TITLE: UNPUBLISHED SYNTHETIC COMPOUND IS ABLE TO INHIBIT THE LEVEDURA-HIFA TRANSITION, IN *Candida albicans.*

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ABSTRACT:

Candida albicans is a commensal microorganism present in the microbiota of humans. However, it can become an opportunistic pathogen, causing infections. By presenting as a polymorphic fungus, *C. albicans* possesses the ability to alternate its yeast status to hyphae, invading tissues and escaping from the host's defenses. Studies have shown that species of *C. albicans* knockout for genes that regulate the yeast-hyphae transition do not have this ability, are considerably less virulent. In addition, there is a growing increase in fungal resistance to the drugs available on the market, making it necessary to develop new antifungal agents. Synthetic compounds derived from marine alkaloids exhibited promising antifungal activity in previous studies developed by our research group. Therefore, this study aimed to evaluate the effect of an unprecedented synthetic marine alkaloid (called NQBIO003) on inhibition of the formation of hyphae of *C. albicans* ATCC 10231. The assay was developed by means of the microdilution technique in broth, using Bovine Fetal Serum as medium (inducing the formation of hyphae). As an antifungal control, ketoconazole (125 µg / mL) and as solvent control, Dimethyl Sulfoxide (DMSO) 2% were used. According to the Minimum Inhibitory Concentration (MIC), NQBIO003 was tested at a concentration of 7.8µg/mL (MIC) and 15.6µg/mL (2xCIM). The microplates were incubated at 37 °C for 24, 48 and 72 hours and at these time intervals, fresh slides containing 20 µL aliquots were prepared and observed under a light microscope at 400X magnification. The results showed that the compound NQBIO003 decreased the formation of hyphae after 72 hours in the concentration of 7.8µg/mL in relation to the growth control and totally inhibited the formation of hyphae in the concentration of 15.6µg/mL, from of 48 hours incubation. Ketoconazole inhibited the formation of hyphae and DMSO did not interfere in the formation of these, with a similar result to growth control, validating the experimental conditions of this study. In conclusion, the synthetic compound derived from marine alkaloids was a potent inhibitor of hyphae formation, highlighting compound NQBIO003 as a potential prototype for the development of novel and novel antifungal agents. Furthermore, *in vitro* experiments and subsequent *in vivo* tests are needed to elucidate their therapeutic potential.

Keywords: *Candida albicans*, virulence factor, inhibition of hyphae, marine alkaloids, synthetic compounds.

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