Supplemental material

Fig. S1

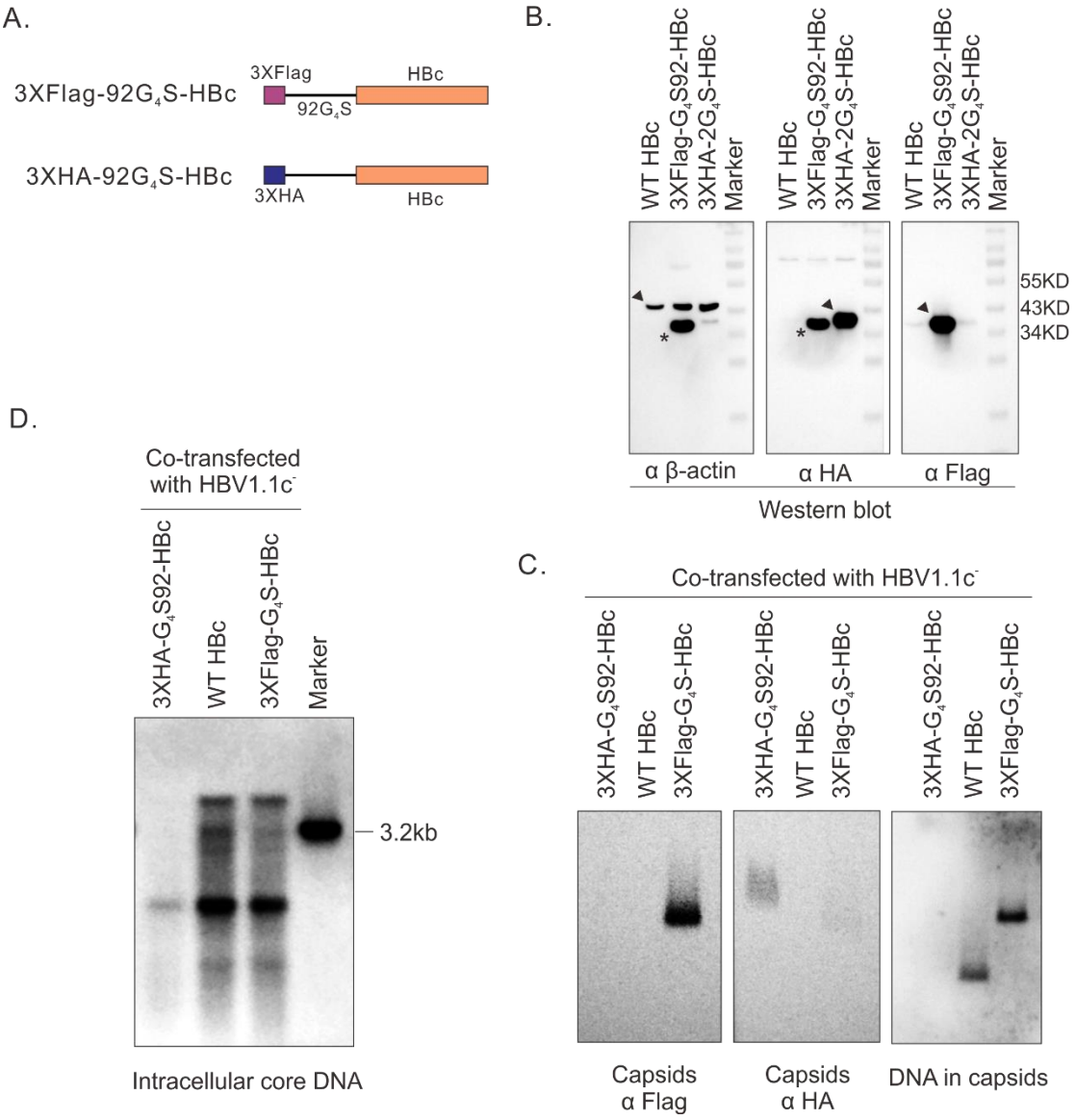

Fig. S1 Function analysis of 3×Flag-G4S92-HBc and 3×HA-G4S92-HBc. (A) Structure of 3×Flag-G$_4$S92-HBc and 3×HA-G$_4$S92-HBc. (B) Confirmation of the expression of 3×Flag-G$_4$S92-HBc and 3×HA-G$_4$S92-HBc. Plasmids were transfected into HEK293 cells respectively. Western blotting was used to confirm the expression of 3×Flag-G$_4$S92-HBc and 3×HA-G$_4$S92-HBc. Antibody against

β-actin we used showed a cross-reaction with 3×Flag-G_4S92-HBc (indicated by an asterisk). Antibody against HA tag used also showed a cross-reaction with 3×Flag-G_4S92-HBc (indicated by an asterisk). The FLAG antibody presented good specificity. (C) Capsid formation of 3×Flag-G_4S92-HBc and 3×HA-G_4S92-HBc. Intracellular capsids were detected by particle gel assays. The 3×Flag-G_4S92-HBc formed an apparent capsid band while the 3×HA-G_4S92-HBc presented a weak capsid band. The capsid formed by both 3×Flag-G_4S92-HBc and wild-type HBc clearly contained HBV DNA. A weak signal of HBV DNA was observed in the capsid formed by 3×HA-G_4 S92-HBc. (D) Intracellular core DNA assay. Southern blotting was used to detect intracellular core DNA. 3×Flag-G_4S92-HBc supported HBV DNA replication with a similar level to the wild-type HBc, while 3×HA-G_4S92-HBc only supported a weak replication of HBV DNA.

Fig. S2

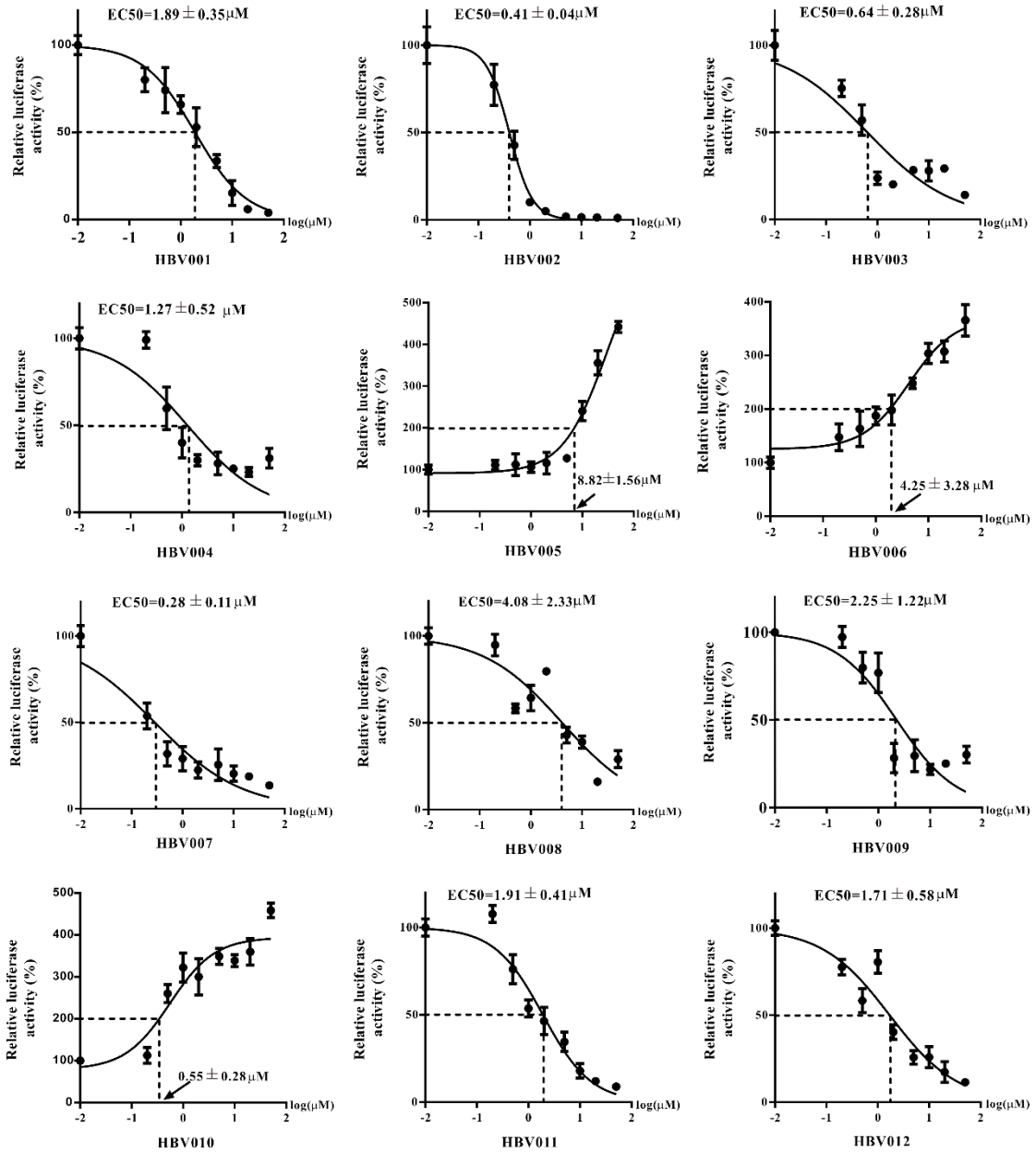

Fig. S2 Dose-effect curves of selected compounds on SRluc-HBc6 cells. Compounds of different concentrations were used to treat SRluc-HBc6 cells for 48h. Rluc activities were tested for plotting dose-effect curves.

Fig. S3

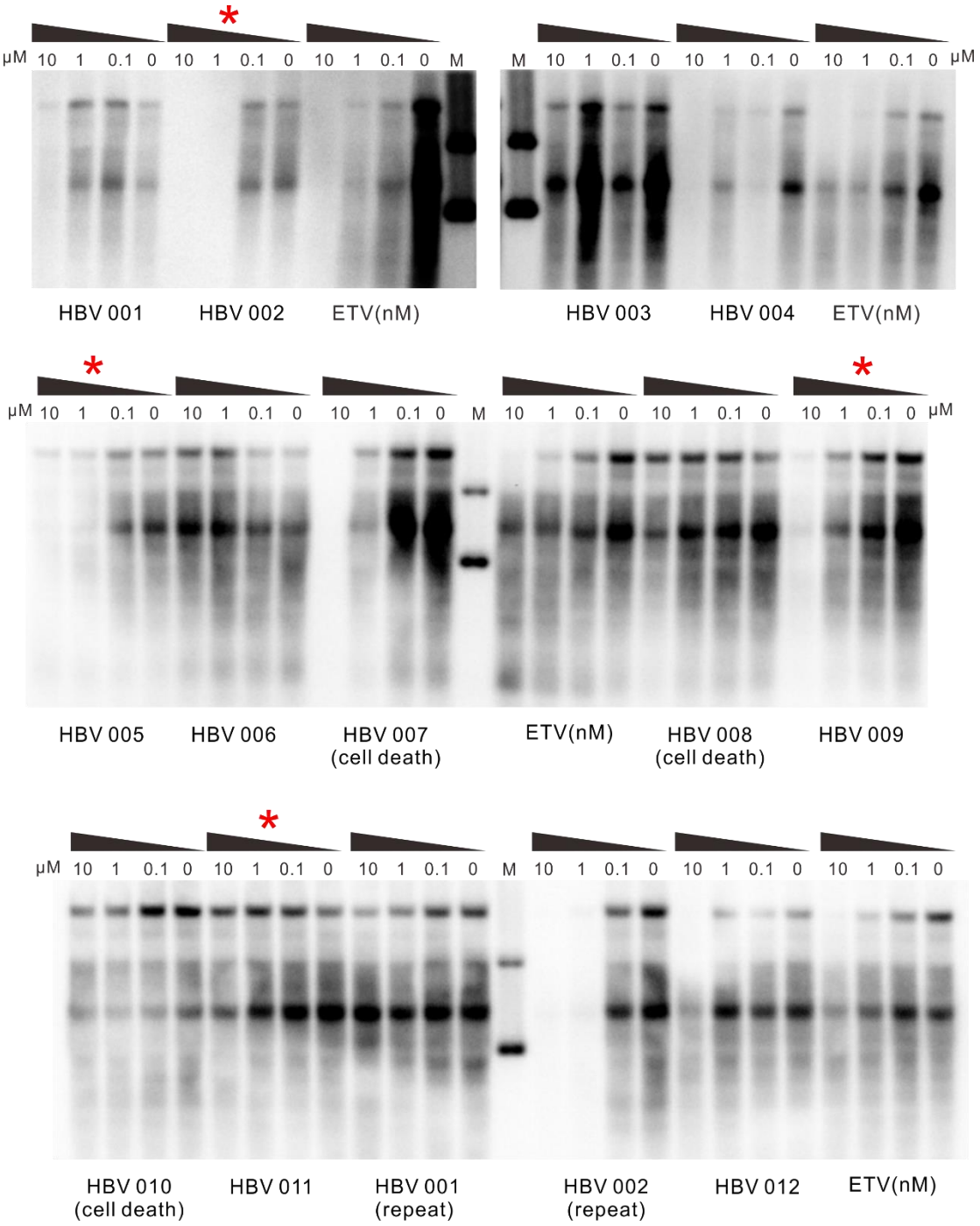

Fig. S3 Anti-HBV activity test of compounds on HepAD38 cells. HepAD38 cells were treated with Compounds of different concentrations for 6 days. Intracellular core DNA was extracted and detected by Southern blotting. Entecavir was used as positive controls. Drugs that induced cell death under

10μM were indicated. Drugs selected for further evaluation were labelled with red asterisks.

Fig. S4

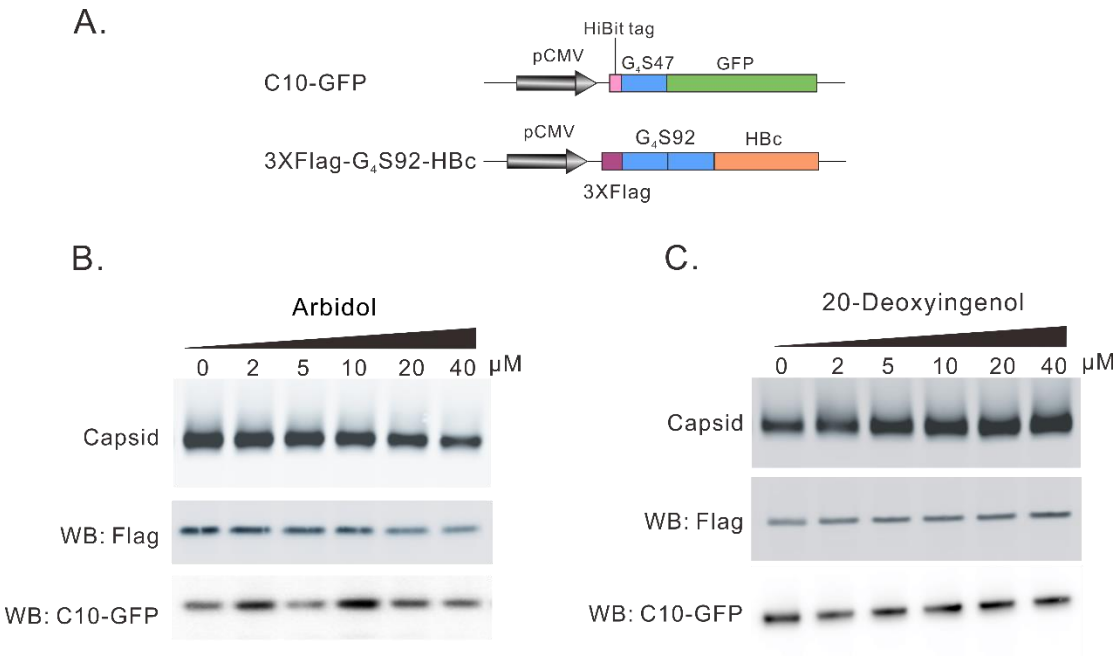

Fig. S4 Influence of Arbidol and 20-Deoxyingenol on the expression of the protein. (A) Structure of C10-GFP. (B) Influence of Arbidol on the expression of C10-GFP and 3×Flag-G4S92-HBc. 3×Flag-G4S92-HBc and C10-GFP were co-transfected into HepG2 cells, and the cells were treated with Arbidol for 6 days. Intracellular capsids were detected by particle gel assay. 3×Flag-G4S92-HBc protein was assayed by Western blotting with an anti-Flag antibody and C10-GFP protein was detected by Western blotting with the Nano-Glo HiBiT Blotting System. The level of capsid and 3×Flag-G4S92-HBc showed a decrease in a dose-dependent manner while C10-GFP did not. (C) Influence of 20-

Deoxyingenol on the expression of C10-GFP and 3×Flag-G_4S92-HBc. The level of capsid and 3×Flag-G_4S92-HBc showed an increase in a dose-dependent manner while C10-GFP did not.

Fig. S5

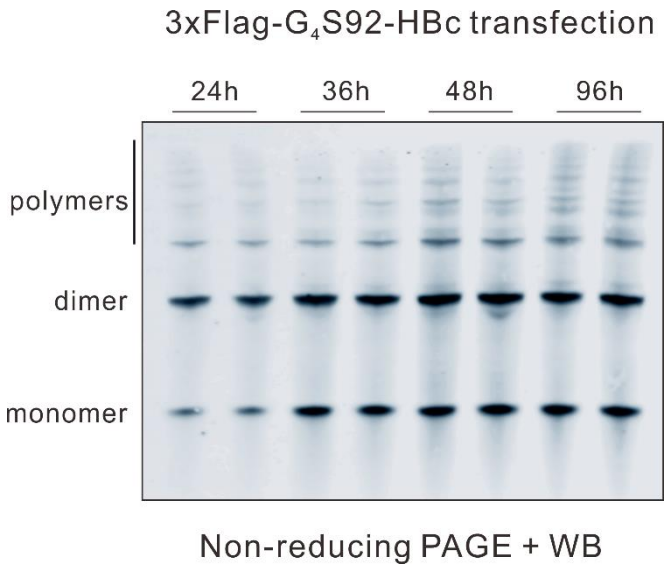

Fig. S5 Detection of HBc oligomerization by non-reducing PAGE. Plasmid 3×Flag-G_4S92-HBc was transfected into HEK293 cells. Cells were lysed at indicated time points with lysis buffer containing 10 mM Tris-HCl (pH 8.0), 1 mM EDTA, 0.2% NP-40. The lysis was loaded on non-reducing PAGEs in the absence of SDS and β-mercaptoethanol. The resolved proteins were transferred onto PVDF membranes and detected by the antibody against the Flag tag.