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Synthesis and Antiviral Evaluation of Novel 5,6-Dichlorobenzimidazole D-Pentofuranonucleosides.

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The adenosine analogue 5,6-dichloro-1-β-D-ribofuranosylbenzimidazole (DRB), a selective and reversible inhibitor of hnRNA synthesis, has received considerable attention during the last decade owing to its wide range of biological properties. For instance, under appropriate conditions DRB on the one hand exhibits antiviral and cytotoxic activities, on the other hand acts as a superinducer of interferon production in human fibroblasts.

Thus, it appeared of interest to synthesize and evaluate new analogues of DRB.

In the present work, we report the unambiguous synthesis and the biological evaluation of some novel D-pentofuranonucleosides of 5,6-dichlorobenzimidazole. Among them, the β-D-lyxofuranosyl derivative showed anti-HIV, anti-herpes and anti-parainfluenza activities at concentrations well below its cytotoxic concentration.

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An Evaluation of Human Recombinant Interferon Beta (rIFN-β) Against Selected Positive-and Negative-Stranded RNA Viruses using an MTT Assay Procedure. J. J. Kirsi[1], W. M. Shannon[1], T. P. Monath[2], and J. W. Huggins[2]. Southern Research Institute, Birmingham, AL 35255 USA[1], and U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 21701 USA[2].

A rapid, *in vitro*, automated MTT (tetrazolium dye) assay protocol was used in Vero-76 cells to evaluate the antiviral effects of human recombinant beta interferon (rIFN-β) against selected representatives of the following virus families: Bunyaviridae (Punta Toro virus, sandfly fever virus), Togaviridae (Venezuelan equine encephalomyelitis virus) and Flaviviridae (yellow fever virus, Japanese encephalitis virus). The results were compared to the effects of two positive control compounds ribavirin and selenazofurin. The suppression of viral CPE by rIFN-β was superior to that of the control compounds against all viruses tested. The Total Antiviral Inhibition (TAI index = area between cytotoxicity and antiviral curves) of rIFN-β was between 50-97% and the 50% virus inhibitory concentrations (IC_{50}'s) were between 17-2400 IU/ml of the rIFN-β depending on the virus. rIFN-β was nontoxic up to 100,000 IU/ml. This was the highest interferon concentration tested. In contrast, the TAI of ribavirin was only 25-45% and the IC_{50} was between 5-25 μg/ml. The maximum antiviral activity of ribavirin was reached at 32 μg/ml, after which the antiviral activity is slowly lost because of cytotoxicity. The TAI of selenazofurin was poor, between 0-20%, and this compound does not consistently reach an IC_{50} value with 10-100 μg/ml of the drug before it becomes maximally toxic at 10 μg/ml. The Selectivity Index (SI = TC_{50}/IC_{50}) for rIFN-β was close to 100 while ribavirin was about 10 and selenazofurin was approximately 1.0 depending on the virus used. The *in vitro* results indicate that these RNA viruses are very sensitive to the action of rIFN-β. Also, that the MTT assay is a good estimator of the viral CPE-inhibition and cytotoxicity of the test compounds *in vitro*. **Supported in part by U.S. Army Medical Research Acquisition Activity Contract No. DAMD17-86-C-6013.**