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THE ANTI-CANDIDA ACTIVITY OF NEW N-METHYL-QUINOLINYL-PORPHYRINS *IN VITRO*

The activity of new N-methyl-quinolinyl-porphyrins against different morphological forms of *Candida albicans* (unattached, free-dividing cells, as well as structures formed in the process of biofilm maturation) was characterized. Modification of porphyrin molecules by N-methyl-6-quinolinyl increases the fungicidal effect on the yeast cells, in contrast to N-methyl-7-quinolinyl derivatives that are effective against hyphal structures. *Candida albicans* biofilm cells are more resistant to low concentrations of the studied compounds.

Key words: *Candida albicans*, biofilm, planktonic cells, porphyrin.

Porphyrins are macroheterocyclic compounds, containing conjugated system, which is based on four pyrrole rings linked by four methine groups in α-positions. Two classes of porphyrins, natural and synthetic, can be distinguished on the basis of their origin and structure. More than 50 different metals can be introduced into the porphyrin ring to create a wide variety of metalloporphyrins in both classes [1].

The *Candida albicans* fungus commonly colonizes the epithelial surfaces of human organism. Impairment of innate and adaptive host defenses, perturbation of normal microbiota or underlying disease can contribute to fungal overgrowth and candidiasis progress. In the course of this infection *C. albicans* forms a massive biofilm on the large surface of affected tissues and organs. *C. albicans* also grows as a biofilm on prosthetic devices, contributing to the failure of antifungal therapy and recurrent infection.

Treatment of superficial *C. albicans* infections with photosensitizing agents and light, termed photodynamic therapy, offers an alternative to conventional treatments. In the presence of molecular oxygen, the irradiation of photosensitizers with the appropriate wavelength of light results in the local production of singlet oxygen, which rapidly oxidizes

cellular macromolecules found nearby, leading to cell damage and death [4].

The *Candida albicans* ATCC 18804 strain obtained from the Microbiology, Virology and Biotechnology Department culture collection was used as the test object. For the experiment 18-24-hrs *C. albicans* cultures that were grown on Nutrient Agar at 37 ^{0}C were used. The working microbial suspension contained 10^6 CFU/ml.

The studies were carried out for a synthetic *meso*-N-methyl-quinolinyl-porphyrins -substituted free porphyrin bases.

The *C. albicans* cultivation in the presence of the studied porphyrins was carried out in sterile polystyrene plate in Sabouraud nutrient medium. The porphyrin concentrations in the culture medium corresponded to the values presented in the following work [2].

The following parameters were noted: planktonic biomass (cells that have developed in the suspension) and the biofilm formation (cells that developed on «solid surface (the well bottoms) – liquid (culture medium)» phase edge). The obtained data were calculated with a spectrophotometer BioTek «μQuant» (at 540 nm and 592 nm, respectively) [3].

The studied culture was sensitive to the porphyrin action.

After 24 hrs the most active compounds was N-methyl-6-quinolinyl porphyrin that inhibited growth by 80 % in comparison with the control value. On the 2nd cultivation day the cell number in suspension did not exceed 60 % of the control.

Formation of *C. albicans* biofilm was subjected to influence of the studied porphyrins, as on the 1st and the 2nd day. The greatest decreasing of the biofilm formation intensity takes place in the presence of the substance N-methyl-7-quinolinyl porphyrin (24–48 hrs) and substances N-methyl-6-quinolinyl porphyrin (48 hrs). However, the most of the results was above the reference values, in some cases up to 2 times higher than that.

So, therapy with porphyrins has the potential to evolve into a useful treatment for difficult to eradicate fungal infections of accessible regions of the body. For example, the prospect of eradicating oral thrush in an AIDS patient, or denture stomatitis in an elderly nursing home resident in a single session, or a once-off curative treatment for *Candida* mycosis, is a scenario that would be attractive to both patients and health service providers [3]. However, this will not become a clinical reality until pharmaceutical companies and grant-awarding bodies devote considerable resources to the development of both photosensitisers specifically designed for antifungal treatment and drug delivery systems that allow such agents to be efficiently delivered to their sites of action.

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