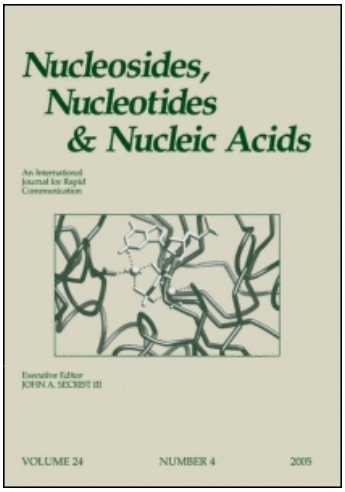

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Carbovir: A Carbocyclic Nucleoside with Potent and Selective Activity Against Human Immunodeficiency Virus (HIV) in Vitro

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CARBOVIR: A CARBOCYCLIC NUCLEOSIDE WITH POTENT AND SELECTIVE ACTIVITY AGAINST HUMAN IMMUNODEFICIENCY VIRUS (HIV) IN VITRO

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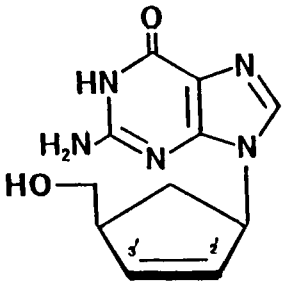
Carbocyclic 2', 3'-didehydro-2',3'-dideoxyquanosine (carbovir), a novel nucleoside analog, emerged as a potent and selective anti-HIV agent from a primary screen of a large number of carbocyclic nucleosides.[1] Carbovir inhibited the infectivity and replication of HIV in T-cells at concentrations 200- to 400-fold below toxicity to host cells. Carbovir was also evaluated for its inhibitory effects on the expression of viral antigen in HIV-infected CEM cells. Production of p 24 core antigen at optimal inhibitory concentrations of the antiviral agents indicated comparable results for AZT, ddA and carbovir.



CARBOCYCLIC ANALOG OF 2',3'-DIDEOXY-2',3'-DIDEHYDROGUANOSINE (CARBOVIR: NSC-614846)

Carbovir also exhibits a surprisingly synergistic anti-HIV efficacy when combined with either AZT or ribavirin. Thus, the MIC_{50} value for carbovir is significantly reduced in a concentration-dependent manner with increasing levels of ribavirin in the two-drug combinations. Cytotoxicity for the host MT-2 cells is increased only at the highest concentrations of ribavirin used in combination with carbovir and synergistic antiviral effects are observed with carbovir + ribavirin at non-cytotoxic concentrations.

Combination treatment of HIV-infected MT-2 cells with non-cytotoxic levels of carbovir + AZT yields potent synergistic antiviral activity in vitro. The concentration of each drug in combination is found to be reduced to 1/10 of that required for 50% inhibition of HIV-induced cytopathic effects by each drug alone.

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