ISSN 2710-1185 (Online)
ISSN 1813-1107 (Print)

ЕҢБЕК ҚЫЗЫЛ ТУ ОРДЕНДІ
«Ә. Б. БЕКТҰРОВ АТЫНДАҒЫ
ХИМИЯ ҒЫЛЫМДАРЫ ИНСТИТУТЫ»
АКЦИОНЕРЛІК ҚОҒАМЫ

ҚАЗАҚСТАННЫҢ ХИМИЯ ЖУРНАЛЫ

ХИМИЧЕСКИЙ ЖУРНАЛ КАЗАХСТАНА

CHEMICAL JOURNAL of KAZAKHSTAN

АКЦИОНЕРНОЕ ОБЩЕСТВО
ОРДЕНА ТРУДОВОГО КРАСНОГО ЗНАМЕНИ
«ИНСТИТУТ ХИМИЧЕСКИХ НАУК
им. А. Б. БЕКТУРОВА»

2 (74)

АПРЕЛЬ – ИЮНЬ 2021 г.

ИЗДАЕТСЯ С ОКТЯБРЯ 2003 ГОДА

ВЫХОДИТ 4 РАЗА В ГОД

АЛМАТЫ
2021

«Қазақстанның химия журналы»
ISSN 2710-1185 (Online); ISSN 1813-1107 (Print)

Құрылтайшы: Еңбек Қызыл Ту орденді Ә.Б. Бектұров атындағы Химия ғылымдары институты

Тіркеу: Қазақстан Республикасының Мәдениет, ақпарат және қоғамдық келісім министрлігінде № 3995-Ж 2003 жылғы 25-маусымдағы

2003 жылы құрылған. Жылына 4 рет шығады.

Редакцияның мекен-жайы: *050010 (A26F3Y1), Қазақстан Республикасы, Алматы қ., Ш. Уалиханов көшесі, 106. тел. 8 (727) 291-24-64, 8 (727) 291-59-31.*
ics_rk@mail.ru

«Қазпошта» АҚ-ның газет-журналдар каталогында немесе оның қосымшаларында жазылу индексі **75241**.

«Химический журнал Казахстана».
ISSN 2710-1185 (Online); ISSN 1813-1107 (Print)

Учредитель: Ордена Трудового Красного Знамени Институт химических наук им. А.Б. Бектурова.

Регистрация: Министерство культуры, информации и общественного согласия Республики Казахстан № 3995-Ж от 25 июня 2003 г.

Основан в 2003 г. Выходит 4 раза в год.

Адрес редакции: *050010 (A26F3Y1), г. Алматы, ул. Ш. Уалиханова, 106, тел. 8 (727) 291-24-64, 8 (727) 291-59-31.*
ics_rk@mail.ru

Подписной индекс **75241** в Каталоге газет и журналов АО «Казпочта» или в дополнении к нему.

«Chemical Journal of Kazakhstan»
ISSN 2710-1185 (Online);
ISSN 1813-1107 (Print)

Founder: Order of the Red Banner of Labor Institute of Chemical Sciences named after A.B. Bekturov.

Registration: Ministry of Culture, Information and Public Accord of the Republic of Kazakhstan No. 3995-Ж dated June 25, 2003 year.

«Chemical Journal of Kazakhstan» was founded in 2003 year, publishes four issues in a year.

Address of the Editorial board: *050010 (A26F3Y1), Republic of Kazakhstan, Almaty, Sh. Ualikhanov str., 106, A.B. Bekturov Institute of chemical sciences awarded by the Order of Red Banner of Labor, Fax: 8(727)291-24-64.*
ics_rk@mail.ru

Chemical Journal of Kazakhstan
ISSN 1813-1107 **https://doi.org/10.51580/2021-1/2710-1185.31**
Volume 2, Number 74 (2021), 86 – 102

УДК 615.017:616.079

STRUCTURE AND PROPERTIES OF THE DI- ((2S) -2-AMINO-3- (1H-INDOL-3-YL) PROPIONATE)-DIHYDRO-TETRAIODIDE

A.N. Sabitov*, S. Turganbay, A. Dzhumagazieva

Test Facility, JSC «Scientific center for anti-infectious drugs», Almaty, Republic of Kazakhstan
*E-mail: aitugans@mail.ru

Abstract: New organic iodine complex in the amino acid - alkali metal salt - iodine - water system was synthesized. The physico-chemical properties of complex di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide were studied. Microscopic analysis shows that particles of complex have elongated needle-like linear stick-like shapes with average size 2.50-4.00 μm. The cytotoxicity test on MDCK cell culture, antimicrobial activity on *S. aureus* ATCC 6538-P (museum susceptible strain); *S. aureus* ATCC-BAA-39 (museum multiresistant strain); *E. coli* ATCC 8739 (museum susceptible strain); *E. coli* ATCC-BAA-196 (museum multiresistant strain); *P. aeruginosa* ATCC 9027 (museum susceptible strain); *P. aeruginosa* TA2 were observed. Complex has low cytotoxicity, direct antiviral effect, and antimicrobial activity against antibiotic-resistant strains of microorganisms. Di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide does not cause any mutagenic effect on mammalian cells of the L5178Y line, both in the presence and in the absence of metabolic activation.

Keywords: iodine polyanion complex, Di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide, x-ray diffraction analysis, mutagenic test on L5178Y line, cytotoxicity.

Introduction. Semiorganic compounds, including metal atoms and various organic molecules are of great interest from the point of view of the diversity of their pharmaceutical and physical properties. For example, the large glycine family of metal halides and metal halides includes a large variety of different crystal structures. The structural units of these compounds are glycine molecules, halide ions, and metal cations. Depending on the combination of building blocks, five different structural families of glycine halides and glycine metal halides were distinguished [1]. Studies of the physical properties have shown that some of these compounds are ferroelectrics, ionic conductors, and exhibit interesting thermal and optical properties [2-9]. Due to the presence of asymmetric centers in most amino acid molecules, coordination compounds with amino acids crystallize within non-centrosymmetric spatial groups, being possible candidates for nonlinear optical materials and are interesting compounds because of their possible use in new optoelectronic technologies [10, 11].

In our early studies, we have already studied semi-organic iodine complexes in the amino acid - alkali metal salt - iodine - water (or organic solvent) system. A number of them had significant biological activity against pathogenic microorganisms and viruses [12-14].

The aim of this research is the synthesis of new compound in the tryptophan-iodine-sodium iodide-water system, determination of the crystal structure of new compound and physico-chemical properties of the obtained complex.

EXPERIMENTAL PART

Synthesis of new semiorganic iodine complex. 2.000 g of tryptophan, 11 mL of purified water, and 3 ml of hydrochloric acid (18%) were added to a 50 mL beaker. The mixture was stirred with a glass rod until complete dissolution of the amino acid, while heating the beaker on a water bath. The molar ratio of tryptophan: NaI : I_2 was 1:0.5:1. 0.7340 g of sodium iodide, 1.0132 g of iodine, previously crushed in an agate mortar to a fine powder, and 20 mL of ethanol (96%) were added to a 100 mL flask with ground-in stopper. The mixture was stirred until complete dissolution, while heating on a water bath. After complete dissolution of the mixture in the flask the sodium triiodide solution was added to the tryptophan solution. The resulting reaction mixture was capped and stirred at room temperature for 5 minutes. The prepared product was kept in a dark place at room temperature.

A day later the complex solution was poured into a crystallizer, a crystallizer with the complex solution was further placed into a desiccator with anhydrous calcium chloride to evaporate the solvent at room temperature. After complete evaporation of the complex solution we took the monocrystals of the new tryptophan:NaI:iodine system and the yield of monocrystals of the complex was 1.95 g (65% of the theoretical).

X-ray diffraction analysis. The purpose of these studies was to determine and refine the crystal structure of the new coordination compound formed in the tryptophan:NaI:iodine:water system. Small crystals were formed after crystallization of the synthesized compound. All diffraction measurements were carried out by using Enraf-Nonius CAD4 autodiffractometer (Nederland) (graphite monochromator, Mo-K_α radiation, $\theta/2\theta$ scan, CAD4 software) [15]. The main fragment of the structure was decoded by a direct method. The coordinates of missing atoms were determined by difference Fourier syntheses of electron density. Due to the presence of heavy atoms in the structure, it was not possible to detect hydrogen atoms by difference Fourier syntheses of electron density.

The coordinates of hydrogen atoms were determined by geometric calculations and refined using the “rider” model with the following conditions: C-H bond length = 0.96Å, U_{iso}(H) =1.5U_{eq} (C) for CH_2 groups, CH = 0.93Å, U_{iso} (H) =1.5U_{eq} (C) for CH groups, NH = 0.86Å, U_{iso} (H) = 1.2U_{eq} (N) for NH groups, NH = 0.89Å, U_{iso} (H) = 1.2U_{eq} (N) for NH_3 groups and O- H = 0.86Å, U_{iso} (H) = 1.2U_{eq} (O) for water molecules. The structure was refined using full

matrix OLS in the anisotropic approximation for non-hydrogen atoms and in the isotropic approximation for hydrogen atoms. All structural calculations were carried out using the SHELXTL [16] and JANA2006 [17] software packages; the purity of structural data was checked using the PLATON software [18].

Investigation of physical-chemical parameters. UV-VIS spectra of the water solution of obtained compound was measured using an UV-Vis spectrophotometer Perkin Elmer Lambda-35 at wavelength from 200 to 900 nm.

Determination of the melting point of the compoundwere carried out using a synchronous thermoanalyzer STA 449 F1 Jupiter (NETZSCH) combining simultaneous measurement of mass changes (thermogravimetry) and heat fluxes. Samples weighing 0.8-2 mg were heated in the temperature range from 28 to 320 °C in 85 μl closed corundum crucibles at a rate of 10 K/min in a dry nitrogen atmosphere (gas flow rate 40 ml/min). The thermograms were recorded differential curves of change in the heat capacity of the sample.

The determination of the melting temperature of substances was carried out by using the Netzsch-Proteus program at the intersection point of the tangents held to the beginning of the endothermic peak on the Differential Scanning Calorimetry (DSC) curve. The temperature of the beginning of the peak, which corresponds to the melting point of the sample, was determined.

Bulk density (kg/m^3) is determined by weighing a graduated cylinder filled with a substance after repeated compaction. Particle shape and size were determined using a Nikon Eclipse 50 i microscope and NIS Elements AR software. Solubility is determined in purified water, as well as several polar and non-polar solvents. The measurement of pH is carried out by potentiometric method using a combined electrode on an ionometer Basic pH Meter PB-11, manufactured by Sartorius. The test was carried out on 1% aqueous solutions of the substance.

Determination of cytotoxicity. Cytotoxicity is the indicator of the quality of being toxic to cells. The in vitro cytotoxicity of substances was determined using the MTT test. Cells were seeded into 96-well plates at a concentration of 200,000 cells in 1 ml. Dies were cultivated in a thermostat at 37 ºC, 5% CO_2. After 24 hours of incubation, the growth medium was removed from the wells of the plate, and 200 μl of the medium containing the test substances was added. 200 μl DMEM nutrient medium was added to the negative control wells.

After 48 and 72 hours, the medium with the substance was removed from the wells, 200 μl of fresh nutrient medium and 50 μl of MTT working solution (5 mg/ml) were added, the plate was incubated for 4 hours at 37 °C. After the expiration of the incubation period, the supernatant was removed. 100μl of DMSO was added to each well. The optical density in the wells was measured on a Tecan Sunrise RC.4 microplate reader, Austria, at the wavelength of the main filter - 492 nm and the reference filter - 620 nm. The calculation of the results was performed using formulas 5–7:

- calculated the arithmetic average value of optical density ($\overline{Y}$) for the negative control by theequation (5):

$$\overline{Y} = \frac{y_1 + ... + y_n}{n} = \frac{1}{n}\sum_{i=1}^{n} y_i \quad (5)$$

Where, y_i - measurement result of the optical density (OD) of each object of the group; n - is the number of objects in the group; - calculated the percentage of surviving cells for each repetition of each concentration of the test substance according to the (6):

$$Percentage\ of\ surviving\ cells\ = \frac{Y_1}{\overline{Y}_{NC}} * 100\%. \quad (6)$$

Where, Y_i – the result of the measurement of the OD for each group; $\overline{Y}_{NC}$ – arithmetic average OD ($\overline{Y}$) for negative control; - calculated the arithmetic average value of the percentage of surviving cells ($\overline{Y}$) for each concentration of the analyte by the formula (3);

- CTC_{50} (concentration of substances at which 50% of cells die) for each test substance was calculated as in (7):

$$CTC_{50} = \left[\frac{X1 - 50}{X1 - X2} * (Mx2 - Mx1) \right] + Mx1. \quad (7)$$

Where $X1$ - > 50 % surviving cells; $X2$ - < 50 % surviving cells; $Mx1$ – concentration of matter where survived > 50 %; $Mx2$ - concentration of matter where survived < 50 %.

Studies on antimicrobial activity. The antimicrobial activity of the coordination compound was studied by using the twofold serial dilution method in a liquid nutrient medium [19].

The procedure for antimicrobial activity was performed by the method of twofold serial dilutions in a liquid nutrient medium (CLSI M100, 2016). For the method of two-fold serial dilutions, an inoculum of the test strain of the microorganism at a concentration of 1.5×10^6 CFU/ml was used. The primary suspension of the test strain was prepared in a physiological solution (0.9% NaCl). An aliquot of a day-cultured test strain was taken with a sterile loop. After that it was introduced into a sterile tube with 5 ml of 0.9% NaCl. The turbidity of the inoculum obtained was monitored by measuring the optical density on a DEN-1 densitometer (Biosan, Latvia). The density of the primary suspension was 0.5 units. According to McFarland, which corresponds to 1.5×10^8 CFU / ml. Next, the primary suspension in an amount of 0.1 ml was introduced into a test tube with 9.9 ml of isotonic solution to achieve a working concentration of 1.5 × 106 CFU / ml. Testing was carried out on a liquid nutrient medium - Muller-Hinton broth (Himedia, India).

A 48-well plate (BIOLOGIX, China) was used to determine the antimicrobial activity. In all the wells, except the 1st (from 2 to 16), poured nutrient broth Muller-Hinton (MHB) in an amount of 0.5 ml. Working solutions of coordination compounds were introduced in a volume of 0.5 ml into the 1st tube, and the

second with MHB already present in it (0.5 ml). Next, serial dilutions were made, which were carried out by taking the mixture (MHB (0.5 ml) + test compound (0.5 ml)) from the 2nd tube in the amount of 0.5 ml to the 3rd tube, which already contains 0, 5 ml of broth, etc. From the last tube, 0.5 ml of the mixture was removed. Thus, the following dilutions were obtained: 1: 0; 1: 1; 1: 2; 1: 4; 1: 8; 1:16; 1:32; 1:64; 1: 128; 1: 256; 1: 512; 1: 1024; 1: 2048; 1: 4096; 1: 8192; 1: 16384, which corresponds to the tubes from the 1st to the 16th. The 17th test tube was the control of culture growth.

After conducting a series of dilutions, 0.05 ml of microorganism test strain was added to all tubes at a concentration of 1.5×10^6 CFU/ml. The procedure was repeated for all test cultures. All samples were incubated for 18-24 hours at a temperature of (37±1) °C. After the time of incubation, seeding was carried out on a dense nutrient medium - Muller-Hinton agar (Himedia, India) to determine viable cells. After seeding the cups were placed in a thermostat for 18-24 hours, the cultivation was carried out at a temperature of (37±1) °C.

The results were recorded by the presence / absence of visible growth of microorganisms on the surface of a dense nutrient medium. The minimum bactericidal concentration (MBC) was considered the lowest concentration in the well, which completely suppressed the growth of microorganisms. All experiments were performed in triplicate.

Test strains used in the study were obtained from the American Type Culture Collection (ATCC). The museum susceptible, museum multiresistant, and one clinical test strains were used in the experiment: *S. aureus* ATCC 6538-P (museum susceptible strain); *S. aureus* ATCC-BAA-39 (museum multiresistant strain); *E. coli* ATCC 8739 (museum susceptible strain); *E. coli* ATCC-BAA-196 (museum multiresistantstrain); *P. aeruginosa* ATCC 9027 (museum susceptible strain); *P. aeruginosa* TA2 (clinical multiresistant strain) [20].

Investigation of mutagenic properties in in vitro micronucleus assay. The choice of the investigated concentrations of the complexes based on the range of concentrations of drugs recommended for their study on the putative mutagenic activity in vitro. According to the OECD Guideline for Research on Chemical Substances No. 487 "In vitro micronucleus test of mammalian cells", adopted on September 26, 2014 [21], for non-toxic, highly soluble compounds, the maximum dose can be up to 5 mg / ml,

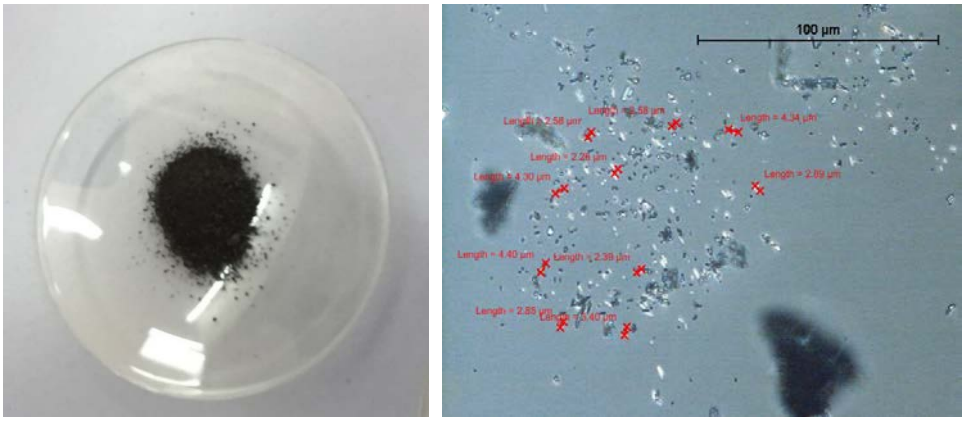
The suspension culture of L5178Y cells is recommended for MNvit by the OECD Guidelines for Testing Chemical Substances No. 487.

Murine L5178Y lymphoma cells are used because they are sensitive indicators of mutagenic activity of a wide range of chemical compounds.

RESULTS AND DISCUSSION

Structure of the obtained crystals. The resulting organic complex is a dark gray-green with a weak iodine odor (Figure 1). Particles have elongated needle-like linear stick-like shapes. All synthesized amount of the monocrystals of new

compound were stored at dark place for further use. The parameters of triclinic unit cell were determined (Table 1) and refined based on 25 reflexes with 10.2 <θ<12.9.



a b

Figure 1 – Photo (a) of the obtained di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide complex and its particles sizes (b)

Table 1 – Crystallographic data for $C_{11}H_{12}N_2O_2$•$(C_{11}H_{13}N_2O_2)^+$•$(I_4)^{2-}$ •Na^+ •$2H_2O$, determination accuracy is given in parentheses

Crystallographic data	
Formula	$C_{11}H_{12}N_2O_2 \cdot (C_{11}H_{13}N_2O_2)^+ \cdot Na^+ \cdot 2H_2O \cdot (I_4)^{-2}$
Molecular weight	976.08
Syngony; Spacegroup	Triclinic, P1
Lattice parameters a, b, c [Å]	5.4298(11), 11.427(2), 13.388(3)
alpha, beta, gamma [deg]	101.58(3), 100.96(3), 93.43(3)
V $[Å]^3$; Z	794.8(3); 1
D(calc) $[g/cm^3]$; F(000)	2.039; 460
Mu (MoKα) [mm^{-1}]	3.973
Crystalsizes [mm]	0.22x0.10x0.005
Measurements	
Temperature (K); Radiation+ [Å]	293; MoKα; λ=0.71073
θ_{min}; θ_{max} [Deg]	1.6, 30.0
Measuring area	-7≤h≤7; -16≤k≤16; -18≤l≤18
Number of reflexes	7080
Observed data [I > 2.0 sigma(I)]	2408

Refinement	
Number of reflexes, Number of parameters	7080, 363
R, wR^2, S	0.0784, 0.2176, 0.97
w = 1/[\s^2^(Fo^2^)+(0.0349P)^2^+8.8867P] where P=(Fo^2^+2Fc^2^)/3	
Max. and Av. Shift/Error	0.00, 0.00
Min. and Max. Resd. Dens. [e/Å^3]	-0.45, 0.41

According to the results of the calculations performed, the chemical structure of the compound can be represented as $C_{11}H_{12}N_2O_2$•$(C_{11}H_{13}N_2O_2)^+$ •Na^+ •$2H_2O$ •$(I_4)^{2-}$. By IUPAC it will be di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide. Interatomic distances in the crystal structure are given in Table 2.

Table 2 – Main interatomic distances in the structure $C_{11}H_{12}N_2O_2$•$(C_{11}H_{13}N_2O_2)^+$ •Na^+ •$2H_2O$ •$(I_4)^{2-}$

Atoms	Distance (Å)	Atoms	Distance (Å)	Atoms	Distance (Å)
I1-I2	2.762(4)	C4-C5	1.38(5)	C1-C2	1.44(4)
I1-I3A	3.431(4)	I1-I3B	3.444(4)	C1-C6	1.41(3)
I2-I4B	3.628(4)	I2-I4A	3.629(4)	C1-C9	1.42(5)
Na1-O1W	2.30(2)	C5-C6	1.35(4)	C2-C3	1.41(5)
Na1-O2W	2.36(3)	N7-H7	0.8600	C3-C4	1.40(5)
Na1-O35	2.43(2)	C8-C9	1.41(4)	C5-H5	0.9300
Na1-O14_b	2.39(2)	C9-C10	1.45(4)	C8-H8	0.9300
Na1-O15	2.42(2)	C10-C11	1.55(3)	C10-H10A	0.9700
Na1-O34_b	2.34(3)	C11-C13	1.51(3)	C10-H10B	0.9800
O14-C13	1.29(3)	N12-H12B	0.8900	C11-H11	0.9800
O15-C13	1.21(3)	N12-H12C	0.8900	C22-H22	0.9300
O34-C33	1.35(4)	N12-H12A	0.8900	C23-H23	0.9300
O35-C33	1.17(4)	C21-C22	1.34(4)	N32-H32C	0.8900
O1W-H1W2	0.87(11)	C21-C26	1.49(4)	N32-H32B	0.8900
O1W-H1W1	0.86(7)	C21-C29	1.40(5)	C2-H2	0.9300
O2W-H2W1	0.86(17)	C22-C23	1.31(4)	C3-H3	0.9300
O2W-H2W2	0.86(6)	C23-C24	1.47(5)	C4-H4	0.9300
N7-C6	1.37(3)	C24-C25	1.30(5)	C24-H24	0.9300
N7-C8	1.39(4)	C25-C26	1.37(4)	C25-H25	0.9300
N12-C11	1.43(3)	N27-H27	0.8600	C28-H28	0.9200
O14-H14	0.8200	C28-C29	1.37(4)	C30-H30B	0.9700
N27-C28	1.34(4)	C29-C30	1.50(4)	C30-H30A	0.9700
N27-C26	1.36(4)	C30-C31	1.52(3)	C31-H31	0.9800
N32-C31	1.49(4)	C31-C33	1.51(4)		
O34-H34	0.8200	N32-H32A	0.8900		

The independent part of the unit cell contains two molecules of tryptophan $C_{11}H_{12}N_2O_2$, two molecules of water H_2O, sodium cation Na^+, and iodine polyanion $(I_4)^{-2}$. At the same time, one of the tryptophan molecules is positively charged $(C_{11}H_{13}N_2O_2)^+$ due to the addition of a proton. The negative charge of the polyanion $(I_4)^{-2}$is compensated by the positive charge of tryptophanium $(C_{11}H_{13}N_2O_2)^+$and Na^+ cation (Figure 2).

In three-dimensional packing of the crystal structure of the compound $C_{11}H_{12}N_2O_2$•$(C_{11}H_{13}N_2O_2)^+$ •Na^+ •$2H_2O$ •$(I_4)^{2-}$, Na^+ cations are octahedral coordinated by six oxygen atoms, forming infinite tapes in the plane direction (Figure 3).

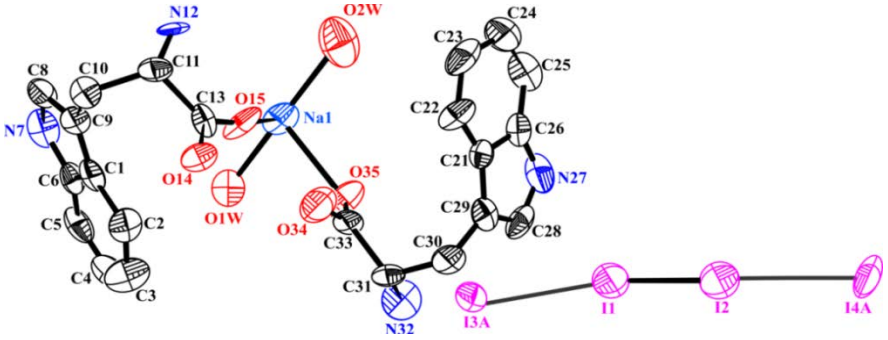


Figure 2 – Model of atomic structure $C_{11}H_{12}N_2O_2$•$(C_{11}H_{13}N_2O_2)^+$•Na^+•$2H_2O$•$(I_4)^{2-}$. Ellipsoids of anisotropic thermal oscillations are shown at the 50% probability level, hydrogen atoms and disordered polyanions $(I_4)^{-2}$are not demonstrated

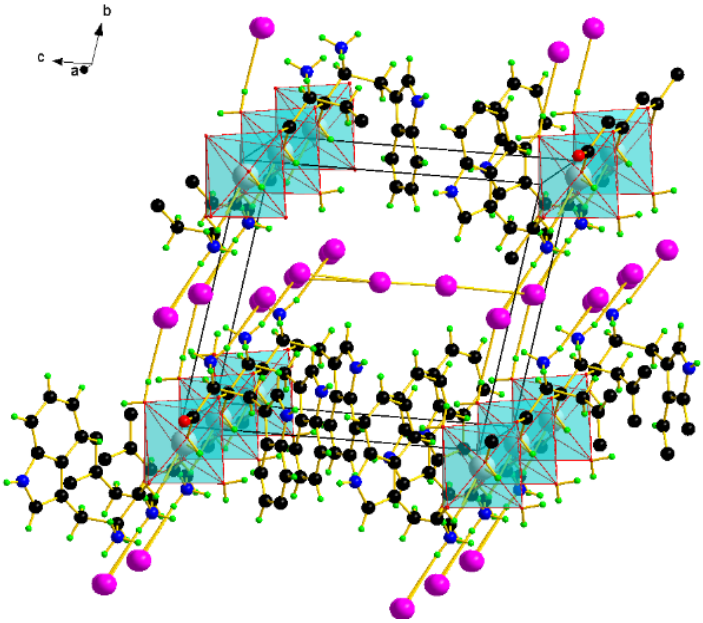


Figure 3 – Perspective view of the crystal structure $C_{11}H_{12}N_2O_2$•$(C_{11}H_{13}N_2O_2)^+$ •Na^+ •$2H_2O$ •$(I_4)^{2-}$

According to the obtained structural data, a search was conducted in the Cambridge Structural Database in order to establish the originality of the results or find analogues in the case of their availability. The search indicated that these crystals are original, were not previously obtained and studied, and new crystallographic data in the CIF format were deposited in the Cambridge Crystallographic Data Centre, the deposit number is CCDC 1877292.

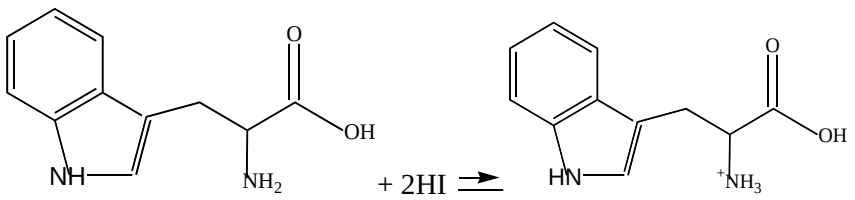
The composition of the semiorganic complex compound formed in the tryptophan-sodium iodide-iodine-water system indicates that the system is non-equilibrium. The iodine hydrolysis reaction takes place in it.

$$H_2O + I_2 \rightarrow HI + HOI \quad (1)$$

$$2HOI \rightarrow 2HI + O_2\uparrow \quad (2)$$

The resulting hydroiodic acid protonates part of the tryptophan molecules at the nitrogen atom of -NH_2 -group.Therefore, in the equilibria in the tryptophan-NaI-I_2-H_2O system, along with the initial components there are protonated tryptophan and triiodide ions, which are formed by the reaction $I_2 + I^- \rightarrow I_3^-$.

Na^+ cation coordinates one tryptophan molecule and one protonated tryptophan molecule (tryptophanium) on the oxygen atoms of the carboxyl groups, as well as two water molecules.Iodide ions formed during dissociation of sodium iodide and iodide ions of hydroiodic acid form with molecular iodine tetraiodide I_4^{2-}.



(3)

The bond length in the iodine molecule (I1-I2, Table 2) is 2.762 Å, while the bond length of ions I_3^- and I_4^-attached to the molecule is as follows: I1-I3 - 3.431 Å I2-I4 - 3.628 Å. In the polyanion I_4^- a rare case is realized when two iodide anions polarize the electrons of the iodine molecule with the formation of a partially positive charge on each atom

$$I^- \overset{3.431Å}{\underline{\quad}} I^{\delta+} \overset{2.762Å}{\underline{\quad}} I^{\delta+} \overset{3.628\ Å}{\underline{\quad}} I^- \quad (4)$$

Determination of the physical-chemical parameters of the compound. UV spectra, a 0.1% aqueous solution of tryptophan as the control and a 0.05% aqueous solution of the obtained iodine complex were measured. The UV spectrum of tryptophan displays two peaks at 218.45 nm at 0.83 A and 278.41 at 0.13A (Figure 4).

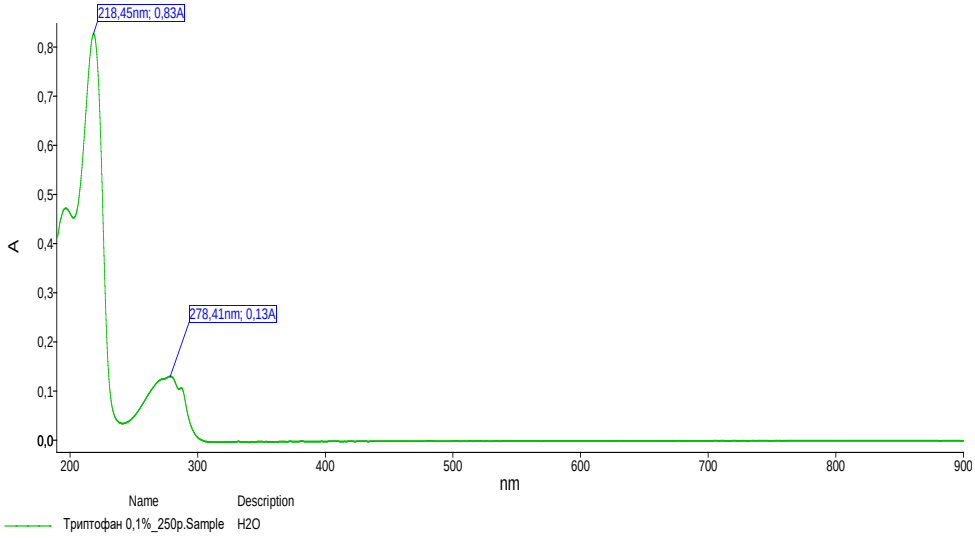


Figure 4 – UV-spectrum of tryptophan.

The pictures below show the UV spectrum of tryptophan and tryptophan complexes: NaI: iodine. The spectra show real absorption bands that do not exist in the spectra of a pure tryptophan sample. These are bands at 190 and 280 nm for the corresponding complex formed by the reaction of tryptophan and potassium iodide with iodine (Figure 5)

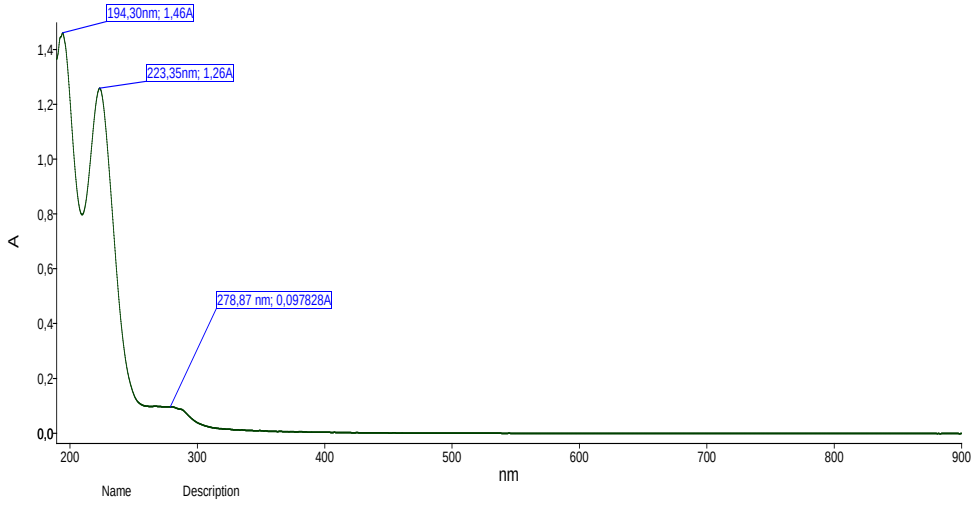


Figure 5 – UV-spectrum of di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide

The thermograms were recorded differential curves of change in the heat capacity of the sample. The DSC curves of tryptophan shows the peak of melting point of tryptophan is 298.1ºC. Starting value of the melting point at the peak is 292ºC. The table data for the melting point of tryptophan is 293-295ºC (Figure 6).

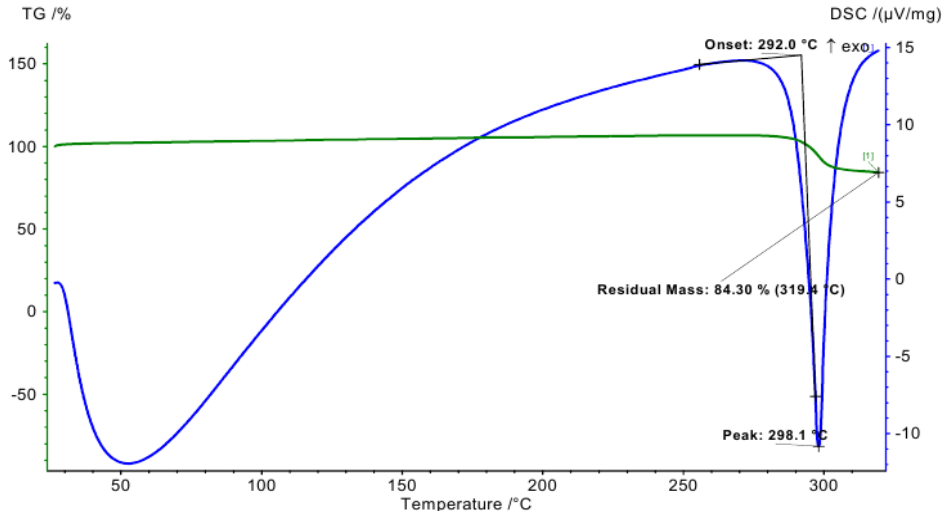


Figure 6 – DSC and TG curves of Tryptophan

The DSC and TG curves of complex shows the peak of melting point of complex is 58.9ºC (Figure 7). The TG curve of the new complex shows us the single stage decomposition.

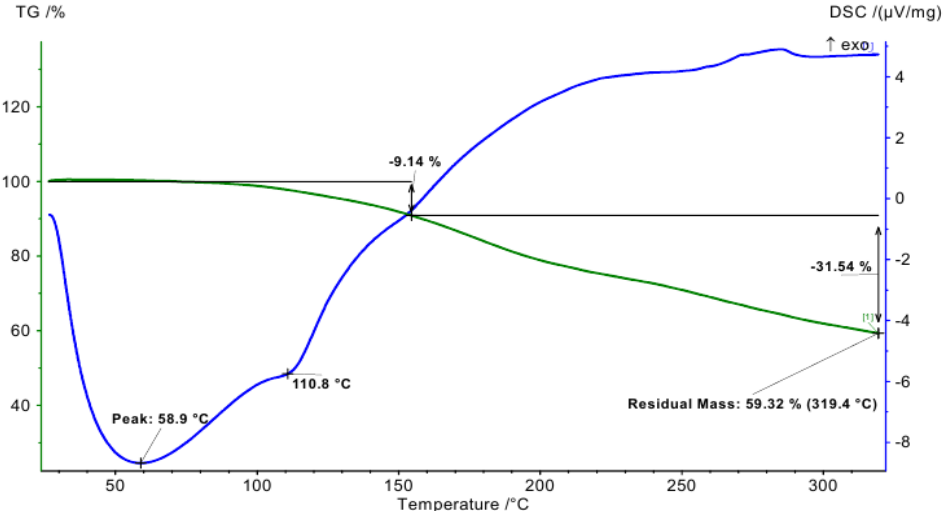


Figure 7 – DSC and TG curves of di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide

Some physicochemical parameters of the di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate) -dihydro-tetraiodide complex is presented at Table 3.

Table 3 – Physicochemical parameters of the di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate) -dihydro-tetraiodide complex

Parameter	Value
Particle shape	elongated needle-like linear stick-like shape
Bulk density, g/cm^3	0,767
Particle size, μm	3,20
Solubility	It is soluble in water, DMSO, slightly soluble in ethanol, acetone and cyclohexane.
pH of aqueous solutions	4,30-4,40

Solubility studies show that the complex dissolves well in solvents with a polarity index of 7.2 and 10.2, and in solvents with an index of 5.1; 4.3 and 0.04 are slightly soluble. The dissolution process in organic solvents is accompanied by the formation of an intense brown color.

Cytotoxicity of the complex. The cytotoxic effect of the coordination compound was studied to determine the maximum concentrations that do not have toxic properties. Monolayer transplantable cell culture MDCK was used to evaluate the toxicity. The results of the study assessing the cytotoxic effect of the coordination compound on MDCK cell culture are presented in Figure 8.

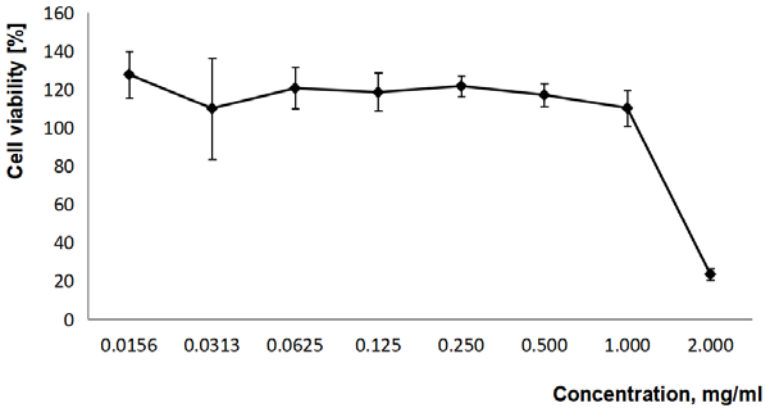


Figure 8 – Cytotoxic effect of the coordination compound on MDCK culture

The toxicity value for the coordination compound was 1.70 mg/mL, which characterizes the examined substance as a low toxic compound.

Antimicrobial activity of complex. The results of testing for antimicrobial activity are presented in Table 4.

Table 4 – Minimum bactericidal concentrations values of the di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide, μg/mL

Sample	Teststrain	Minimum bactericidal concentrations of the complex, μg/mL
$C_{11}H_{12}N_2O_2$• $(C_{11}H_{13}N_2O_2)^+$ • Na^+•$2H_2O$ •$(I_4)^{2-}$	*S. aureus* ATCC 6538-P	125
	S. aureus ATCC-BAA-33591	125
	E. coli ATCC 8739	250
	E. coli ATCC-BAA 2523	125
	P. aeruginosa ATCC 9027	250
	P. aeruginosa TA 2	250

As may be seen from the above, the semiorganic complex contains molecular iodine in its structure, which has antimicrobial properties. Its content in the complex is 26 mass% , and the coordination compound is therefore of particular interest due to its potential antimicrobial activity. This compound is effective against both susceptible and resistant strains of *S. aureus* ATCC 6538-P and *S. aureus* ATCC-BAA-33591, value of the minimum bactericidal concentration is125 μg/mL. The coordination compound is effective against the susceptible P. aeruginosa strain ATCC 9027, as well as the clinical multiresistant of *P. aeruginosa strain TA2*, at a concentration of 250 μg/mL.

The minimum bactericidal concentrations of the compound under testing against the susceptible *E. coli* strain ATCC 8739 and multiresistant *E. coli* strain ATCC-BAA 2523 are 250 μg/mL and 125 μg/mL, respectively. The complex exhibits bactericidal activity against both susceptible and multiresistant bacterial strains.

Determination of the mutagenic activity of the complex in the in vitro micronucleus assay. In these studies, the maximum concentration used is 5 mg / ml, followed by 2-fold dilution in exposure medium. The analysis is carried out with a 4-hour exposure with metabolic activation (+ S9) and without metabolic activation (- S9). For the analysis of micronuclei, slides with L5178Y cells treated with complex di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodide at concentrations from 0.625 to 0.039 mg / ml in the presence or absence of metabolic activation are taken.

Calculation of the number of micronuclei per 1000 mononuclear cells with new complex shows (Figure 9) an unreliable increase in the frequency of micronuclei with an increase in the concentration of complex in the presence and absence of metabolic activation.

Evaluation of the results of the experiment. If the validity of the analysis is satisfied, the following criteria are met:

- Positive response: a test substance is considered a mutagenic substance if it induces a statistically significant, dose-dependent increase in the frequency of mononuclear cells compared to a negative control.

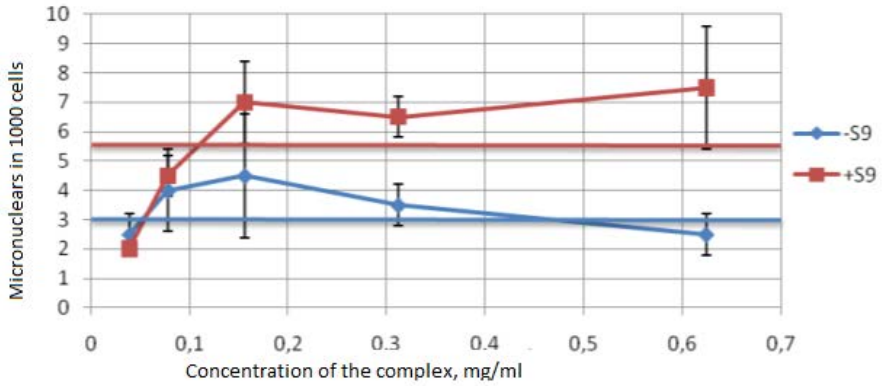


Figure 9 – Frequency of micronuclei in the presence of a new complex

- Negative response: a test substance is considered a non-mutagenic substance if there is no statistically significant increase in the frequency of mononuclear cells compared to a negative control.

Thus, the new complex does not cause any mutagenic effect on mammalian cells of the L5178Y line, both in the presence and in the absence of metabolic activation.

Conclusion. New iodine complex from system tryptophan:NaI:iodine:water system was synthesized. The parameters of triclinic unit cell were determined. As follows from the obtained data, a new complex di- ((2S) -2-amino-3- (1H-indol-3-yl) propionate)-dihydro-tetraiodideor $C_{11}H_{12}N_2O_2$•$(C_{11}H_{13}N_2O_2)^+$ •Na^+ •$2H_2O$ •$(I_4)^{2-}$has low cytotoxicity, direct antiviral effect, antimicrobial activity against antibiotic-resistant strains of microorganisms and is therefore promising for further use as an active antimicrobial substance. New complex does not cause any mutagenic effect on mammalian cells of the L5178Y line, both in the presence and in the absence of metabolic activation.

Acknowledgments. The research was carried out with the financial support of the Republic of Kazakhstan for a fundamental research on the topic "Development of new anti-infectious drugs".

The authors express their gratitude to the staff of the laboratories of virology and microbiology of JSC «Scientific center for anti-infectious drugs», Almaty, Republic of Kazakhstan who provided assistance in preparing the materials of the article.

References

1. Michel F. Compounds of glycine with halogen or metal halogenides: review and comparison // Z. Kristallogr. 2008. Vol. 223. P. 222–232. DOI 10.1524/zkri.2008.0020

2. Sorochinsky A.E., Aceña J.L., Moriwaki H., Sato T., Soloshonok V.A. Asymmetric synthesis of α-amino acids via homologation of Ni(II) complexes of glycine Schiff bases; Part 1:

alkyl halide alkylations // Amino Acids. 2013. Vol. 45. P. 691–718. https://doi.org/10.1007/s00726-013-1539-4

3. Anbu A.M., Alagar M., Raja P.M. Growth of γ-glycine single crystals using the tailored additive of potassium chloride and L-Proline and analyzing micro structural, optical, mechanical and electrical parameters // Chemical Physics Letter. 2021. Vol. 765. P. 138-151. https://doi.org/10.1016/j.cplett.2020.138301

4. Dacko S., Czapla Z., Baran J., Drozd M. Ferroelectricity in $Gly^{\cdot}H_3PO_3$ crystal // Physics Letters A. 1996. Vol. 223. P. 217–220. https://doi.org/10.1016 /S0375-9601(96)00698-6

5. Balashova E. V., Lemanov V.V., Pankova G.A. Acoustic and Dielectric Anomalies in the Temperature Range of a Ferroelectric Phase Transition in Glycine Phosphite Crystals // Phys. Solid State. 2001. Vol. 43. P. 1328–1335. https://doi.org/10.1134/1.1386474

6. Cherouana A., Benali-Cherif N., Bendjeddou L., Merazig H. Diglycinium sulfate // Acta Cryst. 2002. Vol.58. P. 1351–1353. https://doi.org/10.1107/S1600536802019785

7. Ambujam K., Rajarajan K., Selvakumar S., Madhavan J., Mohamed G., Sagayaraj P. Growth and characterization of gelgrown single crystals of bis-glycine hydrogen chloride (BGHC) // Optical Materials. 2007. Vol. 29. P. 657–662. https://doi.org/10.1016/j.optmat.2005.11.008

8. Balakrishnan T, Ramamurthi K. Growth and characterization of glycine lithium sulphate single crystal // Cryst. Res. Technol. 2006. Vol. 41, P.1184–1188. https://doi.org/10.1002/crat.200610746

9. Fleck M., Becker P.,Bohaty L., Held P.,Monteagudo J., Tillmanns E. Physical properties of glycine zinc chloride compounds // 15th Slovenian- Croatian Crystallographic Meeting, Jezersko, Slovenia. Book of Abstracts. 2006. Vol. 37, P. 212. doi 10.1524/zkri.2008.0019.

10. Marcy H. O., Warren L. F., Webb M. S., Ebbers C. A., Velsko S. P., Kennedy G.C. // Appl. Opt. 1992. Vol. 31. P. 5051–5060. doi.org/10.1364/AO.31.005051

11. Wang X.Q., Xu D., Yuan D.R., Tian Y.P., Yu W.T., Sun S. Y. Synthesis, structure and properties of a new nonlinear optical material: zinc cadmium tetrathiocyanate // Mater. Res. Bull. 1999. Vol. 34. P. 2003–2011. https://doi.org/10.1016/S0025-5408(99)00211-1

12. Berdibay S., Sabitov A., Paretskaya N., Islamov R., Tamazyan R. Phenylalanine – iodine complex and its structure // Bul. of the Nat. academy of sciences of the Republic of Kazakhstan. Physico-mathematical series. 2017. Vol. 3, No 312. P. 5-9.

13. Berdibay S., Ermolaev V., Paretskaya N., Sabitov A., Martirosyan K. S. Structure and physical properties of new lithium- and iodine-containing adducts // Proc. of SGEM, Sofia. 2017. Vol. 17, No. 61. P. 319. doi:10.5593/sgem2017/61/S24.042

14. Berdibay S., Sabitov A., Islamov R., Tamazyan R., Paretskaya N., Tokmoldin S., Ilin A., Martirosyan, K. Coordination compounds of lithium halides with certain amino acids // Bul. of Nat. academy of sciences of the Republic of Kazakhstan. 2017. Vol. 367, P. 5-7.

15. CAD-4 Software: Enraf-Nonius. / CAD-4 Software (CAD-4 EXPRESS) Enraf-Nonius. Delft, the Netherlands. 1989. DOI: 10.1107/S0021889894004589

16. Sheldrick G. M. All programs beginning with SHELX // Acta Cryst. 2008. Vol. 64. P. 112-122. https://doi.org/10.1107/S0108767307043930

17. Petricek V., Dusek M., Lukas P. Crystallographic Computing System JANA2006: General features // Zeitschrift für Kristallographie - Crystalline Materials. 2014. Vol. 229. P. 345-352. https://doi.org/10.1515/zkri-2014-1737

18. Spek A. L. PLATON // Acta Cryst. 2009. Vol.65. P.148-155. https://doi.org/10.1107/S090744490804362X

19. M26-A CLSI Methods for Determining Bactericidal Activity of Antimicrobial Agents / Approved Guideline.1999. Vol.19, No. 18.

20. Clinical and Laboratory Standards Institute Performance Standards for Antimicrobial Susceptibility Testing, 26th ed. / CLSI supplement M100S. 2016. Clinical and Laboratory Standards Institute. 950 West Valley Road, Pennsylvania, 19087 USA.

21. Guideline for Research on Chemical Substances No. 487 *In vitro* micronucleus test of mammalian cells, adopted on September 26, 2014.

Information about authors:

Sabitov A.N. – Candidate of chemical sciences (PhD), JSC "Scientific Center for Anti-Infectious Drugs", Almaty, the Republic of Kazakhstan, ORCID ID: 0000-0003-3677-86856,

E-mail: aitugans@mail.ru

Turganbay S. – Doctor PhD, JSC "Scientific Center for Anti-Infectious Drugs", Almaty, the Republic of Kazakhstan, ORCID ID: 0000-0001-9621-3534, E-mail: serik530@mail.ru

Jumagaziyeva A.B. – PhD Student, JSC "Scientific Center for Anti-Infectious Drugs", Almaty, the Republic of Kazakhstan, ORCID ID: 0000-0002-8610-7321, E-mail: r_dawa@mail.ru

Түйіндеме

ДИ- ((2S) -2-АМИН-3- (1Н-ИНДОЛ-3-ИЛ) ПРОПИОНАТ) -ДИГИДРО-ТЕТРАИОДИДТІҢ ҚҰРЫЛЫМЫ ЖӘНЕ ҚАСИЕТТЕРІ

А.Н. Сабитов, С. Тұрғанбай, А. Джумагазиева

Амин қышқылы - сілтілік метал тұзы - иод - су жүйесі негізінде жаңа органикалық комплекс синтезделді. ди- ((2S) -2-амино-3- (1Н-индол-3-ил) пропионат) – дигидро-тетраиодид ретінде анықталған комплекстің физика-химиялық қасиеттері зерттелді. Микроскопиялық талдау көрсеткендей, комплекстің бөлшектері ұзын ине тәрізді сызықты таяқша тәрізді пішінде, орташа мөлшері 2,50-4,00 мм. Комплекстің микробқа қарсы белсенділігі *S. aureus* ATCC 6538-P (мұражайсезімтал штаммы); *S. aureus* ATCC-BAA-39 (мұражайдың тұрақты штаммы); *E. coli* ATCC 8739 (мұражай сезімтал штаммы); *E. coli* ATCC-BAA-196 (мұражайдың тұрақты штаммы); *P. aeruginosa* ATCC 9027 (мұражай сезімтал штаммы); *P. aeruginosa* TA2 жасушаларында тікелей вирусқа және антибиотикке төзімді микроорганизмдердің штамдарына қарсы белсенділігі бар екені анықталды. MDCK жасушасына жасалған зерттеу нәтижесінде цитотоксикалық әсерінің төмендігі көрсетілді. Di- ((2S) -2-амино-3- (1Н-индол-3-ил) пропионат) -дигидро-тетраиодид L5178Y сызықты сүтқоректілер жасушаларына қатысты мутагендіәсер етпейді.

Түйін сөздер: Иод полианион кешені, ди- ((2S) -2-амин-3- (1Н-индол-3-ыл) пропионат) -ди-гидро-тетраиодид, рентгендік құрылымдық талдау, L5178Y сызықты жасушаларына мутагендік тест, цитотоксикалық әсер.

Резюме

СТРУКТУРА И СВОЙСТВА ДИ- ((2S) -2-АМИН-3- (1Н-ИНДОЛ-3-ИЛ) ПРОПИОНАТ) -ДИГИДРО-ТЕТРАИОДИДА

А.Н. Сабитов, С. Турганбай, А. Джумагазиева

Синтезирован новый комплекс йода в системе аминокислота - соль щелочного металла - йод - вода. Изучены физико-химические свойства комплекса ди- ((2S) -2-амино-3- (1Н-индол-3-ил) пропионат) дигидротетраиодид. Микроскопический анализ показывает, что частицы комплекса имеют продолговатую игольчатую

линейную палочковидную форму со средним размером 2,50-4,00 мкм. Определяли цитотоксичность на культуре клеток MDCK, антимикробную активность на *S. aureus* ATCC 6538-P (музейно-чувствительный штамм); *S. aureus* ATCC-BAA-39 (музейный мультирезистентный штамм); *E. coli* ATCC 8739 (музейно-чувствительный штамм); *E. coli* ATCC-BAA-196 (музейный мультирезистентный штамм); *P. aeruginosa* ATCC 9027 (музейно-чувствительный штамм); *P. aeruginosa* TA2. Комплекс обладает низкой цитотоксичностью, прямым противовирусным действием и антимикробной активностью в отношении устойчивых к антибиотикам штаммов микроорганизмов. Ди- ((2S) -2-амино-3- (1H-индол-3-ил) пропионат) дигидротетраиодид не оказывает мутагенного действия на клетки млекопитающих линии L5178Y как в присутствии, так и в отсутствии метаболической активации.

Ключевые слова: иод-полианионный комплекс, ди- ((2S) -2-амино-3- (1H-индол-3-ил) пропионат) -дигидротетраиодид, рентгеноструктурный анализ, мутагенный тест на клетках L5178Y, цитотоксичность.

Ғылыми жарияланымдардың этикасы

Редакциялық алқа және "Қазақстанның химия журналы" ғылыми журналының (бұдан әрі – Журнал) бас редакторы "Жарияланымдар жөніндегі этика комитеті" (Committee on Publication Ethics – COPE) (http://publicationethics.org/about), **"Еуропалық ғылыми редакторлар қауымдастығы"** (European Association of Science Editors – EASE) (http://www.ease.org.uk) **және "Ғылыми жарияланымдар әдебі жөніндегі комитеттің"** (http://publicet.org/code/) **қабылданған халықаралық стандарттарды ұстанады.**

Баспа қызметіндегі әділетсіз тәжірибені болдырмау мақсатында (плагиат, жалған ақпаратты ұсыну және т.б.) және ғылыми жарияланымдардың жоғары сапасын қамтамасыз ету, автордың алған ғылыми нәтижелерін жұртшылықпен тану мақсатында редакциялық кеңестің әрбір мүшесі, автор, рецензент, сондай-ақ баспа процесіне қатысатын мекемелер этикалық стандарттарды, нормалар мен ережелерді сақтауға және олардың бұзылуын болдырмау үшін барлық шараларды қабылдауға міндетті. Осы процеске қатысушылардың барлығының ғылыми жарияланым этикасы ережелерін сақтауы авторлардың зияткерлік меншік құқықтарын қамтамасыз етуге, басылым сапасын арттыруға және авторлық материалдарды жеке тұлғалардың мүддесі үшін заңсыз пайдалану мүмкіндігін болдырмауға ықпал етеді.

Редакцияға келіп түскен барлық ғылыми мақалалар міндетті түрде екі жақты шолудан өтеді. Журнал редакциясы мақаланың журнал профиліне, ресімдеу талаптарына сәйкестігін белгілейді және оны қолжазбаның ғылыми құндылығын айқындайтын және мақала тақырыбына неғұрлым жақын ғылыми мамандандырулары бар екі тәуелсіз рецензент – мамандарды тағайындайтын журналдың жауапты хатшысының бірінші қарауына жібереді. Мақалаларды рецензиялауды редакциялық кеңес және редакциялық алқа мүшелері, сондай-ақ басқа елдердің шақырылған рецензенттері жүзеге асырады. Мақалаға сараптама жүргізу үшін белгілі бір рецензентті таңдау туралы шешімді Бас редактор қабылдайды. Рецензиялау мерзімі 2-4 аптаны құрайды, бірақ рецензенттің өтініші бойынша ол ұзартылуы мүмкін.

Редакция мен рецензент қарауға жіберілген жарияланбаған материалдардың құпиялылығын сақтауға кепілдік береді. Жариялау туралы шешімді журналдың редакциялық алқасы рецензиялаудан кейін қабылдайды. Қажет болған жағдайда қолжазба авторларға рецензенттер мен редакторлардың ескертулері бойынша пысықтауға жіберіледі, содан кейін ол қайта рецензияланады. Редакция этика ережелерін бұзған жағдайда мақаланы жариялаудан бас тартуға құқылы. Егер ақпаратты плагиат деп санауға жеткілікті негіз болса, жауапты редактор жариялауға жол бермеуі керек.

Авторлар редакцияға ұсынылған материалдардың жаңа, бұрын жарияланбаған және түпнұсқа екендігіне кепілдік береді. Авторлар ғылыми нәтижелердің сенімділігі мен маңыздылығына, сондай-ақ ғылыми этика қағидаттарын сақтауға, атап айтқанда, ғылыми этиканы бұзу фактілеріне жол бермеуге (ғылыми деректерді тұжырымдау, зерттеу деректерін бұрмалауға әкелетін бұрмалау, плагиат және жалған тең авторлық, қайталау, басқа адамдардың нәтижелерін иемдену және т. б.) жауапты болады.

Мақаланы редакцияға жіберу авторлардың мақаланы (түпнұсқада немесе басқа тілдерге немесе басқа тілдерге аударылған) басқа журналға(журналдарға) берме-

генін және бұл материал бұрын жарияланбағанын білдіреді. Әйтпесе, мақала авторларға авторлық құқықты бұзғаны үшін мақаланы қабылдамау туралы ұсыныспен дереу қайтарылады. Басқа автор жұмысының 10 пайызынан астамын оның авторлығын және дереккөзге сілтемесіз сөзбе-сөз көшіруге жол берілмейді. Алынған фрагменттер немесе мәлімдемелер автор мен бастапқы көзді міндетті түрде көрсете отырып жасалуы керек. Шамадан тыс көшіру, сондай-ақ кез-келген нысандағы плагиат, оның ішінде рәсімделмеген дәйексөздер, өзгерту немесе басқа адамдардың зерттеулерінің нәтижелеріне құқықтар иемдену этикалық емес және қолайсыз. Зерттеу барысына қандай да бір түрде әсер еткен барлық адамдардың үлесін мойындау қажет, атап айтқанда, мақалада зерттеу жүргізу кезінде маңызды болған жұмыстарға сілтемелер ұсынылуы керек. Қосалқы авторлардың арасында зерттеуге қатыспаған адамдарды көрсету болмайды.

Егер жұмыста қате табылса, редакторға тез арада хабарлау керек және бірге түзету туралы шешім қабылдау керек.

Қолжазбаны жариялаудан бас тарту туралы шешім рецензенттердің ұсынымдарына сәйкес редакциялық алқа отырысында қабылданады. Редакциялық алқаның шешімімен жариялауға ұсынылмаған мақала қайта қарауға қабылданбайды. Жариялаудан бас тарту туралы хабарлама авторға электрондық пошта арқылы жіберіледі.

Редакциялық алқа мақаланы жариялауға жіберу туралы шешім қабылдағаннан кейін редакция бұл туралы авторға хабарлайды және жариялау мерзімін көрсетеді. Рецензиялардың түпнұсқалары журналдың редакциясында 3 жыл бойы сақталады.

Этика научных публикаций

Редакционная коллегия и главный редактор научного журнала «Химический журнал Казахстана» (далее – Журнал) придерживаются принятых международных стандартов «Комитета этики по публикациям» (Committee on Publication Ethics – COPE) (http://publicationethics.org/about), **«Европейской ассоциации научных редакторов»** (European Association of Science Editors – EASE) (http://www.ease.org.uk) и «**Комитета по этике научных публикаций**» (http://publicet.org/code/).

Во избежание недобросовестной практики в публикационной деятельности (плагиат, изложение недостоверных сведений и др.) и в целях обеспечения высокого качества научных публикаций, признания общественностью, полученных автором научных результатов, каждый член редакционного совета, автор, рецензент, а также учреждения, участвующие в издательском процессе, обязаны соблюдать этические стандарты, нормы и правила и принимать все меры для предотвращения их нарушений. Соблюдение правил этики научных публикаций всеми участниками этого процесса способствует обеспечению прав авторов на интеллектуальную собственность, повышению качества издания и исключению возможности неправомерного использования авторских материалов в интересах отдельных лиц.

Все научные статьи, поступившие в редакцию, подлежат обязательному двойному слепому рецензированию. Редакция Журнала устанавливает соответствие статьи профилю Журнала, требованиям к оформлению и направляет ее на первое рассмотрение ответственному секретарю Журнала, который определяет научную ценность рукописи и назначает двух независимых рецензентов – специалистов, имеющих наиболее близкие к теме статьи научные специализации. Рецензирование статей осуществляется членами редакционного совета и редакционной коллегии, а также приглашенными рецензентами других стран. Решение о выборе того или иного рецензента для проведения экспертизы статьи принимает главный редактор. Срок рецензирования составляет 2-4 недели, но по просьбе рецензента он может быть продлен.

Редакция и рецензент гарантируют сохранение конфиденциальности неопубликованных материалов присланных на рассмотрение работ. Решение о публикации принимается редакционной коллегией Журнала после рецензирования. В случае необходимости рукопись направляется авторам на доработку по замечаниям рецензентов и редакторов, после чего она повторно рецензируется. Редакция оставляет за собой право отклонить публикацию статьи в случае нарушения правил этики. Ответственный редактор не должен допускать к публикации информацию, если имеется достаточно оснований полагать, что она является плагиатом.

Авторы гарантируют, что представленные в редакцию материалы являются новыми, ранее неопубликованными и оригинальными. Авторы несут ответственность за достоверность и значимость научных результатов, а также соблюдение принципов научной этики, в частности, недопущение фактов нарушения научной этики (фабрикация научных данных, фальсификация, ведущая к искажению исследовательских данных, плагиат и ложное соавторство, дублирование, присвоение чужих результатов и др.)

Направление статьи в редакцию означает, что авторы не передавали статью (в оригинале или в переводе на другие языки или с других языков) в другой журнал(ы)

и что этот материал не был ранее опубликован. В противном случае статья немедленно возвращается авторам с рекомендацией отклонить статью за нарушение авторских прав. Не допускается дословное копирование более 10 процентов работы другого автора без указания его авторства и ссылок на источник. Заимствованные фрагменты или утверждения должны быть оформлены с обязательным указанием автора и первоисточника. Чрезмерные заимствования, а также плагиат в любых формах, включая неоформленные цитаты, перефразирование или присвоение прав на результаты чужих исследований, неэтичны и неприемлемы. Необходимо признавать вклад всех лиц, так или иначе повлиявших на ход исследования, в частности, в статье должны быть представлены ссылки на работы, которые имели значение при проведении исследования. Среди соавторов недопустимо указывать лиц, не участвовавших в исследовании.

Если обнаружена ошибка в работе, необходимо срочно уведомить редактора и вместе принять решение об исправлении.

Решение об отказе в публикации рукописи принимается на заседании редакционной коллегии в соответствии с рекомендациями рецензентов. Статья, не рекомендованная решением редакционной коллегии к публикации, к повторному рассмотрению не принимается. Сообщение об отказе в публикации направляется автору по электронной почте.

После принятия редколлегией Журнала решения о допуске статьи к публикации редакция информирует об этом автора и указывает сроки публикации. Оригиналы рецензий хранятся в редакции Журнала в течение 3 лет.

Ethics of scientific publications

The editorial board and editor-in-chief of the scientific journal "Chemical Journal of Kazakhstan" (hereinafter - the Journal) adhere to the accepted international standards of "the Committee on Publication Ethics" (COPE) (http://publicationethics.org/about), **"European Association of Science Editors – EASE"** (http://www.ease.org.uk) **and "Committee on the Ethics of Scientific Publications"** (http://publicet.org/code/).

Public recognition of the scientific results obtained by the author, each member of the editorial board, author, reviewer, as well as institutions involved in the publishing process is obliged to comply with ethical standards, norms, and rules and take all measures to prevent violations thereof. This is needed to avoid unfair practice in publishing activities (plagiarism, presentation of false information, etc.) and to ensure the high quality of scientific publications. Compliance with the rules of ethics of scientific publications by all participants in this process contributes to ensuring the rights of authors to intellectual property, improving the quality of the publication, and excluding the possibility of illegal use of copyright materials in the interests of individuals.

All scientific articles submitted to the editorial office are subject to mandatory double-blind review. The editorial board of the Journal establishes the correspondence of the article to the profile of the Journal, the requirements for registration and sends it for the first consideration to the executive secretary of the Journal, who determines the scientific value of the manuscript and appoints two independent reviewers - specialists who have scientific specializations closest to the topic of the article. Reviewing of articles is carried out by members of the editorial board and editorial board, as well as invited reviewers from other countries. The decision on choosing a reviewer for the examination of the article is made by the editor-in-chief. The review period is 2-4 weeks, but it can be extended at the request of the reviewer.

The editorial board and the reviewer guarantee the confidentiality of unpublished materials sent for consideration. The decision on publication is made by the editorial board of the Journal after reviewing. The manuscript is sent to the authors for revision based on the comments of reviewers and editors if necessary. After which, it is re-reviewed. The editors reserve the right to reject the publication of an article in case of a violation of the rules of ethics. The executive editor should not allow information to be published if there are sufficient grounds to believe that it is plagiarism.

The authors guarantee that the submitted materials to the editorial office are new, previously unpublished, and original. Authors are responsible for the reliability and significance of scientific results, as well as adherence to the principles of scientific ethics, in particular, the prevention of violations of scientific ethics (fabrication of scientific data, falsification leading to distortion of research data, plagiarism, and false co-authorship, duplication, appropriation of other people's results, etc.).

The submission of an article to the Editorial Board means that the authors did not transmit the article (in original or translation into other languages or from other languages) to another journal (s), and this material has not been previously published. Otherwise, the article is immediately returned to the authors with a recommendation to reject the article for copyright infringement. Verbatim copying of more than 10 percent of another author's work is not allowed without indicating his authorship and links to the source. Borrowed fragments or statements must be made with the obligatory indication of

the author and the source. Excessive borrowing as well as plagiarism in any form, including unofficial quotations, paraphrasing, or appropriation of rights to the results of other people's research, is unethical and unacceptable. It is necessary to recognize the contribution of all persons, who in one way or another influenced the course of the research in particular the article, should contain references to works that were of importance in the conduct of the research. Among the co-authors, it is inadmissible to indicate persons who did not participate in the study.

If an error is found in work, it is necessary to notify the editor and together make a decision on the correction.

The decision to refuse publication of the manuscript is made at a meeting of the editorial board by the recommendations of the reviewers. An article not recommended for publication by the decision of the editorial board is not accepted for reconsideration. The refusal to publish is sent to the author by e-mail.

After the editorial board of the Journal decides on the admission of the article for publication, the editorial board informs the author about it and indicates the terms of publication. The originals of the reviews are kept in the editorial office for three years.

Верстка на компьютере *Д. Н. Калкабековой*

Подписано в печать 25.06.2021.
Формат 70x100 $^{1}/_{16}$. 9,8 п.л. Бумага офсетная. Тираж 500.

Типография ТОО «Luxe Media Group»
г. Алматы, ул. Станиславского, 43