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Differential Effects of Capsid-binding Antivirals on the Adsorption of Rhinoviruses

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The effect of a series of capsid-binding antiviral agents on the adsorption of a series of rhinoviruses has been determined using an infectious center assay. Compounds selected for this study were a pyridazinamine (R61837), a flavan (4-6' dichloroflavan), a chalcone (Ro-09410), and an isoxazole (WIN 51711). Rhinoviruses selected included HRV1A and HRV29 (minor receptor group, antiviral group B), HRV9 and HRV 39 (major receptor group, antiviral group B), HRV 14 and HRV35 (major receptor group, antiviral group A).

Three patterns of inhibition could be observed. A complete inhibition of adsorption at concentrations exceeding 5 to 10x the MIC; an absence of inhibition (<10 %) at concentrations exceeding 25x the MIC; and an intermediate pattern of inhibition. Three serotypes displayed two patterns of inhibition, depending on the antiviral used, one serotype displayed all three types, and two serotypes displayed only one type. Our results suggest that the conformational alterations induced by antiviral compounds can vary considerably within a given serotype, depending on the nature of the antiviral compound used. A correlation between the effect on adsorption and receptor group or antiviral group could not be found.

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Antiviral Activity of Protease Inhibitors on the Replications of Ortho- and Paramyxoviruses.

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The glycoproteins, HA of influenza viruses and F of paramyxoviruses, undergo post-translational proteolytic cleavage. This cleavage is a precondition for the fusion activity of these glycoproteins, and thus for the infectivity of virions and spred of the virus in the host organism. The cleavage is accomplished by host cellular protease. We tested several protease inhibitors for the antiviral activity on the multicycle replications of various ortho and paramyxovirusses and the cytotoxicity to the host cells based on the MTT (a tetrazolium dye) method. Some of tested compounds inhibited virus replication at concentrations that were significantly lower than their cytotoxic concentrations. The in vitro and in vivo antiviral activities of protease inhibitors will be presented.