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Antiviral Effect of Compound 2'-nor-cGMP Against Cytomegalovirus Infection in the Guinea Pig Model. Z.H. YANG, R.L. TOLMAN, R.J. COLONNO and G.D. HSIUNG. Yale University School of Medicine, New Haven, CT. 06510, Merck, Sharp & Dohme Research Laboratory, West Point, PA. 19486 and VA Medical Center, West Haven, CT. 06516 U.S.A.

Previous studies showed that 2'-nor-cGMP (9[(2-hydroxy-1,3,2-dioxaphosphorinan-5yl) oxymethyl)] guanine P-oxide, sodium salt), had broad spectrum of activity against DNA viruses in cell cultures. In the present study, the antiviral activity of this compound against guinea pig cytomegalovirus (GPCMV) infection was evaluated in both in vitro and in vivo. First 2'-nor-cGMP was found to be highly potent against GPCMV infection in guinea pig embryo (GPE) cell cultures. In the plaque reduction assay, the ED_{50} of the compound against GPCMV replication in cell cultures was 3.3 μM, which was about 15-fold lower than that of DHPG and 150-fold lower than that of ACV. Virus infectivity titers were reduced by 2 and 4 $\log_{10}$ $TCID_{50}$ at concentrations of 3.75 μM and 7.5 μM respectively, when compared with the drug-free virus infected control. In an in vivo study, Hartley guinea pigs infected intraperitoneally (I.P.) with GPCMV were treated with the compound 25 mg/kg/day (I.P.) for 4 days, starting 24 hr. after virus inoculation. Virus infectivity titers were significantly lower in the lung, spleen and liver of 2'-nor-cGMP treated guinea pigs than those obtained in the sham-treated animals on day 8 post-infection. The differences were statistically significant ($p<0.01$). These results indicated that 2'-nor-cGMP was highly effective in inhibiting GPCMV infections both in vitro and in vivo.

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Cytomegalovirus (CMV) Infection In Immunocompromised Guinea Pigs: A Model For Testing Antiviral Agents In Vivo. M.J.C. Aquino-De Jesus and B.P. Griffith. Yale Univ. Sch. Med., New Haven, CT and V.A. Med. Cent., West Haven, CT, USA.

Therapy for CMV infections is urgently needed in the immunocompromised patient. This study aimed at establishing a convenient experimental model for testing antivirals agents in immunocompromised hosts. Groups of guinea pigs inoculated with CMV were given cyclophosphamide (Cy) and compared to sham treated CMV infected animals. Group A received one dose of 300mg/kg two days prior to virus inoculation. Group B received one dose of 300 mg/kg one day after virus inoculation. Group C received one daily dose of 30 mg/kg for 5 days starting one day before virus inoculation. Deaths occurred only in Cy treated animals, and mortality rates ranged from 33% to 100%. Clinical disease was most severe in animals from group B. Virus titers measured in blood on days 7-8 after virus inoculation were higher in blood of Cy than in sham treated animals and were highest in animals from group A. CMV infected guinea pigs given Cy and treated with 9-(1,3-dihydroxy-2-propoxymethyl)guanine (50 mg/kg daily for 8 days) had death rates and virus titers in blood that were each reduced by a mean of 50% as compared to Cy treated CMV infected controls. These data indicate that this guinea pig model can be used for studies of CMV therapy in the immunocompromised host.