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THE ROLE OF ORAL MICROBIOTA IN THE COLONIZATION AND ANTIFUNGAL RESISTANCE OF CANDIDA SPP.

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Abstract

The oral microbiota is made of microorganisms, including bacteria and fungi, that live in the mouth and help protect against infections. This balance is important for oral and overall health. When the balance is disturbed, for example, due to antibiotic use, weak immune system, or poor oral hygiene, certain fungi, especially *Candida albicans*, can grow too much and cause infections like oral candidiasis.

C. albicans is usually a harmless organism in the mouth, but it can become dangerous under the right conditions. It can change shapes which helps it invade tissues. It can also form biofilms, protective layers that make it harder for the immune system and antifungal drugs to remove it. These biofilms are difficult to treat and can lead to chronic or repeated infections.

This fungus does not live alone. It interacts with different types of bacteria in the mouth. Some bacteria support *C. albicans* by helping it stick to surfaces and protect it from antifungals. Others, like lactic acid bacteria, can stop it from growing or forming biofilms. These interactions show how important the whole microbial community is when it comes to preventing or treating fungal infections.

Thanks to modern technologies like gene sequencing and metagenomics, scientists can now study the entire oral microbiome, including both bacteria and fungi. These tools have shown how changes in bacterial populations can increase the risk of fungal infections. Understanding how the oral microbiota influences Candida resistance is essential for developing more effective diagnostic tools and treatment strategies. This review examines current knowledge on the synergistic and antagonistic interactions between *C. albicans* and the oral microbiota, focusing on how these interactions affect oral health and lead to antifungal resistance.

Keywords: *oral microbiota, Candida albicans, oral candidiasis, biofilm, fungal-bacterial interaction, antifungal resistance*

Introduction

1.1 Oral microbiota

The human oral cavity hosts one of the most diverse microbial communities in the body, comprising bacteria, fungi, viruses, and archaea. This complex ecosystem, referred to as the oral microbiota [1], plays a fundamental role in maintaining oral and systemic health, ensuring oral homeostasis, protecting

the oral cavity and preventing disease development. The oral cavity's microbial community is the second most complex in the human body, after the gut-associated microbiome. It plays a key role in defending against opportunistic fungal pathogens, especially Candida species. These fungi naturally inhabit the oral cavity as commensal organisms, mostly in a planktonic state but can become pathogenic under certain conditions, leading to oral candidiasis and other mucosal infections [2]. The balance between microbial residents and host factors is essential for preventing fungal overgrowth. Disruptions to this microbial balance, a phenomenon known as dysbiosis, [3] can lead to a range of oral pathologies including caries, periodontitis, cavities endodontic disease and tonsillitis and can be associated with the development of several systemic diseases, for example cardiovascular disease, diabetes, pneumonia, obesity, digestive system diseases, colon cancer, and psychological disorders [4]. Oral microbial communities are not uniform, different areas of the mouth harbor distinct microbial niches due to variations in surface types and environmental conditions. This diversity impacts how different microbes, including Candida species, interact and thrive. For example, the tongue›s papillary structure facilitates the colonization of *C. albicans*. These variations in microbial composition and function make certain areas more prone to specific infections [5].

1.2 *Candida albicans* virulence

Among the fungal species present, *C. albicans* is the most prevalent due to its lifestyle as a powerful and commensal pathogen and the fact that its pathobiology has been studied more thoroughly than that of most other fungal pathogens [6,18]. Based on the World Health Organization (WHO) fungal priority pathogens list [7], *C. albicans* is categorized as a critical priority pathogen. This means it is considered a high-risk fungal pathogen requiring urgent research and development attention.

C. albicans cells can exist in multiple forms, with hyphae recognized as the invasive and pathogenic form responsible for host cell penetration. These forms include blastospores (yeast cells), pseudo hyphae (elongated yeast cells in chains), and hyphae (branched, tubular cells) [6,8]. The transition between these forms is crucial for the fungus's ability to cause infection and disease and can be triggered by several environmental factors such as temperature, pH, and the presence of host factors like serum. The hyphal form is invasive and pathogenic and can penetrate host tissues due to its elongated shape and ability to produce enzymes that aid in invasion.

In addition, another virulence mechanism include biofilm formation which begins with adhesion of Candida cells to surfaces like oral epithelial cells, denture materials, or medical devices, followed by the formation of microcolonies and the production of extracellular matrix composed of polysaccharides, that encases the cells. In the final phase, when mature biofilm has already been formed, some cells can detach and disperse, spread to other locations and potentially start new biofilm formations. These biofilms protect them from external factors such as host immune system defenses and antifungal drugs [9].

1.3 *C. albicans* and Oral Bacteria Interactions

C. albicans pathogenicity is further increased by its interactions with oral bacteria such as Streptococcus, Actinomyces, Fusobacterium, and lactic acid bacteria which can be synergistic or antagonistic involve physical adhesion, extracellular signaling and metabolic exchanges [10,11]. These interactions, especially those involving polymicrobial biofilm formation increase antifungal resistance through several mechanisms, including the production of extracellular matrix (which can sequester drugs), horizontal gene transfer of resistance genes, overexpression of the efflux pump or phenotypic switching like hyphal development [12]. Streptococcus mutans, for instance, have been shown to enhance Candida biofilm formation and support its survival through extracellular polymeric substances and inter-kingdom signaling pathways [13]. On the other hand, lactic acid bacteria can release compounds that prevent *C. albicans* from forming hyphal production and biofilms, demonstrating antagonistic microbial–fungal interaction [14].

In the past, research on the oral microbiome was limited by traditional culture-based methods, which could not detect many of the bacteria because they cannot grow in laboratory conditions. However, the

new advanced molecular techniques, especially next-generation sequencing (NGS) that targets the 16S rRNA gene in bacterial DNA and metagenomic analysis allowed to evidence the dynamic and complex nature of the bacterial communities living in the mouth. These methods give a thorough understanding of the oral microbial community by enabling them to examine the entire microbial community (metagenome) without having to cultivate individual bacteria [15]. Furthermore, they have revealed that changes community in the oral bacterial community can significantly impact fungal growth and pathogenicity. Shifts in bacterial populations can create environments that favor the growth of harmful fungi or reduce the presence of beneficial bacteria that can suppress fungal growth.

1.4 Non- albicans species

Unlike *C. albicans*, non- albicans species such as C. glabrata, C. krusei, C. tropicalis, show intrinsic or rapidly acquired resistance to first-line antifungal medications, especially azoles like fluconazole and sometimes even to echinocandins [16]. This resistance makes treatment more difficult, leading to poor outcomes, recurrent infections and increased morbidity. The growing incidence of antifungal-resistant strains is further complicated by the polymicrobial nature of the oral environment. Changes in the oral microbiota, due to factors such as antibiotic use, poor oral hygiene, and systemic diseases can alter the balance between commensal and pathogenic organisms, facilitating the overgrowth of resistant Candida species.

Furthermore, the incidence of oral candidiasis is increasing due to rising numbers of immunocompromised individuals, overuse of antibiotics, poor oral hygiene, and widespread use of prosthetic dental devices. Despite the availability of effective antifungal therapies, primarily azoles (e.g., fluconazole) and polyenes (e.g., nystatin and amphotericin B), the clinical management of oral candidiasis has become increasingly complicated. Prolonged and frequent use of antifungal medications, particularly in patients with weakened immune systems, might potentially favor resistant forms of Candida, which can cause recurring or chronic infections.

When local Candida infections are not effectively contained by the host immune system or local microbiota, they can penetrate mucosal barriers and enter the bloodstream, a condition known as candidemia [11]. Once in the circulatory system, Candida species can invade various organs, and spread throughout the body, leading to systemic candidiasis. The progression to systemic disease is associated with high morbidity and mortality, particularly in immunocompromised individuals (e.g., those with HIV/AIDS, cancer, or undergoing chemotherapy), or in patients undergoing intensive care. In elderly and intubated patients, for example, aspiration of Candida-laden oral biofilms has been associated with respiratory infections, including pneumonia. Additionally, oral dysbiosis may worsen diseases like periodontitis and has been linked to poor glycemic control in diabetic patients. These correlations highlight how important it is to manage Candida colonization as part of comprehensive oral and systemic health strategies.

Methodology

An electronic literature search was performed on databases including PubMed, Scopus, and Google Scholar, focusing on publications from 2020 to 2025. Key words included ‘oral microbiota’, *‘Candida albicans’*, ‘oral candidiasis’, ‘biofilm’, ‘fungal-bacterial interaction’. Articles were selected based on relevance, recency, and the presence of clinical or experimental data. Key findings were synthesized to identify common themes, mechanisms, and therapeutic developments related to Candida colonization and oral microbiota interactions.

Discussion

This review shows that the microorganisms living in our mouth such as bacteria, fungi, viruses, and archaea play an important role in keeping our mouth healthy. When this balance is disturbed, for example:

by antibiotics, poor oral hygiene, or health problems, fungi like *C. albicans* can grow and cause infections. It can create a strong layer called a biofilm, which helps it survive and makes it harder to treat.

Also, *C. albicans* interact with different bacteria in the mouth. Some bacteria help them grow and become more resistant to medicine, while others stop it from growing. This means that the way fungi and bacteria live together in the mouth is very important. Learning more about these relationships can help us find better ways to prevent and treat oral infections.

Conclusion

In conclusion, the oral microbiota plays a key role in protecting the mouth from infections, including those caused by *C. albicans*. Although *C. albicans* is a frequent commensal bacterium in the oral cavity, the disturbance of microbial homeostasis is linked to its transformation into a pathogenic condition. The ability of *C. albicans* to form biofilms and interact with oral bacteria, whether synergistic or antagonistic, can enhance or inhibit its virulence, biofilm development, and resistance to antifungal therapies. Contemporary molecular techniques like metagenomics and next-generation sequencing have increased our knowledge of the oral microbiome and the complex inter-kingdom connections between fungi and bacteria. Understanding how they work together in the oral cavity can help to develop better treatments. It is important to focus on keeping a healthy balance in the oral microbiome to prevent infections and improve both oral and overall health.A comprehensive strategy including good oral hygiene, careful use of antifungal drugs, and possibly using probiotics is required to tackle antifungal resistance and to properly manage Candida infections. Future research should investigate microbial interactions at the molecular level and investigate personalized treatments and new diagnostic tools based on the microbiome to reduce the impact of the oral fungal infections.

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