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EVALUATION OF AEROSOLIZED APROTININ THERAPY FOR INFLUENZA AND PARAINFLUENZA INFECTIONS IN HUMANS

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Aprotinin is a basic proteinase inhibitor from bovine organs (an active ingredient of Trasylol). Aprotinin aerosol inhalations are protective against experimental influenza and parainfluenza bronchopneumonia [Antiviral Res. (1994) 23:107-118]. This randomized, placebo-controlled trial determined the therapeutic efficacy of aerosoloized aprotinin in naturally occurring influenza (H3N2) and parainfluenza (type 1) disease of <48 hours duration. Adults (n=52) were randomly assigned to inhalations of aerosolized 2% sodium bicarbonate (plecebo) or 350 TIU/ml aprotinin solution (~3000 TIU per inhalation) 3 times/day for 4-5 days. In subjects with virus disorders no important differences existed in gender, mean age, or time from cold onset. The median durations (days) of symptoms for placebo and ap-treated patients were: fever (2.5 vs 1.8), headache (2.0 vs 1.5), weakness (2.8 vs 1.6), sore in throat (3.0 vs 1.6), hyperemic throat (4.1 vs 2.6), rhinorrhea and nasal obstruction (3.9 vs 2.6), cough (4.9 vs 3.0), hoarseness (3.5 vs 1.3) [$p<0.05$]. Aprotinin inhalations were generally well tolerated and did not cause local irritant reactions and allergy. In summary, aprotinin inhalation was associated with clinical benefit in treatment of naturally occurring Influenza and Parainfluenza respiratory illnesses.

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Anti-respiratory Syncytial Virus Activity of Selected Polyoxometalates.

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A series of polyoxometalate analogs were evaluated for inhibitory activity against several respiratory viruses of clinical significance, including adeno, measles, parainfluenza and respiratory syncytial (RSV) viruses. Five compounds, $Cs_4[SiW_{11}O_{39}\text{-}(SiCH_2CH_2CH_2Cl)_2]$ (HS-081), $[(CH_3)_4N^+]_4SiW_{11}O_{39}\text{-}O(SiCH{=}CH_2)_2$ (HS-086), $[(CH_3)_4N^+]_4SiW_{11}O_{39}\text{-}O(SiC(CH_3)_3)_2$ (HS-087), $(Me_3NH)_8Si_2W_{18}Nb_6O_{77}.nH_2O$ (HS-106) and $(LysH^+)_7KSi_2W_{18}Nb_6O_{77}.18H_2O$ (HS-116), potently inhibited several strains of RSV when compared to ribavirin. When tested against a clinical isolate of RSV (Utah 89) in a CPE inhibition assay confirmed by neutral red staining, 50% inhibitory concentrations (EC_{50}) ranged from 0.1 μM for HS-116 to 1.5 μM for HS-081. The order of potency was HS-116 > HS-106 > HS-086 > HS-087 > HS-081. The selective indices ranged from >1000 for HS-116 to >100 for HS-087. In virus yield assays, HS-116 had a 90% inhibitory concentration (EC_{90}) of 0.1 μM, while HS-086 had the highest EC_{90} value at 2 μM. Effects of these compounds on cells in log phase growth were determined by enumerating cells in a Coulter counter using the trypan blue exclusion method. The 50% cell inhibitory concentration for each compound was greater than 100 μM. These data suggest that these polyoxometalate analogs warrant evaluation in animals as potentially useful clinical therapeutics for RSV infections.

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