Using Matrix Assays to Analyze the Synergistic Efficacy of Antiviral Drugs Against HSV-2
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Over 400 million people world-wide have genital HSV-2 infections. The current therapies against HSV-2 infections include Acyclovir (ACV), which is incompletely effective, and Foscarnet for ACV-resistant herpes virus strains, which causes nephrotoxicity. We hypothesize that the nucleotidyl transferase superfamily (NTS) inhibitors, ciclopirox olamine (#41), an FDA-approved drug for topical use, and piroctone olamine (#191) will synergize with acyclovir (ACV) in vitro to act as a safe and effective agent against HSV-2 infections. Previous studies have indicated that ACV loses effectiveness 5 hours post-infection. However, Compound #41 and #191 were found to inhibit viral replication at an early stage against one or more targets. This data provided sufficient evidence to suggest that these compounds could be effective in suppressing HSV infection. To test this hypothesis, I performed synergy assays that contained both drugs in Vero cells, and quantitatively analyzed titers using the CompuSyn application. This computational method produced a combination index (CI) value greater than 1 for each synergy assay, indicating antagonism. This experiment was only performed once for each drug, and more rounds of synergy assays are necessary to make an accurate conclusion. The purpose of this research was to identify a new combination of drugs with antiviral properties that work synergistically to yield the lowest concentration of herpes virus. If one of these, or other, NTS inhibitors is found to work synergistically with acyclovir, then it will be a critical step in developing effective antiviral drug therapy for herpes infection.