cost less since 1 or 2 g of ribavirin can be used daily instead of 6 g.

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Therapy of Advanced Arenaviral Infection in Hamsters with T-705

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Severe arenaviral diseases such as Lassa fever are insidious in their progression and generally do not present with distinguishing symptoms, making them difficult to clinically diagnose at early stages. Consequently, it is of utmost importance to identify antiviral therapies that can be effective when given at later times during the course of infection, which is consistent with the time whereby patients would actually seek medical attention due to illness. T-705 has proven to be efficacious in the Pichinde virus (PICV) hamster infection model of severe arenaviral disease when treatment is initiated within 3 days of viral challenge with a highly lethal viral inoculum. Here we present efficacy data based on the initiation of therapy as late as 7 days post-PICV challenge and compare the antiviral activity of T-705 with that of ribavirin. Both drugs offered significant protection when given as late as day 6 of infection, but hamsters receiving ribavirin lost considerably more weight and those that survived recovered at a much slower rate. At equitoxic doses, T-705 was found to be more effective than ribavirin when treatment was started on day 5 of infection, but comparable when started on day 6. T-705 activity was also compared to the related pyrazine analog, T-1106, reported to be highly active in the hamster model of yellow fever. In contrast to T-705, only limited protection was seen with T-1106 in the PICV infection model when treatment was begun 4 days after viral challenge. Determining the efficacy of T-705 when treatment is started at later stages of infection and in the face of substantial viral burden is important from a practical standpoint, as therapy in human cases would most likely start when patients are viremic. In this regard, the significant protection of PICV-challenged hamsters by therapy with T-705 initiated 2 days prior to the time when animals begin to succumb to the infection is encouraging. Moreover, T-705 appears to be as effective as ribavirin at treating PICV infection in hamsters and considerably less toxic.

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Virucidal Activity of Extracts from Four Algae Species Against Herpes Simplex Virus

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Herpes simplex virus types 1 and 2 (HSV-1, HSV-2) are the cause of a wide variety of human diseases. These viruses are opportunistic and their infection can result in major problems in immunocompromised individuals. The drugs currently used to treat cutaneous or genital HSV infections are effective in limiting disease, although the emergence of drug resistant viruses is observed after prolonged therapy. Prophylactic systemic treatment with antiviral drugs reduces transmission but there is continuing need for topical microbicides with virucidal activity that have the potential to limit transmission of the virus. Previous reports demonstrated the antiviral activity of complex carbohydrates extracted from some seaweed species and suggested that they interfered with the attachment of virions to host cells. Here, we evaluated the antiviral activity of extracts from *Undaria pinnatifida*, *Splachnidium rugosum*, *Gigartina atropurpurea*, and *Plocamium cartilagineum* against HSV-1 and HSV-2 in standard laboratory assays. This series of compounds exhibited good activity when added during viral infection, but were ineffective if they were added after the first hour of infection. Pretreatment plaque reduction assays with these compounds yielded EC_{50} values that ranged from (1.9–45 μg/ml) for HSV-1, (0.8–7.4 μg/ml) for HSV-2. None of the compounds exhibited significant toxicity in a neutral red uptake assay ($IC_{50} > 100$ μg/ml). Subsequent assays revealed that the compounds possessed virucidal activity and were capable of inactivating virus at very low concentrations. We conclude that these extracts are nontoxic and effective virucidal agents that warrant further investigation to determine their potential role in the treatment of HSV infections of humans.

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Luciferase-based Assay for Rapid Screening of Antivirals against Human Cytomegalovirus

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Human cytomegalovirus (HCMV) infections continue to be a problem in the immunocompromised host. There is a growing need for new classes of compounds that are effective against nucleoside-resistant mutants and are also less toxic than the currently available compounds. A recombinant virus was described previously that expresses luciferase from an immediate early promoter (McVoy and Mocarski, 1999). An assay was developed using this virus to facilitate the evaluation of large numbers of new compounds for potential antiviral activity. In this assay,