Prospects for clinical use of the drug Camelin® in the treatment and prevention of viral infections

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SUMMARY

Researchers from the International Institute of Biotherapy (Kyiv, Ukraine) conducted a
A placebo-controlled study of the antiviral efficacy of Kamellin® drug substance on the L929 model using vesicular stomatitis virus (RNA virus). The results obtained testify to the significant antiviral activity of the Kamellin drug under the conditions of its use against RNA viruses, including the Rhabdoviridae family. Proven efficacy
Kamelin's antiviral activity against RNA genomic viruses is important for the prospects of the drug's use in current diseases such as hepatitis C, Coxsackie, hemorrhagic fever, coronavirus infection, and seasonal rhinovirus infections. Action
The antiviral activity of the drug Kamelin is mainly due to the activity of natural peptides anti-infectives, whose antiviral properties arose naturally during evolution over the more evolutionarily ancient RNA viruses.
Prospects for the clinical use of Camelyn® for the treatment and prevention of viral infections

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SUMMARY
Researchers at the International Institute of Biotherapy (Kiev, Ukraine) conducted a placebo-controlled study of the antiviral efficacy of the substance of the drug Camelyn® on the L929 model using the vesicular stomatitis virus (RNA virus). The data obtained indicate a significant antiviral activity of the drug Camelyn in the conditions of its use against RNA-containing viruses, including the family Rhabdoviridae. Camelyn's proven antiviral efficacy against RNA-genomic viruses is important for the prospects of using the drug for actual diseases such as hepatitis C, Coxsackie, hemorrhagic fever, coronavirus infection, seasonal rhinovirus infections. The antiviral effect of the drug Camelyn is mainly due to the activity of natural anti-infectious peptides, the antiviral properties of which were naturally formed during evolution in relation to more evolutionarily ancient RNA viruses.
During research in laboratories in various countries, including Japan, South Korea, the United Kingdom and the United States, it was found that peptides of natural origin, in particular RJP-1, apidaecin, defensin have ancient, evolutionary properties: to activate immunity and destroy viruses. Understanding these mechanisms reasonably led to the introduction of drugs based on natural peptides into medical practice.
In recent years, Kamelin®, an immunotropic drug containing anti-infective peptides of natural origin, has been successfully used for the treatment and prevention of seasonal viral infections (SEIs) [1-4].
The design of the placebo-controlled study of the antiviral efficacy of Kamelina® was developed by a team of infectious disease physicians within the antiviral program
International Institute of Biotherapy (Kyiv, Ukraine). In this study, cells of line L929 (mouse fibroblasts) and RNA-containing vesicular stomatitis virus (WPZJU, ATCC No. VR-158) with an infectious titer of at least 105 TCD50/0.1 ml were used. The test systems listed meet the requirements of the USP "Draft Guidance for Industry on Analytical Procedures and Methods
Validation for Drugs and Biologics; Availability, 2014". Evaluation of the antiviral effect of different concentrations of Kamelin prepared ex tempore in saline solution
was carried out by determining the number of viable cells in the tear after staining with crystal violet [Saotome K, Morita H, Umeda M.
Cytotoxicity test with simplified crystal violet staining method using microtitre plates and its application to injection drugs // Toxicol In Vitro. - 1989. - Vol.3, № 4. - P. 317-321. PMID: 20702298].

Twenty-four hours after infection, the cytopathic effect of the virus was checked: after the supernatant fluid was removed from the tears, 0.2% was added to the disinfectant solution and to the cells Crystal Violet ("Sigma", USA) dye solution in 2% ethanol. After 15 minutes, the dye was removed, and the stained cell monolayer was rinsed under running water. The optical density of the stained cells was measured at 540 nm.
The results were taken into account only if there were no cytodestructive changes in the virus-free control cultures (placebo - isotonic 0.9% sodium chloride solution), and complete cell destruction was observed in the virus control. Testing of antiviral effect was carried out with 24-hour contact of cells with the drug, which was administered 40 minutes after the
Test virus infection (Table 1).

3	1	2	3	4	5	6	7	8	9	10	11	12
A	KW	Virus + Placebo	Virus + A 1230	Virus + A 1230	Virus + A 1230	Virus + A 1230	Placebo	A 1230	A 1230	A 1230	A 1230	KK
B	KW	Virus + Placebo	Virus + A 123	Virus + A 123	Virus + A 123	Virus + A 123	Placebo	A 123	A 123	A 123	A 123	KK
C	KW	Virus + Placebo	Virus + A 12,3	Virus + A 12,3	Virus + A 12,3	Virus + A 12,3	Placebo	A 12,3	A 12,3	A 12,3	A 12,3	KK
D	KW	Virus + Placebo	Virus + A 1,23	Virus + A 1,23	Virus + A 1,23	Virus + A 1,23	Placebo	A 1,23	A 1,23	A 1,23	A 1,23	KK
E	KW	Virus + Placebo	Virus + A 0,123	Virus + A 0,123	Virus + A 0,123	Virus + A 0,123	Placebo	A 0,123	A 0,123	A 0,123	A 0,123	KK
F	KW	Virus + Placebo	Virus + A 0,012	Virus + A 0,012	Virus + A 0,012	Virus + A 0,012	Placebo	A 0,012	A 0,012	A 0,012	A 0,012	KK
G	KW	Virus + Placebo	Virus + A 0,001	Virus + A 0,001	Virus + A 0,001	Virus + A 0,001	Placebo	A 0,001	A 0,001	A 0,001	A 0,001	KK
H	KW	Virus + Placebo	Virus + A 0,0001	Virus + A 0,0001	Virus + A 0,0001	Virus + A 0,0001	Placebo	A 0,0001	A 0,0001	A 0,0001	A 0,0001	KK

* Conventional designations *KW - virus control; KK - cell control; Placebo - solvent (0.9% sodium chloride solution, isotonic); A 1230 - Kamelin drug substance at a concentration of 1230 µg/ml of culture medium.*
The study determined the antiviral effect of the drug Kamelin against the virus u RNA vesicular stomatitis (VRS) and determined the EC 50 - the effective drug concentration (µg/ml) required to inhibit the cytopathic effect of the virus by 50%, which was 10 µg/ml.
Camellin at a concentration of 16 µg/ml contributes to the survival of 96% of cells, and at a concentration of 500 µg/ml 100% of L929 culture cells (Figure 1-2).

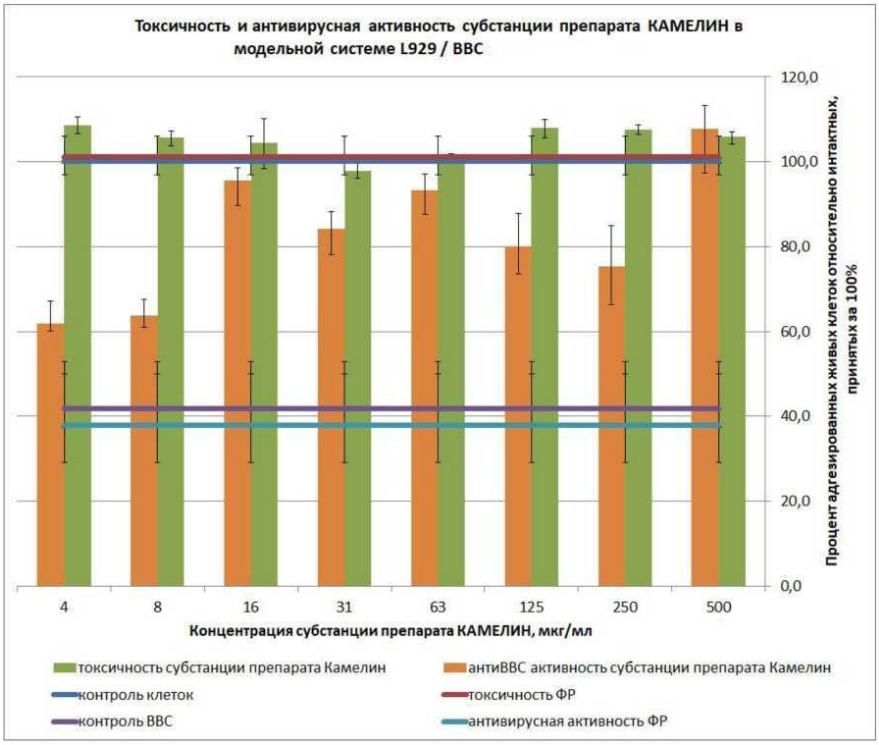

Figure 1 Application of Kamelin drug substance in the L929 / WPZJU model system. *Assays: cell control - number of intact cells of L929 lineage; RF (saline?) toxicity - number of cells of L929 lineage after contact with RF for 24 hours; Kamelin drug substance toxicity - number of cells of L929 lineage after contact with Kamelin drug substance for 24 hours; CSF control - number of cells of L929 lineage after 24 hours after infection with CSF virus; RF antiviral activity - number of cells of L929 lineage after infection with CSF virus and treatment of cells with RF for 24 hours; activity against CSF of Kamelin drug substance - number of cells of line L929 after infection with CSF virus and treatment of cells with Kamelin drug substance for 24 hours; % live cells - the number of adherent live cells of the L929 line relative to intact cells, considered 100%.*

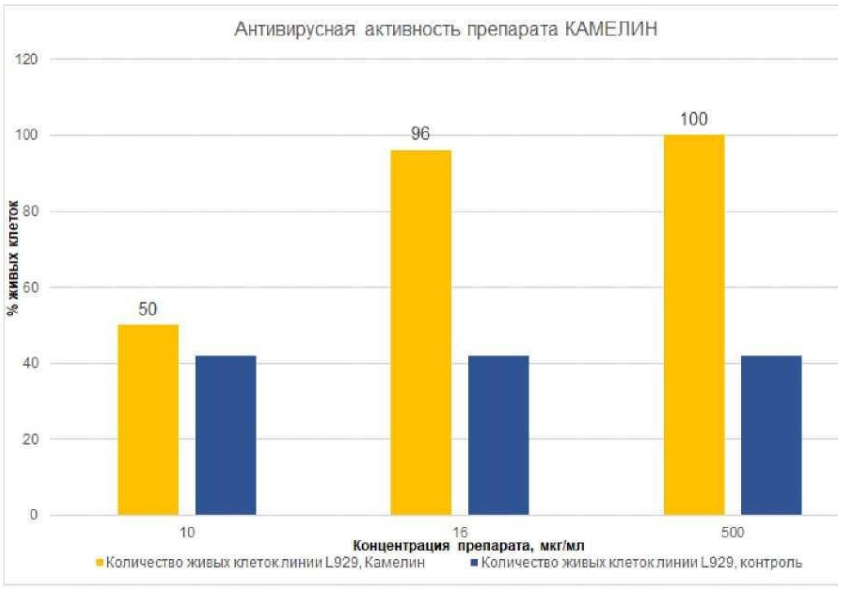

Figure 2: Substance use of the drug Kamelin in the L929 / WPZJU model system.

The results obtained demonstrate the significant antiviral activity of the drug Kamellin under the conditions of its use against RNA viruses, including the Rhabdoviridae family. Kamellin's proven antiviral efficacy against RNA genomic viruses is important for the prospects of the drug's use in current diseases such as hepatitis C, Coxsackie, hemorrhagic fever, coronavirus infection, seasonal rhinovirus infections, etc.

It should also be noted that when planning the prevention and treatment of acute respiratory viral infections, including Covid-19, it is important to take into account new data from 2020 scientific article materials obtained by specialists when treating this disease. In the article

Published in April in the scientific journal The Lancet (The Lancet) Dr. Varga (Zurich, Switzerland) with a group of scientists

have discovered that the SARS-CoV-2 virus can infect endothelial cells lining the inner walls of blood vessels. Endothelial cells protect the cardiovascular system and release proteins,
that affect its structural and functional indicators: from blood clot formation to immune response. "The concept we've tracked down is that coronavirus infection is not just a respiratory disease; it's considered a systemic disease
Respiratory due to the initial symptoms, but overall it is a vascular disease that threatens to
patients with fatal consequences due to cardiovascular interference," the researchers report. In their publication, the researchers reveal damage to vascular endothelial cells in the lungs,
heart, kidney, liver and other internal organs in patients with Covid-19 infection [9]. In view of the above, it is necessary to point out the clear angioprotective properties of the peptide RJP-1, which is part of the drug Kamelin. Patients with vascular pathology who took the Kamelin drug to restore immune homeostasis were ordered to test the drug's angioprotective potential by testing the expression level of vascular endothelial growth factor-VEGF-A.
Determination of VEGF-A in serum was carried out by indirect solid-phase immunoassay using kits from Bender MedSystems GmbH (Austria). Drug substance
Kamelin due to evolutionary properties of exogenous peptides react with regulatory proteins of cell membranes, stimulates expression of endothelial growth factor
Vascular. Increased VEGF-A activity promotes neovascularization, reduces hypoxia and improves trophism of ischemic tissues at the microlevel, provides repair of
damaged vascular endothelium, leading to better outcomes for patients with vascular pathology [10]. In the context of the above, the data obtained allow us to recommend Kamelin® as a promising drug for improving the prognosis of patients with viral infections accompanied by vascular damage, in particular the Covid-19 virus variant.

Applications

1. A placebo-controlled study confirms that the drug Kamelin shows clear antiviral activity in the L929/WPZJU (RNA virus) model.

2. The antiviral activity of the drug Kamelin is mainly due to the activity of natural anti-infective peptides, whose antiviral properties arose naturally during evolution against the more evolutionarily ancient RNA viruses.
3. Proven antiviral efficacy is important for the clinical perspective of the inclusion of Kamelin in treatment and prevention regimens for socially relevant diseases: seasonal rhinovirus (OWZDR) infections, tick-borne encephalitis, hemorrhagic fever
Ebola, coronavirus infection, hepatitis C, etc.

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