Photodynamic inactivation of planktonic cells, pseudohyphae and biofilms *Candida albicans* by cationic porphyrins

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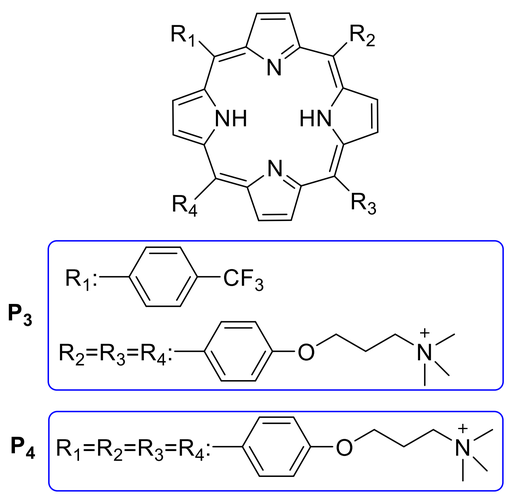
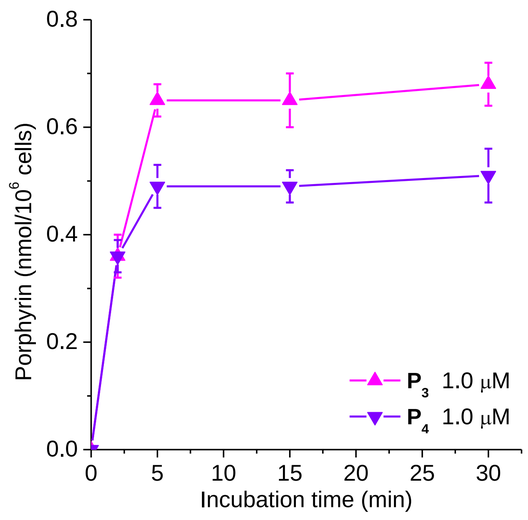
Candidiasis is an opportunistic fungal infection that is considered to be the most common in humans [1]. Recently, *Candida albicans* infections have increased worldwide due to enlarged use of antifungals and medical devices, such as heart valves, vascular bypasses, dental implants, and catheters, where fungal biofilms can form [2]. In this work, two cationic porphyrins (**P_3** and **P_4**) were evaluated as photosensitizing agents for the photodynamic inactivation (PDI) of *C. albicans* under different culture conditions [3,4].

Porphyrin structures

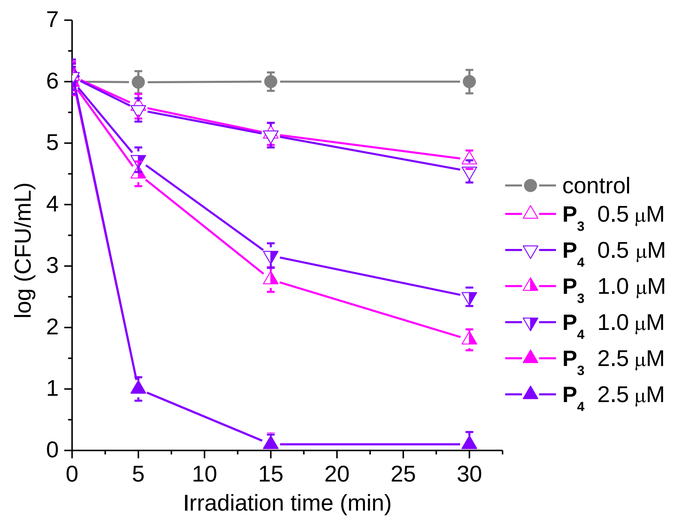


Uptake of porphyrin



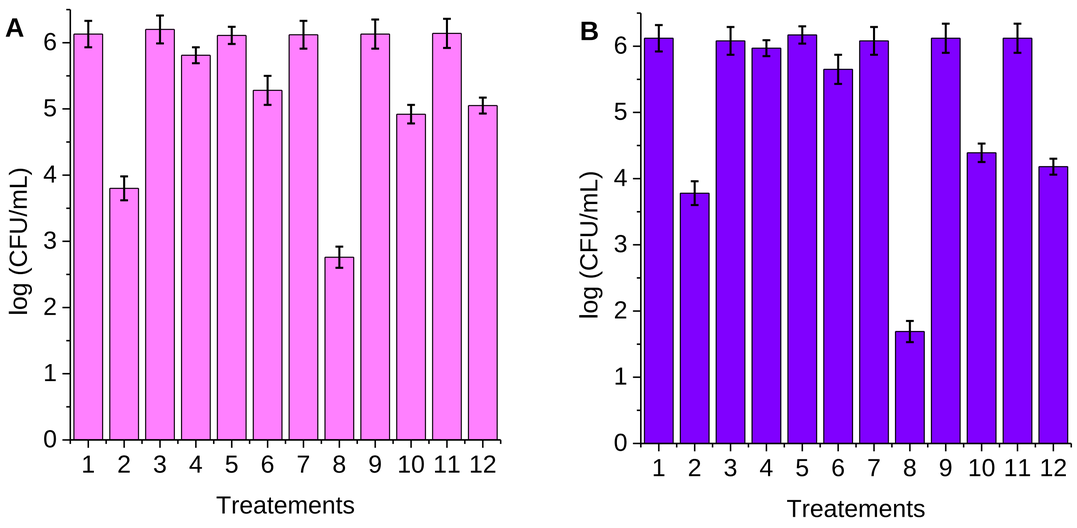
Amount of porphyrin recovered from *C. albicans* treated with **P_3** and **P_4** for 30 min at 37 ºC in the dark.

PDI of planktonic cells



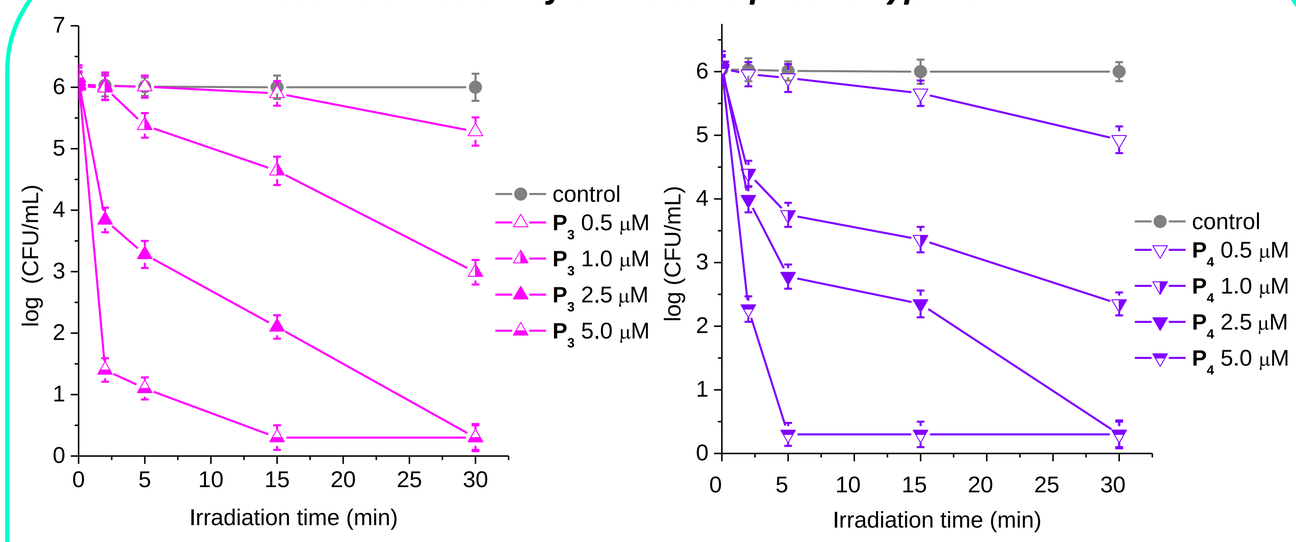
Survival of *C. albicans* planktonic cells treated with **P_3** and **P_4** for 30 min at 37 ºC in the dark and irradiated with white light (90 mW/cm^2).

Photodynamic mechanism in C. albicans cells



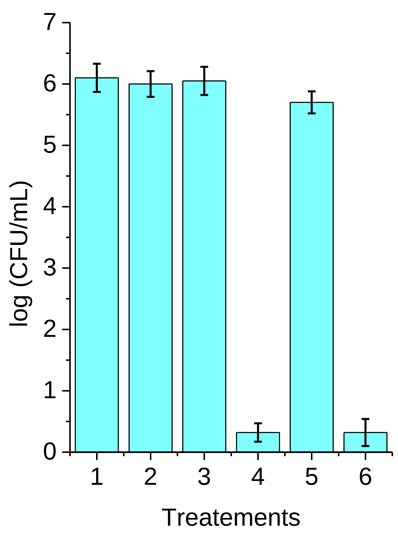
C. albicans treated with 1.0 μM (A) **P_3** and (B) **P_4** for 30 min at 37 ºC in the dark and irradiated with white light (90 mW/cm^2) for 15 min; (1) cells; (2) cells treated with porphyrin; (3) cells treated with 50 mM sodium azide; (4) cells treated with 50 mM sodium azide and porphyrin; (5) cells treated with 50 mM DABCO; (6) cells treated with 50 mM DABCO and porphyrin (7) cells in D_2O; (8) cells in D_2O and treated with porphyrin; (9) cells treated with 50 mM D-mannitol; (10) cells treated with 50 mM D-mannitol and porphyrin; (11) cells treated with 50 mM cysteine; (12) cells treated with 50 mM cysteine and porphyrin.

Photoinactivation of C. albicans pseudohyphae



Survival of *C. albicans* pseudohyphae treated with **P_3** and **P_4** for 30 min at 37 ºC in the dark and irradiated with white light (90 mW/cm^2).

Photokilling of *C. albicans* biofilms



C. albicans incubated with 5.0 μM porphyrin for 18 h at 37 ºC in the dark during biofilm proliferation and irradiated with white light (90 mW/cm^2) for 60 min; (1) cells in the dark; (2) irradiated cells; 3) cells treated with **P_3** in the dark; (4) irradiated cells treated with **P_3**; (5) cells treated with **P_4** in the dark; (6) irradiated cells treated with **P_4**

Conclusions. Both porphyrins were rapidly bound to cells in 5 min. *C. albicans* planktonic cells treated with 2.5 and 5.0 μM were eliminated after 5 and 15 min of irradiation, respectively. The addition of reactive oxygen species scavengers showed that singlet molecular oxygen was mainly involved in the photoinactivation. These porphyrins were effective to photoinactivate *C. albicans* pseudohyphae suspentions, producing a reduction of 6 log after 15 min of irradiation. Furthermore, the biofilms of *C. albicans* that incorporated the porphyrins (5.0 μM) during the proliferation stage were completely photoinactivated after 60 min of irradiation. Therefore, both porphyrins, **P_3** and **P_4**, present potential applications as a phototherapeutic agent for fungal inactivation under different culture conditions.

References

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[2] S. Wijnants, J. Vreys, P. Van Dijck, Trends Pharmacol. Sci. 2022, 43, 69-79.
[3] P. V. Cordero, M. G. Alvarez, E. J. Gonzalez Lopez, D. A. Heredia, E. N. Durantini, Antibiotics 2023, 12, 105.
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