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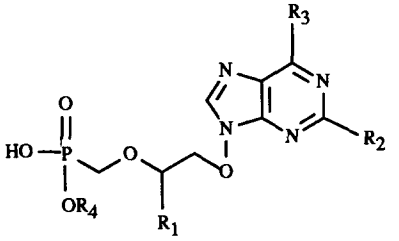
Antiviral Activity of 9-{2-(Phosphonomethoxy)ethoxy}purines Against HIV, FIV and Visna virus. R.M. Perkins[1], A. Immelmann[2], L. Elphick[1], D.M. Duckworth[1], M.R. Harnden[1], M. D. Kenig, D.N. Planterose[1], A.G. Brown[1]. SmithKline Beecham Pharmaceuticals, Gt. Burgh, UK[1], Diagen GmbH, Dusseldorf, FRG[2].

The antiviral activities of a novel series of acyclic nucleotide analogues against HIV, FIV, and visna virus, are described. These compounds are the first acyclic nucleotides in which a phosphonic acid bearing moiety is attached to the N-9 of a purine via an N-O bond.Many of these compounds display potent activity against HIV replication



	R_2	R_3	R_4	R_1	HIV-1/PBL IC_{50} (uM)
1	H	NH_2	H	H	0.3
2	NH_2	NH_2	H	H	0.03
3	H	NH_2	H	CH_2OH	0.63
4	NH_2	NH_2	H	CH_2OH	NT
5	H	OH	H	H	10
6	NH_2	OH	H	H	0.01
7	NH_2	Cl	H	H	<9
8	NH_2	OMe	H	H	0.01
9	NH_2	OH	H	CH_2OH	0.06
10	NH_2	OH	—CH_2—		0.44

in human peripheral blood lymphocytes (PBLs), e.g. compounds **6** and **8** have a 50% inhibitory concentration (IC_{50}) of 0.01μM, a value similar that found for AZT in this system. Although compounds **6** and **8** have poor selectivity when the concentrations required for antiviral activity and inhibition of PBL replication are compared, compound **1** was found to be highly selective, with an IC_{50} of 0.3μM, at least 2 orders of magnitude less than concentrations at which effects on PBL replication are observed. Some of these compounds also display potent and selective antiviral activity against FIV and visna virus.

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Comparison of Rauscher and LP-BM5 MuLV for Assessing Anti-AIDS Drugs *In Vitro*.

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Since the identification of a human retrovirus as the causative agent of AIDS, significant effort has been directed at defining appropriate animal models for evaluating potential chemotherapeutic agents. Several murine leukemia virus (MuLV) systems, including Rauscher and LP-BM5, have been used in evaluations of the *in vivo* efficacy of potential anti-HIV chemotherapeutic agents. Our interest in the utility of these two murine retrovirus models led us to determine if they differ in their *in vitro* sensitivity to anti-HIV compounds. Antiviral activity against the MuLVs was measured by UV-XC plaque reduction assay. Test compounds were added to triplicate cultures of SC-1 cells grown in 6-well plates following which the viral inoculum was added. After incubation for 3 days (37°C, 5% CO_2), the medium was decanted, the cultures were UV-irradiated and rat XC cells were added. Following a 3-day incubation, the cultures were fixed, stained and the plaques were counted. Cell, virus and cytotoxicity controls were assayed in parallel. In addition, drug cytotoxicity was assessed by MTT assay in 96 well tissue culture trays. For anti-HIV drug evaluations, CEM cells were grown in 96 well trays in the presence of serial dilutions of the test compounds. Activity was assessed by measuring cell viability in an XTT assay. Cell, virus and cytotoxicity controls were included on each assay plate. For both assay systems the antiviral activity was assessed by comparing the amount of virus-induced cytopathicity in the compound-treated wells to that present in the untreated, virus-infected controls and a 50% effective dose (ED_{50}) was calculated. For cytotoxicity evaluations, the cell viability in compound-treated wells was compared to the viability of the untreated, uninfected cell controls and the 50% inhibitory dose (ID_{50}) was calculated. These studies indicate no real differences in the *in vitro* antiviral drug sensitivity between the 2 murine retroviruses. As expected, some of the compounds with anti-HIV activity were not active against the murine leukemia viruses. This work was supported, in part, by NCI Contract Nos. NO1-CM-87274 and NO1-CM-87237.