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In Vitro Anti-Hepatitis B Virus and Anti-Human Cytomegalovirus Activities of Selected 2',2'-Difluoro Purine and Pyrimidine Nucleoside Analogs. J. M. Colacino, C. S. Grossman, K. A. Staschke, A. J. Schilke, J. S. Kroin and L. W. Hertel. Lilly Research Laboratories, Indianapolis, Indiana, USA.

Recently, a number of 2'-deoxy-2',2'-difluoro nucleoside analogs were evaluated for their ability to inhibit the replication of hepatitis B virus (HBV) in an HBV producing human hepatoma cell line by quantifying extracellular virion DNA using PCR analysis. Of seven purine nucleoside analogs tested, two compounds displayed anti-HBV activity: 1) 2'-deoxy-2',2'-difluoro-2-amino-6-methylaminopurine (# 296416) displayed a 50% inhibitory concentration (IC_{50}) of <0.32 μM and a 50% cytotoxic concentration (TC_{50}) of 26.2 μM, thus yielding a selective index (TC_{50}/IC_{50}) of >80; 2) 2'-deoxy-2',2'-difluoroguanosine (# 223592) displayed an IC_{50} of 0.24 and a TC_{50} of <8.2 thus yielding a selective index of <34.2. Other 2',2'-difluoro purine nucleoside analogs tested displayed marginal or no anti-HBV activity. Compound 296416 inhibited HCMV replication with an IC_{50} of approximately 3 μM, as determined in a plaque reduction assay. Two other analogs, 2'-deoxy-2',2'-difluoro-2-amino-6-methyleneaminopurine and 2'-deoxy-2',2'-difluoro-2-chloro-6-hydroxypurine displayed no anti-HBV activity but were at least as potent as 296416 against HCMV replication. Among 2',2'-difluoro pyrimidine nucleoside analogs tested, 2'-deoxy-2',2'-difluoro-5-iodocytosine (# 188114) displayed only marginal anti-HBV activity with an IC_{50} of 9.4 μM. Compound 188114 is the difluoro analog of the mono arabino-fluoro compound, FIAC, which has demonstrated potent in vitro and in vivo anti-HBV activity. The compounds, 2'-deoxy-2',2'-difluorouridine (#198791) and 2'-deoxy-2',2'-difluoro-4-methoxy-pyrimidinyl-2-one (# 303373) were not inhibitory to HBV replication. Additionally, compound 198791 displayed no activity against HCMV replication. Interestingly, those compounds above which inhibited HBV and HCMV replication, displayed no antiviral activity against herpes simplex virus types 1 or 2 indicating that the mechanism underlying the antiviral activity of these compounds is not dependent on the presence of a virus specified purine or pyrimidine nucleoside kinase.

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Revealing of Virus Hepatis A Inhibitors Among Spasmolitic Drugs. S.V.Orlova, N.P.Mischaeva, A.B.Tarasenko, A.A.Zgirovskaya, T.V.Amvrosieva. Byelorussian Research Institute for Epidemiology & Microbiology, Minsk, Republic of Byelarus

Virus hepatitis A (HAV) morbidity is a prevalent feature in the patology of individuals, one of the main reason being the lack of etiotropic drugs to treat HAV-patients. We conducted investigations on antiviral properties of officinal drugs - Nicoverinum and Trental. They used as spasmolytic drugs to reveal HAV inhibitors. The investigation was carried out with macaque rhesus renal embryo (FRHK-4) cell culture. Different concentrations were prepared from the drugs and used them for prevention (two hours before infection) and treatment (one hour after infection) regimes. The cells were injected with HAS-15 strain of HAV, isolated from feces of HAV-patients in dose 2.0 - 3.0 lg LD_{50}/ml. For the first time, we revealed Nicoverinum potential effect on they nhibition of HAV replication in cell culture FRHK-4 (inhibition ratio 2.74). We also proved Trental antiviral properties against HAV (inhibition ratio 2.3). This findings permites to reccomend Nicoverinum and Trental not only as spasmolitic drugs, but antiviral ones as well.