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4-Guanidino Neu5Ac2en is a potent and broad spectrum inhibitor of influenza A and B viruses, *in vitro* and *in vivo*. J.M. Woods, S.A. Hiscox, D.M. Ryan and C.R. Penn. Glaxo Group Research Limited, Virology Department, Greenford Road, Greenford, Middlesex UB6 0HE U.K.

The sialidase (neuraminidase) inhibitor 4-guanidino Neu5Ac2en is a potent inhibitor of influenza virus both *in vitro* and *in vivo* (von Itzstein *et al* submitted for publication). A detailed study of the *in vitro* antiviral activity of 4-guanidino Neu5Ac2en against a range of influenza A and influenza B viruses have shown that this compound has a broad spectrum of activity. The viruses included in this study are representative of different time periods and geographic locations and include examples of all the major subtypes of influenza virus know to infect man. Amantadine/rimantadine resistant clinical isolates were also evaluated. All isolates tested, were sensitive to 4-guanidino Neu5Ac2en (IC50 16-0.0005μM) and in all cases 4-guanidino Nen5Ac2en was more active than amantadine, rimantadine or ribavirin. The least sensitive isolate to 4-guanidino Neu5Ac2en determined *in vitro* was equally sensitive in an animal model as other strains of influenza found to be more sensitive *in vitro*. 4-Guanidino Neu5Ac2en is more potent and demonstrates the broadest spectrum of activity of any specific anti-influenza compound described to date.

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Comparative Anti-Influenza Virus Activity of 2′-Deoxy-2′ Fluororibosides In Vitro. F Hayden, A Elkatieb, and B Rollins. University of Virginia, Charlottesville, VA.

The anti-influenza virus activity of 2′-deoxy-2′-fluoroguanosine (DFG) was determined in cell culture and in explants of human respiratory epithelium by yield reduction assay. The concentration causing at least 1.0 $\log_{10}$ reduction in influenza A (H3N2) virus yield (EC_{90}) at 24 hrs was 2.5 ug/ml in primary rhesus monkey kidney and 12 ug/ml in Madin-Darby canine kidney (MDCK) cells, compared to 0.5 ug/ml and 0.9 ug/ml, respectively, for ribavirin. The estimated therapeutic ratios for both compounds were less than 5 in these cell types. In contrast, the EC_{90}s of DFG at 48 hrs for influenza A and B viruses were $\leq$ 0.1 ug/ml in human respiratory epithelial explants, and concentrations up to 100 ug/ml did not inhibit explant outgrowth or ciliary activity. Ribavirin was ~50 fold less active in this system and inhibited outgrowth at 10 ug/ml. DFG was also ~50 fold more potent than the corresponding adenosine and inosine compounds in explants. Partially resistant variants, with ~5 fold increases in EC_{50} values, could be selected by serial influenza A virus passage in MDCK cells in the presence of DFG, which indicated that its activity is at least partially virus specific. The exceptional activity of DFG in respiratory epithelial cells against both influenza A and B viruses makes this compound a promising candidate for further investigation.