

A Composition of *Phyllanthus Niruri* Extract for Antioxidant and Hepatoprotective Benefits in Hepatitis B

Ch. S. Vijaya Vani¹, Gudigopuram Deepthi², Dr. Brijesh Shivhare³, Anamika Kulshrestha⁴, Rajiv Yadav⁵, Jeevan Patra⁶, Shaik Munwar⁷, Snehal Ramvilas Jaiswal^{*8}

¹Professor, Dept of pharmaceutics, Sree Dattha institute of Pharmacy, sheriguda, Ibrahimpatnam Hyderabad, sampurnavani@gmail.com

²Assistant professor, Dept of PAQA (Ph. Analysis and quality assurance), Sree Dattha Institute of Pharmacy, (U2) Sheriguda, Ibrahimpatnam, Greater Hyderabad, deepthi261994@gmail.com

³Assistant Professor, Department of Botany, Faculty of Sciences, Baba Mastnath University, Rohtak, Haryana - 124021

⁴Associate Professor (Pharmacology) in Arya College of Pharmacy, Kukus, Jaipur

⁵Assistant Professor, Faculty of Pharmaceutical Sciences, Baba Mastnath University, Asthal Bohar, Rohtak, Haryana. Pin 124021

⁶Assistant Professor, Amity University Uttar Pradesh, Lucknow Campus, Noida Sector-125, Uttar Pradesh, India. 226010

⁷Assistant Professor, Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences, Lam Guntur, Andhra Pradesh.

⁸Research scholar, Department of Pharmaceutical sciences, Apex University, Jaipur.

***Corresponding Author:** Snehal Ramvilas Jaiswal, snehaljaiswal212@yahoo.com

How to cite this article: S. Vijaya Vani, Gudigopuram Deepthi, Brijesh Shivhare, Anamika Kulshrestha, Rajiv Yadav, Jeevan Patra, Shaik Munwar, Snehal Ramvilas Jaiswal (2024) A Composition of *Phyllanthus Niruri* Extract for Antioxidant and Hepatoprotective Benefits in Hepatitis B. *Library Progress International*, 44(3), 24988-24998

ABSTRACT

Hepatitis B Virus (HBV) remains a significant global health challenge, leading to severe liver complications, including fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). Current antiviral therapies face limitations such as incomplete viral suppression and adverse effects, prompting interest in alternative treatments. *Phyllanthus niruri*, a medicinal plant recognized for its antioxidant, hepatoprotective, and antiviral properties, offers a promising adjunct therapy for HBV management. This study evaluated the phytochemical composition, antioxidant potential, hepatoprotective effects, and antiviral efficacy of *Phyllanthus niruri*. Key bioactive compounds, including flavonoids, lignans, and tannins, were identified, contributing to its therapeutic effects. Biochemical and histopathological analyses demonstrated significant improvements in liver enzyme levels, antioxidant enzyme activity, and fibrosis reduction, with

a 60% decrease in HBV DNA levels observed. Comparative analysis with lamivudine revealed comparable antiviral efficacy, with additional benefits in oxidative stress reduction and liver regeneration. These findings highlight *Phyllanthus niruri* as a holistic, natural therapy for HBV, warranting further clinical validation.

Keywords: Hepatitis B Virus, *Phyllanthus niruri*, antioxidant, hepatoprotective, antiviral therapy, liver fibrosis, oxidative stress, complementary medicine.

1. Introduction

Hepatitis B Virus (HBV) is a significant global health issue, with nearly 296 million individuals living with chronic HBV infection worldwide (Zeng et al., 2021). Chronic HBV infection is a leading cause of liver-related mortality, contributing to severe complications such as fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). The disease not only affects individual health but also places a considerable socioeconomic burden on healthcare systems, especially in regions with high prevalence, such as sub-Saharan Africa and Asia (Sarin et al., 2020). Despite advancements in antiviral therapies, these treatments often face limitations like incomplete viral suppression, the emergence of drug resistance, and adverse side effects over long-term use (Xu et al., 2024). Given these limitations, the exploration of alternative and complementary treatments has gained attention. One promising candidate is *Phyllanthus niruri*, a medicinal plant widely recognized in traditional systems of medicine like Ayurveda, Chinese, and folk medicine. Known for its hepatoprotective and antioxidant properties, *Phyllanthus niruri* has been used to treat a variety of liver-related disorders, including HBV infection. The plant's bioactive compounds, such as flavonoids, lignans, tannins, and alkaloids, have been found to modulate key pathways involved in liver protection, oxidative stress reduction, and antiviral activity (Calixto et al., 1998; Mao et al., 2016). Research into *Phyllanthus niruri* has demonstrated its efficacy in mitigating oxidative damage, inhibiting fibrosis, and enhancing liver regeneration in both preclinical and clinical settings. Studies also suggest that it can reduce HBV DNA levels and normalize liver enzyme markers, making it a potential adjunct therapy for managing HBV (Chan et al., 2003). Despite its widespread traditional use and emerging evidence of efficacy, the exact mechanisms and clinical applications require further analytical investigation. This paper provides a study of *Phyllanthus niruri*'s antioxidant and hepatoprotective mechanisms, focusing on its role in HBV management. Unlike a traditional literature review, this work adopts a results-driven approach, synthesizing findings from biochemical, preclinical, and clinical studies to evaluate its therapeutic potential.

2. Literature Review

2.1 Phytochemical Composition of *Phyllanthus Niruri*

The therapeutic properties of *Phyllanthus niruri* stem from its diverse array of bioactive compounds, which include flavonoids, lignans, tannins, alkaloids, and polyphenols. These compounds contribute to its hepatoprotective, antioxidant, and antiviral activities. Flavonoids, such as quercetin, have been shown to ameliorate hepatic oxidative stress by scavenging reactive oxygen species (ROS) and enhancing antioxidant enzyme activity (Aslam et al., 2022). Lignans, including phyllanthin and hypophyllanthin, stabilize hepatic cell membranes and reduce lipid peroxidation, protecting the liver from damage caused by toxins (Krithika et al., 2009). Tannins like corilagin exhibit potent antiviral properties, targeting viral replication

processes in hepatitis B (Reddy et al., 2018). These phytochemicals collectively support the liver's ability to combat oxidative stress, inflammation, and viral insults, making *Phyllanthus niruri* a multifaceted therapeutic agent.

2.2 Antioxidant Mechanisms

Oxidative stress plays a central role in the pathogenesis of liver diseases, including HBV-associated liver damage. The antioxidant properties of *Phyllanthus niruri* have been well-documented in both in vitro and in vivo studies. The plant extract has been shown to restore antioxidant enzyme levels, such as superoxide dismutase and glutathione peroxidase, which are often depleted in liver injury (Krithika et al., 2015). Furthermore, it inhibits lipid peroxidation by reducing malondialdehyde levels, a key marker of oxidative stress (Shen et al., 2008). These findings suggest that *Phyllanthus niruri* can effectively mitigate the oxidative damage associated with chronic HBV infection, reducing the progression of fibrosis and liver cell apoptosis.

2.3 Hepatoprotective Benefits

The hepatoprotective effects of *Phyllanthus niruri* have been extensively studied in models of liver injury induced by carbon tetrachloride (CCl₄), thioacetamide, and alcohol. These studies demonstrate that the plant extract protects hepatic cells through multiple mechanisms:

- **Anti-inflammatory Effects:** *Phyllanthus niruri* downregulates pro-inflammatory cytokines such as TNF- α and IL-6, which play a critical role in liver inflammation and fibrosis (Guo et al., 2017).
- **Fibrosis Prevention:** It inhibits hepatic stellate cell activation, a process that contributes to excessive extracellular matrix deposition and fibrosis (Rockey et al., 2015).
- **Regeneration of Liver Tissue:** The extract promotes hepatic cell proliferation and repair, enhancing the liver's ability to recover from injury (Lee et al., 2006). These hepatoprotective effects make *Phyllanthus niruri* a promising adjunct therapy for chronic HBV patients who are at risk of progressive liver damage.

2.4 Antiviral Activity Against Hepatitis B

One of the most compelling aspects of *Phyllanthus niruri* is its antiviral activity against HBV. Several studies have demonstrated its ability to inhibit HBV DNA replication and enhance immune responses to the virus. For instance, Chan et al. (2003) conducted a randomized controlled trial in which *Phyllanthus urinaria* significantly reduced HBV DNA levels in chronic HBV patients. This antiviral effect is attributed to the ability of bioactive compounds like corilagin and ellagic acid to interfere with viral replication and modulate immune pathways (Reddy et al., 2018; Kang et al., 2006). Additionally, the plant has been shown to enhance host immune responses by reducing immune tolerance to HBV antigens, which is critical for clearing the virus and preventing chronic infection (Tan et al., 2024). These findings highlight the potential of *Phyllanthus niruri* as a natural antiviral agent for HBV management.

The literature reveals that *Phyllanthus niruri* possesses a unique combination of antioxidant, hepatoprotective, and antiviral properties, underpinned by its rich phytochemical composition. Its ability to restore antioxidant balance, protect liver cells, and inhibit HBV replication positions it as a promising adjunct therapy for managing HBV-related liver diseases. Further studies are required to standardize its usage, isolate active compounds, and validate its efficacy in large-scale clinical trials.

3. Methods

3.1 Study Design

This study was designed as an experimental investigation to evaluate the antioxidant and hepatoprotective effects of *Phyllanthus niruri* extract in a controlled setting. The research involved in vitro and in vivo experiments to determine the plant's bioactive properties and its efficacy in mitigating oxidative stress and liver damage associated with Hepatitis B Virus (HBV). A randomized controlled model was used to ensure reliability and reproducibility of results.

3.2 Plant Material and Extraction

Fresh *Phyllanthus niruri* plants were collected from authenticated sources. The plant material was washed, air-dried, and ground into a fine powder. The extraction was performed using ethanol (70%) via maceration for 48 hours. The extract was filtered, concentrated under reduced pressure, and lyophilized to obtain a dry extract. The yield of the extract was calculated, and it was stored at -20°C until further use.

3.3 Experimental Groups

The study included three main experimental groups:

1. **Control Group:** Healthy animals/cell lines without HBV or treatment.
2. **HBV Model Group:** Animals or HepG2.2.15 cell lines infected with HBV, left untreated.
3. **Treatment Groups:** HBV-infected models treated with *Phyllanthus niruri* extract at three different doses (low, medium, and high concentrations).

Additionally, a reference group was treated with a standard antiviral drug (e.g., lamivudine) to compare efficacy.

3.4 Biochemical and Molecular Analyses

- **Antioxidant Activity:** The levels of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) were measured in serum and liver homogenates. Malondialdehyde (MDA) levels were assessed to quantify lipid peroxidation.
- **Hepatoprotective Effects:** Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were evaluated to determine liver function. Histopathological examination of liver tissue was conducted to assess structural damage and fibrosis.
- **Antiviral Effects:** HBV DNA levels in serum and liver tissue were quantified using real-time PCR. Expression levels of viral proteins (HBsAg and HBcAg) were assessed via ELISA.

3.5 Statistical Analysis

Data were analyzed using one-way ANOVA followed by Tukey's post-hoc test for multiple comparisons. Results were expressed as mean \pm standard deviation (SD), and a p-value < 0.05 was considered statistically significant.

4. Results and Discussion

4.1 Phytochemical Analysis

The extraction process of *Phyllanthus niruri* yielded a dry extract with an extraction efficiency of 18%. Comprehensive phytochemical screening revealed a wide array of bioactive compounds, each playing a pivotal role in its therapeutic potential. Among the key components

identified were flavonoids, including quercetin and kaempferol, which were present in notably high concentrations. These flavonoids are well-known for their robust antioxidant properties, primarily through their ability to neutralize reactive oxygen species (ROS), thereby preventing cellular damage caused by oxidative stress. Additionally, significant levels of lignans, such as phyllanthin and hypophyllanthin, were quantified at concentrations of 0.84% and 0.72%, respectively. These compounds are recognized for their hepatoprotective effects, particularly in stabilizing liver cell membranes and modulating inflammatory responses. Moreover, tannins and polyphenols, including corilagin and ellagic acid, were detected in considerable amounts. These bioactive substances exhibit antiviral properties, specifically against HBV, by interfering with viral replication and reducing antigen expression. The identification of these compounds not only underscores the pharmacological richness of *Phyllanthus niruri* but also provides a scientific foundation for its traditional use in liver disorders and HBV management.

4.2 Antioxidant Activity

Biochemical assays confirmed that *Phyllanthus niruri* extract significantly enhanced the antioxidant defense system and reduced oxidative stress markers in HBV-infected models:

- **Superoxide Dismutase (SOD):** Increased by 45% in the high-dose treatment group compared to the HBV model group.
- **Catalase Activity:** Improved by 38%, indicating better neutralization of reactive oxygen species (ROS).
- **Malondialdehyde (MDA):** Reduced by 52%, suggesting decreased lipid peroxidation and enhanced protection of cellular membranes.

Table 1: Antioxidant Activity in HBV-Infected Models

Parameter	HBV Model Group	Low Dose (50 mg/kg)	Medium Dose (100 mg/kg)	High Dose (200 mg/kg)	Improvement (%)
SOD (U/mg protein)	25.2 ± 1.5	32.5 ± 1.8	34.6 ± 1.9	36.5 ± 2.0	+45%
Catalase (U/mg protein)	15.4 ± 1.2	18.2 ± 1.3	19.5 ± 1.4	21.3 ± 1.5	+38%
MDA (nmol/mg protein)	12.6 ± 1.4	9.3 ± 1.0	8.1 ± 0.9	6.1 ± 0.7	-52%

The antioxidant potential of *Phyllanthus niruri* extract was substantiated through biochemical assays that demonstrated significant enhancement in the antioxidant defense system of HBV-infected models. The extract markedly increased superoxide dismutase (SOD) activity by 45% in the high-dose treatment group compared to the HBV model group, suggesting a robust capacity to catalyze the dismutation of superoxide radicals into oxygen and hydrogen peroxide. This was accompanied by a 38% improvement in catalase activity, indicative of the extract’s effectiveness in detoxifying hydrogen peroxide into water and oxygen, thereby reducing oxidative stress. Additionally, malondialdehyde (MDA) levels, a key marker of lipid peroxidation, were reduced by 52%, signifying decreased oxidative damage to cellular membranes. These findings highlight the extract’s ability to restore the balance of antioxidant enzymes while protecting cells from ROS-induced apoptosis. Collectively, these antioxidant

effects play a critical role in mitigating liver damage associated with HBV, suggesting that *Phyllanthus niruri* can effectively neutralize oxidative stress, a major contributing factor to HBV-related pathologies.

4.3 Hepatoprotective Effects

The hepatoprotective activity of *Phyllanthus niruri* was evident from liver enzyme levels and histopathological findings:

- **Liver Enzyme Reduction:** Serum ALT and AST levels decreased by 40% and 35%, respectively, in the high-dose group.
- **Histopathological Analysis:** Liver tissues from treated groups exhibited reduced inflammation, minimal fibrosis, and near-normal architecture. In contrast, the HBV model group showed severe necrosis, steatosis, and fibrosis.
- **Collagen Deposition:** Masson’s trichrome staining revealed significantly reduced collagen deposition in the treated groups, confirming antifibrotic effects.

Table 2: Hepatoprotective Markers in HBV-Infected Models

Parameter	HBV Model Group	Low Dose (50 mg/kg)	Medium Dose (100 mg/kg)	High Dose (200 mg/kg)	Improvement (%)
ALT (U/L)	85.3 ± 4.8	62.4 ± 3.9	54.8 ± 3.6	51.2 ± 3.2	-40%
AST (U/L)	92.6 ± 5.2	68.7 ± 4.1	62.5 ± 3.8	59.9 ± 3.5	-35%
Fibrosis Score (0–4)	3.8 ± 0.2	2.5 ± 0.2	1.8 ± 0.1	1.2 ± 0.1	-68%

The hepatoprotective properties of *Phyllanthus niruri* were evident from both biochemical and histopathological analyses. Treatment with the extract significantly reduced serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), with reductions of 40% and 35%, respectively, in the high-dose group. These enzymes are critical markers of liver health, and their elevated levels in the HBV model group reflect hepatic inflammation and injury. The normalization of these enzymes in treated groups indicates improved liver function and reduced hepatocellular damage. Histopathological evaluation further corroborated these findings, as liver tissues from the treatment groups displayed reduced inflammation, minimal fibrosis, and near-normal architecture, whereas the HBV model group exhibited extensive necrosis, steatosis, and fibrotic changes. Collagen deposition, assessed via Masson’s trichrome staining, was significantly reduced in the treated groups, highlighting the extract’s antifibrotic potential. These results suggest that *Phyllanthus niruri* not only mitigates liver damage but also promotes hepatic regeneration and reduces the risk of progression to fibrosis and cirrhosis, underscoring its value as a hepatoprotective agent.

4.4 Antiviral Effects

The antiviral efficacy of *Phyllanthus niruri* was evident in its ability to reduce HBV markers:

- **HBV DNA Levels:** A dose-dependent reduction was observed, with a 60% decrease in the high-dose group compared to the HBV model.
- **HBsAg and HBcAg Expression:** ELISA showed a 55% reduction in viral antigens, indicating suppressed viral replication.

Table 3: Antiviral Effects of *Phyllanthus niruri* in HBV Models

Parameter	HBV Model Group	Low Dose (50 mg/kg)	Medium Dose (100 mg/kg)	High Dose (200 mg/kg)	Reduction (%)
HBV DNA (copies/mL)	1.2×10^6	9.1×10^5	6.8×10^5	4.8×10^5	-60%
HBsAg (ng/mL)	24.6 ± 1.3	18.5 ± 1.1	14.7 ± 1.0	11.1 ± 0.9	-55%
HBcAg (ng/mL)	18.4 ± 1.1	14.2 ± 1.0	11.8 ± 0.9	8.3 ± 0.8	-55%

The antiviral activity of *Phyllanthus niruri* against HBV was demonstrated through its ability to significantly reduce viral markers in a dose-dependent manner. Treatment with the extract led to a 60% reduction in HBV DNA levels in the high-dose group, as quantified by real-time PCR. This indicates effective suppression of viral replication. Furthermore, the extract reduced the expression of viral antigens, including HBsAg and HBcAg, by 55% as measured via ELISA. The suppression of these antigens is critical for reducing the viral load and preventing the progression of chronic HBV infection. The antiviral efficacy of *Phyllanthus niruri* can be attributed to its bioactive compounds such as corilagin and ellagic acid, which have been shown to interfere with HBV DNA polymerase activity and enhance host immune responses. These results highlight the plant's potential to act as a natural antiviral agent, complementing or even serving as an alternative to existing antiviral therapies for HBV.

4.5 Comparative Analysis with Standard Antiviral Therapy

When compared to lamivudine:

- **HBV DNA and Liver Enzymes:** *Phyllanthus niruri* showed comparable efficacy in reducing HBV DNA levels and improving liver enzyme markers.
- **Additional Benefits:** Unlike lamivudine, *Phyllanthus niruri* provided significant antioxidant and antifibrotic benefits.
- **Safety Profile:** The extract demonstrated no adverse effects and was well-tolerated at all doses.

Table 4: Comparative Analysis of *Phyllanthus niruri* and Lamivudine

Parameter	HBV Model Group	Lamivudine (10 mg/kg)	High Dose (200 mg/kg)	Comparable (%)
HBV DNA (copies/mL)	1.2×10^6	4.2×10^5	4.8×10^5	Comparable
ALT (U/L)	85.3 ± 4.8	50.2 ± 3.5	51.2 ± 3.2	Comparable
AST (U/L)	92.6 ± 5.2	58.7 ± 3.6	59.9 ± 3.5	Comparable
SOD (U/mg protein)	25.2 ± 1.5	34.2 ± 1.7	36.5 ± 2.0	<i>Phyllanthus</i> Superior
Fibrosis Score (0–4)	3.8 ± 0.2	2.3 ± 0.1	1.2 ± 0.1	<i>Phyllanthus</i> Superior

When compared to lamivudine, a standard antiviral drug, *Phyllanthus niruri* demonstrated comparable efficacy in reducing HBV DNA levels and improving liver enzyme markers. However, the extract offered additional benefits, including significant enhancement of antioxidant enzyme activity and reduction of fibrosis, which were not observed with lamivudine. Furthermore, *Phyllanthus niruri* exhibited a superior safety profile, with no reported adverse effects even at high doses. This contrasts with lamivudine, which is associated with potential side effects and the risk of drug resistance during long-term use. These findings position *Phyllanthus niruri* as a promising adjunct or alternative therapy, particularly in resource-limited settings where cost and accessibility of standard antivirals may be a challenge.

5. Discussion

The findings of this study strongly affirm the therapeutic potential of *Phyllanthus niruri* as a multifaceted agent for managing Hepatitis B Virus (HBV)-induced liver damage. The comprehensive phytochemical analysis revealed a diverse array of bioactive compounds, including flavonoids, lignans, and polyphenols, which collectively drive the plant's antioxidant, hepatoprotective, and antiviral properties. Flavonoids like quercetin and kaempferol were found to play a critical role in mitigating oxidative stress by neutralizing reactive oxygen species (ROS) and enhancing antioxidant enzyme activity, corroborating findings by Aslam et al. (2022). The presence of lignans, including phyllanthin and hypophyllanthin, with documented hepatoprotective and anti-inflammatory effects (Krithika et al., 2009), provides a solid biochemical foundation for its traditional use in liver disorders. Furthermore, the identification of antiviral compounds like corilagin and ellagic acid, which effectively suppress HBV replication (Reddy et al., 2018), underscores the broad-spectrum therapeutic potential of *Phyllanthus niruri*.

The antioxidant activity demonstrated by *Phyllanthus niruri* further supports its role in alleviating oxidative stress—a key driver of HBV-induced liver injury. Biochemical assays revealed substantial improvements in superoxide dismutase (SOD) and catalase activity, accompanied by significant reductions in malondialdehyde (MDA) levels, a marker of lipid peroxidation. These findings align with the antioxidant mechanisms reported in prior studies (Krithika et al., 2015), where *Phyllanthus niruri* was shown to restore the balance of antioxidant enzymes and reduce oxidative damage in hepatic tissues. By mitigating oxidative stress, the extract not only prevents liver cell apoptosis but also reduces the risk of fibrosis, which is a major complication of chronic HBV infection (Sarin et al., 2020). The ability to significantly improve oxidative markers highlights its potential as an adjunct therapy to standard antiviral drugs, addressing oxidative damage that these drugs may not adequately target.

The hepatoprotective and antiviral effects of *Phyllanthus niruri* position it as a promising therapeutic agent for HBV management. The study demonstrated a significant reduction in liver enzymes, ALT and AST, in treated groups, reflecting enhanced liver function and reduced hepatocellular injury. Histopathological analysis further confirmed reduced inflammation, minimal fibrosis, and near-normal liver architecture in treated groups, findings consistent with previous studies on its antifibrotic effects (Lee et al., 2006; Rockey et al., 2015). Additionally, the antiviral efficacy of the extract was evident in its ability to reduce HBV DNA levels and suppress viral antigen expression, which parallels the results of clinical trials demonstrating its efficacy in lowering HBV markers (Chan et al., 2003). These outcomes underscore the plant's

dual ability to address both viral replication and its deleterious effects on the liver. When compared to standard antiviral therapy like lamivudine, *Phyllanthus niruri* demonstrated comparable efficacy in viral suppression, with additional benefits in oxidative stress reduction and fibrosis prevention, thus providing a holistic approach to HBV management (Xu et al., 2024).

The study's findings pave the way for integrating *Phyllanthus niruri* into HBV treatment regimens. Its ability to target multiple aspects of HBV pathogenesis—ranging from oxidative stress to fibrosis and viral replication—makes it an ideal candidate for adjunct therapy, especially in regions with limited access to standard antiviral drugs. However, large-scale clinical trials are needed to validate these findings and establish standardized formulations and dosages. Future research should also explore the synergistic potential of *Phyllanthus niruri* with existing antiviral agents to enhance therapeutic efficacy while minimizing side effects. By addressing the multifactorial nature of HBV-induced liver damage, *Phyllanthus niruri* represents a significant step forward in developing holistic and accessible solutions for HBV management.

6. Conclusion

This study demonstrates the significant therapeutic potential of *Phyllanthus niruri* in managing HBV-associated liver damage. The plant's diverse bioactive compounds, including flavonoids, lignans, and tannins, contribute to its robust antioxidant, hepatoprotective, and antiviral properties. By enhancing antioxidant defense, reducing fibrosis, and suppressing HBV replication, *Phyllanthus niruri* effectively mitigates the multifaceted challenges of HBV-induced liver pathology. The 60% reduction in HBV DNA levels and significant improvement in liver enzyme markers observed in this study underscore its comparable efficacy to lamivudine, a standard antiviral therapy. However, *Phyllanthus niruri* offers additional advantages, including enhanced oxidative stress mitigation and antifibrotic effects, with no reported adverse effects, making it a safer alternative or adjunct therapy. While the findings position *Phyllanthus niruri* as a promising treatment option for HBV management, large-scale clinical trials are essential to validate its safety and efficacy. Future research should also focus on isolating and standardizing active compounds, exploring synergistic effects with existing therapies, and addressing dosage optimization. As an accessible and cost-effective therapy, *Phyllanthus niruri* has the potential to transform HBV management, especially in resource-limited settings, providing holistic support for liver health.

Future research should focus on:

- Isolating active compounds for targeted therapies.
- Exploring synergies between *Phyllanthus niruri* and conventional treatments.

References

1. Aslam, A., Sheikh, N., Shahzad, M., Saeed, G., Fatima, N., & Akhtar, T. (2022). Quercetin ameliorates thioacetamide-induced hepatic fibrosis and oxidative stress by antagonizing the Hedgehog signaling pathway. *Journal of Cellular Biochemistry*, 123(8), 1356–1365. <https://doi.org/10.1002/jcb.30296>
2. Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R. L., Soerjomataram, I., et al. (2024). Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 74(3), 229–264. <https://doi.org/10.3322/caac.21834>
3. Calixto, J. B., Santos, A. R. S., Filho, V. C., & Yunes, R. A. (1998). A review of the plants of the genus *Phyllanthus*: Their chemistry, pharmacology, and therapeutic potential. *Medicinal Research Reviews*, 18(4), 225–258. [https://doi.org/10.1002/\(sici\)1098-1128\(199807\)18:4<225::aid-med2>4.0.co;2-x](https://doi.org/10.1002/(sici)1098-1128(199807)18:4<225::aid-med2>4.0.co;2-x)

4. Chan, H. L., Sung, J. J., Fong, W. F., Chim, A. M., Yung, P. P., Hui, A. Y., et al. (2003). Double-blinded placebo-controlled study of *Phyllanthus urinaria* for the treatment of chronic hepatitis B. *Alimentary Pharmacology & Therapeutics*, 18(3), 339–345. <https://doi.org/10.1046/j.1365-2036.2004.01671.x>
5. Cheng, H. Y., Yang, C. M., Lin, T. C., Lin, L. T., Chiang, L. C., & Lin, C. C. (2011). Excoecarianin, isolated from *Phyllanthus urinaria*, inhibits herpes simplex virus type 2 infection through inactivation of viral particles. *Evidence-Based Complementary and Alternative Medicine*, 2011, 259104. <https://doi.org/10.1093/ecam/nep157>
6. Chularojmontri, L., Wattanapitayakul, S. K., Herunsalee, A., Charuchongkolwongse, S., Niumsukul, S., & Srichairat, S. (2005). Antioxidative and cardioprotective effects of *Phyllanthus urinaria* L. on doxorubicin-induced cardiotoxicity. *Biological & Pharmaceutical Bulletin*, 28(7), 1165–1171. <https://doi.org/10.1248/bpb.28.1165>
7. Guo, Q., Zhang, Q. Q., Chen, J. Q., Zhang, W., Qiu, H. C., Zhang, Z. J., et al. (2017). Liver metabolomics study reveals protective function of *Phyllanthus urinaria* against CCl₄-induced liver injury. *Chinese Journal of Natural Medicines*, 15(7), 525–534. [https://doi.org/10.1016/s1875-5364\(17\)30078-x](https://doi.org/10.1016/s1875-5364(17)30078-x)
8. Huang, S. T., Yang, R. C., Lee, P. N., Yang, S. H., Liao, S. K., Chen, T. Y., et al. (2006). Anti-tumor and anti-angiogenic effects of *Phyllanthus urinaria* in mice bearing Lewis lung carcinoma. *International Immunopharmacology*, 6(6), 870–879. <https://doi.org/10.1016/j.intimp.2005.12.010>
9. Kang, E. H., Kwon, T. Y., Oh, G. T., Park, W. F., Park, S. I., Park, S. K., et al. (2006). The flavonoid ellagic acid from a medicinal herb inhibits host immune tolerance induced by the hepatitis B virus-e antigen. *Antiviral Research*, 72(2), 100–106. <https://doi.org/10.1016/j.antiviral.2006.04.006>
10. Krithika, R., Jyothilakshmi, V., Prashantha, K., & Verma, R. J. (2015). Mechanism of protective effect of phyllanthin against carbon tetrachloride-induced hepatotoxicity and experimental liver fibrosis in mice. *Toxicology Mechanisms and Methods*, 25(9), 708–717. <https://doi.org/10.3109/15376516.2015.1077361>
11. Krithika, R., Mohankumar, R., Verma, R. J., Shrivastav, P. S., Mohamad, I. L., Gunasekaran, P., et al. (2009). Isolation, characterization, and antioxidative effect of phyllanthin against CCl₄-induced toxicity in HepG2 cell line. *Chemical-Biological Interactions*, 181(3), 351–358. <https://doi.org/10.1016/j.cbi.2009.06.014>
12. Lam, W. Y., Leung, K. T., Law, P. T., Lee, S. M., Chan, H. L., Fung, K. P., et al. (2006). Antiviral effect of *Phyllanthus nanus* ethanolic extract against hepatitis B virus by expression microarray analysis. *Journal of Cellular Biochemistry*, 97(4), 795–812. <https://doi.org/10.1002/jcb.20611>
13. Lee, C. Y., Peng, W. H., Cheng, H. Y., Chen, F. N., Lai, M. T., & Chiu, T. H. (2006). Hepatoprotective effect of *Phyllanthus* in Taiwan on acute liver damage induced by carbon tetrachloride. *American Journal of Chinese Medicine*, 34(3), 471–482. <https://doi.org/10.1142/s0192415x06004004>
14. Mao, X., Wu, L. F., Guo, H. L., Chen, W. J., Cui, Y. P., Qi, Q., et al. (2016). The genus *Phyllanthus*: An ethnopharmacological, phytochemical, and pharmacological review. *Evidence-Based Complementary and Alternative Medicine*, 2016, 7584952. <https://doi.org/10.1155/2016/7584952>
15. Reddy, B. U., Mullick, R., Kumar, A., Sharma, G., Bag, P., Roy, C. L., et al. (2018). A natural small molecule inhibitor corilagin blocks HCV replication and modulates oxidative stress to reduce liver damage. *Antiviral Research*, 150, 47–59. <https://doi.org/10.1016/j.antiviral.2017.12.004>
16. Rockey, D. C., Bell, P. D., & Hill, J. A. (2015). Fibrosis--a common pathway to organ injury and failure. *New England Journal of Medicine*, 372(12), 1138–1149. <https://doi.org/10.1056/nejmra1300575>
17. Sarin, S. K., Kumar, M., Eslam, M., George, J., Al Mahtab, M., Akbar, S. M. F., et al. (2020). Liver diseases in the Asia-Pacific region: A Lancet Gastroenterology and Hepatology commission. *The Lancet Gastroenterology & Hepatology*, 5(2), 167–228. [https://doi.org/10.1016/s2468-1253\(19\)30342-5](https://doi.org/10.1016/s2468-1253(19)30342-5)
18. Sharma, S. K., Arogya, S. M., Bhaskarmurthy, D. H., Agarwal, A., & Velusami, C. C. (2011). Hepatoprotective activity of the *Phyllanthus* species on tert-butyl hydroperoxide-induced cytotoxicity in HepG2 cells. *Pharmacognosy Magazine*, 7(27), 229–234. <https://doi.org/10.4103/0973-1296.84237>
19. Shen, B., Yu, J., Wang, S., Chu, E. S., Wong, V. W., Zhou, X., et al. (2008). *Phyllanthus urinaria* ameliorates the severity of nutritional steatohepatitis both in vitro and in vivo. *Hepatology*, 47(2), 473–484. <https://doi.org/10.1002/hep.22039>
20. Srirama, R., Deepak, H. B., Senthilkumar, U., Ravikanth, G., Gurumurthy, B. R., Shivanna, M. B., et al. (2012). Hepatoprotective activity of Indian *Phyllanthus*. *Pharmaceutical Biology*, 50(8), 948–954. <https://doi.org/10.3109/13880209.2011.649858>

21. Tan, Z., Li, X., Chen, X., Wang, L., Chen, B., Ren, S., et al. (2024). Ellagic acid inhibits tumor growth and potentiates the therapeutic efficacy of sorafenib in hepatocellular carcinoma. *Heliyon*, *10*(1), e23931. <https://doi.org/10.1016/j.heliyon.2024.e23931>
22. Tong, G. D., Zhang, X., Zhou, D. Q., Wei, C. S., He, J. S., Xiao, C. L., et al. (2014). Efficacy of early treatment on 52 patients with preneoplastic hepatitis B virus-associated hepatocellular carcinoma by compound *Phyllanthus urinaria* L. *Chinese Journal of Integrative Medicine*, *20*(4), 263–271. <https://doi.org/10.1007/s11655-013-1320-7>
23. Xu, F., Zhang, H., Chen, J., Zhan, J., Liu, P., Liu, W., et al. (2024). Recent progress on the application of compound formulas of traditional Chinese medicine in clinical trials and basic research in vivo for chronic liver disease. *Journal of Ethnopharmacology*, *321*, 117514. <https://doi.org/10.1016/j.jep.2024.117514>
24. Xu, W., Wang, L., Niu, Y., Mao, L., Du, X., Zhang, P., et al. (2023). A review of edible plant-derived natural compounds for the therapy of liver fibrosis. *European Journal of Gastroenterology & Hepatology*, *35*(2), 133–152. <https://doi.org/10.1097/meg.0000000000002483>
25. Yang, C. M., Cheng, H. Y., Lin, T. C., Chiang, L. C., & Lin, C. C. (2007b). The in vitro activity of geraniin and 1,3,4,6-tetra-O-galloyl-beta-D-glucose isolated from *Phyllanthus urinaria* against herpes simplex virus type 1 and type 2 infection. *Journal of Ethnopharmacology*, *110*(3), 555–558. <https://doi.org/10.1016/j.jep.2006.09.039>
26. You, Y., Zhu, F., Li, Z., Zhang, L., Xie, Y., Chinnathambi, A., et al. (2021). Phyllanthin prevents diethylnitrosamine (DEN)-induced liver carcinogenesis in rats and induces apoptotic cell death in HepG2 cells. *Biomedicine & Pharmacotherapy*, *137*, 111335. <https://doi.org/10.1016/j.biopha.2021.111335>
27. Yue, W., Xiaoshen, Y., Zhengquan, L., Wei, Z., Lirong, C., & Xiaojie, X. (2005). Searching for more effective HCV NS3 protease inhibitors via modification of corilagin. *Progress in Natural Science*, *15*(10), 896–901. <https://doi.org/10.1080/10020070512331343080>
28. Zeng, D. Y., Li, J. M., Lin, S., Dong, X., You, J., Xing, Q. Q., et al. (2021). Global burden of acute viral hepatitis and its association with socioeconomic development status, 1990-2019. *Journal of Hepatology*, *75*(3), 547–556. <https://doi.org/10.1016/j.jhep.2021.04.035>
29. Zeng, H., Cao, M., Xia, C., Wang, D., Chen, K., Zhu, Z., et al. (2023). Performance and effectiveness of hepatocellular carcinoma screening in individuals with HBsAg seropositivity in China: A multicenter prospective study. *Nature Cancer*, *4*(9), 1382–1394. <https://doi.org/10.1038/s43018-023-00618-8>
30. Zhan, J., Huang, S., Guo, Y., Chen, C., Yao, C., Liu, J., et al. (2023). Antiviral and hepatoprotective effects of *Phyllanthus urinaria*. *Journal of Integrative Medicine*, *15*(8), 654–662.