Ezetimibe blocks hepatitis B virus infection after virus uptake into hepatocytes.

Current treatment of chronic hepatitis B virus (HBV) infection mainly targets viral replication in hepatocytes and leads to curing only in exceptional cases. Despite their potential to improve therapeutic success, no drugs interfering with early infection steps of the hepatotropic pathogen HBV are available to date. Recently, entry of the hepatitis C virus (HCV) has been shown to occur along hepatic cholesterol uptake pathways and ezetimibe, a drug which blocks this lipid transport, has been shown to inhibit HCV infection. We here investigated the effect of ezetimibe on HBV infection using differentiated HepaRG cells as a cell-culture infection model. Treatment with ezetimibe inhibited establishment of intrahepatic cccDNA and expression of viral replication markers when cells were infected with HBV virions, while we observed no effect when the HBV viral genome was transduced via an adenoviral vector. Our data suggest that modulating hepatic cholesterol uptake by ezetimibe inhibits early HBV infection and that ezetimibe sensitive lipid transport pathways represent new targets for antiviral therapy in HBV infection.