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***In Vivo* Anti-Influenza Virus Activity of Kampo (Japanese Herbal) Medicine "Sho-Seiryu-To (Xiao-Qing-Long-Tang)"**

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Several Kampo medicines (crude drugs) have traditionally been used for the treatment of the "cold" syndromes. Because influenza viruses are known as one of the causes of the cold syndrome, some Kampo medicines may be effective against the virus infection. We previously reported that "Sho-seiryu-to (SST)", which has been used clinically for the treatment of the cold syndrome, showed potent antiviral activity in BALB/c mice against mouse-adapted influenza virus A/PR/8/34 (H1N1 subtype) by nasal site-restricted infection, and the antiviral IgA antibody in the nasal and broncho-alveolar washes of the SST treated mice increased significantly.[1] SST also showed antiviral activities in the broncho-alveolar cavity of aged mice (~6 months old) against A/PR8 virus, and in the nasal and broncho-alveolar cavities of young mice (7 weeks old) against mouse-adapted influenza viruses A/Guizhou/54/89 (H3N2) and B/Ibaraki/2/85. Although SST was effective only when it was administrated to the mice before viral infection, when mice preinfected with mouse non-adapted influenza virus A/Fukuoka/C29/85 (H3N2) were infected with mouse-adapted A/PR8 virus, SST showed therapeutic antiviral activity. SST augmented nasal antiviral IgA antibody and broncho-alveolar and serum antiviral IgG antibodies against secondary nasal inoculation of influenza HA vaccine. These results suggest that SST is useful for influenza virus infection on aged persons, for cross-protection of subtypes of influenza A viruses and influenza B virus and for the treatment of influenza virus infection on human which has a history of influenza virus infection and/or influenza vaccination.

1) T. Nagai and H. Yamada, *Int. J. Immunopharmacol.*, **16**, 605-613 (1994).

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Dramatic Combination therapy with Ribavirin and Polyoxometalate in the treatment of Influenza A virus infected mice.

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Polyoxometalate, $[PriNH_3]_6H[PTi_2W_{10}O_{38}(O_2)]H_2O$ (PM523) have emerged as inhibitor of Influenza virus A, B by tissue culture system. Furthermore, combination use of PM523 and ribavirin showed a synergistic antiviral effect against infection to MDCK cells. Combination therapy of 10mg/ml ribavirin and 10mg/ml PM523 administered as a small particle aerosol given 2h twice daily for 4 days in Influenza virus A infected mice was examined and compared with their monotherapy. As a results, survival rate of Influenza virus A infected mice increased dramatically by contrast with their monotherapy (100% in combination Vs 10% monotherapy on 7 days). Monotherapy with 20mg/ml of each compound hardly recovered the infected mice survival. This study indicated that the combination therapy with Ribavirin and PM523 may permit significantly shorter treatment schedules without loss of efficacy and reduce adverse effects of each compound.

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EFFECTIVENESS OF THE COMBINED USE OF INACTIVATED VACCINE (IV) AND THE INHIBITOR OF PROTEOLYSIS E-AMINOCAROIC ACID (E-ACA) IN PREVENTION OF EXPERIMENTAL INFLUENZA.

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The prophylactic effects produced by different types of antiviral preparations such as IV and E-ACA, used separately or in combination in experimental letal infection induced by influenza virus A/Leninqrad/49/32 (H1N1) in mice are compared. The quantitative evalution of the antiinfluenza effect were carried out by the method of multifactor analysis after the optimum second-order plan based on the mathematical theory of experiment. This made it possible to determine the best combination of the preparations and their doses to estabilish the time of the formation of reliable protection from influenza in mice. The prophylactic effect produced by the use of E-ACA alone and the capacity of this preparation for enhancinq the protective action of IV were estabilished. The hiqhest effectiveness had place if we injected subcutaneusly IV (512 HAU; 0,1 ml) in combination with E-ACA (300 mg/ml; 0,1 ml) 6 days before intranasal infecting of mice by influenza virus.

Novel Anti-Respiratory Syncytial (RS) Viral Compounds; Benzoditiin Derivatives.

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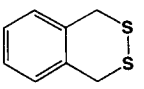
We found the benzoditiin structure compound RD3-0028 was an anti-RS viral agent. Using the modified MTT assay developed in our laboratory, the 50% effective concentration and 50% cytotoxic concentration values of this compound were 0.3 and 43.0 μg/ml, respectively, and which were superior to that of ribavirin. The structure-activity relationship of the benzoditiin derivatives was discussed by comparison to RD3-0028. We also tested the antiviral activity spectrum of this compound against several kinds of viruses (influenza A virus, human immunodeficiency virus, herpes simplex virus etc.). This compound had only the anti-RS viral activity. We proved this compound acted on the stage of virus entry to cell.



RD3-0028