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THE SECRETION OF HUMAN HEPATITIS B VIRUS IS INHIBITED BY THE IMINO SUGAR, N-BUTYL-DEOXYNOJIRIMYCIN

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The imino sugar, N-butyldeoxynojirimycin (NBDNJ), is a potent inhibitor of the oligosaccharide trimming enzyme, α-glucosidase I. Hepatitis B Virus (HBV) contains three surface proteins (HBs) of different sizes which are singly or doubly N-glycosylated and are essential for the formation of infectious virus. Therefore, the replication and secretion of HBV in the human hepatoma cell line, HepG2, was studied in the presence of NBDNJ. In both the stably HBV transfected HepG 2.2.15 cells and in HBV *infected* HepG2 cells, NBDNJ suppressed secretion of HBV particles and caused intracellular retention of HBV DNA. The secretion of sub-viral particles was less affected. These data suggest that inhibitors of oligosaccharide trimming may be useful for antiviral therapy of hepatitis B and for the study of the intracellular transport of the viral glycoproteins.

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Antiviral activity of penciclovir, a novel antiherpesvirus compound, against duck hepatitis B virus *in vitro*.

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In vitro anti-hepadnaviral activities of penciclovir ([9-[4-hydroxy-3-hydroxymethylbut-1-yl] guanine) and ganciclovir ([9-[2-hydroxy-1-(hydroxymethyl) ethoxymethyl] guanine) were compared in primary duck hepatocyte (PDH) cultures congenitally infected with the duck hepatitis B virus (DHBV). Both compounds inhibited DHBV DNA replication to a comparable extent during continuous short-term treatment of the cultures. However, penciclovir was more effective both during longer-term continuous treatment and in "wash-out" experiments designed to compare the persistence of inhibitory activity after removal of extracellular compound. In these experiments, IC50s for penciclovir and ganciclovir were 0.7 and 4.0 μM (continuous) and 3.0 and 46.0 μM ("wash-out") respectively. Effects on viral preS1, pre-S2 and core antigen synthesis were similar to effects on viral DNA replication. Reason(s) for the greater antiviral activity shown by penciclovir are unknown, but may include increased rate or efficiency of activation of the parent compound, increased intracellular stability of its nucleotides compared with those of ganciclovir, or yet other factor(s). These data suggest that penciclovir or its oral form famciclovir may have clinical utility in the treatment of chronic hepatitis B virus infection.