

ISSN 2224-526X

ҚАЗАҚСТАН РЕСПУБЛИКАСЫ
ҰЛТТЫҚ ҒЫЛЫМ АКАДЕМИЯСЫНЫҢ
Қазақ ұлттық аграрлық университеті

Х А Б А Р Л А Р Ы

ИЗВЕСТИЯ

НАЦИОНАЛЬНОЙ АКАДЕМИИ НАУК
РЕСПУБЛИКИ КАЗАХСТАН
Қазақстан Республикасының
Ұлттық ғылым академиясының
Қазақ ұлттық аграрлық университеті

IZVESTIĀ

NATIONAL'NOJ AKADEMII NAUK
RESPUBLIKI KAZAHSTAN
Kazakh national
agrarian university

SERIĀ AGRARNYH NAUK

5 (53)

SEPTEMBER – OCTOBER 2019

PUBLISHED SINCE JANUARY 2011

PUBLISHED 6 TIMES A YEAR

ALMATY, NAS RK

Б а с р е д а к т о р

Есполов Т.И.,

э.ғ.д, профессор,

ҚР ҰҒА академигі және вице-президенті

Р е д а к ц и я а л қ а с ы:

Байзақов С.Б., э.ғ.д, проф., ҚР ҰҒА академигі (бас редактордың орынбасары); **Тиреуов К.М.**, э.ғ.д, проф., ҚР ҰҒА академигі (бас редактордың орынбасары); **Елешев Р.Е.**, т.ғ.д., проф., ҚР ҰҒА академигі; **Рау А.Г.**, т.ғ.д., проф., ҚР ҰҒА академигі; **Иванов Н.П.**, в.ғ.д, проф., ҚР ҰҒА академигі; **Кешуов С.А.**, т.ғ.д., проф., ҚР ҰҒА академигі; **Мелдебеков А.**, а.ш.ғ.д., проф., ҚР ҰҒА академигі; **Чоманов У.Ч.**, т.ғ.д., проф., ҚР ҰҒА академигі; **Елюбаев С.З.**, а.ш.ғ.д., проф., ҚР ҰҒА академигі; **Садықұлов Т.**, а.ш.ғ.д., проф., академигі; **Баймұқанов Д.А.**, а.ш.ғ.д., проф., ҚР ҰҒА корр-мүшесі; **Сансызбай А.Р.**, а.ш.ғ.д., проф., ҚР ҰҒА корр-мүшесі; **Умбетаев И.**, а.ш.ғ.д., проф., ҚР ҰҒА академигі; **Оспанов С.Р.**, а.ш.ғ.д., проф., ҚР ҰҒА құрметті мүшесі; **Олейченко С.И.**, а.ш.ғ.д., проф.; **Кененбаев С.Б.**, а.ш.ғ.д., проф., ҚР ҰҒА корр-мүшесі; **Омбаев А.М.**, а.ш.ғ.д., проф. ҚР ҰҒА корр-мүшесі; **Молдашев А.Б.**, э.ғ.д., проф., ҚР ҰҒА құрметті мүшесі; **Сагитов А.О.**, б.ғ.д., ҚР ҰҒА академигі; **Сапаров А.С.**, а.ш.ғ.д., проф., ҚР АШҒА академигі; **Балгабаев Н.Н.**, а.ш.ғ.д., проф.; **Умирзаков С.И.**, т.ғ.д, проф.; **Султанов А.А.**, в.ғ.д., проф., ҚР АШҒА академигі; **Алимкулов Ж.С.**, т.ғ.д., проф., ҚР АШҒА академигі; **Сарсембаева Н.Б.**, в.ғ.д., проф.

Р е д а к ц и я к е ñ е с і:

Fasler-Kan Elizaveta, Dr., University of Basel Switzerland; **Koolmees Petrus Adrianus**, Prof. Dr., Utrecht University, The Netherlands; **Babadoost-Kondri Mohammad**, Prof., University of Illinois, USA; **Yus Aniza Binti Yusof**, Dr., University Putra, Malaysia; **Hesseln Hayley Fawn**, As. Prof., University of Saskatchewan, Canada; **Alex Morgounov**, Pr., International Maize and Wheat Improvement Center Turkey; **Андреш С.**, Молдова Республикасы ҰҒА академигі; **Гаврилюк Н.Н.**, Украина ҰҒА академигі; **Герасимович Л.С.**, Беларусь Республикасының ҰҒА академигі; **Мамедов Г.**, Азербайжан Республикасының ҰҒА академигі; **Шейко И.П.**, Беларусь Республикасының ҰҒА академигі; **Жалнин Э.В.**, т.ғ.д., проф., Ресей; **Боинчан Б.**, а.ш.ғ.д, проф., Молдова Республикасы; **Юлдашбаев Ю.А.**, а.ш.ғ.д, проф., РФА корр-мүшесі, Ресей.

Главный редактор

Есполов Т.И.,

доктор эконом. наук, проф.,
вице-президент и академик НАН РК

Редакционная коллегия:

Байзаков С.Б., доктор эконом. наук, проф., академик НАН РК (заместитель главного редактора); **Тиреуов К.М.**, доктор эконом. наук, проф., академик НАН РК (заместитель главного редактора); **Елешев Р.Е.**, доктор техн. наук, проф., академик НАН РК; **Рау А.Г.**, доктор техн. наук, проф., академик НАН РК; **Иванов Н.П.**, доктор ветеринар. наук, проф., академик НАН РК; **Кешуов С.А.**, доктор техн. наук, проф., академик НАН РК; **Мелдебеков А.**, доктор сельхоз. наук, проф., академик НАН РК; **Чоманов У.Ч.**, доктор техн. наук, проф., академик НАН РК; **Елюбаев С.З.**, доктор сельхоз. наук, проф., академик НАН РК; **Садыкулов Т.**, доктор сельхоз. наук, проф., академик НАН РК; **Баймуқанов Д.А.**, доктор сельхоз. наук, проф., член-корр. НАН РК; **Сансызбай А.Р.**, доктор сельхоз. наук, проф., член-корр. НАН РК; **Умбетаев И.**, доктор сельхоз. наук, проф., академик НАН РК; **Оспанов С.Р.**, доктор сельхоз. наук, проф., Почетный член НАН РК; **Олейченко С.И.**, доктор сельхоз. наук, проф.; **Кененбаев С.Б.**, доктор сельхоз. наук, проф., член-корр. НАН РК; **Омбаев А.М.**, доктор сельхоз. наук, проф. член-корр. НАН РК.; **Молдашев А.Б.**, доктор эконом. наук, проф., Почетный член НАН РК; **Сагитов А.О.**, доктор биол. наук, академик НАН РК; **Сапаров А.С.**, доктор сельхоз. наук, проф., академик АСХН РК; **Балгабаев Н.Н.**, доктор сельхоз. наук, проф.; **Умирзаков С.И.**, доктор техн. наук, проф.; **Султанов А.А.**, доктор ветеринар. наук, проф., академик АСХН РК; **Алимкулов Ж.С.**, доктор техн. наук, проф., академик АСХН РК; **Сарсембаева Н.Б.**, доктор ветеринар. наук, проф.

Редакционный совет:

Fasler-Kan Elizaveta, Dr., University of asel Switzeland; **Koolmees Petrus Adrianus**, Prof. Dr., Utrecht University, The Netherlands; **Babadoost-Kondri Mohammad**, Prof., University of Illinois, USA; **Yus Aniza Binti Yusof**, Dr., University Putra, Malaysia; **Hesseln Hayley Fawn**, As.Prof., University of Saskatchewan, Canada; **Alex Morgounov**, Pr., International Maize and Wheat Improvement Center Turkey; **Андреш С.**, академик НАН Республики Молдова; **Гаврилюк Н.Н.**, академик НАН Украины; **Герасимович Л.С.**, академик НАН Республики Беларусь; **Мамедов Г.**, академик НАН Республики Азербайджан; **Шейко И.П.**, академик НАН Республики Беларусь; **Жалнин Э.В.**, доктор техн. наук, проф., Россия; **Боинчан Б.**, доктор сельхоз. наук, проф., Республика Молдова; **Юлдашбаев Ю.А.**, доктор сельхоз. наук, проф., член-корр. РАН, Россия.

Известия Национальной академии наук Республики Казахстан. Серия аграрных наук.

ISSN 2224-526X

Собственник: ООО «Национальная академия наук Республики Казахстан» (г. Алматы)

Свидетельство о постановке на учет периодического печатного издания в Комитете информации и архивов Министерства культуры и информации Республики Казахстан № 10895-Ж, выданное 30.04.2010 г.

Периодичность 6 раз в год

Тираж: 300 экземпляров

Адрес редакции: 050010, г. Алматы, ул. Шевченко, 28, ком. 219-220, тел. 272-13-19, 272-13-18

<http://agricultural.kz/index.php/en/>

© Национальная академия наук Республики Казахстан, 2019

Адрес типографии: ИП «Аруна», г. Алматы, ул. Муратбаева, 75

Chief Editor

Espolov T.I.,

Dr. economy. Sciences, prof.,
Vice President and academician of the NAS RK

Editorial Board:

Baizakov S.B., Dr. of economy sciences, prof., academician of NAS RK (deputy editor); **Tireuov K.M.**, Doctor of Economy Sciences., prof., academician of NAS RK (deputy editor); **Eleshev R.E.**, Dr. Of agricultural sciences, prof., academician of NAS RK; **Rau A.G.**, Dr. sciences, prof., academician of NAS RK; **Ivanov N.P.**, Dr. of veterinary sciences, prof., academician of NAS RK; **Keshuov S.A.**, Dr. sciences, prof., academician of NAS RK; **Meldebekov A.**, doctor of agricultural sciences, prof., academician of NAS RK; **Chomanov U.Ch.**, Dr. sciences, prof., academician of NAS RK; **Yelyubayev S.Z.**, Dr. of agricultural sciences, prof., academician of NAS RK; **Sadykulov T.**, Dr. Farm. Sciences, prof., academician of NAS RK; **Baimukanov D.A.**, doctor of agricultural sciences, prof., corresponding member NAS RK; **Sansyzbai A.R.**, doctor of agricultural sciences, prof., corresponding member NAS RK; **Umbetaev I.**, Dr. Farm. Sciences, prof., academician of NAS RK; **Ospanov S.R.**, Dr. agricultural sciences, prof., Honorary Member of NAS RK; **Oleychenko S.N.**, Dr. Of agricultural sciences, prof.; **Kenenbayev S.B.**, Dr. Agricultural sciences, prof., corresponding member NAS RK; **Ombayev A.M.**, Dr. Agricultural sciences, Prof. corresponding member NAS RK; **Moldashev A.B.**, Doctor of Economy sciences, prof., Honorary Member of NAS RK; **Sagitov A.O.**, Dr. biol. sciences, academician of NAS RK; **Saparov A.S.**, Doctor of agricultural sciences, prof., academician of NAS RK; **Balgabaev N.N.**, the doctor agricultural sciences, Prof.; **Umirzakov S.I.**, Dr. Sci. Sciences, Prof.; **Sultanov A.A.**, Dr. of veterinary sciences, prof., academician of the Academy of Agricultural Sciences of Kazakhstan; **Alimkulov J.C.**, Dr. of tekhncial sciences, prof., academician of the Academy of Agricultural sciences of Kazakhstan; **Sarsembayeva N.B.**, Dr. veterinary sciences, prof.

Editorial Board:

Fasler-Kan Elizaveta, Dr., University of Basel Switzzeland; **Koolmees Petrus Adrianus**, Prof. Dr., Utrecht University, The Netherlands; **Babadoost-Kondri Mohammad**, Prof., University of Illinois, USA; **Yus Aniza Binti Yusof**, Dr., University Putra, Malaysia; **Hesseln Hayley Fawn**, As. Prof., University of Saskatchewan, Canada; **Alex Morgounov**, candidate of agricultural sciences, International Maize and Wheat Improvement Center Turkey; **Andresh S.**, academician of NAS of Moldova; **Gavriluk N.N.**, academician of NAS of Ukraine; **Gerasimovich L.S.**, academician of NAS of Belorassia; **Mamadov G.**, academician of NAS of Azerbaijan; **Sheiko I.P.**, academician of NAS of Belorassia; **Zhalnin E.V.**, Dr. of technical sciences, professor, Russia, **Boinchan B.**, doctor of agricultural sciences, prof., Moldova; **Yuldashbayev Y.A.**, doctor of agricultural sciences, prof., corresponding member of RAS, Russia.

News of the National Academy of Sciences of the Republic of Kazakhstan. Series of Agrarian Sciences.

ISSN 2224-526X

Owner: RPA "National Academy of Sciences of the Republic of Kazakhstan" (Almaty)

The certificate of registration of a periodic printed publication in the Committee of Information and Archives of the Ministry of Culture and Information of the Republic of Kazakhstan N 10895-Ж, issued 30.04.2010

Periodicity: 6 times a year

Circulation: 300 copies

Editorial address: 28, Shevchenko str., of.219-220, Almaty, 050010, tel. 272-13-19, 272-13-18,

<http://nauka-nanrk.kz/agricultural.kz>

© National Academy of Sciences of the Republic of Kazakhstan, 2019

Address of printing house: ST "Aruna", 75, Muratbayev str, Almaty

NEWS

OF THE NATIONAL ACADEMY OF SCIENCES OF THE REPUBLIC OF KAZAKHSTAN

SERIES OF AGRICULTURAL SCIENCES

ISSN 2224-526X

Volume 5, Number 53 (2019), 32 – 38

<https://doi.org/10.32014/2019.2224-526X.57>

UDC 619.9:615.2.014

B. F. Kerimzhanova, L. N. Ivanova, A. I. Ilyin

JSC "Scientific Center for Anti-Infectious Drugs", Almaty, Kazakhstan.

E-mail: scaid@scaid.kz, scaid@mail.ru, kbf19@mail.ru

**EFFICIENCY OF THE IODINE-CONTAINING COMPLEX
AGAINST AVIAN INFLUENZA A VIRUS SERIES**

Abstract. The paper contains materials on the study of exposure to avian influenza A virus iodine-containing complexes synthesized in the JSC "Scientific Center of Anti-Infectious Drugs". Conducted screening of educed the most active iodine-containing complex from a nine investigational. It was found that the iodine-containing complex is a low-toxic compound and exhibiting antiviral activity against influenza A virus. It has a high potentiating effect when combined with commercial antiviral drugs.

Keywords: iodine-containing complexes, cytotoxicity, acute toxicity, influenza viruses, antiviral activity, potentiating action.

Introduction. The problem of improving systems of ant epizootic measures for the prevention and treatment of infectious diseases has always been and remains very relevant. According to the literature, an analysis of the epizootic situation shows that in recent years there has been an increasing threat of widespread infectious diseases throughout the world, which brought a significant economic damage and posing a danger to human infection. Among viral diseases, bird flu comes first. This virus - refers to a highly contagious and widespread viral infection. The causative agent of the infection - the influenza virus is divided into three serological types: A, B and C. Type A viruses causes diseases in animals and humans [1-6].

Currently, bird flu remains a global problem in veterinary medicine. According to the World Organization for Animal Health (OIE), in 2018 507 foci of highly pathogenic avian influenza were registered in 35 countries such as Afghanistan (3), Bangladesh (2), Bulgaria (25), United Kingdom (21), Vietnam (10), Germany (5), Denmark (30), India (11), Iraq (15), Cambodia (7), China (13), Russia (82), Saudi Arabia (22), Sweden (11), Japan (14) and etc. The virus have been reported in herds of agricultural and wild bird populations in 15 countries in Asia, Africa, Europe and United States. There were registered cases of highly pathogenic influenza in the world: H5N1 (17 countries), H5N2 (3 countries), H5N5 (Germany, Holland, Montenegro), H5N6 (5 countries), H5N9 (France), H7N7 (Italy), H7N1 (Algeria). The most propagation is the H5N6 influenza virus, as well as similar viruses of the subtypes H5N8, H5N1. Seasonal migrations of birds from Southeast Asia to the Russian Federation during the nesting period are the main prerequisites for the possibility of influenza infection of poultry in industrial bird's farms and private farmsteads. The likelihood of a bird flu virus entering the territory of Kazakhstan with migratory flows of migratory birds remains quite high. According to the WHO experts, every year from 3 to 5 million people become ill with severe forms of influenza and from 250,000 to 500,000 people die around the world (Uchaykin V.F., 2004, I. Toshihiro, 2001).

Despite this, the practice of modern veterinary medicine uses a relatively small set of drugs with a wide range of antiviral effects. The emergence of drug resistance in viral pathogens to antiviral drugs leads to a decrease or complete loss of the effectiveness of the therapy and the flightiness of spread of infection goes down, this leads with searching of new drugs (Sidorenko S.V., 2004, Abraham EP, 1940, Walsh C. 2000). One of the main directions in the development of antiviral drugs is the synthesis of

analogues from known drugs. So iodine-containing drugs widely used in veterinary medicine and medicine, determine high biological activity and versatile pharmacological action, without causing resistance in the pathogen [7-10]. This work will present the results of studies, which will indicate new synthesized iodine – containing complexes for avian influenza virus type A [11, 12].

Methodology and research method. For the research were used: transplantable cell line MDCK (Madin-Darby canine kidney); - seven-day-old chickens weighing 250-350 g, - sexually mature outbred mice of both sexes, weighing 18-24 g, rats weighing 160-230 g, 7-18 day old developing chicken embryos. During the conducting of research the following strains of influenza viruses were used: - Waybrige strain A/78, (H7N7)/FPV /; Rostock strain A/34, (H7N1), /FPV/black laughter strain A, Atyrau 744/04, (H13N6); Almaty strain A 5/98, (H3N2).

Cell and virus types were cultured in a monolayer using DMEM medium and 10% cattle serum was added (Applichem, Sigma, USA). The propagation of influenza viruses was carried out on seven to nine chicken embryos by introducing 0.2 ml of the virus into the allantois cavity and on the MDCK cell culture by infection of the cell monolayer. Infectious virus titer was determined in a hem agglutination reaction (RGA according to Reed & Muench).

Results of own research. A study was made of 9 iodine-containing α -dextrin complexes capable of penetrating the membrane and nucleus of a microbial cell. The molecular iodine of the active drugs' complex compound is located inside of the α -dextrin helix and is coordinated by alkali metal halides and polypeptides. In this structure, molecular iodine difficulty to interact with blood components and reaches the pathogen cell unchanged, because only nucleotides of the DNA of a pathogen can compete with polypeptides for complexation with iodine. The biopharmaceutical solubility of the iodine-containing complexes which were taken for the study was researched in the pH range of 1.2; 4,5; 6.8 corresponding to physiological fluids of the gastrointestinal tract. The determination of the permeability of iodine-containing complexes was carried out on an MDCK cell culture. In 96 well plates with MDCK cell culture, 0.2 ml of DMEM medium containing the test substances at a concentration of 0.5 mg / ml was added. The results of studies of the active complex substance's ability to dissolve when applied internally are presented in figures 1.

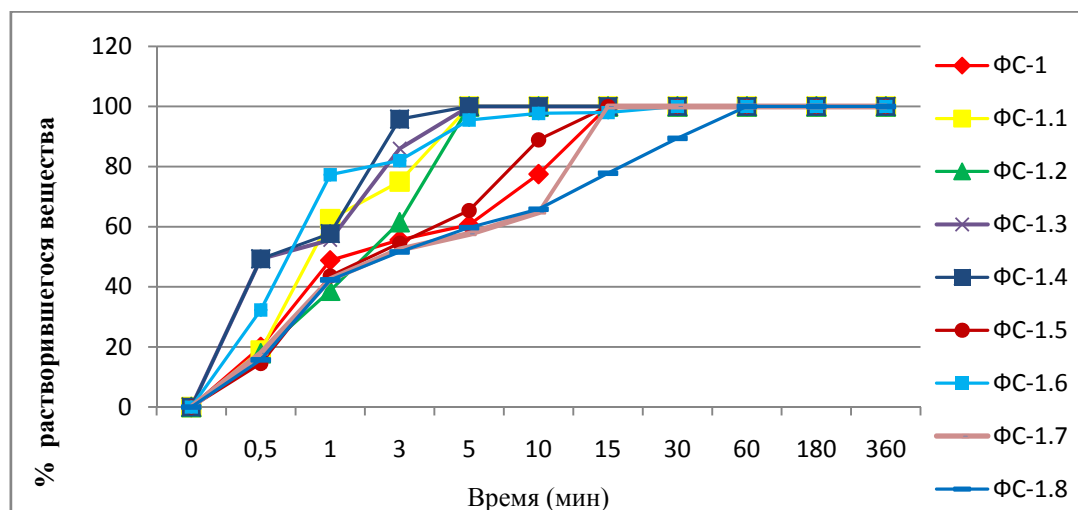


Figure 1 – Pharmacopoeia solubility of FS-1 in water, a buffer solution with a pH of 1.2, 4.5 and 6.8

According to the results of the studies, it was found that the biopharmaceutical properties of all iodine-containing complexes based on the degree of their solubility in water, buffer solutions with a pH of 1.2; 4.5; 6.8 and permeability in an experiment on an MDCK cell culture corresponded to class III bioequivalence of drugs. The studied complexes divided by substances with “high” solubility and “low” permeability.

The safety of iodine-containing complexes was determined on an MDCK cell culture by the MTT test and by using concentrations from 0.03 to 25.0 mg/ml.

Although, an experiment in mice by determining toxicological studies of the maximum tolerated doses of the active substance from 0.6 - 13.4 ml/kg. The results of the MTT test on the MDCK cell line for iodine-containing complexes are shown in figures 2 and 3. The results of acute toxicity of iodine-containing complexes in an experiment in mice with intraperitoneal administration are shown in figure 4.

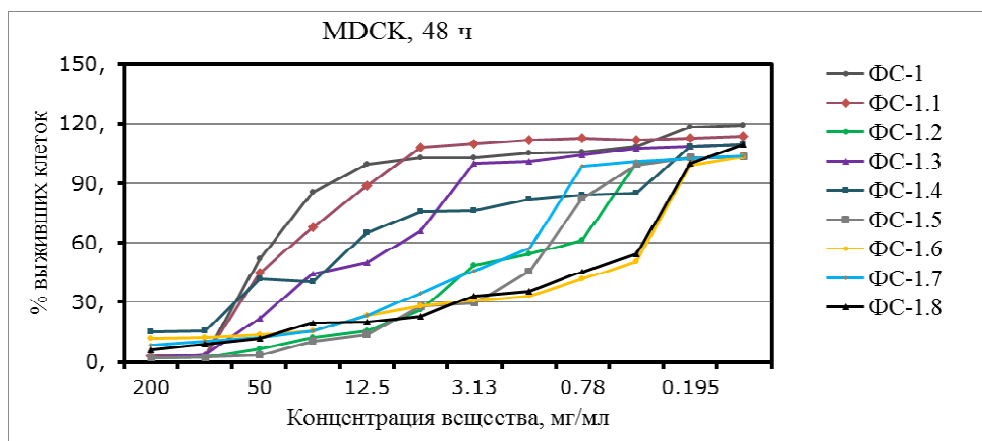


Figure 2 – The effect of iodine-containing complexes on the survival of the MDCK cell line after 48 hours of incubation

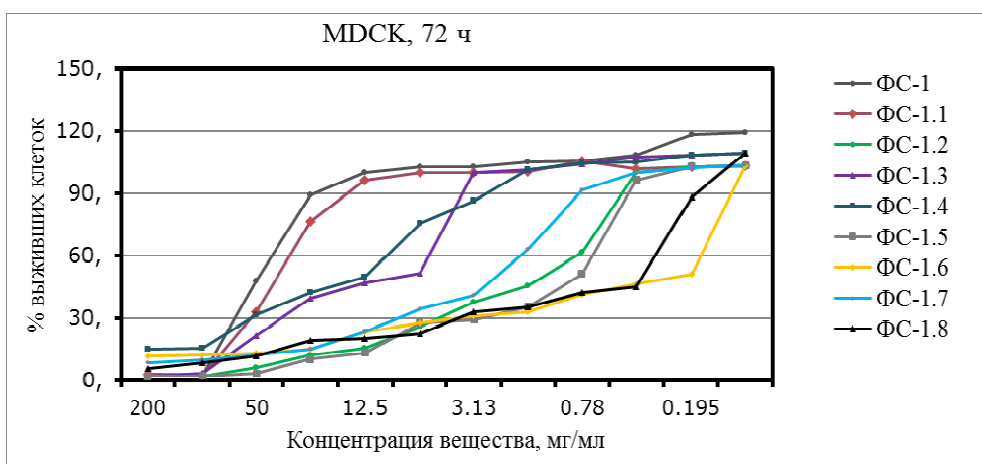


Figure 3 –The effect of iodine-containing complexes on the survival of the MDCK cell line after 72 hours of incubation

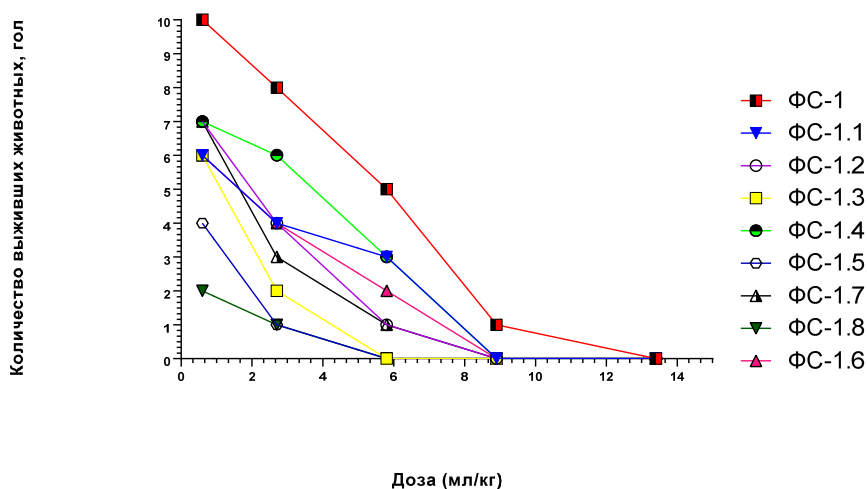


Figure 4 – Determination of FS-1's acute toxicity in an experiment in mice with intraperitoneal administration

As shown in figure 2 and figure 3 iodine-containing complexes FS-1, FS-1.1, FS-1.3, FS-1.4 have a low toxic. The CC_{50} of complexes FS-1, FS-1.1, FS-1.3, FS-1.4 after 48 hours of cultivation was in the concentration range from 10.0 to 50.0 mg/ml and after 72 hours of cultivation was in the concentration range from 5.0 to 50.0 mg/ml. Toxicity did not increase depending on the duration of cultivation. The iodine-containing complexes FS-1.2, FS-1.5, FS-1.6, FS-1.7, FS-1.8 had moderate toxicity. Their CC_{50} ranged from 0.39 to 2.13 mg/ml after 48 hours of incubation on an MDCK cell culture and from 0.20 to 1.77 mg/ml after 72 hours.

Determination of acute toxicity in mice from Figure 4 showed that all the iodine-containing compounds FS-1.1, FS-1.2, FS-1.3, FS-1.4, FS-1.5, FS-1.6, FS-1.7, FS-1.8, except FS-1, in doses of 0.6 up to 13.4 ml/kg caused a pronounced toxic effect. At the same time, the FS-1 complex under study showed the least toxic properties in doses from 0.6 to 5.8 ml/kg.

An *in vitro* study of the antiviral effect of iodine-containing compounds was carried out using the Waybrige/78 strain A virus (H7N7) as an example. It was found that the reproduction of influenza A virus on an inoculated cell culture of MDSK was suppressed under the influence of complexes FS-1.1, FS-1.2, FS-1.3, FS-1.5, FS-1.6, FS-1.8 in comparison with the control titer by no more than 2.0 log. At the same time, the FS-1.4 complex reduced the titer of the virus by 5.0-6.0 log in comparison with the control. The greatest antiviral effect among the studied iodine-containing complexes was found in the FS-1 and FS-1.7 complexes, which reduced the virus titer by 6.0-8.0 log. However, the FS-1.7 complex showed high toxicity in further experiments on animals. Therefore, as a result of studies of iodine-containing complexes based on physicochemical properties, determination of cytotoxicity in an MDCK cell culture, acute toxicity in an experiment in mice, antiviral activity using the example of influenza virus strain A Waybrige/78, (H7N7), *in vitro*, showed the most effective composition of the iodine-containing complex FS-1. Our further studies were aimed at studying the antiviral activity of the iodine-containing complex FS-1 against avian influenza A virus in experiments on chicken embryos, chickens, as well as determining the potentiating effect in experiments *in vitro*, *in ovo*, *in vivo*.

By determining the safety of the FS-1 complex in mice, an accumulation coefficient of 1.45 was calculated, and the absence of chronic toxicity of the FS-1 complex with repeated administration (24 times) to animals was established.

Studies of the determination of acute toxicity in rats showed that oral administration of FS-1 made it possible to calculate active doses effective in 50% of cases and toxic (lethal) doses equal to LD16 - 571 mg/kg, LD50 - 922 mg/kg, LD84 - 1273 mg/kg, LD100 - 1449 mg/kg.

According to the toxicity scale of substances administered *per os* (Hodg G., Gleason S., 1975; S. A. Kutsenko, 2002) the studied complex FS-1 can be attributed to low-toxic substances of the third class of biological safety.

The study of embryo toxicity of FS-1 was carried out on 10, 12 and 18 day old chicken embryos. Into the chorion-allantois cavity 0.2 ml of the studied concentrations of FS-1. Based on the data obtained, it was found that the studied FS-1 in concentrations from 0.8 to 1.6 mg/ml did not have a toxic effect. In concentrations from 3.3 to 6.6 mg/ml, 10 % to 20 % of embryos died. The embryo toxic effect of FS-1 is expressed in concentrations from 13.1 to 52.5 mg/ml, where from 50 % to 100 % of chicken embryos died. It is also shown that the embryo toxicity of FS-1 depends not only on its concentrations, but also on the timing of development of the chicken embryo. With the introduction of FS-1 to embryos with a developmental period of 10; 12 and 18 days at a concentration of 52.5 mg/ml killed 100 %, 80 % and 50 % of chicken embryos, respectively. With the introduction of FS-1 at a concentration of 26.3 mg/ml, 80% of chicken embryos died with a development period of 10 days, 60 % of 12-day-old chicken embryos and 10 % of 18-day-old chicken embryos.

The lowest toxic concentration that caused the death of 70 % - 10-day-old embryos is 13.1 mg/ml. With the introduction of FS-1 at a concentration of 26.3 mg/ml, 80 % of chicken embryos died with a development period of 10 days, 60 % of 12-day-old chicken embryos and 10% of 18-day-old chicken embryos. The obtained concentration of toxicity of FS-1 in an experiment on embryos was used to study antiviral activity. The study of acute toxicity of FS-1 was carried out in an experiment on seven-day-old chickens. Studies have shown that - the dose of LD₅₀ for FS-1 was 52.5 mg/kg when administered orally and subcutaneously to the chicken. Medium toxic doses were established with subcutaneous administration of FS-1 in concentrations from 1/8 LD₅₀ to 1/2 LD₅₀ mg/kg. At the same time, the tolerated

concentration of the antiviral drug named «remantadine» (control substance) was fixed at a dose of 8.33 mg/kg.

Studies of the antiviral activity of FS-1 were measured in experiments with influenza viruses with various strains: strain A Rostock / 34, (H7N1), black-headed laughter, strain A Atyrau 744/04, (H13N6); Almaty strain A 5/98, (H3N2) on ten-day-old chicken embryos by neutralizing the virus at a dose of 100 EID₅₀ /0.2 ml with experimental concentrations. It was found that FS-1 at a concentration of 3.3 mg/ml suppressed the reproduction of viruses by 2.0 log, and at a concentration of 6.6 mg / ml completely suppressed 100 infectious doses of influenza A virus of different strains: strain A Rostock / 34, (H7N1); black-headed laughter, Atyrau strain A 744/04, (H13N6); Almaty strain A 5/98, (H3N2).

The determination of the antiviral therapeutic efficacy of FS-1 was carried out in an experiment on seven-day-old chickens against the influenza virus strain A/Rostock/34, (H7N1). Three doses of FS-1 were used in the experiment: 6.6 mg/kg, corresponding to 1/8 LD₅₀; 13.1 mg/kg corresponding to 1/4 LD₅₀ and 26.3 mg/kg corresponding to 1/2 LD₅₀. As a control, a commercial drug «remantadine» was used at a therapeutic dose of 8.33 mg/kg for comparison. The results of the study are presented in figure 5.

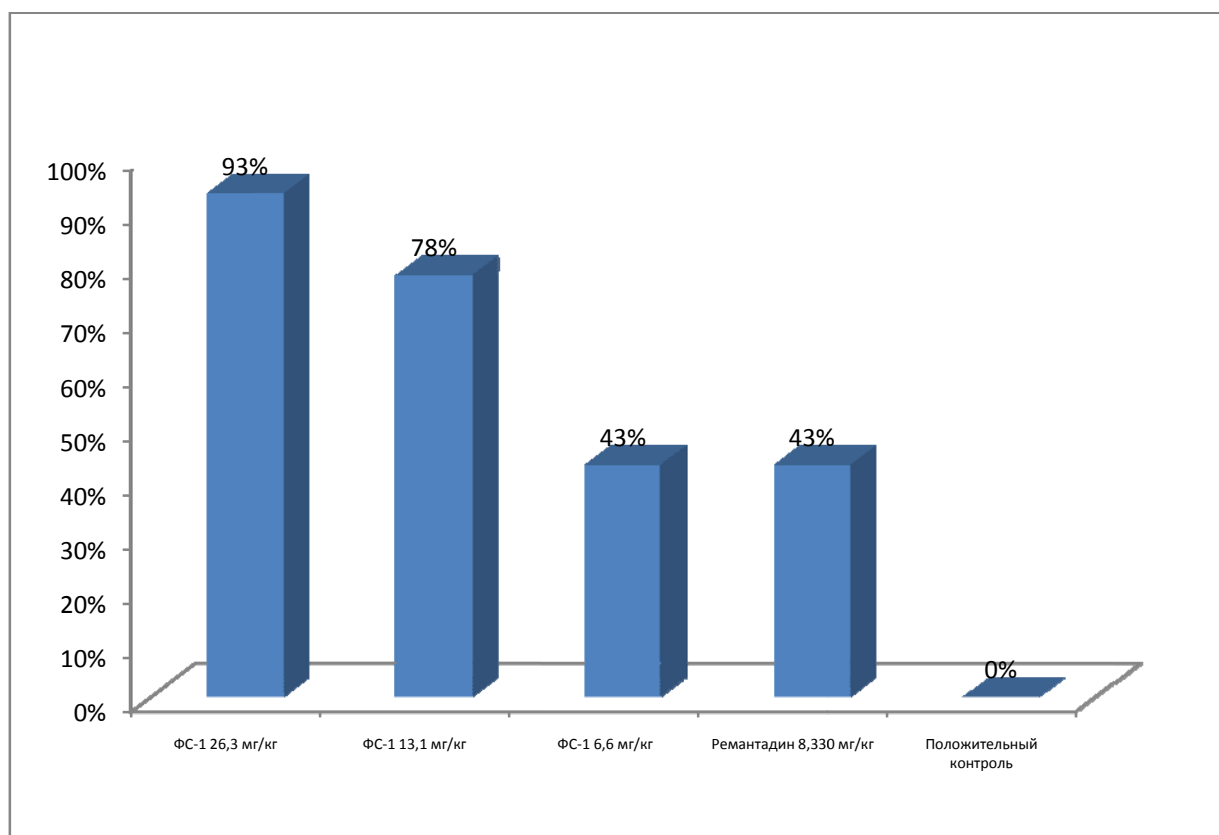


Figure 5 – The therapeutic effect of the drug FS-1

The results indicate that FS-1 showed high therapeutic efficacy at doses of 13.1 and 26.3 mg/kg against influenza virus in infected chickens. The use of the FS-1 complex as a therapeutic agent in doses of 26.3 and 13.1 mg/kg led to 93 % and 78 % survival of chickens, while the use of the drug «remantadine» in a therapeutic dose of 8.33 mg/ml retained only 43 % of the livestock.

The antiviral prophylactic efficacy of FS-1 was determined in an experiment on seven-day-old chickens against the influenza virus strain A Rostock / 34, (H7N1). In this case, four doses of FS-1 were used: 3.3 mg/kg corresponding to 1/16 LD₅₀; 6.6 mg/kg, corresponding to 1/8 LD₅₀; 13.1 mg/kg corresponding to 1/4 LD₅₀ and 26.3 mg/kg corresponding to 1/2 LD₅₀. The multiplicity of per os administration of the studied iodine-containing complexes and «remantadine» was seven days. As a control, a commercial drug «remantadine» at a dose of 8.33 mg/kg was used for comparison. The results of the study are presented in figure 6.

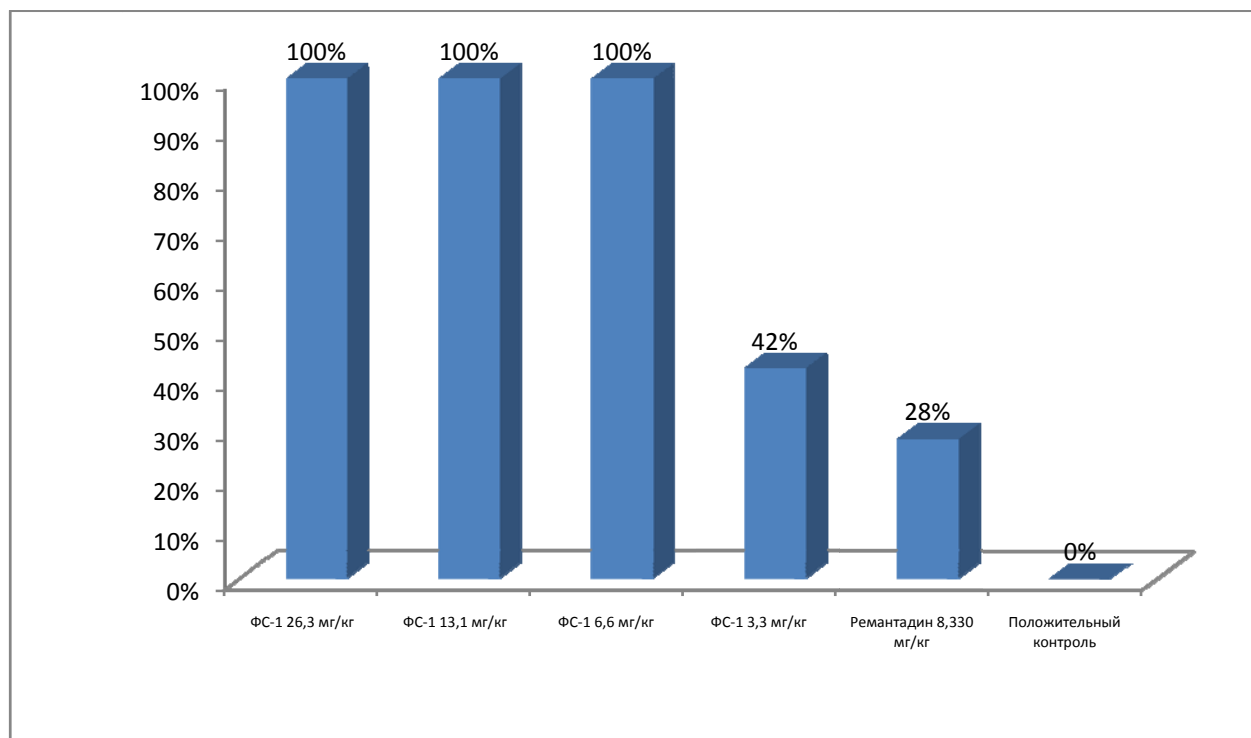


Figure 6 – The preventive effect of the drug FS-1's action

The results of studying the antiviral prophylactic effectiveness of FS-1 in experiments on chickens infected with Rostock/34 strain A influenza virus, (H7N1), showed pronounced prophylactic efficacy (100 %) in the studied doses of 26.3; 13.1 and 6.6 mg/kg more than three times the prophylactic effectiveness of the control antiviral drug «remantadine». However, at a dose of 3.3 mg/kg, the prophylactic efficacy of the investigated iodine-containing complex FS-1 is 1.5 times higher than the prophylactic dose of 8.33 mg/kg of the antiviral drug «remantadine».

In our experiments, we also established a significant pharmacological effect on influenza A virus. In various models with antiviral drugs widely used in practice, remantadine, oseltamivir, ribazole and amixin revealed a potentiation effect under the influence of the FS-1 iodine-containing complex. The results of potentiation with the combined use of the iodine-containing complex FS-1 with the studied antiviral drugs were accompanied by an increase in their therapeutic effect. Based on the results, we have compiled and filed an application for an invention with the patent department of NTsGNTe RK.

Thus, the studies and the results obtained allow us to conclude that the iodine-containing complex FS-1 is a low-toxic compound, exhibits antiviral activity against influenza A virus, and has a high potentiating effect when used in conjunction with commercial drugs. Further studies of the drug are actively continues.

Б. Ф. Керимжанова, Л. Н. Иванова, А. И. Ильин

«Инфекцияға қарсы материалдардың ғылыми орталығы» АҚ, Алматы, Қазақстан

ҚУСТАРДЫҢ А ТҰМАУЫНА ҚАРСЫ КҮРЕСТЕ ИОДТЫ ҚОСЫЛЫСЫНЫҢ ЭФФЕКТИВТІЛІГІНЕ БАҒА БЕРУ

Аннотация. Жұмыста «Инфекцияға қарсы дәрі-дәрмектердің ғылыми орталығы» АҚ-да синтезделген құрамында йод бар кешендерді зерттеуге арналған материалдар ұсынылған. Зерттелген зерттеуінде кешендер құрамында ең белсенді йод бар кешені анықталды. Алынған құрамында йод бар кешендердің құс тұмауына әсерін зерттеу нәтижелері сипатталған.

Түйін сөздер: құрамында йод бар кешендер, цитотоксикалық, жедел уыттылық, тұмау вирустары, вирусқа қарсы белсенділік, потенциалды әсер.

Б. Ф. Керимжанова, Л. Н. Иванова, А. И. Ильин

АО «Научный центр противоинфекционных препаратов», Алматы, Казахстан

ОЦЕНКА ЭФФЕКТИВНОСТИ ИОДСОДЕРЖАЩЕГО КОМПЛЕКСА В БОРЬБЕ С ГРИППОМ ПТИЦ А

Аннотация. В работе изложены материалы по изучению воздействия на вирус гриппа птиц А иодсодержащих комплексов, синтезированных в АО «Научный центр противоинфекционных препаратов». Проведенный скрининг из девяти исследованных комплексов выявил наиболее активный иодсодержащий комплекс. Установлено, что иодсодержащий комплекс является малотоксичным соединением, проявляет противовирусную активность в отношении вируса гриппа А, обладает высоким потенцирующим действием при совместном применении с коммерческими противовирусными препаратами.

Ключевые слова: иодсодержащие комплексы, цитотоксичность, острая токсичность, вирусы гриппа, противовирусная активность, потенцирующее действие.

Information about authors:

Kerimzhanova Bakhytzhana Fazylyzhanovna, Deputy Head of the laboratory, Doctor of Veterinary Sciences, Professor of JSC "Scientific Center for Anti-Infectious Drugs", Almaty, Kazakhstan; kbf19@mail.ru; <https://orcid.org/0000-0002-6860-3751>

Ilin Alexander Ivanovich, Doctor of chemical sciences, Chairman of the board. JSC "Scientific Center for Anti-Infectious Drugs", Almaty, Kazakhstan; ilin_ai@mail.ru; <https://orcid.org/0000-0001-9528-9721>

Ivanova Ludmila Nikolaevna, Deputy Head of Virology Laboratory, JSC "Scientific Center for Anti-Infectious Drugs", Almaty, Kazakhstan; lyudmila_69.69@mail.ru; <https://orcid.org/0000-0002-7194-0556>

REFERENCES

- [1] Antipov V.A., Talanovsky V.F. (1997) Iodine preparations in veterinary. Krasnodar. 47 p. (in Russ.).
- [2] Gendon Yu.Z. (1995) Pandemic flu: can you fight it? Questions of virology. 2:8-12 (in Russ.).
- [3] Ito Toshihiro, Goto Hideo, Yamamoto Eiji et al. (2001) Generation of a highly pathogenic avian influenza virus from an avirulent field isolate by passaging in chickens // J. Virol. 75:9:4439-4443.
- [4] Karpukhin G.I. Influenza: A Guide for Doctors. (2001). SPb.: Hippocrates, 360 p. (in Russ.).
- [5] Monto A.S., Fleming D.M., Henry D. (1999) Efficacy and neuraminidase inhibitor zanamivir in the treatment of influenza A and B infections // J. Infect. Dis. 180:(2):254-261.
- [6] Monto A.S., Robinson D.P., Herlocher L. et al. (1999) Zanamivir in healthy adults // J. Am. Med. Assoc. 282:31-36.
- [7] Mokhnach V.O. (1967) Yodvysokopolymer and their application in medicine and veterinary medicine. Iodinol in medicine and veterinary medicine. L.: Nauka. 188 p. (in Russ.).
- [8] Mokhnach V.O. (1974) Iodine and the problems of life. M.: Kolos. 254 p. (in Russ.).
- [9] Nikitin V.Ya., Kucheruk N.Kh., Kuzmenko P.I., Vinnikov V.V. (1999) Iodine and its preparations as antiseptics with a wide spectrum of action // Bulletin of veterinary medicine. 12:3-52 (in Russ.).
- [10] Uchaikin V.F., Kharlamov S.G., Cheshik S.G. (2004) The use of arbidol and amixin as etiotropic treatment of influenza and ARVI in children // Pediatrics. 5:73-77 (in Russ.).
- [11] Paretskaya N.A., Tamazyan R.A., Akhmatullina N.B., Amanzholyzy A., Sabitov A.N., Berdibai S.B., Kerimzhanova B.F., Dzhumagazieva A.B., Korotetskii I.S., Ilin A.I. (2019) New Semiorganic Iodine Complex, Its Structure And Biological Activity // News of NAS RK. Series of chemistry and technology. ISSN 2224-5286. 1:433:9:70-76 (in Russ.).
- [12] Kulmanov M.E., Ivanova L.N., Sokolova N.N., Korotetsky I.S., Kerimzhanova B.F., Ilyin A.I. (2015) Anti-influenza effect of the drug substance FS-1 in the experiment on chickens Series biological and medical. ISSN 2224-5308. 5:311:27-35 (in Russ.).

Publication Ethics and Publication Malpractice in the journals of the National Academy of Sciences of the Republic of Kazakhstan

For information on Ethics in publishing and Ethical guidelines for journal publication see <http://www.elsevier.com/publishingethics> and <http://www.elsevier.com/journal-authors/ethics>.

Submission of an article to the National Academy of Sciences of the Republic of Kazakhstan implies that the described work has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis or as an electronic preprint, see <http://www.elsevier.com/postingpolicy>), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. In particular, translations into English of papers already published in another language are not accepted.

No other forms of scientific misconduct are allowed, such as plagiarism, falsification, fraudulent data, incorrect interpretation of other works, incorrect citations, etc. The National Academy of Sciences of the Republic of Kazakhstan follows the Code of Conduct of the Committee on Publication Ethics (COPE), and follows the COPE Flowcharts for Resolving Cases of Suspected Misconduct (http://publicationethics.org/files/u2/New_Code.pdf). To verify originality, your article may be checked by the Cross Check originality detection service <http://www.elsevier.com/editors/plagdetect>.

The authors are obliged to participate in peer review process and be ready to provide corrections, clarifications, retractions and apologies when needed. All authors of a paper should have significantly contributed to the research.

The reviewers should provide objective judgments and should point out relevant published works which are not yet cited. Reviewed articles should be treated confidentially. The reviewers will be chosen in such a way that there is no conflict of interests with respect to the research, the authors and/or the research funders.

The editors have complete responsibility and authority to reject or accept a paper, and they will only accept a paper when reasonably certain. They will preserve anonymity of reviewers and promote publication of corrections, clarifications, retractions and apologies when needed. The acceptance of a paper automatically implies the copyright transfer to the National Academy of Sciences of the Republic of Kazakhstan.

The Editorial Board of the National Academy of Sciences of the Republic of Kazakhstan will monitor and safeguard publishing ethics.

Правила оформления статьи для публикации в журнале смотреть на сайте:

www:nauka-nanrk.kz

<http://agricultural.kz/index.php/en/>

Редактор *М. С. Ахметова, Т. М. Апендиев, Д. С. Аленов*
Верстка на компьютере *Д. Н. Калкабековой*

Подписано в печать 14.10.2019.
Формат 60x881/8. Бумага офсетная. Печать – ризограф.
8,2 п.л. Тираж 300. Заказ 5.