

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

Carbovir: A Carbocyclic Nucleoside with Potent and Selective Activity Against Human Immunodeficiency Virus (HIV) in Vitro

Robert Vince^a; Mel Hua^a; Jay Brownell^a; George C. Lavelle^b; Jeanine Qualls^b; William M. Shannon^b

^a College of Pharmacy, University of Minnesota, Minneapolis, MN ^b Southern Research Institute, Birmingham, AL

To cite this Article Vince, Robert , Hua, Mel , Brownell, Jay , Lavelle, George C. , Qualls, Jeanine and Shannon, William M.(1989) 'Carbovir: A Carbocyclic Nucleoside with Potent and Selective Activity Against Human Immunodeficiency Virus (HIV) in Vitro', *Nucleosides, Nucleotides and Nucleic Acids*, 8: 5, 1127 — 1128

To link to this Article: DOI: 10.1080/07328318908054307

URL: <http://dx.doi.org/10.1080/07328318908054307>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

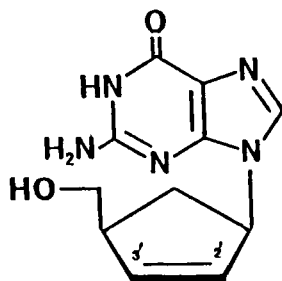
**CARBOVIR: A CARBOCYCLIC NUCLEOSIDE WITH POTENT AND SELECTIVE
ACTIVITY AGAINST HUMAN IMMUNODEFICIENCY VIRUS (HIV) IN VITRO**

Robert Vince,¹ Mei Hua,¹ Jay Brownell¹ George C. Lavelle,² Jeanine Qualls,² and
William M. Shannon.²

¹College of Pharmacy, University of Minnesota, Minneapolis, MN 55455

²Southern Research Institute, Birmingham, AL 35255

Carbocyclic 2', 3'-didehydro-2',3'-dideoxyquanosine (carbovir), a novel nucleoside analog, emerged as a potent and selective anti-HIV agent from a primary screen of a large number of carbocyclic nucleosides.¹ Carbovir inhibited the infectivity and replication of HIV in T-cells at concentrations 200- to 400-fold below toxicity to host cells. Carbovir was also evaluated for its inhibitory effects on the expression of viral antigen in HIV-infected CEM cells. Production of p 24 core antigen at optimal inhibitory concentrations of the antiviral agents indicated comparable results for AZT, ddA and carbovir.



**CARBOCYCLIC ANALOG OF 2',3'-DIDEOXY-
2',3'-DIDEHYDROGUANOSINE
(CARBOVIR: NSC-614846)**

Carbovir also exhibits a surprisingly synergistic anti-HIV efficacy when combined with either AZT or ribavirin. Thus, the MIC₅₀ value for carbovir is significantly reduced in a concentration-dependent manner with increasing levels of ribavirin in the two-drug combinations. Cytotoxicity for the host MT-2 cells is increased only at the highest concentrations of ribavirin used in combination with carbovir and synergistic antiviral effects are observed with carbovir + ribavirin at non-cytotoxic concentrations.

Combination treatment of HIV-infected MT-2 cells with non-cytotoxic levels of carbovir + AZT yields potent synergistic antiviral activity in vitro. The concentration of each drug in combination is found to be reduced to 1/10 of that required for 50% inhibition of HIV-induced cytopathic effects by each drug alone.

Acknowledgment: This work was supported by NIH grant R01-CA 23263

REFERENCES

1. R. Vince, M. Hua, J. Brownell, S. Daluge, F. Lee, W.M. Shannon, G.C. Lavelle, J. Qualls, O.S. Weislow, R. Kiser, P.G. Canonico, R.H. Schultz, V.L. Narayanan, J.G. Mayo, R.H. Shoemaker, and M.R. Boyd, *Biochem. Biophys. Res. Commun.*, in press (1988).