pound after iv was in urine (50–60%), with 10–20% in feces. After po administration, radioactivity was excreted about equally in urine and feces, ~35% each in 24 h. Thus, acyloxyalkly derivatization represents a novel strategy for the oral delivery and liver-targeting of dinucleotide compounds and oligonucleotides.

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CYSTUS052, a New Compound Against Seasonal and Pandemic Influenza Virus

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Influenza still represents a major threat to humans and several animal species. Beside vaccination, only two classes of drugs are available for antiviral treatment against this pathogen. The appearance of pandemic H1N1 and highly pathogenic avian influenza viruses of the H5N1 subtype being able to infect humans reveal the urgent need for new and efficient countermeasures against this disease. Even though several antiviral compounds have been developed against influenza virus, their long-term efficacy is often limited, because of their toxicity or the emergence of drug-resistant virus mutants. Moreover, it is also widely discussed that neuraminidase inhibitors the most common anti-influenza agents, are less effective against new H5N1 isolates and seasonal H1N1 strains. In this regard, we were able to show that a polyphenol rich plant extract from a special variety of Cistus incanus named CYSTUS052 exhibits antiviral activity against influenza viruses *in vitro* and in a mouse model and a randomized, placebo controlled clinical study. The recovery from clinical symptoms was 2.5 days faster in the CYSTUS052 group compared to patients from the placebo group. In addition, we investigated the antiviral potential of CYSTUS052 in comparison to oseltamivir against the swine origin influenza virus (SOIV) H1N1 and various H5N1 influenza viruses. Using an *in vitro* infectivity inhibition assay we found that during the first 24 h after infection a single treatment of CYSTUS052 was highly effective against these H5N1 viruses compared. Therefore, we conclude that CYSTUS052 might be an effective antiviral with prophylactic and therapeutic potential against influenza viruses including the current pandemic strain and A/H5N1.

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Lectins and T-20, but not Neutralizing Antibodies, Inhibit HIV-1 Env-mediated Syncytium Formation between Clone69t1RevEnv and Supt1 Cells Monitored by Fluorescence Microscopy

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Objectives: The HIV-1 envelope protein Env (gp120/gp41) mediates the fusion of the viral envelope with the host cell membrane. We developed an HIV fusion assay, using fluorescent Clone69T1RevEnv cells expressing Env, and highly CD4+ SupT1 cells. We examined whether previously established inhibitors of HIV-1 infection, including a peptide, lectins, and neutralizing antibodies, inhibit Env-mediated syncytium formation.

Methods: Clone69TRevEnv cells were induced to express Env by removing tetracycline from the medium. The cells were labeled with Calcein-AM Green, incubated for 3 h with SupT1 cells labeled with CellTrace™ Calcein red-orange, with or without the inhibitors, and observed under a Nikon inverted fluorescence microscope. Co-localization of the two fluorescent probes following syncytium formation resulted in orange fluorescence. Antibodies were obtained from the NIH AIDS Research & Reference Reagent Program, Polymun (2G12) and D. Dimitrov (m14; NIH). T-20 was from the AIDS Reagent Program.

Results: The lectins *Hippeastrum hybrid* agglutinin (HHA) and *Galanthus nivalis* agglutinin (GNA), and the peptide T-20, inhibited syncytium formation at 1 μg/ml. Antibodies to gp120 (IgG1B12, m14 IgG, F105 and 2G12), and gp41 (2F5 and 4E10) that inhibit HIV-1 infection had little or no inhibitory effect on syncytium formation.

Conclusions: The observation that antibodies that inhibit HIV infection are not effective against syncytium formation, suggests that the mechanisms of interaction of Env with cell membrane CD4 and co-receptors may be different in cell–cell and virus-cell membrane fusion, as suggested previously (J. Gen. Virol., 1995, 76, 669–679). These results also indicate that "neutralizing" antibodies may not be able to inhibit the spread of viral genetic material from infected cells to uninfected cells. This fluorescence assay can be adapted to screen novel inhibitors of membrane fusion in high-throughput assays.

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CYSTUS052, a Polyphenol Rich Plant Extract, Exerts Potent Antiviral Activity Against Influenza- and Rhinoviruses by Preventing Viral Attachment to Host Cells

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Infections with influenza A viruses (IAV) still pose a major threat to humans and several animal species. The appearance of highly pathogenic avian H5N1 viruses and new H1N1v swine-origin influenza virus in humans as well as the increasing incidence of resistance to the currently available medication highlight the urgent need for novel antiviral drugs for prophylaxis and therapy. Here we demonstrate that the polyphenol rich plant extract CYSTUS052 from a variety the Mediterranean plant *Cistus incanus* exerts a potent anti-influenza virus activity in cells infected with various influenza viruses including those of the H5N1 and H1N1v type. The extract is also highly active against different types of human rhinoviruses (HRV). CYSTUS052 did not exhibit apparent harming effects on cell viability and did not influence metabolism, proliferation or cell activation by extracellular ligands. Furthermore, viruses did not develop resistance to CYSTUS052 upon consecutive passaging. Mechanistically, the protective effect appears to be due to a binding of the CYSTUS052-ingredients to the virus surface, preventing virus-binding to cellular receptors. Since these plant extracts are already in use in traditional medicine for centuries without reports of side effects, local application of CYSTUS052 to the respiratory tract may be a promising approach for