108

SITE OF ACTION OF 9-/1,3-DIHYDROXY-2-PROPOXYMETHYL/GUANINE /DHPG/ IN THE VIRUS REPLICATION CYCLE. M. Dragúň and B. Rada, Institute of Virology, Slovak Academy of Sciences, 842 46 Bratislava, Czecho-Slovakia.

The time-course of the DHPG-sensitive step in the herpesvirus replication cycle /strain Kupka in the one-step growth experiments in suspensions of VERO cells/ has been studied by addition of the analog to infected cultures at various times post infection /p.i./ and determining the virus yield at 12 hr p.i. Formation of the component essential for virus replication is completely inhibited by DHPG up to 2-3 hr p.i. The kinetics of formation of the DHPG-sensitive component precedes the appearance of infectious virus by 2 hr. - Using the modified agar-diffusion plaque-inhibition test nine deoxy- and ribonucleosides were tested for the reversal of the antiviral effect of DHPG incorporated in an agarose medium overlay. Only thymidine and deoxyuridine were found to be able to reverse the inhibition of herpesvirus plaque formation caused by DHPG. In one-step growth experiments thymidine caused partial reversal of the inhibition. Thereby we confirm the previous results of Cheng et al. Even in the presence of a tenfold higher concentration of thymidine /than that of DHPG/ this metabolite was not able to cause complete reversal of the inhibition by DHPG. A competition for nucleoside kinase and DNA polymerase between DHPG and thymidine and their triphosphates may occur in the virus infected cell.

109

Inhibition of HSV-2 replication and glycoprotein expression in human fibroblast cells by HPMPC. S. Chatterjee, P. Burns, R.J. Whitley, and E.R. Kern, Department of Pediatrics, University of Alabama School of Medicine, Birmingham, Alabama 35294, U.S.A.

An acyclic nucleotide analogue, (S)-1-[(3-hydroxy-2-phosphonyl methoxy) propyl] cytosine (HPMPC) inhibited the replication of herpes simplex virus type 2 (HSV-2) in human fibroblast cells by more than 99% at a concentration of 1 µg/ml. Release of total extracellular virus particles from HSV-2-infected and HPMPC-treated human cells was also significantly reduced. The inhibition of HSV-2 replication in human cells was greater than that previously observed with HSV-1 in the same cells. Electron microscopic observation of infected and treated cells demonstrated few extracellular complete virions. Immunoblot analysis of virus-specific proteins showed that HPMPC blocked the expression of HSV-2 proteins including glycoproteins B, E and H. The expression of glycoprotein D was also reduced although not as significantly as observed with other glycoproteins. Furthermore, HPMPC inhibited the synthesis of viral DNA as determined by in situ hybridization. These results indicate that HPMPC inhibits the replication of HSV-2 by blocking one of the early events involved in DNA synthesis. Further studies are in progress to define it's exact mechanism of action against HSV-2 in human cells.