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# Inhibition of HBV replication and HBV-related inflammatory responses by KCT-01 through suppression of cccDNA formation

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Chronic hepatitis B (CHB) remains incurable because hepatitis B virus (HBV) nuclear covalently closed circular DNA (cccDNA) undergoes persistent maintenance in hepatocytes. Due to the fact that no current antiviral strategies with nucleos(t)ide analogs or interferon completely eradicate cccDNA, a novel antiviral option to suppress effectively cccDNA formation is urgently required. KCT-01 is a newly developed herbal mixture consisted of *Artemisia capillaris, Sanguisorba officinalis*, and *Curcuma longa*, which each plant has been revealed to cure viral infection and hepatic inflammation in previous studies. Thus, we investigated whether KCT-01 inhibits HBV virion replication as well as HBV-related hepatic inflammation through inhibition of cccDNA levels using HepG2.2.15 cell line and HBV hydrodynamic injection mouse model. KCT-01 significantly reduced HBsAg production, virion particle excretion, and intracellular 3.5 kb pregenomic RNA (pgRNA) quantity in HepG2.2.15 cells, which antiviral effects were comparable to entecavir, a representative antiviral. In accordance with *in vitro* results, KCT-01 administration dose-dependently suppressed HBsAg production and HBV virion excretion in serum and cccDNA formation and viral DNA levels in the liver tissue were also inhibited in mouse models. Besides, HBV-related inflammation mediators, such as TNF-α, IL-6, IL-1β, and MCP, were significantly downregulated under the treatment of KCT-01, validating that it could mediate both viral replication and inflammatory responses induced by HBV pathogen. Furthermore, KCT-01 produced according to Good Manufacturing Practices(GMP) regulations showed no toxicity in a preclinical study. Consequently, this study suggests that KCT-01 may play an effective regulatory role for treating CHB through suppression of cccDNA formation, a major challenge to cure HBV infection.

## Biography

Eungyeong Jang completed her MD and PhD from Kyung Hee University in Republic of Korea.

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