Determination of antimicrobial activity of some 1,2,4-triazole derivatives

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We carried out MIC of the derivatives of 1,2,4-triazole II (4-(5-nitrofuran-2-yl) methylamino)-1-propyl-4H-1,2,4-triazolium bromide) and I (N-(5-nitrofuran-2-yl)methylene)-4-amino-1,2,4-triazolidinium chloride) against Escherichia coli ATCC 3912/4 and E. coli K88ad, Klebsiella pneumonia ATCC 25923 and S. aureus K99, Salmonella typhimurium ATCC 144, S. enteritidis. All test cultures were sensitive to compound II at concentrations of 1.25–0.039 μg/ml. Similar MIC (0.039 μg/ml) of compounds II and I were set for E. coli K88ad and S. aureus K99 test cultures – 0.156 μg/ml. Only S. aureus ATCC 25923 and K. pneumonia K56 had sensitivity to ceftriaxone (MIC = 0.097 μg/ml). Antiviral activity of Trifuzol (piperidine 2-[5-(furan-2-il)-4-phenil-1,2,4-triazol-3-llithio]acetate) and avistim (morpholines 3-[4-pyridyl]-1,2,4-triazolil-5-thioacetate) against the chicken infectious bronchitis virus (VIB) strain 4/91 was characterized by a decrease in mortality and pathological changes of chicken embryos (CE) which were induced by the virus. Death of infected CE provoked by the strain 4/91 of VIB in dilution 10–3 occurred at 57.1%. The reduction in the percentage of deaths of CE infected by the virus in dilution 10–3 in the presence of Avistim was 28.6%, and with Trifuzol 14.3%. The use of avistim and Trifazol compounds reduced VIB infectious activity when it was cultivated in CE, reducing the titre of the virus (strain 4/91) by 3 log EID 50 cm-1.

Keywords: derivatives of 1,2,4-triazole; Trifuzol; Avistim; antibacterial activity; antiviral activity

Introduction

The compounds of 1,2,4-triazole-5 and 3-nitro-1,2,4-triazole-5 were obtained at the beginning of the 20th century, and considered as effective compounds in decreasing of the influence of many diseases (Gehlen et al., 1964). The typical species in a range of compounds of 1,2,4-triazole are 5-amino-1,2,4-triazole-3-carboxylic and 5-amino-1,2,4-triazole-3-thioacetic acid. The first of these was known at the end of the 19th century. Dyes, plant protection products and antivirals (ribavirin) were synthesized in industry on its basis (Abo-Bakr, 2014). Derivatives of 1,2,4-triazoles are used in industry, agriculture, veterinary and humane medicine. Among a large number of various agents that have antibacterial, antifungal and antiviral effects, these compounds deserve special attention in veterinary practice (Parchenko, 2011; Pattan et al., 2012; Zoumpoulakis et al., 2012).

The analysis of scientific and technical studies in recent years has shown that the nucleus of 1,2,4-triazole is a structural fragment of antifungal drugs (Fluconazole, Itaconazole, antidepressant (Trazodone, Alprazolam), hepatoprotective, wound healing and antiviral (Thiotiazolin) effects (Plech Tomaz et al., 2013).

Currently 1,2,4-triazoles attract interest in antimicrobial chemotheraphy due to their high spectrum of biological activity. The emergence of new pathogens and the difficult problem of resistance give rise to the need for new antimicrobial agents with greater selectivity and low accidental effects (Jyoti Sinha et al., 2017).

Among the compounds that have antibacterial activity, special attention should be paid to 2-pyrazolines, 1,3,4-oxadiazoles, glycosides, salicylates, quinolines, amino acids (glycopeptides), isatins, oxindoles and triazoles. The spectrum of use of morpholinos 2-[5-(pyridine-4-il)-1,2,4-triazole-3-llithio]acetate for the treatment and prevention of poultry diseases is very wide. The main indications for the successful use of any drug in the poultry sector are activation of the general resistance, increa-
**Materials and methods**

For bacteriological studies, blood and red bone marrow from 1-day, 10-day and 21-day Hådbard cross chickens were collected. Sensitivity of microorganisms to antibiotics was carried out relative to NCCLS “Methods for the determination of susceptibility of bacteria to antimicrobial agents” (1999) and EUCAST Definitive document CLSI “Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems” (2015).

List of compounds, studied in the research:

I – N-(5-Nitrofuran-2-yl)methylene-4H-4-amino-1,2,4-triazolidin chloride (formula 1);

II – 4-(5-Nitrofuran-2-yl)methyleneamino)-1-propil-4H-1,2,4-triazolidin bromide (formula 2);

Avistim – morpholines 3-(4-pyridyl)-1,2,4-triazolil-5-thioacetate (formula 3);

Trifuzol – piperidine 2-[5-(furan-2-il)-4-phenil-1,2,4-triazolil-3-ilthio] acetate (formula 4);

The compounds were synthesized in Zaporizhzhia State Medical University, Ukraine.

**Dimethylformamide (DMF)** – N,N-Dimethylformamide (formula 5);

Ceftriaxone – [6R-[alpha][beta][gamma]-7]-[(2-Amino-4-triazolil) methoxyiminocetyl]amino]-8-oxo-3-[[1,2,5-tetrahydro-2-metil-5,6, bicyclo(1,2,3)-triazin-3-yl]tio][metil]-5-tia-1-azabicyclo[4.2.0]octa-2-ene-2-carboxylic acid (formula 6);

**Preparation of solutions and serial dilutions of the studied substances.** The compounds are synthesized in Zaporizhzhia State Medical University, Ukraine.

The dilution of compounds 1 and II were prepared from 1:20 to 1:0,039 based on a matrix solution (dilution of compounds 1:10 in DMF) on the sterile physiological solution for 24 units of McFarland.

Ceftriaxone is a dry powder for injection of 1,000 active units (1 g), was diluted in 2 ml of meat infusion broth (MIB), and a working solution of 500 units/ml was obtained. Then dilutions were repeated, by adding 1 ml of the working solution of antibiotic with 500 units/ml to 4 ml of MIB. Thus, the working solution was obtained at a concentration of 100 units/ml. Subsequently 1 ml of MIB was added to the same solution.
and received 50 units/ml (McFarland 0.5). Thus, the tested concentrations of Ceftriaxone were from 25 to 0.0488 units.

Preparation of inoculum of test cultures. Typical representatives of Gram-positive and Gram-negative bacteria were selected as test objects: Staphylococcus aureus ATCC 29523 and k99; Escherichia coli ATCC 39124/1 k88 ad.; Klebsiella pneumoniae k56 and Salmonella typhimurium 144. For the production of inoculums of microorganism cultures, daily cultures were grown on Mueller-Hinton Agar (HiMedia Laboratories Ltd., India).

Inoculum was prepared from the daily culture of microorganisms, on MIB. The inoculum concentration was 0.5 units by McFarland, which is 1.5·10^7 CFU/ml. The working concentration of the inoculum was 5 CFU/ml (10^6 CFU/ml).

Serial dilutions in the broth were accompanied by control of crop growth in MIB without the use of compounds I or II, Ceftriaxone and DMF.

The purity of the suspension of microorganisms was confirmed by sowing on agar, followed by Gram-staining and microscopy. The assessment of sensitivity of microorganisms to the studied compounds was carried out on the basis of a minimum inhibitory concentration (MIC). The results of the experiment were taken into account after the assessment control of the inoculums, which was at temperature 40°C and in the thermostat (37°C).

**Disc-diffusion method.** Disks of sterile filter paper, 5 mm diameter, were soaked in appropriate concentrations of the studied compounds I and II. The content of the studied compounds on the disk was 25 and 50 µg. Petri dishes with the Mueller-Hinton agar were sown by test culture in the concentration equal to the turbid standard McFarland 0.5. After that the disks, which contained the test substances and antibiotics, were replaced on the agar surface, in accordance to the stencil. Petri dishes were maintained at room temperature for 30 minutes and placed in the thermostat at the temperature of 8°C in an inverted position. Antibiotics: Ofloxacin, Norfloxacin, Ciprofloxacin, Levomycetin, Erythromycin, Azithromycin, Josamycin, Cefuroxime, Ceftriaxone, Cefepime, Gentamicin, Amoxicillin were control. In 24 h, the sensitivity of test-cultures to compounds I and II was determined by the diameter of retardation zone (Patel, 2013).

**Studying of antiviral activity of triazolin range compounds against the virus of the infection of chicken bronchitis.** Chicken embryos (CE) were inoculated in a laboratory. Biological evaluation of eggs was carried out according to the recommendations of Dyadichkin (2010) and Besarabov (2010). Vaccine strain that was used in this research: the lyophilized live vaccine against chicken bronchitis infectious (Nobilis IB 491, virus titer10^6 EID₅₀/cm³). The preparation of the virus from 10⁻¹ to 10⁻⁴ was prepared in a sterile physiological solution. The determination of the antiviral activity of the compounds of Trifuzol and Avistim in concentration 1% was carried out by simultaneous infection by the strain of 491 VIB of chicken embryos 9-day incubation on the CAM in a dose of 0.2 cm². The incubation of infected and control CE were carried out in a laboratory incubator at the temperature of 37°C and a humidity of 65% for 4 days. Evaluation of pathological changes induced by VIB strain 491 and the effects of triazolin range compounds, selection of the restrictive virus material were carried out at 4 days incubation of CE and pre-cooling at the temperature of 40°C for 12 h. The criterion for assessing the reproduction of the virus was patho-anatomical changes in the embryo, special to the action of the virus and the titre of the virus, which was calculated by Reed and Mencch and expressed in EID₅₀/cm³ (Stefanov, 2001).

**Statistical processing of the results.** Statistical data were processed by program Statistica 7.0 (StatSoft, USA) (Rebrova, 2006).

**Results**

Strains of E. coli and S. aureus were isolated from 1, 10 and 21-day chickens. As a result of serological typing, there were 78 enterotropic bacteria cultures, 87% of them were classified into serological variants of k88 ad; k88 ad, ab; k99. E. coli and S. aureus were detected from the blood of 1-day chickens, E. coli of serovariant k 88 ad were detected from the red bone marrow, whereas in the blood of 10-day old chickens – E. coli serovariant k 88 ad, ab and S. aureus k99 were detected. E. coli serovariants k99 were isolated from red bone marrow of 21-day old chickens. The frequency of detection of S. aureus – 16.2% and E. coli – 13.2% (Fig. 1).

Isolated strains of E. coli and S. aureus had the highest sensitivity to erythromycin (diameter of the growth inhibition zones 32 ± 3.5 mm and 25 ± 2.8 mm respectively).

Both S. aureus and E. coli were sensitive to gentamicin (diameter of the growth inhibition zones 19 ± 2.1 mm and 21 ± 2.3 mm respectively). In this case, the S. aureus culture had an average sensitivity to Doxycycline. Thus, microorganism cultures isolated from chickens at different incubation periods have the high sensitivity to antibiotics of the Macrolide and Aminoglycoside classes.

The evaluation of isolated E. coli 88 showed the resistance to Doxycycline (diameter of the growth inhibition zone 2.5 ± 0.27 mm), Josamycin (4.3 ± 0.47 mm), and Azithromycin (3.1 ± 0.56 mm). The resistance of S. aureus k99 was also detected to Azithromycin, Josamycin, Ceftriaxone and Ciprofloxacin. In the subsequent study we expanded the antibiotics spectrum of different groups and tested the potential antimicrobial action of new derivatives of 1,2,4-triazole.

![Fig. 1. Clinically sick chicken Hubbard cross (a) and pathological changes in chicken with coli bacillosis (b)](image)

**Antimicrobial activity of triazolin compounds.** The sensitivity to Cefuroxim was shown by E. coli ATCC 39124 and S. aureus ATCC 25923. The diameter of the growth inhibition zone exceeded the norm for this antibiotic. Cultures, which were isolated from the chickens, stayed insensitive to Cefuroxim.

E. coli ATCC 39124/1 detected high sensitivity to Ceftriaxone that also exceeded the normative index. All studied cultures were highly susceptible to Gentamicin and only test-cultures were susceptible to Ciprofloxacin and Norfloxacin. The sensitivity of S. aureus culture, isolated both from the chickens and among the museum strains, should be noted.

Antibacterial activity of the new triazolin range compounds can be compared with the normative indices, in the case of their sensitivity to the action of Cefuroxin, Cefepim, Norfloxacin, Levomycetin, and Doxycline in the growth delay zone, as tested and as isolated cultures (Table 1).
The decrease in the percentage of CE with an increased amount of studied concentrations, with Avistim at the same time.

The increase of this feature occurred after the injection of the virus in dilution 10⁻³ with Avistim was 14.3%, which is believed to be lower than control by 71.4% (Fig. 3).

The detection of antimicrobial activity of triazolinium group compounds by the method of serial dilutions. The experimental data on effect of compounds I and II indicates the high bactericidal and bacteriostatic effects of the compound on the epizootic strains of bacteria, isolated from chicken. The minimum bactericidal concentration of compound II for E. coli k88 ad cultures was 0.039 µg/ml. The minimum inhibitory concentration of compound II to S. aureus k99 culture was 0.16 µg/ml (Table 2).

The detection of sensitivity of test cultures and isolated strains of E. coli and S. aureus to new derivatives of 1,2,4-triazolo N-(5-nitrofuran-2-il)methylene)-4H-4-amino-1,2,4-triazolium chloride (I) and 4-(5-nitrofuran-2-il)methylene-amino)-1-propyl-4H-1,2,4-triazolium bromide (II), in comparison with the antibiotics of different groups, indicates their antimicrobial action. The most effective antimicrobial activity was shown by the compound I at a concentration of 50 µg against the S. aureus (diameter of inhibition of growth zone 18.8 ± 1.65 mm). The compound I had lower activity with respect to E. coli (17.8 mm), respectively, serovariant k88 ad and ATCC 3912/41. Compound II inhibited the growth of S. aureus k99 (diameter of inhibition of growth zone 17.3 mm).

Table 1

<table>
<thead>
<tr>
<th>Drug class or subclass / antibiotic</th>
<th>The content of the antibiotic on the disk, μg</th>
<th>The diameter of the growth inhibition zone, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E. coli, 5×10⁴ CFU/cm²</td>
<td>S. aureus, 5×10⁴ CFU/cm²</td>
</tr>
<tr>
<td>K88 ad</td>
<td>ATCC 055 K59 91/241</td>
<td>ATCC 29223</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>15</td>
<td>32 ± 3.5</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>15</td>
<td>5.1 ± 0.56</td>
</tr>
<tr>
<td>Josamicin</td>
<td>15</td>
<td>4.3 ± 0.47</td>
</tr>
<tr>
<td>Cefuroxim</td>
<td>30</td>
<td>6.2 ± 0.68</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>30</td>
<td>7.8 ± 0.86</td>
</tr>
<tr>
<td>Ceftelip</td>
<td>30</td>
<td>6.5 ± 0.72</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>20</td>
<td>10.1 ± 1.12</td>
</tr>
<tr>
<td>Ofloxacine</td>
<td>5</td>
<td>–</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>5</td>
<td>9.3 ± 1.03</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>10</td>
<td>10 ± 1.11</td>
</tr>
<tr>
<td>Doxycline</td>
<td>30</td>
<td>2.5 ± 0.27</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>120</td>
<td>21 ± 2.33</td>
</tr>
<tr>
<td>Levomycetin</td>
<td>30</td>
<td>17.8 ± 0.48</td>
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<td>N-(5-Nitrofuran-2-il)methylene)-4H-4-amino-1,2,4-triazolium chloride (I)</td>
<td>25</td>
<td>158.0 ± 15.5</td>
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<tr>
<td>4-(5-Nitrofuran-2-il)methylene-amino)-1-propyl-4H-1,2,4-triazolium bromide (II)</td>
<td>50</td>
<td>17.8 ± 1.44</td>
</tr>
<tr>
<td>4-(5-Nitrofuran-2-il)methylene-amino)-1-propyl-4H-1,2,4-triazolium bromide (II)</td>
<td>25</td>
<td>14.8 ± 1.7</td>
</tr>
<tr>
<td>4-(5-Nitrofuran-2-il)methylene-amino)-1-propyl-4H-1,2,4-triazolium bromide (II)</td>
<td>50</td>
<td>12.0 ± 2.16</td>
</tr>
</tbody>
</table>

Note: “–” – not sensitive.

Fig. 2. CE infected with VIB strain 4/91: a – control; c – infected by VIB in dilution 10⁻²; e – infected VIB in dilution 10⁻³ simultaneously with Avistim; g – infected with VIB in dilution 10⁻³ simultaneously with Avistim.

The increase of this feature occurred after the injection of the virus at a concentration of 10⁻³ simultaneously with Avistim, that was 28.5%. The decrease in the percentage of CE with an increased amount of extraembryonic liquid was registered after the injection of the virus in studied concentrations, with Avistim at the same time.

Thus, the reduction of this index (by 73.2%) occurred in CE which had been infected by 10⁻³ dilution of the virus with Avistim, when compared with CE which were infected with the virus at the same concentration without Avistim.

In the control CE group and the groups that have been injected only by Avistim or Trifuzol, in contrast to the experimental CE, the amount of allantoic fluid decreased. The presence of uremic salts in CE of these groups was observed at the level of 85.7% in the control group, and 28.5% after the injection of Avistim, and 14.3% in the group receiving Trifuzol. When compared with the CE control group, the percentage of this index in CE infected by the virus in dilution 10⁻¹ decreased by 56.9%, whereas in the CE group after the injection of Avistim, the difference was 57.5%. The percentage of uremic salts in allantoic fluid infected by the virus at a concentration of 10⁻³ and infected by the virus at a concentration of 10⁻² with Avistim was 14.3%, which is believed to be lower than control by 71.4% (Fig. 3).

In the CE group, infected by the virus from dilution of 10⁻³ simultaneously with Trifuzol, the presence of uremic salts was detected at a large value, and was 42.9%.
Transparent allantoic fluid in CE was present in the group which had been injected by the virus in the studied concentrations, in contrast to the control group and CE groups which had been injected by Avistim and Trifuzol. The highest percentage of transparent allantoic fluid was observed in CE infected by the virus in dilution of $10^{-3}$ (71.4%), the lowest rate index in CE, infected by the virus in dilution $10^{-2}$ (25.0%). This index remained stable in CE infected by all investigated concentrations with the simultaneous injection of Trifuzol compounds and amounted to 42.9%. In the CE group infected with the virus in combination with Avistim, this feature decreased simultaneously with the decrease of virus concentration.

The highest death rate of the embryo was in the CE group infected by the virus in dilution $10^{-3}$ (57.1%). The death of the embryos rose to 28.5%, while in the CE infected by the virus at the same concentration simultaneously with Avistim and in the group infected by Trifuzol the death rate was 42.9%. The position of the embryos during the autopsy observed in CE infected by the virus in dilution of $10^{-1}$ (71.4%), the decrease of virus concentration.

The percentage of CE with limbs on the head in the CE group, which was infected with the virus, simultaneously with injection of Avistim was lower than in CE which had been infected with only the virus, however it was higher than in the CE group with Trifuzol.

Growth delay was marked in CE infected by the virus at the concentrations of $10^{-2}$, $10^{-3}$ (12.5% and 14.3% respectively) and in the group infected by the virus in dilution $10^{-4}$ simultaneously with Trifuzol (14.3%). The Avistim and Trifuzol compounds reduce the VIB infectious activity during its cultivation in CE, reducing the titre of the virus (strain 4/91) by 3 lg EID$_{50}$/cm$^2$.

**Discussion**

Use of the preparations, containing the nucleus of 1,2,4-triazole into the veterinary practice is increasing very rapidly (Dal Pozzo & Thiry, 2014; Krajczyk et al., 2014; Jefferey et al., 2015; Wenda et al., 2017).

Search for new antiviral and antibacterial means is being undertaken all over the world. This is connected with the emergence of new variants of viruses and antibiotic resistant bacteria (Wang & Zhou, 2011; de Oliveira et al., 2012; Asl, 2015). Testing a number of triazole derivative compounds that were obtained as the result of directed synthesis has proven their ability to suppress the reproduction of test-cultures of microorganisms (Zhao Chen et al., 2010; Ferreini et al., 2013).

Derivatives of 1,2,4-triazole are distinguished among other drugs by the capacity for a wide range of biological activity and low toxicity. The priority of their use in antimicrobial therapy is confirmed by the prolonged effect of the formation of resistance bacteria (Sidhiqui et al., 2011; Gross & Bryson, 2015). Reduction of the infectious activity of the infectious bronchitis virus (strain 4/91) in the EC bio-system, caused by Trifuzol and Avistim, makes it possible to register them as antiviral and immunomodulatory agents for use in veterinary medicine.

Investigation of the compound 2-[(5-furan-2-yl-4-phenyl-1,2,4-triazole-3-ylii)-acetate on 9-day chicken embryos against the action of the infectious encephalomyelitis virus (Calnek 1143 strain) and the infectious bronchitis virus H-120 revealed the decrease of titre of strain H-120 at 1.8 log and strain Calnek 1143 at 1.0 log (Parchenko et al., 2009; Fotina, 2015).

A comparative assessment of the sensitivity E. coli and S. aureus cultures, isolated from chickens and test-cultures, against new triazolin compounds with the results of antibacterial drug sensitivity proves that they are worth studying further. The growth inhibition zones of test-cultures, caused by compounds I and II, were indexed in the range from 12.0 to 19.8 mm. Norfloxacin, Levomycin, Doxycycline and Eritromicin induced similar inhibition of growth zones of test-cultures, simultaneously. Sahu (2014) defined the MIC of new compounds that are derivatives of 1,2,4-triazole compared to Gentamicin. By the method of dilutions, it was determined that MIC ranges for compounds against E. coli and S. aureus were from 1.6 to 25.0 mg/ml, and for Gentamicin for these test-cultures – 1.6 mg/ml. The diameter of inhibition of growth zone of test-cultures of E. coli and S. aureus, induced by the compounds, changed from 0.6 to 5.0 mm, while for Gentamicin – 16.0 mm.

According to Malladi (2013), MIC of Ceftriaxone for E. coli was 1.61 mg/ml and for S. aureus – 3.13 mg/ml. Sceiala (2016) showed the ability of triazolin compounds to suppress the growth of E. coli test-culture (MTCC 433) at MIC from 50 to 3.13 mg/ml. In this case, Streptomycin and Chloramphenicol had a MIC of 6.25 mg/ml.

Wahi et al. (2011) proved the antimicrobial activity of new derivatives of 1,2,4-triazole by the method of serial dilutions. Only 2 compounds out of the 8 compounds were indexed against Gram-negative and Gram-positive bacteria in low MIC (3.12 mg/ml). MIC of the compounds against Streptococcus pyogenes, Micrococcus luteus, Staphylococcus epidermidis, Clostridium sporogenes, Salmonella typhimurium ranged from 3.12 to 50 mg/ml. The standard example had a lower MIC (1.56-6.25 mg/ml). In research by Popiolek et al. (2013), MIC of novel 1,2,4-triazole and 1,3,4-dihiaziol derivatives against Gram-negative and Gram-positive bacteria (S. aureus ATCC 25923, S. aureus ATCC 6538, S. epidermidis ATCC 12228, B. subtilis ATCC 6633, B. cereus ATCC 10876, M. luteus ATCC 10240) ranged from 15.6 to 500 mg/ml. The inhibitory concentration of Ceftriaxone on S. epidermidis ATCC 12228 was 0.24 mg/ml, and for B. cereus ATCC 10876 – 62.5 mg/ml.

Screening of 15 new derivatives of 1,2,4-triazole with antibacterial activity made by Bektaş et al. (2010) detected for 4 compounds: MIC for E. coli ATCC 25923 ≥ 500 mg/ml to 1.95 mg/ml. S. aureus ATCC 25923 was susceptible to these compounds in the range of 1.95 to 500 mg/ml. Ampicillin had a higher MIC compared to E. coli (10 mg/ml) and 35 mg/ml – to S. aureus. The ability of new derivatives of 1,2,4-triazole to have an effect against the bacterial and viral pathogens of poultry infections, has been carried out in the process of the research, and is the basis for their use in schemes for prevention of infectious diseases. The agents of Trifuzol and Avistim have antiviral action against the chicken infectious virus bronchiitis strain 4/91 (reduction of the virus titre by 3.0 logs). In this case, defined antiviral activity was higher than the data obtained by Fotina et al. (2015), against the VIB strain N-120 and the virus of encephalomyelitis of bird strain Calnek 1143.

The biological activity of the new derivatives of 1,2,4-triazole, determined by us against the different groups of microorganisms, proves the prospect of their further use in veterinary medicine.
Antibacterial activity of compounds I and II against collection strains, isolated from broiler chickens is established. Against S. aureus, compound I in 50 μg concentration on a disk, induced the growth inhibition zone at 18.5 ± 1.65 mm and for E. coli - 17.8 ± 1.44 – 17.8 ± 0.25 mm respectively to serovarants k88 ad and ATCC 39214. Compound II in a concentration of 50 μg on a disk induced the growth inhibition zone of S. aureus 99, isolated from chicken broilers, at a level of 17.3 mm. Trifuzol and Avistim cause antibacterial activity against the VIB strain 4/91 during cultivation in EC. The percentage of deaths of EC infected with the virus in dilution 10^{-3} in the presence of Avistin was lower by 28.6%, and with Trifuzol lower by 14.3%. The Avistin and Trifuzol compounds reduced the VIB infectious activity when it was cultivated in CE, reducing the titre of the virus (strain 4/91) by 3.0 log EID_{50}/cm².

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