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The study of effect of a new antiviral drug arbidol on different stages of viral reproduction.

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Arbidol(hydrochloride monohydrate I-methyl-2phenyltiomethyl 3-carbooxy-4-dimethyl-amino-methyl-5-oxy-6-bromindole) is an antiviral drug active against influenza A and B viruses.We have studied the action of arbidol on different stages of viral reproduction.The drug produced no inhibitory effect on translation virus-specific proteins.It did not inhibit transcriptase activity of influenza virus A ribonucleoprotein complex in vitro.Cell-ELISA revealed that arbidol affected early stages of viral reproduction. The method of fluorescence dequeching was used to study the effect of arbidol on early stages of viral reproduction.Experiments with endocytosis inhibitors and fluorescence dequenchers have shown that the fluorescence dequenching observed at pH=5,0 resulted from the fusion of viral lipid envelopes with the cell plasma membranes,while that at pH=7,4 was with the endosomal membranes.Arbidol and its active analogues unhibited the fusion of viral lipid envelopes with cell plasma membranes at pH=5,0 as well as with endosomal membranes at pH=7,4 under physiological conditions.Inactive analogues inhibited the fusion of viral lipid envelopes with plasma cell membranes at pH=5,0 only.This results suggest, that virusspecific effect of arbidol is due to its action upon the fusion of viral lipid envelopes with ehdosomal membranes,wich occurs when the virus nucleocapsid is released from external proteins and lipid envelopes.

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Antiviral Activity of Mizoribine (4-Carbamyl-1-B-D-Ribofuranosylimidazolium -5-olate) against ortho- and paramyxoviruses.

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Mizoribine, an nucleoside analogue with a similar structure as ribavirin was isolated from Eupenicillium brefeldianum first and has been developed for anticancer and immunosuppressive drug. We examined antiviral activity of mizoribine for orthomyxo- and paramyxoviruses with MTT method in vitro. Mizoribine was 9 to 10 fold more active and 3 fold more active against measles and RS viruses respectively than ribavirin(EC_{50} were 1.7 and 0.6 μg/ml for each virus). Mizoribine was inhibitory against FluV-A, FluV-B, PFluV-2 and mumps virus at less concentration than 10 μg/ml. Antiviral effects of mizoribine against measles V and RSV were reversed by addition of 6.25 and 100 ug/ml of GMP and also reversed by 100 and 400 ug/ml of XMP. Mizoribine and some (S)-adenosylhomocystein hydrolase inhibitors showed strong synergistic anti-RSV activity by plaque reduction method using HeLa cells. Mizoribin did not show cytotoxicity for MDCK, Vero and HeLa cells at concentration of 250 μg/ml. Mizoribine is a promissing antiviral compound against ortho- and paramyxoviruses.