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Modulation of Antiherpes Activity by Deoxyguanosine.
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5-Methoxymethyl-2'-deoxycytidine (MMdCyd) is an antimetabolite with specificity against Herpes Simplex Virus type 1 (HSV-1). MMdCyd potency was significantly increased in the presence of 24 μM deoxyguanosine (dGuo) and maximal enhancement occurred at 100 μM dGuo [Aduma *et al.*, Antiviral Res. 15, 301-313 (1991)]. This finding was not only interesting but also surprising because a natural constituent of cells potentiated the action of an antiherpes compound. We have extended these investigations and determined the effect of 100 μM dGuo on other antiherpes agents by plaque reduction assay. There was marked potentiation of antiviral activity for all 5-substituted deoxyuridine (dUrd) and deoxycytidine (dCyd) compounds tested. The order of potentiation for dUrd compounds was: EtdUrd > IdUrd > BrVdUrd. For the dCyd series, marked enhancement of antiherpes activity was observed for BrVdCyd, IdCyd and MMdCyd (IdCyd > MMdCyd > BrVdCyd). The potency of acyclovir and PFA against HSV-1 in the presence of dGuo was not affected to a significant degree.
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Allopurinol Potentiates the Activity of Vidarabine Against Herpes Simplex Virus In vitro. S.N. Pancheva and T. Venkova. Institute of Microbiology, Bulg Acad Sci, Sofia, Bulgaria.

The inhibition of the metabolic drug degradation may be an useful approach in antiviral chemotherapy. It may allow relatively toxic antiviral agents to be delivered to cells in lower doses with effective antiviral activity and less toxicity. Allopurinol (4-hydroxypyrazolopyrimidine, HPP) is a potent inhibitor of xanthine oxidase, which catalyzes the degradation of AraA. In this study it was shown that when HPP is combined with AraA an enhancement of antiherpes activity is established. The results were confirmed by virus yield assays in human embryonic skin-muscle fibroblasts. HPP shows no effect on the replication of the virus and the degree of enhancement appears not to be a function of HPP concentrations. Optimal effect was established in the presence of HPP by ID_{50} of AraA (20 μg/ml) with an increase of the inhibitory effect of AraA with 2 $\log_{10}$. The potentiation of the antiherpes activity of AraA by HPP in a function of the ability of HPP to impair the degradation of AraA by inhibition of xanthine oxidase is discussed. (Supported by NFSI Grant, Bulgaria).

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Synthesis and Properties of Fluorescent Analogues of Acyclovir.
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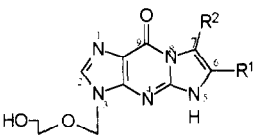
Substitution of 1,N^2-ethenoacyclovir {3,9-dihydro-3-[(2-hydroxyethoxy)methyl]-9-oxo-5*H*-imidazo[1,2-*a*]purine} (1, R^1=R^2=H) in the 6 position with phenyl or 4-biphenylyl has recently been reported to result in fluorescent selective antiherpetic agents [1]. A series of novel fluorescent analogues of acyclovir is now synthesized and characterized. It comprises monosubstituted derivatives bearing various aromatic groups either in the 6- or in the 7- position and 6,7-disubstituted ones with aromatic groups accompanied by other substituents of potential influence on solubility and biological activity.



R^1, R^2 = Ar, CHO, CH_2OH, CH_2NH_2, $CH(NH_2)COOH$

[1]Golankiewicz, B.; Ostrowski, T.; Andrei, G.; Snoeck, R.; De Clercq, E. *J.Med.Chem.* **1994**, *37*, 3187-3190.

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Antiviral Drug Susceptibility of Herpes Simplex Virus Type 2 (HSV-2) Strains Emerging Under the Selective Pressure of Various Acyclic Nucleoside Phosphonate Analogues *In Vitro*
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Drug-resistant HSV-2 strains were selected under the pressure of the 3-hydroxy-2-phosphonylmethoxypropyl (HPMP) derivatives of cytosine (HPMPC, Cidofovir) and adenine (HPMPA), the 2-phosphonylmethoxyethyl (PME) derivatives of adenine (PMEA) and 2,6-diaminopurine (PMEDAP) and foscarnet (PFA). The resistant strains ($HPMPC^r$, $HPMPA^r$, $PMEA^r$, $PMEDAP^r$ and PFA^r) were obtained by serial passages of the HSV-2 Lyons strain in the presence of increasing concentrations of the compounds in Vero cell cultures. Drug-susceptibility of the strains was determined by a viral CPE reduction assay in human embryonic lung cells. A considerable degree of cross-resistance against HPMPC and HPMPA was noted for the $HPMPA^r$ and $HPMPC^r$ strains. No changes in susceptibility to PMEA, PMEDAP, PFA, acyclovir (ACV), ganciclovir (GCV) and penciclovir (PCV) were detected for the $HPMPC^r$ and $HPMPA^r$ strains when compared to the wild-type virus. On the other hand, a significant degree of cross-resistance was noted with the $PMEA^r$, $PMEDAP^r$ and PFA^r strains against PMEA, PMEDAP and PFA. No differences in susceptibility to HPMPC, HPMPA and GCV were observed for the $PMEA^r$, $PMEDAP^r$ and PFA^r strains as compared to the wild-type virus; however, a 10-fold decrease in the sensitivity to ACV and PCV was noted. These results are in agreement with the patterns of cross-resistance that we have already reported for HSV-1. Thus, the HPMP derivatives may be assumed to differ from PFA and the PME derivatives in their mode of action.