dosages and minimize the development of drug resistance. The results of these experiments indicate that combinations of CMX-001 and ST-246 are particularly effective in the treatment of orthopoxvirus infections in vitro and suggest that this combination may also be optimal in treating these infections in animals and humans.

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Inhibition of Cellular Entry and Spread of Lymphocytic Choriomeningitis Virus by Amphipathic DNA Polymers

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Arenaviruses merit significant attention as powerful experimental models and the causative agents of several severe human hemorrhagic fevers with high mortality. Lymphocytic choriomeningitis virus (LCMV) serves as the prototype of the Old World arenavirus family and represents a powerful experimental model system for the study of arenavirus pathogenesis and treatments. In the present study, we tested the activity of novel sequence-independent amphipathic DNA polymers for activity against LCMV. Our findings indicate that REP 9, a 40mer degenerate PS-ON is a potent antiviral drug against LCMV infection, and revealed a novel antiviral mechanism for this class of drugs against this family of viruses. We determined that REP 9 targets the viral glycoprotein and blocks the initial steps of infection and cell-cell propagation of the virus. REP 9 blocks the binding of LCMV to its cellular receptor, a-dystroglycan, and can dissociate the stable virus-receptor complex. There is no apparent effect of REP 9 on the association between GP1 and GP2 or on the conformation of neutralizing antibody epitopes. Structure-function studies revealed that the action of REP 9 is sequence independent but has a critical dependence on size and hydrophobicity as seen for antiviral activity against type 1 enveloped viruses targeted by this class of compounds. The results herein suggest REP 9 has potential for treatment and prevention of arenavirus infection, and highlight our efforts towards the development of a unique class of anti-arenaviral drugs with a novel mechanism of action.

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Benzimidazole with Broad Spectrum of Antiviral Action

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Benzimidazoles show large-scale biological activity. The series of benzimidazoles and their derivatives were synthesized. An antiviral action of 2-methyl-4-dimethyl-aminomethyl-5-oxybenzimidazole was studied. Antiviral efficacy of this compound was predicted using developed by us hierarchical QSAR technology for molecular design of the promising antiviral compounds. Anti-HSV action was tested using cytomorphological method. Hep-2 cells were infected with HSV-1 strain US in dose 5 IFU/cell. The cells were incubated in Eagle's Medium that contained compound in experimental samples or without them in control samples. Then cells were fixed with 96% ethanol and stained with 0.01% acridine orange solution. The amount of infected cells with DNA-containing virus inclusion bodies was counted by fluorescent microscopy. Anti-HSV activity of compound was calculated as the difference between of the percentage of infected cells in treated cell cultures to the percentage of infected cells in untreated cell cultures.

Anti-influenza activity of the compound was studied on the model of replication of human A/Hong Kong/1/68 (H3N2) and avian H5N3 and H7N3 strains in tissue culture of chorioallantoic membranes of chicken embryos.

Anti-NDV activity was tested on the same model. 2-Methyl-4-dimethyl-aminomethyl-5-oxybenzimidazole in dose 20 mg/ml decreased amount of cells infected with HSV-1 by 60%. This compound in concentration 100 mg/ml inhibited of human influenza virus A/Hong Kong/1/68 (H3N2) replication on 1.0 $\log_{10}$ TID_{50}. In dose 100 mg/ml it decreased of avian influenza virus H5N3 reproduction on 1.0 $\log_{10}$ TID_{50}. 2-Methyl-4-dimethyl-aminomethyl-5-oxybenzimidazole did not show antiviral action in dose 200 mg/ml toward avian influenza virus H7N3, but this compound was active toward NDV. In concentration 100 mg/ml it decreased virus amount on 0.8 $\log_{10}$ TID_{50}.

The results of this research show that benzimidazoles are the perspective class of compounds for search of new agents with broad spectrum of antiviral activity.

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