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ТҮЙІН

Түйе шешегіне қарсы бейбелсендірілген дамылсыз дамитын торша өсіндісінде өсірілген вакцинаны әзірлеу кезінде Маңғыстау облысы Бейнеу ауданының шаруа қожалығының түйелерінен 2020 жылы оқшауланып, бөлініп алған М-0001 түйе шешек вирусының депозиттелген штаммы пайдаланылды. Иммундық жауапты ынталандыру үшін 1% концентрацияда montanide GEL 01 адъюванты қолданылды.

Иммунопрофилактика кезіндегі мал иммунитетінің шынайы жай-күйі жоспарлы иммунологиялық (серологиялық) мониторинг және инфекцияның пайда болған ошағын жою нәтижелері бойынша айқындалатын болады. "М-0001" штаммынан түйе шешегіне қарсы инактивтендірілген торша өсіндісінде өсірілген вакцинаны сынақтан өткізу мақсатында өндірістік жағдайларда ЖШС "Антиген" өндірістік ғылыми кешенінің виварийін база ретінде пайдаланылды. Вакцинаның иммуногенділігін зерттеу мақсатында вакцина түйелердің шап аймағының тері астына 3,0 см^3 дозада енгізіп, 3 бас 6 айлық жас түйелерде сыналды. Зерттеуге шешек ауруынан қолайлы аймақтан алынған түйелерге жүргізілді. Вакцинацияланған жануарларда "М-0001" штаммынан түйе шешегіне қарсы инактивтендірілген дамылсыз дамитын торша өсіндісінде өсірілген вакцинамен 0 тәулікке шешекке қарсы антиденелердің титрі теріс нәтиже көрсетті, 7 тәулікке 1:2 – 1:4, 14 тәулікке 1:4-1:8, 21 тәулікке антиденелердің титрі 1:8 құрады.

РЕЗЮМЕ

При разработке инактивированной культуральной вакцины против оспы верблюдов был использован депонированный штамм вируса оспы верблюдов М-0001, выделенный в одном из КХ Мангистауской области Бейнеуовском районе в 2020 г. Для инактивации использовали 0,05 % конечных концентрации инактивант ß-пропиолактон. Для стимулирования иммунного ответа был использован адъювант Montanidae Gel01 в 1% концентрации.

Истинное состояние иммунитета поголовья при иммунопрофилактике будет определяться по результатам планового иммунологического (серологического) мониторинга и ликвидации возникшего очага инфекции. С целью апробации культуральной инактивированной противооспенной вакцины из штамма «М-0001» против оспы верблюдов в производственных условиях в качестве базы был использован виварий ТОО НПП «Антиген». Иммуногенность вакцины испытали на 3-х верблюдах, которым вводили вакцину подкожно в дозе 3,0 см^3 в паховую область. У вакцинированных животных инактивированной культуральной вакциной против оспы верблюдов из штамма «М-0001» на 0 сутки титр антител против оспы показал отрицательный результат, на 7 сутки составлял 1:2 – 1:4, на 14 сутки составлял 1:4-1:8, на 21 сутки титр антител составлял 1:8.

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STUDY OF IMMUNOSTIMULATORY PROPERTIES OF ADJUVANT MONTANIDE™ GEL 01 AND VARIOUS INACTIVANTS IN THE COMPOSITION OF INACTIVATED CULTURE CAMEL SMALLPOX VACCINE

ANNOTATION

Chemical methods of virus inactivation have found wide application in production due to their ease of use, gentle effect on the antigenic structure of pathogens, reliable inactivation and high reproducibility of results. Of all known chemical compounds used as inactivants, formaldehyde and ß-propiolactone are the most widely used.

In experiments to determine the inactivation mode of the camel pox virus, a culture strain that had undergone 15 consecutive passages on the culture of lamb kidney cells was used. For virus inactivation, formaldehyde was used at concentrations of 0.02; 0.03; 0.05 and 0.1% relative to the total biomass volume. During the course of the experiment, the timing of complete inactivation of the virus by OM was determined at temperatures of 4°C, 27°C and 37°C, at pH of the suspension 7.4-7.6. The initial biological activity was 6.25 lgTCD50/cm^3.

The choice of adjuvant in vaccine development is critical to the properties of the vaccine. There is no universal adjuvant and there is always a trade-off between safety and efficacy. Consequently, the adjuvant chosen will depend on the target species, antigen, route of inoculation and the desired immune response and its duration. This study provides direct evidence that Montanide™ GEL 01 can act as a potent adjuvant in a synthetic peptide-based vaccine and represents an easy-to-use and inexpensive veterinary vaccine with a higher safety profile for large animals.

Key words: *camels, smallpox, smallpox vaccine virus, адъювант, attenuation, infection.*

Introduction. The development of domestic prophylactic agents against camel pox is urgent due to periodic recurrent outbreaks of the disease caused by new virulent strains of the pathogen, the lack of biopreparations used for the prevention of this disease and the presence of susceptible livestock [1].

There are multifaceted effective strategies and methods to enhance the immunogenicity of vaccines. In this regard, the inactivated camelpox vaccine we are developing using a local field strain could be a key element for an effective national strategy for progressive control of the above infection. The results of this work will make it possible to optimize anti-epizootic measures to prevent and spread this disease among camels in the Republic of Kazakhstan [2-3].

Currently, much attention is paid to the development and improvement of inactivated vaccines for the prevention of viral diseases. One of the most important points in their development is the selection of inactivators that would inactivate the virus at low concentrations and retain its antigenic activity. In recent years, ethylenimine, dimerethylenimine, acetylethylenimine and other derivatives have been widely used abroad and in the former USSR. These compounds inactivate both RNA- and DNA-containing viruses. In addition, ethylenimine derivatives are easily able to neutralize the virus without any damage to the quality of the biopreparation [4].

At different times in the world, studies on inactivation of infectious activity of viruses by physical effects: ultrahigh pressure, gamma rays, ultraviolet irradiation, photodynamic action of dyes, high temperature, ultrasound, etc. have been conducted.

Borisova I.A. [5] developed an optimal scheme for obtaining viral raw material from the strain "PVOZ-B" of avian metapneumovirus using a grafted culture of green marmoset Vero kidney cells. In the course of research she substantiated the modes of inactivation of avian Newcastle disease by beta propiolactone and the dynamics of virus inactivation.

Nikiforova A.I. [6] developed an inactivated trivalent trivalent subunit influenza vaccine with copolymer of 2-methyl-5-vinylpyridine and vinylpyrrolidone (Sovidone), evaluated its safety and immunogenicity, and determined its optimal content with a new adjuvant in the composition of the influenza preparation.

Chernos V.I. and Gendon Y.Z. [7] carried out inactivation of poliovirus by beta-propiolactone at 24 °C, pH of the medium 8.0, at a concentration of beta-propiolactone 1:1000. Inactivation was stopped by adding sodium thiosulfate to the sample. Beta-propiolactone inactivates FMD and Newcastle disease viruses at 25-37°C faster than formaldehyde.

Fayet M.T. [8] compared the inactivating effect of beta-propiolactone on FMD virus with acetylenimine, glycidaldehyde, and formaldehyde. It was found that in the process of virus inactivation, beta-propiolactone hydrolyzes as a first-order reaction, as a result of which its content in the reaction medium decreases and the inactivation rate slows down.

However, the difficulties associated with obtaining avirulent and immunogenic preparations, as well as the low reproducibility of the results, prevented the widespread introduction of inactivated vaccines with a physical method of virus inactivation into industrial production.

The practice of making preparations for active immunization of animals with inactivated vaccines has shown the advantage of chemical inactivation of viruses, when they lose the ability to reproduce, but retain the antigenic and immunogenic properties of the original virus.

Various chemical agents are used to inactivate viruses, which, interacting with the viral particle, cause either incomplete oxidation of functional groups or acylation of the protein molecule. All inactivating agents alter both the nucleic acid and protein of the virus.

Formalin was the first chemical reagent used to prepare inactivated vaccines. Formalin is a 34.9-38.0% aqueous solution of formaldehyde in the form of methylene glycol hydrate, which has high chemical activity with a wide range of reactions The mechanism of the inactivating effect of formalin on viruses is fairly well understood. Formalin reacts not only with nucleic acid, but also with acid within the undestroyed virion. The inactivation curve of rhinopneumonia virus is similar to that of poliovirus inactivation by formaldehyde. In the first hours of exposure, there is a sharp decline in the infectivity curve, which then turns into a more or less continuous line [9].

Inactivation of smallpox virus with formaldehyde does not guarantee a completely safe vaccine. Some investigators have found smallpox virus capable of replicating in vaccines regardless of the viral raw material used in vaccine manufacture. Beta-propiolactone was used in the manufacture of vaccines against Aujeszky's disease, rinderpest, Newcastle disease, and vesicular stomatitis. Inactivation with this preparation was much faster than with formaldehyde. In addition, there is evidence that the immunogenicity of preparations of rinderpest virus inactivated with beta-propiolactone is inferior to that of preparations inactivated with formaldehyde [10].

Zhugunusov K.D., Taranov D.S. et al. conducted comparative studies to evaluate the effectiveness of different adjuvants in the manufacture of inactivated bluetongue vaccine. The results of the study showed good stability of the emulsified vaccine with an oil adjuvant and the absence of reactogenicity in sheep when administered intramuscularly [11].

Studies on the use of phenol, formaldehyde, hydroxylamine, and acetylethylenimine as inactivants showed that the efficacy of vaccines produced using the above compounds was significantly lower than the immunogenicity of ß-propiolactone.

Analysis of literature data indicates that the search for the most effective inactivants remains one of the topical issues in the production of effective smallpox vaccines [12-20].

Thus, the results of the study of the epizootic situation, as well as the development of prophylactic preparations for camelpox will make it possible to optimize anti-epizootic measures to prevent the emergence and spread of this disease among camels in the Republic of Kazakhstan.

Materials and methods. Blood serum from camels of different ages from Mangistau, Atyrau, Turkestan and Kyzylorda regions (710 samples) was used for serologic studies. Trained specialists with smallpox vaccination were allowed, as people are susceptible to camelpox virus due to the kinship of the causative agent with the causative agent of smallpox. Detection of antibodies to camelpox virus was

carried out by ELISA method (Abbexa, UK). In the studies to determine the sensitivity to camelpox virus, transfected cell lines sheep kidney, Vero, MDVK, TT and primary-trypsinized cultures of lamb kidney and testicle of lambs were used. For the neutralization reaction, the tested sera were inactivated at 56 ^{0}C for 30 minutes and double dilutions were prepared from 1:2 to 1:16.

The methods of infection, cultivation, virus collection, sensitivity assessment and adaptation of cell cultures in the second and subsequent passages were similar to those in the first passage. To determine the titer of biological activity of camelpox virus, cell cultures (Vero, sheep kidney, calf testicle, MDVK, lamb testicle, lamb kidney) were seeded on 96-well plates 24 hours before infection. Concentrated camelpox virus was layered on a 30% sucrose density gradient and purified by ultracentrifugation at 30000 rpm for 2 h (4 ^{0}C). The virus precipitate was collected and resuspended 2 times with Tris-HCl buffer (pH 7.2-7.4). The virus was stored at minus 70 ^{0}C until use. The resources of the National Center of Biotechnology (Astana) and software utilities "BLAST" and "Vector NTI 9.1.0" were used in the study of molecular genetic characteristics.

Plasmid DNA with a marker insert was used for PCR amplification. The DNA sample isolated from the isolate was identified by determining the direct nucleotide sequence of the ATI gene fragment and then determining its nucleotide identity with sequences deposited in the GeneBank international database. Sequencing was performed using BigDye® Terminator v3.1 Cycle Sequencing Kit (Applide Biosystems) according to the manufacturer's instructions. Bioinformatic analysis of sequencing sequences was performed using Eneious 11.0 computer program (Biomatters, New Zealand). Alignment and phylogenetic analysis of sequenced genes with nucleotide sequences from GenBank were performed using the computer program MEGA 6.0 using the maximum likelihood method based on 500 samples, GTR model.

Results and discussion. In the development of inactivated culture vaccine against camelpox, the deposited strain of camelpox virus M-0001, isolated in one of the farms of Mangistau region in 2020, was used. During inactivation 0.05 % of final concentrations of inactivant ß-propiolactone was used. To stimulate the immune response, adjuvant Montanidae Gel01 in 1% concentration was used. The technology of this experimental series of inactivated camelpox vaccine consisted of several steps: inactivation of camelpox virus; residual virulence test was performed on PJ cell culture. When testing the avirulence of the suspension on sensitive animals, five guinea pigs were injected with inactivated material in the volume of 1 cm3 subcutaneously. The animals were monitored for 14 days.

The results of the literature analysis allowed us to choose formaldehyde and β-propiolactone as the most promising and effective chemical compounds for inactivation of M-0001 camelpox strain. All works were carried out at the production base of DiaVak-ABN LLP.

Given the insufficient information on the regulations of camelpox virus inactivation by β-propiolactone, in the present studies we considered it necessary to establish the optimal final concentration of the inactivant, temperature of the reaction medium, and duration of inactivation of strain M-0001 of camelpox virus. Formaldehyde and β-propiolactone at different final concentrations and temperature conditions were used as camelpox virus inactivant. Working solutions of the inactivants were used in this work, which were prepared immediately before inactivation. Inactivation with β-propiolactone can be obtained by combining β-propiolactone solution with virus suspension to a final concentration of β-propiolactone of about 1-2 mM. It was incubated at 35-40 ºC with constant stirring for 36-72 h.

For preparation of 3% formaldehyde we used technical formalin, highest grade, with formaldehyde content not lower than 36%.

Based on the concentration of formaldehyde in formalin, a 3% formaldehyde solution was prepared using sterile distilled water. The formaldehyde solution was prepared in glass bottles on the day of making the experimental trial series.

The content of formaldehyde in the initial formalin is 36 %. To prepare a 3% formaldehyde solution, the following formula (2) was used:

$$X = 3 \times 100 / 36 = 8,3 \quad (2)$$

36 g formaldehyde is contained in 100 g formalin, 3 g formaldehyde is contained in X formalin.

The calculated amount of formalin (8.3) in milliliters was diluted to 100 ml with sterile distilled water.

In studying the virulicidal activity of formaldehyde, 3% formaldehyde solution was added to samples of clarified suspension of OV virus to final concentrations of 0.02; 0.04; 0.08 and 0.1%.

Inactivation was continued for 10-38 hours at temperatures of 4, 27 and 37 ºC and pH in the suspension 7.4-7.6. After the expiration of the specified period of inactivant action, the suspension was cooled at 4-6 ºC and neutralizing solution of sodium thiosulfate was added.

In experiments to determine the mode of camelpox virus inactivation, a culture strain that had undergone 15 consecutive passages on lamb kidney cell culture was used. For virus inactivation, formaldehyde was used at concentrations of 0.02; 0.03; 0.05 and 0.1% relative to the total biomass volume. In the course of the experiment, the terms of complete inactivation of camelpox virus were established at temperatures of 4, 27 and 37℃, at pH of the suspension 7.4-7.6. The initial biological activity was 6.25 lgTCD50/cm^3.

Avirulence of preparations was determined by the method of cytopathogenic effect on lambs kidney cell culture and infection of guinea pigs. As a result, the concentrations of the inactivant at which there is no residual infectivity were determined.

The results of studies to determine the optimal concentration of inactivants are presented in Table 1.

Table 1 – Inactivation of camelpox virus by formaldehyde and beta-propiolactone at different temperatures and concentrations of inactivants.

Concentration Inactivant concentration, %	Time of complete inactivation of smallpox virus at temperatures, hours					
	Formaldehyde			Beta-propiolactone		
	4ºC	27ºC	37ºC	4ºC	27ºC	37ºC
0,1	96	30	14	94	20	10
0,05	144	33	27	144	24	25
0,03	184	37	30	184	33	30
0,02	195	42	35	196	39	31

The data of table 1 reflect the virulicidal activity of camelpox virus at different concentrations of formaldehyde and beta-propiolactone, at pH of suspension 7.5 and temperature regimes of 4^{0}C, 27^{0}C and 37^{0}C. The duration of camelpox virus inactivation time was directly dependent on the concentration of virus suspension inactivants and exposure temperature. Increasing the inactivation temperature by 23^{0}C and 10^{0}C accelerated the loss of infectivity by 3.5 and 2.5 times, respectively. Data analysis shows that the kinetics of camelpox virus inactivation by formaldehyde deviates from the first-order reaction. First there is a relatively sharp decline in infectivity, followed by a transition into a more or less prolonged "log phase". The lowest concentration of 0.02% formaldehyde inactivated the camelpox virus within 35 hours at 37 ^{0}C, and at 27^{0}C within 42 hours, and when using 0.1% reagent concentration, the inactivation time was sharply reduced, and the infectivity of the virus was not established after 14 and 30 hours, respectively. The use of 0.1% formaldehyde significantly reduced the inactivation time and increased the likelihood of complete loss of virus infectivity. Beta-propiolactone concentration of 0.02% inactivated camelpox virus within 31 hours at 37^{0}C, and at 27^{0}C within 39 hours, and when 0.1% reagent concentration was used, the inactivation time was sharply reduced and the infectivity of the virus was not established after 10 and 20 hours, respectively.

The inactivation process with beta-propiolactone with a concentration of 0.05% was recognized as optimal, as this concentration is not toxic to the animal organism in contrast to the concentration of 0.1% and provides complete inactivation and reliability within 24 hours at 27^{0}C.

The data in the table also indicate that decreasing the concentration of inactivants resulted in an increase in virus survival time, and increasing the concentration of inactivants resulted in a decrease in inactivation time, regardless of exposure temperature.

The avirulence of suspensions of inactivated camelpox virus was tested on guinea pigs to avoid distortions of the obtained results. In parallel, we switched to the determination of avirulence of inactivated preparations by cytopathogenic effect on lamb kidney cell culture.

The choice of these parameters is due to the preservation of the initial antigenic activity of the virus and practically threefold reserve of the inactivation period, which theoretically guarantees the obtaining of avirulent virus-containing suspension.

Avirulence of the inactivated suspension using the above inactivation parameters was determined by titration in lamb kidney cell culture on guinea pigs, to which the inactivated suspension was injected

subcutaneously at a dose of 1 cm3. The guinea pigs were clinically monitored for 14 days at 26-28°C. The guinea pigs remained clinically healthy during the observation period.

Control of inactivation completeness was carried out on lamb kidney cell culture during three consecutive passages, within 5-7 days. No visible changes in the cytopathogenic effect of the virus were observed in the cell culture, indicating complete inactivation of the virus.

Thus, inactivation of camelpox virus by β-propiolactone at 0.05% concentration at 27°C and at pH of reaction medium 7.4-7.6 for 24 hours allows complete inactivation of the virus with preservation of antigenic properties of the virus.

The inactivated viral suspension was supplemented with 1% adjuvant Montanide™ GEL 01, which has a nonspecific stimulating effect. The prepared preparation was injected into laboratory animals (guinea pig) intramuscularly in a volume of 0.3 cm^3. At 7, 14, 21 and 28 days after vaccination, blood serum samples were collected and analyzed by complement binding reaction to determine the level of antibodies. The level of antibodies was used to judge the immunogenicity of the tested preparation; the data of these studies are shown in table 2.

Table 2 – Titer of virus neutralizing antibodies in serum of guinea pigs inoculated with inactivated preparation against camel pox

№	*Name of material*	*Time of onset of immunity (days)*	*Antibody titer in neutralization reaction*	*Results*
1	*Guinea pig blood serum*	*7*	*1:2-1:4*	*positively*
2	*Guinea pig blood serum*	*14*	*1:4 - 1:8*	*positively*
3	*Guinea pig blood serum*	*21*	*1:16*	*positively*
4	*Guinea pig blood serum*	*28*	*1:16*	*positively*

The results of the studies show that the antibody titer against camelpox on 7 days was 1:2-1:4, on 14 days 1:4 - 1:8, on 21 and 28 days 1:16. These data will be taken into account in further studies when developing an inactivated preparation for this infection.

To study the immunobiological properties of the preparation and subsequent substantiation and experimental confirmation of optimal schemes of camel immunization, 1 experimental-laboratory series of culture inactivated vaccine against camel pox from strain M-0001 was prepared according to the developed technology.

Conclusion. Formaldehyde and β-propiolactone were chosen as the most promising and effective chemical compounds for inactivation of camelpox strain M-0001. Inactivation with beta-propiolactone was continued for 24-196 hours at temperatures of 4, 27 and 37ºC and pH in suspension 7.4-7.6. According to the results of these studies, the optimal mode of camelpox virus inactivation with β-propiolactone at 0.05% concentration at 27°C and at pH of the reaction medium 7.4-7.6 for 24 hours was recognized. The choice of these parameters is due to the preservation of the initial antigenic activity of the virus and practically threefold reserve of the inactivation period, which theoretically guarantees obtaining an avirulent virus-containing suspension.

Avirulence of the inactivated suspension was determined by titration in cell culture of lambs kidney, as well as on guinea pigs, to which the inactivated suspension was injected subcutaneously at a dose of 1 cm3. The guinea pigs were clinically monitored for 10 days. The guinea pigs remained clinically healthy during the observation period. The control of inactivation completeness was carried out on the cell culture of lambs kidney during three consecutive passages, during 5-7 days in the cell culture no visible changes of cytopathogenic effect of the virus were observed, which indicates complete inactivation of the virus.

1% adjuvant Montanide™ GEL 01 was added to the inactivated viral suspension, and the preparation was administered to laboratory animals (guinea pig) intramuscularly in the volume of 0.3 cm^3. In 7, 14, 21 and 28 days after vaccination we took samples of blood sera, which were examined in the complement binding reaction to determine the level of antibodies, the level of antibodies was used to judge the immunogenicity of the study drug, that the titer of antibodies against camelpox on 7 days

was 1:2-1:4, on 14 days 1:4 - 1:8, on 21 and 28 days 1:16. These data will be taken into account in further studies when developing an inactivated preparation for this infection.

To study the immunobiological properties of the preparation and subsequent substantiation and experimental confirmation of optimal schemes of camel immunization, 1 experimental-laboratory series of inactivated vaccine against camel pox from strain M-0001 was prepared according to the developed technology. The experimental-laboratory series of the vaccine was tested on naturally susceptible animals to study its harmlessness and immunogenic properties.

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ТҮЙІН

Вирустарды инактивациялаудың химиялық әдістері оларды қолданудың қарапайымдылығына, қоздырғыштардың антигендік құрылымына жұмсақ әсер етуіне, сенімді инактивациясына және нәтижелердің жоғары қайталануына байланысты өндірісте кеңінен қолданылды. Инактиванттар ретінде қолданылатын барлық белгілі химиялық қосылыстардың ішінде формальдегид пен β-пропиолактон ең көп таралған.

Шешек вирусын инактивациялау режимін анықтау тәжірибелерінде қозы бүйрегінің торша өсіндісінде қатарынан 15 үздіксіз пассаждау қолданылды. Вирусты инактивациялау үшін формальдегид 0,02; 0,03; 0,05 және 0,1% концентрациясында биомассаның жалпы көлеміне қатысты қолданылды. Эксперимент барысында шешек вирусын 4°С, 27°С және 37°С температурада, суспензияның pH 7,4-7,6 температурада толық инактивациялау мерзімдері белгіленді. Бастапқы биологиялық белсенділік 6,25 ТЦӘ50 / см3.

Вакцинаны әзірлеу кезінде адъювантты таңдау вакцинаның қасиеттері үшін өте маңызды екені белгілі. Әмбебап адъювант жоқ және қауіпсіздік пен тиімділік арасында әрқашан компаға келу бар. Сондықтан таңдалған адъювант мақсатты түрге, антигенге, егу әдісіне және қажетті иммундық жауапқа және оның ұзақтығына байланысты болады. Бұл зерттеу Montanide ™ GEL 01 синтетикалық пептидке негізделген вакцинада күшті адъювант ретінде әрекет ете алатынын және ірі жануарлар үшін жоғары қауіпсіздік профилі бар қолдануға оңай және арзан ветеринарлық вакцина екенін тікелей дәлелдейді.

РЕЗЮМЕ

Химические методы инактивации вирусов нашли широкое применение в производстве в связи с простотой их использования, щадящего воздействия на антигенную структуру возбудителей, надежной инактивацией и высокой воспроизводимостью результатов. Из всех известных химических соединений, применявшихся в качестве инактивантов, наибольшее распространение нашли формальдегид и ß-пропиолактон.

В опытах по определению режима инактивации вируса ОВ использовали культуральный штамм, прошедший 15 последовательных пассажей на культуре клеток ПЯ. Для инактивации вируса использовали формальдегид в концентрациях 0,02; 0,03; 0,05 и 0,1% по отношению к общему объему биомассы. В процессе проведения эксперимента устанавливали сроки полной инактивации вируса ОВ при температуре 4, 27 и 37˚С, при pH суспензии 7,4-7,6. Исходная биологическая активность 6,25 lgТЦД50/см^3.

Хорошо известно, выбор адъюванта при разработке вакцины имеет решающее значение для свойств вакцины. Универсального адъюванта не существует, и всегда существует компромисс между безопасностью и эффективностью. Следовательно, выбранный адъювант будет зависеть от вида мишени, антигена, способа инокуляции и желаемого иммунного ответа и его продолжительности. Это исследование предоставляет прямые доказательства того, что Montanide™ GEL 01 может действовать как мощный адъювант в синтетической вакцине на

основе пептидов и представляет собой простую в использовании и недорогую ветеринарную вакцину с более высоким профилем безопасности для крупных животных.

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