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Susceptibility of human immunodeficiency virus replication to acyclic adenosine analogues, and synergy in combination with azidothymidine. M.S. Smith, E.L. Brian, E. DeClercq, and J.S. Pagano. Lineberger Cancer Research Center [1] and Departments of Medicine[2] and Microbiology and Immunology[3], University of North Carolina, Chapel Hill, N.C., USA, and Division of Microbiology[4], Rega Institute, Katholieke Universiteit Leuven, Belgium.

The replication of human immunodeficiency virus *in vitro* is inhibited by azidothymidine and by some acyclic adenosine derivatives [9-(2-phosphonylmethoxyethyl) adenine (PMEA) and (S)-HPMPDAP]. In our *in vitro* system, at 6 days post infection, the ED_{50} of AZT was 0.018 uM, the ED_{90} was 0.47 uM, and for PMEA, the ED_{50} was 1 uM. and the ED_{90} was 29 uM. For the compound (S)-HPMPDAP, the ED_{50} was 2.3 uM, and the ED_{90} was 36 uM. (S)-HPMPA had no inhibitory effect against virus replication up to the toxic level of 40 uM. A synergistic effect was found with the combination of PMEA and AZT. In experiments in the T cell line C3, where the reverse transcriptase activity in supernatant medium was assayed at 6 days p.i., the combination indices for 50 to 90% inhibition of virus replication ranged from 0.22 to 0.62. If PMEA or other members of this group show low toxicity *in vivo*, combinations of these drugs with low doses of AZT may show an effect in treatment of AIDS, while reducing toxicity due to AZT.

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3-METHYLQUERCETIN PREVENTS SYNTHESIS OF NEGATIVELY STRANDED VIRAL RNA IN POLIOVIRUS INFECTED CELLS.

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In order to study the influence of 3-MQ on the synthesis of viral RNA we infected a number of monolayer cultures with Poliovirus 1 at a high multiplicity of infection in the presence and absence of MQ. At different times p.i. aliquots of the infected cells were lysed and two aliquotes of each lysate separated in two agarose gels. After incubation with methylmercurohydroxyde, the gels were dried and the RNA of each gel hybridyzed "in situ" against ^{32}P labeled RNA. One of the gels was hybridized against RNA of positive and the other against RNA of negative polarity with respect to poliovirus.
Positive stranded viral RNA was detectable in both, the MQ-treated and the untreated control culture from the very beginning of the experiment. But whereas in the MQ-treated culture the amount of positively stranded RNA stayed unchanged, in the untreated cultures it began to increase after appr. 3 hours p.i. and continued going up throughout the experiment. In the MQ-treated culture the amount of positively stranded RNA at time zero (i.e. exposure to the viruses immediately followed by washing and harvesting) was essentially the same as in the other samples harvested later on. No negatively stranded RNA was detected in the culture treated with MQ, whereas in the untreated culture high molecular weight negatively stranded RNA began showing up at 3 hours postinfection.