ABSTRACT

TITLE:	Sattabacin Inhibits Replication of the Varicella Zoster Virus in Human Fibroblast Cells
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ABSTRACT: Herpes simplex virus 3 (HSV3) is commonly known as the Varicella zoster virus (VZV), which is a DNA virus within the Herpesviridae family. Infection with VZV, commonly in children, results in chickenpox (varicella) and reactivation of the virus in the elderly or in immunocompromised adults leads to shingles (zoster). The Census Bureau predicts that by 2050 more than 21 million American will be 85 years of age or older; therefore, a large population will be susceptible to shingles. New compounds against VZV infection must be developed now and tested for anti-viral efficacy. We hypothesize that sattabacin and other structurally related compounds will have anti-viral activity against VZV infection in human fibroblast cells (MRC-5 cell line). Our study utilizes sattabacin, 4, which has been synthetically produced in the Chemistry Department and is known to exhibit antiviral activity against Herpes simplex virus type 1 (HSV1) and Herpes simplex virus type 2 (HSV2). To identify effective anti-viral compounds against VZV infection a traditional viral plaque assay was performed. Microarray analysis and realtime PCR were also used to determine a cellular mechanism by which these compounds inhibit VZV replication by analyzing global gene expression changes in human fibroblast cells. Our results indicate that, although sattabacin is cytotoxic to human cells at concentrations of 1000 M and greater, sattabacin also possesses anti-viral activity against VZV infection at concentrations ten-fold less than the cytotoxic concentrations. Compound concentrations that reduced viral replication by 50% (IC50) and 90% (IC90) were 58 M and 109 M, giving antiviral coefficients of 13.2 and 35.6, respectively. Inhibition of active viral replication by sattabacin may occur at the translational level in human cells. However, this assertion will need to be clearly identified in future studies. This study demonstrates that sattabacin is an effective anti-viral compound against VZV infection.