AI and Herbal Therapeutics in Hepatitis B

Dr. Sneha Agrawal[1], Shravani D. Deolikar[1]

[1]Bharati Vidyapeeth's College of Pharmacy, Sector-8, C.B.D. Belapur, Navi Mumbai - 400 614, India.

Corresponding author: sdd9337@gmail.com
Doi: **https://doi.org/10.5281/zenodo.22302926**
Received: 01st July 2026
Accepted: 10th July 2026

Abstract

Chronic hepatitis B virus infection is still a major global health problem, with an estimated 240 million people living with the disease in 2024. Yet less than 5% are currently receiving treatment. Persistent gaps in early diagnosis and long-term treatment access, especially in the WHO African and Western Pacific regions, hinder progress towards the WHO 2030 elimination target. This review comprises two distinct but emerging intersecting approaches to addressing these gaps: artificial intelligence and herbal medicine. AI models, which include imaging-based fibrosis staging and laboratory-based machine learning tools, enable earlier non-invasive diagnosis of liver fibrosis in HBV patients. Though most models to date have been geographically concentrated predominantly in China, herbal therapeutics, most notably genus *Phyllanthus*, have acquired over two decades of randomized clinical trial evidence, which demonstrate antiviral activity and improved viral marker clearance. In retrospect, long-term clinical outcome data is absent. Furthermore, it explores the emerging convergence between the fields in which network pharmacology and computational target prediction methods are applied to hepatitis-related herbal formula to identify specific bioactive compounds and mechanisms with precision that traditional whole extract trials cannot achieve. While this integration holds genuine translational promise, major gaps remain, which include limited clinical validation of AI-predicted herbal mechanisms, inconsistent standardization practices, and less geographic diversity in existing research. Narrowing these gaps through long-term planning of clinical trials, collaboration, and clearer regulatory pathways is essential to realizing the full potential of this convergence in supporting global hepatitis B elimination efforts.

Keywords- Hepatitis B; Artificial Intelligence; Phyllanthus; Hepatoprotective Herbs; Network Pharmacology; Machine Learning

Introduction

One of the leading causes of cirrhosis and hepatocellular carcinoma is chronic hepatitis B virus (HBV)[1][2]. It progresses silently from chronic infection to advanced liver disease, which later becomes clinically apparent. The WHO goal to eliminate hepatitis by 2030 can only be achieved if there is proper early diagnosis, long-term monitoring, and accessible treatment in low- and middle-income regions where HBV is prevalent.

Following distinct approaches for diagnosis and treatment could be a step towards achieving the WHO goal. Artificial Intelligence (AI), which includes medical imaging, viral load trends, electronic health records, etc., for

the detection of liver fibrosis, accurate progression prediction of disease, and improved risk stratification for patients. Whereas herbal medicine, especially the genus *Phyllanthus*, has been emerging, with validated clinical trial evidence available for its antiviral and hepatoprotective effectiveness in hepatitis B virus [3][4]. These two are separate frameworks: one is computational precision and long-term data analysis, and the other is centuries of plant-based practice. Emerging research shows that these two have started to intersect; network pharmacology and AI-driven methods are being highly researched to map the molecular targets of the HBV active phytochemicals to attain more precision in the therapeutic traditions, which was initially done by clinical trials of variable methodological quality.

This chapter includes research documents reporting this intersection and is classified into three parts. First, it outlines current applications of AI in hepatitis B diagnosis and prognosis. Then it reviews the clinical evidence base for herbal approaches to disease management; finally, it discusses the emerging intersection of the two fields, which is used to validate the mechanism of HBV activity. This conclusion highlights both the genuine promise and the evidence gaps in this research direction, informing future efforts toward global HBV elimination.

1. Global Burden of Chronic Hepatitis B and the Diagnostic-Treatment Gap

In the WHO 2026 global hepatitis report, approximately 240 million people were living with HBV infection in 2024, i.e around 2.9 % of the world population. The Western Pacific and African regions of the WHO account for most of these infections, with 102 million and 64 million people affected respectively [1][2]. Whereas in Southeast Asia, Eastern Mediterranean, Europe, and America, fewer patients were reported. There were approximately 1.34 million deaths in 2024 from HBV and hepatitis C together [1][2]. Other related complications, such as cirrhosis and hepatocellular carcinoma, are also leading factors that cause liver-related mortality. A major source of new chronic infection is transmission from the HBsAg- or HBeAg-positive mother to child. 90% of the infants born to such mothers develop chronic disease if untreated, thus underscoring the importance of timely birth dose vaccination [5]. Here is when the diagnostic treatment gap becomes the most relevant or apparent. The WHO reports that less than 5% of the 240 million with chronic HBV were receiving treatment even after the availability of effective antiviral therapy [1]. The birth dose vaccination rates reported in the WHO African Region are just 17% in 2024, whereas by 2025, 20 out of 47 countries of the region still had not introduced the vaccination at all [6][7]. Thus, the global target toward 2030 elimination is off track despite the decline in new infections since 2015[6][8]. Such gaps in diagnosis and treatment access need to be addressed. Advances in both technology and therapeutic approaches can contribute and are discussed in the following section, also positioned as stones for closing this gap rather than differentiating solutions.

2. Artificial Intelligence in Hepatitis B Diagnosis and Prognosis

AI is now applied to nearly every stage of HBV care, from non-invasive fibrosis assessment to long-term risk reduction [9][10]. A recent review of the AI models found 21 eligible studies. Approximately 81% of the research in this aspect originates from China, wherein focus specifically on hepatitis B-related liver disease, thus becoming a testing ground for this technology [11].

Imaging-based AI for fibrosis staging- This has reduced the reliance on liver biopsy and is a major focus area. One of the multidisciplinary teams developed fully automated AI models using non-contrast MRI to stage liver fibrosis.It has been trained on 1208 patients and validated across both internal and external datasets, it was found

that the resulting model outperformed radiologists and traditional non-invasive scoring methods [12]. For more widely accessible and low-cost imaging than MRIs, deep learning approaches have been applied to ultrasound imaging to automate liver fibrosis classification [13][14].

Laboratory-based machine learning models- Several studies have built machine learning models using routine blood-based biomarkers to predict fibrosis stage without imaging or biopsy at all. A study analysed 618 chronic HBV patients, identified serum markers, and constructed a machine learning model to predict the fibrosis stage [15]. At the same time, a separate diagnostic framework was built from routine laboratory tests in 268 biopsy-confirmed CHB patient tested eight different ML algorithms to identify significant fibrosis [16]. In resource-limited settings where imaging equipment or biopsy capacity is scarce, these lab-based models become particularly valuable.

Models for comorbid and complex presentations. In more complex clinical scenarios, wherein hepatitis B coexists with other liver conditions, AI is used. One 2025-26 study has developed an interpretable machine learning model which predicts significant liver fibrosis in patients with both chronic HBV and non-alcoholic fatty liver disease [17][18]. This reflects a broader trend which has been tailored to overlapping disease scenarios rather than single condition assessment alone.

A broader review of AI's status and future directions across liver disease shows that detection, accurate diagnosis, and effective treatment remain substantial for improving patient survival [19]. Thus, AI tools are a direct response to diagnostic gaps outlined previously. Together, this suggests that AI's role in Habitus B care is shifting from experimental proof toward models that are validated on real multicenter clinical cohorts. Furthermore, the geographic concentration of this review suggests that broader international validation is still an open need [11][20].

3. Herbal and Phytochemical Approaches to Hepatitis B Management

Herbal medicine has a significantly longer research history in chronic hepatitis B disease as compared to AI. This includes several plant-derived compounds accumulating decades of clinical trial evidence. The evidence is more extensive in this regard than the other liver conditions, but also of mixed quality compared to the newer AI literature as reviewed in section 2.

Phyllanthus is the most extensively studied herbal candidate for hepatitis B. The plants of this genus are found throughout the tropical and subtropical regions and contain major bioactive constituents, phyllanthins, hypophyllanthins, and several polyphenols, which have been experimentally shown to interfere with HBV polymerase activity and viral mRNA transcription and replication, which offers a plausible antiviral mechanism [3][21]. A review of 22 randomized controlled trials involving 1947 patients found that this species produced significantly better clearance of the serum HBsAg when compared with placebo [3]. They found no significant difference from interferon therapy on HBsAg, HBeAg, or HBV DNA clearance. Noting that combining *Phyllanthus* with interferon produced better clearance than only interferon alone. This suggests a possible adjunct role rather than just substitution. A 2013 review extended this comparison against the model antiviral drug such as lamivudine, interferon-alpha, thymosin, not just the placebo, which reflects the field's shift towards more clinically relevant comparisons over the period of time [4]. No serious adverse events were reported.

Glycyrrhizin (liquorice root extract) - Glycyrrhizin has been used to treat chronic viral hepatitis broadly. The earlier reviews from 2002-2007 concluded that the evidence did not support a strong clinical recommendation because of availability and bioavailability limitations in older formulations. Orally bioavailable Glycyrrhizin preparation development was identified as a step that could enable better controlled, feasible long-term studies in the future. Indicating that this compound has both formulation science and biological activity as a limiting factor [22].

Silymarin and polyherbal formulations- Silymarin is derived from milk thistle and is primarily valued for its antifibrotic property, rather than direct HBV antiviral activity [23]. Therefore, it is more of a complementary hepatoprotective agent than a specific therapy. Polyherbal formulation such as Liv.52 is a multi-herb combination product, which in published review reports among is the most used herbal preparations for liver disease [23][24]. Hence, stating that herbal therapeutics in practice often combine several agents rather than just relying on a single compound.

Beyond *Phyllanthus*, glycyrrhizin, and Liv.52, there have been other traditional formulas used in the HBV-related liver disease management. But with less mechanistic clarity until recently. Yinzhihuang granules is a four-herb formula used for jaundice and hepatic inflammation, clinically applied for its anti-inflammatory and bilirubin-lowering effects [25]. Forsythiae *Fructus*, a herb earlier used in heat-clearing formulas, has emerged as a research interest in its relevance to HPV-related hepatocellular carcinoma [26]. At the same time, one of the most classic combinations in traditional Chinese medicines used for hepatitis is herb pair, *Radix Bupleuri* and *Radix Paeoniae Alba* as they show combined anti-inflammatory and hepatoprotective effects [27]. In contrast to *Phyllanthus*, the precise molecular mechanism behind these formulas' clinical effects is unclear. A gap which is recently addressed, as discussed in the next section.

A lot of evidence gaps in herbal therapeutics is observed despite the substantial trial volume. The critical limitation is that no randomized controlled trial data exists on definitive long-term clinical outcomes, even for *Phyllanthus*, which is the best-studied compound [3]. For the progression of cirrhosis or hepatocellular carcinoma or the overall survival. The existing trials have focused on short-to-medium-term viral marker clearance and liver enzyme normalization instead of the hard clinical endpoint, which matters most for elimination. In addition, the 2001 original systematic review noted that the trial methodological quality was high in only five of the 22 included double-blind trials, the rest being rated lower quality [3]. And the variation between *Phyllanthus* species and preparation further complicates concluding. Reviews of herbal hepatoprotectants have documented cases of liver injuries following ingestion of certain other herbal products marketed for liver health [28][29]. Thus, showing that herbal does not inherently mean risk-free. The standardization and quality control remain unresolved issue across the field. It is limited due to variable methodological quality, absence of long-term outcome data, and inconsistent product standardization [23]. Thus, these limitations set up a role for computational approaches.

4. The Convergence: AI-Assisted Validation and Discovery in Hepatitis B Herbal Therapeutics

The limitations such as variable trial quality, unclear mechanistic specificity, and inconsistent product standardization identified previously are the problems that network pharmacology and AI-driven methods were developed to address. Instead of testing a whole herbal extract empirically and hoping for a clinical signal, these

methods work backward. It identifies the bioactive compound within a plant, which binds to which biological target, and map how those targets relate to the known disease pathway.[30][31][32]

How does this method work in practice? An example comes from the study of Yinzhihuang granules, a traditional Chinese herbal formulation used for hepatitis. The researchers used computational target prediction databases to identify the formula's chemical compounds and their likely protein targets and then cross-referenced these against known hepatitis B-related targets from the databases and built a target interaction network. This analysis identified 13 potential targets linked to hepatitis B treatment. Molecular docking, a computational technique, shows how strongly a compound binds to a target protein and confirms the strong interactions between them, such as CDK6, CDK2, TP53, and BRCA1. Furthermore, pathway analysis links the formula's activity to the hepatitis and viral carcinogenesis pathway. Most importantly, this analyses which individual compounds within the mixture were driving the most network activity. In this case, luteolin, baicalein, and caffeic acid show the most highly connected compounds, thus showing a compound-level specificity that traditional whole-extract clinical trials cannot provide on their own [25].

Extension to HBV-related liver cancer. This approach has also been applied further in the release process. One study used network pharmacology combined with molecular docking and lab validation to investigate *Forsythiae Fructus* extract against hepatitis B virus-related hepatocellular carcinoma. The analysis identified three target proteins- C-jun, ESR1, and MMP9. These interactions were confirmed through both computational modeling and follow-up in vitro and in vivo experiments [26]. This combined study of computational prediction and wet lab confirmation shows the more rigorous end of current practice in the AI herbal convergence research, which addresses a common criticism that purely computational studies can overstate certainty without experimental follow-up.

Herb-pair and formula-level analysis

Network pharmacology is well suited for formula-level analysis, as traditional herbal medicine frequently uses a combination of herbs rather than a single compound. To illustrate, a study of the herb pair *Radix bupleuri* and *Radix paeoniae* Alba, a combination which was used traditionally against hepatitis, used the same target prediction and docking pipeline to identify 14 core targets and 10 associated biological pathways, illustrating how this methodology can explain the mechanism behind multi-herb formulas rather than only a single compound like *Phyllanthus*[27]

As these above examples focus on a traditional hepatitis B formula, the same methodology is directly applicable and has already been applied to *Phyllanthus*, as it has well-characterized bioactive compounds[3][25]. Applying both compound target network analysis and molecular docking to these specific constituents can help resolve one of the central limitations identified previously. It distinguishes which of Phyllanthus's many chemical constituents are responsible for the antiviral and hepatoprotective effects, which were observed across the clinical trials, instead of just treating the whole plant as a single extract. This represents a concrete near-term opportunity where AI methods and herbal evidence reviewed previously could genuinely intersect.

Most published network pharmacology studies on hepatitis-related herbs to date focus on formulas other than *Phyllanthus*. Much of this research is at the computational prediction and preclinical validation stage [25][32][33]. Instead of being tested in a randomized trial, the clinical trial population is discussed in section 3. This gap, which

is found between methodically well-characterized empirical prediction and generalized validated outcome, is one of the most important open opportunities in the field, which forms a natural bridge into the challenges and future directions.

5. Challenges and Limitations

Several substantial challenges currently limit the clinical and translational impact of AI-integrated organ health tracking research. Despite the genuine progress documented across the previous sections, they fall mainly into four broad categories as follows.

Limitations in AI-based diagnostic models.

Many of the AI fibrosis staging and prediction models reviewed previously, both imaging-based and laboratory-based, are developed and validated on single-country or even single-hospital cohorts. Nonetheless external validation across diverse populations is rare. This raises a question about generalizability [11][20][34]. If a model is trained commonly on one population, genetic, dietary, and disease progression patterns may not perform as well elsewhere. The data quality and consistency also remain issues since the ML models are only reliable as the labelled training data they are built on. The biopsy, the ground standard truth these models are often trained against, carry their own sampling variability, interpretation, and subjectivity.

Limitations on herbal evidence base.

The best studied herbal candidate, *Phyllanthus*, also suffers from methodological weakness as only 5 out of 22 trials in a foundational systematic review met high-quality double-blind standards [3]. And no trial has measured long-term clinical endpoints, which include cirrhosis, hepatocellular carcinoma, or survival. Various factors further complicate drawing firm conclusions, such as variation in plant species, preparation methods, and dosing between studies. The lack of standardization is not only in *Phyllanthus*, but it also affects herbal medicine research broadly. Safety monitoring also remains underdeveloped when compared with conventional pharmaceuticals. Additionally, previous documented cases of liver injury linked to other herbal product ingestion marketed for liver health suggest that the hepatoprotective claim requires the same rigorous safety evaluation as any other therapeutic intervention [28][29].

Geographic and institutional concentration.

Both the AI and network pharmacological literatures that have been reviewed are heavily concentrated in China [25][35]. This reflects both the country's large hepatitis B patient population and the national investment in computational medicine and traditional medicine modernization. This has led to rapid methodological progress, but at the same time, independent replication in other populations and healthcare systems is limited. To illustrate, the African and Western Pacific region, which carries the highest HBV burden, remains largely untested[6][7].

Challenges specific to AI and human convergence

The network pharmacology studies reviewed in Section 4 are almost entirely computational or preclinical; very few have progressed to testing AI-identified compounds or mechanisms in the same randomized clinical trial populations used for whole-extract herbal research [25][26][27]. This creates a translational gap: computational methods can generate plausible, mechanistically grounded hypotheses about which compounds and targets matter

most, but these hypotheses largely remain clinically unverified for Hepatitis B specifically. There is also a methodological standardization issue within network pharmacology itself; different studies use different target-prediction databases and thresholds for what counts as a "significant" target, which can affect reproducibility across research groups [30][31][36].

Regulatory and integration gaps

Diagnostic tools face inconsistent approval for clinical deployment, whereas herbal products, despite their widespread use, remain outside formal pharmaceutical regulation in most of the jurisdictions. This means that product quality and standardization are often left to the manufacturers rather than being enforced by the regulatory bodies. Until these regulatory and evidentiary gaps can be addressed, the promising computational and clinical findings are likely to remain confined to research settings rather than translating into routine hepatitis B care.

6. Future Directions

Addressing the challenges identified in Section 5 will require deliberate, coordinated effort across several fronts rather than incremental progress on any single front alone.

Higher quality long-term clinical trials

Designing a randomized controlled trial that tracks the long-term clinical endpoints, progression to cirrhosis, hepatocellular carcinoma incidence, and survival, instead of just relying on short-term viral marker clearance, is the most valuable next step for herbal hepatitis B research. Given that *Phyllanthus* alone has already had over 1900 trial participants across existing studies, a coordinated long-term follow-up cohort building on this existing patient base could be more feasible than just starting from scratch [3].

Bridging computational predictions with clinical validation.

The network pharmacology studies reviewed previously have generated numerous plausible compound-target hypotheses for HBV-related formulas, but very few have been tested prospectively in patients [25][26][27]. The next step is designing clinical trials that are specifically structured to validate AI-predicted metabolism. For example, testing patients whose HBV genotype profile aligns with computationally projected target pathways responds better to a specific herbal compound than those who do not. Thus, this will move the field from AI explains why an herb might work towards AI predicts who and what will work for whom. This becomes a more meaningful standard.

Broader international cross-institutional collaboration.

As stated earlier, due to the geographic concentration in both AI and network pharmacology research in China, expanding these studies to the WHO American and Western Pacific region, which together carry the largest share of global HBV burden, can be a priority [6][7][37]. This would ensure whether the existing AI diagnostic and herbal findings can be generalized across genetically and epidemiologically diverse populations. This helps ensure that any resulting innovation reaches the regions that need them the most, instead of just being confined to the place where they were developed.

Standardization efforts.

A stronger methodological standardization affects both fields. The AI models would benefit from common reporting standards and external validation requirements before clinical deployment. In the case of herbal medicine research, it would benefit from the standardization of extraction methods, dosing, and quality control across studies [24][28]. This helps so that the different trials of the same drugs become more directly comparable.

Regulatory modernization.

For both AI-based diagnostic tools and evidence-based herbal therapeutics, regulatory bodies should be encouraged to develop clear approval pathways. This can potentially include intermediate regulatory categories that acknowledge promising but not definitively proven interventions, thus allowing continued research under appropriate safety monitoring. Does it avoid leaving these approaches entirely outside the formal healthcare system? In retrospect, these steps would help transform the current state of the AI urban hepatitis B research, which is now promising but fragmented, into a more coherent and clinically actionable body of evidence, which directly supports the WHO's goal of elimination of hepatitis by 2030[6][8][38].

7.Conclusion

An estimated 240 million people live with the infection in 2024, and less than 5% receive treatment; this gap stands in the way of the WHO's 2030 hepatitis elimination targets, which conclude that chronic hepatitis B is a substantial global health burden [1]. This review has examined two distinct approaches to narrow down this gap. Artificial intelligence, which helps enable earlier and more accurate diagnosis through imaging and laboratory-based predictive models, and herbal medicine, which has accumulated a decade of clinical trial evidence for antiviral and hepatoprotective activity [3][4][39]. Building on this, this review proposes that their genuine value lies in convergence instead of just treating them as competitive paradigms, one computational and modern, the other empirical and traditional. These methods are already applied to hepatitis-focused herbal formulation, which identify specific bioactive compounds and molecular targets with a mechanistic precision that whole extract clinical trials cannot provide. Beyond this, applying these methods to *Phyllanthus* bio constituents shows a concrete and achievable next step, capable of addressing the most persistent limitation [25][26]. That is to distinguish which specific compound within a traditionally used plant is responsible for its clinical effects. At the same time, this review has been deliberate in identifying where the evidence remains thin. Neither AI diagnostic models nor herbal-AI convergence studies have yet been validated at scale in the WHO regions carrying the highest Hepatitis B burden, and no trial of any hepatoprotective herb has yet demonstrated impact on the long-term outcomes, cirrhosis, liver cancer, and survival, that ultimately matter most [3]. Bridging these gaps will require sustained investment in longer-term clinical trials, broader international research collaboration, and regulatory frameworks capable of supporting both technologies as they mature. Achieved together, technology and tradition offer a genuinely complementary path toward global Hepatitis B elimination.

REFERENCES

1. World Health Organization. *Global hepatitis report 2026* [Internet]. Geneva: World Health Organization; 2026 [cited 2026 Jul 25]. Available from: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hepatitis/reports/global-hepatitis-report-2026

2. World Hepatitis Alliance. WHO Global Hepatitis Report 2024: summary [Internet]. London: World Hepatitis Alliance; 2024 [cited 2026 Jul 25]. Available from: https://www.worldhepatitisalliance.org/wp-content/uploads/2024/07/WHA-Global-Hepatitis-Report_FINAL.pdf
3. Liu J, Lin H, McIntosh H. Genus Phyllanthus for chronic hepatitis B virus infection: a systematic review. J Viral Hepat. 2001 Sep;8(5):358-66. doi: 10.1046/j.1365-2893.2001.00307.x. PMID: 11555193.
4. Xia Y, Luo H, Liu JP, Gluud C. Phyllanthus species versus antiviral drugs for chronic hepatitis B virus infection. Cochrane Database Syst Rev. 2013 Apr 30;2013(4):CD009004. doi: 10.1002/14651858.CD009004.pub2. PMID: 23633363; PMCID: PMC11930397.
5. World Health Organization. *Hepatitis B* [Internet]. Geneva: World Health Organization; [cited 2026 Jul 25]. Available from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b
6. World Health Organization. Efforts to eliminate hepatitis delivers gains but more action needed to meet 2030 targets [Internet]. Geneva: World Health Organization; 2026 Apr 28 [cited 2026 Jul 25]. Available from: https://www.who.int/news/item/28-04-2026-efforts-to-eliminate-hepatitis-delivers-gains-but-more-action-needed-to-meet-2030-targets
7. Al-Busafi SA, Alwassief A. Global Perspectives on the Hepatitis B Vaccination: Challenges, Achievements, and the Road to Elimination by 2030. Vaccines (Basel). 2024 Mar 9;12(3):288. doi: 10.3390/vaccines12030288. PMID: 38543922; PMCID: PMC10975970.
8. Cao G, Jing W, Liu J, Liu M. Countdown on hepatitis B elimination by 2030: the global burden of liver disease related to hepatitis B and association with socioeconomic status. Hepatol Int. 2022 Dec;16(6):1282-1296. doi: 10.1007/s12072-022-10410-y. PMID: 36048317.
9. Abd El-Latif AA, et al. Explainable machine learning for hepatitis prediction. PLoS One. 2025;20:e0319078. doi:10.1371/journal.pone.0319078.
10. Malik S, Das R, Thongtan T, Thompson K, Dbouk N. AI in Hepatology: Revolutionizing the Diagnosis and Management of Liver Disease. J Clin Med. 2024 Dec 22;13(24):7833. doi: 10.3390/jcm13247833. PMID: 39768756; PMCID: PMC11678868.
11. Yoshida T, Asahi Y, Ganchiku Y, Kakisaka T, Hirata K, Kudo K, Taketomi A. Multimodal artificial intelligence models for liver fibrosis staging: a scoping review. Abdom Radiol (NY). 2026 Jul 1. doi: 10.1007/s00261-026-05667-y. PMID: 42380350.
12. Li C, Wang Y, Bai R, et al. Development of fully automated models for staging liver fibrosis using non-contrast MRI and artificial intelligence: a retrospective multicenter study. EClinicalMedicine. 2024 Oct 17;77:102881. doi: 10.1016/j.eclinm.2024.102881. PMID: 39498462; PMCID: PMC11532432.
13. Nduma BN, Al-Ajlouni YA, Njei B. The Application of Artificial Intelligence (AI)-Based Ultrasound for the Diagnosis of Fatty Liver Disease: A Systematic Review. Cureus. 2023 Dec 15;15(12):e50601. doi: 10.7759/cureus.50601. PMID: 38222117; PMCID: PMC10788148.
14. Yin C, Zhang H, Du J, Zhu Y, Zhu H, Yue H. Artificial intelligence in imaging for liver disease diagnosis. Front Med. 2025;12:1591523. doi: 10.3389/fmed.2025.1591523.
15. Zhang C, Shu Z, Chen S, et al. A machine learning-based model analysis for serum markers of liver fibrosis in chronic hepatitis B patients. Sci Rep. 2024 May 27;14(1):12081. doi: 10.1038/s41598-024-63095-8. PMID: 38802526; PMCID: PMC11130122.

16. Hou L, Tang J, He W, Qin W. Machine learning diagnostic framework for liver fibrosis in chronic hepatitis B based on routine laboratory tests. Medicine (Baltimore). 2026 Mar 13;105(11):e47412. doi: 10.1097/MD.0000000000047412. PMID: 41824881; PMCID: PMC12991754.
17. Rui F, Yeo YH, Xu L, et al. Development of a machine learning-based model to predict hepatic inflammation in chronic hepatitis B patients with concurrent hepatic steatosis: a cohort study. EClinicalMedicine. 2024 Jan 16;68:102419. doi: 10.1016/j.eclinm.2023.102419. PMID: 38292041; PMCID: PMC10827491.
18. Gu J, Chai J. An interpretable machine learning model for prediction of significant liver fibrosis in comorbid chronic hepatitis B and nonalcoholic fatty liver disease: a retrospective development and validation study. BMC Gastroenterol. 2026 Jan 16;26(1):116. doi: 10.1186/s12876-025-04594-4. PMID: 41545932; PMCID: PMC12896100.
19. Gao B, Duan W. The current status and future directions of artificial intelligence in the prediction, diagnosis, and treatment of liver diseases. Digit Health. 2025 Apr 13;11:20552076251325418. doi: 10.1177/20552076251325418. PMID: 40290269; PMCID: PMC12033675.
20. Žigutytė L, Sorz-Nechay T, Clusmann J, Kather JN. Use of artificial intelligence for liver diseases: A survey from the EASL congress 2024. JHEP Rep. 2024 Sep 6;6(12):101209. doi: 10.1016/j.jhepr.2024.101209. PMID: 39583096; PMCID: PMC11585758.
21. Martin KW, Ernst E. Antiviral agents from plants and herbs: a systematic review. Antivir Ther. 2003 Apr;8(2):77-90. PMID: 12741619.
22. Stickel F, Schuppan D. Herbal medicine in the treatment of liver diseases. Dig Liver Dis. 2007 Apr;39(4):293-304. doi: 10.1016/j.dld.2006.11.004. PMID: 17331820.
23. Dhiman RK, Chawla YK. Herbal medicines for liver diseases. Dig Dis Sci. 2005 Oct;50(10):1807-12. doi: 10.1007/s10620-005-2942-9. PMID: 16187178.
24. Służały P, Paśko P, Galanty A. Natural Products as Hepatoprotective Agents-A Comprehensive Review of Clinical Trials. Plants (Basel). 2024 Jul 20;13(14):1985. doi: 10.3390/plants13141985. PMID: 39065511; PMCID: PMC11280762.
25. Zhang J, Liu X, Zhou W, et al. A bioinformatics investigation into molecular mechanism of Yinzhihuang granules for treating hepatitis B by network pharmacology and molecular docking verification. Sci Rep. 2020 Jul 10;10(1):11448. doi: 10.1038/s41598-020-68224-7. PMID: 32651427; PMCID: PMC7351787.
26. Chen F, Cai Y, Chen C, Zhou J. Network pharmacology integrated with molecular docking and experimental validation elucidates the therapeutic potential of Forsythiae Fructus extract against hepatitis B virus-related hepatocellular carcinoma. Front Oncol. 2025;15:1571537. doi: 10.3389/fonc.2025.1571537.
27. Huang L, Yu Q, Peng H, Zhen Z. Network pharmacology and molecular docking technology for exploring the effect and mechanism of Radix Bupleuri and Radix Paeoniae Alba herb-pair on anti-hepatitis: A review. Medicine (Baltimore). 2023 Dec 1;102(48):e35443. doi: 10.1097/MD.0000000000035443. PMID: 38050220; PMCID: PMC10695497.
28. Saraswat I, Goel A, Gupta J. Herbal remedies for hepatic diseases: A review of medicinal herbs in the treatment of liver disorders. Chin Herb Med. 2026 Feb 14;18(2):329-342. doi: 10.1016/j.chmed.2026.02.015. PMID: 41971583; PMCID: PMC13069626.

29. Islam Shawon S, Nargis Reyda R, Qais N. Medicinal herbs and their metabolites with biological potential to protect and combat liver toxicity and its disorders: A review. Heliyon. 2024 Feb 1;10(3):e25340. doi: 10.1016/j.heliyon.2024.e25340. PMID: 38356556; PMCID: PMC10864916.
30. Wang X, Hu Y, Zhou X, Li S. Editorial: Network pharmacology and traditional medicine: Setting the new standards by combining *In silico* and experimental work. Front Pharmacol. 2022 Oct 21;13:1002537. doi: 10.3389/fphar.2022.1002537. PMID: 36339546; PMCID: PMC9634580.
31. Zhang P, Zhang D, Zhou W, et al. Network pharmacology: towards the artificial intelligence-based precision traditional Chinese medicine. Brief Bioinform. 2024 Jan;25(1):bbad518. doi: 10.1093/bib/bbad518.
32. Zhao W, Wang B, Li S. Network pharmacology for traditional Chinese medicine in era of artificial intelligence. Chin Herb Med. 2024 Sep 3;16(4):558-560. doi: 10.1016/j.chmed.2024.08.004. PMID: 39606265; PMCID: PMC11589279.
33. Cui G, Li M, Guo W, Gao M, Zhu Q, Liao J. AI driven network pharmacology: Multi-scale mechanisms of traditional Chinese medicine from molecular to patient analysis. Comput Struct Biotechnol J. 2025;27:5087-5104. doi: 10.1016/j.csbj.2025.11.016.
34. Morel SMG, Wu S, Kendall TJ, et al. Opportunities and challenges of artificial intelligence in hepatology. npj Gut Liver. 2026;3:3. https://doi.org/10.1038/s44355-025-00052-w
35. Liu Z, Lin C, Mao X, et al. Changing prevalence of chronic hepatitis B virus infection in China between 1973 and 2021: a systematic literature review and meta-analysis of 3740 studies and 231 million people. Gut. 2023 Nov 24;72(12):2354-2363. doi: 10.1136/gutjnl-2023-330691. PMID: 37798085; PMCID: PMC10715530.
36. Zhao W, Liu Q, Zhang T, Sutcharitchan C, Wang B, Zhang D, Li S. Network pharmacology: Advancing the application of large language models in traditional Chinese medicine research. Science of Traditional Chinese Medicine. 2025;3(2):113-123. https://doi.org/10.1097/st9.0000000000000073
37. Hiebert-Suwondo L, Manning J, Tohme RA, et al. A 2024 global report on national policy, programmes, and progress towards hepatitis B elimination: findings from 33 hepatitis elimination profiles. Lancet Gastroenterol Hepatol. 2025 Jul;10(7):671-684. doi: 10.1016/S2468-1253(25)00069-X. PMID: 40409324; PMCID: PMC12308976.
38. eClinicalMedicine. Global hepatitis elimination 2030: immediate action is the need of the hour. EClinicalMedicine. 2024 Jul 23;73:102763. doi: 10.1016/j.eclinm.2024.102763. PMID: 39429810; PMCID: PMC11490652.
39. Thyagarajan S, Thirunalasundari T, Subramanian S, et al. Effect of Phyllanthus amarus on chronic carriers of hepatitis B virus. Lancet. 1988;332:764-766.