Studies on Two New Antiviral Agents Against Guinea Pig Lymphotropic Herpesvirus Infection in vitro. J.M. HU and G.D. HSIUNG. Yale University School of Medicine, New Haven, CT 06510 and VA Medical Center, West Haven, CT 06516 U.S.A.

Guinea pig lymphotropic herpesvirus (GPHLV) has been shown to share many common biological properties with human Epstein-Barr virus (EBV). Two new antiviral agents, Compound 102 (4-amino-5-bromo-7-(2-hydroxyethoxymethyl) pyrrolo [2,3-d] pyrimidine) and 2'-nor-cGMP (9-[(2-hydroxy-1,3,2-dioxaphosphorinan-5-yl) oxymethyl] guanine P-oxide), were evaluated for their antiviral activity against GPHLV infection in guinea pigs as an animal model for EBV infection. For the determination of ED_{50} and ED_{99}, the plaque reduction assay and virus yield reduction assay were done respectively using guinea pig embryo cell cultures.

Drugs	ED_{50} (μM)	ED_{99} (μM)
ACV (acyclovir)	145.5	2500
Compound 102	35.5	630
2'-nor-cGMP	2.0	28

These data indicate that both drugs were more active than ACV against GPHLV infection in cell culture. Ultrastructural studies revealed that Compound 102 reduced the formation of viral dense cores, production of viral nucleocapsids and development of enveloped virions. Our findings suggest that these two new antiviral agents warrant further investigation against lymphotropic herpesvirus infection.

Activity of 5-Bromovinyl-2'-deoxycytidine in Combination with Deaminase Inhibitors Against Herpes Simplex Virus Type 1. Philip J. Aduma*, Sagar V. Gupta* and Erik De Clercq+. *Department of Physiological Sciences, WCVM, University of Saskatchewan, Saskatoon, Canada and +Rega Institute for Medical Research, Katholieke University, Leuven, Belgium.

Most deoxyuridine analogs with selective antiherpes activity are rapidly catabolized to inactive pyrimidine bases by thymidine phosphorylase, thus reducing their usefulness for the treatment of systemic Herpes Simplex Virus (HSV) infections. This limitation can be overcome by use of the deoxycytidine (dCyd) compounds provided deamination can be prevented in vivo. Reasons for this hypothesis are: (i) dCyd analogs will be anabolized exclusively using HSV-induced dCyd/deoxycytidylate (dCydMP) kinase pathway in HSV-infected cells to triphosphates; and (ii) these analogs will be stable to phosphoryltic cleavage because they do not serve as substrates of phosphorylases. To test this hypothesis, we have determined the antiviral activity and cytotoxicity of 5-bromovinyl-2'-deoxycytidine against HSV-1 singly and in combination with deaminase inhibitors, tetrahydrouridine (inhibits dCyd deaminase) and tetrahydrodeoxyuridine (inhibits both dCyd and dCydMP deaminase) using rabbit kidney (contains primarily dCMP deaminase), HEP-2 and Vero cells (contain both deaminases) and Chinese hamster ovary cells (lack both deaminases) in cell culture. Results of these investigations will be discussed.