virus is due to inhibition of viral DNA synthesis. Interestingly, both vidarabine and prodrugs were more active against vaccinia (IC_{50}'s = 2.5–6 μM) than cowpox (IC_{50}'s = 8–54 μM). Both the D- and L-val prodrugs were stable at three pH's but D-val was more stable in intestinal and liver homogenates and in plasma. These properties make the D-amino acid prodrugs good candidates for further study as orally bioavailable anti-pox virus agents.

Acknowledgements: Supported by NIH grant R43 AI071400-01A1 and funds from TSRL Inc., and the University of Michigan.

doi:10.1016/j.antiviral.2008.01.113

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Antiviral Activity of (−)-D-Carbocyclic Cytosine (Carbodine) Against Avian Influenza Virus (H5N1)

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Natural and synthetic carbocyclic nucleosides are well known for their interesting biological properties, including antitumor as well as antiviral activities against a wide variety of RNA and DNA viruses. The carbocyclic analogue of cytosine (carbodine) was previously prepared as a racemic mixture and has been shown to possess inhibitory activity against human influenza type-A virus, measles, vesicular stomatitis virus and herpes simplex viruses. These interesting biological properties of carbodine, prompted us to develop an efficient synthetic method for the enantiomerically pure (−)-D-carbodine for further antiviral evaluations. Herein, we report the antiviral activity of carbodine against various strains of avian influenza virus (H5N1). Anti-influenza activity of (−)-D-carbodine was evaluated in comparison to its (+)-L- as well as (+)-DL analog against Duck, Gull, Hong Kong/2003 and Vietnam/2004 (H5N1) strains in vitro, and the results indicate that (−)-D-carbodine demonstrated potent antiviral activity with EC50 values of 0.57, 0.27, 0.18 and 0.18 μM, respectively, while the (+)-L-analog was inactive. Further biological and biochemical studies of (−)-D-carbodine as a potential antiviral agent for H5N1 virus are warranted.

Acknowledgement: Supported by NIH AI 056540 and NO1-AI-30048.

doi:10.1016/j.antiviral.2008.01.114

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Application of the Phosphoramidate Protide Approach to the Antiviral Drug Ribavirin

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Ribavirin is a nucleoside analogue with antiviral activity against a number of DNA and RNA viruses in vitro and in vivo (Sidwell et al., 1972). Ribavirin has been approved for the treatment of respiratory syncytial virus and for the treatment of hepatitis C virus in association with interferon. The bioactivation of ribavirin involves intracellular phosphorylation to its 5′-monophosphate mediated by adenosine kinase followed by further phosphorylation to the di- and tri-phosphate. Its broad spectrum of antiviral activity prompted us to design and synthesise a new series of ribavirin phosphoramidates in order to investigate its activity against different viruses. The synthesis and the biological evaluation for these compounds will be reported.

Reference

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doi:10.1016/j.antiviral.2008.01.115

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Design, Synthesis and Biological Evaluation of Novel Acyclovir ProTides

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Acyclovir and its prodrug valacyclovir are currently the treatments of choice for herpes simplex virus (HSV) and varicella-zoster virus (VZV) infections. Intracellular conversion of acyclovir to its active triphosphate form is severely limited by the first phosphorylation step, which is carried out by a herpes virus encoded thymidine kinase (Elion et al., 1977). Further conversions to the di- and triphosphate are mediated by cellular guanosine monophosphate kinase and nucleoside diphosphate kinase respectively. Importantly, the activation of the compound by the viral nucleoside kinase is a target for drug resistance in both HSV and VZV strains (Larder et al., 1983). Our phosphoramidate ProTide approach was applied to acyclovir as a means to bypass the limiting step of its activation. However, no signifi-