

In Vitro Efficacy of Cidofovir and Acyclovir against Frog Virus 3

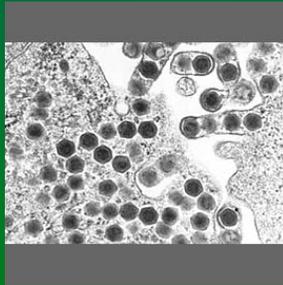
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Objective

Evaluate the *in vitro* efficacy of antiviral drugs Acyclovir and Cidofovir to reduce ranavirus titers in cell cultures.

Background

- ❖ Frog virus 3 is a *Ranavirus* in the family *Iridoviridae*
- ❖ Large double-stranded DNA viruses
- ❖ Significant die-offs in wild and captive amphibian, reptile, and non-tetrapod fish populations
- ❖ Little is understood about chemotherapeutics for Iridoviral diseases
- ❖ Acyclovir, a chain terminator prodrug, treats herpesvirus infections
 - ❖ Requires viral phosphorylation to become active
- ❖ Cidofovir is a chain terminator drug that does not require viral activation

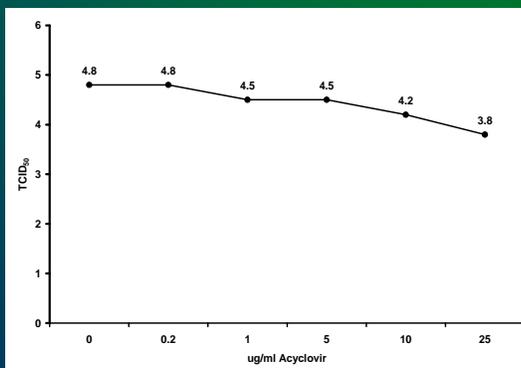


Methods

- ❖ *Terrapene* heart cells (TH-1) grown to confluency in 10% complete media in 24 2 cm² well cell culture plates, incubated at 28°C in 5% CO₂
- ❖ Isolated and partially characterized ranavirus from a Burmese Star tortoise used to inoculate cells at starting concentration of 10⁵TCID₅₀/ml
- ❖ Antivirals added
 - ❖ Acyclovir diluted into 25 mL cell culture media in 0, 0.2, 1, 5, 10, and 25µg/ml concentrations
 - ❖ Lipid-encapsulated cidofovir diluted into 25 mL cell culture media in 0, 0.2, 1, 5, and 10µg/ml concentrations
- ❖ Cells allowed to incubate for four days
- ❖ Wells evaluated for cytopathic effects (CPE)
- ❖ Virus titers estimated using a tissue culture infectious dose (TCID₅₀) assay

Results

- ❖ After four days, all wells with various concentrations of acyclovir showed CPE
- ❖ While there was a trend observed towards a decreasing titer with increasing acyclovir concentrations, the decrease was not statistically significant (p=0.287)
- ❖ Preliminary investigations demonstrated acyclovir to be insufficient at completely inhibiting viral replication
- ❖ Cidofovir testing is still underway



Effect of increasing concentrations of acyclovir on the TCID₅₀ of *Terrapene* cells inoculated with the Burmese star tortoise isolate.

Discussion

- ❖ While this study did not find acyclovir to be effective for ranavirus, doses higher than 25µg/ml were not evaluated
 - ❖ Nephrotoxicity and bone marrow suppression seen with acyclovir in cats
 - ❖ Anorexia seen in a pharmacokinetic study in box turtles at 40 mg/kg PO
- ❖ Acyclovir has been found to be 50% effective against feline herpesvirus-1 at a concentration of 56µg/ml warranting more studies at higher concentrations
- ❖ If effective, cidofovir will require further *in vivo* safety and pharmacokinetic studies.

Acknowledgements

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