TITLE: **Synergistic activity of gold nanoparticles with Amphotericin B on persister cells of *Candida tropicalis* biofilms**

AUTHOR NAMES: M.A. da Silva[a,b], K.F. Crespo Andrada[b], M. Maldonado Torales[b], I. Manrrique Hughes[b], P. Páez[b,c], M.G. Paraje[a,b*]

AUTHOR AFFILIATIONS

[a] Instituto Multidisciplinario de Biología Vegetal (IMBIV), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Córdoba, Argentina.

[b] Cátedra de Microbiología, Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba, Córdoba, Argentina.

[c] Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina.

* AUTHOR FOR CORRESPONDENCE: Prof. Dr. María Gabriela Paraje, Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba, X5000HUA, Córdoba, Argentina. Phone: +54 351-5353800 int. 29731 E-mail: gparaje@unc.edu.ar; gabrielaparaje@gmail.com

ABSTRACT

Aim: The antifungal activity was studied on sessile and persister cells (PCs) of *Candida tropicalis* biofilms of gold nanoparticles (AuNPs) stabilized with cetyltrimethylammonium bromide (CTAB-AuNPs) and those conjugated with cysteine, in combination with Amphotericin B (AmB). **Materials/methods:** The PC model was used and synergistic activity was tested by the checkerboard assay. Biofilms were studied by crystal violet and scanning electron microscopy. **Results/Conclusions:** After the combination of both AuNPs and AmB the biofilm biomass was reduced, with significant differences in architecture being observed with a reduced biofilm matrix. In addition, the CTAB-AuNPs-AmB combination significantly reduced PCs. Understanding how these AuNPs aid in the fight against biofilms and the development of new approaches to eradicate PCs has relevance for chronic infection treatment.

KEYWORDS

antibiofilm activity; gold nanoparticles; Amphotericin B; synergy; *Candida tropicalis*; sessile cells; persister cells.

ACKNOWLEDGEMENTS

PLP and MGP are members of the Scientific and Technological Researcher Career (CIC - CONICET). The authors gratefully acknowledge the support of Ma. Agustina Farchetto for graphical abstract design. We thank Dr. Paul Hobson, native speaker, for revision of the manuscript. This work was supported by grants to MGP from Proyectos de Investigación Plurianuales (PIP) - Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), and Proyectos de Investigación Científica y Tecnológica (PICT) - Fondo para la Investigación Científica y Tecnológica (FONCyT) of Argentina. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.