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HPMPG: An Acyclic Guanosine Phosphonate Which Exhibits Broad Spectrum, Antiviral Activity.
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(R,S)-9-(3-Hydroxy-2-phosphonylmethoxypropyl)guanine[(R,S)-HPMPG] exhibited broad spectrum antiviral activity; with ED_{50} less than 1μM against herpes simplex virus types (HSV) 1 and 2, varicella zoster virus, human cytomegalovirus (HCMV) and vaccinia in plaque reduction assays. Both HSV-2 and a thymidine kinase (TK) deficient variant were equally sensitive to HPMPG. HPMPG was about 100-fold more potent than acyclovir (ED_{50} = 0.45μM *vs.* 44μM, respectively) against HCMV in cell culture, and 10-fold more active than acyclovir in extending survival time in mice infected with 100 LD_{50} HSV-1 i.p. However, HPMPG was toxic when given repeatedly at 44 mg/kg/day in adult mice. HPMPG triphosphate was synthesized and acted as a competitive inhibitor relative to dGTP in an HSV-1 DNA polymerase assay (K_i = 0.03μM); 40-fold more active against HSV DNA polymerase than against HeLa alpha polymerase. Consistent with inhibition of viral DNA synthesis, 3 to 10μM HPMPG reduced late (γ) viral polypeptide synthesis in HSV-1 infected cells. Taken together, these data indicate that HPMPG is a TK independent broad spectrum antiviral drug which is probably effective by selective inhibition of viral DNA polymerase.

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Studies on the mode of action of the new antiviral agent hydroxyphosphonylmethoxypropyl adenine (HPMPA) using bovine herpesvirus-1.
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HPMPA was found to be a selective inhibitor of bovine herpesvirus-1 (BHV-1) in bovine tissue culture having an ED50 against several different strains of the virus of approximately 0.1 ug/ml. Resistant mutants of BHV-1 were isolated by passage in the presence of the inhibitor. It was of interest that one mutant (6660, RP1) showed unusual growth characteristics. Attention was focussed on the DNA polymerase induced by this mutant and these observations together with those from biochemical and electron microscopic studies will be discussed in relation to the molecular basis for the mode of action of the drug.