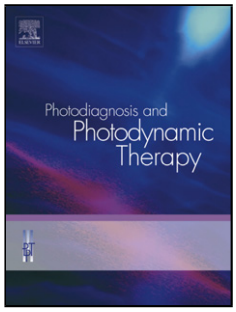

Title: *In vitro* photodynamic inactivation effects of benzylidene cyclopentanone photosensitizers on clinical fluconazole-resistant *Candida albicans*

Authors: Shaona Zhou, Zhiyuan Sun, Zulin Ye, Ying Wang, Leili Wang, Limei Xing, Haixia Qiu, Naiyan Huang, Yanping Luo, Yuxia Zhao, Ying Gu

PII: S1572-1000(17)30466-0
DOI: https://doi.org/10.1016/j.pdpdt.2018.04.001
Reference: PDPDT 1140

To appear in: *Photodiagnosis and Photodynamic Therapy*

Received date: 8-10-2017
Revised date: 30-3-2018
Accepted date: 3-4-2018

Please cite this article as: Zhou S, Sun Z, Ye Z, Wang Y, Wang L, Xing L, Qiu H, Huang N, Luo Y, Zhao Y, Gu Y, *In vitro* photodynamic inactivation effects of benzylidene cyclopentanone photosensitizers on clinical fluconazole-resistant *Candida albicans*, *Photodiagnosis and Photodynamic Therapy* (2010), https://doi.org/10.1016/j.pdpdt.2018.04.001

In vitro photodynamic inactivation effects of benzylidene cyclopentanone photosensitizers on clinical fluconazole-resistant *Candida albicans*

Shaona Zhou[1#], Zhiyuan Sun[2#], Zulin Ye[3], Ying Wang[1], Leili Wang[4], Limei Xing[1], Haixia Qiu[1], Naiyan Huang[1], Yanping Luo[4], Yuxia Zhao[2], Ying Gu[1*]

1 Department of Laser Medicine, Chinese PLA General Hospital, Beijing 100853, China

2 Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing 100190, China

3 Department of Rehabilitation, Tianjin Hospital, Tianjin 300211, China

4 Department of Microbiology, Chinese PLA General Hospital, Beijing, China

* Corresponding author. Tel.: +86 010 6693 9394; fax: +86 010 6822 2584.E-mail address: guyinglaser301@163.com (Y. Gu).

# These authors contributed equally to this work.

Highlights

- The three BCB PSs all have remarkable PDI effects on *C. albicans.*
- BCB PSs-PDI was not affected by the fluconazole susceptibility of *C. albicans*.
- The respective subcellular localization of PSs led to different PDI mechanisms.
- The best effect is obtained by P1, which is lipophilic and has one cationic charge.

ABSTRACT

Background: The incidence of *Candida* infections has increased for various reasons, for instance, the more frequent use of immunosuppresants or broad-spectrum antibiotics. Photodynamic inactivation (PDI) is a promising approach for treating localized *Candida* infections.

Methods: The PDI efficacies of three benzylidene cyclopentanone-based (BCB) photosensitizers (PSs: P1, P2 and Y1) against three fluconazole-resistant *C. albicans* (*cal*-1, *cal*-2, and *cal*-3) and one control *C. albicans* (ATCC 90028), respectively, were evaluated using an established plate dilution method. The binding of PSs to *C. albicans* was determined by fluorescence spectroscopy. The mechanism of antifungal PDI was investigated using confocal laser scanning microscopy (CLSM) and transmission electron microscopy (TEM).

Results: Three BCB PSs all bound rapidly to *C. albicans*. After incubation with PSs for 30 min and irradiation with a 532 nm laser for 10 min (40 mW cm^{-2}, 24 J cm^{-2}), the fungicidal activity was achieved as 7.5 μM for P1 and P2, and 25 μM for Y1. CLSM confirmed that P1 and Y1 were located in intracellular components, including mitochondria, while P2 bound to the protoplast exterior and failed to enter the cells. TEM revealed the damage of mitochondria ultrastructures after P1- or Y1-mediated PDI, consistenting with the CLSM results. However, most cells became edematous, enlarged or deformation after P2-mediated PDI.

Conclusions: The three BCB PSs all have remarkable PDI effects on *C. albicans*. The best effect is obtained by P1, which has one cationic charge with a proper lipophilicity. The respective subcellular localization of the three PSs led to different PDI mechanisms.