Kutapressin Inhibits In Vitro Infection of Human Herpesvirus Type 6. D. V. ABLASHI, Z. BERNEMAN, C. LAWYER, AND A. KOMAROFF. *From the National Cancer Institute, Bethesda, Maryland; Georgetown University School of Medicine, Washington, D.C.; Private Practice, Mequon, Wisconsin; Division of General Medicine, Brigham and Women's Hospital, and Harvard University, Boston, Massachusetts.*

Kutapressin (KU; Schwarz Pharma, Milwaukee, WI), is a prescription drug consisting of processed extract from porcine livers that contains peptides; it has been used in the treatment of patients with herpes zoster, keloids, seborrhea, other skin diseases, and neurasthenia. More recently, results of uncontrolled studies have indicated that treatment with KU results in the abatement of symptoms of many patients with chronic fatigue syndrome (CFS). One large study found evidence of reactivation of human herpesvirus type 6 (HHV-6) in many patients with CFS. Moreover, HHV-6 DNA was detected by Southern blot analysis in lymphocytes from patients with CFS. Because treatments with KU may have positive clinical effects on patients with CFS and the evidence that CFS is associated with reactivation of HHV-6, we investigated the possibility that KU might have direct activity against HHV-6.

KU that was free of phenol was dissolved in tissue culture medium (RPMI 1640 supplemented with 10% fetal calf serum and antibiotics) for in vitro studies. A human T lymphocyte cell line (HSB-2) was infected with HHV-6.

KU blocked HHV-6 (variant A, GS strain) infection of HSB-2 cells most effectively at doses of 300 and 500 μg/mL. These doses of the drug were not toxic to the cells. Inhibition of HHV-6 infection (1,000 $TCID_{50}$) was most effective (>95%) when cells (>10^6/mL) were pretreated with KU overnight, prior to viral infection, and then were maintained in the presence of KU throughout the experiment (14 days after infection). In addition, inhibition (>80%) of HHV-6 infection was observed when HSB-2 cells were first infected with 1,000 $TCID_{50}$ of HHV-6 and were then maintained in the presence of 300- and 500-μg doses of KU. When 300 and 500 μg/mL doses of KU were added to cells 3 days after the start of infection with HHV-6, it inhibited only 22% and 33% of viral infection, respectively. When the cells were simultaneously treated with virus and 300 and 500 μg/mL of KU, ~90% of the HHV-6 infection was inhibited.

These data show that KU is a potent inhibitor of HHV-6 infection. Although the mechanism of HHV-6 inhibition by KU is under investigation, electron microscopic examination of cells treated with KU prior to HHV-6 infection revealed abundant extracellular virus particles, which suggests inhibition of viral attachment and penetration.

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Poly(I)·Poly(C_{12}U) Inhibits In Vitro Replication of Human Herpesvirus Type 6. D. V. ABLASHI, Z. BERNEMAN, D. R. STRAYER, R. J. SUHADOLNIK, NANCY L. REICHENBACH, PATRICIA HITZGES, AND A. KOMAROFF. *From the National Cancer Institute, Bethesda, Maryland; Georgetown University School of Medicine, Washington, D.C.; Hahnemann University and Temple University, Philadelphia, Pennsylvania; and Brigham and Women's Hospital and Harvard University, Boston, Massachusetts.*

Poly(I)·poly(C_{12}U) (Ampligen; HEM Pharmaceuticals, Rockville, MD) is an antiviral drug that has been used to treat human immunodeficiency virus (HIV)–positive patients with AIDS-related complex or AIDS. More recently, Ampligen was also used in vivo to treat a limited number patients with chronic fatigue syndrome (CFS) whose peripheral blood lymphocytes were positive for human herpesvirus type 6 (HHV-6) antigens. Studies have shown that HHV-6 is highly reactivated in patients with CFS. Since the specificity of Ampligen's activity against HHV-6 infection has never been tested directly, we were interested in evaluating the drug in vitro as an anti-HHV-6 agent.

HSB-2 cells (immature T lymphocytes) were infected with HHV-6 (variant A, GS strain). One thousand $TCID_{50}$ of HHV-6 and four dosages of Ampligen (10, 50, 100, and 200 μg/mL) were used in this study. HHV-6 infection was monitored by observation of morphological changes in cells, by detection of HHV-6 antigens by polyclonal and monoclonal antibodies to HHV-6, and by electron microscopy.

Ampligen was most effective in blocking HHV-6 infection (98% inhibition) at the 100- and 200-μg doses (these doses were not toxic to HSB-2 cells) when the cells were pretreated with the drug prior to viral infection and maintained in the presence of the drug. Ampligen also inhibited HHV-6 infection (>95%) when the cells were first infected with HHV-6 and then treated with the drug; HHV-6 infection was blocked (95% inhibition) when virus and drug were added together to the HSB-2 cells. When the Ampligen was removed from the virus-infected cell culture, the HHV-6 infection reappeared slowly but never reached the same level as that observed in only virus-infected cells (55% vs. 95%). Ampligen also significantly (>98%) inhibited HHV-6 DNA polymerase activity. Electron micrographs showed either unassembled virus in the nucleus or extracellular virus particles, which could not enter the cell. This finding suggests that Ampligen may block the receptors on the cell surface, which prevents virus entry and adsorption to the cell.

The data show that Ampligen is a potent inhibitor of HHV-6 replication. The mechanism of action of Ampligen is still to be investigated.

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