

## STUDY OF SYNERGISM OF FLUCONAZOLE WITH THIAZOLIDINE DERIVATIVES

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Nowadays, fungal diseases are the 5th most common among all human infectious diseases. Etiologically, fungal diseases are most often represented by such species as *C. albicans* and *C. tropicalis*. Antifungal drugs are used to treat this type of infection, but more and more information is being received about the resistance of fungi to traditional drugs. To solve this problem, research is being conducted on new alternative compounds and their combination with common drugs.

The aim of our study was to reveal the antifungal properties of new synthetic compounds - thiazolidine derivatives and their effectiveness in combination with fluconazole.

A total screening for the antifungal activity of 330 compounds - thiazolidine derivatives was carried out using the agar diffusion method. The screening results revealed 3 active compounds - 6-oxo-5,6-dihydro [1,3]thiazolo [2,3-b][1,2,4]triazol-6-one derivatives - L95, L1369, and L1558, which then were used to study synergism with fluconazole by the method of serial dilutions in 96-well microplates. Clinical strains *C. albicans* and *C. tropicalis* were used as test strains. The results were evaluated by determining the minimum inhibitory concentration (MIC) of substances.

For *C. albicans*, MIC of L95 was 50 µg/ml, MIC of L1369 - 100 µg/ml and MIC L1558 - >100 µg/ml. For the *C. tropicalis*, MIC of L95 was 25 µg/ml, MIC of L1369 - 25 µg/ml and MIC of L1558 - 25 µg/ml. MIC of fluconazole for *C. albicans* was 1000 µg/ml and for *C. tropicalis* was 4000 µg/ml.

While in combination with fluconazole (1/8 of MIC), MIC of L95 was 25 µg/ml, MIC of L1369 - 100 µg/ml and MIC L1558 - 50 µg/ml for *C. albicans*. For *C. tropicalis* - in combination with 1/8 MIC of fluconazole, MIC L95 is 3.125 µg/ml, MIC L1369 - 6.25 µg/ml and MIC L1558 - 12.5 µg/ml.

Even better results were shown in the combination of MIC of fluconazole with 1/8 MIC of substances. For *C. albicans*, MIC of fluconazole in combination with 1/8 MIC of L95 was 16 µg/ml, with 1/8 MIC of L1369 - 125 µg/ml, with 1/8 MIC of L1558 - 125 µg/ml. For *C. tropicalis*, MIC of fluconazole in combination with 1/8 MIC of L95 was 16 µg/ml, with 1/8 MIC of L1369 - 16 µg/ml, with 1/8 of MIC L1558 - 16 µg/ml.

The obtained results indicate that the synergism of fluconazole with thiazolidine derivatives increases the sensitivity of *Candida* to these compounds by 4-6 times. So, we can talk about the discovery of new, potentially promising compounds with antifungal activity, the effect of which also increases in combination with known antifungal drugs.