I - Photobiology, Optogenetics and Neural Systems

I.01 - Photodynamic Therapy Towards Inactivation of Miltefosine-Resistant Leishmania amazonensis

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INTRODUCTION: Cutaneous leishmaniasis (CL) is a chronic disease developed by Leishmania parasites that promotes destructive lesions. The emergence of drug-resistant parasites has been related to the misuse of drugs, being a major threat to global health. Although antimicrobial photodynamic therapy (APDT) has been reported as an attractive treatment against a broad spectrum of drug-resistant pathogens, the use of APDT against drug-resistant *Leishmania* parasites has never been explored. OBJECTIVES: This study aimed to explore the effects of methylene blue-mediated APDT (MB-APDT) on promastigotes and intracellular amastigotes of two different strains of *Leishmania amazonensis*, a wild-type (WT) and a miltefosine-resistant cell line (MFR). MATERIALS AND METHODS: Promastigotes and intracellular amastigotes were treated at different concentrations of miltefosine. Regarding APDT, we used a red LED (λ= 660±22 nm) at 20 mW/cm ^{2} and two MB concentrations. Parasites were exposed to radiant exposures of 0 to 25 J/cm ^{2} .DISCUSSION AND RESULTS: The miltefosine concentration necessary to reduce 50% (EC50) MFR promastigotes was found to be 5.6-fold higher than that of the WT strain. Amastigotes were even more resistant, and the concentration needed to effectively kill MFR was not able to be calculated once it was toxic to health macrophages. Differently, both promastigotes and intracellular amastigotes were susceptible to MB-APDT. Indeed, promastigotes were equally susceptible to treatment regardless of the MB concentration. EC50 calculated for the light dose delivered was nearly 3 J/cm2, which corresponds to an exposure time of 150 s. Surprisingly, amastigotes of MFR were more susceptible to MB-APDT at 50 µM MB concentration, and the light dose necessary to reduce 50% of resistant parasites was half of that of the WT strain (2.3 J/cm ^{2} and 4.7 J/cm ^{2} , respectively). CONCLUSION: These results indicate that MB-APDT could be a promising treatment to overcome the global issue of antileishmanial drug resistance in CL.

Keywords: methylene blue, miltefosine-resistant parasites, red light

I.02 - Biophotonic Strategy Associated with Hexyl Zinc Porphyrin for Inactivation of Candida spp.

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INTRODUCTION: The genus Candida is among the most frequent fungal pathogens worldwide. The indiscriminate use of antifungals enables the spread of resistant strains, which have been associated with high morbidity and mortality. Photodynamic inactivation (PDI) is a promising technology to treat resistant Candida spp. infections. PDI occurs when light excites a photosensitizer (PS) leading to the production of reactive oxygen species (ROS). Zn(II) porphyrins (ZnPs) present high efficiency for intracellular ROS generation and structural versatility for tailored lipophilicity and ionic character, modulating the bioavailability and interaction with cellular structures. OBJECTIVES: This study aimed to investigate the potential of ZnTnHex-2-PyP4+-mediated PDI to inactivate C. albicans and C. glabrata yeasts. MATERIALS AND METHODS: Candida yeasts (1×10^7 CFU/mL) were evaluated according to the groups: (i) control (without treatment); (ii) only ZnTnHex-2-PyP4+ (dark); (iii) only light (blue LED); and (iv) PDI (ZnP + light) using 10 min of pre-incubation. Different ZnP concentrations (0.15 to 1.25 µM) and light doses were firstly tested with C. albicans. Treated samples were diluted and seeded on Sabouraud agar for colony enumeration after incubation at 37 ºC for 24 h. DISCUSSION AND RESULTS: C. albicans viability decreased with increasing ZnP concentration, achieving complete eradication at 0.8 µM and 3 min of irradiation (24.1 mW/cm²). PDI with 1.25 µM and 1 min of irradiation resulted in a 2 log10 reduction only, demonstrating the importance of light dose in microbial photoinactivation. PDI parameters were subsequently adjusted for inactivation of C. glabrata. Complete C. glabrata eradication was achieved with ZnP at 0.8 µM, and 3 min of irradiation, however, at a higher irradiance (38.4 mW/cm²). Groups treated with either light or ZnP alone did not affect Candida spp. viability. CONCLUSION: These results suggest that the protocols used in this study were efficient for inactivating Candida spp. yeasts at sub-micromolar concentration ZnP and short irradiation times.

Keywords: Candida albicans, Candida glabrata, Photodynamic inactivation