SELENORGANIC COMPOUND 1,5-DI-(M-NITROPHENYL)-3-SELENAPENTADION-1,5 EFFECT ON CLINICAL STRAINS OF PSEUDOMONAS AERUGINOSA

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In work was studied the action of selenorganic compound 1,5-di-(m-nitrophenyl)-3-selenapentadion-1,5 on clinical strains of *Pseudomonas aeruginosa* extracted from patients with suppurative complications of traumatology and orthopedic hospital. Incubation (30–150 minutes) of *P. aeruginosa* with 1,5-di-(m-nitrophenyl)-3-selenapentadion-1,5 in concentration 0,01 mg/ml has led to inhibition of bacterial colonies growth on 34–57%; 0,1 mg/ml – on 70–99% and 1 mg/ml – on 92–100% in comparison with control. It is possible that antibacterial activity of the investigated compound is caused by the presence of lateral nitro-groups in its structure.

Keywords: selenium, selenorganic compound, *Pseudomonas aeruginosa*, antibacterial action

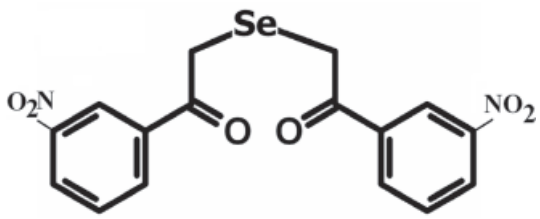
Now significant amount bacterial strains, resistant to antibiotics of a wide spectrum of action are appeared. Therefore the synthesis of new antibacterial compounds and studying of their action mechanisms are pressing question. Throughout several last years antimicrobic activity of organic compounds of selenium is established [3, 4, 8]. For example, selenorganic compound ebselen (2-phenyl-1,2-benzisoselenazol-3(2H)-on) possesses antimicrobic activity on Gram-positive and Gram-negative bacteria in low concentration (MIC = 0,2–1,5 mkg/ml) [1, 5, 6, 9]. Antimicrobic activity of ebselen is comparable to activity of some nitrofuran compounds. It is known that antibacterial activity of nitrofuran-derivatives is caused by nitro-group presence in their structure [2].

Besides, earlier it was informed about antimicrobic activity of selenorganic compounds 1,5-diphenyl-3-selenapentadion-1,5 (diacetophenonylselenide – DAPS-25) and its derivatives on clinical strains of *Pseudomonas aeruginosa* [7].

The aim of the study: to analyze antimicrobial fctivity of selenorganic compound 1,5-di – (m-nitrophenyl)-3-selenapentadion-1,5 (nitro-derivative of DAPS-25) on clinical strains of *Pseudomonas aeruginosa* extracted from patients with suppurative complications of traumatology-orthopedic hospital.

Materials and methods of research

In this work we used selenorganic compound 1,5-di – (m-nitrophenyl)-3-selenapentadion-1,5, kindly given by a professor B.I. Drevko:



Experiment was carried out on 10 taxonomic identical clinical strains of *Pseudomonas aeruginosa* (*P. aeruginosa*) extracted from patients with suppurative complications which are on treatment in a traumatology and orthopedic hospital of the Saratov scientific research institute of traumatology and orthopedics Generic identification of strains has carried out on the basis of studying phene. Bacteria had resistance to five and more structural antibiotics. Suspension of bacteria prepared with use the turbidity standard of the State scientific research institute of standardization and the control of medical biological preparations n.a. L.A. Tarasevich, by consecutive cultivations to final concentration of bacteria – $3 \cdot 10^5$ cells in 1 ml.

For investigation of antibacterial action we prepared 4 dilutions of selenorganic compound in concentrations 0,001–1 mg/ml. The mix of dimethylformamide (DMFA) in 0,9% solution NaCl in the relation 1:10 is used as a solvent. Aliquot of 100 µl of final suspension of microorganisms was added in test tubes with diluted compound and incubated for 30, 60, 90, 120 and 150 minutes at a room temperature. As the control group used the same quantities of bacterial suspension dissolved in similar proportions with the solvent (DMFA in 0,9% solution NaCl) and incubated for the same time interval. Then aliquot of 100 µl of bacterial suspensions from each test tube inoculated and spread on nutrient meat-peptonic agar which was incubated for 24 hours at 37°C. Counting of colonies was made next day.

Statistical analysis of finding carried out by means of software package Statistica 6.0. We checked hypotheses about a kind of distributions (Shapiro-Wilk's criterion). A lot of findings did not fit of distribution law. For comparison of values the U-Mann-Whitney's criterion, Z – Fisher's criterion and a p-value were determined. A critical significance of p-value in this research accepted equal 0,05.

Results of research and their discussion

The results depicted in Table 1 show strong activity of selenorganic compound 1,5-di – (m-nitrophenyl)-3-selenapentadion-1,5 against clinical strains of *P. aeruginosa*. This compound in concentration 0,01 mg/ml inhibited the bacterial colonies growth on 34% (30 minutes), 38% (60 minutes), 51% (90 minutes), 36% (120 minutes) ($p < 0,001$) and 57% (150 minutes) correspondingly ($p < 0,05$) in comparison with the control.

The compound in concentration 0,1 mg/ml has led to inhibition of bacterial colonies

growth on 70% (30 minutes), 73% (60 minutes), 82% (90 minutes), 92% (120 minutes) and 99% (150 minutes) ($p < 0,001$) correspondingly in comparison with the control.

The compound 1,5-di-(m-nitrophenyl)-3-selenapentadion-1,5 in concentration 1 mg/ml demonstrated the greatest antibacterial activity. The incubation of *P. aeruginosa* with this compound in concentration 1 mg/ml during 30, 60 and 90 minutes led to reduction of bacterial colonies quantity on 92, 93 and 99% correspondingly in comparison with control ($p < 0,001$). The growth of bacterial colonies was inhibited completely after 120 and 150 minutes incubation of P. aeruginosa with 1,5-di-(m-nitrophenyl)-3-selenapentadion-1,5.

Table 1

Antibacterial effect of 1,5-di – (m-nitrophenyl)-3-selenapentadion-1,5 on clinical strains of *Pseudomonas aeruginosa*

		The quantity of colonies on nutrient agar				
		Control group	Experimental groups, concentration of compound, mg/ml			
			1	0,1	0,01	0,001
Time of incubation, minutes	30	1002 (967; 1107)	83(67; 178) $Z_k = 3,77$; $p_k = 0,000157$	298(256; 348) $Z_k = 3,77$; $p_k = 0,000157$	661(563; 781) $Z_k = 3,55$; $p_k = 0,000377$	975(896; 1176) $Z_k = 0,22$; $p_k = 0,227206$
	60	1034 (867; 1143)	76(43; 153) $Z_k = 3,77$; $p_k = 0,000157$	278(229; 395) $Z_k = 3,77$; $p_k = 0,000157$	641(508; 765) $Z_k = 3,36$; $p_k = 0,000765$	1016(947; 1078) $Z_k = 0,30$; $p_k = 0,762369$
	90	947 (805; 993)	9(0; 81) $Z_k = 3,77$; $p_k = 0,000157$	170(104; 197) $Z_k = 3,77$; $p_k = 0,000157$	462(405; 765) $Z_k = 2,94$; $p_k = 0,003197$	894(856; 956) $Z_k = 0,68$; $p_k = 0,496292$
	120	977 (894; 1171)	0(0; 0) $Z_k = 3,77$; $p_k = 0,000157$	74(27; 183) $Z_k = 3,77$; $p_k = 0,000157$	627(408; 680) $Z_k = 3,77$; $p_k = 0,000157$	762(654; 905) $Z_k = 2,60$; $p_k = 0,009109$
	150	885 (764; 937)	0(0; 0) $Z_k = 3,77$; $p_k = 0,000157$	6(0; 81) $Z_k = 3,77$; $p_k = 0,000157$	378(128; 645) $Z_k = 3,25$; $p_k = 0,001152$	803(549; 874) $Z_k = 1,51$; $p_k = 0,130571$

N o t e s : In each case is given median value, lower and top quartiles (25; 75%). Z_k, p_k – differences in comparison with control group.

Thus, selenorganic compound 1,5-di – (m-nitrophenyl)-3-selenapentadion-1,5 in concentrations 0,01–1 mg/ml demonstrated strong activity on clinical strains of *P. aeruginosa*. However low concentration 0,001 mg/ml of this compound slightly decreased bacterial colonies quantity (on 22% after incubation 120 minutes). At other incubation time intervals it was not observed authentic antibacterial effect of the compound.

Finally, we assume that compound action is caused by presence of two nitro-groups in its structure. It allows drawing an analogy with antibacterial action of nitrofurans. It is known, that nitrofurans get antibacterial activity after reduction of nitro-groups by flavin-dependent nitro-reductases, localized in bacteria, protozoa and tissues of organism. Intermediate products of consecutive one-or two-electronic stages of reduction are highly reactive, especially nitro-radical anion, thanks to which nitrofurans get antibacterial activity [2].

In this connection, it is possible to assume, that antibacterial activity of 1,5-di – (m-nitrophenyl)-3-selenapentandion-1,5 is caused the presence in its structure of two nitro-groups which, being treated by bacterial enzymes action, show the cytotoxic activity concerning clinical strains of *Pseudomonas aeruginosa*.

Conclusion. Findings allow suggesting the perspectives of using of 1,5-di – (m-nitrophenyl)-3-selenapentandion-1,5 as antibacterial compound against antibiotic-resistant bacterial strains of *Pseudomonas aeruginosa*.

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