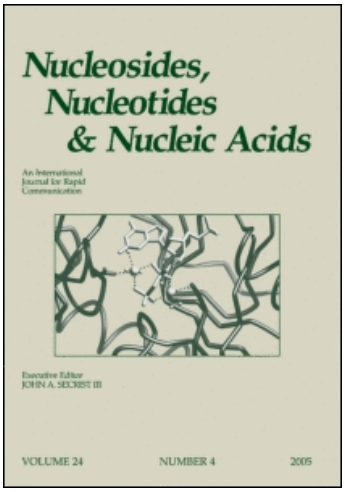

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Antiviral Activity of Magnesium and Magnesium/poly r(A-U) Combinations Against two RNA Viruses

J. Jamison[a]; J. Gilloteaux[b]; M. R. Nassiri[c]; C. C. Tsai[d]; J. Summers[a]
[a] Department of Urology, Summa Health System/N. E. Ohio Universities College of Medicine, Rootstown, Ohio [b] Departments of Anatomy, [c] Pharmacology/Virology, Lake Erie College of Osteopathic Medicine, Erie, PA [d] Department of Chemistry, Kent State University, Kent, OH

To cite this Article Jamison, J. , Gilloteaux, J. , Nassiri, M. R. , Tsai, C. C. and Summers, J.(1999) 'Antiviral Activity of Magnesium and Magnesium/poly r(A-U) Combinations Against two RNA Viruses', Nucleosides, Nucleotides and Nucleic Acids, 18: 6, 1221 — 1222
To link to this Article: DOI: 10.1080/07328319908044668
URL: http://dx.doi.org/10.1080/07328319908044668

NUCLEOSIDES & NUCLEOTIDES, 18(6&7), 1221–1222 (1999)

ANTIVIRAL ACTIVITY OF MAGNESIUM AND MAGNESIUM/POLY r(A-U) COMBINATIONS AGAINST TWO RNA VIRUSES

J. Jamison[1]*, J. Gilloteaux[2], M.R. Nassiri[3], C-c. Tsai[4] and J. Summers[1].

Department of Urology[1], Summa Health System/N.E. Ohio Universities College of Medicine, 4209 St. Rt 44, P.O. Box 95, Rootstown Ohio 44272,

Departments of Anatomy[2] and Pharmacology/Virology[3], Lake Erie College of Osteopathic Medicine, 1858 W. Grandview Blvd., Erie PA 16509,

Department of Chemistry[4], Kent State University, Kent, OH 44242

ABSTRACT: Magnesium (Mg^{2+}) potentiated the anti-vesicular stomatitis virus (VSV) activity of poly r(A-U) or poly r(G-C) and the anti-HIV-1 activity of poly r(A-U). Mg^{2+} did not affect the anti-VSV activity of poly (rI) • poly (rC), poly (dA-dT) • poly (dA-dT) or poly (dG-dC) • poly (dG-dC). Modulation of one or more nuclear (nucleolar) processes of the host cell may be responsible for the synergistic antiviral activity.

The role of Mg^{2+} in modulating the antiviral activity of poly r(A-U) and poly r(G-C) was examined using a human foreskin fibroblast - VSV bioassay in which the concentration of poly r(A-U) or poly r(G-C) was fixed at 0.2 mM while the Mg^{2+} concentration was varied to produce variable Mg^{2+}/ribonucleotide ratios ranging from 1:16 to 2:1. Poly (rI) • poly (rC), poly

Table 1. Effect of Magnesium on the Antiviral Activity of Polynucleotides.

Test agent	Nucleotide 50% effective dose (μM)	Mg^{2+}/Nucleotide ratio of 50% effective doses (μM)	Enhancement of nucleotide antiviral activity (n-fold)
poly r(A-U)	6.8	0.17/0.68	10
poly r(G-C)	5.9	0.16/0.64	9
poly (rI) • poly (rC)	0.71	0.32/1.28	0.55
poly (dA-dT) • poly (dA-dT)	NI	NI	NA
poly (dG-dC) • poly (dG-dC)	NI	NI	NA
Mg^{2+} alone	18.00	NA	NA

NI = not inhibitory NA = not applicable

Twelve serial twofold dilutions of test solutions were co-incubated with HSF cells for 3 h at 37° C. The test solutions were removed and the cells were washed twice with PBS, overlaid with media, incubated for 17 h at 37° C and challenged with VSV (MOI = 0.1). Antiviral activity was evaluated by 50% CPE 17 h post-infection.

(dA-dT) • poly (dA-dT) and poly (dG-dC) • poly (dG-dC) were also tested at a Mg^{2+}/nucleotide ratio of 1:4 and a polynucleotide concentration of 0.20 mM.

None of the test agents alone or Mg^{2+}/polydeoxyribonucleotide combinations were efficacious antiviral agents (Table I). When Mg^{2+} was combined with poly r(A-U) or poly r(G-C), the 50 % effective dose (ED_{50}) of the Mg^{2+} decreased 106- to 112-fold and the ED_{50} of the poly r(A-U) and poly r(G-C) decreased 9- to 10-fold. The ED_{50} of the Mg^{2+}/poly (rI) • poly (rC) showed no change. Additional bioassays demonstrated that the enhanced antiviral activity was not due to increased interferon production or direct viral inactivation. A p24 ELISA assay system demonstrated that Mg^{2+} and the Mg^{2+}/poly r(A-U) combination exhibit antiviral activity against HIV-1 3B infected peripheral blood mononuclear cells (PBMCs) (Figure 1). No host cell toxicity was observed with the concentrations of test agents employed during these studies. Phase contrast micrographs of Eriochrome Blue SE-treated HSF cells illustrated that the Mg^{2+}/poly r(A-U) combinations display altered subcellular distribution with the Mg^{2+} being localized in the nucleoli and chromatin. Taken together, these results suggest that the enhancement phenomenon is not virus-specific nor host cell-specific and may be due to the modulation of one or more nuclear (nucleolar) processes. The low toxicity of Mg^{2+} and the Mg^{2+}/poly r(A-U) combination suggest that they may be employed alone or as part of a cocktail in the chemotherapy of HIV-1.

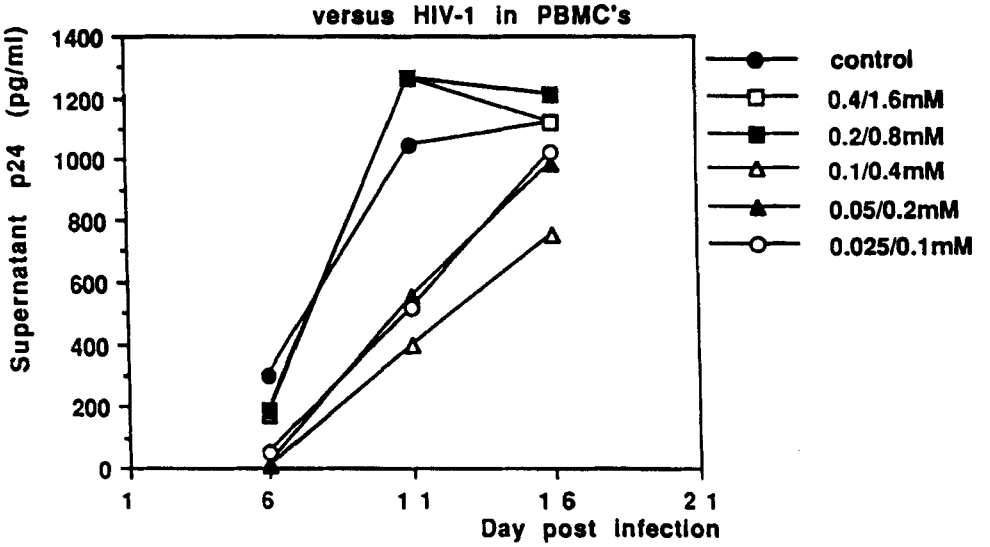

Figure 1. **Magnesium anions and poly r(A-U) in combination**

Five serial 2-fold dilutions of test agents were incubated with PBMCs for 3 h, diluted 1:3 with media, incubated 17 h and exposed to HIV-1 (3B, MOI = 0.02) for 5 h at 37 °C. Cell-free virus was removed and the PBMCs were resuspended in drug-free media. On days 6, 11 and 16, supernatant was tested for p24 antigen using the Coulter ELISA assay system. Zidovudine-treated and sham-treated, HIV-1 infected PBMCs served as controls.

Funded by Summa Health System Foundation and Kent State University.