

# Mycosis: Understanding Fungal Infections and Their Impact on Human Health

José D Sidrim\*

Department of Pathology, Federal University of Ceará, Ceará, Brazil

\*Corresponding author: José D Sidrim, Department of Pathology, Federal University of Ceará, Ceará, Brazil, E-mail: josedsid@gmail.com

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## Description

Mycosis, or fungal infection, is a common and diverse group of diseases caused by various species of fungi. These infections can affect different parts of the body, including the skin, nails, respiratory tract, and internal organs. In this article, we explore the intricacies of mycosis, its classification, risk factors, and treatment options.

Mycosis, especially candidiasis, are important pathologies in the medical and dental consultation, particularly for immunodeficient patients. Their extension and severity, added to pharmacological interactions and development of resistance to antifungal agents, justify the search for new drugs and pharmacological strategies. Among the microorganisms involved, *Candida albicans* stands out because it produces important infections. Its hyphae have been shown in connective tissues of periodontal patients, in association with highly invasive anaerobic bacteria.

The prenylated flavonoid was isolated and identified from *Dalea elegans* roots. It was extracted with EtOH and chromatographed on a silica gel column using C, H, -EtOAc with increasing concentrations of EtOAc as eluent. The eluate was rechromatographed on silica gel TLC using C,H,-EtOH. Its structure was characterized by spectroscopic and spectrophotometric methods.

As mitochondria are often used as targets in studies of potential medicinal drugs, 8PP was tested initially in cells rich in such organelles, like those of liver, given the relevance of such organ in metabolic processes. In rat hepatocytes, 8PP inhibited the activity of mitochondrial enzymes associated to the electron transport chain and the adenosine-5'-triphosphate (ATP) synthesis. By inhibiting their mitochondrial respiration, reflected through cell oxidoreductase activity assays in human HEP-2 tumor whole cells, 8PP kills them.

In azole-resistant *C. albicans*, 8PP inhibits cell growth and bears additive interactions with fluconazole (FCZ). These results are relevant since treatment of candidiasis is generally carried out with azole antifungals and resistance to these drugs has widely developed in the last times. The prenylated flavonoid also inhibits biofilms by accumulation of endogenous Reactive Oxygen Species (ROS) and reactive nitrogen intermediates (RNI). Besides killing per se, 8PP helps FCZ to achieve an almost complete fungicidal effect, which would be crucial to eradicate

fungal infections, since the major disadvantage of azole antifungals is their fungistatic nature that favours the onset of drug resistance..

Extrusion of antimicrobials is a crucial mechanism of drug resistance. Inhibition of the transporters involved would increase the intracellular concentration of such drugs with the subsequent reversion of resistance. In this context, 8PP was the first prenylated flavonoid reported to inhibit azole extrusion in resistant *C. albicans*, acting on the carrier site of ATP-binding cassette (ABC) *cdr* transporters. The transporters *cdr1* and *cdr2* are among the main responsible molecules for resistance to antifungal agents reported in recent decades. *Cdr1* has been purified and tested in different biological studies and seems to share many features with *cdr2*. So far, six mechanisms of action related to *cdr1* have been proposed to inhibit the drug efflux in *C. albicans*.

*Cdr* transporters have two main types of sites: 1) one which carries compounds like azoles or 8PP and 2) other that generates the energy necessary for transport through ATP hydrolysis. They are located at the transmembrane and cytosolic domain, respectively.

In this work we study the effects of 8PP and FCZ on the ATPase activity associated to *cdr* transporters. In addition, we measure the cell oxidoreductase activity as an approach to evaluate the energy available for the efflux pump activation in *C. albicans*.

## Understanding *Candida albicans*

**Biology and Morphology:** *Candida albicans* is an oval-shaped, unicellular fungus belonging to the genus *Candida*. It is a dimorphic organism, meaning it can exist in two distinct forms: yeast and filamentous. In its yeast form, it appears as a single-cell organism, whereas in its filamentous form, it develops elongated hyphae that allow it to invade tissues. This adaptability contributes to its ability to cause infections in various host niches. **Prevalence and Colonization:** *Candida albicans* is a commensal inhabitant of the human microbiota, commonly found in the oral cavity, gastrointestinal tract, and vaginal mucosa. It coexists harmoniously with other microorganisms in these locations, without causing harm. However, when the balance of the microbial ecosystem is disrupted, *C. albicans* can flourish and become pathogenic.

## Pathogenicity of *Candida albicans*

**Factors Influencing Pathogenesis:** Several factors contribute to the transition of *C. albicans* from a commensal to a pathogenic organism. These include host factors (e.g., compromised immune system, underlying medical conditions), microbial factors (e.g., biofilm formation, secretion of virulence factors), and environmental factors (e.g., antibiotic use, high sugar diets). Together, these factors create an environment conducive to *C. albicans* overgrowth and invasion.

**Types of Candidiasis: Oropharyngeal Candidiasis:** Commonly known as thrush, oropharyngeal candidiasis affects the oral cavity, primarily seen in infants, elderly individuals, and those with weakened immune systems. It presents as white patches on the tongue, inner cheeks, and throat, causing discomfort and difficulty swallowing.

**Vulvovaginal Candidiasis:** Vulvovaginal candidiasis is a prevalent infection affecting many women during their lifetime. Symptoms include itching, burning, abnormal discharge, and redness of the vulva and vagina. Hormonal fluctuations,

antibiotic use, and compromised immune function can increase the risk of developing this condition.

**Invasive Candidiasis:** Invasive candidiasis is a severe systemic infection that occurs when *C. albicans* enters the bloodstream and spreads throughout the body. It primarily affects individuals with weakened immune systems, such as those with HIV/AIDS or undergoing chemotherapy. Invasive candidiasis can lead to severe complications and is associated with high mortality rates.

**Diagnosis and Treatment: A. Diagnosis of Candidiasis:** The diagnosis of candidiasis involves a combination of clinical evaluation, microscopic examination, and laboratory tests. In most cases, a healthcare professional will collect samples from the affected site, such as oral swabs or vaginal discharge, and culture them in a laboratory setting. Molecular techniques, such as polymerase chain reaction (PCR), may also be employed for accurate identification.

**B. Treatment Options:** The treatment of *Candida albicans* infections depends on the type and severity of the infection. Antifungal medications, such as azoles (e.g., fluconazole) or echinocandins.