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ANTIVIRAL EFFECT OF COUMARIN ANALOGUE AGAINST RESPIRATORY SYNCYTICAL VIRUS INFECTION IN VITRO AND IN VIVO

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A new compound, the coumarin analogue, had been extracted from the alternantherae philoxeroides griseb. The antiviral and therapeutic effect on respiratory syncytical virus in Hep-2 cell and Kauming mice was examined. The antiviral activity of coumarn analogue was evaluated on the basis of checking viral antigen and virus titer inside and outside of the infected cells and tissues by immunofluorescence assay and ELISA. The results shown that coumarin analogue can clearly innibite the replication of virus at 100ug/ml in vitro. The antiviral activity increased with the increasing of the concentration of the coumarin analogue. Cytotoxicity was not seen in vitro and in vivo.

Coumarin analogue given orally to adult mice at concentrations with 25, 45 and 85mg/kg daily for 5 days. The detection rate of virus were 20.0, 6.6 and 0.0% in lungs for each groups, virus titer were Log1.6PFU/ml, Log1.1PFU/ml and Log0.6PFU/ml. At the same time, ribavirin given orally to adult mice at concentrations with 20 and 60mg/kg daily for 5 days. The detection rate of virus and virus titer were 40.0 and 50.3% as well as Log 2.1 and 2.6 PFU/ml in lung for each groups respectively. These results suggest that the coumarin analogue was effective in treatment of respiratory syncytical virus infection, the antivirus activity is better than ribavirin.

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Synthetic Peptides from Conserved Regions of Respiratory Syncytial Virus Fusion (F) Protein are Potent Inhibitors of Viral Fusion. **A.L. Lambert, S. Barney, K. Guthrie, R. Medinas, D.E. Davis-Rhodes, T. Bucy, J. Erickson, G. Merutka, S.R. Petteway, Jr., D.M. Lambert. Trimeris, Inc., Durham, NC**

Human respiratory syncytial virus (RSV) is considered the most important viral etiologic agent of lower respiratory illness in infants and is the major cause of bronchiolitis and pneumonia severe enough to warrant hospitalization of children. There are no vaccines to prevent infection and current therapies are limited. Therefore, safe and effective treatments for RSV infections represent a significant unmet medical need. The surface attachment and fusion glycoproteins of enveloped viruses are intimately involved in the adsorption and penetration steps of the infectious process. These fusion proteins are required for infection and fusion. In RSV, F_0 (the 68 kDa uncleaved, inactive form) is cleaved into two active disulfide-bonded subunits, F_1 (48 kDa) and F_2 (19-21 kDa). Inhibition of the function of the F proteins blocks infection as demonstrated by neutralizing antibodies. Inhibitors targeted to these proteins would represent a novel class of antiviral agents that act at the cell surface. Recent discoveries by Wild et al. and Carr et al. provide a structural and functional basis for the discovery of antivirals targeted to viral fusion proteins. In particular, two synthetic peptides derived from distinct domains of the HIV-1 gp41 fusion protein, DP-107 and DP-178, have been shown to be potent inhibitors of HIV-1 fusion and infection. Structural similarities to the HIV gp41 site were identified in several regions of RSV F protein, using computer algorithms. Overlapping 35-mer peptides spanning these regions were synthesized and assayed for their ability to block virus-mediated fusion and infection. Active peptides that block virus-mediated fusion and infection at sub-micromolar concentrations *in vitro* were identified and three chosen as leads for further study. These fusion-inhibiting peptides represent a new class of RSV antivirals acting at the cell surface.