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Comparative Inhibitory Effects of Ribavirin, Pyrazofurin, and EICAR on Measles (SSPE) Virus Replication In Vitro and In Vivo.

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We have evaluated three nucleoside analogues, i.e. ribavirin, 3-(β-D-ribofuranosyl)-4-hydroxypyrazole-5-carboxamide (pyrazofurin), and 5-ethynyl-1-β-D-ribofuranosylimidazole-4-carboxamide (EICAR), for their inhibitory effects on the in vitro replication of various measles (SSPE) virus strains, including wild type strains recently isolated from measles patients, and for their therapeutic efficacy in hamster SSPE model. Pyrazofurin and EICAR were more inhibitory than ribavirin to the replication of various strains of measles (SSPE) virus, in vitro. Ribavirin improved the survival of infected hamsters in a dose-dependent manner by intracranial administration, and ribavirin at a dose of 10 mg/kg/day completely prevented mortality. Pyrazofurin did not improve the survival of infected hamsters at the maximum tolerate dose. EICAR improved the survival by 50% at a dose of 5 mg/kg/day, whereas the survival decreased when the dose increased to 10 or 20 mg/kg/day. Therapeutic efficacy in vivo of pyrazofurin or EICAR was less than that of ribavirin.

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An Antiviral Synthetic Coiled-Coil Peptide Displays Sustained Blood Levels in Rats. **D.M. Lambert, T. Venetta, E.I. DiMassimo, J. Matthews*, S.R. Petteway, Jr. Trimeris, Inc., Durham, NC, and *Research Triangle Institute, RTP, NC**

DP-107, a 36-mer synthetic peptide, has been shown to be a potent inhibitor of HIV-1 fusion and infection (Wild et al., 1992). The antiviral activity of this peptide appears to be related to its coiled-coil structure. In the course of evaluating DP-107 as a potential therapeutic agent, we have investigated the pharmacokinetic properties of this peptide in the cannulated rat model. An iv bolus injection of 4 mg/Kg was administered to four rats in a total volume of 200 μl, and blood samples were taken at various intervals. Blood levels were determined by recovering DP-107 from the plasma after precipitation of the bulk of serum proteins with two volumes of methanol. Recovered peptide was quantified by (1) SDS-PAGE and Western blot analysis with specific polyclonal antibody and (2) a sandwich capture ELISA. Results demonstrate that this peptide exhibited a surprisingly long half-life with sustained blood levels. Peptide concentrations above the IC_{50} level for this peptide were maintained for approximately 6 hours post injection. These results suggest that DP-107 and its analogs may be suitable for investigation as potential therapeutic peptides for the treatment of HIV-1 infection in AIDS.