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Pseudomonas chlororaphis subsp. *aureofaciens* NATIVE AND MODIFIED BY COMPLEXES OF GE(IV) AND SN(IV) LIPOPOLYSACCHARIDE ANTIVIRAL ACTIVITY

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The purpose of the research was to investigate changes of antiviral activity of *Pseudomonas chlororaphis* subsp. *aureofaciens* lipopolysaccharides as a result of their modifications by coordination compounds of Sn(IV) and Ge(IV) synthesised on the basis of aromatic, pyridinecarboxylic acids hydrazides and appropriate hydrazones of aromatic aldehydes. A wide range of Ge(IV) and Sn(IV) coordinative compounds was chosen for *P. chlororaphis* subsp. *aureofaciens* UCM-306 LPS modification. "Tobacco mosaic virus – hypersensitive plant" model study of lipopolysaccharide and its modified preparations (1–35) antiviral activity showed that a lot of the tested preparations exhibit high antiviral activity due to their composition and structural peculiarities. Such preparations are of interest as perspective agents in struggle against plant virus diseases. Antiviral action of preparations (% of inhibition, I,%) which neutralizes virus infectivity depends on: complexing metal [complexes of Sn(IV) are more active (I, % 65–79) as compared to Ge(IV) complexes (I,% 26–62)]; amount of functional groups in ligand molecules [hydrazone complexes of Sn(IV) are more active (I, % 69–79) then hydrazide ones (I, % 48–63)]; and also on coordination form of ligand coupling with different substituents [complexes with salicyloyl hydrazones of 4-metoxy- (I, % 71), 4-hydroxybenzaldehydes (I, % 77) and pyrogallol (I, % 72) with ketone $O_{(C=O)}$–$N_{(CH=N)}$ form of a ligand are more active than with enol $O_{(C-O)}$–$N_{(CH=N)}$ form of isonicotinoyl hydrazones of the same aldehydes (I, % 32–63)]. Introduction of two substituents (OH- and Br-) into the hydrazide fragment of hydrazone molecule significantly increases the activity of Sn(IV) complexes with enol form of the ligand (I, % 79).

Key words: *Pseudomonas chlororaphis* subsp. *aureofaciens*, lipopolysaccharide, Ge(IV) and Sn(IV) coordination compounds, antiviral action, tobacco mosaic virus.

Viral plant diseases are widespread in agro- and biocenoses, therefore they play an important role in crops yield reducing, which leads to significant economic losses in crop production. There are various methods of plants viral disease control; disease prevention and resistant to viruses species breeding are the most effective among them. All stages of viruses reproduction are closely related to the metabolic, energy and enzymatic reactions of the cell, so chemicals usage to virus infections control is often ineffective because drugs that inhibit the reproduction of viruses tend to inhibit the normal metabolic processes in plants. Such compounds are characterized by a significant phytotoxicity, so the problem of plants therapy and viral infections prophylaxis by biological agents usage is urgent nowadays. At the Institute of Microbiology and Virology of the National Academy of Sciences of Ukraine on the basis of two strains of *Pseudomonas chlororaphis* subsp. *aureofaciens,* earlier [1] a complex biopreparation gaupsin, inhibiting the growth of pathogenic bacteria and fungi, possessing as antimicrobial activity as strong entomopathogenic activity, has been created and patented. In subsequent years it has been found that gaupsin is characterized by pronounced antiviral properties as it inhibits by 80–97% the progression of induced by tobacco mosaic virus (TMV) necroses [2]. The authors have shown that gaupsin antiviral activity is associated with exometabolites synthesis; in particular, it has been hypothesized that high molecular weight

polysaccharides, primarily lipopolysaccharide (LPS) and exopolysaccharides, probably participate in these antiviral mechanisms. We have found [3] that lipopolysaccharide of *P. chlororaphis* subsp. *aureofaciens* B-111 and B-306 are highly active antiviral agents. It is interesting that lipopolysaccharides derived from microorganisms belonging to other genera and species (*Rahnella aquatilis* and *Ralstonia solanacearum*), were not active against TMV, and sometimes even stimulated necrosis formation.

One of the methods for biopolymers activity alteration is their modification, in particular by binding to activators (inhibitors) such as biometals and bioligands complexes. It is known [4] that the complex compounds of germanium with nitrogen-containing compounds of the purine row provide a high level of biological activity against herpes viruses of the 1st and the 2nd types and also are effective when used in the comprehensive treatment of HIV-infected and cancer patients; for a series of germanium (IV) complexes the effect on the activity of glycosidases [5] and proteases [6, 7] is revealed. The effect of tin complex compounds is less studied; as it is known [7], tin is a part of the gastric enzyme gastrin, affects the activity of flavin enzymes, and is also an effective inhibitor of hemeoxidase [8].

The aim of this work was to study the changes in antiviral activity of *P. chlororaphis* subsp. *aureofaciens* lipopolysaccharides by modifying them with new coordination compounds of tin (IV) and germanium (IV), which are synthesized by Seifullina and Shmatkova [9–15] on the basis of aromatic, pyridinecarboxylic acids hydrazides and corresponding aromatic aldehyde hydrazones. These ligands, due to the presence in their molecules composition as an analog of peptide C (O) NH-group and other functional groups, are biologically active compounds [16, 17]. Thus, germanium (IV) with hydrazones complexes are characterized by anti-inflammatory activity [18–20], and complexes of a tin (IV) exhibit antiseptic [11, 12] and antibacterial [13–15] action.

Materials and Methods

The object of the study was the strain of *Pseudomonas chlororaphis* subsp. *aureofaciens* UCM B-306, isolated from the rhizosphere of cabbage and was deposited in Institute of Microbiology and Virology of the National Academy of Sciences of Ukraine, number IMV B-7096.

Cultivation of the strain was performed in semi-synthetic King medium of the following composition (g/l): peptone — 20, K_2SO_4 — 20, glycerol — 20, $MgCl_2$ — 7, in Erlenmeyer flasks of 750 ml filled with 150 ml of culture medium, for 24 hours, on a shaker (220 rev / min) at 28 °C.

Lipopolysaccharides were obtained by extraction from the cells, dried with acetone and ether, with 45% aqueous phenol solution at 65–68 °C. The resulting aqueous fractions were dialyzed against tap water, and then against distilled water to remove phenol, hereafter clarified from nucleic acids by precipitation with trichloroacetic acid and also by ultracentrifugation (104 000 g, 4 h). Purified LPS was lyophilized [21].

To modify the LPS of *P. chlororaphis* subsp. *aureofaciens* UCM-306 a wide range of coordination compounds was selected:

– germanium (IV) with 2-R-benzoyl (R-H_2Bs), nicotinoyl- (H_2Ns) and isonicotinoyl — (H_2Is) hydrazones of salicyl aldehyde of compositions: [Ge (R-Bs)$_2$], where R = 2-OH (1), 2-NH_2 (2), [Ge(Ns)$_2$] (3), [Ge(Is)$_2$] (4) with $O_{(C\text{-}O)}$–$N_{(CH=N)}$–$O_{(Ph\text{-}O)}$ form of the ligand;

– tin (IV) with hydrazides of R-benzoic (R-HBg), 2-OH-5Br-benzoic and 2-naphthoic (HLg) acids of compositions:[$SnCl_4$(R-HBg)], where R=H (12), 2-OH (13), 2-OCH_3 (15), [$SnCl_4$(2-OH-5Br-HBg)] (14), [$SnCl_4$(HLg)] (17) with $O_{(C=O)}$–$N_{(NH2)}$ form of the ligand;

– tin (IV) with hydrazides of 2-NH_2-benzoic (NH_2-HBg), nicotinic (HNg) and isonicotinic (HIg) acids of compositions: [$SnCl_4$(NH_2-HBg·H)] (16), [$SnCl_4$(Ng·H)] (18), [$SnCl_4$(Ig·H)] (19) with $O_{(C\text{-}O)}$ –$N_{(NH_2)}$ form of the ligand;

– tin (IV) with aroyl- and pyridinoyl-hydrazones of 4-N(CH_3)$_2$-benzaldehyde: R-benzoyl-(R-HBdb) [$SnCl_4$(R-Bdb·H)],where R=H (5), 2-OH (6), 2-OCH_3 (8), 2-NH_2-(28), 2-OH-5-Br-benzoyl-[$SnCl_4$(2-OH-5Br-Bdb·H)] (7), nicotinoyl-[$SnCl_4$(Ndb·H)] (9), isonicotinoyl- [$SnCl_4$(Idb·H)] (10) and 2-naphthoyl-[$SnCl_4$(Ldb·H)] (11) with $O_{(C\text{-}O)}$–$N_{(CH=N)}$ form of the ligand;

– tin (IV) with salicyloylhydrazones of aromatic aldehydes: R-benzoic (2-OH-HB-R-b) of compositions: [$SnCl_4$(2-OH-HB-R-b)], where R= H (24), 4-OCH_3 (20), 4-OH (21) , 4-Br (22), and also pyrogallol (23) and 4-OH-3-OCH_3-benzoic aldehyde (35) with $O_{(C=O)}$–$N_{(CH=N)}$ form of the ligand;

– tin (IV) with isonicotinoylhydrazones of aromatic aldehydes: R-benzoic (HI-R-b) of the compositions: [$SnCl_4$(I-R-b ·H)], where R=H (31), 4-OCH_3 (30), 4-OH (21) , 4-Br (32), and also of pyrogallol (33) and 4-OH-3-OCH_3 of

benzoic aldehyde (34) with $O_{(C\text{-}O)}$–$N_{(CH=N)}$ form of the ligand;

– tin (IV) with hydrazone — product of 2-aminobenzoic acid hydrazide and 4-$N(CH_3)_2$-benzaldehyde [2-NH_2-HB$(db)_2$] double condensation of the composition [$SnCl_4(Bdb)_2 \cdot H$)] (29) with $O_{(C\text{-}O)}$–$N_{(CH=N)}$ form of the ligand;

– tin (IV) with terephthaloyldihydrazones of 4-$N(CH_3)_2$-benzaldehyde (H_2Tfdb) and 2-OH-benzaldehyde (H_4Tfs) [$(SnCl_4)_2$(μ-Tfdb·2H)] (26), [$(SnCl_3)_2$(μ-H_2Tfs)] (25) $O_{(C\text{-}O)}$–$N_{(CH=N)}$ (26) and $O_{(C=O)}$–$N_{(CH=N)}$–$O_{(Ph\text{-}O)}$ (25) forms of bridge ligands; [$SnCl_4$(H_4Oxs)] (27) with $O_{(C=O)}$–$O_{(C=O)}$ form of 2-OH-benzaldehyde (H_4Oxs) oxaloylhydrazone.

The choice of these compounds makes it possible to trace the several factors (complexing agent (Ge, Sn), coordination site composition and variety of substituents presence in the ligand molecule) impact on the investigated LPS antiviral activity.

The antiviral activity of *P. chlororaphis* subsp. *aureofaciens* was studied in a model of tobacco mosaic virus (TMV U1 strain), derived from systemically infected *Nicotiana tabacum* L. varieties Immune 580 (revertant) plants according to [22, 23]. Investigations were carried out on leaves of hypersensitive to TMV datura plant *Datura stramonium* L., reacting to virus inoculation by the formation of local necrosis. Experimental halves of leaves previously carborundum dusting were inoculated with a mixture of virus and each of the test preparations (1–35) in a ratio of 1:1, and control halves of leaves — with virus only. LPS preparations at concentrations of 1.5, 1.0 or 0.75 mg/ml were added to TMV (1 or 0.75 g/ml) for 30 min before plants inoculation (in control distilled water was added to TMV). Lipopolysaccharides antiviral action *in vitro* against TMV was evaluated by the number of local necrosis induced by virus. The inhibitory effect (I) of preparations was determined using the formula:

$$I = (1 - E / C) \times 100\ \%,$$

where E and C — an average number of necrosis formed on the experimental and control halves of leaves respectively.

To assess the reliability of experimental data the parametric criteria of normal distribution were used; calculating the arithmetic mean (X_a), mean square inaccuracy measure (S_{x_a}) at a significance level of 0.05 or 0.01, the Student's t test (t) was determined and according to the table for small samples the levels of significance (P) of the mean values difference or ratio were found. Results of statistical processing were represented in the form of confidence intervals or $X_a \pm S_{x_a}$. The relative mean values error was obtained by the processing of 15–20 repetitions [24].

Results and Discussion

Previously [3] we have shown that lipopolysaccharides (ЛПС) of *P. chlororaphis* subsp. *aureofaciens* B-111 and B-306 (gaupsin components) are highly active antiviral agents. In studies in 2010–2012 they invariably showed efficacy against TMV on the model of three types of indicator plants of the family *Solanaceae*. Inhibition of virus infectivity was 98–100% by LPS at a concentration of 1–10 mg/ml, 57–69% — at a concentration of 0.1 mg/ml, 43–44% — at a concentration of 0.01 mg/ml. LPS at a concentration of 1 μg / ml caused reduction of virus infectivity at various indicator datura (*Datura stramonium* L.) and tobacco (*Nicotiana sanderae* H., *Nicotiana tabacum* L.) plants ranged from 10.2 to 46.0%. LPS activity of both *P. chlororaphis* subsp. *aureofaciens* strains was approximately the same. Therefore, in this study the effect of LPS modified by different complexes was carried out using LPS of one strain only — *P. chlororaphis* subsp. *aureofaciens* B-306.

It is known [25] that the complexes of biopreparations with metals may induce non-specific resistance of plants to viruses or enhance the inhibitory effect of the drug. Therefore, it was interesting to study the antiviral activity of the modified LPS (LPS-m). Along with the modified LPS we investigated the original unmodified LPS (LPS-o) antiviral activity as positive control.

It should be noted that all LPS preparations in a concentration of 1.5 mg/ml possessed phytotoxicity that appeared on the treated leaves as burns. The first signs of burns in the form of whitish or brown spots on the leaves appeared 2–3 days after treatment (Figure). Preparations 6–10, 16–35 caused focal burns of lamina at an initial concentration of 1 mg/ml, so in subsequent experiments they were investigated in a concentration of 0.75 mg/ml.

As is evident from the results shown in the table, all investigated LPS-m have antiviral activity, which manifested in virus-induced local necrosis number in the experimental halves of leaves decreasing compared to controls. The inhibitory effect of the preparations at LPS-m concentration of 1.0–0.75 mg/ml was 32–77%. For preparations 3, 4, 24, 28, 30, it was lower than that of LPS-o which inhibited the formation of local

a *b*

Phytotoxic action of investigated LPS at concentration of 1 mg/ml (*a*) and 1.5 mg/ml (*b*)

necrosis in the experimental halves of leaves by 40%. Preparations 2, 6, 8, 9, 11, 13, 19, 22, 25, 27, 31, 32, 34, on account of table data, have no significant effect on antiviral activity. Preparations 7, 14, 20, 21, 23, 26, 12 inhibited TMV infectivity by 65–79% and exhibited the highest activity against the tobacco mosaic virus. Among the designated groups of complexes some regularities can be found:

– among germanium (IV) complexes (1–4) the composition of hydrazide fragment of hydrazone influence on LPS antiviral activity is observed, salicylic acid derivatives (1) contribute to its increase (I, % 62), and nicotinic (3) and isonicotinic (4) — a significant decrease (I,% 26 and 28, respectively);

– among tin (IV) complexes with hydrazides (12–19) [$SnCl_4$(2-OH-5Br-Bg)] (14) with two OH- and Br- substituents in the ligand molecule showed the highest activity (I, %, 73) as compared to [$SnCl_4$(HBg)] (12) (I, % 65), wherein the substituents are absent;

– among tin (IV) complexes with hydrazones of 4-N$(CH_3)_2$-benzaldehyde (5-11) [$SnCl_4$(2-OH-5Br-Bdb H)] (7) (I, % 79) containing the same substituents in hydrazide moiety as (14) (I, 73%) had the highest activity;

– activity of tin (IV) complexes with salicyloylhydrazones (20–24, 35) changes depending on the aldehyde moiety in their molecules, the maximum inhibition of TMV infectivity the complexes with derivatives of 4-OCH_3-benzaldehyde (20) (I, 71%), of 4-OH-benzaldehyde (21) (I, 77%) and of pyrogallol (23) (I, 72%) have exerted;

– tin (IV) complexes with isonicotinoyl-hydrazones (30–34) is significantly inferior in activity to the complexes with salicyloylhydrazones; from this group hydrazone pyrogallol complex (33) (I, 63%) stands out;

– among tin (IV) complexes with dihydrazones (25–27) and double condensation product (29) the maximum inhibition of TMV infectivity (I, 69%) binuclear (26) complex with terephthaloyldihydrazone of 4-N$(CH_3)_2$-benzaldehyde has expressed.

From the above it follows that preparations virucidal effect neutralizing virus infectivity depends on: metal-complexing agent [tin (IV) compounds are more active (I, % 65–79) as compared to germanium (IV) complexes (I, % 26–62)], the number of functional groups in ligand molecules [hydrazone complexes of tin (IV) are more active (I, 69–79%) than hydrazide (I, % 48–63)], as well as coordination form of the ligand in combination with various substituents [complexes with salicyloylhydrazones of 4-methoxy- (I, % 71), 4-hydroxybenzaldehydes (I, % 77) and pyrogallol (I, % 72) with ketone $O_{(C=O)}$–$N_{(CH=N)}$ form of the ligand are more active than with enol $O_{(C-O)}$–$N_{(CH=N)}$ isonicotinoylhydrazones form of the same aldehydes (I, % 32–63)]. Introduction of two substituents (OH- and Br-) into the hydrazide moiety of hydrazone molecule significantly increases the activity of tin (IV) with the enol form of the ligand complexes (I, % 79).

The most active complexes antivirus action possible mechanisms may be the TMV direct inhibition by attaching to the structural proteins of TMV and conglomerates formation (aggregates of the virus and the modified LPS) or the degradation of viral RNA (by host RNAase at mechanical inoculation). It is possible involvement of preparations in the induction (stimulation) of plant defense mechanisms, which consequence is the increased resistance of plants to TMV and inhibition of viral reproduction (obstacle to the development of productive infection).

Thus, "TMV — ultrasensitive plant" model study of LPS and its modified preparations (1–35) antiviral activity showed high antiviral activity of preparations 7, 21, 14, 23, 20 and 26, which may be due to their composition and structural features. Such preparations are of interest as promising agents in the fight against viral diseases of plants.

In available literature we have not found the data on antiviral effect of bacteria of the genus *Pseudomonas* LPS, however, based on the above data it is fair to assume that the observed activity of *P. chlororaphis* subsp. *aureofaciens* strains may be associated with non-specific stimulation of infected with TMV plants protective forces.

Lipopolysaccharide preparations of *P. chlororaphis* subsp. *aureofaciens* UCM-306 effect on TMV infectivity

LPS	LPS, mg/ml	Number of necrosis		E/C	I,%
		experiment	control		
Original (LPS-o)	1.0	31.2	50.6	0.62 ± 0.06	38
Modified (LPS-m):					
1	1	8.6	22.6	0.38 ± 0.08	62 ± 5*
2	1	29.5	53.6	0.55 ± 0.05	45 ± 9^0
3	1	62.1	83.8	0.74 ± 0.02	26 ± 2^0
4	1	46.3	64.3	0.72 ± 0.08	28 ± 11^0
5	1	24.1	60.2	0.40 ± 0.01	60 ± 2*
11	1	63.2	100.3	0.63 ± 0.02	37 ± 3^0
12	1	17.3	49.1	0.35 ± 0.03	65 ± 8*
13	1	22.9	44.9	0.51 ± 0.08	49 ± 16^0
14	1	20.0	74.1	0.27 ± 0.03	73 ± 11*
15	1	25.7	64.3	0.40 ± 0.03	60 ± 8*
Original (LPS-o)	0.75	26.5	44.2	0.60 ± 0.06	40 ± 10^0
Modified (LPS-m):					
6	0.75	26.5	46.3	0.57 ± 0.007	43 ± 1^0
7	0.75	10.1	47.9	0.21 ± 0.05	79 ± 23*
8	0.75	39.1	63.1	0.62 ± 0.06	38 ± 9^0
9	0.75	82.6	135.4	0.61 ± 0.05	39 ± 8
10	0.75	21.4	49.7	0.43 ± 0.01	57 ± 2*
16	0.75	8.2	20.5	0.40 ± 0.05	60 ± 12*
17	0.75	19.3	43.8	0.44 ± 0.06	56 ± 13^0
18	0.75	41.8	112.8	0.37 ± 0.04	63 ± 10*
19	0.75	39.4	75.6	0.52 ± 0.05	48 ± 9^0
20	0.75	37.3	128.0	0.29 ± 0.02	71 ± 7*
21	0.75	10.9	46.6	0.23 ± 0.03	77 ± 13*
22	0.75	24.5	47.7	0.51 ± 0.06	49 ± 11^0
23	0.75	11.6	41.4	0.28 ± 0.01	72 ± 4*
24	0.75	26.7	39.2	0.68 ± 0.04	32 ± 5
25	0.75	20.8	45.2	0.46 ± 0.06	54 ± 13^0
26	0.75	11.3	36.5	0.31 ± 0.03	69 ± 9*
27	0.75	37.7	78.5	0.48 ± 0.09	52 ± 18^0
28	0.75	38.4	59.1	0.65 ± 0.06	35 ± 9^0
29	0.75	24.8	55.1	0.45 ± 0.01	55 ± 2^0
30	0.75	45.9	67.6	0.68 ± 0.06	32 ± 80
31	0.75	35.9	61.6	0.58 ± 0.06	42 ± 10^0
32	0.75	28.5	51.8	0.55 ± 0.05	45 ± 9^0
33	0.75	17.6	47.6	0.37 ± 0.03	63 ± 8*
34	0.75	35.8	70.2	0.51 ± 0.02	49 ± 3^0
35	0.75	29.6	68.8	0.43 ± 0.04	57 ± 9*

Note: LPS-m is LPS modified with variety of complexes 1-35; LPS-o is original LPS;
* — confidence level P is within $0{,}1\% \le P \le 1\%$; ^{0} — $P > 5\%$.

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АНТИВІРУСНА АКТИВНІСТЬ НАТИВНОГО ТА МОДИФІКОВАНОГО КОМПЛЕКСАМИ GE(IV) І SN(IV) ЛІПОПОЛІСАХАРИДУ *Pseudomonas chlororaphis* subsp. *aureofaciens*

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Метою роботи було вивчити зміни противірусної активності ліпополісахариду *Pseudomonas chlororaphis* subsp. *aureofaciens* за модифікації його координаційними сполуками олова (IV) і германію (IV), синтезованими на основі гідразидів ароматичних, піридинкарбонових кислот та відповідних гідразонів ароматичних альдегідів. Для модифікації ліпополісахариду *P. chlororaphis* subsp. *aureofaciens* УКМ-306 було вибрано широкий ряд координаційних сполук германію (IV) та олова (IV). Вивчення антивірусної активності ліпополісахариду та його модифікованих препаратів (1-35) на моделі «Вірус тютюнової мозаїки — надчутлива рослина» показало, що багато з досліджуваних препаратів виявляють високу антивірусну активність, що пов'язано з їхнім складом та структурними особливостями. Такі препарати становлять інтерес як перспективні агенти у боротьбі з вірусними захворюваннями рослин. Антивірусна дія препаратів (% інгібування, I, %), що нейтралізує інфекційність вірусу, залежить від: металу-комплексоутворювача [сполуки олова (IV) активніші (I, % 65–79) порівняно із комплексами германію (IV) (I, % 26–62)], кількості функціональних груп у молекулах лігандів [(гідразонні комплекси олова (IV) активніші (I, % 69–79) за гідразидні (I, % 48–63)], а також від форми ліганду, що координується, у поєднанні з різними замісниками [комплекси із саліцилоїлгідразонами 4-метокси- (I, % 71), 4-гідроксибензальдегідів (I, % 77) та пірогалолу (I, % 72) з кетонною $O_{(C=O)}$–$N_{(CH=N)}$ формою ліганду більш активні, ніж з енольною $O_{(C-O)}$–$N_{(CH=N)}$ формою ізонікотиноїлгідразонів тих самих альдегідів (I, % 32–63)]. Уведення двох замісників (OH- і Br-) у гідразидний фрагмент молекули гідразону істотно підвищує активність комплексів олова (IV) з енольною формою ліганду (I, % 79).

Ключові слова: *Pseudomonas chlororaphis* subsp. *aureofaciens*, ліпополісахарид, координаційні сполуки Ge(IV) і Sn(IV), антивірусна дія, вірус тютюнової мозаїки.

АНТИВИРУСНАЯ АКТИВНОСТЬ НАТИВНОГО И МОДИФИЦИРОВАННОГО КОМПЛЕКСАМИ GE(IV) И SN(IV) ЛИПОПОЛИСАХАРИДА *Pseudomonas chlororaphis* subsp. *aureofaciens*

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Цель работы — изучить изменение противовирусной активности липополисахаридов *Pseudomonas chlororaphis* subsp. *aureofaciens* при модификации их координационными соединениями олова (IV) и германия (IV), синтезированными на основе гидразидов ароматических, пиридинкарбоновых кислот и соответствующих гидразонов ароматических альдегидов. Для модификации липополисахарида *P. chlororaphis* subsp. *aureofaciens* УКМ-306 был выбран широкий ряд координационных соединений германия (IV) и олова (IV). Изучение антивирусной активности липополисахарида и его модифицированных препаратов (1–35) на модели «Вирус табачной мозаики — сверхчувствительное растение» показало, что многие из исследуемых препаратов проявляют высокую антивирусную активность, что связано с их составом и структурными особенностями. Такие препараты представляют интерес как перспективные агенты в борьбе с вирусными заболеваниями растений. Антивирусная активность препаратов (% ингибирования, I, %), нейтрализующая инфекционность вируса, зависит от: металла-комплексообразователя [соединения олова (IV) более активны (I, % 65–79) по сравнению с комплексами германия (IV) (I, % 26–62)], количества функциональных групп в молекулах лигандов [гидразонные комплексы олова (IV) активнее (I, % 69–79) гидразидных (I, % 48–63)], а также от координируемой формы лиганда в сочетании с различными заместителями [комплексы с салицилоилгидразонами 4-метокси- (I, % 71), 4-гидроксибензальдегидов (I, % 77) и пирогаллола (I, % 72) с кетонной $O_{(C=O)}$–$N_{(CH=N)}$ формой лиганда более активны, чем с енольной $O_{(C-O)}$–$N_{(CH=N)}$ формой изоникотиноилгидразонов тех же альдегидов (I, % 32–63)]. Введение двух заместителей (OH- и Br-) в гидразидный фрагмент молекулы гидразона значительно повышает активность комплексов олова (IV) с енольной формой лиганда (I,% 79).

Ключевые слова: *Pseudomonas chlororaphis* subsp. *aureofaciens*, липополисахарид, координационные соединения Ge(IV) и Sn(IV), антивирусное действие, вирус табачной мозаики.