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Photodynamic inactivation of *Candida albicans* in different growth forms mediated by BODIPY derivatives

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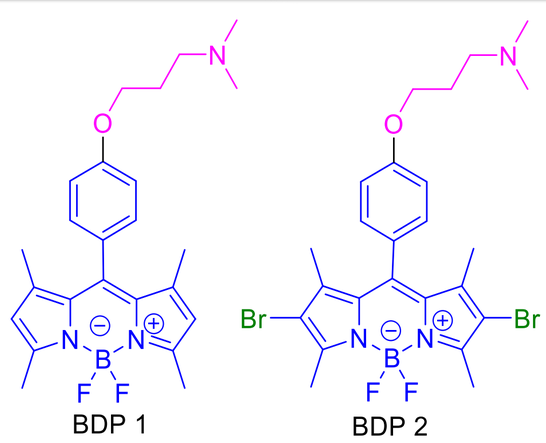
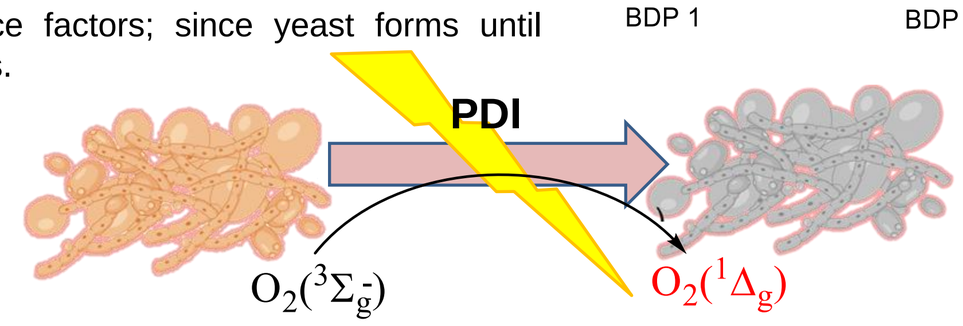
INTRODUCTION & AIM

Photodynamic inactivation (PDI) has emerged as a promising non-conventional approach to control this microorganism [1]. In this study, the PDI activity of two BODIPY derivatives: a compound bearing a dimethylaminopropoxy group attached to a phenylene unit (BDP 1) and its dibrominated analogue (BDP 2) [2] were evaluated against the opportunistic pathogen *Candida albicans* and their virulence factors; since yeast forms until biofilms.

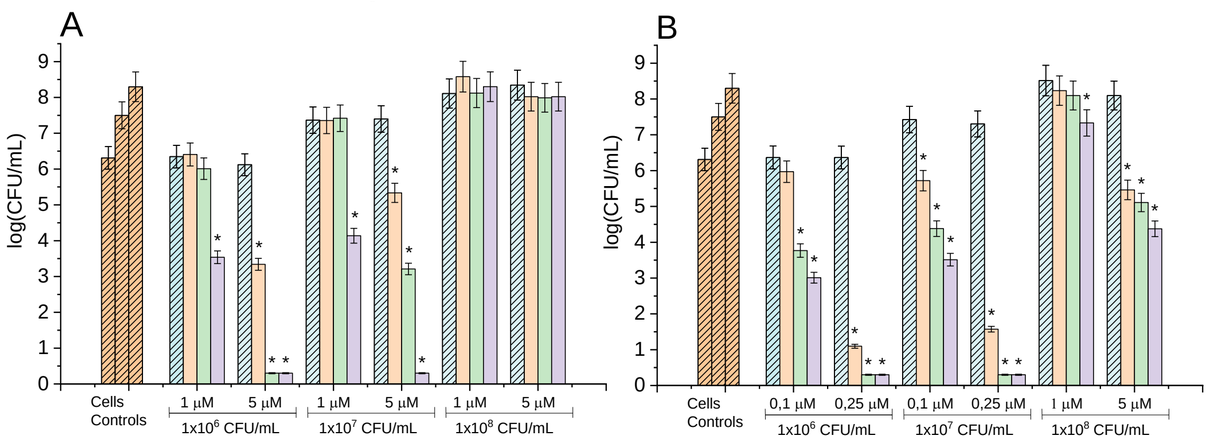




METHOD

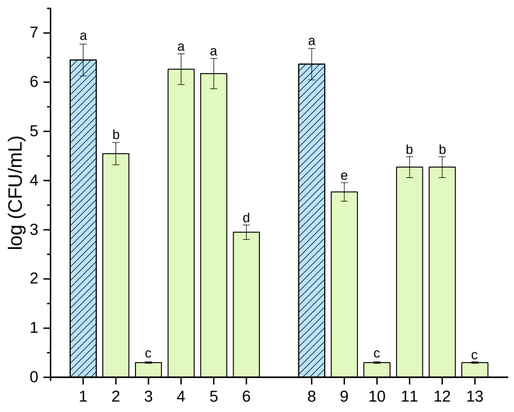
BODIPY derivatives were obtained as reported [2]. *C. albicans* cultivation and PDI experiments were performed as previously described [3].

Photoinactivation of planktonic cells



Survival of *C. albicans* planktonic cells treated with **BDP1** (A) and **BDP 2** (B) irradiated with white light (90 mW/cm^2) during 5 ( ) , 15 ( ) or 30 min ( ). Controls (dash bars) were made with the same conditions but maintained in the dark for 30 min at 37 ºC.

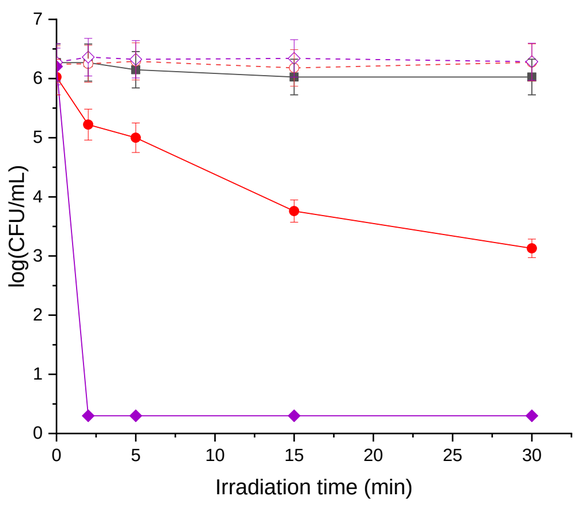
Photodynamic action mechanisms



C. albicans treated with 1.0 μM of BDP 1 (1-6) or with 0.1 μM of BDP 2 (8-13) for 30 min at 37ºC in the dark, followed by irradiation with white light (90 mW/cm^2) for 15 min ; (1,8) control cells maintained in the dark; (2,9) PDI treatment; (3,10) cells treated with 50 mM sodium azide + PSs; (4,11) cells treated with 50 mM D-mannitol + PSs; (5,12) cells treated with 50 mM cysteine + PSs; (6,13) cells in D_2O + PSs.

RESULTS & DISCUSSION

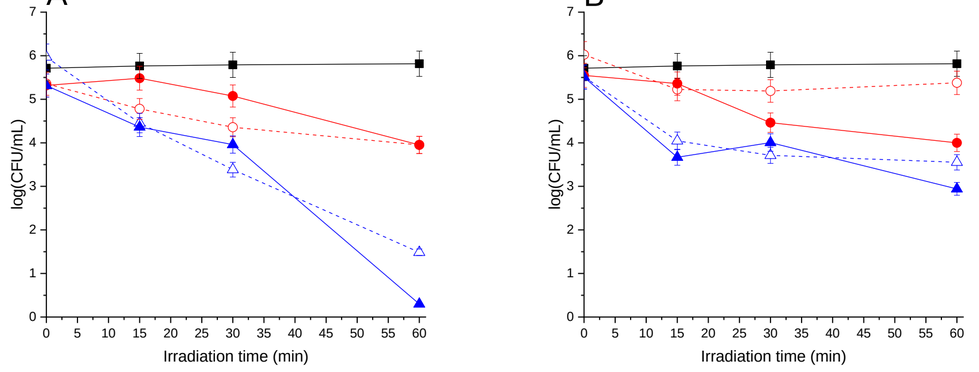
Photoinactivation of C. albicans pseudohyphae



Survival of *C. albicans* pseudohyphae treated with BDP 1 (red) and BDP 2 (violet) for 30 min at 37ºC in the dark, followed by irradiation with white light (90 mW/cm^2). Dashed lines indicate PDI performed on pseudohyphae suspended in human serum, whereas solid lines represent PDI conducted on pseudohyphae suspended in PBS. The control of untreated cells in PBS is shown as a solid black line.

Photokilling of C. albicans biofilms

C. albicans biofilms incubated with 5 μM (dashed lines) or 10 μM (solid lines) of BODIPYs during the entire proliferation phase (A) or for 30 min after 18 h of growth (B) at 37ºC in the dark, followed by irradiated with white light (90 mW/cm^2) for 15, 30 and 60 min. Red lines correspond to BDP 1 and blue lines to BDP 2. Black squares represent untreated biofilm growth.



Photodynamic treatment were performed using different concentrations of the photosensitizer BDP 1 (1.0-5.0 μM) or BDP 2 (0.1-5.0 μM), various irradiation times (5-30 min) with white light (90 mW/cm^2) and different cell densities.

BDP1 was reduced approximately 3 logs of *C. albicans* planktonic cells (from ~10^6 to ~10^3 CFU/mL) with 1.0 μM after 30 min of irradiation, and achieved complete eradication at 5.0 μM and 30 min for 10^6 and 10^7 CFU/mL yeast densities. No changes were observed at the highest cell density (10^8 CFU/mL). In contrast, BDP 2 exhibited mayor photokilling activity since a completely eradication was achieved with only 0.25 μM at inocula of 10^6 and 10^7 CFU/mL. Moreover, 5 μM reduces approximately 2 log at the highest cell density.

The addition of reactive oxygen species scavengers indicated that $O_2(^1\Delta_g)$ was involved in the photoinactivation mediated by BDP 2. In addition, evidence of type I mechanism was detected in the yeast inactivation with BDP 1.

In pseudohyphae suspended in PBS, 1.0 μM BDP 1 with 15 min of irradiation reduces in 99,99% the viability, whereas BDP 2 required only 2 min for the complete eradication of this virulence factor. No inhibition was observed in pseudohyphae suspended in serum.

Biofilm inhibition was assessed at two developmental stages: during proliferation and in 18 h mature biofilms. The most effective photokilling was observed when BODIPYs were incorporated throughout the entire proliferation phase, followed by 60 min of white light irradiation. Notably, treatment of 18 h mature biofilms with BDP 2 and 60 min irradiation resulted in a ~3 logs reduction in the viability of this resistant structure of *C. albicans*.

CONCLUSION

Both BDP 1 and BDP 2 showed photodynamic activity against *C. albicans*, with BDP 2 displaying superior efficacy. BDP 1 reduced planktonic cells at moderate concentrations but was ineffective at high densities, whereas BDP 2 achieved complete eradication at low doses and remained active even at the highest inoculum. Mechanistic assays indicated that BDP 2 acted mainly through singlet oxygen, while BDP 1 involved type I pathways. In pseudohyphae, BDP 2 was faster and more potent. For biofilms, the best inhibition occurred when BODIPYs were incorporated during proliferation, with BDP 2 also significantly reducing mature biofilms.

REFERENCES

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