

A Comparison of the *In Vitro* Antiviral Potency of 2-Thio-6-Azauridine with Ribavirin and Selenazofurin Against Selected Positive- and Negative-Stranded RNA Viruses. J. J. Kirs<sup>1</sup>, B. Gabrielsen<sup>2</sup>, J. T. Rankin<sup>2</sup>, W. M. Shannon<sup>1</sup>, T. P. Monath<sup>2</sup> and J. W. Huggins<sup>2</sup>. Southern Research Institute, Birmingham, AL 35255, USA<sup>1</sup> and Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 21701, USA<sup>2</sup>.

Our large scale antiviral screening program (~50,000 single drug/single virus assays thus far), is using ribavirin and selenazofurin as control compounds to verify the uniformity of assay execution and to monitor the day-to-day variabilities of the MTT-assay system itself. In these parallel experiments, 2-thio-6 azauridine (2T6AU) performs equally or better than ribavirin and selenazofurin against the representatives of the following RNA virus families: Flaviviridae (yellow fever virus - Asibi strain; Japanese encephalitis virus - Beijing strain), Togaviridae (Venezuelan equine encephalomyelitis virus - Trinidad donkey strain), and Bunyaviridae (Punta Toro virus - Adames strain; sandfly fever virus - Sicilian strain). The comparison is based upon the Maximum Antiviral Reduction Values (MARV-concentration) and TAI INDEX = Total Antiviral Inhibition = area between cytotoxicity and antiviral curves, which takes into account drug's cytotoxicity. The general, overall antiviral *in vitro* potency of 2T6AU against Flaviviridae (YF, JE) is around twice of that of selenazofurin. Against Togaviridae (VE) the 2T6AU works equally well or slightly less than selenazofurin. The overall *in vitro* antiviral potency of 2T6AU against Bunyaviridae (PT) is better than ribavirin and is reached at a 10-fold lower drug concentration than ribavirin. However, against SF virus 2T6AU is less active than ribavirin although the maximum antiviral activity is reached at a 5-fold lower drug concentration. The cytotoxicity values of 2T6AU are closely comparable to those of selenazofurin and ribavirin. Further studies are underway to determine if the measured antiviral suppression is virustatic or virucidal or if any related compound would be a more potent antiviral. Supported in part by U. S. Army Medical Research Acquisition Activity Contract No. DAMD17-91-C-1050.

Search for Antiviral Compounds against Influenza and Some Other Viruses causing Respiratory Diseases. G.M.Ryazantseva, N.A.Zamyatina, L.L.Firstova. A.Kirchenstein Institute of Microbiology, Latvian Academy of Sciences, Riga, Latvia.

Results from studies of antiviral activity of different compounds against influenza A and B viruses, rhino- (HRV-13) and respiratory syncytial (RSV, Long strain) viruses are reported. The *in vitro* tests were carried out in CAM and monolayers of MDCK, Hep-2 and M-6 (human fibroblasts) cells by micro-titer assay.  $IC_{50}$ s of compound (a concentration causing 50% inhibition of 100<sup>5</sup> infectious doses of virus) were determined. Effective antiinfluenza compounds were revealed among the adamantane derivatives but their efficacies were comparable with rimantadine one. Among 30 tested benzimidazole derivatives one compound strongly inhibited reproduction of A/Bangkok/1/79 (H3N2) and B/Hong Kong/5/72 influenza strains and A/Krasnodar/101/59 (H2N2) strain resistant to rimantadine. This compound was active in experimental influenza infection of white mice reducing lethality by 35% at prophylactic and therapeutic compound administration together. Adenosine aliphatic derivative and 5 benzimidazole derivatives were shown to be active against HRV-13 in M-6 cell culture (therapeutic indexes - 30 and 8 - 19.5 correspondingly). One from the *in vitro* effective benzimidazole derivatives manifested its activity in experimental rhinovirus infection in Swiss mice reducing the titer of virus in nose washes by 2.5 lg TCID<sub>50</sub> after 24 h post infection. Dextran sulfate and chitosane sulfate were shown to be effective against RSV in Hep-2 cells.