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Prospects for the use of N-stearoylethanolamine as an effective antiviral agent for the pharmacotherapy of herpes infection caused by human herpes simplex virus

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Endogenous N-acylethanolamines (NAEs) are part of a large group of endocannabinoids - compounds that, together with the corresponding cannabinoid receptors, make up the endocannabinoid regulatory system. NAE - derivatives of N-acylated phospholipids (NAPE) - a large and diverse class of signaling minor lipids. The data presented in the literature and the results of our own research indicate that NAE is an attractive target for the development of drugs for the treatment and prevention of cardiovascular, cancer,

neurodegenerative diseases, viral infections and more. We have previously shown that administration of saturated C18: 0 NAE N-stearoylethanolamine (NSE) to influenza virus-infected mice reduced the death of animals from influenza infection (Gula NM et al., 2014). It was also found that NSE in doses of 10-300 mg / kg is non-toxic and does not cause side effects. The aim of our study was to investigate the antiviral activity of NSE against herpes simplex viruses type 1 and 2 in vitro and in vivo.

Methods. In vitro studies used herpes simplex virus type 2 (HSV-2) - a strain of VN obtained from the Museum of Viruses of the Institute of Virology. DI Ivanovsky RAMS. The virus was maintained by serial passages in Vero cell culture. Infectious titer for JRS in cell culture was - 5.0 - 7.0 lg TCD50 / 0.1 ml. A model of herpes meningoencephalitis in mice was used to study the antiherpetic effect of NSE in vivo. Used lyophilized herpes simplex virus type 1 (HSV-1), strain VC. Animals (n = 10) were infected with herpes virus by intracerebral injection in a volume of 0.03 ml of viral suspension. The value of the infectious dose in the experiments was equal to 1-10 LD50 (lethal doses for mice). NSE was administered to animals (n = 10) intraperitoneally at a dose of 0.2 mg / kg body weight. Virolex from KRKA (Slovenia) was used as a reference drug. Infectious activity of the herpes virus was studied by animal mortality and infectious titer of the virus in brain tissue. NSE was administered in two ways: 24 hours before infection - a prophylactic way and 24 h after infection with the herpes virus - a treatment way. Evaluation of drug activity was performed by comparing mortality and inhibition of infectious titer in brain tissue in experimental and control groups.

Results. The mortality of control animals infected with the herpes virus was 100%. NSE was found to be effective in inhibiting the reproduction of herpes virus type 2 at concentrations of 10-6 to 10-8 M in Vero cell culture (selectivity index 103). In the group of mice receiving NSE at a dose of 0.2 mg / kg body weight before infection with the herpes virus, 40% of the animals survived. In the group receiving virolex at a dose of 10 mg / kg body weight, 50% of the animals survived. Inhibitory infectious titer in mouse brain tissue in lg ID50 was 2.0 for NSE, and 2.5 for virolex. In the case of NSE according to the treatment regimen, 75% of the animals survived, and in the group of mice treated with virolex - 50% of the animals. In this case, the inhibitory infectious titer in the brain tissue of mice in lg ID50 was equal to 2.5 for NSE and Virolex.

Conclusion. Therefore, NSE exhibits pronounced antiviral activity against herpes simplex virus in both in vitro and in vivo studies and is effective in both prophylactic and therapeutic ways of application. This indicates the

prospect of developing NSE-based drugs for the prevention and treatment of human herpes infections.