

# FORMULATION STRATEGIES AND THERAPEUTIC EVALUATION OF A POLYHERBAL HEPATOPROTECTIVE DOSAGE FORM

Shilpa, Deepak Saini\*, Sunita Rani

Smt. Tarawati Institute of Biomedical & Allied Sciences, Roorkee, Uttarakhand-247667.

Article Received: 15 April 2026 | Article Revised: 05 May 2026 | Article Accepted: 26 May 2026

\*Corresponding Author: Deepak Saini

Smt. Tarawati Institute of Biomedical & Allied Sciences, Roorkee, Uttarakhand-247667.

DOI: <https://doi.org/10.5281/zenodo.20446451>

**How to cite this Article:** Shilpa, Deepak Saini, Sunita Rani (2026) FORMULATION STRATEGIES AND THERAPEUTIC EVALUATION OF A POLYHERBAL HEPATOPROTECTIVE DOSAGE FORM. World Journal of Pharmaceutical Science and Research, 5(6), 682-689.



Copyright © 2026 Deepak Saini | World Journal of Pharmaceutical Science and Research.

This work is licensed under creative Commons Attribution-NonCommercial 4.0 International license (CC BY-NC 4.0).

## ABSTRACT

Liver diseases represent a significant global health burden, accounting for substantial morbidity and mortality due to their progressive and often irreversible nature. Despite advances in conventional pharmacotherapy, the management of liver disorders remains challenging due to drug-induced toxicity, limited efficacy in chronic conditions, and high treatment costs. In recent years, herbal medicines have emerged as a promising alternative owing to their natural origin, safety profile, and therapeutic versatility. Among these, polyherbal formulations have gained considerable attention as they combine multiple medicinal plants to achieve synergistic therapeutic effects, enhance efficacy, and minimize adverse reactions. This review provides a comprehensive and critical evaluation of formulation strategies and therapeutic assessment of polyherbal hepatoprotective dosage forms. It explores the pathophysiological mechanisms underlying liver disorders, highlights key hepatoprotective medicinal plants and their phytoconstituents, and discusses advanced formulation approaches including conventional and novel drug delivery systems. Furthermore, the review elaborates on standardization techniques, preclinical and clinical evaluation methods, toxicological considerations, and regulatory frameworks governing herbal medicines. The integration of modern pharmaceutical technologies with traditional knowledge is emphasized to improve the quality, safety, and global acceptance of polyherbal hepatoprotective therapies.

**KEYWORDS:** Hepatoprotective formulations, Polyherbal therapy, Liver diseases, Herbal medicine.

## 1. INTRODUCTION

The liver is a multifunctional organ responsible for vital physiological processes such as metabolism of carbohydrates, lipids, and proteins, detoxification of xenobiotics, synthesis of plasma proteins, and regulation of biochemical homeostasis. Due to its central metabolic role and continuous exposure to endogenous and exogenous toxins, the liver is highly vulnerable to injury. Liver diseases such as viral hepatitis, alcoholic liver disease, non-alcoholic fatty liver

disease (NAFLD), cirrhosis, and hepatocellular carcinoma are increasingly prevalent worldwide, posing a serious challenge to public health systems.<sup>[1-3]</sup>

Conventional therapeutic approaches for liver disorders are often limited by their inability to reverse liver damage completely, along with associated adverse effects and high economic burden. These limitations have led to increased interest in alternative and complementary medicine systems, particularly herbal medicine. Medicinal plants have been used for centuries in traditional systems such as Ayurveda, Unani, and Traditional Chinese Medicine for the treatment of liver disorders.<sup>[4-5]</sup>

Polyherbal formulations, which combine multiple plant extracts, are designed based on the principle of synergism, where different components act on multiple targets or pathways to produce enhanced therapeutic effects. This holistic approach not only improves efficacy but also reduces toxicity and enhances patient compliance. The present review aims to provide an in-depth and systematic analysis of formulation strategies and therapeutic evaluation of polyherbal hepatoprotective dosage forms, bridging traditional knowledge with modern scientific advancements.<sup>[6-7]</sup>

## 2. Pathophysiology of Liver Disorders

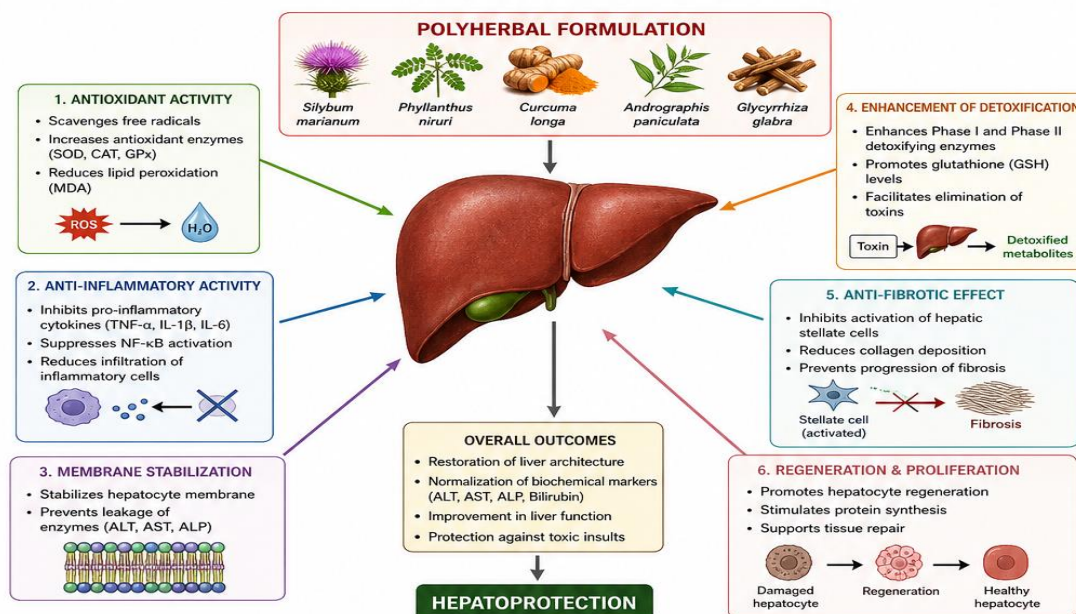
The pathogenesis of liver disorders involves complex and interrelated mechanisms, including oxidative stress, inflammation, apoptosis, necrosis, and fibrosis. One of the primary mechanisms of liver injury is oxidative stress, which results from an imbalance between the generation of reactive oxygen species (ROS) and the antioxidant defense system. Excess ROS leads to lipid peroxidation, protein oxidation, and DNA damage, ultimately causing hepatocellular injury.

Inflammation plays a critical role in the progression of liver diseases. Activation of Kupffer cells and other immune cells leads to the release of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-6, which exacerbate liver damage. Chronic inflammation can further lead to fibrosis, characterized by excessive deposition of extracellular matrix proteins mediated by hepatic stellate cells.<sup>[8-11]</sup>

Drug-induced liver injury (DILI) is another major cause of liver damage, often associated with commonly used drugs such as paracetamol. In overdose conditions, paracetamol is metabolized into a highly reactive intermediate, N-acetyl-p-benzoquinone imine (NAPQI), which depletes glutathione and causes oxidative damage to hepatocytes.

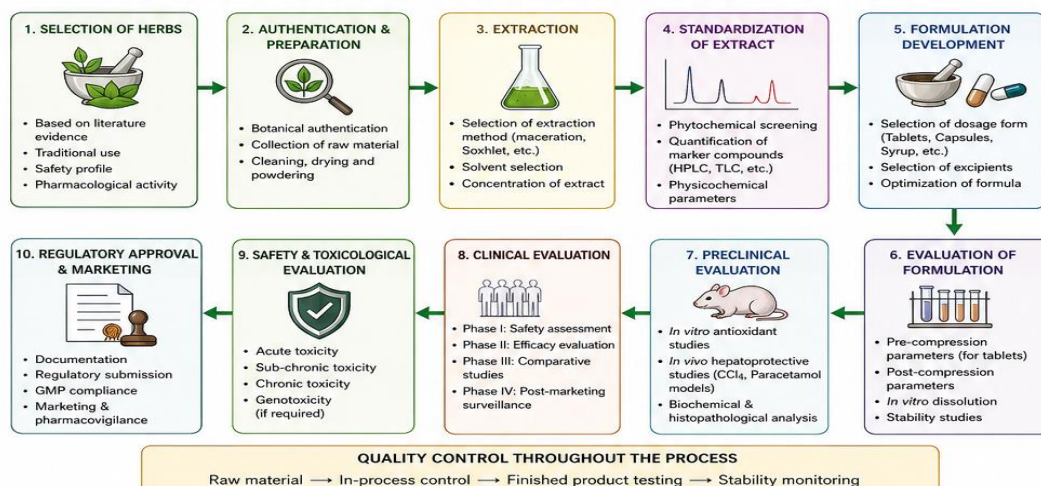
Biochemical markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin are widely used for assessing liver function. Histopathological examination of liver tissue provides further insights into the extent of cellular damage, inflammation, and fibrosis.<sup>[12-14]</sup>

Figure 1. Mechanism of Hepatoprotective Action of Polyherbal Formulations



Polyherbal formulations exert hepatoprotective effects through multiple mechanisms including antioxidant, anti-inflammatory, membrane stabilization, detoxification enhancement, anti-fibrotic and regenerative activities.

Figure 2. Formulation Development Flowchart of Polyherbal Hepatoprotective Dosage Form



GMP: Good Manufacturing Practices; HPLC: High Performance Liquid Chromatography; TLC: Thin Layer Chromatography.

### 3. Herbal Drugs with Hepatoprotective Activity

A wide variety of medicinal plants have been reported to possess hepatoprotective properties, primarily due to the presence of bioactive phytoconstituents such as flavonoids, alkaloids, terpenoids, glycosides, and phenolic compounds. These phytochemicals exert their effects through multiple mechanisms, including antioxidant activity, anti-inflammatory action, inhibition of lipid peroxidation, and enhancement of liver regeneration.<sup>[15]</sup>

*Silybum marianum* (milk thistle) is one of the most extensively studied hepatoprotective plants. Its active constituent, silymarin, is a flavonolignan complex known for its potent antioxidant and membrane-stabilizing properties. It protects hepatocytes by scavenging free radicals and enhancing protein synthesis.<sup>[16]</sup>

*Phyllanthus niruri* has demonstrated significant antiviral and hepatoprotective activity, particularly in the management of hepatitis B. It inhibits viral replication and promotes liver cell regeneration.<sup>[17]</sup>

*Andrographis paniculata* contains andrographolide, which exhibits anti-inflammatory, antioxidant, and hepatoprotective effects by modulating immune responses and reducing oxidative stress.<sup>[18]</sup>

*Curcuma longa* (turmeric) contains curcumin, a polyphenolic compound with strong antioxidant and anti-inflammatory properties. It inhibits lipid peroxidation and protects against liver injury.<sup>[19]</sup>

*Glycyrrhiza glabra* (licorice) contains glycyrrhizin, which has hepatoprotective, anti-inflammatory, and immunomodulatory effects. It stabilizes liver cell membranes and enhances detoxification processes.<sup>[20]</sup>

#### 4. Concept of Polyherbal Formulation

Polyherbal formulations are based on the concept of combining multiple medicinal plants to achieve enhanced therapeutic efficacy through synergistic interactions. This approach is deeply rooted in traditional medicine systems, where formulations are designed to target multiple aspects of disease pathology.<sup>[21]</sup>

The advantages of polyherbal formulations include improved efficacy due to synergistic action, reduced toxicity, and the ability to address multiple pathways involved in disease progression. However, the complexity of such formulations presents challenges in terms of standardization, quality control, and reproducibility.<sup>[22]</sup>

#### 5. Formulation Strategies for Polyherbal Dosage Forms

##### 5.1 Selection of Herbs

The selection of herbs is a critical step in the development of polyherbal formulations. It is based on pharmacological activity, safety profile, traditional usage, and compatibility with other herbs. Scientific validation through experimental studies is essential to ensure efficacy and safety.

##### 5.2 Extraction Methods

Extraction methods play a crucial role in isolating bioactive compounds from plant materials. Conventional methods such as maceration and Soxhlet extraction are widely used, while advanced techniques such as supercritical fluid extraction and microwave-assisted extraction offer improved efficiency and selectivity.

##### 5.3 Dosage Forms

Polyherbal formulations can be developed in various dosage forms, including tablets, capsules, syrups, and suspensions. Novel drug delivery systems such as phytosomes, liposomes, and nanoparticles have been developed to enhance bioavailability, stability, and targeted delivery of herbal drugs.

##### 5.4 Excipients and Compatibility

Excipients are essential components of pharmaceutical formulations that influence stability, bioavailability, and patient acceptability. Compatibility studies are conducted to evaluate interactions between herbal extracts and excipients.

##### 5.5 Standardization and Quality Control

Standardization is essential to ensure consistency and reproducibility of polyherbal formulations. It involves phytochemical screening, chromatographic analysis, and adherence to WHO guidelines for herbal medicines.<sup>[23-26]</sup>

## 6. Preformulation and Stability Studies

Preformulation studies involve the evaluation of physicochemical properties such as solubility, pH, particle size, and moisture content. These parameters influence formulation design and performance.

Stability studies are conducted under various environmental conditions to determine shelf life and storage requirements. These studies are performed according to ICH guidelines and are essential for ensuring product quality and safety.<sup>[27-29]</sup>

## 7. Therapeutic Evaluation of Polyherbal Formulations

### 7.1 In Vitro Studies

In vitro studies are conducted to evaluate antioxidant activity, cytoprotective effects, and mechanisms of action. Assays such as DPPH and FRAP are commonly used to assess free radical scavenging activity.<sup>[30-31]</sup>

### 7.2 In Vivo Studies

Animal models such as CCl<sub>4</sub>-induced and paracetamol-induced hepatotoxicity are widely used to evaluate hepatoprotective activity. Biochemical parameters and histopathological analysis provide insights into the therapeutic efficacy of formulations.<sup>[32-34]</sup>

### 7.3 Clinical Evaluation

Clinical trials are conducted to assess the safety and efficacy of polyherbal formulations in humans. These studies are essential for validating traditional claims and ensuring regulatory approval.

## 8. Toxicological Evaluation

Toxicological studies are essential for determining the safety profile of polyherbal formulations. These include acute, sub-chronic, and chronic toxicity studies, which evaluate potential adverse effects on various organ systems.<sup>[35]</sup>

## 9. Regulatory Aspects

The regulation of herbal medicines involves compliance with guidelines provided by WHO, AYUSH, and other regulatory bodies. Good Manufacturing Practices (GMP) and quality control measures are essential for ensuring product safety and efficacy.

## 10. Challenges in Polyherbal Formulation Development

Despite their advantages, polyherbal formulations face challenges such as variability in raw materials, lack of standardization, herb-drug interactions, and stability issues. Advanced analytical techniques and rigorous quality control are required to overcome these challenges.

## 11. Future Perspectives

The integration of nanotechnology and modern pharmaceutical approaches offers new opportunities for improving the efficacy and bioavailability of polyherbal formulations. Evidence-based research and clinical validation are essential for global acceptance.

## 12. CONCLUSION

Polyherbal formulations have emerged as a highly promising and effective approach for hepatoprotection because of their synergistic therapeutic effects, natural origin, and comparatively better safety profile when compared with many synthetic drugs. The combination of multiple medicinal herbs in a single formulation not only enhances therapeutic efficacy but also helps in reducing toxicity and adverse effects through complementary mechanisms of action. These formulations possess significant potential in the prevention and management of various liver disorders, including drug-induced hepatotoxicity, alcoholic liver disease, fatty liver disease, and other hepatic dysfunctions.

Despite their growing popularity and widespread traditional use, there remains a strong need for comprehensive scientific validation through pharmacological, toxicological, and clinical studies to establish their efficacy, safety, and mechanism of action. In addition, proper standardization of raw materials, quality control procedures, dosage consistency, and identification of active phytoconstituents are crucial to ensure reproducibility and reliability of therapeutic outcomes. Regulatory compliance and adherence to national and international guidelines are also essential for gaining wider acceptance of polyherbal medicines in evidence-based healthcare systems.

Therefore, with continued research, advanced analytical techniques, and well-designed clinical investigations, polyherbal formulations can play a vital role in the development of safer, more affordable, and effective hepatoprotective therapies. Their successful integration into modern healthcare systems has the potential to provide a valuable bridge between traditional herbal medicine and contemporary scientific medicine for the better management of liver-related diseases.

## 13. ACKNOWLEDGMENT

The authors acknowledge the support of their institution for providing necessary resources.

## 14. CONFLICT OF INTEREST

The authors declare no conflict of interest.

## 15. REFERENCES

1. Gonfa YH, Bachheti A, Semwal P, Rai N, Singab AN, Bachheti RK. Hepatoprotective activity of medicinal plants, their phytochemistry, and safety concerns: a systematic review. *Z Naturforsch C.*, 2025; 80(3-4): 61–73.
2. Służały P, Paśko P, Galanty A. Natural products as hepatoprotective agents—A comprehensive review of clinical trials. *Plants (Basel)*, 2024; 13(14): 1985.
3. Balkrishna A, Kumar A, Rohela A, Arya V, Gautam AK, Sharma H, et al. Traditional uses, hepatoprotective potential, and phytopharmacology of *Tinospora cordifolia*: A review. *J Pharm Pharmacol*, 2024; 76(3): 183–200.
4. Aladejana EB, Aladejana AE. Hepatoprotective activities of polyherbal formulations: A systematic review. *J Med Plants Econ Dev*, 2023; 7(1): a206.
5. Alkandahri MY, Pamungkas BT, Oktoba Z, Shafirany MZ, Sulastri L, Arfania M, et al. Hepatoprotective effect of kaempferol: A review. *J Food Qual*, 2023; 2023: 1387665.
6. Arman M, Chowdhury KAA, Bari MS, Khan MF, Huq MMA. Hepatoprotective potential of medicinal plants: Ethnomedicinal and pharmacological evidence. *Phytochem Rev*, 2022; 21: 1863–1886.
7. Autade KA, et al. Toxicity profiling of a polyherbal formulation for hepatic health: Acute and subacute evaluation. *Toxicol Res (Camb)*, 2025.

8. Sharma A, Gupta R, Singh S. Herbal hepatoprotective agents: A review of current perspectives. *J Ethnopharmacol*, 2022; 282: 114623.
9. Yadav NP, Dixit VK. Recent approaches in herbal drug standardization. *Int J Integr Med*, 2020; 12(2): 45–56.
10. Efferth T, Oesch F. Anti-inflammatory and hepatoprotective properties of plant-derived compounds. *Biotechnol Adv*, 2021; 49: 107–120.
11. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: An overview. *Sci World J.*, 2020; 2020: 162750.
12. Li S, Tan HY, Wang N, Zhang ZJ, Lao L, Wong CW, et al. The role of oxidative stress in liver diseases. *Int J Mol Sci.*, 2020; 21(3): 942.
13. Zhang CY, Yuan WG, He P, Lei JH, Wang CX. Liver fibrosis and hepatic stellate cells: Etiology and therapeutic targets. *World J Gastroenterol*, 2021; 27(16): 1889–1907.
14. Ahmed S, Khan RA, Jamil S. Pharmacological evaluation of hepatoprotective herbal formulations. *Pharmacogn Rev*, 2021; 15(29): 45–55.
15. Singh D, Gupta R, Saraf SA. Herbs-are they safe enough? An overview. *Crit Rev Food Sci Nutr*, 2020; 60(5): 876–898.
16. Patel VR, Patel PR, Kajal SS. Antioxidant activity of herbal plants: A review. *J Pharm Sci Res*, 2021; 13(4): 234–241.
17. Wang K, Liu R, Li J. Advances in hepatoprotective herbal medicines. *Front Pharmacol*, 2022; 13: 876543.
18. Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 11th ed. Elsevier, 2021.
19. Gupta AK, Mishra AK. Herbal drug delivery systems: Current perspectives. *Int J Pharm Sci Rev Res*, 2022; 72(1): 112–120.
20. Singh R, Lobo R. Phytosome technology: A novel drug delivery system. *J Drug Deliv Sci Technol*, 2021; 61: 102–110.
21. Choudhary N, Sekhon BS. An overview of advances in herbal drug formulation. *J Pharm Educ Res*, 2020; 11(2): 45–52.
22. WHO. Quality control methods for herbal materials. Geneva: World Health Organization, 2021.
23. ICH. Stability testing of new drug substances and products Q1A(R2), 2020.
24. OECD. Guidelines for testing of chemicals: Acute oral toxicity, 2021.
25. Kaur R, Sharma A. Evaluation of hepatoprotective activity of polyherbal formulations. *Int J Pharm Sci Res.*, 2023; 14(5): 2100–2108.
26. Singh P, Mehta A. Hepatoprotective herbs and their mechanisms of action. *Phytother Res*, 2022; 36(2): 789–805.
27. Devi VK, Jain N, Valli KS. Importance of novel drug delivery systems in herbal medicines. *Pharmacogn Rev*, 2021; 15(30): 50–56.
28. Shende S, Patel J. Role of tannin-rich plant fractions in hepatoprotection: A nanotechnology perspective. *Discover Nano*, 2026; 21: 44.
29. Polunina TE. Phytotherapy in chronic liver diseases. *Meditinskiy Sovet*, 2025; 15: 139–145.
30. Otuokere IE, Iheanyichukwu JI, Ngwu CM, et al. GC–MS and antioxidant studies of polyherbal formulation. *Discover Chemistry*, 2025; 2(1): 202.
31. Singh B, Sharma RA. Plant terpenes: Defense responses and hepatoprotection. *Phytochemistry*, 2021; 182: 112–120.

32. Jain PK, Kharya MD, Gajbhiye A. Pharmacological evaluation of medicinal plants for hepatoprotection. *Asian J Pharm Clin Res*, 2020; 13(2): 12–18.
33. Verma S, Singh SP. Current and future status of herbal medicines. *Vet World*, 2020; 13(3): 425–431.
34. Bhardwaj P, Alok U. Herbal remedies for liver disorders: A review. *J Drug Deliv Ther*, 2021; 11(3): 230–238.
35. Raza A, Khan RA. Evaluation of hepatoprotective effect of medicinal plants. *Pak J Pharm Sci*, 2022; 35(4): 1235–1242.