Z-Gly-Gly-ABC) were synthesized using thiazole-containing amino acid glycine – Gly and evaluated for anti-HIV activity on MT-4 cells. Cytotoxicity experiments showed Z-Gly-Gly-ABC and Z-Gly-ABC were more cytotoxic (CC50 = 70 μM and 100 μM respectively) than Gly-ABC (CC50 = 650 μM) which in turn proved less cytotoxic than ABC (CC50 = 160 μM). Gly-ABC inhibited HIV-1 III B replication measured by infectivity and reverse transcriptase (RT) activity, IC50 was detected to be 6.5 μM. Mitochondrial toxicity was established, although decline in both mitochondrial and nuclear DNA were found. Further, 32 passages of HIV-1 in MT-4 cells with increasing concentrations of Gly-ABC were carried out and RT region of the resulting virus was sequenced using Opengene, TRUGENE kit. IC50 increased up to 5 times compared to initial IC50. Both mutations found – K122E and T165I are not related to ABC as well as to other nucleoside reverse transcriptase inhibitors. Z-Gly-ABC and Z-Gly-Gly-ABC were not further evaluated due to their cytotoxicity. In conclusion, a new less cytotoxic derivative of ABC – Gly-ABC – was synthesized with high anti-HIV activity due to RT inhibition, low mitochondrial toxicity and most probably characterized by a high genetic barrier to resistance.

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Efficacy of Zanamivir Administered by Different Routes and at Different Times for Treatment of an Influenza A/CA/04/2009 (H1N1) Virus Infection in Mice

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Zanamivir is recommended for administration by inhalation. However, the intranasal route is problematic in mice because that route exacerbates the infection. This study determined the dose-responsive effects of zanamivir administered by three routes (i.p., i.m., or p.o.) against challenge infection of mice with influenza A/CA/04/2009 (pandemic H1N1) virus. Zanamivir doses of 3 and 10 mg/kg were effective at increasing survival regardless of the route of administration. The dose of 1 mg/kg also produced significant survival results when administered by the i.m. or p.o. routes. We also evaluated the antiviral effects of delayed zanamivir treatment, when initiated at 4, 24, and 48 h post-challenge infection. Twice daily treatments with zanamivir at 3 and 10 mg/kg for 5 days were compared to placebo controls matched for the route of administration. All mice survived challenge infection in the groups treated with 10 mg/kg zanamivir beginning 4 and 24 h post-infection. In addition, all treatment groups, at all three starting times showed significant improvement in survival compared to placebo controls. However, mortality was observed at the 3 mg/kg dose for the group receiving zanamivir by the i.p. route at all three staring times, and for the i.m. treatment group starting at 24 h post-infection. None of the treatments significantly prevented weight loss during the initial 8–10 days following infection. However, an improvement in mean body weight, observed as more rapid weight gain after day 12 post-infection, was almost exclusively observed for the 10 mg/kg dose at all three staring times. These results demonstrate that zanamivir administered by different routes can be used effectively to treat an influenza virus infection in mice, and that treatment can be delayed for 24 or 48 h post-infection and remain efficacious.

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Inactivated Vaccine Against Tick-Borne Encephalitis Virus as Surrogate Vaccine Against Omsk Hemorrhagic Fever Virus

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Tick-borne encephalitis virus (TBEV) and Omsk hemorrhagic fever virus (OHFV) are mammalian tick-borne flaviviruses. Viruses are closely related, and the *p*-distance is about 0.25 counted for the whole ORF. These viruses show cross-reactivity in neutralization test and other serological reactions. OHFV cause an acute disease with hemorrhagic syndrome and neurological symptoms. The virus is spread in Siberia (Russia) with sporadic cases, and there are shared foci of TBEV and OHFV in the area. Nowadays there is no any vaccine against OHFV.

In the present work we tried to evaluate the protective immunity against OHFV that is caused by immunization with inactivated vaccine against TBEV in mice and monkeys. First of all we modeled the Omsk hemorrhagic fever in BALB/c mice with hemorrhagic syndrome and neurological symptoms like paralysis. Virological and pathomorphological studies showed that two-time intramuscular vaccination of mice with TBEV vaccine protected 70% of animals from infection with $100LD_{50}$ OHFV.

The acute clinical symptoms did not registered in green monkeys (Cercopithecus aethiops) after OHFV inoculation. The OHFV infection in the monkeys was observed by clinical blood analysis and viremia, and by virus spread in CNS and viscerals after the autopsy. The two-time intramuscular vaccination with TBEV vaccine did not prevent the OHFV infection but strikingly decreased the level of virus spread and abnormal changes in blood samples. The TBEV vaccine does not prevent the OHFV infection but weakens the symptoms.

Summarizing all the facts we can conclude that TBEV vaccine could be considered only as a surrogate vaccine in urgent cases OHFV infection.

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Efficacy of Aminocaproic Acid use for Prevention of Some Infectious Diseases in Organized Collectives

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Previously, our studies have established the participation of proteolysis in the interaction of virus with the host organism. Aminocaproic acid (ACA), an inhibitor of proteolysis slows proteolysis raising and penetration of viruses into cells. Inhibition of replication of influenza virus types A and B, parainfluenza, adenoviruses, with the ACA in different cell systems was revealed. ACA leads to the stimulation of defense reactions of organism. Application of ACA on