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Effect of 2-Acetylpyridine Thiosemicarbazones on *In Vivo* Type 2 Herpesvirus Infections. J. H. Huffman, R. W. Sidwell, T. W. Schafer, and C. Shipman Jr. Utah State Univ., Logan, UT, CytRx Corp., Norcross, GA, and Univ. of Michigan, Ann Arbor, MI.

2-Acetylpyridine semicarbazone (APSC), 2-acetylpyridine thiosemicarbazone (APTSC) and 2-acetylpyridine-4-methyl-3-thiosemicarbazone (APMTSC) were compared with acyclovir (ACV) against type 2 herpesvirus (HSV-2) genitalis and encephalitis in mice and guinea pigs. Using 1,3-butanediol as topical vehicle, thrice daily treatment with 1% APSC and APTSC beginning 24 hr post-virus inoculation significantly increased survivors and decreased genital lesion severity. APTSC also reduced virus recovered from vaginal lesions. Results of 5% ACV in polyethylene glycol (PEG) were comparable in survivors and lesion reduction, but virus titer reduction was better. Eight vehicles were compared to determine which would provide most efficacy when 1% APTSC was applied to the HSV-2 genital infection in mice. Squibb creme, Eucerin and K-Y jelly bases were most effective. A genital guinea pig infection was similarly treated with 1% APMTSC and APTSC comparing Squibb and K-Y vehicles; APMTSC was more effective in the creme, whereas APTSC was more active in the jelly base. 5% ACV in PEG was more effective than either thiosemicarbazone, but 1% ACV was less inhibitory to the infection. Parenteral treatment of mice intraperitoneally infected with HSV-2 using 12.5, 25 or 50 mg/kg/day of APTSC prevented death comparable to 120 mg/kg/day of ACV.

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Antiviral Activity of Compound 102 Against Guinea Pig Cytomegalovirus Infection.
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The antiviral activity of a new compound (4-amino-5-bromo-7-(2-hydroxyethoxymethyl) pyrrolo [2,3-d] pyrimidine) or Compound 102 against guinea pig cytomegalovirus (GPCMV) replication was evaluated in vitro using guinea pig embryo cells and in vivo using Hartley guinea pigs. This compound was significantly effective in cell cultures tested. The ED_{50} of Compound 102 was 233 μM as determined by the plaque reduction assay. Using MOI at 0.01 in the virus yield reduction method, the ED_{99} was 200 μM. In an in vivo study, 40 one-week old guinea pigs were divided into four groups. Each group was inoculated with different dosages of GPCMV, i.e. 2.25, 3.25, 4.25 and 5.25 $\log_{10}$ $TCID_{50}$ by intraperitoneal route. One day after virus inoculation, six animals in each group were treated with Compound 102 at 50 mg/kg/day by i.p. for 5 days. Non-infected drug-treated control group was also included. Whole blood, spleen, lung and salivary gland were assayed for virus infectivity titers 7, 14 and 21 days post infection. There was no significant difference between drug-treated and sham-treated animals even in those animals who received only 2.25 $\log_{10}$ $TCID_{50}$ of virus. Compound 102 was found non-toxic to these guinea pigs. These results suggest that Compound 102 was effective against GPCMV replication in cell cultures, but lacked activity against GPCMV infection in guinea pigs.