B13

Antiviral Effects of a Deoxynojirimycin Derivative on the HBV and HCV Viral Replication

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Alpha-glucosidase inhibitors, which block the trimming pathway of *N*-linked glycosylation, have been shown to eliminate the production of several ER-budding viruses in the Endoplasmic Reticulum (ER). These glucose-derived iminosugar derivatives *N*-butyl- and *N*-nonyl-deoxynojirimycin (DNJ) have been largely purified from the midgut of the silkworm, *Bombyx mori*. Here we investigated the effects of those DNJ molecules on the replication and release of HBV and BVDV viruses (flavivirus) in the *in vitro* and *in vivo* experiments. In the presence of DNJ, a functional HBV pol expressed in the Sf9 insect cell by a recombinant FPL-pol baculovirus was greatly inhibited and verified by HBV-pol priming reaction. And also, viral release in the body fluid of the HBV-producing transgenic mice was drastically decreased and tested by real-time PCR experiment. The purified DNJ was analyzed in the BVDV surrogate assay and its relative activity compared to the standards Ribavirin and INF-alpha. The DNJ sample inhibited viral-induced cell killing over a broad range with a calculated CKEC50=2.96 mM, and at high concentrations reduced progeny viral yields 3 logs with a calculated tEC90=0.24 mM. Cytotoxicity was not observed up to 50 mM. In reference to a compounds effective antiviral concentration relative to its cytotoxicity, a selective index (S.I.=CC50/EC90) was calculated as of 208. The only two drugs approved by the FDA for clinical use against HCV are effective in the BVDV model. DNJ compound tested in this system exhibited similar or greater antiviral activity. This DNJ may also inhibit HCV.