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Syntheses of a Series of 6-Substituted Pyrimidines Including Orotidylic Acid Decarboxylase Inhibitors, and *In Vitro* Evaluation of their Antiviral Efficacy. B. Gabrielsen, J. W. Huggins, H. A. Blough, T. P. Monath, (U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, USA 21702), J. J. Kirsi, C. D. Kwong, L. K. Hanna, L. A. Krauth, J. A. Secrist III, W. M. Shannon, (Southern Research Institute, Birmingham, AL, USA, 35255).

6-Azauridine analogues (including the known orotidylic acid decarboxylase, ODCase, inhibitors, 6-aza- and 6-thiocarboxamido-uridine), 6-substituted [$-NH_2$. -CN, $-CS(NH_2)$, and $-C\equiv C$] uridines and uracils, and 5-aza- and amino-pyrimidines were synthesized or obtained commercially. Several potential transition state analogues of ODCase were synthesized. Antiviral evaluation using an MTT-based assay in Vero cells revealed a broad spectrum of antiviral activity against selected representatives of the RNA viruses including: flaviviruses (Japanese encephalitis, yellow fever and dengue-4 viruses); bunyaviruses (Punta Toro and sandfly fever viruses); alphavirus (Venezuelan equine encephalomyelitis virus); lentivirus (HIV-1 in CEM cells) and the DNA virus, vaccinia virus. In general, the *in vitro* antiviral spectrum and potency of these analogues were either better, comparable or considerably lower than the corresponding antiviral values for 2-thio-6-azauridine, which itself performed slightly better than the well-known antiviral agents, selenazofurin and ribavirin. Supported in part by U. S. Army Medical Research Acquisition Activity Contract No. DAMD17-91-1050 and No. DAMD 17-91-C-1034.

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The effect of glycosylation inhibitors on the replication of Junin virus.E. Damonte,A.Silber,N.Candurra,S.E.Mersich.Laboratorio de Virología.Facultad de Ciencias Exactas y Naturales.Universidad de Buenos Aires.Argentina.

Glycosylation inhibitors have been devised as potential antiviral agents with variable effect on different viruses.In the present study we have investigated the antiviral activity of several drugs which interfere with the diverse stages of the oligosaccharide biosynthetic pathway on the replication of Junin virus (JV),agent of Argentine Hemorrhagic Fever.The drugs tested were: monensin (M), a sodium ionophore which disturbs the trans-golgi function affecting post-translational glycosylation;deoxynojirimycin (DNJ) and bromoconduritol (BC),two glucosidase inhibitors;deoxymannojirimycin (DMN) and swainsonine (SW),mannosidase I and II inhibitors,respectively.M inhibited the formation of both cell-associated and cell-free virus in JV infected Vero cells although the release of extracellular virus was significantly more sensitive.A similar level of inhibition (app.90%) was achieved if M was added immediately after virus adsorption or so late as 16 h post-infection.The mature JV envelope glycoprotein GP38 was not detected by PAGE and immunoprecipitation in the presence of M whereas its precursor GPC was accumulated and bound to lectins Concanavalin A and Ricinus communis agglutinin, indicating a specific inhibition of proteolytic cleavage by the drug. Among the inhibitors of glycoprotein trimming reactions, BC was one of the most active against JV replication.Both extracellular and intracellular virus yields were significantly reduced by BC which inhibits the trimming of the innermost glucose residue.By contrast,DNJ an inhibitor of the trimming of the outermost glucose residues, did not show activity.The different structural alteration produced by BC might be responsible for an increased proteolysis of the glycoproteins which in turn gives reduced yields of JV.