Antimicrobial and cytotoxic activities of thiazolo[4,5-b]pyridine derivatives

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**Aim.** The screening of antimicrobial and cytotoxic activities of thiazolo[4,5-b]pyridine derivatives was accomplished. **Methods.** The antibacterial and antifungal activities of synthesized thiazolopyridines were evaluated *in vitro* with the agar diffusion and broth microdilution methods using clinical and reference strains of Gram-positive, Gram-negative bacteria and yeasts. The structure-antibacterial/antifungal activity relationships of the screened compounds were established. The target compounds were screened for their cytotoxicity effects on HaCaT and HEK293 cells using MTT assay. **Results.** The highest antimicrobial activity was observed for compound V 2-oxo-7-thiophen-2-yl-2,3-dihydrothiazolo[4,5-b]pyridine-5-carboxylic acid with minimal inhibitory concentration (MIC) 12.5 μg/mL against *Candida albicans*. At the same time, the synthesized compounds were explored in the interaction with amoxicillin against multidrug resistant clinical isolates of ESβL⁺ *Klebsiella pneumoniae* and *Staphylococcus haemolyticus* (MRSH). The best synergistic activity with amoxicillin was exhibited by compound VI. HaCaT human keratinocytes and HEK293 human embryonic kidney cells demonstrated resistance to the thiazolopyridine derivatives treatment and did not reach the IC₅₀ value up to 100 μM. **Conclusions.** The tested thiazolopyridines constitute an interesting background for further development of new chemotherapeutic agents.

**Keywords:** heterocyclic compounds, thiazolidinones, thiazolo[4,5-b]pyridines, antimicrobial activity, antiproliferative activity

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Introduction

A wide range of infectious diseases caused by different pathogens is a main focus of the searching for new highly active and low-toxic antimicrobials in modern drug discovery. A special issue in this contest is occupied by heterocyclic compounds, due to their unique ability to mimic the structure of prokaryotic cell metabolites and to bind reversibly to diverse biotargets [1, 2]. Thus, considerable interest among antimicrobial drug-design strategies has been paid to thiazole derivatives and their structure-related analogues [3].

Noteworthy, the thiazole/thiazolidinone skeleton underlies the structure of wide antimicrobial drugs, namely, penicillins, monobactam antibiotics and sulfadruugs. Additionally, thiazolidinones have been identified as the multi-inhibitors of bacterial lactamase [4], UDP-galactopyranose mutase (UGM) [5], Sortase A (SrtA) [6], Protein mannosyl transferase 1 [5], Peptide deformylase [7], UDP-N-acetylmuramate/L-alanine ligase (MurC) [8] and MurD ligase [9]. However, the mentioned heterocycles possess wide spectra of other biological

Fig. 1. Structures of fused thiazole/thiazolidinones with antimicrobial activity.
activities, especially anticancer [10, 11], anti-
tripanosomal [12, 13], anti-inflammatory [14,
15]. Interestingly, the significant antimicro-
bial activity was also observed for fused thia-
zoles, especially thiopyrano[2,3-d]thiazoles
[16], imidazo[2,1-b]thiazoles [17], azo[2,1-b]
thiazoles [18], thiazolo[4,5-d]pyrimidines [19]
and benzo[h]thiazolo[2,3-b]quinazolinones
[20] (Figure 1). As a part of our research in
the field of biologically active fused thiazoles,
herein we report the antimicrobial and antip-
roliferative properties of some thiazolo[4,5-b]
pyridine derivatives. Moreover, the pharma-
cological potential of thiazolopyridines has
been associated with their affinity to various
biotargets, especially the EGFR/ErbB family
of protein-tyrosine kinases [21], histamine H3-
receptors [22], G-protein coupled receptors
(mGluR 5) [23], fibrillar amyloid-β peptide
(AB) [24], liver-selective glucokinase (GK)
[25], 3',5’-cyclic adenosine monophosphate
phosphodiesterase (PDE) III [26] etc.
Noteworthy, we have previously established a
significant antitumor activity of this class of
compounds [27]. To take into account the
above facts, it is promising to evaluate the
biological activity of the mentioned com-
pounds as realization of the polypharmaco-
logical strategy in the design of prospective
drug-like molecules among the condensed
4-thiazolidinone derivatives.

Materials and Methods

Chemistry

The antimicrobial activity of three subtypes of
thiazolopyridines, namely 5,7-diaryl-3H-
thiazolo[4,5-b]pyridin-2-ones (compounds
I-II), 2-oxo-7-aryl-2,3-dihydrothiazolo[4,5-b]
pyridine-5-carboxylic acids (compounds III–
VI) and their amides (VII), was evaluated
(Figure 2). A series of 5,7-diaryl-3H-
thiazolo[4,5-b]pyridin-2-ones (I-II), 2-oxo-
7-aryl-2,3-dihydrothiazolo[4,5-b]pyridine-
5-carboxylic acids (III–VI) were obtained via
[3+3]-cyclization of 4-aminio-5H-thiazol-2-one
and chalcones or arylidene pyruvic acids
(APAs) [28]. The target 7-(4-chlorophenyl)-2-
oxo-2,3-dihydrothiazolo[4,5-b]pyridine-5-car-
boxylic acid (4-chlorophenyl)amide (VII) was
synthesized from appropriate 2-oxo-7-phen-
yl-2,3-dihydrothiazolo[4,5-b]pyridine-5-car-
boxylic acid, which was transformed into acid
chlorides and used in the acylation reaction of
respective amine according to the protocol
described previously [27].

Antimicrobial activity

The antimicrobial activity of the synthesized
thiazolopyridines was estimated with the agar
diffusion method [29]. Nutrient agar (0.5 %
peptone, 0.3 % beef extract, 1.5 % agar, 0.5 %
sodium chloride, distilled water, pH ~ 6.8) was
used as a nutrient medium for in vitro antibac-
terial activity. In vitro antifungal activity was
determined by using Sabouraud Agar plates.
The test cultures suspensions (in concentration
1×10^7 CFU/ml), standardized previously by
the optical standard of turbidity, were uni-
formly sown in Petri dishes with the nutrient
agar. Aliquot part (20 μL) of 0.1 % tested
thiazolopyridine derivatives (concentration
1000 μg/ml) in ethanol/dimethyl sulfoxide/
water (2:1:1) was placed into wells (diameter
of 4.0±0.1 mm) in agar in Petri plates with test
microorganisms. Antibacterial and antifungal
activities were estimated by measuring the
diameter of inhibition zone of microbial
growth. The plates were incubated for 24 h at 37 °C for bacteria and for 24 h at 25 °C for fungi. The inhibition zone appeared after 24 h was measured in mm around the well in each plate. The digital images of culture growth on dishes were obtained and processed with a computer program UTHSCSA ImageTool 2.0 (UT Health San Antonio, © 1995–1996) for calculation of diameters of the growth inhibition zone. Each experiment was performed by three independent researchers. The results were expressed as the means ± S.D. The experiments were carried out on the microorganism strains, which were isolated from the ambulatory patients. The following isolated clinical strains of conditionally pathogenic bacteria were used: methicillin-sensitive Staphylococcus aureus (MSSA); methicillin-resistant Staphylococcus aureus (MRSA); methicillin-resistant Staphylococcus haemolyticus (MRSH) (extended spectrum β-lactamase (ESβL) producing); Gram-negative bacteria Escherichia coli; yeasts Candida albicans. All clinical strains were multidrug resistant (MDR) [30] and Candida albicans were resistant to fluconazole and clotrimazole. All compounds were also tested against the reference strains of Staphylococcus aureus (ATCC 25923 (F-49)), Escherichia coli (ATCC 25922), Bacillus subtilis (ATCC 6633), Klebsiella pneumoniae (ATCC 700603) and Candida albicans (ATCC 885-653) from the culture museum. Test-cultures were identified using chemical micro-tests “STAPHYtest 16” and “ENTEROtest 24” (Erba Lachema, Czech Republic). Fungi cultures were identified on the basis of 40 biochemical tests using the VITEK 2 system with the VITEK® 2 YST ID card (bioMérieux Corporate, France).

The sensitivity of strains to antibiotics was determined by disc-diffusion method and serial dilutions in agar. The MICs of the com-

![Fig. 2. Structures of tested thiazolo[4,5-b]pyridine derivatives I–VII.](image-url)
pounds were determined using the microdilution methods for antimicrobial susceptibility [31, 32]. Microorganism suspensions were inoculated to the corresponding wells and incubated at 36 °C for 18 h for bacteria and at 25 °C for 24 h for fungi. The presence of the microorganism growth in the bouillon (bouillon turbidity) suggested that the concentration of the compound was insufficient to suppress its viability. The first lowest concentration of the tested compounds (from a series of dilutions), where the bacterial growth was not visually determined, was the minimum inhibitory concentration (MIC). The estimation of synergy with amoxicillin for synthesized compounds has been performed by comparison of amoxicillin MICs in the presence of compounds in subinhibitory concentrations [33]. The following bacterial strains with the resistance to β-lactam antibiotics were used: EsβL (extended spectrum β-lactamase)-producing Klebsiella pneumoniae ATCC 700603; methicillin-resistant Staphylococcus haemolyticus (MRSH) with double mechanisms of β-lactam resistance included both atypical penicillin-binding protein PBP2* and β-lactamase activities. The production of the atypical penicillin-binding protein PBP2* was proved by the latex agglutination reaction (Slidex® MRSA Detection, bioMérieux Corporate, France). The results have been refined by variation statistics methods.

Antiproliferative activity
The HaCaT human keratinocites and HEK293 human embryonic kidney cells were obtained from Cell Collection of R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology (Kyiv, Ukraine). The cells were cultured in Dulbecco’s-modified Eagle medium (DMEM, Biowest, Nuaille, France) containing 10 % fetal bovine serum (Biowest, Nuaille, France) under standard conditions (37 °C, 5 % CO₂, 95 % humidity). The stock solution of studied compounds was prepared in DMSO and diluted with the culture medium to obtain a concentration range from 0.29 to 41.63 µg/mL. Cell viability was assessed after 72 h cultivation in the medium containing the studied compounds with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay kit (EZ4U, Biomedica, Vienna, Austria) according to the manufacturer’s protocol. The optical density was measured with the Absorbance Reader BioTek ELx800 (BioTek Instruments, Inc., USA) at 490 nm with 630 nm as a reference wavelength. The percentage of the viability inhibition was calculated in comparison with the untreated control cells. The IC₅₀ values (inhibition concentrations) are the compounds concentrations that inhibit the cell viability by 50 %, and were calculated by GraphPad Prism 6 software (San Diego, CA, USA) using nonlinear regression. Statistical analyses were performed using two-way ANOVA test with Dunnett’s multiple comparisons test. P < 0.05 was considered as statistically significant.

Results and Discussion
Antimicrobial activity of the synthesized thiazolopyridines in vitro was evaluated with the agar diffusion method. The screening was carried out against reference and clinical strains of Gram-positive and Gram-negative bacteria and yeasts: Staphylococcus aureus, Bacillus subtilis, Escherichia coli and Candida albicans. Amoxicillin for bacteria and Amphotericin-B
for fungi are taken as standard drugs. The screened compounds showed different mean zone of inhibition in the range of 0.0–9.42 mm against tested microorganisms (Table 1). The obtained results reveal that some thiazolopyridine derivatives possess a moderate activity towards the tested microorganisms in the dose of 20 µg per well. Thus, antimicrobial activity assay allowed the identification of 2-oxo-7-thiophen-2-yl-2,3-dihydrothiazolo[4,5-b]pyridine-5-carboxylic acid V and 7-(4-chlorophenyl)-2-oxo-2,3-dihydrothiazolo[4,5-b]pyridine-5-carboxylic acid (4-chlorophenyl)amide VII with good growth inhibition against some tested microorganisms. The compound V shows the highest activity against clinical strain Candida albicans compared to standard drug Amphotericin-B. The compound VII displays a moderate antibacterial activity against S. aureus methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) strains. MICs for compounds I–VII against several microorganisms were calculated using the broth microdilution method (Table 2). The tested compounds exhibited the inhibitory activity against MSSA and MRSA Staphylococcus aureus, Escherichia coli and Candida albicans with MIC 12.5–>50 µg/mL. Compound V showed a moderate activity towards Candida albicans with MIC 12.5 µg/mL. Compound VII exhibited at the same dilution inhibitory activity with MIC against MSSA and MRSA Staphylococcus aureus with MIC 50 µg/mL.

The derivatives I–VII were studied in the interaction with amoxicillin against multidrug

Table 1. Antimicrobial activity of thiazolopyridine derivatives.

| Compound | S. aureus (ATCC 25923) | S. aureus MSSA | S. aureus MRSA | E. coli (ATCC 25922) | E. coli | B. subtilis (ATCC 6633) | C. albicans (ATCC 885-653) | C. albicans |
|----------|-------------------------|----------------|-----------------|-----------------------|---------|-------------------------|-----------------------------|------------|
|          | Zone of growth inhibition, mm* |                 |                 |                       |         |                          |                             |            |
| I        | 4.15±0.08               | 4.65±0.08      | 7.03±0.64       | 0                     | 0       | 0                       | 5.43±0.21                   | 5.91±0.22  |
| II       | 5.01±0.35               | 4.78±0.45      | 4.95±0.46       | 0                     | 0       | 0                       | 0                           | 0          |
| III      | 3.71±0.21               | 4.76±0.29      | 4.47±0.41       | 0                     | 0       | 6.74±0.45               | 5.12±0.22                   | 6.21±0.36  |
| IV       | 5.71±0.22               | 4.75±0.29      | 4.21±0.29       | 4.21±0.29             | 5.06±0.32| 4.36±0.14               | 5.66±0.34                   | 4.30±0.42  |
| V        | 5.88±0.81               | 6.28±0.80      | 4.59±0.38       | 4.22±0.31             | 4.22±0.31| 5.14±0.36               | 8.47±0.42                   | 9.42±0.45  |
| VI       | 4.35±0.22               | 4.20±0.27      | 6.18±0.83       | 4.74±0.29             | 4.74±0.29| 0                       | 6.19±0.40                   | 6.39±0.50  |
| VII      | 6.71±0.43               | 7.67±0.47      | 8.16±0.65       | 5.04±0.28             | 5.04±0.28| 0                       | 6.16±0.33                   | 5.16±0.39  |
| Amoxicillin | 12.78±0.41           | 6.37±0.45      | 5.60±0.41       | 10.05±0.36            | 8.20±0.35| 7.97±0.42               | -                           | -          |
| Amphotericin-B | -                 | -              | -               | -                     | -       | -                       | 11.00±0.51                  | 9.00±0.65  |

* Data are given as mean ± SD.

# clinical isolates

Table 2. Minimum inhibitory concentration of tested compounds, µg/mL.

| Compound | S. aureus MSSA | S. aureus MRSA | E. coli | C. albicans |
|----------|----------------|----------------|---------|-------------|
| I        | > 50           | > 50           | > 50    | > 50        |
| II       | > 50           | > 50           | > 50    | > 50        |
| III      | > 50           | > 50           | > 50    | > 50        |
| IV       | > 50           | > 50           | > 50    | > 50        |
| V        | > 50           | > 50           | > 50    | 12.5        |
| VI       | > 50           | > 50           | > 50    | > 50        |
| VII      | 50             | 50             | > 50    | > 50        |
resistant clinical isolates of ESβL+ *K. pneumonia* and MRSH (Tables 3–5). According to the preliminary results of interaction screening, the thiazolopyridine derivative with a styrene fragment in the molecule VI displays the promising synergistic activity with amoxicillin against ESβL + *K. pneumonia* and MRSH strains. Interestingly, in numerous literature reports, the styrene fragment combined with various heterocyclic systems exhibits a significant synergistic effect with beta-lactam antibiotics [34]. Especially it can be observed for the quinoline/quinaxoline-styrene hybrid molecules structurally related to thiazolopyridines [34, 35].

The SAR analysis showed that the antibacterial effect of compounds I–VII did not depend on the substituents at C5 and C7 of thiazolopyridine core. However, the thiazolo[4,5-b]pyridine-5-carboxylic acid V with thienyl substituent was the most active and demonstrated a good effect against *Candida albicans* with MIC 12.5 µg/mL. Compound V possessed also a slight activity on renal cancer A498 cell line (GP = 73.76 %) as described previously [28]. The antimicrobial activity of thiophene-based derivatives has already been observed in the previous systematic studies, especially for condensed benzothiophene [36], thieno[2,3-d]pyrimidine [37] and thieno[3,2-c]pyrazole derivatives [38]. Additionally, the experimental study revealed that the presence of an amide fragment in thiazolopyridine core of the compound VII is also favorable for antimicrobial potency. The data concerning a critical impact of electron withdrawing groups in amide fragment are also presented in our previous paper about thiazolopyridine-5-carboxylic acid amides as possible anticancer agents [27]. On the other hand, the compounds with phenyl, 4-chlorophenyl, 4-methoxyphenyl, styryl and carboxylic substituents at C5 and C7 on thiazolo[4,5-b]pyridine core were insufficient to show enhanced activity and didn’t correlate with other types of activity typical for these compounds [27, 28].

Next, we used the MTT assay to investigate cytotoxicity of the thiazolopyridine derivatives towards the pseudo-normal cell line (HaCaT human keratinocytes and HEK293 human em-

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**Table 3. The synergistic interaction of thiazolopyridine derivatives with amoxicillin against ESβL+ Klebsiella pneumonia ATCC 700603, zone of growth inhibition (mm), M±S(σ), MIC amoxicillin 250 µg/mL.**

| Compounds | Control (medium without amoxicillin) | Media with amoxicillin |
|-----------|-------------------------------------|------------------------|
| EtOH+DMSO | 2.86±0.21                           | 2.75±0.52 | 2.63±0.21 | 3.38±0.71 | 3.06±0.33 |
| I         | 3.85±0.51                           | 4.37±0.48 | 3.85±0.46 | 3.14±0.17 | 2.91±0.32 |
| II        | 3.28±0.59                           | 3.47±0.61 | 3.25±0.43 | 3.20±0.07 | 3.24±0.43 |
| III       | 3.31±0.33                           | 3.75±0.22 | 5.18±1.14 | 3.47±0.44 | 4.30±0.60 |
| IV        | 3.46±0.57                           | 2.95±0.39 | 2.95±0.17 | 4.70±0.39 | 2.66±0.14 |
| V         | 3.03±0.43                           | 4.04±0.65 | 3.16±0.45 | 3.05±0.19 | 2.67±0.36 |
| VI        | 6.02±0.48                           | 8.37±1.38 | 6.27±0.29 | 6.03±0.58 | 5.90±0.66 |
|           | [12.73±0.83]                        | [13.20±1.05] | [11.06±1.25] | [15.47±2.16] | - |
| VII       | 3.25±0.37                           | 2.34±0.16 | [4.04±0.81] | [8.83±1.02] | 3.79±0.68 |

# in brackets — zones of partial inhibition of the bacterial growth (bacteriostatic effect).
Table 4. The synergistic interaction of thiazolopyridine derivatives with amoxicillin against MRSH, zone of growth inhibition (mm), M±S(σ), MIC amoxicillin 4000 µg/mL.

| Compounds | Control (medium without amoxicillin) | Media with amoxicillin |
|-----------|-------------------------------------|------------------------|
| EtOH+DMSO | 2.83±0.57                           | 2.94±0.27              |
| I         | 2.92±0.12                           | 2.85±0.44              |
| II        | 4.11±0.27                           | 3.42±0.31              |
| III       | 4.78±1.01                           | 5.55±0.56              |
| IV        | 2.92±0.25                           | 3.25±0.47              |
| V         | 3.28±0.56                           | 3.75±0.40              |
| VI        | 7.34±0.36                           | 14.28±0.53             |
| VII       | 3.52±0.65                           | 3.18±0.11              |

# in brackets — zones of partial inhibition of the bacterial growth (bacteriostatic effect).

Table 5. The synergistic interaction of thiazolopyridine derivatives (50 µg/mL) with amoxicillin against β-lactamase producing bacteria.

| Compounds | Klebsiella pneumonia ATCC 700603 | Staphylococcus haemolyticus MRSH |
|-----------|----------------------------------|----------------------------------|
| Amoxicillin| 256                             | 4096                             |
| + Clavulanate | 8                               | 32                               |
| I         | 256                             | 4096                             |
| II        | 256                             | 1024                             |
| III       | 256                             | 2048                             |
| IV        | 256                             | 4096                             |
| V         | 256                             | 2048                             |
| VI        | 32                              | 8                                |
| VII       | 256                             | 4096                             |

# clinical isolate with both atypical penicillin-binding protein PBP2* and β-lactamase activities.

bryonic kidney cells). We found that HaCaT and HEK293 demonstrated resistance to the thiazolopyridine derivatives treatment and did not reach the IC<sub>50</sub> value at 28.73–41.63 µg/mL (Figure 3). Compound I at 36.88 µg/mL inhibited the growth of HaCaT cells by 30.2 %, HEK293 cells — by 42.8 %. Compound IV at 30.67 µg/mL inhibited the growth of HaCaT cells by 24.1 %, HEK293 cells — by 33.0 %. Compound V at 28.73 µg/mL reduced the viability of HaCaT cells by 14.3 %, of HEK293 cells — by 31.3 %. Compound VI reduced the viability of HaCaT cells by 7.0 %, of HEK293 cells — by 15.8 %. Under compound VII treatment at 41.63 µg/mL, we found 26.3 % of HaCaT cells growth inhibition, and 26.5 % of HEK293 cells growth inhibition (Figure 3).

Conclusions

The various subtypes of thiazolopyridines I–VII were evaluated for in vitro antibacterial activity against Staphylococcus aureus,
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Bacillus subtilis and Escherichia coli as well as for antifungal activity against Candida albicans using the agar diffusion and microbroth dilution methods. The antimicrobial screening led to the identification of the active compound V with the highest activity against Candida albicans (MIC = 12.5 µg/mL). The synergism of action with amoxicillin allowed the distinguishing of the most active compound VI with good antimicrobial activity against ESβL + K. pneumoniae and Staphylococcus haemolyticus (MRSH) strains. Compounds I, IV–VII in concentrations of 0–41.63 µg/mL demonstrated low cytotoxicity against HaCaT human keratinocytes and HEK293 human embryonic kidney cell lines. Considering the above, the thiazolopyridine derivatives are justified as a fruitful template for the development of a new class of chemotherapeutic agents in the modern drug discovery.

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Антимікробна та цитотоксична активність похідних тіазоло[4,5-b]піридина.

Висновки. Встановлено взаємозв’язок структура-антибактеріальна/протимікробна активність синтезованих соединений. Проведена оцінка цитотоксичності цільових сполук відносно клітинних ліній HaCaT та HEK293 (МТТ-тест). Встановлено взаємозв’язок структура-антибактеріальна/протимікробна активність для досліджуваних сполук. Проведено оцінку цитотоксичної активності похідних тіазолопіридину.

Результати. Наивисша антибактеріальна активність наблюдалася для 2-оксо-7-тиофен-2-ил-2,3-дигідротіазоло[4,5-b]піридин-5-карбонової кислоти (сполука V) із значенням мінімальної інгібуючої концентрації (МИК) 12.5 μg/mL відносно Candida albicans. Одночасно для синтезованих сполук досліджувався синергізм взаємодії з амоксициліном відносно мультирезистентних клінічних ізолятів ESβL+ Klebsiella pneumoniae та Staphylococcus haemolyticus (MRSH).

Висновки. Досліджувані похідні тіазолопіридину становлять цікаву платформу для подальшої розробки нових хіміотерапевтичних лікарських засобів.

Ключові слова: гетероциклічні сполуки, тіазолідинони, тіазоло[4,5-b]піридини, протимікробна активність, антипроліферативна активність

Цель. Осуществить скрининг противомикробной и цитотоксической активности производных тиазоло[4,5-b]пиреидина. Методы. Изучение антибактериальной и противогрибковой активности синтезированных соединений проведено in vitro методом диффузии в агар и микрометодом серийных разведений в агаре относительно клинических и музейных штаммов грамположительных, грамотрицательных бактерий и дрожжей. Установлена взаимосвязь структура-антимикробная/противогрибковая активность для исследуемых соединений. Проведена оценка цитотоксичности целевых соединений относительно клеточных линий HaCaT и HEK293 (MTT-тест). Результаты. Наивысшая антимикробная активность наблюдалась для 2-оксо-7-тиофен-2-ил-2,3-дигидротиазоло[4,5-b]пирин-5-карбоновой кислоты (соединение V) со значением минимальной ингибирующей концентрации (МИК) 12.5 μg/mL относительно Candida albicans. Одновременно для синтезированных соединений исследовался синергизм взаимодействия с амоксициллином относительно мультирезистентных клинических изолятов ESβL+ Klebsiella pneumoniae и Staphylococcus haemolyticus (MRSH).

Лучший синергизм взаимодействия с амоксициллином наблюдался для соединения V. Кератиноциты человека линии HaCaT и клетки эмбриональной почки человека HEK293 продемонстрировали устойчивость к действию на них производных тиазолопиридина со значением IC₉₀ менее 100 μM.

Выводы. Исследуемые производные тиазолопиридина составляют интересную платформу для дальнейшей разработки новых химиотерапевтических лекарственных средств.

Ключевые слова: гетероциклические соединения, тиазолидиноны, тиазоло[4,5-b]пиринды, противомикробная активность, антипролиферативная активность.

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