Disruption of the self-assembly pathway of hepatitis B virus capsid by antivirals

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The hepatitis B virus (HBV) is a major health problem worldwide. Despite the existence of a safe and effective vaccine, more than 292 million people are chronically infected by HBV, mainly in Africa and South Asia, due to a poor vaccination rate. Capsid assembly modulators (CAM) are antiviral molecules that disrupt the formation of HBV capsids, some of them being currently in clinical trial. I will first review the self-assembly and disassembly pathways of HBV capsids under various ionic conditions investigated by time-resolved X-ray scattering and cryoelectron microscopy. Then, I will detail our recent findings about the effects of various CAMs on the morphology and assembly kinetics of HBV capsids. In particular, I will show that CAMs alter the elastic properties of capsids leading to either slightly elongated or aberrant shapes. Elucidating the mechanisms by which antivirals disrupt the capsid self-assembly pathways is not only essential to combat viral infection, but it can help design bio-inspired nanocapsules with controlled morphology for delivery applications.