

Synergistic Effects of 3-Deazaneplanocin A, Carbocyclic 3-deazaadenosine, Neplanocin A and Ribavirin against Measles Virus.
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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				Effect
Drug 1	Drug 2	Drug 1	Drug 2	Drugs 1 + 2		
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

^aED₅₀ = median efficacious dose; S.I. = selective index.

Similar testing against other measles and paramyxoviruses is proceeding.

SYNERGISTIC INHIBITION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 IN VITRO BY COUMERMycin A1 AND HUMAN LEUKOCYTE INTERFERON.

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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 (CAL) and human leukocyte interferon (IFN- α) in HIV-infected peripheral blood leukocytes. Cells were pretreated with IFN- α for 24 hr at 37°C prior to the addition of CAL, 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 CAL and IFN- α 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- α were observed at the concentrations tested. The CAL and IFN- α concentrations at which synergy was observed are achievable in vivo.