

PHOTODYNAMIC INACTIVATION OF *Candida glabrata* BOOSTED BY ASSOCIATION OF SILVER NANOPARTICLES WITH CATIONIC ZnTE-2-PyP⁴⁺ PORPHYRIN

Geyse S. de Lima¹, Sueden O. de Souza¹, Bruno L. Raposo¹, Gleyciane S. de Santana¹, José Ferreira Sarmiento-Neto², Beate S. Santos³, Rejane P. Neves⁴, Martha S. Ribeiro⁵, Júlio S. Rebouças², Paulo E. Cabral Filho¹, Adriana Fontes¹

¹Biophysics and Radiobiology Department, Federal University of Pernambuco, Recife, PE, Brazil (E-mail: geyse.santos@ufpe.br)

²Chemistry Department, Federal University of Paraíba, João Pessoa, PB, Brazil

³Pharmaceutical Science Department, Federal University of Pernambuco, Recife, PE, Brazil

⁴Mycology Department, Federal University of Pernambuco, Recife, PE, Brazil

⁵Center for Lasers and Applications, Nuclear and Energy Research Institute (IPEN-CNEN), São Paulo, SP, Brazil

Candida glabrata, a high priority fungal pathogen, presents alarming incidence and resistance potential to available antifungals. In this scenario, photodynamic inactivation (PDI) introduces a promising antifungal approach, especially in resistant cases. PDI occurs when a photosensitizer (PS) is excited by an appropriate light source, leading to production of reactive oxygen species (ROS). Zinc porphyrins (ZnPs) are attractive PSs for their efficient ROS generation and cellular uptake. The plasmonic effect of silver nanoparticles (AgNPs) can be explored to potentiate the action of PSs, such as ZnPs, in PDI. Therefore, this work aimed to study the association of AgNPs with ZnTE-2-PyP⁴⁺ (ZnP-ethyl) in PDI against *C. glabrata*. AgNPs were synthesized and characterized by absorption spectroscopy and electron microscopy. The association AgNP:ZnP-ethyl was evaluated by zeta potential (ζ) analyses as well as absorption and emission spectroscopies. The systems containing AgNP:ZnP-ethyl (at different proportions; v/v) and different ZnP-ethyl concentrations (0.5 – 1.5 μM) were prepared and incubated with a resistant isolate of *C. glabrata*, followed by illumination with a blue LED. The PDI effect was assessed by quantifying colony forming units. AgNPs presented spherical morphology and extinction maximum at ~ 410 nm, overlapping with the ZnP-ethyl absorption spectra. Variations in ζ confirmed the association between AgNPs and ZnP-ethyl, corroborated by subtle changes in the ZnP spectroscopic profile. The AgNP:ZnP-ethyl combination promoted complete fungal eradication at 0.6 μM of PS, while at 0.5 μM , the association led to a yeast reduction of about 6.8 \log_{10} . Individual ZnP-ethyl (1.5 μM) promoted a 2 \log_{10} reduction. These results show the benefit of AgNPs:ZnP-ethyl association to boost PDI efficiency against resistant *C. glabrata* isolates. This is a promising antifungal approach to treat resistant candidiasis.

This work was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Portaria nº 206/2018), the Wellcome Trust (grant 219677/Z/19/Z), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, 406450/2021-8, 314241/2021-3, 424159/2018-0); Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE, APQ-0573-2.09/18); and Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, nº 2018/20226-7). The Instituto Nacional de Ciência e Tecnologia em Fotônica (INCT-INFo) is also acknowledged.