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Synergistic Effects of 3-Deazaneplanocin A, Carbocyclic 3-deazaadenosine, Neplanocin A and Ribavirin against Measles Virus. J.B. Pfeifer, B.E. Gilbert and P.R. Wyde. Baylor College of Medicine, Houston, TX, USA.

Measles virus (MV) is a major cause of death among children, ages 1-5, in developing countries. In the United States, significant epidemics continue to occur despite the availability of vaccines. Hence, a need exists for effective measles chemotherapy. The drugs 3-deazaneplanocin A (DANA), carbocyclic 3-deazaadenosine (Cc3Ado), neplanocin A (NPA) and ribavirin (RIB) have been reported to have activity against paramyxoviruses. In this study each drug was tested alone and in a 1:1 (wt/wt) ratio in VERO cells against the clinical MV isolate, AC705. Although most of these compounds had little to no anti-MV activity alone, in combination, marked inhibition of MV was observed as indicated by the examples in the following table:

Test compounds		ED_{50} [ug/ml] (S.I.)[a]						
Drug 1	Drug 2	Drug 1		Drug 2		Drugs 1 + 2		Effect
DANA	RIB	72	(>3)	66	(15)	3.5	(>71)	Synergy
DANA	Cc3Ado	72	(>3)	104	(>2)	1.2	(>208)	Synergy
Cc3Ado	RIB	104	(>2)	66	(15)	2.0	(>125)	Synergy
NPA	RIB	3	(>83)	66	(15)	0.4	(>625)	Synergy

[a] ED_{50} = median efficacious dose; S.I. = selective index.

Similar testing against other measles and paramyxoviruses is proceeding.

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SYNERGISTIC INHIBITION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 IN VITRO BY COUMERMYCIN A1 AND HUMAN LEUKOCYTE INTERFERON.
G. TACHEDJIAN, D. TYSSEN, D. JARDINE and C. BIRCH. Macfarlane Burnet Centre for Medical Research and Virology Department, Fairfield Hospital, Yarra Bend Rd, Fairfield, Victoria 3078, Australia.

The use of synergistic drug combinations for the treatment of HIV infection has benefits in terms of antiviral efficacy, potential for reduction in drug-related toxicity, and the prevention of the emergence of antiviral drug resistance. Drugs acting at different stages of the HIV replication cycle are of particular importance. Accordingly, we examined the in vitro interaction of coumermycin A1(CA1) and human leukocyte interferon (IFN-alpha) in HIV-infected peripheral blood leukocytes. Cells were pretreated with IFN-alpha for 24 hr at 37°C prior to the addition of CA1, then infected with HIV-1. At 6-7 days post-infection, culture supernates were clarified and particle-associated reverse transcriptase (RT) activity determined. Results were analysed using the multiple drug effect analysis programme of Chou and Talalay and by the classical isobologram technique. Analysis of data for CA1 and IFN-alpha at fixed ratios of 1:12.8 and 1:25.6 revealed synergy at a wide range of effect levels. Analysis of data using the isobologram technique also revealed synergy. Neither combined toxicity nor anti-proliferative effects due to IFN-alpha were observed at the concentrations tested. The CA1 and IFN-alpha concentrations at which synergy was observed are achievable in vivo.