Phytocompounds from Indian medicinal plants with anti-Hepatitis B virus activity: A Systematic Review of in vitro evidence

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Background: Hepatitis B virus (HBV) infection remains a leading cause of liver related morbidity and mortality worldwide. Current nucleos(t)ide analogue therapies are constrained by drug resistance and an inability to eliminate covalently closed circular DNA (cccDNA). Medicinal plant metabolites represent a chemically diverse source of potential anti-HBV agents with favorable cytotoxicity profiles. This systematic review aimed to identify and rank plant extracts and phytocompounds with reported in vitro anti-HBV activity and to characterize their mechanisms of action.

Methods: A systematic literature search was conducted across PubMed, Scopus, and Google Scholar to identify medicinal plants of the Indian subcontinent with reported anti-HBV activity. Of 3,834 articles retrieved, 110 met inclusion criteria. Data extracted included compound identity, plant source, HBV cell line used, cytotoxicity, HBsAg (Hepatitis B surface antigen) and HBeAg (Hepatitis B envelope antigen) inhibition, HBV DNA reduction, and selectivity index (SI).

Results: 73 in vitro studies were identified from 110 primary studies. Predominant metabolite classes included flavonoids, polyphenols, diterpenoids, alkaloids, and caffeic acid derivatives. Among the most promising candidates, a caffeic acid derivative isolated from *Artemisia capillaris* exhibited one of the highest composite selectivity profiles (HBsAg SI >37.7, HBeAg SI >8.4, and HBV DNA SI >155.0). A piperidine alkaloid from *Piper longum* demonstrated notable antiviral activity with an HBeAg SI >16.4, while the polyphenolic compound 1,2,4,6-tetra-O-galloyl-β-D-glucose from *Phyllanthus emblica* showed potent inhibition of HBsAg production (IC_{50} = 0.69 µg/mL). Mechanistically, compounds acted through HBV promoter suppression (*Hypericum perforatum*), redox-mediated disruption of capsid assembly and cccDNA (isochlorogenic acid A), ER dependent blockade of virion secretion (*Boehmeria nivea*), direct inhibition of cccDNA formation (*Polygonum perfoliatum*), and p53-mediated transcriptional suppression of viral replication (*Curcuma longa*).

Conclusion: Plant extracts and compounds derived from Indian medicinal plants exhibit significant in vitro anti-HBV activity through diverse mechanisms rendering them as adjuncts to existing antiviral therapies.

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