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Inhibition of phosphorylation and viral protein kinase activity by D609 (tricyclodecan-9-yl-xanthogenate). D.G. Walro and K.S. Rosenthal, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 USA.

D609 (Merz & Co., Frankfurt, FDR) inhibits the replication of both enveloped and nonenveloped DNA and RNA viruses. D609 was recently shown to inhibit the phosphorylation of the regulatory protein, NS, of VSV-infected cells, thereby presumably preventing secondary transcription (Muller-Decker et al., J. Gen. Virol., 68: 3045-3056, 1987). We have shown that 10 ug/ml of D609 reduces the yield of HSV-1 by 90% when added at any time up to 9 hours post-infection. D609 reduces the level of protein kinase specific activity in infected cells when compared to untreated infected cells. The incorporation of $^{32}P_i$ into virion polypeptides was analysed by SDS-PAGE and found to be inhibited when D609 was added at concentrations greater than 7.5 ug/ml. Concentrations of D609 as low as 1 ug/ml completely inhibited the in vitro activity of the HSV-specific kinase obtained from virions. Furthermore, the serine kinase activity associated with the rel oncogene product of REV-T transformed cells was inhibited by 5 and 10 ug/ml of D609. These studies show that D609 abolished activity of virus-specific protein kinases in vitro which may account for the diminished protein kinase levels and altered phosphorylation patterns observed in vivo. The importance of phosphorylation reactions for virus reproduction and the target for D609 antiviral activity is suggested by these studies.

I-11

The Antiviral Properties of Adenosine Analogues are Correlated with the Inhibition of S-Adenosylhomocysteine Hydrolase. M. Cools and E. De Clercq. Rega Institute for Medical Research, B-3000 Leuven, Belgium.

Various adenosine analogues have been described which share a unique antiviral activity spectrum: they are particularly active against (-)-RNA viruses, double-stranded (+)-RNA viruses and poxviruses. These viruses require a viral methyltransferase for $5'$-capping of their mRNAs. S-Adenosylhomocysteine (AdoHcy) is both a product and a negative feedback inhibitor of these methylation reactions. Inhibition or inactivation of the enzyme (AdoHcy hydrolase) that hydrolyzes AdoHcy leads to an accumulation of AdoHcy and a concomitant inhibition of the methyltransferases. AdoHcy hydrolase was isolated and purified from murine L929 cells, which were also used in the antiviral studies. The inhibitory effect of the adenosine analogues on AdoHcy hydrolase correlated closely with the antiviral activity against vaccinia virus and vesicular stomatitis virus. In terms of their (increasing) inhibitory effect on both virus replication and AdoHcy hydrolase activity the compounds ranked as follows: (S)-DHPA < (RS)-AHPA (isobutyl ester) < C-c^3-Ado and c^3-neplanocin < adenosine dialdehyde < neplanocin A.