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Tromantadine Inhibits Herpes Simplex Virus Induced Syncytia. D.E. Ickes, T.M. Venetta, K.S. Rosenthal, N.E. Ohio Universities College of Medicine, Rootstown, OH 44272 USA

Tromantadine (TRO)(N-1-adamantyl-N-[2-(dimethylamine) ethoxy] acetamide hydrochloride) (Merz & Co.) inhibits both the number and size of HSV-1 (GC + strain) induced syncytia in Vero and HEp-2 cells. The minimal fusion inhibitory concentration was 50 ug/ml. The area of the syncytia was determined by computer assisted image analysis. Reversal of TRO treatment was seen within 12 to 24 hours of drug removal. No recovery of fusion activity followed cycloheximide treatment upon removal of TRO, indicating that new protein synthesis is required for the recovery from TRO treatment. Immunofluorescence with monoclonal antibodies to gB and/or gD showed their presence on the cell surface at fusion inhibitory concentrations of TRO. Expression of the viral glycoproteins, but not fusion, indicates that TRO does not interfere directly with viral fusion, but most likely blocks the proper synthesis of the fusion glycoproteins. TRO treatment induced changes in the viral glycoprotein pattern of SDS-PAGE gels. It is likely that TRO interferes with the proper processing of these glycoproteins.

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Studies on the Mechanism of Antiviral Action of 5-(2-Chloroethyl)-2'-Deoxyuridine Against Herpes Simplex Virus. R. Bernaerts, P. Sterkens, P. Herdewijn, B. Rosenwirth* and E. De Clercq. Rega Institute for Medical Research, B-3000 Leuven, Belgium and *Sandoz Forschungsinstitut, A-1235 Vienna, Austria.

Amongst the 5-substituted 2'-deoxyuridines 5-(2-chloroethyl)-2'-deoxyuridine (CEDU) is one of the most potent and selective inhibitors of herpes simplex virus (HSV). Its mode of action is assumed to depend on a preferential phosphorylation by the virus-encoded thymidine kinase since it lacks activity against thymidine kinase-deficient (TK^-) mutants of HSV-1. The phosphorylation of [2-^{14}C]CEDU was examined in both mock- and HSV-1-, HSV-2-, and TK^- HSV-1-infected cells. Our results demonstrated that [2-^{14}C]CEDU was phosphorylated to its 5'-mono-, 5'-di- and 5'-triphosphate in both HSV-1- and HSV-2-infected cells. Its incorporation into viral and cellular DNA was studied by cesium chloride gradient analysis of HSV-1-infected cell lysates. In parallel experiments its effect on DNA synthesis was measured by monitoring [^{32}P]orthophosphate incorporation into DNA in the presence of varying concentrations of CEDU. A close correlation was found between the incorporation of [2-^{14}C]CEDU into viral DNA, the inhibition of viral DNA synthesis and the reduction in virus progeny formation.