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# Influence of Photodynamic Therapy Combined with Antimicrobial Peptides on Oral Biofilm and 3D Reconstructed Human Oral Epithelium Model

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By

LUANA MENDONÇA DIAS SANTANA

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**ABSTRACT**

This thesis explores innovative approaches to treat *Candida albicans* infections in single and mixed-species biofilms when combined also with *Streptococcus mutans*. The experimental publication 1 evaluated the antimicrobial peptides/proteins (AMPs) Hylin-a1, Temporin-SHa, and KR-12-a5, against fluconazole-resistant and susceptible *C. albicans* and identified Temporin-SHa as the most promising AMP with significant antifungal and biocompatibility abilities, inhibiting biofilm formation and reducing fungal biomass. Publication 2 assessed the AMPs DR9-RR14, RR14, Histatin 3, and Histatin 5 on mixed biofilms formed on acrylic resin, showing reduced biofilm biomass and extracellular matrix (ECM) vital components disruption. Publication 3 investigated the combined effects of His3 and His5, the most promising AMPs evaluated previously, with antimicrobial photodynamic therapy (aPDT) on mixed biofilms containing three resistant strains of *C. albicans* and *S. mutans*, showing enhanced biofilm inhibition and reduced extracellular matrix (ECM) components, also minimizing the virulence of resistant strains and highlighting the synergistic potential of this new approach. Lastly, publication 4 validated the combination of His3 and His5 with aPDT in a 3D oral epithelium model, demonstrating limited infection penetration into deeper layers, reduced hyphal invasion, and compatibility with host tissue. These findings collectively highlight the potential of combining aPDT with AMPs as a targeted approach to overcome microbial resistance and biofilm complexity. Proteomic profiling provided information about the molecular mechanisms by which this combination treatment works, proving its efficacy as a therapy. As a future investigation, the combined treatment validated in this study needs to be extended to in vivo models to evaluate tissue regeneration behavior, particularly after the remission of the lesions.

Santana LMD. Influência da terapia fotodinâmica combinada com peptídeos antimicrobianos sobre biofilme oral e modelo 3D de epitélio oral humano reconstruído[Thesis Doctor]. University of Saskatchewan, Saskatoon; São Paulo State University (UNESP), School of Dentistry, Araraquara; 2025.

**RESUMO**

Esta tese explora abordagens inovadoras para o tratamento de infecções por *Candida albicans* em biofilmes de espécie única e em associação com *Streptococcus mutans*. A primeira publicação experimental avaliou os peptídeos/proteínas antimicrobianos (AMPs) Hylin-a1, Temporin-SHa e KR-12-a5 contra cepas de *C. albicans* resistentes e suscetíveis ao fluconazol, identificando o Temporin-SHa como o AMP mais promissor, com significativa atividade antifúngica e biocompatibilidade, capaz de inibir a formação de biofilmes e reduzir a biomassa fúngica. A segunda publicação analisou os AMPs DR9-RR14, RR14, Histatina 3 (His3) e Histatina 5 (His5) em biofilmes mistos formados sobre resina acrílica, demonstrando redução da biomassa do biofilme e redução de componentes vitais da matriz extracelular (MEC). Na terceira publicação, foram investigados os efeitos combinados de His3 e His5, identificados anteriormente como os AMPs mais promissores, com a terapia fotodinâmica antimicrobiana (aPDT) em biofilmes mistos contendo três cepas resistentes de *C. albicans* associadas a *S. mutans*. Os resultados revelaram inibição significativa dos biofilmes, redução de componentes da MEC e diminuição da virulência das cepas resistentes, destacando o potencial sinérgico desta nova abordagem. Por fim, a quarta publicação validou a combinação de His3 e His5 com a aPDT em um modelo tridimensional (3D) de epitélio oral, evidenciando penetração limitada da infecção em camadas mais profundas, redução da invasão hifal e compatibilidade com o tecido hospedeiro. Coletivamente, esses achados ressaltam o potencial da combinação entre aPDT e AMPs como uma estratégia direcionada para superar a resistência microbiana e a complexidade dos biofilmes. A análise proteômica forneceu informações relevantes sobre os mecanismos moleculares pelos quais esse tratamento combinado atua, comprovando sua eficácia terapêutica. Como perspectiva futura, destaca-se a necessidade de expandir a investigação deste tratamento combinado para modelos in vivo, a fim de avaliar o comportamento de regeneração tecidual, especialmente após a remissão das lesões.

**Palavras – chave:** Biofilmes, Candida albicans, Streptococcus mutans

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# SUMMARY

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**LIST OF ABBREVIATIONS**

| | |
|---|---|
| AMPs | Antimicrobial peptides |
| CFU | Colony-forming unit |
| CaF | *Candida albicans* fluconazole-resistant strain |
| CaP | *Candida albicans* polyene-resistant strain |
| CaR | *Candida albicans* fluconazole-resistant strain |
| CaS | *Candida albicans* susceptible strain |
| CaW | *Candida albicans* wild-type strain |
| DR9-RR14 | Derived peptide from statherin DR9 sequence combined with RR14 motif |
| ECM | Extracellular matrix |
| FGH | Fibroblasts of human gingiva |
| GO | Gene Ontology |
| HPLC | High-performance liquid chromatography |
| His3 | Histatin 3 |
| His5 | Histatin 5 |
| KEGG | Kyoto Encyclopedia of Genes and Genomes |
| LED | Light-emitting diode |
| MFC | Minimum fungicidal concentration |
| MIC | Minimum inhibitory concentration |
| MS | Mass spectrometry |
| MTT | 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide |
| NOK | Normal oral keratinocytes |
| OHAT | Office of Health Assessment and Translation |
| OSF | Open Science Framework |
| PBS | Phosphate-buffered saline |
| PCA | Principal component analysis |
| PPIs | Protein-protein interactions |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| PS | Photosensitizer |
| ROS | Reactive oxygen species |
| RR14 | Arginine-rich peptide composed of 14 amino acids |
| Sm | *Streptococcus mutans* |
| aPDT | Antimicrobial photodynamic therapy |

## THESIS ORGANIZATION

This thesis adheres to the formatting guidelines outlined by the College of Graduate Studies and Postdoctoral Research, University of Saskatchewan for a manuscript-based thesis, consequently, there is some repetition of content across chapters.

- Chapter 1, the current chapter is a comprehensive introduction to the thesis topic, along with an overview of the thesis objectives.
- Chapter 2, representing literature review, is a systematic review of the literature which summarized several aspects of the thesis topic related to the application.
- Chapter 3 gives details about the study rationale, hypotheses, and objectives.
- Chapters 4 – 7, the main body of thesis, were structured as a manuscript-based format, consisting of three different research projects (objectives).
- Chapter 8 and 9 serve as general discussion section with a conclusion, summarizing the scientific gaps addressed and filled throughout this thesis and providing conclusion of the thesis. Moreover, it discusses the limitations and outlines future directions, with a potential focus on the potential translational clinical utility in oral health.
- Chapter 10 contains all the references cited in this work.

# 1 INTRODUCTION

## 1.1 Background

### 1.1.1 Oral Biofilms

Biofilms are complex, structured communities of microorganisms attached to a surface. Their development is coordinated through various mechanisms, including metabolic signaling, genetic exchange, and quorum sensing—an intercellular communication system. The biofilm lifecycle typically progresses through four main stages: (1) initial surface adhesion, (2) microcolony formation, (3) maturation, and (4) dispersion (Kaplan, 2010). The dispersion phase is particularly critical, as it may facilitate the spread of infection to new anatomical sites, promoting the establishment of additional biofilms. These developmental stages result in distinct cellular physiology and phenotypic traits that differ markedly from those of planktonic (free-floating) cells (Mirghani et al., 2022) (Figure 1).

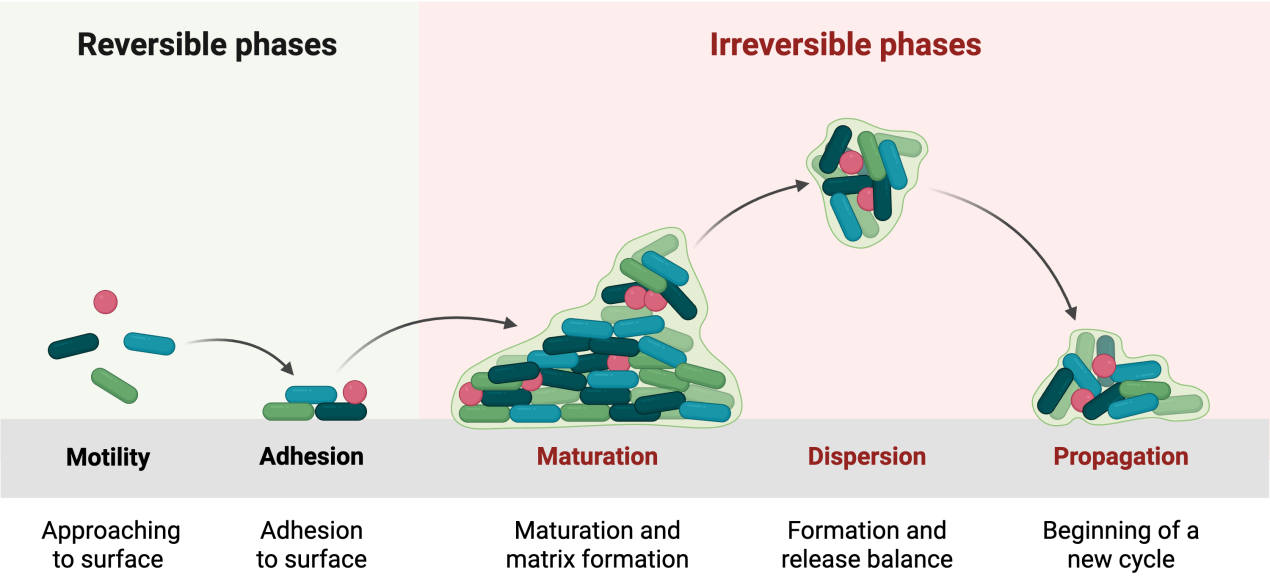


Figure 1. Biofilm Cycle. Created in BioRender. Lab, S. (2025) https://BioRender.com/nl247rq.

Biofilm cells are embedded within a self-produced extracellular matrix (ECM), composed of extracellular polymeric substances (EPS) synthesized by the microorganisms themselves (Flemming et al., 2007). The ECM plays a critical role in mediating cell-to-cell interactions within the biofilm and supports essential biological processes required for biofilm maintenance and stability. Its composition can dynamically adapt in response to environmental conditions, such as temperature, pH, and nutrient availability(Flemming et al., 2023). It because ECM can prevent the host's phagocytes from recognizing the fungi and activating the complement system. Additionally, it binds to antimicrobial agents, blocking their diffusion or neutralizing them, thus hindering their action(Kaplan, 2010). EPS components provide the necessary structural adhesion and cohesion, for three-dimensional organization of the biofilm(Bowen et al., 2018a).

In addition to structural functions, the ECM also serves as a recycling hub, retaining the components of lysed cells—including extracellular DNA (eDNA), which may act as a reservoir for horizontal gene transfer and contribute to the dissemination of genetic traits within the microbial community(Jiang et al., 2020). The ECM also impedes the host's immune defense mechanisms by preventing recognition by phagocytes and inhibiting activation of the complement system. Moreover, it restricts the diffusion of antimicrobial agents, either neutralizing them or reducing their access to deeper biofilm layers (Kaplan, 2010).

This three-dimensional structure creates gradients of nutrients and oxygen, which result in reduced metabolic activity in the innermost layers (Flemming et al., 2007). Consequently, antimicrobial agents that rely on active microbial metabolism for their mode of action become less effective (Kadosh & Mundodi, 2020). The ability to form such structured and protective communities makes biofilm-associated infections one of the most resilient forms of microbial persistence in clinical settings. (Thompson et al., 2011).

### 1.1.2 Role of *Candida albicans*

Given its highly adaptable nature, *Candida albicans* is one of the most studied fungal species in the context of oral biofilms. *Candida albicans* is the most prevalent species of *Candida*,

being a commensal microorganism typically found in the intestinal tract, genitourinary system, and the normal flora of the skin and mucous membranes(Scully et al., 1994). Immunosuppression in an individual can allow this microorganism to act as an opportunistic pathogen, penetrating the tissues and providing infections (Ishikawa et al., 2015). Individuals with conditions that weaken the immune system, such as kidney failure, AIDS, and diabetes, are more susceptible to developing oropharyngeal candidiasis. However, healthy individuals can also develop an infection due to an imbalance in the host's immune system (Scully et al., 1994). This fungus could adapt to changes in environmental pH through metabolic flexibility and robust nutrient acquisition systems, including a strong response to oxidative stress(Scully et al., 1994).

Aspects related to the virulence of *C. albicans* are mediated by factors such as substrate adherence, biofilm formation, and self-defense against the host's immune system(Thompson et al., 2011). The production of hydrolytic enzymes, such as proteases and phospholipases, can also be considered a virulence factor and is closely associated with tissue damage(Moyes & Naglik, 2011). Moreover, this fungus exhibits distinct morphologies such as blastoconidia and chlamydoconidia (yeast form), pseudohyphae, and hyphae, making it highly morphologically heterogeneous.

Biofilm formation begins with the adhesion of yeast cells to a substrate, followed by surface proliferation and the emergence of filamentous projections—comprising hyphae and, in some cases, pseudohyphae—that contribute to the maturation and structural complexity of the biofilm. Hypha formation is known to enhance virulence by enabling the invasion of epithelial cell layers, penetration of individual cells, disruption of endothelial cells, and lysis of macrophages and neutrophils. Pseudohyphae, in turn, are considered elongated yeast cells that lack the ability to separate from the mother cell during the cell cycle. Despite their different shapes, pseudohyphae more closely resemble yeast cells than true hyphae(Kadosh & Mundodi, 2020). In addition, the development of *C. albicans* biofilms can be influenced by several environmental factors, including the nature of the surface (substrate), culture medium, and pH. Study demonstrated this by evaluating biofilm formation on a polystyrene surface, revealing that both adhesion capacity and the expression of adhesion-related genes were affected under these conditions(Wu et al., 2014).

Additionally, *C. albicans* exhibits the ability to adapt to environmental pH changes through metabolic flexibility and robust nutrient acquisition systems, such as an effective response to oxidative stress(Cannon et al., 1995). Moreover, *C. albicans* expresses a variety of genes (such as CAT1 – catalase and SOD1 – superoxide dismutase) that activate pathways aiding in protection against free radicals and reactive oxygen species(Dantas et al., 2015). These features demonstrate that *C. albicans* possesses a wide range of biological tools that enable invasion, survival, and protection within host tissues.

### 1.1.3 Cross-Kingdom Interactions with *Streptococcus mutans*

Although *C. albicans* is the primary pathogen associated with denture stomatitis, bacteria such as *Streptococcus mutans* are also frequently found in biofilms formed under acrylic dentures, and these organisms may exhibit synergistic interactions (Bulet & Stöcklin, 2005). *C. albicans* is unable to efficiently metabolize sucrose but benefits from the free glucose and fructose generated from sucrose metabolism by *S. mutans* (Hwang et al., 2015). The synergy between these two microorganisms promotes the growth of *C. albicans* and consequently the development of polymicrobial biofilms, further enhancing the virulence potential of this model(D. Kim et al., 2017a; Rocha et al., 2018). Therefore, the biofilm of *C. albicans* and *S. mutans* exhibits a wide array of biological tools that facilitate invasion, survival, and protection within the host tissue (Pereira-Cenci et al., 2008).

Cross-kingdom metabolic cooperation promotes *C. albicans* proliferation and the development of stronger polymicrobial biofilms(D. Kim et al., 2017a). Mixed biofilm communities demonstrate greater structural intricacy and enhanced resilience against stress factors than single-species biofilms(Hwang et al., 2015). The interaction between species leads to increased virulence factor expression in *C. albicans* which subsequently boosts its ability to invade and persist in hosts(Y. Li et al., 2023). The surrounding extracellular matrix and interaction with *S. mutans* facilitate immune evasion by shielding fungal cells from phagocytosis and oxidative stress (D. Kim et al., 2017a).

Recent findings have shown that this cooperative behavior can be able to enhance the resistance of this biofilm to antimcirobial approaches. For instance, biofilms containing *C. albicans* and *S. mutans* demonstrate higher extracellular matrix (ECM) production, including increased levels of proteins, water-soluble polysaccharides (WSP), and extracellular DNA (eDNA)(Abreu-Pereira et al., 2023; Dias, Paul, et al., 2025). This process provides immune system evasion abilities and reduction drug penetration(Xiao et al., 2023).

### 1.1.4 Antimicrobial Resistance

The use of standardized conventional antifungal therapies may be limited due to the resistance that microorganisms can develop following drug exposure(Ho et al., 2025). Resistance to antifungal agents is considered a potential cause of treatment failure, leading to the persistence or progression of infection(Robbins et al., 2017).

The antimicrobial resistance can be classified as either primary or secondary. Intrinsic or primary resistance occurs when a microorganism exhibits low susceptibility to a given drug prior to any exposure to the agent(Brauner et al., 2016). The literature reports species in which all known isolates possess innate resistance to a specific antifungal, such as *Candida glabrata* and *Candida krusei*, which are intrinsically resistant to antifungal drugs, especially fluconazole(Silva et al., 2017a). Secondary or acquired resistance refers to resistance that may be developed by the microorganism after prolonged exposure to antifungal drugs(Brauner et al., 2016). The development of acquired resistance can occur through various mechanisms, including overexpression of the drug target, amino acid substitutions in the target that prevent binding of the inactivating enzyme, activation of stress response signaling pathways, upregulation of efflux pumps, or alterations in cellular pathways(Robbins et al., 2017). This resistance may be further accelerated by the organism's genetic plasticity or the presence of already-resistant strains. In this context, the combined effect of these contributing mechanisms leads to the selection of increasingly resistant organisms, resulting in high rates of recurrent infections (Christaki et al., 2020).

Variations in resistance phenotypes have been observed not only between different species and isolates of the same species but also across distinct growth states of the same strain(Pokharel et al., 2022). The formation of fungal biofilms can reduce susceptibility to conventional antifungal agents due to the difficulty of drug penetration through the biofilm layers to reach the target cell, thereby decreasing compound efficacy. It has been reported that in *C. albicans* biofilms, the surrounding glucan-rich matrix can act as a physical barrier, limiting the bioavailability of antifungal agents(Silva et al., 2017a).

Given the challenges related to fungal resistance, alternative strategies for inactivating Candida species have recently been suggested.

### 1.1.5 Antimicrobial Photodynamic Therapy (aPDT) as an Adjunctive Strategy

Antimicrobial photodynamic therapy (aPDT) has been employed in the inactivation of microorganisms and in the treatment of infections (Hu et al., 2018). aPDT involves the application of a photosensitizer (PS), a light source corresponding to the PS absorption band, and the presence of oxygen (Dantas et al., 2015; Demidova & Hamblin, 2005). The process of photosensitization begins with the treatment of the target cell with the PS. After, a light source with an appropriate wavelength for PS activation must be applied to illuminate the sensitized target (Donnelly et al., 2008). The interaction of light with the PS in the presence of oxygen promotes the formation of reactive oxygen species (ROS) that can induce cellular inactivation. It is suggested that this mechanism promotes the absorption of photons from the light source by the PS, which raises its electrons to an excited state. This excitation process occurs in the presence of oxygen and PS, which, when excited by light, can react with neighboring molecules through electron or hydrogen transfer (Type I reaction) or energy transfer to oxygen (Type II reaction) (Bonnett & Martínez, 2001). This therapy offers several advantages in treating infections caused by microorganisms, such as a broad spectrum of action and low mutagenic potential in exposed cells (Huang et al., 2012). However, compared to bacteria, photoinactivation of fungi appears to be more challenging

to achieve due to the larger cell size of these microorganisms, requiring a greater amount of singlet oxygen for cell death to occur (Demidova & Hamblin, 2005).

Another important aspect that has been observed is that the resistant strains of *C. albicans* are also less susceptible to aPDT alone. An application of aPDT (100 mg/L of PDZ combined with LED) led to a 4.36 $\log_{10}$ reduction in fluconazole-susceptible *C. albicans* (CaS) in an animal model (Carmello et al., 2015). In another study, aPDT using the same photosensitizer combined with LED light for the inactivation of fluconazole-resistant *C. albicans* (CaR) resulted in a reduction of approximately 1.96 $\log_{10}$ (Alves et al., 2019). When animals were subjected to treatment (5 sessions of aPDT), the results demonstrated that aPDT was as effective as Nystatin in inactivating CaS, achieving reductions of 3 and 3.2 $\log_{10}$, respectively. Additionally, it was observed that animals treated with aPDT showed complete remission of oral lesions (Carmello et al., 2016). Conversely, in the same animal model contaminated with a CaR strain (ATCC 96901), animals treated with either aPDT or Nystatin alone showed similar reductions in CaR viability (1.3 and 1.1 $\log_{10}$, for aPDT and Nystatin, respectively); however, no improvement in the macroscopic appearance of the lesion on the tongue was noted (Hidalgo et al., 2019). Therefore, treatments for infections caused by resistant strains require enhancements to improve their efficacy.

### 1.1.6 Antimicrobial Peptides Potential

Antimicrobial peptides (AMPs) are oligopeptides containing up to 50 amino acids with a broad spectrum of action against microorganisms, including viruses, bacteria, fungi, and parasites (Boparai & Sharma, 2020). AMPs occur naturally in both prokaryotes and eukaryotes and, in multicellular organisms, are part of the innate immune system's defense line against potentially harmful microorganisms (Bechinger & Gorr, 2017). Interestingly AMPs have grown primarily due to their low cost and their small molecular size, high biocompatibility, and antimicrobial action at low concentrations (Fosgerau & Hoffmann, 2015). AMPs with antibacterial activity have an overall positive charge and amphipathic nature, primarily targeting the lipid bilayer of the plasma membrane, along with intracellular targets (Bahar & Ren, 2013a). The action mechanism of AMPs

on bacterial plasma membranes depends on their electrostatic and hydrophobic interactions with the lipid bilayer, either intracellularly or extracellularly (Bechinger & Gorr, 2017).

Due to its significant antibacterial activity and reduced structural size, several types of AMPs have been becoming an extremely viable model for infection control assays. Peptides such as Hylin-a1 exhibit broad-spectrum antimicrobial activity against Gram-negative and Gram-positive bacteria, as well as diverse species of *Candida spp.* (*C. albicans, Candida krusei, Candida parapsilosis,* and *Cryptococcus neoformans*) (Castro et al., 2009; Vignoli Muniz et al., 2020). Another peptide that has been studied for its antimicrobial properties is KR-12-a5, a derivative of LL-37, classified as an α-helix, making it one of the smallest known peptides with antimicrobial activity (B. Mishra et al., 2013). Additionally, the peptide temporin-SHa also showed antimicrobial activity due to its secondary structure, net positive charge, hydrophobicity, helicity, and amphipathicity (Q. Chen et al., 2004). Despite numerous investigations testing the effects of various AMPs on different pathogens, there is a lack of studies in the literature addressing the antifungal potential of these AMPs in biofilm models involving resistant-*Candida* strains and *S. mutans* in the same biofilm.

Histatin 3 (His3) and Histatin 5 (His5), antimicrobial proteins with peptide sizes that come from saliva, also have distinct antimicrobial activity against oral microorganisms (Kavanagh & Dowd, 2004a). His5 particularly has an effect against *C. albicans*, inhibits its growth, and damages mitochondria and ATP production (Moffa, Mussi, et al., 2015a). Additionally, His3 also reduces *S. mutans* adhesion to hydroxyapatite (Marin et al., 2022). In addition, derived peptides like DR9, from statherin, inhibit *C. albicans* hyphal formation, reducing virulence and cell proliferation, while RR14, from His3, reduces S. mutans biofilm biomass (Moussa & Siqueira, 2021; Pellissari et al., 2021a). Despite their effectiveness, studies on Hist3, Hist5 and the AMP's derived (DR9-RR14 and RR14) have focused only on single-species biofilm, with limitations also in complex-biofilms involving more than one species (Gyurko et al., 2000; Kavanagh & Dowd, 2004a; Komatsu et al., 2011, 2019a; Mochon & Liu, 2008; Moffa, Machado, et al., 2015; Moussa &

# 9 CONCLUSION

This thesis collectively demonstrates the therapeutic potential of combining AMPs with aPDT as an innovative strategy to manage *C. albicans* and *S. mutans* biofilms, particularly those exhibiting antifungal resistance, with His3 and His5 identified as the most promising peptides through progression from simple biofilm models to mixed species and 3D oral tissue models.

# 10 REFERENCES


Abrahamse, H. & Hamblin, M. R. (2016). New photosensitizers for photodynamic therapy. *The Biochemical Journal*, *473*(4), 347–364. https://doi.org/10.1042/BJ20150942

Abreu-Pereira, C. A., Gorayb-Pereira, A. L., Menezes Noveletto, J. V., Jordão, C. C. & Pavarina, A. C. (2023). Zerumbone Disturbs the Extracellular Matrix of Fluconazole-Resistant Candida albicans Biofilms. *Journal of Fungi*, *9*(5), 576. https://doi.org/10.3390/jof9050576

Ahmad, P., Marin, L. M., Lowe, C., Katselis, G. S. & Siqueira, W. L. (2024). Salivary protein homology between humans and dogs: Mass spectrometry-based proteomics analysis. *Journal of Dentistry*, *142*, 104855. https://doi.org/10.1016/j.jdent.2024.104855

Allison, R. R. & Moghissi, K. (2013). Photodynamic Therapy (PDT): PDT Mechanisms. *Clinical Endoscopy*, *46*(1), 24–29. https://doi.org/10.5946/ce.2013.46.1.24

Alves, F., Carmello, J. C., Mima, E. G. de O., Costa, C. A. de S., Bagnato, V. S. & Pavarina, A. C. (2019). Photodithazine-mediated antimicrobial photodynamic therapy against fluconazole-resistant Candida albicans in vivo. *Medical Mycology*, *57*(5), 609–617. https://doi.org/10.1093/mmy/myy083

Amirshaghaghi, A., Yan, L., Miller, J., Daniel, Y., Stein, J. M., Busch, T. M., Cheng, Z. & Tsourkas, A. (2019). Chlorin e6-Coated Superparamagnetic Iron Oxide Nanoparticle (SPION) Nanoclusters as a Theranostic Agent for Dual-Mode Imaging and Photodynamic Therapy. *Scientific Reports*, *9*(1), 2613. https://doi.org/10.1038/s41598-019-39036-1

Astuty, S. D., Suhariningsih, Baktir, A. & Astuti, S. D. (2019). The Efficacy of Photodynamic Inactivation of the Diode Laser in Inactivation of the Candida albicans Biofilms With Exogenous Photosensitizer of Papaya Leaf Chlorophyll. *Journal of Lasers in Medical Sciences*, *10*(3), 215–224. https://doi.org/10.15171/jlms.2019.35

Bahar, A. A. & Ren, D. (2013a). Antimicrobial peptides. *Pharmaceuticals (Basel, Switzerland)*, *6*(12), 1543–1575. https://doi.org/10.3390/ph6121543

Bahar, A. A. & Ren, D. (2013b). Antimicrobial peptides. *Pharmaceuticals (Basel, Switzerland)*, *6*(12), 1543–1575. https://doi.org/10.3390/ph6121543

Basiri, T., Johnson, N. D., Moffa, E. B., Mulyar, Y., Serra Nunes, P. L., Machado, M. A. A. M. & Siqueira, W. L. (2017). Duplicated or Hybridized Peptide Functional Domains Promote Oral Homeostasis. *Journal of Dental Research*, *96*(10), 1162–1167. https://doi.org/10.1177/0022034517708552

Batoni, G., Maisetta, G. & Esin, S. (2016). Antimicrobial peptides and their interaction with biofilms of medically relevant bacteria. *Biochimica et Biophysica Acta (BBA) - Biomembranes*, *1858*(5), 1044–1060. https://doi.org/10.1016/j.bbamem.2015.10.013

Bechinger, B. & Gorr, S.-U. (2017). Antimicrobial Peptides: Mechanisms of Action and Resistance. *Journal of Dental Research*, *96*(3), 254–260. https://doi.org/10.1177/0022034516679973

Bonnett, R. & Martínez, G. (2001). Photobleaching of sensitisers used in photodynamic therapy. *Tetrahedron*, *57*(47), 9513–9547. https://doi.org/10.1016/S0040-4020(01)00952-8

Boparai, J. K. & Sharma, P. K. (2019). Mini Review on Antimicrobial Peptides, Sources, Mechanism and Recent Applications. *Protein & Peptide Letters*, *27*(1), 4–16. https://doi.org/10.2174/0929866526666190822165812

Boparai, J. K. & Sharma, P. K. (2020). Mini Review on Antimicrobial Peptides, Sources, Mechanism and Recent Applications. *Protein and Peptide Letters*, *27*(1), 4–16. https://doi.org/10.2174/0929866526666190822165812

Bourré, L., Giuntini, F., Eggleston, I. M., Mosse, C. A., Macrobert, A. J. & Wilson, M. (2010). Effective photoinactivation of Gram-positive and Gram-negative bacterial strains using an HIV-1 Tat peptide-porphyrin conjugate. *Photochemical & Photobiological Sciences : Official Journal of the European Photochemistry Association and the European Society for Photobiology*, *9*(12), 1613–1620. https://doi.org/10.1039/c0pp00146e

Bowen, W. H., Burne, R. A., Wu, H. & Koo, H. (2018a). Oral Biofilms: Pathogens, Matrix, and Polymicrobial Interactions in Microenvironments. *Trends in Microbiology*, *26*(3), 229–242. https://doi.org/10.1016/j.tim.2017.09.008

Bowen, W. H., Burne, R. A., Wu, H. & Koo, H. (2018b). Oral Biofilms: Pathogens, Matrix, and Polymicrobial Interactions in Microenvironments. *Trends in Microbiology*, *26*(3), 229–242. https://doi.org/10.1016/j.tim.2017.09.008

Brauner, A., Fridman, O., Gefen, O. & Balaban, N. Q. (2016). Distinguishing between resistance, tolerance and persistence to antibiotic treatment. *Nature Reviews Microbiology*, *14*(5), 320–330. https://doi.org/10.1038/nrmicro.2016.34

Brunet, K., Verdon, J., Ladram, A., Arnault, S., Rodier, M.-H. & Cateau, E. (2022). Antifungal activity of [K $^{3}$ ]temporin-SHa against medically relevant yeasts and moulds. *Canadian Journal of Microbiology*, *68*(6), 427–434. https://doi.org/10.1139/cjm-2021-0250

Bulet, P. & Stöcklin, R. (2005). Insect antimicrobial peptides: structures, properties and gene regulation. *Protein and Peptide Letters*, *12*(1), 3–11. https://doi.org/10.2174/0929866053406011

Caiaffa, K. S., Dos Santos, V. R., Abuna, G. F., Santos-Filho, N. A., Cilli, E. M., Sakai, V. T., Cintra, L. T. A. & Duque, C. (2021). Cytocompatibility and Synergy of EGCG and Cationic Peptides Against Bacteria Related to Endodontic Infections, in Planktonic and Biofilm Conditions. *Probiotics and Antimicrobial Proteins*, *13*(6), 1808–1819. https://doi.org/10.1007/s12602-021-09830-3

Caiaffa, K. S., Massunari, L., Danelon, M., Abuna, G. F., Bedran, T. B. L., Santos-Filho, N. A., Spolidorio, D. M. P., Vizoto, N. L., Cilli, E. M. & Duque, C. (2017). KR-12-a5 is a non-cytotoxic agent with potent antimicrobial effects against oral pathogens. *Biofouling*, *33*(10), 807–818. https://doi.org/10.1080/08927014.2017.1370087

Campos, M. S., Marchini, L., Bernardes, L. A. S., Paulino, L. C. & Nobrega, F. G. (2008). Biofilm microbial communities of denture stomatitis. *Oral Microbiology and Immunology*, *23*(5), 419–424. https://doi.org/10.1111/j.1399-302X.2008.00445.x

Cannon, R. D., Holmes, A. R., Mason, A. B. & Monk, B. C. (1995). Oral Candida: clearance, colonization, or candidiasis? *Journal of Dental Research*, *74*(5), 1152–1161. https://doi.org/10.1177/00220345950740050301

Cantón, E., Pemán, J., Gobernado, M., Viudes, A. & Espinel-Ingroff, A. (2004). Patterns of Amphotericin B Killing Kinetics against Seven *Candida* Species. *Antimicrobial Agents and Chemotherapy*, *48*(7), 2477–2482. https://doi.org/10.1128/AAC.48.7.2477-2482.2004

Carmello, J C, Dovigo, L. N., Mima, E. G., Jorge, J. H., de Souza Costa, C. A., Bagnato, V. S. & Pavarina, A. C. (2015). In vivo evaluation of photodynamic inactivation using Photodithazine® against Candida albicans. *Photochemical & Photobiological Sciences : Official Journal of the European Photochemistry Association and the European Society for Photobiology*, *14*(7), 1319–1328. https://doi.org/10.1039/c4pp00368c

Carmello, Juliana Cabrini, Alves, F., G Basso, F., de Souza Costa, C. A., Bagnato, V. S., Mima, E. G. de O. & Pavarina, A. C. (2016). Treatment of Oral Candidiasis Using Photodithazine®-Mediated Photodynamic Therapy In Vivo. *PloS One*, *11*(6), e0156947. https://doi.org/10.1371/journal.pone.0156947

Castro, M. S., Ferreira, T. C. G., Cilli, E. M., Crusca, E., Mendes-Giannini, M. J. S., Sebben, A., Ricart, C. A. O., Sousa, M. V. & Fontes, W. (2009). Hylin a1, the first cytolytic peptide isolated from the arboreal South American frog Hypsiboas albopunctatus ("spotted treefrog"). *Peptides*, *30*(2), 291–296. https://doi.org/10.1016/j.peptides.2008.11.003

Cavalheiro, M. & Teixeira, M. C. (2018). Candida Biofilms: Threats, Challenges, and Promising Strategies. *Frontiers in Medicine*, *5*. https://doi.org/10.3389/fmed.2018.00028

Chandra, J., Mukherjee, P. K., Leidich, S. D., Faddoul, F. F., Hoyer, L. L., Douglas, L. J. & Ghannoum, M. A. (2001). Antifungal Resistance of Candidal Biofilms Formed on Denture Acrylic in vitro. *Journal of Dental Research*, *80*(3), 903–908. https://doi.org/10.1177/00220345010800031101

Chen, Q., Wade, D., Kurosaka, K., Wang, Z. Y., Oppenheim, J. J. & Yang, D. (2004). Temporin A and Related Frog Antimicrobial Peptides Use Formyl Peptide Receptor-Like 1 as a Receptor to Chemoattract Phagocytes. *The Journal of Immunology*, *173*(4), 2652–2659. https://doi.org/10.4049/jimmunol.173.4.2652

Chen, S., Ye, X., Yu, X., Xu, Q., Pan, K., Lu, S. & Yang, P. (2015). Co-culture with periodontal ligament stem cells enhanced osteoblastic differentiation of MC3T3-E1 cells and osteoclastic differentiation of RAW264.7 cells. *International Journal of Clinical and Experimental Pathology*, *8*(11), 14596–14607.

Chen, Z., Yang, J., Wu, B. & Tawil, B. (2014). A Novel Three-Dimensional Wound Healing Model. *Journal of Developmental Biology*, *2*(4), 198–209. https://doi.org/10.3390/jdb2040198

Cho, J.-A., Jeon, S., Kwon, Y., Roh, Y. J., Lee, C.-H. & Kim, S. J. (2024). Comparative proteomics analysis of biofilms and planktonic cells of Enterococcus faecalis and Staphylococcus lugdunensis with contrasting biofilm-forming ability. *PloS One*, *19*(5), e0298283. https://doi.org/10.1371/journal.pone.0298283

Christaki, E., Marcou, M. & Tofarides, A. (2020). Antimicrobial Resistance in Bacteria: Mechanisms, Evolution, and Persistence. *Journal of Molecular Evolution*, *88*(1), 26–40. https://doi.org/10.1007/s00239-019-09914-3

Conlon, J. M., Kolodziejek, J. & Nowotny, N. (2004). Antimicrobial peptides from ranid frogs: taxonomic and phylogenetic markers and a potential source of new therapeutic agents. *Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics*, *1696*(1), 1–14. https://doi.org/10.1016/j.bbapap.2003.09.004

Costa-de-Oliveira, S. & Rodrigues, A. G. (2020). Candida albicans Antifungal Resistance and Tolerance in Bloodstream Infections: The Triad Yeast-Host-Antifungal. *Microorganisms*, *8*(2). https://doi.org/10.3390/microorganisms8020154

Czajka, K. M., Venkataraman, K., Brabant-Kirwan, D., Santi, S. A., Verschoor, C., Appanna, V. D., Singh, R., Saunders, D. P. & Tharmalingam, S. (2023). Molecular Mechanisms Associated with Antifungal Resistance in Pathogenic Candida Species. *Cells*, *12*(22). https://doi.org/10.3390/cells12222655

Dai, T., Huang, Y.-Y. & Hamblin, M. R. (2009). Photodynamic therapy for localized infections—State of the art. *Photodiagnosis and Photodynamic Therapy*, *6*(3–4), 170–188. https://doi.org/10.1016/j.pdpdt.2009.10.008

Dantas, A. da S., Day, A., Ikeh, M., Kos, I., Achan, B. & Quinn, J. (2015). Oxidative stress responses in the human fungal pathogen, Candida albicans. *Biomolecules*, *5*(1), 142–165. https://doi.org/10.3390/biom5010142

Darzi, Y., Letunic, I., Bork, P. & Yamada, T. (2018). IPath3.0: Interactive pathways explorer v3. *Nucleic Acids Research*, *46*(W1), W510–W513. https://doi.org/10.1093/NAR/GKY299

David, C. C. & Jacobs, D. J. (2014). Principal component analysis: a method for determining the essential dynamics of proteins. *Methods in Molecular Biology (Clifton, N.J.)*, *1084*, 193–226. https://doi.org/10.1007/978-1-62703-658-0_11

de Freitas, L. F. & Hamblin, M. R. (2016). Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. *IEEE Journal of Selected Topics in Quantum Electronics*, *22*(3), 348–364. https://doi.org/10.1109/JSTQE.2016.2561201

de Freitas, L. M., Lorenzón, E. N., Santos-Filho, N. A., Zago, L. H. de P., Uliana, M. P., de Oliveira, K. T., Cilli, E. M. & Fontana, C. R. (2018). Antimicrobial Photodynamic therapy enhanced by the peptide aurein 1.2. *Scientific Reports*, *8*(1), 4212. https://doi.org/10.1038/s41598-018-22687-x

Demchenko, A. P. (2020). Photobleaching of organic fluorophores: quantitative characterization, mechanisms, protection. *Methods and Applications in Fluorescence*, *8*(2), 022001. https://doi.org/10.1088/2050-6120/ab7365

Demidova, T. N. & Hamblin, M. R. (2005). Effect of cell-photosensitizer binding and cell density on microbial photoinactivation. *Antimicrobial Agents and Chemotherapy*, *49*(6), 2329–2335. https://doi.org/10.1128/AAC.49.6.2329-2335.2005

Dias, L. M., Cilli, E. M., Medeiros, K. S., Brasil, M. C. O. de A., Marin, L. M., Siqueira, W. L. & Pavarina, A. C. (2024). Antibiofilm Activity and Biocompatibility of Temporin-SHa: A Promising Antimicrobial Peptide for Control of Fluconazole-Resistant Candida albicans. *Microorganisms*, *12*(1). https://doi.org/10.3390/microorganisms12010099

Dias, L. M., Ferrisse, T. M., Medeiros, K. S., Cilli, E. M. & Pavarina, A. C. (2022a). Use of Photodynamic Therapy Associated with Antimicrobial Peptides for Bacterial Control: A

Systematic Review and Meta-Analysis. *International Journal of Molecular Sciences*, *23*(6), 3226. https://doi.org/10.3390/ijms23063226

Dias, L. M., Ferrisse, T. M., Medeiros, K. S., Cilli, E. M. & Pavarina, A. C. (2022b). Use of Photodynamic Therapy Associated with Antimicrobial Peptides for Bacterial Control: A Systematic Review and Meta-Analysis. *International Journal of Molecular Sciences*, *23*(6). https://doi.org/10.3390/ijms23063226

Dias, L. M., Klein, M. I., Ferrisse, T. M., Medeiros, K. S., Jordão, C. C., Bellini, A. & Pavarina, A. C. (2023). The Effect of Sub-Lethal Successive Applications of Photodynamic Therapy on Candida albicans Biofilm Depends on the Photosensitizer. *Journal of Fungi*, *9*(1), 111. https://doi.org/10.3390/jof9010111

Dias, L. M., Marin, L. M., Pavarina, A. C. & Siqueira, W. L. (2025). Unlocking Histatin Potential against *Candida albicans* and *Streptococcus mutans* Biofilms: Targeting the Extracellular Matrix While Preserving Oral Cell Integrity. *ACS Omega*. https://doi.org/10.1021/acsomega.5c02108

Dias, L. M., Paul, P., Pavarina, A. C. & Siqueira, W. L. (2025). Salivary proteins-enhanced antimicrobial photodynamic therapy: Overcoming three distinct cultures of resistant mixed biofilms. *Journal of Dentistry*, *157*, 105778. https://doi.org/10.1016/j.jdent.2025.105778

Donnelly, R. F., McCarron, P. A. & Tunney, M. M. (2008). Antifungal photodynamic therapy. *Microbiological Research*, *163*(1), 1–12. https://doi.org/10.1016/j.micres.2007.08.001

Dosselli, R., Ruiz-González, R., Moret, F., Agnolon, V., Compagnin, C., Mognato, M., Sella, V., Agut, M., Nonell, S., Gobbo, M. & Reddi, E. (2014). Synthesis, spectroscopic, and photophysical characterization and photosensitizing activity toward prokaryotic and eukaryotic cells of porphyrin-magainin and -buforin conjugates. *Journal of Medicinal Chemistry*, *57*(4), 1403–1415. https://doi.org/10.1021/jm401653r

Dosselli, R., Tampieri, C., Ruiz-González, R., De Munari, S., Ragàs, X., Sánchez-García, D., Agut, M., Nonell, S., Reddi, E. & Gobbo, M. (2013). Synthesis, characterization, and photoinduced antibacterial activity of porphyrin-type photosensitizers conjugated to the antimicrobial peptide apidaecin 1b. *Journal of Medicinal Chemistry*, *56*(3), 1052–1063. https://doi.org/10.1021/jm301509n

DUBOIS, M., GILLES, K., HAMILTON, J. K., REBERS, P. A. & SMITH, F. (1951). A colorimetric method for the determination of sugars. *Nature*, *168*(4265), 167. https://doi.org/10.1038/168167a0

Enjalbert, B., Nantel, A. & Whiteway, M. (2003). Stress-induced gene expression in Candida albicans: absence of a general stress response. *Molecular Biology of the Cell*, *14*(4), 1460–1467. https://doi.org/10.1091/mbc.e02-08-0546

Fan, F., Liu, Y., Liu, Y., Lv, R., Sun, W., Ding, W., Cai, Y., Li, W., Liu, X. & Qu, W. (2022). Candida albicans biofilms: antifungal resistance, immune evasion, and emerging therapeutic strategies. *International Journal of Antimicrobial Agents*, *60*(5–6), 106673. https://doi.org/10.1016/j.ijantimicag.2022.106673

Feese, E., Gracz, H. S., Boyle, P. D. & Ghiladi, R. A. (2019). Towards microbe-targeted photosensitizers: Synthesis, characterization and *in vitro* photodynamic inactivation of the

tuberculosis model pathogen *M. smegmatis* by porphyrin-peptide conjugates. *Journal of Porphyrins and Phthalocyanines*, *23*(11n12), 1414–1439. https://doi.org/10.1142/S1088424619501505

Feese, E., Gracz, H. S., Boyle, P. D. & Ghiladi, R. A. (2021). Towards microbe-targeted photosensitizers: Synthesis, characterization and *in vitro* photodynamic inactivation of the tuberculosis model pathogen *M. smegmatis* by porphyrin-peptide conjugates. In *Porphyrin Science by Women* (pp. 335–360). WORLD SCIENTIFIC. https://doi.org/10.1142/9789811223556_0027

Finkel, J. S. & Mitchell, A. P. (2011). Genetic control of Candida albicans biofilm development. *Nature Reviews Microbiology*, *9*(2), 109–118. https://doi.org/10.1038/nrmicro2475

Flemming, H.-C., Neu, T. R. & Wozniak, D. J. (2007). The EPS matrix: the "house of biofilm cells". *Journal of Bacteriology*, *189*(22), 7945–7947. https://doi.org/10.1128/JB.00858-07

Flemming, H.-C., van Hullebusch, E. D., Neu, T. R., Nielsen, P. H., Seviour, T., Stoodley, P., Wingender, J. & Wuertz, S. (2023). The biofilm matrix: multitasking in a shared space. *Nature Reviews. Microbiology*, *21*(2), 70–86. https://doi.org/10.1038/s41579-022-00791-0

Fosgerau, K. & Hoffmann, T. (2015). Peptide therapeutics: current status and future directions. *Drug Discovery Today*, *20*(1), 122–128. https://doi.org/10.1016/j.drudis.2014.10.003

Fusco-Almeida, A. M., de Matos Silva, S., dos Santos, K. S., de Lima Gualque, M. W., Vaso, C. O., Carvalho, A. R., Medina-Alarcón, K. P., Pires, A. C. M. da S., Belizario, J. A., de Souza Fernandes, L., Moroz, A., Martinez, L. R., Ruiz, O. H., González, Á. & Mendes-Giannini, M. J. S. (2023). Alternative Non-Mammalian Animal and Cellular Methods for the Study of Host–Fungal Interactions. *Journal of Fungi*, *9*(9), 943. https://doi.org/10.3390/jof9090943

Gad, M. & Fouda, S. (2020). Current perspectives and the future of Candida albicans-associated denture stomatitis treatment. *Dental and Medical Problems*, *57*(1), 95–102. https://doi.org/10.17219/dmp/112861

Gad, M. M. & Fouda, S. M. (2020a). Current perspectives and the future of Candida albicans-associated denture stomatitis treatment. *Dental and Medical Problems*, *57*(1), 95–102. https://doi.org/10.17219/dmp/112861

Gad, M. M. & Fouda, S. M. (2020b). Current perspectives and the future of Candida albicans-associated denture stomatitis treatment. *Dental and Medical Problems*, *57*(1), 95–102. https://doi.org/10.17219/dmp/112861

Galdiero, E., de Alteriis, E., De Natale, A., D'Alterio, A., Siciliano, A., Guida, M., Lombardi, L., Falanga, A. & Galdiero, S. (2020). Eradication of Candida albicans persister cell biofilm by the membranotropic peptide gH625. *Scientific Reports*, *10*(1), 5780. https://doi.org/10.1038/s41598-020-62746-w

Gao, L., Xu, T., Huang, G., Jiang, S., Gu, Y. & Chen, F. (2018). Oral microbiomes: more and more importance in oral cavity and whole body. *Protein & Cell*, *9*(5), 488–500. https://doi.org/10.1007/s13238-018-0548-1

Gao, Q., Huang, D., Deng, Y., Yu, W., Jin, Q., Ji, J. & Fu, G. (2021). Chlorin e6 (Ce6)-loaded supramolecular polypeptide micelles with enhanced photodynamic therapy effect against

Pseudomonas aeruginosa. *Chemical Engineering Journal*, *417*, 129334. https://doi.org/10.1016/j.cej.2021.129334

Gao, Y., Wang, J., Hu, D., Deng, Y., Chen, T., Jin, Q. & Ji, J. (2019). Bacteria-Targeted Supramolecular Photosensitizer Delivery Vehicles for Photodynamic Ablation Against Biofilms. *Macromolecular Rapid Communications*, *40*(4), e1800763. https://doi.org/10.1002/marc.201800763

Garcia, B. A., Panariello, B. H. D., Freitas-Pontes, K. M. de & Duarte, S. (2021). Candida biofilm matrix as a resistance mechanism against photodynamic therapy. *Photodiagnosis and Photodynamic Therapy*, *36*, 102525. https://doi.org/10.1016/j.pdpdt.2021.102525

Garcia de Carvalho, G., Maquera-Huacho, P. M., Silva Pontes, C., Annunzio, S. R. de, Fontana Mendonça, C. R., Nara de Souza Rastelli, A., de Oliveira, K. T., Teughels, W., Chorilli, M., Leal Zandim-Barcelos, D. & Palomari Spolidorio, D. M. (2023a). Chlorin-e6 conjugated to the antimicrobial peptide LL-37 loaded nanoemulsion enhances photodynamic therapy against multi-species biofilms related to periodontitis. *Photodiagnosis and Photodynamic Therapy*, *43*, 103725. https://doi.org/10.1016/j.pdpdt.2023.103725

Garcia de Carvalho, G., Maquera-Huacho, P. M., Silva Pontes, C., Annunzio, S. R. de, Fontana Mendonça, C. R., Nara de Souza Rastelli, A., de Oliveira, K. T., Teughels, W., Chorilli, M., Leal Zandim-Barcelos, D. & Palomari Spolidorio, D. M. (2023b). Chlorin-e6 conjugated to the antimicrobial peptide LL-37 loaded nanoemulsion enhances photodynamic therapy against multi-species biofilms related to periodontitis. *Photodiagnosis and Photodynamic Therapy*, *43*, 103725. https://doi.org/10.1016/j.pdpdt.2023.103725

Goodyear, M. C., Seidel, L., Krieger, J. R., Geddes-McAlister, J., Levesque, R. C. & Khursigara, C. M. (2023). Quantitative proteomics reveals unique responses to antimicrobial treatments in clinical Pseudomonas aeruginosa isolates. *MSystems*, *8*(5), e0049123. https://doi.org/10.1128/msystems.00491-23

Gulati, M. & Nobile, C. J. (2016a). Candida albicans biofilms: development, regulation, and molecular mechanisms. *Microbes and Infection*, *18*(5), 310–321. https://doi.org/10.1016/j.micinf.2016.01.002

Gulati, M. & Nobile, C. J. (2016b). Candida albicans biofilms: development, regulation, and molecular mechanisms. *Microbes and Infection*, *18*(5), 310–321. https://doi.org/10.1016/j.micinf.2016.01.002

Guo, Y., Yang, B., Zhou, X., Gong, Z., Wang, E., Pan, Y., Zhao, Y. & Liu, H. (2025). Proteomic Analysis Reveals the Phenotypic Heterogeneity and Tolerance Mechanisms of Halophilic Vibrio parahaemolyticus Under Dual Stress of Low Salinity and Bile Salts in the Human Intestine. *Biomolecules*, *15*(4). https://doi.org/10.3390/biom15040518

Gyurko, C., Lendenmann, U., Troxler, R. F. & Oppenheim, F. G. (2000). *Candida albicans* Mutants Deficient in Respiration Are Resistant to the Small Cationic Salivary Antimicrobial Peptide Histatin 5. *Antimicrobial Agents and Chemotherapy*, *44*(2), 348–354. https://doi.org/10.1128/AAC.44.2.348-354.2000

Hamblin, M. R. (2016). Antimicrobial photodynamic inactivation: a bright new technique to kill resistant microbes. *Current Opinion in Microbiology*, *33*, 67–73. https://doi.org/10.1016/j.mib.2016.06.008

Hamblin, M. R. & Abrahamse, H. (2018). Inorganic Salts and Antimicrobial Photodynamic Therapy: Mechanistic Conundrums? *Molecules (Basel, Switzerland)*, *23*(12). https://doi.org/10.3390/molecules23123190

Hampe, I. A. I., Friedman, J., Edgerton, M. & Morschhäuser, J. (2017). An acquired mechanism of antifungal drug resistance simultaneously enables Candida albicans to escape from intrinsic host defenses. *PLoS Pathogens*, *13*(9), e1006655. https://doi.org/10.1371/journal.ppat.1006655

Hansen, P. R. & Oddo, A. (2015). Fmoc Solid-Phase Peptide Synthesis. In *Methods Mol Biol* (pp. 33–50). https://doi.org/10.1007/978-1-4939-2999-3_5

Heberle, H., Meirelles, V. G., da Silva, F. R., Telles, G. P. & Minghim, R. (2015). InteractiVenn: A web-based tool for the analysis of sets through Venn diagrams. *BMC Bioinformatics*, *16*(1). https://doi.org/10.1186/S12859-015-0611-3

Hefny, Z. A., Ji, B., Elsemman, I. E., Nielsen, J. & Van Dijck, P. (2024). Transcriptomic meta-analysis to identify potential antifungal targets in Candida albicans. *BMC Microbiology*, *24*(1), 66. https://doi.org/10.1186/s12866-024-03213-8

Ho, C. S., Wong, C. T. H., Aung, T. T., Lakshminarayanan, R., Mehta, J. S., Rauz, S., McNally, A., Kintses, B., Peacock, S. J., de la Fuente-Nunez, C., Hancock, R. E. W. & Ting, D. S. J. (2025). Antimicrobial resistance: a concise update. *The Lancet. Microbe*, *6*(1), 100947. https://doi.org/10.1016/j.lanmic.2024.07.010

Hojo, K., Nagaoka, S., Ohshima, T. & Maeda, N. (2009). Bacterial interactions in dental biofilm development. *Journal of Dental Research*, *88*(11), 982–990. https://doi.org/10.1177/0022034509346811

Hou, Y., Yang, M., Jiang, H., Li, D. & Du, Y. (2019). Effects of low-intensity and low-frequency ultrasound combined with tobramycin on biofilms of extended-spectrum beta-lactamases (ESBLs) Escherichia coli. *FEMS Microbiology Letters*, *366*(3). https://doi.org/10.1093/femsle/fnz026

Hu, X., Huang, Y.-Y., Wang, Y., Wang, X. & Hamblin, M. R. (2018). Antimicrobial Photodynamic Therapy to Control Clinically Relevant Biofilm Infections. *Frontiers in Microbiology*, *9*, 1299. https://doi.org/10.3389/fmicb.2018.01299

Huang, L., Xuan, Y., Koide, Y., Zhiyentayev, T., Tanaka, M. & Hamblin, M. R. (2012). Type I and Type II mechanisms of antimicrobial photodynamic therapy: An in vitro study on gram-negative and gram-positive bacteria. *Lasers in Surgery and Medicine*, *44*(6), 490–499. https://doi.org/10.1002/lsm.22045

Humphries, R. M., Ambler, J., Mitchell, S. L., Castanheira, M., Dingle, T., Hindler, J. A., Koeth, L. & Sei, K. (2023). Erratum for Humphries et al., "CLSI Methods Development and Standardization Working Group Best Practices for Evaluation of Antimicrobial Susceptibility Tests." *Journal of Clinical Microbiology*, *61*(10). https://doi.org/10.1128/jcm.00739-23

Hwang, G., Marsh, G., Gao, L., Waugh, R. & Koo, H. (2015). Binding Force Dynamics of Streptococcus mutans-glucosyltransferase B to Candida albicans. *Journal of Dental Research*, *94*(9), 1310–1317. https://doi.org/10.1177/0022034515592859

International Organization for Standardization (ISO). (2020. October). *23. ISO 10993-5:2009 (Biological evaluation of medical devices – part 5: tests for in vitrocytotoxicity).* Https://Www.Iso.Org/Standard/36406.Html. https://www.iso.org/standard/36406.html

Ishikawa, K. H., Mayer, M. P. A., Miyazima, T. Y., Matsubara, V. H., Silva, E. G., Paula, C. R., Campos, T. T. & Nakamae, A. E. M. (2015). A Multispecies Probiotic Reduces Oral *Candida* Colonization in Denture Wearers. *Journal of Prosthodontics*, *24*(3), 194–199. https://doi.org/10.1111/jopr.12198

Janeth Rimachi Hidalgo, K., Carmello, J. C., Carolina Jordão, C., Aboud Barbugli, P., de Sousa Costa, C. A., Mima, E. G. de O. & Pavarina, A. C. (2019). Antimicrobial Photodynamic Therapy in Combination with Nystatin in the Treatment of Experimental Oral Candidiasis Induced by Candida albicans Resistant to Fluconazole. *Pharmaceuticals (Basel, Switzerland)*, *12*(3). https://doi.org/10.3390/ph12030140

Jayatilake, J. A. M. S., Samaranayake, Y. H. & Samaranayake, L. P. (2005). An ultrastructural and a cytochemical study of candidal invasion of reconstituted human oral epithelium. *Journal of Oral Pathology & Medicine : Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology*, *34*(4), 240–246. https://doi.org/10.1111/j.1600-0714.2005.00307.x

Jeong, H., Mason, S. P., Barabási, A.-L. & Oltvai, Z. N. (2001). Lethality and centrality in protein networks. *Nature*, *411*(6833), 41–42. https://doi.org/10.1038/35075138

Jiang, Y., Geng, M. & Bai, L. (2020). Targeting Biofilms Therapy: Current Research Strategies and Development Hurdles. *Microorganisms*, *8*(8). https://doi.org/10.3390/microorganisms8081222

Jiao, Y., Tay, F. R., Niu, L. & Chen, J. (2019). Advancing antimicrobial strategies for managing oral biofilm infections. *International Journal of Oral Science*, *11*(3), 28. https://doi.org/10.1038/s41368-019-0062-1

Johnson, G. A., Ellis, E. A., Kim, H., Muthukrishnan, N., Snavely, T. & Pellois, J.-P. (2014). Photoinduced membrane damage of E. coli and S. aureus by the photosensitizer-antimicrobial peptide conjugate eosin-(KLAKLAK)2. *PloS One*, *9*(3), e91220. https://doi.org/10.1371/journal.pone.0091220

Johnson, G. A., Muthukrishnan, N. & Pellois, J.-P. (2013). Photoinactivation of Gram positive and Gram negative bacteria with the antimicrobial peptide (KLAKLAK)(2) conjugated to the hydrophilic photosensitizer eosin Y. *Bioconjugate Chemistry*, *24*(1), 114–123. https://doi.org/10.1021/bc3005254

Jordão, C. C., Klein, M. I., Barbugli, P. A., Mima, E. G. de O., de Sousa, T. V., Ferrisse, T. M. & Pavarina, A. C. (2023a). DNase improves the efficacy of antimicrobial photodynamic therapy in the treatment of candidiasis induced with Candida albicans. *Frontiers in Microbiology*, *14*. https://doi.org/10.3389/fmicb.2023.1274201

Jordão, C. C., Klein, M. I., Barbugli, P. A., Mima, E. G. de O., de Sousa, T. V., Ferrisse, T. M. & Pavarina, A. C. (2023b). DNase improves the efficacy of antimicrobial photodynamic therapy in the treatment of candidiasis induced with Candida albicans. *Frontiers in Microbiology*, *14*, 1274201. https://doi.org/10.3389/fmicb.2023.1274201

Jordão, C. C., Klein, M. I., Carmello, J. C., Dias, L. M. & Pavarina, A. C. (2021). Consecutive treatments with photodynamic therapy and nystatin altered the expression of virulence and ergosterol biosynthesis genes of a fluconazole-resistant Candida albicans in vivo. *Photodiagnosis and Photodynamic Therapy*, *33*, 102155. https://doi.org/10.1016/j.pdpdt.2020.102155

Judzewitsch, P. R., Corrigan, N., Wong, E. H. H. & Boyer, C. (2021). Photo-Enhanced Antimicrobial Activity of Polymers Containing an Embedded Photosensitiser. *Angewandte Chemie (International Ed. in English)*, *60*(45), 24248–24256. https://doi.org/10.1002/anie.202110672

Kadosh, D. & Mundodi, V. (2020). A Re-Evaluation of the Relationship between Morphology and Pathogenicity in Candida Species. *Journal of Fungi (Basel, Switzerland)*, *6*(1). https://doi.org/10.3390/jof6010013

Kaiser, E., Colescott, R. L., Bossinger, C. D. & Cook, P. I. (1970). Color test for detection of free terminal amino groups in the solid-phase synthesis of peptides. *Analytical Biochemistry*, *34*(2), 595–598. https://doi.org/10.1016/0003-2697(70)90146-6

Kang, J., Dietz, M. J. & Li, B. (2019). Antimicrobial peptide LL-37 is bactericidal against Staphylococcus aureus biofilms. *PLOS ONE*, *14*(6), e0216676. https://doi.org/10.1371/journal.pone.0216676

Kaplan, J. B. (2010). Biofilm dispersal: mechanisms, clinical implications, and potential therapeutic uses. *Journal of Dental Research*, *89*(3), 205–218. https://doi.org/10.1177/0022034509359403

Karatan, E. & Watnick, P. (2009). Signals, regulatory networks, and materials that build and break bacterial biofilms. *Microbiology and Molecular Biology Reviews : MMBR*, *73*(2), 310–347. https://doi.org/10.1128/MMBR.00041-08

Karygianni, L., Ren, Z., Koo, H. & Thurnheer, T. (2020). Biofilm Matrixome: Extracellular Components in Structured Microbial Communities. *Trends in Microbiology*, *28*(8), 668–681. https://doi.org/10.1016/j.tim.2020.03.016

Kavanagh, K. & Dowd, S. (2004a). Histatins: antimicrobial peptides with therapeutic potential. *The Journal of Pharmacy and Pharmacology*, *56*(3), 285–289. https://doi.org/10.1211/0022357022971

Kavanagh, K. & Dowd, S. (2004b). Histatins: antimicrobial peptides with therapeutic potential. *The Journal of Pharmacy and Pharmacology*, *56*(3), 285–289. https://doi.org/10.1211/0022357022971

Kavanagh, K. & Dowd, S. (2004c). Histatins: antimicrobial peptides with therapeutic potential. *The Journal of Pharmacy and Pharmacology*, *56*(3), 285–289. https://doi.org/10.1211/0022357022971

*KEGG Mapper – Convert ID*. (n.d.). Retrieved March 27, 2025, from https://www.kegg.jp/kegg/tool/conv_id.html
*KEGG Mapper Color*. (n.d.). Retrieved March 27, 2025, from https://www.kegg.jp/kegg/mapper/color.html
Kim, D., Sengupta, A., Niepa, T. H. R., Lee, B.-H., Weljie, A., Freitas-Blanco, V. S., Murata, R. M., Stebe, K. J., Lee, D. & Koo, H. (2017a). Candida albicans stimulates Streptococcus mutans microcolony development via cross-kingdom biofilm-derived metabolites. *Scientific Reports*, *7*(1), 41332. https://doi.org/10.1038/srep41332
Kim, D., Sengupta, A., Niepa, T. H. R., Lee, B.-H., Weljie, A., Freitas-Blanco, V. S., Murata, R. M., Stebe, K. J., Lee, D. & Koo, H. (2017b). Candida albicans stimulates Streptococcus mutans microcolony development via cross-kingdom biofilm-derived metabolites. *Scientific Reports*, *7*, 41332. https://doi.org/10.1038/srep41332
Kim, H.-E., Liu, Y., Dhall, A., Bawazir, M., Koo, H. & Hwang, G. (2020). Synergism of Streptococcus mutans and Candida albicans Reinforces Biofilm Maturation and Acidogenicity in Saliva: An In Vitro Study. *Frontiers in Cellular and Infection Microbiology*, *10*, 623980. https://doi.org/10.3389/fcimb.2020.623980
Kmeid, J. G., Youssef, M. M., Kanafani, Z. A. & Kanj, S. S. (2013). Combination therapy for Gram-negative bacteria: what is the evidence? *Expert Review of Anti-Infective Therapy*, *11*(12), 1355–1362. https://doi.org/10.1586/14787210.2013.846215
Kobayashi, H., Oethinger, M., Tuohy, M. J., Procop, G. W. & Bauer, T. W. (2009). Improved detection of biofilm-formative bacteria by vortexing and sonication: a pilot study. *Clinical Orthopaedics and Related Research*, *467*(5), 1360–1364. https://doi.org/10.1007/s11999-008-0609-5
Komatsu, T., Kobayashi, K., Helmerhorst, E., Oppenheim, F. & Chang-Il Lee, M. (2019a). Direct assessment of the antioxidant property of salivary histatin. *Journal of Clinical Biochemistry and Nutrition*, *65*(3), 217–222. https://doi.org/10.3164/jcbn.19-53
Komatsu, T., Kobayashi, K., Helmerhorst, E., Oppenheim, F. & Chang-Il Lee, M. (2019b). Direct assessment of the antioxidant property of salivary histatin. *Journal of Clinical Biochemistry and Nutrition*, *65*(3), 217–222. https://doi.org/10.3164/jcbn.19-53
Komatsu, T., Kobayashi, K., Helmerhorst, E., Oppenheim, F. & Chang-Il Lee, M. (2019c). Direct assessment of the antioxidant property of salivary histatin. *Journal of Clinical Biochemistry and Nutrition*, *65*(3), 217–222. https://doi.org/10.3164/jcbn.19-53
Komatsu, T., Salih, E., Helmerhorst, E. J., Offner, G. D. & Oppenheim, F. G. (2011). Influence of histatin 5 on Candida albicans mitochondrial protein expression assessed by quantitative mass spectrometry. *Journal of Proteome Research*, *10*(2), 646–655. https://doi.org/10.1021/pr100861k
Komiyama, S., Miyasaka, R., Kikukawa, K. & Hayman, R. (2019). Can nano-hydroxyapatite permeate the oral mucosa? A histological study using three-dimensional tissue models. *PLOS ONE*, *14*(4), e0215681. https://doi.org/10.1371/journal.pone.0215681

Konopka, K., Dorocka-Bobkowska, B., Gebremedhin, S. & Düzgüneş, N. (2010). Susceptibility of Candida biofilms to histatin 5 and fluconazole. *Antonie van Leeuwenhoek*, *97*(4), 413–417. https://doi.org/10.1007/s10482-010-9417-5

Koo, H, Xiao, J., Klein, M. I. & Jeon, J. G. (2010). Exopolysaccharides produced by Streptococcus mutans glucosyltransferases modulate the establishment of microcolonies within multispecies biofilms. *Journal of Bacteriology*, *192*(12), 3024–3032. https://doi.org/10.1128/JB.01649-09

Koo, Hyun & Yamada, K. M. (2016). Dynamic cell-matrix interactions modulate microbial biofilm and tissue 3D microenvironments. *Current Opinion in Cell Biology*, *42*, 102–112. https://doi.org/10.1016/j.ceb.2016.05.005

Kragh, K. N., Alhede, M., Rybtke, M., Stavnsberg, C., Jensen, P. Ø., Tolker-Nielsen, T., Whiteley, M. & Bjarnsholt, T. (2018). The Inoculation Method Could Impact the Outcome of Microbiological Experiments. *Applied and Environmental Microbiology*, *84*(5). https://doi.org/10.1128/AEM.02264-17

Last, A., Maurer, M., S. Mosig, A., S. Gresnigt, M. & Hube, B. (2021). *In vitro* infection models to study fungal–host interactions. *FEMS Microbiology Reviews*, *45*(5). https://doi.org/10.1093/femsre/fuab005

Le Guern, F., Sol, V., Ouk, C., Arnoux, P., Frochot, C. & Ouk, T.-S. (2017). Enhanced Photobactericidal and Targeting Properties of a Cationic Porphyrin following the Attachment of Polymyxin B. *Bioconjugate Chemistry*, *28*(9), 2493–2506. https://doi.org/10.1021/acs.bioconjchem.7b00516

Li, X. S., Reddy, M. S., Baev, D. & Edgerton, M. (2003). Candida albicans Ssa1/2p is the cell envelope binding protein for human salivary histatin 5. *The Journal of Biological Chemistry*, *278*(31), 28553–28561. https://doi.org/10.1074/jbc.M300680200

Li, Y., Huang, S., Du, J., Wu, M. & Huang, X. (2023). Current and prospective therapeutic strategies: tackling Candida albicans and Streptococcus mutans cross-kingdom biofilm. *Frontiers in Cellular and Infection Microbiology*, *13*. https://doi.org/10.3389/fcimb.2023.1106231

Lin, Q., Zheng, Y., Wang, G., Shi, X., Zhang, T., Yu, J. & Sun, J. (2015). Protein adsorption behaviors of carboxymethylated bacterial cellulose membranes. *International Journal of Biological Macromolecules*, *73*, 264–269. https://doi.org/10.1016/j.ijbiomac.2014.11.011

Lin, S., Liu, C., Han, X., Zhong, H. & Cheng, C. (2021). Viral Nanoparticle System: An Effective Platform for Photodynamic Therapy. *International Journal of Molecular Sciences*, *22*(4). https://doi.org/10.3390/ijms22041728

Liu, F., Soh Yan Ni, A., Lim, Y., Mohanram, H., Bhattacharjya, S. & Xing, B. (2012). Lipopolysaccharide neutralizing peptide-porphyrin conjugates for effective photoinactivation and intracellular imaging of gram-negative bacteria strains. *Bioconjugate Chemistry*, *23*(8), 1639–1647. https://doi.org/10.1021/bc300203d

Liu, H., Jiang, Y., Wang, Z., Zhao, L., Yin, Q. & Liu, M. (2022). Nanomaterials as carriers to improve the photodynamic antibacterial therapy. *Frontiers in Chemistry*, *10*. https://doi.org/10.3389/fchem.2022.1044627

Lobo, C. I. V., Rinaldi, T. B., Christiano, C. M. S., De Sales Leite, L., Barbugli, P. A. & Klein, M. I. (2019). Dual-species biofilms of *Streptococcus mutans* and *Candida albicans* exhibit more biomass and are mutually beneficial compared with single-species biofilms. *Journal of Oral Microbiology*, *11*(1), 1581520. https://doi.org/10.1080/20002297.2019.1581520

Macias-Paz, I. U., Pérez-Hernández, S., Tavera-Tapia, A., Luna-Arias, J. P., Guerra-Cárdenas, J. E. & Reyna-Beltrán, E. (2023). Candida albicans the main opportunistic pathogenic fungus in humans. *Revista Argentina de Microbiologia*, *55*(2), 189–198. https://doi.org/10.1016/j.ram.2022.08.003

Macri, N., Dias, L. M., Pavarina, A. C., Siqueira, W. L. & Sperandio, F. F. (2025). Saliva-derived components can enhance the performance of toluidine blue in photodynamic therapy. *Frontiers in Pharmacology*, *16*, 1538520. https://doi.org/10.3389/fphar.2025.1538520

Mangoni, M. L. (2006). Temporins, anti-infective peptides with expanding properties. *Cellular and Molecular Life Sciences*, *63*(9), 1060–1069. https://doi.org/10.1007/s00018-005-5536-y

Marconi, A., Mattioli, E. J., Ingargiola, F., Giugliano, G., Marforio, T. D., Prodi, L., Di Giosia, M. & Calvaresi, M. (2023). Dissecting the Interactions between Chlorin e6 and Human Serum Albumin. *Molecules (Basel, Switzerland)*, *28*(5). https://doi.org/10.3390/molecules28052348

Marin, L. M., Xiao, Y., Cury, J. A. & Siqueira, W. L. (2022). Modulation of Streptococcus mutans Adherence to Hydroxyapatite by Engineered Salivary Peptides. *Microorganisms*, *10*(2). https://doi.org/10.3390/microorganisms10020223

Meyer, M. De, Ryck, J. De, Goormachtig, S. & Van Damme, P. (2020). Keeping in Touch with Type-III Secretion System Effectors: Mass Spectrometry-Based Proteomics to Study Effector-Host Protein-Protein Interactions. *International Journal of Molecular Sciences*, *21*(18). https://doi.org/10.3390/ijms21186891

Mirghani, R., Saba, T., Khaliq, H., Mitchell, J., Do, L., Chambi, L., Diaz, K., Kennedy, T., Alkassab, K., Huynh, T., Elmi, M., Martinez, J., Sawan, S. & Rijal, G. (2022). Biofilms: Formation, drug resistance and alternatives to conventional approaches. *AIMS Microbiology*, *8*(3), 239–277. https://doi.org/10.3934/microbiol.2022019

Mishra, B., Epand, R. F., Epand, R. M. & Wang, G. (2013). Structural location determines functional roles of the basic amino acids of KR-12, the smallest antimicrobial peptide from human cathelicidin LL-37. *RSC Advances*, *3*(42), 19560. https://doi.org/10.1039/c3ra42599a

Mishra, P., Pandey, C., Singh, U., Keshri, A. & Sabaretnam, M. (2019). Selection of appropriate statistical methods for data analysis. *Annals of Cardiac Anaesthesia*, *22*(3), 297. https://doi.org/10.4103/aca.ACA_248_18

Mochon, A. B. & Liu, H. (2008). The Antimicrobial Peptide Histatin-5 Causes a Spatially Restricted Disruption on the Candida albicans Surface, Allowing Rapid Entry of the Peptide into the Cytoplasm. *PLoS Pathogens*, *4*(10), e1000190. https://doi.org/10.1371/journal.ppat.1000190

Moffa, E. B., Machado, M. A. A. M., Mussi, M. C. M., Xiao, Y., Garrido, S. S., Giampaolo, E. T. & Siqueira, W. L. (2015). In Vitro Identification of Histatin 5 Salivary Complexes. *PloS One*, *10*(11), e0142517. https://doi.org/10.1371/journal.pone.0142517

Moffa, E. B., Mussi, M. C. M., Xiao, Y., Garrido, S. S., Machado, M. A. A. M., Giampaolo, E. T. & Siqueira, W. L. (2015a). Histatin 5 inhibits adhesion of C. albicans to Reconstructed Human Oral Epithelium. *Frontiers in Microbiology*, *6*, 885. https://doi.org/10.3389/fmicb.2015.00885

Moffa, E. B., Mussi, M. C. M., Xiao, Y., Garrido, S. S., Machado, M. A. A. M., Giampaolo, E. T. & Siqueira, W. L. (2015b). Histatin 5 inhibits adhesion of C. albicans to Reconstructed Human Oral Epithelium. *Frontiers in Microbiology*, *6*, 885. https://doi.org/10.3389/fmicb.2015.00885

Moussa, D. G. & Siqueira, W. L. (2021). Bioinspired caries preventive strategy via customizable pellicles of saliva-derived protein/peptide constructs. *Scientific Reports*, *11*(1), 17007. https://doi.org/10.1038/s41598-021-96622-y

Moyes, D. L. & Naglik, J. R. (2011). Mucosal immunity and Candida albicans infection. *Clinical & Developmental Immunology*, *2011*, 346307. https://doi.org/10.1155/2011/346307

Nakonieczna, J., Wolnikowska, K., Ogonowska, P., Neubauer, D., Bernat, A. & Kamysz, W. (2018). Rose Bengal-Mediated Photoinactivation of Multidrug Resistant Pseudomonas aeruginosa Is Enhanced in the Presence of Antimicrobial Peptides. *Frontiers in Microbiology*, *9*, 1949. https://doi.org/10.3389/fmicb.2018.01949

Navarro-Mendoza, M. I., Pérez-Arques, C., Parker, J., Xu, Z., Kelly, S. & Heitman, J. (2024). Alternative ergosterol biosynthetic pathways confer antifungal drug resistance in the human pathogens within the Mucor species complex. *MBio*, *15*(8), e0166124. https://doi.org/10.1128/mbio.01661-24

Nett, J. E. & Andes, D. R. (2020). Contributions of the Biofilm Matrix to Candida Pathogenesis. *Journal of Fungi (Basel, Switzerland)*, *6*(1). https://doi.org/10.3390/jof6010021

Nett, J., Lincoln, L., Marchillo, K., Massey, R., Holoyda, K., Hoff, B., VanHandel, M. & Andes, D. (2007). Putative role of beta-1,3 glucans in Candida albicans biofilm resistance. *Antimicrobial Agents and Chemotherapy*, *51*(2), 510–520. https://doi.org/10.1128/AAC.01056-06

Olleik, H., Baydoun, E., Perrier, J., Hijazi, A., Raymond, J., Manzoni, M., Dupuis, L., Pauleau, G., Goudard, Y., de La Villéon, B., Goin, G., Sockeel, P., Iqbal Choudhary, M., Di Pasquale, E., Nadeem-ul-Haque, M., Ali, H., Iftikhar Khan, A., Shaheen, F. & Maresca, M. (2019). Temporin-SHa and Its Analogs as Potential Candidates for the Treatment of Helicobacter pylori. *Biomolecules*, *9*(10), 598. https://doi.org/10.3390/biom9100598

Oppenheim, F. G., Helmerhorst, E. J., Lendenmann, U. & Offner, G. D. (2012). Anti-candidal activity of genetically engineered histatin variants with multiple functional domains. *PloS One*, *7*(12), e51479. https://doi.org/10.1371/journal.pone.0051479

Panariello, Beatriz H D, Klein, M. I., Dias, L. M., Bellini, A., Costa, V. B., Barbugli, P. A. & Pavarina, A. C. (2021). Lactobacillus casei reduces the extracellular matrix components of fluconazole-susceptible Candida albicans biofilms. *Biofouling*, *37*(9–10), 1006–1021. https://doi.org/10.1080/08927014.2021.2001645

Panariello, Beatriz Helena Dias, Klein, M. I., Mima, E. G. D. O. & Pavarina, A. C. (2018a). Fluconazole impacts the extracellular matrix of fluconazole-susceptible and -resistant

*Candida albicans* and *Candida glabrata* biofilms. *Journal of Oral Microbiology*, *10*(1), 1476644. https://doi.org/10.1080/20002297.2018.1476644

Panariello, Beatriz Helena Dias, Klein, M. I., Mima, E. G. D. O. & Pavarina, A. C. (2018b). Fluconazole impacts the extracellular matrix of fluconazole-susceptible and -resistant *Candida albicans* and *Candida glabrata* biofilms. *Journal of Oral Microbiology*, *10*(1), 1476644. https://doi.org/10.1080/20002297.2018.1476644

Paramanantham, P., Siddhardha, B., Lal Sb, S., Sharan, A., Alyousef, A. A., Al Dosary, M. S., Arshad, M. & Syed, A. (2019). Antimicrobial photodynamic therapy on Staphylococcus aureus and Escherichia coli using malachite green encapsulated mesoporous silica nanoparticles: an in vitro study. *PeerJ*, *7*, e7454. https://doi.org/10.7717/peerj.7454

Pellissari, C. V. G., Jorge, J. H., Marin, L. M., Sabino-Silva, R. & Siqueira, W. L. (2021a). Statherin-derived peptides as antifungal strategy against Candida albicans. *Archives of Oral Biology*, *125*, 105106. https://doi.org/10.1016/j.archoralbio.2021.105106

Pellissari, C. V. G., Jorge, J. H., Marin, L. M., Sabino-Silva, R. & Siqueira, W. L. (2021b). Statherin-derived peptides as antifungal strategy against Candida albicans. *Archives of Oral Biology*, *125*, 105106. https://doi.org/10.1016/j.archoralbio.2021.105106

Pereira-Cenci, T., Deng, D. M., Kraneveld, E. A., Manders, E. M. M., Del Bel Cury, A. A., ten Cate, J. M. & Crielaard, W. (2008). The effect of Streptococcus mutans and Candida glabrata on Candida albicans biofilms formed on different surfaces. *Archives of Oral Biology*, *53*(8), 755–764. https://doi.org/10.1016/j.archoralbio.2008.02.015

Petrovic, S., Mobbs, G. W., Bley, C. J., Nie, S., Patke, A. & Hoelz, A. (2022). Structure and Function of the Nuclear Pore Complex. *Cold Spring Harbor Perspectives in Biology*, *14*(12). https://doi.org/10.1101/cshperspect.a041264

Pimentel, B. N. A. da S., de Foggi, C. C., Barbugli, P. A., de Oliveira, R. C., de Avila, E. D., Longo, E. & Vergani, C. E. (2020). Antifungal activity and biocompatibility of α-AgVO3 microcrystals: A promising material against oral Candida disease. *Materials Science and Engineering: C*, *108*, 110405. https://doi.org/10.1016/j.msec.2019.110405

Pimentel, B. N. A. da S., Marin-Dett, F. H., Assis, M., Barbugli, P. A., Longo, E. & Vergani, C. E. (2022). Antifungal Activity and Biocompatibility of α-AgVO3, α-Ag2WO4, and β-Ag2MoO4 Using a Three-Dimensional Coculture Model of the Oral Mucosa. *Frontiers in Bioengineering and Biotechnology*, *10*. https://doi.org/10.3389/fbioe.2022.826123

Pokharel, K., Dawadi, B. R. & Shrestha, L. B. (2022). Role of Biofilm in Bacterial Infection and Antimicrobial Resistance. *Journal of Nepal Medical Association*, *60*(253), 836–840. https://doi.org/10.31729/jnma.7580

Pourhajibagher, M., Pourakbari, B. & Bahador, A. (2022). Contribution of antimicrobial photo-sonodynamic therapy in wound healing: an in vivo effect of curcumin-nisin-based poly (L-lactic acid) nanoparticle on Acinetobacter baumannii biofilms. *BMC Microbiology*, *22*(1), 28. https://doi.org/10.1186/s12866-022-02438-9

Prather, D., Krogan, N. J., Emili, A., Greenblatt, J. F. & Winston, F. (2005a). Identification and Characterization of Elf1, a Conserved Transcription Elongation Factor in Saccharomyces

cerevisiae . *Molecular and Cellular Biology*, *25*(22), 10122–10135. https://doi.org/10.1128/mcb.25.22.10122-10135.2005

Prather, D., Krogan, N. J., Emili, A., Greenblatt, J. F. & Winston, F. (2005b). Identification and characterization of Elf1, a conserved transcription elongation factor in Saccharomyces cerevisiae. *Molecular and Cellular Biology*, *25*(22), 10122–10135. https://doi.org/10.1128/MCB.25.22.10122-10135.2005

Puri, S. & Edgerton, M. (2014a). How does it kill?: understanding the candidacidal mechanism of salivary histatin 5. *Eukaryotic Cell*, *13*(8), 958–964. https://doi.org/10.1128/EC.00095-14

Puri, S. & Edgerton, M. (2014b). How does it kill?: understanding the candidacidal mechanism of salivary histatin 5. *Eukaryotic Cell*, *13*(8), 958–964. https://doi.org/10.1128/EC.00095-14

Qiu, L., Wang, C., Lan, M., Guo, Q., Du, X., Zhou, S., Cui, P., Hong, T., Jiang, P., Wang, J. & Xia, J. (2021). Antibacterial Photodynamic Gold Nanoparticles for Skin Infection. *ACS Applied Bio Materials*, *4*(4), 3124–3132. https://doi.org/10.1021/acsabm.0c01505

Qiu, L., Wang, C., Lei, X., Du, X., Guo, Q., Zhou, S., Cui, P., Hong, T., Jiang, P., Wang, J., Li, Y.-Q. & Xia, J. (2021). Gelatinase-responsive release of an antibacterial photodynamic peptide against Staphylococcus aureus. *Biomaterials Science*, *9*(9), 3433–3444. https://doi.org/10.1039/d0bm02201b

Quishida, C. C. C., de Oliveira Mima, E. G., Dovigo, L. N., Jorge, J. H., Bagnato, V. S. & Pavarina, A. C. (2015). Photodynamic inactivation of a multispecies biofilm using Photodithazine® and LED light after one and three successive applications. *Lasers in Medical Science*, *30*(9), 2303–2312. https://doi.org/10.1007/s10103-015-1811-9

Raja, Z., André, S., Abbassi, F., Humblot, V., Lequin, O., Bouceba, T., Correia, I., Casale, S., Foulon, T., Sereno, D., Oury, B. & Ladram, A. (2017). Insight into the mechanism of action of temporin-SHa, a new broad-spectrum antiparasitic and antibacterial agent. *PLOS ONE*, *12*(3), e0174024. https://doi.org/10.1371/journal.pone.0174024

Rapacka-Zdończyk, A., Woźniak, A., Michalska, K., Pierański, M., Ogonowska, P., Grinholc, M. & Nakonieczna, J. (2021). Factors Determining the Susceptibility of Bacteria to Antibacterial Photodynamic Inactivation. *Frontiers in Medicine*, *8*, 642609. https://doi.org/10.3389/fmed.2021.642609

Ribeiro, A. B., Pizziolo, P. G., Clemente, L. M., Aguiar, H. C., Poker, B. de C., Silva, A. A. M. E., Makrakis, L. R., Fifolato, M. A., Souza, G. C., Oliveira, V. de C., Watanabe, E. & Lovato da Silva, C. H. (2024). Strategies for Preventing and Treating Oral Mucosal Infections Associated with Removable Dentures: A Scoping Review. *Antibiotics (Basel, Switzerland)*, *13*(3). https://doi.org/10.3390/antibiotics13030273

Ribeiro, M., Gomes, I. B., Saavedra, M. J. & Simões, M. (2022). Photodynamic therapy and combinatory treatments for the control of biofilm-associated infections. *Letters in Applied Microbiology*, *75*(3), 548–564. https://doi.org/10.1111/lam.13762

Rikken, G., Meesters, L. D., Jansen, P. A. M., Rodijk-Olthuis, D., van Vlijmen-Willems, I. M. J. J., Niehues, H., Smits, J. P. H., Oláh, P., Homey, B., Schalkwijk, J., Zeeuwen, P. L. J. M. & van den Bogaard, E. H. (2023). Novel methodologies for host-microbe interactions and

microbiome-targeted therapeutics in 3D organotypic skin models. *Microbiome*, *11*(1), 227. https://doi.org/10.1186/s40168-023-01668-x

Robbins, N., Caplan, T. & Cowen, L. E. (2017). Molecular Evolution of Antifungal Drug Resistance. *Annual Review of Microbiology*, *71*(1), 753–775. https://doi.org/10.1146/annurev-micro-030117-020345

Rocha, G. R., Florez Salamanca, E. J., de Barros, A. L., Lobo, C. I. V. & Klein, M. I. (2018). Effect of tt-farnesol and myricetin on in vitro biofilm formed by Streptococcus mutans and Candida albicans. *BMC Complementary and Alternative Medicine*, *18*(1), 61. https://doi.org/10.1186/s12906-018-2132-x

Rothstein, D. M., Helmerhorst, E. J., Spacciapoli, P., Oppenheim, F. G. & Friden, P. (2002). Histatin-derived peptides: potential agents to treat localised infections. *Expert Opinion on Emerging Drugs*, *7*(1), 47–59. https://doi.org/10.1517/14728214.7.1.47

Roy, S. & Gow, N. A. R. (2023). The role of the Candida biofilm matrix in drug and immune protection. *Cell Surface (Amsterdam, Netherlands)*, *10*, 100111. https://doi.org/10.1016/j.tcsw.2023.100111

Sampaio, L. S., de Annunzio, S. R., de Freitas, L. M., Dantas, L. O., de Boni, L., Donatoni, M. C., de Oliveira, K. T. & Fontana, C. R. (2020). Influence of light intensity and irradiation mode on methylene blue, chlorin-e6 and curcumin-mediated photodynamic therapy against Enterococcus faecalis. *Photodiagnosis and Photodynamic Therapy*, *31*, 101925. https://doi.org/10.1016/j.pdpdt.2020.101925

Scully, C., EI-Kabir, M. & Samaranayake, L. P. (1994). Candida and Oral Candidosis: A Review. *Critical Reviews in Oral Biology & Medicine*, *5*(2), 125–157. https://doi.org/10.1177/10454411940050020101

Shah, Z. A., Farooq, S., Ali, S. A., Hameed, A., Choudhary, M. I. & Shaheen, F. (2018). New analogs of temporin-LK1 as inhibitors of multidrug-resistant (MDR) bacterial pathogens. *Synthetic Communications*, *48*(10), 1172–1182. https://doi.org/10.1080/00397911.2018.1437450

Shaikh, S. & Kumar, S. M. (2017). Beneficial effects of specific natural substances on oral health. *Saudi Medical Journal*, *38*(12), 1181–1189. https://doi.org/10.15537/smj.2017.12.20516

Sherrington, S. L., Sorsby, E., Mahtey, N., Kumwenda, P., Lenardon, M. D., Brown, I., Ballou, E. R., MacCallum, D. M. & Hall, R. A. (2017). Adaptation of Candida albicans to environmental pH induces cell wall remodelling and enhances innate immune recognition. *PLoS Pathogens*, *13*(5), e1006403. https://doi.org/10.1371/journal.ppat.1006403

Silva, S., Rodrigues, C., Araújo, D., Rodrigues, M. & Henriques, M. (2017a). Candida Species Biofilms' Antifungal Resistance. *Journal of Fungi*, *3*(1), 8. https://doi.org/10.3390/jof3010008

Silva, S., Rodrigues, C. F., Araújo, D., Rodrigues, M. E. & Henriques, M. (2017b). Candida Species Biofilms' Antifungal Resistance. *Journal of Fungi (Basel, Switzerland)*, *3*(1). https://doi.org/10.3390/jof3010008

Sims, K. R., Maceren, J. P., Liu, Y., Rocha, G. R., Koo, H. & Benoit, D. S. W. (2020). Dual antibacterial drug-loaded nanoparticles synergistically improve treatment of Streptococcus mutans biofilms. *Acta Biomaterialia*, *115*, 418–431. https://doi.org/10.1016/j.actbio.2020.08.032

Siqueira, W L, Helmerhorst, E. J., Zhang, W., Salih, E. & Oppenheim, F. G. (2007). Acquired enamel pellicle and its potential role in oral diagnostics. *Annals of the New York Academy of Sciences*, *1098*, 504–509. https://doi.org/10.1196/annals.1384.023

Siqueira, W L, Margolis, H. C., Helmerhorst, E. J., Mendes, F. M. & Oppenheim, F. G. (2010a). Evidence of intact histatins in the in vivo acquired enamel pellicle. *Journal of Dental Research*, *89*(6), 626–630. https://doi.org/10.1177/0022034510363384

Siqueira, W L, Margolis, H. C., Helmerhorst, E. J., Mendes, F. M. & Oppenheim, F. G. (2010b). Evidence of intact histatins in the in vivo acquired enamel pellicle. *Journal of Dental Research*, *89*(6), 626–630. https://doi.org/10.1177/0022034510363384

Siqueira, Walter L, Zhang, W., Helmerhorst, E. J., Gygi, S. P. & Oppenheim, F. G. (2007). Identification of protein components in in vivo human acquired enamel pellicle using LC-ESI-MS/MS. *Journal of Proteome Research*, *6*(6), 2152–2160. https://doi.org/10.1021/pr060580k

Skog, A. E., Corucci, G., Tully, M. D., Fragneto, G., Gerelli, Y. & Skepö, M. (2023). Interaction of a Histidine-Rich Antimicrobial Saliva Peptide with Model Cell Membranes: The Role of Histidines. *Langmuir : The ACS Journal of Surfaces and Colloids*, *39*(22), 7694–7706. https://doi.org/10.1021/acs.langmuir.3c00498

Soares, A. B., de Albuquerque, M. C., Rosa, L. M., Klein, M. I., Pavarina, A. C., Barbugli, P. A., Dovigo, L. N. & Mima, E. G. de O. (2024). Quantification methods of Candida albicans are independent irrespective of fungal morphology. *Microbial Cell (Graz, Austria)*, *11*, 265–277. https://doi.org/10.15698/mic2024.07.831

Song, N., Zhou, X., Li, D., Li, X. & Liu, W. (2022). A Proteomic Landscape of Candida albicans in the Stepwise Evolution to Fluconazole Resistance. *Antimicrobial Agents and Chemotherapy*, *66*(4), e0210521. https://doi.org/10.1128/aac.02105-21

Soukos, N. S. & Goodson, J. M. (2011). Photodynamic therapy in the control of oral biofilms. *Periodontology 2000*, *55*(1), 143–166. https://doi.org/10.1111/j.1600-0757.2010.00346.x

Subramanian, A., Tamayo, P., Mootha, V. K., Mukherjee, S., Ebert, B. L., Gillette, M. A., Paulovich, A., Pomeroy, S. L., Golub, T. R., Lander, E. S. & Mesirov, J. P. (2005). Gene set enrichment analysis: A knowledge-based approach for interpreting genome-wide expression profiles. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(43), 15545–15550. https://doi.org/10.1073/PNAS.0506580102

Sun, C., Zhao, X., Jiao, Z., Peng, J., Zhou, L., Yang, L., Huang, M., Tian, C. & Guo, G. (2022). The Antimicrobial Peptide AMP-17 Derived from Musca domestica Inhibits Biofilm Formation and Eradicates Mature Biofilm in Candida albicans. *Antibiotics*, *11*(11), 1474. https://doi.org/10.3390/antibiotics11111474

Szklarczyk, D., Kirsch, R., Koutrouli, M., Nastou, K., Mehryary, F., Hachilif, R., Gable, A. L., Fang, T., Doncheva, N. T., Pyysalo, S., Bork, P., Jensen, L. J. & Von Mering, C. (2023). The

STRING database in 2023: protein-protein association networks and functional enrichment analyses for any sequenced genome of interest. *Nucleic Acids Research*, *51*(1 D), D638–D646. https://doi.org/10.1093/NAR/GKAC1000

Tasso, C. O., Ribeiro Ribas, B., Morandin Ferrisse, T., Silva de Oliveira, J. & Jorge, J. H. (2024a). The antimicrobial activity of an antiseptic soap against Candida Albicans and Streptococcus Mutans single and dual-species biofilms on denture base and reline acrylic resins. *PLOS ONE*, *19*(7), e0306862. https://doi.org/10.1371/journal.pone.0306862

Tasso, C. O., Ribeiro Ribas, B., Morandin Ferrisse, T., Silva de Oliveira, J. & Jorge, J. H. (2024b). The antimicrobial activity of an antiseptic soap against Candida Albicans and Streptococcus Mutans single and dual-species biofilms on denture base and reline acrylic resins. *PloS One*, *19*(7), e0306862. https://doi.org/10.1371/journal.pone.0306862

Thein, Z. M., Samaranayake, Y. H. & Samaranayake, L. P. (2006). Effect of oral bacteria on growth and survival of Candida albicans biofilms. *Archives of Oral Biology*, *51*(8), 672–680. https://doi.org/10.1016/j.archoralbio.2006.02.005

Thein, Z. M., Samaranayake, Y. H. & Samaranayake, L. P. (2007). Characteristics of dual species Candida biofilms on denture acrylic surfaces. *Archives of Oral Biology*, *52*(12), 1200–1208. https://doi.org/10.1016/j.archoralbio.2007.06.007

Thompson, D. S., Carlisle, P. L. & Kadosh, D. (2011). Coevolution of Morphology and Virulence in Candida Species. *Eukaryotic Cell*, *10*(9), 1173–1182. https://doi.org/10.1128/EC.05085-11

Topaloglu, N., Guney, M., Aysan, N., Gulsoy, M. & Yuksel, S. (2016). The role of reactive oxygen species in the antibacterial photodynamic treatment: photoinactivation vs proliferation. *Letters in Applied Microbiology*, *62*(3), 230–236. https://doi.org/10.1111/lam.12538

Tornesello, A. L., Borrelli, A., Buonaguro, L., Buonaguro, F. M. & Tornesello, M. L. (2020). Antimicrobial Peptides as Anticancer Agents: Functional Properties and Biological Activities. *Molecules*, *25*(12), 2850. https://doi.org/10.3390/molecules25122850

Trigo-Gutierrez, J. K., Calori, I. R., de Oliveira Bárbara, G., Pavarina, A. C., Gonçalves, R. S., Caetano, W., Tedesco, A. C. & Mima, E. G. de O. (2023). Photo-responsive polymeric micelles for the light-triggered release of curcumin targeting antimicrobial activity. *Frontiers in Microbiology*, *14*, 1132781. https://doi.org/10.3389/fmicb.2023.1132781

Valente, M. T., Moffa, E. B., Crosara, K. T. B., Xiao, Y., de Oliveira, T. M., Machado, M. A. de A. M. & Siqueira, W. L. (2018). Acquired Enamel Pellicle Engineered Peptides: Effects on Hydroxyapatite Crystal Growth. *Scientific Reports*, *8*(1), 3766. https://doi.org/10.1038/s41598-018-21854-4

Van Dijck, P., Sjollema, J., Camue, B. P. A., Lagrou, K., Berman, J., d'Enfert, C., Andes, D. R., Arendrup, M. C., Brakhage, A. A., Calderone, R., Cantón, E., Coenye, T., Cos, P., Cowen, L. E., Edgerton, M., Espinel-Ingroff, A., Filler, S. G., Ghannoum, M., A.R. Gow, N., … Thevissen, K. (2018). Methodologies for in vitro and in vivo evaluation of efficacy of antifungal and antibiofilm agents and surface coatings against fungal biofilms. *Microbial Cell*, *5*(7), 300–326. https://doi.org/10.15698/mic2018.07.638

Vandeputte, P., Ferrari, S. & Coste, A. T. (2012). Antifungal Resistance and New Strategies to Control Fungal Infections. *International Journal of Microbiology*, *2012*, 1–26. https://doi.org/10.1155/2012/713687

Verma-Gaur, J. & Traven, A. (2016). Post-transcriptional gene regulation in the biology and virulence of Candida albicans. *Cellular Microbiology*, *18*(6), 800–806. https://doi.org/10.1111/cmi.12593

Vignoli Muniz, G. S., De la Torre, L. I., Duarte, E. L., Lorenzón, E. N., Cilli, E. M., Balan, A. & Lamy, M. T. (2020). Interaction of synthetic antimicrobial peptides of the Hylin a1 family with models of eukaryotic structures: Zwitterionic membranes and DNA. *Biochemistry and Biophysics Reports*, *24*, 100827. https://doi.org/10.1016/j.bbrep.2020.100827

Wiederhold, N. P. (2023). *Antifungal Susceptibility of Yeasts and Filamentous Fungi by CLSI Broth Microdilution Testing* (pp. 3–16). https://doi.org/10.1007/978-1-0716-3155-3_1

Wisplinghoff, H., Bischoff, T., Tallent, S. M., Seifert, H., Wenzel, R. P. & Edmond, M. B. (2004). Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study. *Clinical Infectious Diseases*, *39*(3), 309–317. https://doi.org/10.1086/421946

Wu, S., Baum, M. M., Kerwin, J., Guerrero, D., Webster, S., Schaudinn, C., VanderVelde, D. & Webster, P. (2014). Biofilm-specific extracellular matrix proteins of nontypeable Haemophilus influenzae. *Pathogens and Disease*, *72*(3), 143–160. https://doi.org/10.1111/2049-632X.12195

Xiao, J., Zeng, Y., Rustchenko, E., Huang, X., Wu, T. T. & Falsetta, M. L. (2023). Dual transcriptome of Streptococcus mutans and Candida albicans interplay in biofilms. *Journal of Oral Microbiology*, *15*(1), 2144047. https://doi.org/10.1080/20002297.2022.2144047

Xu, Y., Ambudkar, I., Yamagishi, H., Swaim, W., Walsh, T. J. & O'Connell, B. C. (1999a). Histatin 3-mediated killing of Candida albicans: effect of extracellular salt concentration on binding and internalization. *Antimicrobial Agents and Chemotherapy*, *43*(9), 2256–2262. https://doi.org/10.1128/AAC.43.9.2256

Xu, Y., Ambudkar, I., Yamagishi, H., Swaim, W., Walsh, T. J. & O'Connell, B. C. (1999b). Histatin 3-mediated killing of Candida albicans: effect of extracellular salt concentration on binding and internalization. *Antimicrobial Agents and Chemotherapy*, *43*(9), 2256–2262. https://doi.org/10.1128/AAC.43.9.2256

Yang, K., Gitter, B., Rüger, R., Wieland, G. D., Chen, M., Liu, X., Albrecht, V. & Fahr, A. (2011). Antimicrobial peptide-modified liposomes for bacteria targeted delivery of temoporfin in photodynamic antimicrobial chemotherapy. *Photochemical & Photobiological Sciences : Official Journal of the European Photochemistry Association and the European Society for Photobiology*, *10*(10), 1593–1601. https://doi.org/10.1039/c1pp05100h

Yang, M., Du, K., Hou, Y., Xie, S., Dong, Y., Li, D. & Du, Y. (2019). Synergistic Antifungal Effect of Amphotericin B-Loaded Poly(Lactic-Co-Glycolic Acid) Nanoparticles and Ultrasound against Candida albicans Biofilms. *Antimicrobial Agents and Chemotherapy*, *63*(4). https://doi.org/10.1128/AAC.02022-18

Yang, Yu, Wang, W., Chu, Z., Zhu, J.-K. & Zhang, H. (2017). Roles of Nuclear Pores and Nucleo-cytoplasmic Trafficking in Plant Stress Responses. *Frontiers in Plant Science*, *8*, 574. https://doi.org/10.3389/fpls.2017.00574

Yang, Yufei, Hu, M., Yu, K., Zeng, X. & Liu, X. (2015). Mass spectrometry-based proteomic approaches to study pathogenic bacteria-host interactions. *Protein & Cell*, *6*(4), 265–274. https://doi.org/10.1007/s13238-015-0136-6

Youf, R., Müller, M., Balasini, A., Thétiot, F., Müller, M., Hascoët, A., Jonas, U., Schönherr, H., Lemercier, G., Montier, T. & Le Gall, T. (2021). Antimicrobial Photodynamic Therapy: Latest Developments with a Focus on Combinatory Strategies. *Pharmaceutics*, *13*(12), 1995. https://doi.org/10.3390/pharmaceutics13121995

Zhang, A.-N., Wu, W., Zhang, C., Wang, Q.-Y., Zhuang, Z.-N., Cheng, H. & Zhang, X.-Z. (2019). A versatile bacterial membrane-binding chimeric peptide with enhanced photodynamic antimicrobial activity. *Journal of Materials Chemistry. B*, *7*(7), 1087–1095. https://doi.org/10.1039/c8tb03094d

Zhang, Y., Cai, Y., Zhang, B. & Zhang, Y.-H. P. J. (2024). Spatially structured exchange of metabolites enhances bacterial survival and resilience in biofilms. *Nature Communications*, *15*(1), 7575. https://doi.org/10.1038/s41467-024-51940-3

Zolin, G. V. S., Fonseca, F. H. da, Zambom, C. R. & Garrido, S. S. (2021). Histatin 5 Metallopeptides and Their Potential against Candida albicans Pathogenicity and Drug Resistance. *Biomolecules*, *11*(8). https://doi.org/10.3390/biom11081209

Zou, L., Zhang, Y., Cheraga, N., Abodunrin, O. D., Qu, K.-Y., Qiao, L., Ma, Y.-Q., Chen, L.-J. & Huang, N.-P. (2023). Chlorin e6 (Ce6)-loaded plaque-specific liposome with enhanced photodynamic therapy effect for atherosclerosis treatment. *Talanta*, *265*, 124772. https://doi.org/10.1016/j.talanta.2023.124772