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Resistance of Sindbis Virus to Some Adamantine Compounds.

G.A. Galegov, V.L. Andronova, N.A. Leontieva.
The D.I. Ivanovsky Institute of Virology, The USSR Academy of Medical Sciences, Moscow, USSR

Amantadine and Rimantadine are very active with respect to different strains of influenza A but Amantadine is not effective against alfaviruses, and Rimantadine possesses low activity. We revealed by studying the correlation between structure and activity that Adamantane-1-carbonamide (1) and some of its analogues have the ability for suppression of Sindbis virus reproduction and some other alphaviruses in Vero cell cultures. The effect (1) on this virus is selective. Its toxicity for the cells is 2.7 times less than in Rimantadine. ID_{50} value is 36 μg/ml. (1) is active also in high multiplicity of infection (one-cycle experiment). Lowering of infective virus titre is more than 4 lg PFU/ml. (1) preserves the activity after its addition two hours after cell infection. In passing of the virus in the presence of (1) the resistant to (1) strain of Sindbis virus can be obtained. Its reproduction is not suppressed even by subtoxic concentrations (1). The resistant strain has the duration of latent period two hours longer than in sensitive to (1) virus. Ammonium chloride inhibits the reproduction of the sensitive to (1) virus but does not inhibit the resistant strain.

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Identification and Characterization of a 47 kDa Host Protein Implicated in the Transport of Alphaherpesviruses in Infected Cells

B.W. Banfield and F. Tufaro. Department of Microbiology, University of British Columbia, Vancouver, B.C. Canada V6T 1Z2.

The murine L cell mutant gro29, selected originally for its ability to survive inoculation with herpes simplex virus type 1 (HSV-1), has a moderate defect in the trafficking of glycosylated and non-glycosylated proteins through the Golgi complex. After infection with HSV-1, HSV-2, or pseudorabies virus (PRV), a host cell function becomes limiting such that the assembly of infectious viral particles and their egress from cells is progressively and rapidly blocked as infection proceeds. In an attempt to identify the defective component in gro29 cells, [^{35}S] methionine labeled infected cell extracts were prepared from HSV-1-infected control L cells and gro29 cells. Subcellular fractions were generated by centrifugation and analyzed by polyacrylamide gel electrophoresis. Analysis of the 10,000 x g fraction revealed a 47 kDa protein enriched in infected L cells that was undetectable in the gro29 fraction. Preliminary characterization suggests that is it an acidic transmembrane polypeptide lacking N-linked oligosaccharides. Interestingly, treatment of HSV-1-infected parental L cells with the drug brefeldin A, which blocks net secretion from the Golgi complex, also causes disappearance of the 47 kDa protein. Experiments are underway to purify the protein to homogeneity to further study its role in normal and infected cells. The observation that gro29 affects a cellular function required for the propagation of two rather diverse alphaherpesviruses, yet has only a marginal effect on uninfected cell growth suggests that gro29 defines a new class of targets for broad spectrum antiviral agents.