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CONTENT

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ANTIFUNGAL ACTIVITY OF 5,6-DIHYDROTETRAZOLO[1,5-*c*]-QUINAZOLINE DERIVATIVE AGAINST SEVERAL CANDIDA SPECIES

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Introduction. Candida species stand out as the predominant causes of fungal infections with approximately 92% of infections attributed to five specific species: *Candida albicans*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, and *C. krusei*, besides other rarely identified thirteen other species, that were found with incidences of less than 0.01% [1]. In our previous study of antimicrobial activity, 4-(5-methyl-5,6-dihydrotetrazolo[1,5-*c*]quinazolin-5-yl)benzoic acid (Figure 1) exhibited antibacterial activity against *S. aureus*, *E. coli*, and antifungal efficacy against *C. albicans,* while its toxicity was predicted of Class V [2].

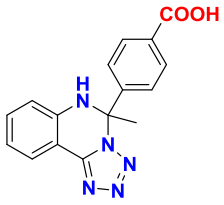

Fig. 1. **Structure of 4-(5-methyl-5,6-dihydrotetrazolo(1,5-*c*]quinazolin-5-yl)benzoic acid**

Aim. So, based on above-mentioned data, it was considered worthwhile to explore antifungal potential of synthesized substance further.

Materials and methods. The method of serial dilutions (2–256 mg/L) of 4-(5-methyl-5,6-dihydrotetrazolo(1,5-*c*]quinazolin-5-yl)benzoic acid (Figure 1, Table 1) on meat-peptone broth was carried out in the bacteriological laboratory of Zaporizhzhia Regional Clinical Hospital of Zaporizhzhia Regional Council (Ukraine) [3] against *Candida glabrata* ATCC 15126, *C. kefyr* ATCC 66058 (*Kluyveromyces marxianus*), *C. utilis* ATCC 9950 (*Cyberlindnera jadinii*), that were isolated from patients' biological material, and identified by chromatic Candida media (Liofilchem, Italy). Microorganism strains didn't reveal sensitivity towards the chosen solvent, namely DMSO (2.5%). All growth experiments were carried out in duplicate.

Results and discussion. *C. kefyr* and *C. utilis*, when isolated and tested, demonstrated no sensitivity to the studied compound (Table 1).

Table 1

Antifungal activity results by serial dilution method

Strain	Number of test tube / Concentration, mg/L								Growth control	Sterility control
	1	2	3	4	5	6	7	8		
	256	128	64	32	16	8	4	2		
*C. glabrata**	-**	-	-	-	-	-	-	-	+	-
C. kefyr	+	+	+	+	+	+	+	+	+	-
C. utilis	+	+	+	+	+	+	+	+	+	-

**Minimum inhibition concentrations of amphotericin B: 8 mg/L, caspofungin: 8 mg/L, micafungin: 4 mg/L; **Absence (–) / presence (+) of opalescence.*

Conversely, *C. glabrata* exhibited resistance to the references amphotericin B and caspofungin (8 mg/L), but displayed sensitivity to micafungin (4 mg/L) as per the testing protocol. Remarkably, this particular strain displayed pronounced sensitivity to the 5,6-dihydrotetrazolo[1,5-*c*]quinazoline derivative, evident even at the lower concentration of 2 mg/L, as illustrated in Figure 2.

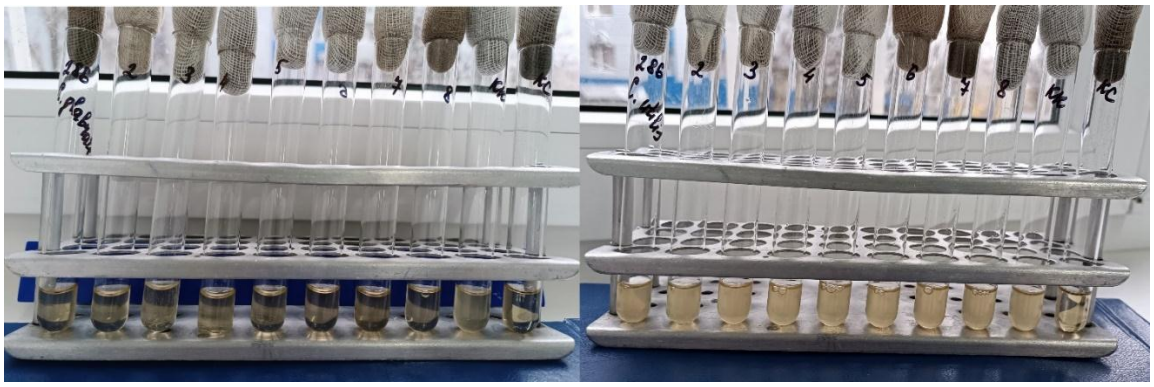

Fig. 2. **Example of *C. glabrata* (left) and *C. utilis* (right) sensitivity**

Conclusions. This study requires further consideration of 4-(5-methyl-5,6-dihydrotetrazolo[1,5-*c*]quinazolin-5-yl)benzoic acid as the treatment of Candida infections, because strains resistant to both fluconazole and echinocandin drugs is a serious problem with limited treatment alternatives [3]. Other 5-phenyl-5,6-dihydrotetrazolo[1,5-c]quinazoline's derivatives are also becoming intriguing targets for investigation of antifungal potential against *C. glabrata.*

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