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# THE EFFECT OF STANUM (IV) AND GERMANIUM (IV) COORDINATION COMPOUNDS ON *Bacillus thuringiensis* var. *israelensis* IMV B-7465 PEPTIDASES ACTIVITY

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The purpose of the research was to investigate the influence of Stannum (IV) and Germanium (IV) coordination compounds on peptidases 1 and 2 of *Bacillus thuringiensis* var. *israelensis* IMV B-7465 activity. The study of coordination compounds effect on peptidase activity was carried out by complexes with the enzymes incubation and residual activity in relation to collagen, elastin and fibrin determination. It was revealed the regularities in the influence of different structure complex compounds on peptidases of *B. thuringiensis* var. *israelensis* IMV B-7465 activity. Stannum (IV) complexes with salicyloylhydrazones of aromatic aldehydes increase collagenase and elastase activities. Substituents replacement in aldehyde fragment of Stannum (IV) complexes with isonicotinoylhydrazones of aromatic aldehydes by the less polar ones contributed to increase of elastase activity of both enzymes while an absence of substituents enables to increase peptidase 2 fibrinolytic activity. The different metal complexes of Germanium (IV) with isonicotinoylhydrazone of salicylic aldehyde, which contain Zn and Co, increased collagenase activity of the peptidase 1 as well as elastase and fibrinolytic activities of the peptidase 2. In general, all tested complexes may be considered as peptidase effectors of *B. thuringiensis* var. *israelensis* IMV B-7465. The difference of complexes effect on activities of the both enzymes is due to the characteristics of the structure of coordination compounds.

***Key words:*** Stannum (IV) and Germanium (IV) complexes with salicyloyl- and isonicotinoylhydrazones of aromatic aldehydes, peptidases with collagenase, elastase and fibrinolytic activity.

Significant advances in basic research in the field of biochemistry, molecular genetics and molecular biology, which have been achieved in the second half of the 20th century, have created the real prerequisites for regulation of cell activity, which have become the impetus for the development of modern biotechnology, an important branch of fundamental research results practical application. One of the important problems is enzymes study because of their use in various fields of human activity becomes increasingly wider. Special researchers' attention is directed to proteolytic enzymes belonging to peptidases, which are aimed at accelerating the hydrolysis of peptide bonds in proteins and peptides.

The researches of proteolytic enzymes are important both in the theoretical aspect — for understanding the structure of proteins and peptides, mechanisms of enzyme catalysis, and for practical ones, given the fact that they are highly necrotic active: no effect on healthy tissue, but dissolve viscous purulent exudates, have the thrombolytic and anti-inflammatory action. Today a number of proteolytic enzymes of different origin producers are known. Thanks to the unlimited availability of raw materials, significant opportunities of selective mutagenesis and producers' artificial selection the most promising are enzymes of microorganisms.

Peptidases of microorganisms and drugs based on them help the cleaning of wounds, the inflammation reducing due to hydrolysis of damaged cell proteins. Thereby they can gain widespread usage in surgery of purulent processes and burns, in ophthalmology, otolaryngology, dentistry, in the treatment of inflammatory conditions, boils, wounds processing.

It is known [1] that fibrin accumulation in blood vessels leads to blood clots. As a result the cardiovascular diseases including myocardial infarction may occur. In this sense, enzymes with fibrinolytic activity attract the attention of researchers due to their low cost and absence of adverse effects. These enzymes are successfully isolated from various microorganisms, but mainly from bacteria of the genus *Bacillus*. In [2] the physicochemical properties of these enzymes are described, and their effectiveness for thrombolysis *in vivo* is shown.

Different methods to increase the activity of enzymes may be used: the optimization of conditions for producer's cultivation, the usage of synthesis inductors and promoters of their activity, and so different compounds that are able to modify the molecules and show both stimulating as well as inhibitory action. Previously [3] we have investigated various coordination compounds of Germanium (IV), Stannum (IV) as modifiers of proteolytic enzymes activity and have found that they show as activating, and so inhibitory effect depending on the composition, structure and charge of the complex, on coordination number of complexing agent, as well as on the enzyme and the strain producing it.

Increased interest in studying the effect of complex metal compounds on the activity of enzymes is caused by the fact that most of them are characterized by biological activity, which can be explained by the presence in their structure of metal atoms (Sn, Ge, Fe, Zn, Co). They are essential for living organisms and are involved in the regulation of biochemical processes as belonging to the proteins, enzymes, vitamins [4–6].

It is known [7] that the compounds of Germanium with nitrogenous compounds of purine row provide a high level of biological activity regarding herpes viruses of the 1$^{st}$ and the 2$^{nd}$ types as well as in the treatment of HIV infection and cancer. The effect of Stannum complex compounds, that is the part of some enzymes and compounds that exhibit antiseptic [8] and antibacterial activity, is less studied [9, 10].

The aim of the work was to investigate the effect of Stannum (IV) and Germanium (IV) coordination compounds on peptidases 1 and 2 activity of *Bacillus thuringiensis* var. *israelensis* IMV B-7465.

## Materials and Methods

The object of the study was the strain of *Bacillus thuringiensis* var. *israelensis* IMV B-7465, isolated from the Black Sea in Snake Island water area and kindly provided to us by the department of microbiology, virology and biotechnology of Mechnikov Odesa National University. Strain is registered in the Depository of Zabolotny Institute of Microbiology and Virology of the National Academy of Sciences of Ukraine, number IMV B-7465 as a producer of peptidase with collagenase activity [11].

For the synthesis of extracellular peptidases *Bacillus thuringiensis* var. *israelensis* IMV B-7465 was cultivated in liquid culture medium [12] of the following composition (g/l): $KH_2PO_4$ — 1,6; $MgSO_4 \cdot 7H_2O$ — 0,75; $ZnSO_4 \cdot 7H_2O$ — 0,25; $(NH_4)_2SO_4$ — 0,5; maltose — 1.0; gelatin — 10.0; yeast autolysate — 0, 15; pH — 6,5–6,7. The culture was grown for 24 h in Erlenmeyer flask rocking 250 rpm/min, 28 °C. Inoculum was grown in an appropriate medium for 24 hours, and then was placed in flasks in an amount of $10^5$–$10^6$ CFU/ml.

The study was carried out with the samples of *Bacillus thuringiensis* var. *israelensis* IMV B-7465 peptidase 1 and peptidase 2 which were received by clearance of 60% salted-out with ammonium sulfate culture supernatant followed by chromatography on charged and neutral gels TSK DEAE-650 (M) and Toyopearl HW-55 (Toyosoda, Japan), according to described earlier cleaning of *B. thuringiensis* IMV B-7324 peptidases [13]. The peptidase 1 with specificity for collagen and elastin and the peptidase 2 with specificity for collagen, elastin and fibrin have been obtained.

In collagenase activity study [14] the incubation mixture with 10 mg of collagen, 2.5 ml of 0.01 Tris-HCl-buffer (pH 9.0–10.0) and 1 ml of investigated enzyme was kept in a water bath for 5 h at 37 °C. Then 0.1 ml of the reaction mixture was transferred into the tubes containing 0.5 ml of ninhydrin 4% solution in a mixture with 0.2 M citrate buffer. Incubation was performed for 20 min in a boiling water bath, whereafter 5 ml of *n*-propanol 50% solution was added into the cooled mixture, and the tubes were held for 15 min at room temperature. Products of splitting were determined by spectrophotometer SP-26 at 600 nm. The unit of collagenase activity was chosen as an amount of released leucine, mmol, according to the standard curve constructed by leucine.

Elastolityc activity was determined colorimetrically by color intensity of the solution at enzymatic hydrolysis of Congo red stained elastin [15]. The incubation mixture contained 2.5 ml of 0.01 M Tris-HCl buffer (pH 7.5), 5 mg of Congo red 0.002% solution

stained elastin and 1 ml of enzyme. The mixture was kept for 5 hours at 37 °C. The reaction was stopped by maintaining the tubes with reaction mixture in an ice bath for 30 min. Not hydrolyzed elastin was separated by centrifugation at 10 000 *g* for 5 min. The color intensity was measured by spectrophotometer SP-26 at 515 nm. The unit of activity was chosen as an enzyme amount that catalyzes the hydrolysis of 1mg of elastin for 1 min.

Determination of fibrinolytic activity was carried out by Masada [16] using fibrin, derived from human plasma at blood transfusion station, as a substrate [17]. Into experimental tube 1 mg of fibrin, 1.8 ml of 0.01 M Tris-HCl-buffer (pH 7.5) and 0.2 ml of studied preparation were added. The reaction mixture was incubated in a water bath at 37 °C for 30–45 min. The reaction was stopped by 2 ml of 10% solution of trichloroacetic acid (TCA) adding. Into the control tube the TCA was added immediately. Samples were kept at room temperature for 20 min, centrifuged for 5 min at 10 000 g. In supernatant the formation of products of fibrin cleavage was measured on a spectrophotometer SP-26 at 275 nm. The unit of fibrinolytic activity was chosen as an enzyme amount that increases the optical density of the reaction mixture by 0.01 for 1 min.

The following complexes were used as modifiers of enzymes activity (Fig. 1 and 2):

– Stannum (IV) with hydrazones, which are different by hydrazide- salicyloyl-(1–10) and isonicotinoyl-(11–20) and also aldehyde fragment respectively — R (R = H (1, 11), 4-$OCH_3$ (2, 12), 2-$OCH_3$ (3, 13), 4-Br (4, 14), 4-$N(CH_3)_2$ (5, 15), 2-OH (7, 17); R, R′ (R = 2-OH, R′- 4-$N(C_2H_5)_2$ (9, 19), R = 2-OH, R′ = 3-$OCH_3$ (10, 20); 2-N –pyridinecarbaldehyde (6, 16), 2-OH-1-naphth- (8, 18).

– Germanium (IV) with isonicotinoyl-hydrazone of 2-hydroxybenzaldehyde ($H_2Is$) with the structure $[Ge(Is{\cdot}HCl)_2]$ (21) and tetrachloride metallates of different metals based on it $[Ge(Is{\cdot}H)(Is{\cdot}H)][FeCl_4]$ (22), $[Ge(Is{\cdot}H)_2][MCl_4]$, M = Zn (23), Co (24).

Complexes (1–24) were first synthesized at the Department of General Chemistry of Mechnikov Odesa National University according to original methods and were isolated from systems "$Sn^{IV}C$ — salicyloyl-(pyridinoylhydrazone) of aromatic aldehydes — $C_2H_5OH$ ($CH_3CN$)" [18–21], "$Ge^{IV}C$ — isonicotinoylhydrazone of salicylic aldehyde — $CH_3OH$" [22], "$Ge^{IV}C$ — isonicotinoylhydrazone of salicylic aldehyde — $FeCl_3$, ($ZnCl_2$, $CoCl_2$) — $CH_3OH$" [23]. Compounds 1, 5, 8, 17, 18 are described by a set of physical and chemical methods: IR and NMR spectroscopy, mass spectrometry, determination of conductivity, thermogravimetry, X-ray analysis (Fig. 1, 2).

We used 0.001% concentration and exposure time — 90 min at studying the impact of coordination compounds on the activity of *Bacillus thuringiensis* var. *israelensis* IMV B-7465 peptidases. Test compounds were dissolved in 0.1% dimethyl sulfoxide. In all experiments an enzymatic activity in the absence of complex compounds (control) was taken as 100%.

To determine the internal structure of the compounds the hierarchical clustering method was used, which is one of the approaches to data analysis in Data Science [24]. The arithmetic mean values by the results of five reps are presented in figures; deviations from the mean values did not exceed 5%.

## Results and Discussion

Selection of coordination compounds (1–24) modifiers was caused as by the low toxicity of these substances as by components high biological activity. The influence of some of these compounds (11, 15, 17, 18) on the growth of opportunistic microorganisms have showed the presence of antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Proteus vulgaris*, *Micrococcus luteus* [9, 10]. Used coordination compounds have biometals and biologically active ligands in their composition that are necessary for the stimulation or inhibition of enzymes. The investigated compounds include Stannum (IV) or Germanium (IV) as complexing agent, or different metals — Iron (II), Cobalt (II), Zinc (II); they are necessary for normal life ensuring. It is known that Stannum is the part of the gastric enzyme gastrin, affects the activity of flavin enzymes, acts as a catalyst for the redox reactions that can accelerate the growth [25]. Germanium is also characterized by a wide range of biological action [26]. In humans, it facilitates the transfer of oxygen and is similar to hemoglobin [27]. Certain complex compounds of Germanium are studied as promising substances for drugs creation. Like Silicium and Aluminum, Germanium natural compounds are low toxic at oral administration [28].

It is shown (Fig. 3) that the most of investigated compounds stimulate peptidase 1 collagenase activity of *Bacillus thuringiensis* var. *israelensis* IMV B-7465.

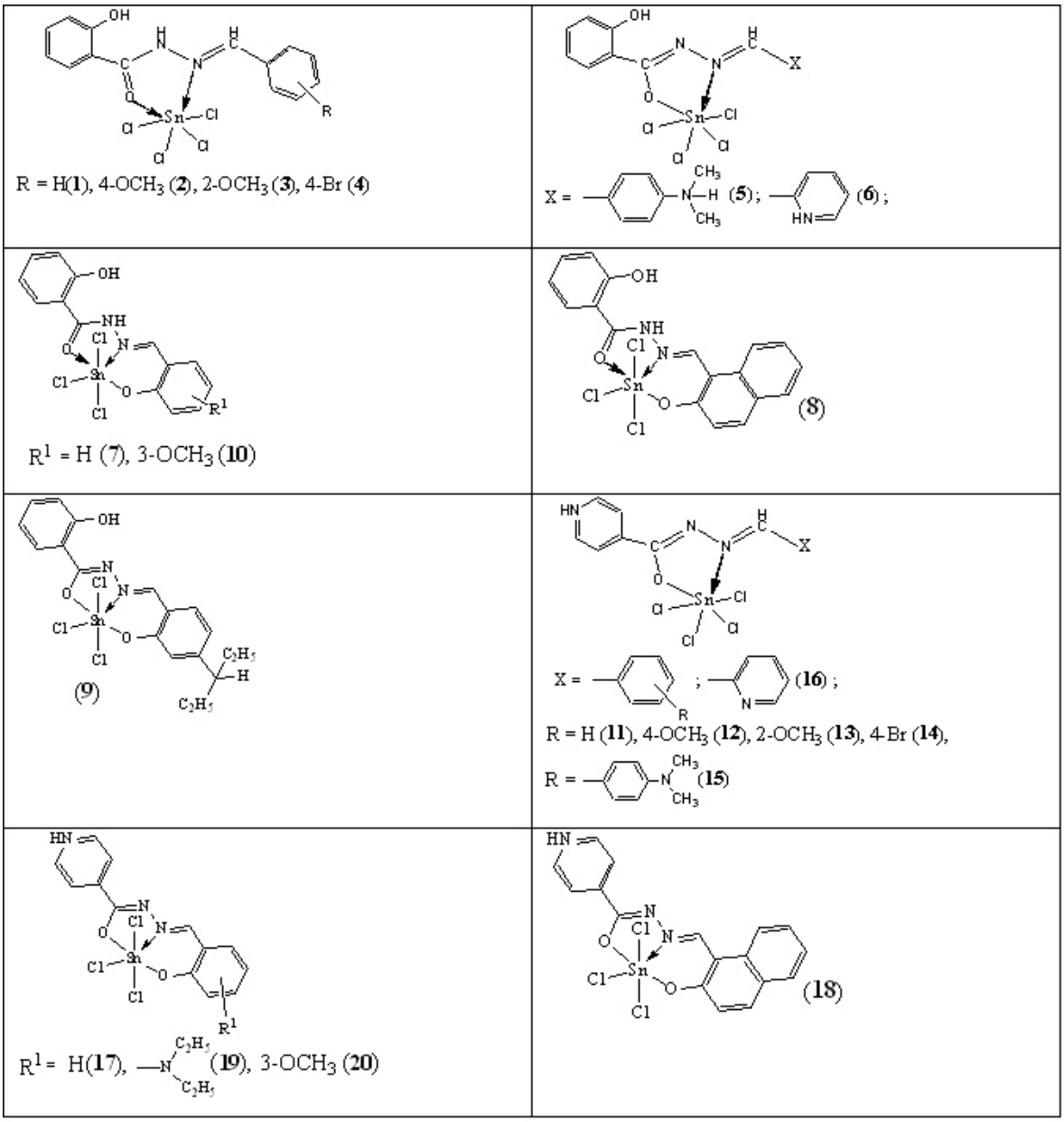


*Fig. 1.* **The diagrams of Stannum (IV) complexes structure with salicyloyl- (1–10) and isonicotinoylhydrazone of aromatic aldehydes (11–20)**

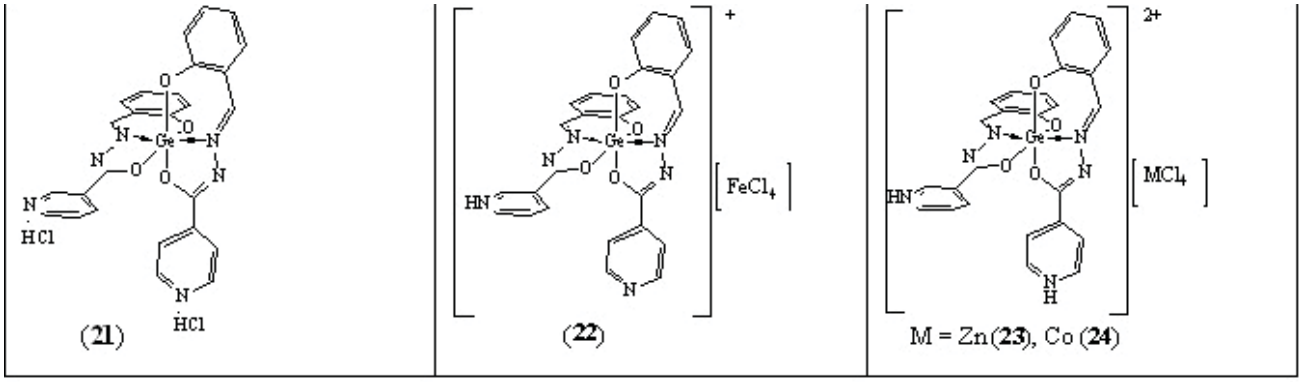


*Fig. 2.* **The diagrams of Germanium (IV) complexes structure with isonicotinoylhydrazone of salicylic aldehyde (21) and of corresponding different metal Ge -M (M = Fe (III), Zn (II), Co (II) tetrachloride metallates (22–24)**

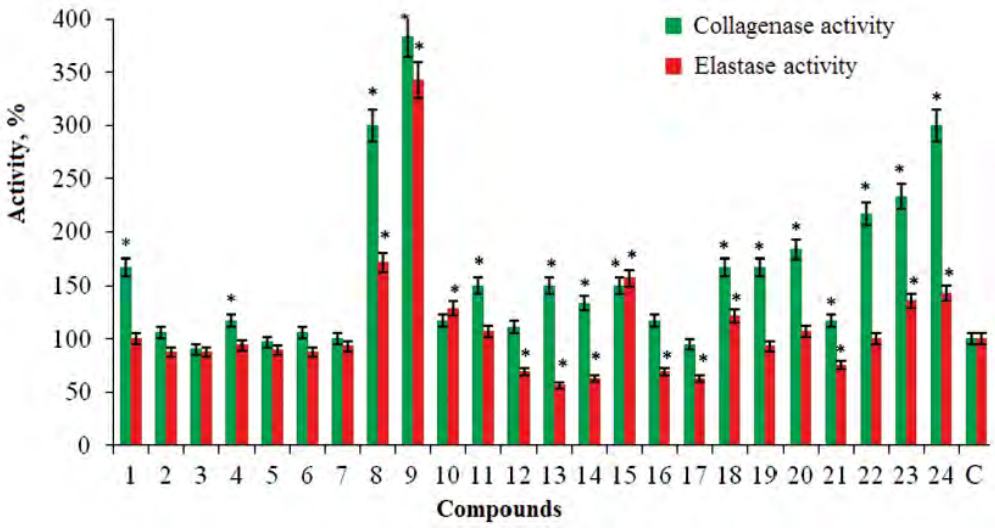


*Fig. 3.* **Impact of coordination compounds on the activity of *Bacillus thuringiensis* var. *israelensis* IMV B-7465 peptidase 1**

Here and in Fig. 4 (* — $P < 0.05$ as compared to control (C) — the reaction mixture without coordination compounds)

Thus, the compounds 8, 9 and 24 significantly increased in 3.0–3.8 times the enzyme collagenase activity. Along with this, the complexes action on peptidase 1 elastase activity was as inhibiting and activating. Significant increase (3.4 times) of the activity took place in the presence of Stannum compound (IV) with salicyloylhydrazone of R, R′-benzoic aldehyde (R = 2-OH, R′- 4-N $(C_2H_5)_2$) (9). Stannum (IV) complexes with isonicotinoylhydrazone of R-benzaldehyde — (R = 4-$OCH_3$ (12), 2-$OCH_3$ (13), 4-Br (14), 2-OH (17) and 2-N-pyridinecarbaldehyde caused the reducing of elastase activity (by 31–44%) (16).

The study of Germanium and Stannum complex compounds impact on the *Bacillus thuringiensis* var. *israelensis* IMV B-7465 peptidase 2 activity have showed that complexes of Stannum with isonicotinoylhydrazone of 2-hydroxybenzaldehyde (17) and its R′- derivatives (R′ = $N(C_2H_5)_2$ (19), $OCH_3$ (20), and also 2-hydroxy-1-naphthaldehyde (18) having the same tridentate coordination of hydrazone enolic form, coordination site {$SnCl_3ON$} and differ, compared to other systems, by the composition of hydrazone molecules aldehyde fragment, have great stimulating effect (2.3–2.6 times) on elastase activity; it increases depending on the aldehyde fragment in complex molecules in a row 18 < 17 < 20 < 19 (Fig. 4).

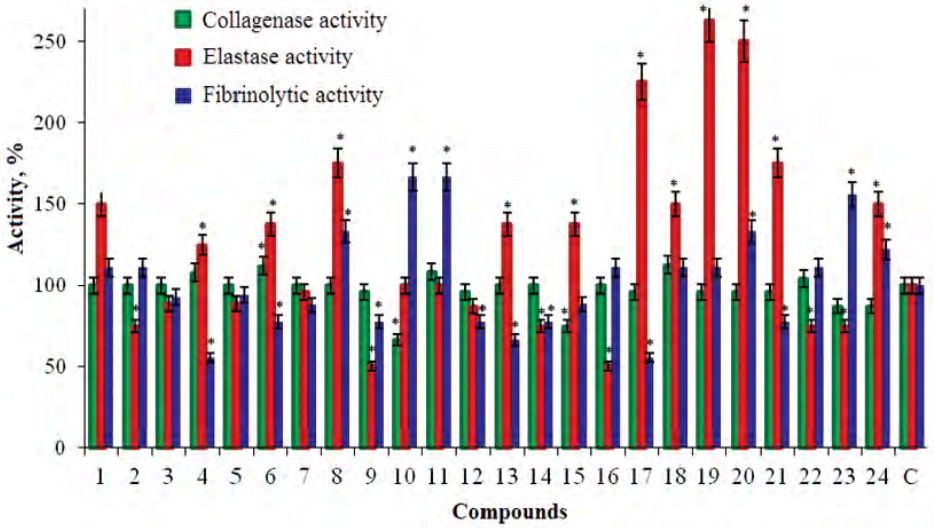


*Fig. 4.* **Impact of coordination compounds on the activity of *Bacillus thuringiensis* var. *israelensis* IMV B-7465 peptidase 2**

Hydrazide fragment replacement in complexes with hydrazones of R, R′-benzaldehyde (R = 2-OH, R′-4-N $(C_2H_5)_2$) — isonicotinoyl — (compound 19) by salicyloyl- (compound 9) led to a sharp decline (5.3 times) of peptidase 2 elastase activity, which may be caused by the presence of vacant hydroxyl group (OH-) (9), which is responsible for the low liophilicity of complex molecule. This dependence is not observed when comparing the rest of the complexes with salicyloyl-(1–8, 10) and pyridinoylhydrazones (11–18, 20) with the corresponding identical aldehyde fragments. This makes it possible to conclude that the simultaneous effect of composition and substituents position in both aldehyde and hydrazide fragments takes place.

The study of Germanium (IV) complex with isonicotinoylhydrazone of salicylic aldehyde (21) and of different metal Ge — M complexes (M = Fe (III) (22), Zn (II) (23), Co (II) (24) have demonstrated that introduction of the second metal to the composition (21) with the formation of different metal complexes significantly affects the expression of collagenase, elastase and fibrinolytic activity of *B. thuringiensis* var. *israelensis* IMV B-7465 peptidase 2 (Fig. 2). Starting Germanium (IV) complex (21) has the maximal elastase activity, the activity is a little bit reduced under the influence of $[CoCl_4]^{2-}$ (24) while $[FeCl_4]^{-}$ (22) and $[ZnCl_4]^{2-}$ (23) cause its inhibition. The complex of Germanium (21) inhibits collagenase activity, while different metal complexes slightly raise it in the following order: $[FeCl_4]^{-} < [CoCl_4]^{2-} < [ZnCl_4]^{2-}$.

Complexes 23, 24, 10, 11, 18, 8 caused fibrinolytic activity increasing by 22–67%.

These data suggest that the investigated complexes selectively inhibit or stimulate collagenase, elastase and fibrinolytic activity of peptidases 1 and 2. The specificity of their interaction with the enzyme is determined by a number of factors:

– Change of coordination site composition $\{SnCl_4ON\}$ (1–6, 11–16) → $\{SnCl_3O_2N\}$ (7–10, 17–20) and ligand denticity rise and a corresponding increase in the durability of the complex;

– Change of coordinated ligand form in Stannum (IV) complexes: ketone (1–4, 7, 8, 10) or enol (5, 9, 11–20);

– Substituents of different nature introduction into some fragments of ligand molecule (hydrazide, aldehyde);

– Different metal ions presence in complexes composition.

Thus, not only metal ion or ligand but also the molecule of complex acts as an intermediary between the enzyme and the substrate, facilitates their interaction and the formation of catalytically active peptidase conformation, which is typical for coordination compounds [6, 29].

In order to reveal the relationship between the complex compounds structure and peptidases of *B. thuringiensis* var. *israelensis* IMV B-7465 activity, to determine possible conceptual schema of grouping and identifying of similarity (or difference) measure of studied compounds, the modern method of cluster analysis of the data — hierarchical clustering was used. This method is that the sample of objects is divided into disjoint subsets, clusters, so that each cluster consists of similar objects, and objects of different clusters are significantly different. Initial information is presented in a matrix of distances [30].

Coordination compounds were divided into separate groups for each peptidase by clustering method (Fig. 5, 6).

With regard to peptidase 1 the complexes may be divided into the following four groups:

1. Increase collagenase and elastase activities by 250–280%.

2. Do not affect collagenase activity, but decrease elastase activity.

3. Increase collagenase activity > 150% and do not affect the elastase one.

4. Increase collagenase activity by ~200%, and elastase activity — by 50% (Fig. 5).

With regard to peptidase 2 the complexes may be divided into seven groups:

1 and 2. Increase elastase activity by 50–120% and not affect collagenase and fibrinolytic activities.

3. Decrease fibrinolytic activity by 50%.

4. Increase elastase activity by 75% without affecting collagenase activity but decrease fibrinolytic one.

5. Do not affect collagenase and elastase activities but increase fibrinolytic one by 60%.

6. Do not affect collagenase and fibrinolytic activities but decrease elastase activity by 50%.

7. Do not affect collagenase activity and decrease fibrinolytic and elastase activities by 25–50% (Fig. 6).

As shown in Fig. 7, *a* the correlation (r = 0.82) between collagenase and elastase activities of peptidase 1 at action of studied coordination compounds is observed.

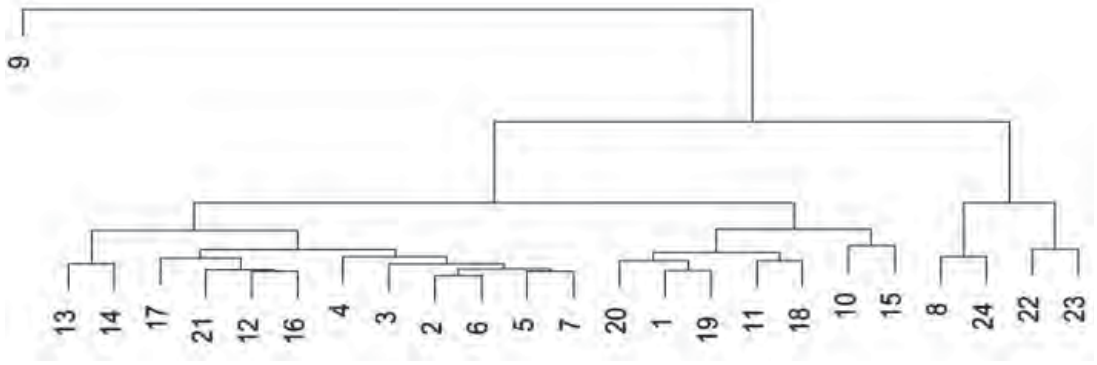


*Fig. 5*. **Hierarchical clustering of coordination compounds by the effect on collagenase and elastase activities of *B. thuringiensis* var. *israelensis* IMV B-7465 peptidase 1**

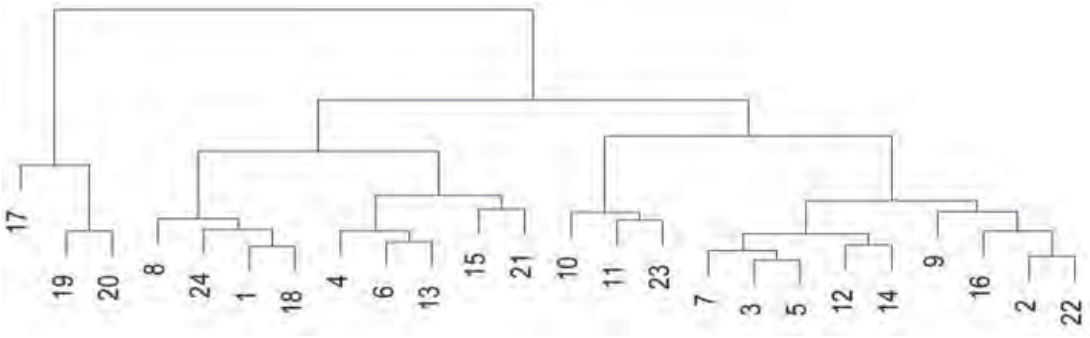


*Fig. 6*. **Hierarchical clustering of coordination compounds by the effect on collagenase, elastase and fibrinolytic activities of *B. thuringiensis* var. *israelensis* IMV B-7465 peptidase 2**

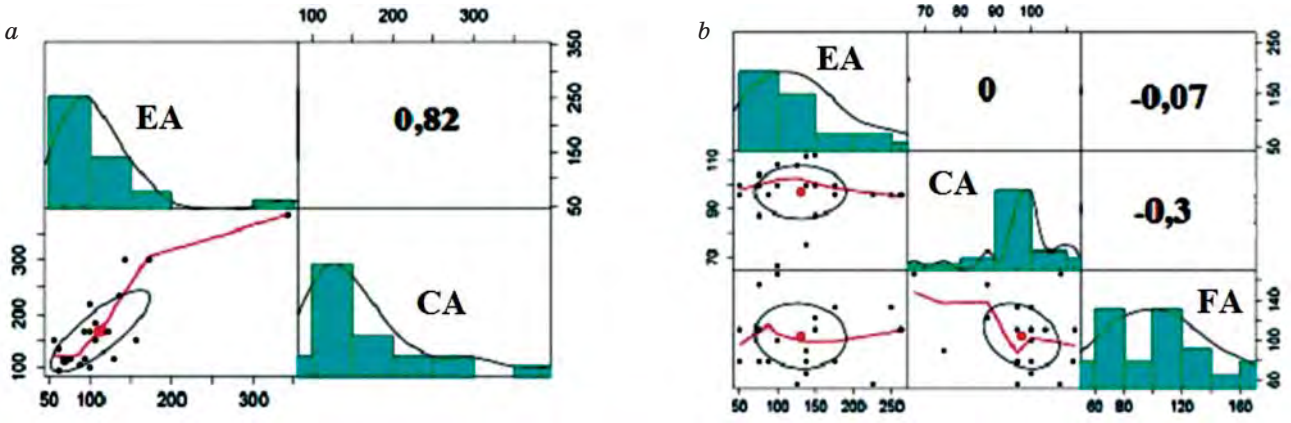


*Fig. 7*. **The diagrams of correlation for collagenase, elastase and fibrinolytic activities of:** *B. thuringiensis* var. *israelensis* IMV B-7465 peptidase 1 (*a*) and peptidase 2 (*b*);
CA — collagenase activity;
EA — elastase activity;
FA — fibrinolytic activity

Negative r values (0, -0.07, -0.3) indicate that for collagenase, elastase and fibrinolytic activities of peptidase 2 this dependence is not revealed (Fig. 7, *b*).

The obtained results allowed establishing the following regularities between complex compounds structure and activity of *B. thuringiensis* var. *israelensis* IMV B-7465 peptidases. Complexes of:

1) Sn (IV) with aromatic aldehydes salicyloylhydrazones increase collagenase and elastase activities by 260%;

2) Sn (IV) with aromatic aldehydes isonicotinoylhydrazones don't significantly affect collagenase activity. Substituents replacement in aldehyde fragment by less polar ones helped to increase elastase activity of both enzymes. The lack of substituents in aldehyde fragment of the molecule enables to increase fibrinolytic activity of peptidase 2;

3) Germanium complexes with salicylic aldehyde isonicotinoylhydrazone which include zinc and cobalt (different metal complexes) increase collagenase activity of peptidase 1 and also elastase and fibrinolytic activity of peptidase 2.

Thus, investigations are currently important both from a theoretical perspective and from a practical standpoint, since the effects on the enzymes activity may be the basis for new preparations creation to hydrolyze slightly soluble collagen, elastin and fibrin protein substrates, which are part of the connective tissue and blood clots. All tested complexes may be considered as peptidase effectors which do not necessarily have to participate in the catalytic hydrolysis of protein substrates of collagen, elastin, and fibrin.

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## ВПЛИВ КООРДИНАЦІЙНИХ СПОЛУК СТАНУМУ(IV) ТА ГЕРМАНІЮ (IV) НА АКТИВНІСТЬ ПЕПТИДАЗ *Bacillus thuringiensis* var. *israelensis* ІМВ В-7465

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Метою роботи було дослідити вплив координаційних сполук стануму (IV) та германію (IV) на активність пептидаз 1 і 2 *Bacillus thuringiensis* var. *israelensis* ІМВ В-7465. Вивчення впливу координаційних сполук на активність пептидаз здійснювали інкубуванням комплексів з ензимом та визначенням залишкової активності щодо колагену, еластину і фібрину. Було виявлено закономірності впливу комплексних сполук різної структури на активність пептидаз 1 і 2 *B. thuringiensis* var. *israelensis* ІМВ В-7465. Комплекси Sn(IV) із саліцилоїлгідразонами ароматичних альдегідів підвищують колагеназну та еластазну активність. Заміна замісників в альдегідному фрагменті комплексів Sn(IV) з ізонікотиноїлгідразонами ароматичних альдегідів на менш полярні сприяла збільшенню еластазної активності обох ензимів. Водночас відсутність замісників дає змогу збільшити фібринолітичну активність тільки пептидази 2. Різнометальні комплекси германію з ізонікотиноїлгідразоном саліцилового альдегіду, до складу яких входять цинк і кобальт, підвищували колагеназну активність пептидази 1, а також еластазну і фібринолітичну активність пептидази 2. Загалом усі досліджені комплекси можна розглядати як ефектори пептидаз *B. thuringiensis* var. *israelensis* ІМВ В-7465. Відмінність у впливі комплексів на активність обох ензимів зумовлена характеристиками будови координаційних сполук.

***Ключові слова:*** комплекси стануму (IV) та германію (IV) із саліцилоїл- та ізонікотиноїлгідразонами ароматичних альдегідів, пептидази з колагеназною, еластазною і фібринолітичною активністю.

## ВЛИЯНИЕ КООРДИНАЦИОННЫХ СОЕДИНЕНИЙ СТАНУМА (IV) И ГЕРМАНИЯ (IV) НА АКТИВНОСТЬ ПЕПТИДАЗ *Bacillus thuringiensis* var. *israelensis* ИМВ В-7465

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Целью работы было исследовать влияние координационных соединений станума (IV) и германия (IV) на активность пептидаз 1 и 2 *Bacillus thuringiensis* var. *israelensis* ИМВ В-7465. Изучение влияния координационных соединений на активность пептидаз осуществляли инкубированием комплексов с энзимом и определением остаточной активности по отношению к коллагену, эластину и фибрину. Были выявлены закономерности влияния комплексных соединений различной структуры на активность пептидаз 1 и 2 *B. thuringiensis* var. *israelensis* ИМВ В-7465. Комплексы Sn(IV) с салицилоилгидразонами ароматических альдегидов повышают коллагеназную и эластазную активность. Замена заместителей в альдегидном фрагменте комплексов Sn(IV) с изоникотиноилгидразонами ароматических альдегидов на менее полярные приводила к повышению эластазной активности обоих энзимов. В то же время отсутствие заместителей позволило повысить фибринолитическую активность только пептидазы 2. Разнометалльные комплексы германия с изоникотиноилгидразоном салицилового альдегида, в состав которых входят цинк и кобальт, повышали коллагеназную активность пептидазы 1, а также эластазную и фибринолитическую активность пептидазы 2. Таким образом, все исследованные комплексы могут выступать в качестве эффекторов пептидаз *B. thuringiensis* var. *israelensis* ИМВ В-7465. Отличие влияния комплексов на активность обоих энзимов обусловлено характеристиками строения координационных соединений.

***Ключевые слова:*** комплексы станума (IV) и германия (IV) с салицилоил- и изоникотиноилгидразонами ароматических альдегидов, пептидазы с коллагеназной, эластазной и фибринолитической активностью.