# Antimicrobial Activity of Some Furans Containing 1,2,4-Triazoles

#### Volodymyr Zazharskyi<sup>1</sup>, Oleksii Bigdan<sup>2\*</sup>, Volodymyr Parchenko<sup>3</sup>, Maryna Parchenko<sup>4</sup>, Tatiana Fotina<sup>5</sup>, Pavlo Davydenko<sup>6</sup>, Oleh Kulishenko<sup>1</sup>, Nadiia Zazharskaya<sup>6</sup>, Iryna Borovik<sup>6</sup>

<sup>1</sup>Department of Epizootology and Infectious Diseases, University of Dnipro State Agrarian and Economics, Ukraine. <sup>2</sup>Department of Clinical Pharmacy, Pharmacotherapy, Pharmacognosy, and Pharmaceutical Chemistry, University of Zaporizhzhya State Medical, Zaporizhzhya, Ukraine. <sup>3</sup>Department of Natural Sciences for Foreign Students and Toxicological Chemistry, University of Zaporizhzhya State Medical, Zaporizhzhya, Ukraine. <sup>4</sup>Department of Pharmacy Management and Economics, University of Zaporizhzhya State Medical, Zaporizhzhya, Ukraine. <sup>5</sup>Department of veterinary examination, microbiology, zoo hygiene and safety and quality livestock products, University of Sumy National Agrarian, Ukraine. <sup>6</sup>Department of parasitology and veterinary examination, University of Dnipro State Agrarian and Economics, Ukraine.

#### Abstract

In this study, the antibacterial activity of 11 preparations of drugs was determined by disc diffusion method in agar. Suspensions  $(0.5 \times 10^8 \text{ CFU})$  were prepared from the daily cultures of Enterobacteriaceae, Pseudomonadaceae, Staphylococcaceae, Bacillaceae, Listeriaceae, Campylobacteraceae, Nocardiaceae, and Saccharomycetaceae family. The resulting suspensions were cultured on Mueller-Hinton agar, followed by cultivation for 24h. Disks impregnated with the studied preparation were placed on top of the passages.

The drug does not dissolve in water, so we used a dilution in 70% ethyl alcohol. The *in vitro* experiment showed the positive antibacterial effect of 11 preparations on cryogenic strains of Enterobacteriaceae microorganisms: *Escherichia coli, Enterococus faecalis, Proteus vulgaris, Serratia marcenses, Klebciella pneumoniae, Salmonella adobraco, Salmonella typhimurium*; Pseudomonadaceae families: *Pseudomonas aeruginosa*, Staphylococcaceae microorganisms: *Staphylococcus aureus; Staphylococcus epidermidis;* Bacillaceae families: *Bacillus subtilis,* Listeriaceae: *Listeria monocytogenes,* Listeria innocua, Listeria ivanovi; Campylobacteraceae: *Campylobacter jejuni;* Nocardiaceae: *Rhodococcus equi*, and yeasts family Saccharomycetaceae: *Candida albicans.* 

The investigated extracts of 5-(furan-2-yl-,5-bromofuran-2-yl)-4H-1,2,4-triazole-3-thiol, 2-(5-(furan-2-yl-, 5-bromofuran-2-yl)-4H-1,2,4-triazole-3-ylthio) acetate, 5-R-2-(furan-2-yl-,5-bromofuran-2-yl) thiazolo [3,2-b] [1,2,4] triazole-4 (5H)-one physicochemical properties can be recommended for additional investigations against polyresistant strains of the mentioned microorganisms.

Effective medicines play a key role in public health care and stable veterinary well-being of livestock. This study indicated that the evaluated preparation more intensively affects multiresistant microorganisms than the kanamycin sodium salt.

Keywords: Physicochemical properties, Enterobacteriaceae, Pseudomonadaceae, Staphylococcaceae, Bacillaceae, Listeriaceae

#### INTRODUCTION

Antibiotic resistance is one of the biggest threats to global health, which critically needs alternative solutions [1, 2]. L'abbé & Beenaerts (1989) reported that 5-Amino-1,2,3-triazoles, having a strong electron-withdrawing N-1 substituent, cannot be converted into the azides using the diazotization methods. Synthesis of 3- (o-nitrophenyl) -5-arylthiazolo [2,3-c] pyridin-2-one (2-octanyl) -6-arylthiazolo [3,2-b] [1,2,4] triazoles and its isomers, - [1,2,4] triazoles have antibacterial and antifungal effects.

Triazoles can also be used to preserve food [3-6]. Increasing heating temperature and pH significantly increase the viscosity of milk concentrates, while the distribution of denatured  $\kappa$ -casein and whey proteins between the micellar phase and serum only marginally affects it.

This work aimed to establish the antibacterial effect of 5-(furan-2-yl-, 5-bromofuran-2-yl)-4H-1,2,4-triazole-3-thiol, 2-(5-(furan-2-yl-,5-bromofuran-2-yl)-4H-1,2,4-triazole-3-ylthio) acetate, 5-R-2-

(furan-2-yl-,5-bromofuran-2-yl)thiazolo[3,2-b][1,2,4]triazole-4(5H)-one on cryogenic strains of *Enterobacteriaceae*, *Pseudomonadaceae*, *Staphylococcaceae*, *Bacillaceae*, *Listeriaceae*, *Corynebacteriaceae*, and *Saccharomycetaceae* families *in vitro*.

Address for correspondence: Oleksii Bigdan, Department of Clinical Pharmacy, Pharmacotherapy, Pharmacognosy, and Pharmaceutical Chemistry Zaporizhzhya State Medical University, Zaporizhzhya, Ukraine. abigdana@gmail.com

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**How to cite this article:** Zazharskyi V, Bigdan O, Parchenko V, Parchenko M, Fotina T, Davydenko P, et al. Antimicrobial Activity of Some Furans Containing 1,2,4- Triazoles. Arch Pharm Pract. 2021;12(2):60-5. https://doi.org/10.51847/RbJb3waUBB

#### MATERIALS AND METHODS

Extracts were filtered through glass funnels using sterile multi-layer gauze filters (fifty 6-mm sterile discs of filter paper) into sterile glass vials for ten days. The discs were dried in a sterile laminar box (BMB-II Laminar-C 1,2 Cytos) under UV rays for 30 minutes before being placed on the agar with the related culture.

Antibacterial effect of the 11 study preparation (Group I 2-(5-(5-bromofuran-2-yl)-4H-1,2,4-triazole-3-ilto)acetate; II-4hydroxyphenyl; III 3-fluorophenyl; IV-3.4-\_ V-3,5-dimethoxyphenyl; dimethoxyphenyl; VI-4fluorophenyl; VII-4-nitrophenyl; VIII-2-carboxyphenyl; IX-4-hydroxyphenyl; X -3,4-dimethoxyphenyl and XI groups 3,5-dimethoxyphenyl) was determined by agar disc diffusion method. A 0.5-Mac Farland suspension was prepared from a fresh culture of the reference cryogenic strains of 17 bacteria. The obtained suspension was subcultured on MHA (Himedia), followed by cultivation in a TCO-80/1 thermostat at 37 °C for 24 and 48 hours. Discs soaked in suitable extracts were put on top of the subcultures. Discs with 30.0µg Kanamycin - 0-3-Amino-3-deoxy-alpha-D-glucopyranosyl-(1 "6) -0- [6-amino-6-deoxy-alpha-D-glucopyrinazyl- [1" 4)] - 2-deoxy- D-streptamine were considered positive control. Kanamycin is a crystalline white powder, aminoglycoside antibiotic of the first generation, anti-tuberculosis drug of the second row, produced by radiant fungus Streptomyces kanamyceticus or other related microorganisms. Discs with (1R,3S,5R,6R,9R, 15.0 Amphotericinin μg 11R,15S,16R,17R,18S,19E,21E,23E,25E,27E,29E,31E,33R, 35S,36R,37S)-33-[(3-amino-3,6-dideoxy-β-Dmannopyranosyl)oxy]-1,3,5,6,9,11,17,37-octahydroxy-

15,16,18-trimethyl-13-oxo-14,39-dioxabicyclo [33.3.1] nonatriaconta-19,21,23,25,27,29,31-heptaene- 36-carboxylic acid) was also used as the second control against Candida albicans.

After 24-hour incubation, the inhibition zone diameter was measured using TpsDig2 program and a template (Antibiotic Zone Scale-C, model PW297, India). The data in tables are shown in the form of  $x \pm 1.96 \cdot SD$ .



**Figure 1.** 0-3-amino-3-deoxy-alpha-d-glucopyranosyl- (1 "6) -0- [6-amino-6-deoxy-alpha-d-glucopyrinazyl- [1" 4)] - 2deoxy- D-streptamine (C18H36N4O11)

## **RESULTS AND DISCUSSION**

It is known from the literature that the reaction of cyclization and the formation of bicyclic 1,2,4-triazole systems follows exactly the scheme of **Figure 1** [1]. The authors also investigated and proved that the reduction of 5-benzylidene-2- (3-fluorophenyl) thiazolo [3,2-b] -1,2,4-triazol-6- (5H) one in the presence of an excess of sodium borohydride leads to ring opening and formation of 3-aryl-2 - ((3- (3fluorophenyl) -1,2,4-triazol-5-yl) thio) -prop-2-en-1-ol [1].

**Table 1** shows the antibacterial effect of the extracts of studied preparation on cryogenic strains of Enterobacteriaceae and Pseudomonadaceae families *in vitro*. We determined the moderate sensitivity of *E. coli* 055 K 59 No. 3912/41 to 1.0% of the preparation of the second experimental group, which is 13.3% (1.9 mm) above the control. Other experimental preparation appeared to be resistant to this strain, although the growth retardation zone ranged from 0.1% of the drugs ranging from 0 (group IV) to 11.2 mm (group I) and at 1% from 10.4 (groups V and X) to 11.2 mm (group I).

Analyzing the effectiveness of the experimental preparation on Enterococcus faecalis ATCC No. 19433, we found fluctuations in the growth retardation zone of more than 10 mm in all groups, and in groups I, V, VI, VI, and XI, this indicator is slightly below the control by 7.4-8.9%. A similar trend was observed when studying the effect of drugs on Klebsiella pneumoniae K-56 No. 3534/51, Salmonella typhimurium 144, and Salmonella adobraco 1: found moderately sensitive growth inhibition of Klebsiella pneumoniae under the influence of 1% concentration of drugs in groups I, II, VII, VII, and IX (growth retardation range 13.1-14.4 mm), as well as Salmonella typhimurium only in group XI (1.0% of the preparation - the growth retardation zone was 14.2 mm). In addition to experimental groups V and VI, when the dilution of drugs was 0.1% (growth retardation zone on Salmonella typhimurium was from 8 mm to absence) in other groups, this figure was higher than 10 mm and ranged within: for 0.1% concentration of drugs from 10.2mm (group II) to 12.6mm (group III), for 1% - from 10.4mm (group IV) to 12.7mm (group III). The effect of drugs on Salmonella adobraco in Groups II, VIII, and VIII was significantly lower than the control (17.9%); (16.6 and 17.2%, respectively).

We found a moderately sensitive antibacterial effect on the strain *Pseudomonas aeruginosa* ATCC No. 2853 (F) under the action of 1.0% concentration of drugs in groups III, VI, and XI (growth inhibition zone was 13.4, 12.1, and 12.3 mm, respectively).

Pseudomonadaceae	iba e far	nilie	ai es m	icroc	organ	stu isms	aiec	зр	repa	arati	on	on	cry	oge	nic	Stra	ains	OT	En	terc	bac	teria	iceae and
		1	:	2	3	3	4	4	;	5	6	6	7	7	8	3	ć	9	1	0	1	1	Reference*
Strains									Dru	g co	ncer	itrati	on. 9	6									
	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	
Escherichia coli 055 K 59 No. 3912/41	$11.2\pm0.89$	$11.2\pm0.97$	$11.3 \pm 0.87$	16.2±1.56	$10.3\pm 1.21$	12.4±0.88	0	$11.3\pm 1.21$	$10.7\pm0.97$	$10.4\pm 1.16$	$10.6 \pm 0.76$	$10.7 \pm 0.67$	6.2±0.56	$10.6\pm 0.87$	0	$10.5\pm0.78$	$10.3 \pm 0.87$	$10.7\pm0.84$	$10.3\pm 1.22$	$10.4\pm0.89$	$10.4 \pm 0.78$	$10.7 \pm 0.88$	14.3±1.21
Enterococus faecalis ATCC No. 19433	$11.4\pm 1.12$	12.5±1.24	$10.1 \pm 0.89$	$10.4 \pm 0.87$	$8.2 \pm 0.78$	11.5±±0.89	$10.3 \pm 0.76$	11.6±1.23	$11.1\pm0.86$	12.2±1.34	$11.1\pm 0.91$	12.4±1.28	$10.3 \pm 0.76$	$12.5\pm 1.18$	$10.4\pm0.89$	$10.2\pm0.89$	$10.4 \pm 0.99$	$11.3 \pm 0.98$	$10.5 \pm 0.78$	$10.5 \pm 0.87$	$11.7\pm0.85$	12.3±1.32	13.5±1.12
Proteus vulgaris HX 19 No. 222	0	18.2±1.76	18.5±2.11	43.2±3.76	$10.7 \pm 0.78$	42.3±3.74	$10.8 \pm 0.89$	40.5±2.34	$15.2\pm 1.33$	$41.2\pm 3.55$	24.6±2.34	40.2±3.76	$10.8 \pm 0.89$	$41.4\pm3.23$	30.5±3.21	42.6±4.21	$13.7 \pm 1.31$	42.2±3.76	40.8±3.44	42.2±4.12	$2.2 \pm 0.18$	32.5±2.78	39.6±3.19
Serratia marcenses 1	$14.7 \pm 1.34$	$20.7\pm 2.11$	$6.2 \pm 0.43$	15.7±1.78	$14.4\pm 1.34$	18.6±2.23	$10.3\pm 1.16$	13.3±0.78	$11.4\pm 1.21$	$12.1\pm 1.31$	14.3±1.33	$14.5\pm 1.42$	$10.7 \pm 0.87$	12.3±1.52	11.7±0.75	12.2±1.21	$10.1 \pm 0.88$	$14.6\pm 1.22$	11.2±0.65	12.1±1.23	12.6±1.28	14.3±1.21	34.6±3.21
Klebciella pneumoniae K- 56 No. 3534/51	$12.2\pm0.93$	$13.1\pm 1.23$	$11.8 \pm 0.76$	13.3±1.23	0	$11.7\pm 1.12$	0	2.1±0.22	0	0	2.1±0.19	$3.3\pm0.31$	$10.2 \pm 1.43$	$13.6\pm 1.22$	2.2±0.19	14.4±1.34	$11.2 \pm 0.89$	$13.5\pm 1.32$	0	$10.5\pm 0.98$	0	0	20.3±2.23
Salmonella typhimurium 144	$10.6 \pm 0.77$	$11.4\pm 1.18$	$10.2\pm0.88$	11.6±1.19	$10.3\pm 1.21$	12.3±1.32	$10.5\pm 1.12$	$10.4\pm 1.21$	$8.2\pm 0.76$	$10.4\pm0.89$	0	$10.2 \pm 0.89$	$11.5\pm 1.23$	$12.8 \pm 0.87$	12.6±1.16	$12.7\pm0.97$	$11.6\pm 1.11$	$11.3\pm 1.21$	$10.4\pm0.45$	$10.9\pm 1.21$	12.2±0.78	14.2±1.21	17.3±1.78
Salmonella adobraco 1	$10.4 \pm 0.86$	$11.3\pm0.95$	$11.6\pm 1.21$	12.4±1.12	8.2±0.76	8.2±0.87	8.3±0.89	$11.3\pm0.97$	$10.5\pm0.85$	$10.2\pm0.79$	$11.4\pm0.78$	12.6±1.21	$12.8\pm 1.41$	$12.5\pm 1.18$	$10.3\pm 1.13$	$11.8 \pm 1.31$	0	$11.1 \pm 0.85$	7.5±0.56	0	0	0	15.1±1.56
Pseudomonas aeruginosa ATCC No. 2853 (F)	6.2±0.56	$11.3\pm0.78$	$2.1\pm0.12$	$10.5\pm 0.87$	11.8±1.12	13.4±1.32	$2.2\pm0.22$	$2.1\pm0.17$	$2.6\pm0.18$	$6.3\pm0.51$	$6.9\pm0.31$	6.6±0.43	6.3±0.67	$12.1\pm 1.21$	$5.4\pm0.32$	$6.6\pm0.44$	$4.3\pm0.23$	$5.2\pm0.45$	$5.1 \pm 0.53$	10.6±1.22	6.7±0.78	12.3±1.31	16.5±1.56

\* Discs with 30.0µg kanamycin were utilized as the positive control (n=12)

At the same time, growth inhibition of microorganisms affected by drugs on ATSC *Staphylococcus aureus* 25923 was detected. (**Table 2**). Using of the test compounds at a concentration of 0.1% causes the sensitivity of microorganisms and growth retardation in groups V, VI, and VIII (13.1; 15.3 and 11.2 mm), in turn, the use of test compounds at a concentration of 1.0% causes the sensitivity of microorganisms and growth retardation already in III-IX and XI samples within 11.2-15.8 mm. A moderate sensitivity of *Staphylococcus epidermidis* ATSC No. 14990 was also detected. Using 1.0% of drugs in groups II, V, VIII, IX, and XI, the growth retardation zone was 11.7, 11.7, 11.4, 13.3, and 13.5 mm, respectively.

We found moderate antibacterial efficacy in the use of experimental drugs on *Bacillus subtilis* ATSC No. 6633. Thus, using 0.1% drug, the growth inhibition of microorganisms was detected only in groups VII and VII, then in 1.0% of the drug, the

growth retardation zone in groups II, III, IV, VIII, VII, and XI, was 11.4, 14.6, 11.9, 11.6, 12.3, and 11.5 mm, respectively).

Antibacterial effect under the influence of experimental drugs was also found on the microorganisms of the family Listeriaceae. It has been experimentally proven that the use of samples on Listeria monocytogenes ATCC No. 19112 moderate inhibition zone in the III and IV groups of 1.0% of the drug (12.4 and 12.7 mm); *Listeria ivanovi* - in I, II, III, IV, and IX groups (within 14.3-16.3 mm), and *Listeria innocua* ATCC No. 33090 already in the I, III, IV, VII, IX and X groups (from 14.2 to 16.7 mm). Also when using 1.0% drug in groups I, III, and IX, the growth retardation zone of the *Listeria ivanovi* was below control by only 13.8, 9.9, and 7.7%, respectively.

Listeriaceae	mic	roor	ganis	sms																			
		1	2	2	3		4		5		6	6	7		8		9		10		11		Poference*
Strains	Drug concentration. %															TREFERENCE							
Otraino	01	10	01	10	01	10	01	10	01	10	01	10	01	10	01	10	01	10	01	10	01	10	
	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	
Staphylococcus aureus ATCC No. 25923	$10.4\pm0.86$	$10.1\pm0.89$	8.3±0.56	10.4±1.32	13.3±1.53	13.6±1.67	0	13.2±0.99	13.1±0.84	14.3±1.65	15.3±1.43	15.8±1.76	10.5±1.12	13.8±0.88	11.2±0.76	11.7±0.95	8.3±0.76	12.6±1.31	10.2±0.89	10.2±0.98	10.5±1.23	11.2±1.34	22.2±3.19
<i>Staphylococcus</i> <i>epidermidis</i> ATCC No. 14990	$10.7\pm 1.23$	$10.4 \pm 0.76$	0	11.7±1.22	$10.2\pm 1.31$	$10.2 \pm 0.78$	$10.1 \pm 0.89$	$10.4 \pm 1.46$	$10.6 \pm 0.87$	$11.7\pm 1.23$	$10.8 \pm 0.67$	$10.7 \pm 0.78$	$10.8 \pm 0.89$	$11.4\pm0.98$	$10.4\pm0.94$	$10.1 \pm 0.95$	12.1±0.87	13.3±1.29	$6.2\pm0.34$	7.5±0.86	$10.2 \pm 0.78$	13.5±1.42	20.6±2.89
<i>Bacillus subtiliss</i> ATCC No. 6633	$10.1 {\pm} 0.88$	$10.1 \pm 1.19$	$8.2 \pm 0.67$	$11.4 \pm 1.12$	$10.6\pm 0.89$	14.6±1.57	8.5±0.76	$11.9\pm 1.24$	0	7.3±0.88	$10.4 \pm 0.78$	$10.3 \pm 0.82$	$11.5 \pm 1.19$	11.6±1.22	$11.6\pm0.69$	12.3±0.78	$10.3 \pm 0.87$	$10.8 \pm 0.98$	$10.4 \pm 0.57$	0	$10.8 \pm 0.79$	$11.5\pm0.89$	30.2±3.41
Listeria ivanovi	12.4±1.13	15.6±1.64	$8.1 \pm 0.77$	14.3±0.77	6.2±0.67	16.3±1.67	$10.3\pm 1.42$	14.3±1.34	$10.3 \pm 0.74$	$10.7 \pm 0.74$	$8.3\pm0.89$	$11.5\pm0.96$	12.3±1.23	12.1±1.45	$10.1 {\pm} 0.89$	$11.5\pm0.96$	$10.7 \pm 0.87$	16.7±1.78	$10.5\pm0.67$	$11.4\pm0.87$	$10.9\pm0.86$	$11.8 \pm 1.28$	18.1±3.21
Listeria innocua ATCC No. 33090	$10.8 \pm 0.87$	15.2±1.45	0	$10.7 \pm 0.89$	12.6±1.11	$14.5\pm 1.34$	$11.8 \pm 0.96$	16.7±1.59	0	$2.2 \pm 0.18$	$11.3\pm 1.24$	$12.1\pm0.93$	13.5±1.34	14.3±1.67	$6.4{\pm}0.54$	$10.1 \pm 0.78$	15.5±1.77	15.3±1.76	0	14.2±1.78	0	0	40.0±4.27
Listeria monocytogenes ATCC No. 19112	$10.3 \pm 0.96$	$10.5 \pm 0.98$	0	0	2.1±0.19	12.4±1.23	8.4±0.76	$10.3\pm0.94$	8.3±0.65	$10.7\pm0.89$	0	$10.2\pm0.85$	0	0	0	$11.4\pm0.89$	12.6±1.27	$12.7\pm 1.44$	8.4±0.56	8.6±0.89	0	0	18.6±2.35

Table 2. The antibacterial effect of studied preparation on cryogenic strains of Staphylococcaceae, Bacillaceae,

Discs with 30.0  $\mu$ g kanamycin were used as a positive control (n=12)

The antibacterial effects of studied preparation on cryogenic strains of Actinobacteria type microorganisms, Actinomycetales series, Corynebacteriaceae family and Ascomycota department,

Saccharomycetes class, Saccharomycetaceae family are presented in Table 3.

Table 3. Antibacterial effect of studied preparation on cryogenic strains of microorganisms of the family   Campylobacteraceae, Nocardiaceae and Saccharomycetaceae																							
		1	4	2	3	3	4	4	Ę	5	(	6	-	7	8	3	9	9	1	0	1	1	Reference <sup>*</sup>
Strains		Drug concentration. %																					
	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	1.0	
Campylobacter jejuni	$12.2\pm 1.42$	$13.7 \pm 1.34$	$12.8 \pm 1.24$	$12.9\pm 1.42$	$11.5 \pm 0.78$	$12.3\pm 1.33$	$11.6\pm 0.88$	$11.7 \pm 0.77$	$10.4 \pm 0.89$	$12.2\pm0.94$	13.7±1.45	14.2±1.44	$12.7\pm0.97$	$13.7 \pm 1.21$	$11.2 \pm 0.69$	16.6±1.75	$13.8 \pm 1.24$	$14.2 \pm 1.55$	$10.7 \pm 0.85$	$13.5 \pm 0.89$	$11.7 \pm 1.21$	$11.6\pm0.87$	20.6±2.86
Rhodococcus equi ATCC No. 6939	12.4±1.37	21.4±2.18	$11.5\pm 0.58$	20.5±2.53	$13.3\pm 1.18$	22.8±2.55	$10.2 \pm 1.02$	14.7±1.32	$12.3\pm 1.33$	14.4±1.34	13.4±1.53	17.8±2.11	0	0	0	$12.8\pm 1.23$	13.7±1.37	14.7±1.31	$10.4 \pm 0.86$	$11.3 \pm 0.89$	13.6±1.32	$13.5\pm 1.23$	23.6±2.95
Candida albicans ATCC No. 885653	12.8±1.19	$14.6\pm 1.32^{**}$	7.5±0.67	14.7±1.45**	11.8±1.27	12.3±1.57	$10.7 \pm 0.76$	11.4±1.31	$10.1 {\pm} 0.87$	12.1±1.23	12.7±1.44	$16.3\pm 1.67^{***}$	$10.2 \pm 0.77$	12.2±1.18	$10.6 \pm 0.87$	12.2±1.19	12.5±1.21	13.4±1.44	$2.2 \pm 0.13$	$12.4 \pm 1.22$	$4.3\pm0.21$	$5.4\pm0.19$	$10.3\pm0.87$ $18.2\pm2.35^{****}$

<sup>\*</sup> Discs with 30.0µg kanamycin were considered as the positive control (n=12) <sup>\*\*</sup> P>0,95; <sup>\*\*\*</sup> P>0,99 <sup>\*\*\*\*</sup> Discs with 15.0µg amphotericin were considered as a positive control for Candida albicans

There is a positive tendency to inhibit the growth of the families Campylobacteraceae, Nocardiaceae, and Saccharomycetaceae. Furthermore, the efficiency of antibacterial effects on Campylobacter jejuni in all test groups, even with 0.1% of the drugs over 10mm, ranged from 10.4 (group V) to 13.8mm (group III). The inhibition zone of Rhodococcus equi ATCC No. 6939 - at 1.0% of drugs in groups I, II, III, and VI was 21.4, 20.5, 22.8, and 17.8 mm, which was below the control by 9.3, 13.1, 3.4, and 24.6%. Moreover, the effect of drugs on all groups (except XI) in general exceeded the control (kanamycin), with the use of 1.0% drog, which led to a growth inhibition zone of 4.3 (P <0.05), 4.4 (P <0.05), and 6.0 (P <0.01) mm in groups I, II, and VI and slightly inferior to the control (amphotericin) which was 3.6, 3.5, and 1.9 mm, respectively.

Global advances in the chemistry of heterocyclic compounds have contributed to the development of organic chemistry as a whole. A special place in organic chemistry is occupied by 1,2,4-triazole derivatives [7, 8]. It is a unique heterocyclic system that attracts the attention of scientists in various fields [9, 10]. In most 1,2,4triazoles, low toxic compounds have a wide range of chemical and biological properties [11, 12]. Some of them are active pharmaceutical ingredients (APIs) of many drugs [13, 14], substances of plant growth regulators and fertilizers [15, 16] biologically active compounds that are in the preclinical trials [12, 17]. Many scientists believe that 1,2,4-triazole is combined with different fragments of other organic compounds [11, 18]. This fact has indisputable scientific evidence of the practical feasibility of the existence of molecules formed by such transformations [9, 11, 19].

Our attention was drawn to the possibility of combining structural fragments of 1,2,4-triazole-3-thiol and furan in one molecule, since each of these systems individually possesses a wide range of biological properties or is already a structural fragment of active pharmaceutical ingredient (AFI) molecules [11, 14].

Thus, the aim of our work was to synthesize new compounds whose fragments of molecules are 1,2,4-triazole-3-thiol and furan residues, namely a series of new 5-R2-2- (furan-2-yl-, 5-bromofuran-2-yl) thiazolo [3,2-b] [1,2,4] triazole-4 (5H) -ones, to study for the last restorations of excess sodium borohydride, to investigate the physicochemical characteristics of the new compounds, and to confirm the identity of the substances.

Analyzing the results of our studies, it was found that the test compounds can compete with kanamycin, a broad-spectrum natural antibiotic of the second generation aminoglycoside group whose action spectrum includes a gram + and - microorganism

The investigational drugs may compete with kanamycin by acting on cryogenic strains of microorganisms: *Candida albicans, irisa equi, subtaris, Bacillus listeria, S. epidermidis, Salmonella typhimurium, Salmonella adobraco, Serratia marcense, P. vulgaris, P. mirabilis, and E. faecalis.*  The investigational drugs may be recommended for further studies against multidrug-resistant strains of these microorganisms.

### CONCLUSION

In vitro experiment showed a positive anti-bacterial effect of the preparation on cryogenic strains of Enterobacteriaceae microorganisms: E. coli 055 K 59 No. 3912/41, Enterococus faecalis ATCC No. 19433, Proteus vulgaris HX 19 No. 222, Serratia marcenses 1, Klebciella pneumoniae K-56 No. 3534/51, Salmonella adobraco 1, Salmonella typhimurium 144; Pseudomonadaceae families: Pseudomonas aeruginosa ATCC Staphylococcaceae No. 2853 (F), microorganisms: Staphylococcus aureus ATCC No. 25923; Staphylococcus epidermidis 14990; Bacillaceae\_families: Bacillus subtilis ATCC No. 6633, Listeriaceae: Listeria ivanovi, Listeria innocua ATCC No 33090, Listeria monocytogenes ATCC No 19112; Campylobacteraceae: Campylobacter jejuni; Nocardiaceae: Rhodococcus equi ATCC No 6939 and mushrooms family Saccharomycetaceae: Candida albicans ATCC No. 885653.

We recommend the evaluated extracts of preparations for further investigations in the fight against polyresistant strains of the mentioned microorganisms.

We determined that all microorganisms tested in the experiment of the Enterobacteriaceae family (*Escherichia coli, Enterococus faecalis, Proteus vulgaris, Serratia marcenses, Klebciella pneumoniae, Salmonella typhimurium, Salmonella adobraco*) are susceptible to MP-3 and MP-5 and MP-5; Pseudomonadaceae (Pseudomonas aeruginosa) - up to MP-3, MP-5, MP-9 and MP-14; Staphylococcaceae (Staphylococcus aureus, Staphylococcus epidermidis) - MP-7, MP-9, MP-12 and MP-14; Bacillaceae (Bacillus subtilis) - MP-4, MP-5, MP-6, MP-9, MP-10 and XI; Listeriaceae (Listeria ivanovi, Listeria innocua, Listeria monocytogenes) - MP-5 and MP-12; Campylobacteraceae (Campylobacter jejuni) - to all preparations of 11 experimental groups; Nocardiaceae (Rhodococcus equi) - to all preparations (except MP-9); Saccharomycetaceae (Candida albicans) - to all preparations (except MP-14).

ACKNOWLEDGMENTS: None CONFLICT OF INTEREST: None FINANCIAL SUPPORT: None ETHICS STATEMENT: None

#### References

- Tiwari R, Sandil S, Nain P, Kaur J. Bacteriological Analysis with Antimicrobial Sensitivity and Resistance Pattern in Blood Culture of Septicemic Patient from Different Wards of a Tertiary Care Hospital in India. Int J Pharm Phytopharmacol Res. 2020;10(4):112-9.
- Alzaid A, Alosaimi M, Alkahtani KF, Alshehri BA, Asiri AE, Asiri AM, et al. Saudi Parents' Knowledge, Attitudes, and Practices Regarding Antibiotic use for Upper Respiratory Tract Infections in Children. Int J Pharm Res Allied Sci. 2020;9(1):115-20.
- Boyko OO, Zazharska NM, Brygadyrenko VV. The influence of the extent of infestation by helminths upon changes in body weight of sheep in Ukraine. Visn Dnipropetr Univ Biol Ecol. 2016;24(1):3-7.

- Zazharska N, Boyko O, Brygadyrenko V. Influence of diet on the productivity and characteristics of goat milk. Indian J Anim Res. 2018;52(5):711-7.
- Zazharskyi VV, Davydenko P, Kulishenko O, Chumak V, Kryvaya A, Biben IA, et al. Bactericidal, protistocidal and nematodicidal properties of mixtures of alkyldimethylbenzyl ammonium chloride, didecyldimethyl ammonium chloride, glutaraldehyde and formaldehyde. Regul Mech Biosyst. 2018;9(4):540-5.
- Tkachenko AA, Davydenko PO, Zazharskiy VV, Brygadyrenko VV. Biological properties of dissociative L- and other forms of Mycobacterium bovis. Visn Dnipropetr Univ Biol Ecol. 2016;24(2):338-46.
- Grigoryan LA, Kaldrikyan MA, Melik-Ogandzhanyan RG, Arsenyan FG. Synthesis and antitumor activity of 2-N-and 3-S-substituted 5-[2-(4-) benzyloxyphenyl]-1, 2, 4-triazoles and acylhydrazides. Pharm Chem J. 2012;46(9):11-5.
- Bansode S, Kamble R. Synthesis of novel 2-(3'-aryl-sydnon-4'ylidene)-5'-substituted-[1, 3, 4]-thiadiazolylamines and [1, 3, 4]thiadiazol-2'-yl-3-oxo-[1, 2, 4]-triazoles as antimicrobial agents. Med Chem Res. 2012;21(6):867-73.
- Bihdan OA. Synthesis, physicochemical and biological properties of 1,2,4-triazole-3-thion derivatives containing fluorophenyl substituents: Diss. PhD of Pharmaceutical science. - Zaporizhzhia; 2015. 205 p.
- Khanage Shantaraman G, Mohite Popat B, Pandhare Ramadas B, Raju Appala S. Synthesis and antimicrobial activity evaluation of some substituted N'[arylidene]-2-(3-methyl-5-pyridin-4-yl-1H-1,2,4-triazol-1-yl) acetohydrazide compounds. Biointerface Res Appl Chem. 2012;2(5):417-23.

- Parchenko VV. Synthesis, physicochemical and biological properties of 1,2,4-triazole-3-thione derivatives containing furan kernel: Diss. PhD of Pharmaceutical science. Kyiv; 2006. 207 p.
- Pruglo ES. Synthesis and biological properties of 3-S-substituted 5-Alk, -Ar, -Het-4 (H) -R-1,2,4-triazole: Diss. Doc. of Pharmaceutical science. – Zaporizhzhia; 2019. 490 p.
- Parchenko VV. Antiviral activity of 1,2,4-triazole derivatives. Pharm J. 2011;(3):49-53.
- Parchenko VV. Synthesis, physico-chemical and biological properties of the 1,2,4-triazole-3-thione 5-furilderivatives: Diss. Doc. of Pharmaceutical science. Zaporizhzhia; 2014. 361 p.
- 15. Paclobutrazole. Available from: http://www.plant-growthregulator.com/plant-growth-regulator/control-overgrowth-planthormones/plant-growth-hormone-paclobutrazol.html
- 16. Fortis Combi. Available from: http://fortis-combi.com
- Shcherbyna RO, Danilchenko DM, Parchenko VV, Panasenko OI, Knysh EH, Hromyh NA, et al. Studying of 2-((5-R-4-R-1-4H-1, 2, 4triazole-3-Yl) Thio) acetic acid salts influence on growth and progress of blackberries (KIOWA Variety) propagules. Res J Pharm Biol Chem Sci. 2017;8(3):975-9.
- Danilchenko DM, Parchenko VV. Antimicrobial activity of new 5-(furan-2-yl)-4-amino-1,2,4-triazole-3-thiol derivatives. Zaporozhye Med Mag. 2017;19(1):105-7.
- Bihdan OA, Parchenko VV. Some aspects of synthesis 3-(2florphenyl)-6-R1-[1,2,4]triazol[3,4-b][1,3,4]thiadiazole and 3-(2-, 3ftorphenyl)-6-R2-7H[1,2,4]triazolo[1,3,4]tiadiazines. Res J Pharm Biol Chem Sci. 2018;9(3):463-70.