hepatoprotective effect. In conclusion, triterpenoids extracted from PG efficiently suppressed HCV replication in HCV replicon system and could be a novel natural anti-HCV therapeutic agent.

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Combinatorial Anti-arenaviral Therapy with the Small Molecule SKI-1/S1P Inhibitor PF-429242 and Ribavirin

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Arenaviruses are enveloped negative strand viruses that cause acute and chronic infections. Several Arenaviruses can cause severe hemorrhagic fever in humans. In West Africa Lassa virus causes several hundred thousand infections per year, while Junin, Machupo, Guanarito, and Sabia virus have emerged in South America. So far, only one drug is licensed against arenaviruses, the nucleoside analogue Ribavirin (Rib), which is effective when given early in disease, but shows only minor therapeutic effects in late stages of the infection. Previous works demonstrated that processing of the arenavirus glycoprotein precursor (GPC) by the cellular proprotein convertase site 1 protease (S1P), also known as subtilisin-kexin-isozyme 1 (SKI-1), is crucial for cell-to-cell propagation of infection and production of infectious virus. Recently, the SKI-1/S1P inhibitor PF-429242 was shown to inhibit Old World arenavirus GPC processing, cell-to-cell propagation, and infectious virus production. In the present study, we assessed the activity of PF-429242 against processing of the GPCs of the genetically and structurally more distant New World arenaviruses and found potent inhibition of processing of the GPCs of Junin, Machupo, and Guanarito virus. Using the prototypic arenavirus lymphocytic choriomeningitis virus (LCMV), we studied the potency of PF-429242 in the context of acute and chronic infection. In line with published data, PF-429242 potently inhibited acute LCMV infection. PF-429242 was also highly active against chronic infection and drug treatment resulted in rapid extinction of the virus without emergence of drug-resistant variants. In a combinatorial drug approach, we found that PF-429242 potentiated the anti-viral effect of Rib in treatment of acute and chronic infection. Taken together, we showed that the SKI-1/S1P inhibitor PF-429242 is broadly active against GPC processing of all major human pathogenic arenaviruses. Apart from being potent in acute infection, the drug is remarkably active in clearing chronic infection and potentiated the anti-arenaviral activity of Rib.

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Generation of dsRNAs Targeting VP1 and VP3 Gene Regions of Coxsackievirus B1 Utilizing Bacteriophage ϕ6 Polymerase Complex

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Coxsackievirus infections can result in a wide variety of disease syndromes including upper respiratory tract symptoms, aseptic meningitis, pericarditis, pleurodynia, myocarditis, and encephalitis. No anti-Coxsackievirus drugs are currently licensed and treatment is directed toward ameliorating symptoms. This places the need of new tools to control virus infections. RNA interference is a mechanism for silencing the transcriptional product of an activated gene. Its high conservancy and sequence-specificity are the basis for its huge potential for therapy against various infectious diseases, genetic disorders, and cancer. A way for high-quality and cost effective production of large quantities of double-stranded RNA is the use of virus-based systems targeting specific regions of the virus genome. T7 RNA polymerase and RNA-dependent RNA polymerase of bacteriophage ϕ6 were used to generate dsRNA molecules from 3′ part of VP3 and 5′ part of VP1 gene regions of Coxsackievirus B1. For large amounts of dsRNA production we utilized *Pseudomonas syringae* cells that constitutively express the bacteriophage ϕ6 complex, and plasmids with the target sequences placed under T7 promoter.

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Inhibition of Herpes- and Adenovirus Replication by Extract of *Artemia salina* Cysts from Crimean Hypersaline Lakes

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Adenoviral infection is a widely distributed human pathology and takes the second place for its spread among acute respiratory infections after influenza. So far, no specific and effective medicines have yet been developed for the treatment of local and systemic forms of adenoviral infection. The diseases caused by Herpes simplex virus (HSV) are widely distributed. Treatment of these infections is the most significant medical problem. At present for the treatment of these diseases nucleoside (acyclovir, ganciclovir, penciclovir, cidofovir) analogues are used. But the appearance of resistant virus is current problem in the treatment of patients and deficiency in the antiviral preparations caused their toxicity. Therefore, it is very important to develop new antiviral drugs against this virus. Very promising approach is the antiviral screening of products derived from natural sources including marine fauna and flora, bacteria, fungi, and green plants. We have studied the antiviral activity against Herpes simplex virus (HSV-1, strain US) and Human adenovirus type 2 (Adh2) of the protein extracts (PE) which were produced from *Artemia* cysts collected in Crimean hypersaline lakes. Anti-viral experiments were performed in vitro on *Hela* cells. PE was tested for antiviral activity against HSV-1 by a plaque reduction assay. The rate of Adh2 like viral reproduction inhibition was evaluated by the decrease percentage of the cells with specific viral intra-nuclear inclusions. The highest inhibitory effect was observed when PE was added to cells immediately after absorption of viruses at 1 h.p.i. It was determined that PE in concentration of 16 μg/ml inhibited the reproduction of HSV-1, EC_{50} of PE was 2.8 μg/ml, and selectivity index (SI) was 7. PE in concentration 2 μg/ml decreased the number of infected Adh2 cells with intranuclear inclusions on 99%, EC_{50} of PE was 0.3 μg/ml, SI was 60. The compounds of these extract probably act on the inhibition of late stages of the viral reproduction. These results suggest that PE have a potential value as a source of new effective compounds against human adenovirus.

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