthmatic patient (14).

Other factors of pathogenicity of these species are certainly the toxins they produce (3).

*Cladosporium cladosporioides* produces cladosporin, emodin (mutagenic and cytotoxic product) as well as some other less toxic compounds. The effect of toxins has been proved *in vivo* in sensitive laboratory animals. A mouse feed on cultures of this species will die of hemolytic jaundice and renal failure. Still, there has not been any proof on the existence of toxic effects after inhaling the spores of this fungus (4,3,13).

Investigation of *Cladosporium sphaerospermum* toxicity has pointed to the toxic effect

registered on chicken embryos, but the chemical content and characteristics have not been completely determined (14,15). *Cladosporium herbarum*, accor-

ding to the investigations so far, has not been classified as a species significantly toxic to humans (12).

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## CLADOSPORIUM SPP. – UZROK OPORTUNISTIČKIH MIKOZA

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### SAŽETAK

Gljive roda *Cladosporium* rasprostranjene su širom sveta i spadaju u najčešće kontaminante vazduha. Neke vrste ovog roda često se u laboratorijskom radu izoluju kao kontaminanti, ali postoje i vrste roda *Cladosporium* koje mogu biti patogene i toksične za čoveka. Do danas je poznato da ove gljive mogu biti izazivači cerebralne ili kutane feohifomikoze. Takođe, gljive roda *Cladosporium* su jaki aero-alergeni, tako da mogu izazvati ozbiljne alergijske bolesti respiratornog trakta, kao i invazivne intrabronhijalne lezije.

Identifikacija roda *Cladosporium*, kao i diferenciranje vrsta ovog roda, moguće je samo na osnovu morfoloških i morfometrijskih karakteristika nakon standardne procedure kultivisanja i izolovanja ovih sojeva u laboratoriji za mikologiju. Procedura rada u izolovanju ovih vrsta podrazumeva bezbedne biološke kabinete i opreznost pri radu. Malo se zna o osetljivosti roda *Cladosporium* prema mikoticima.

***Ključne reči:*** *Cladosporium spp.*, oportunističke mikoze