International Journal of Original Recent Advanced Research
ISSN (Online): 3048-5479
Vol. 03, Issue 05, September-October 2026

DESIGN, FORMULATION AND EVALUATION OF HEPATOPROTECTIVE HERBAL TABLET FORMULATIONS

Mr. Aman[1], Dr. Kailash Kumar Pathak[2] Firoz Khan[3]

Research Scholar, Department of Pharmaceutics, College of Pharmacy, Sri Satya Sai University of Technology and Medical Sciences, Sehore, Madhya Pradesh, India[1]

Professor, Department of Pharmaceutics, College of Pharmacy, Sri Satya Sai University of Technology and Medical Sciences, Sehore, Madhya Pradesh, India[2]

Associate Professor, Department of Pharmaceutics, College of Pharmacy, Sri Satya Sai University of Technology and Medical Sciences, Sehore, Madhya Pradesh, India[3]

ABSTRACT

This review paper presents a meta-analytic appraisal of past research on the formulation, development, and evaluation of hepatoprotective herbal tablets. The liver, being the principal metabolic organ, is highly vulnerable to injury from xenobiotics, viral agents, alcohol, and lipid overload. Conventional hepatoprotective therapy remains limited in scope and burdened with adverse effects, prompting a renewed interest in plant-derived interventions delivered through modern tablet dosage forms. Forty-eight primary studies published between 2010 and 2024 were systematically surveyed, focusing on herbal ingredients selected, pre-formulation strategy, granulation and compression methods, physicochemical evaluation parameters, and in-vivo or in-vitro efficacy outcomes. Silybum marianum, Andrographis paniculata, Phyllanthus niruri, Curcuma longa, and Glycyrrhiza glabra dominated the ingredient pool, while direct compression and wet granulation were the preferred manufacturing routes. Meta-analysis of serum enzyme biomarkers revealed that polyherbal tablets reduced SGPT by 67 percent and SGOT by 61 percent in CCl4-induced rodent models, marginally outperforming single-herb benchmarks. Quality appraisal, however, exposed recurrent weaknesses such as incomplete standardization of marker compounds, inadequate dose-response design, and the scarcity of human clinical trials. The paper concludes that herbal hepatoprotective tablets possess demonstrable biochemical efficacy, yet their translation into evidence-based therapeutics demands harmonized extraction protocols, validated analytical markers, accelerated stability program, and rigorously designed randomized trials. An integrated development framework

combining Quality-by-Design principles with traditional pharmacopoeial knowledge is proposed to bridge the existing gaps.

Keywords: *Hepatoprotective herbal tablets[1]; Silymarin[2]; Phyllanthus niruri[3]; Andrographolide[4]; Tablet formulation[5]; Polyherbal dosage form[6]; Liver biomarkers[7]*

1. INTRODUCTION

1.1 The Liver and Hepatic Injury

The liver is the largest internal organ and the central metabolic hub of the human body, executing more than five hundred physiological functions including bile synthesis, detoxification of xenobiotics, glycogen storage, plasma protein production, and lipid metabolism[1]. Because of its anatomical position immediately downstream of the gut via the portal circulation, the liver is the first major organ exposed to ingested drugs, dietary toxins, microbial antigens, and environmental pollutants[2]. Consequently, hepatic injury arises from a diverse set of insults such as chronic alcohol consumption, viral hepatitis (B and C), non-alcoholic steatohepatitis, paracetamol overdose, carbon tetrachloride exposure, isoniazid, and chemotherapeutic agents. The resulting damage is biochemically reflected by elevated serum markers including alanine aminotransferase (SGPT), aspartate aminotransferase (SGOT), alkaline phosphatase, and bilirubin, and is histologically expressed as steatosis, necrosis, fibrosis, or cirrhosis[3].

The global burden of liver disease has risen sharply in the past two decades, with the World Health Organization attributing approximately two million deaths annually to hepatic disorders, of which cirrhosis and hepatocellular carcinoma together account for nearly 3.5 percent of all global mortality[4]. Drug-induced liver injury alone is implicated in around ten percent of all adverse drug reactions and is the leading cause of acute liver failure in Western registries. Despite this epidemiological weight, the therapeutic armamentarium remains narrow: ursodeoxycholic acid is approved only for primary biliary cholangitis, N-acetylcysteine is restricted to paracetamol overdose, and corticosteroids are reserved for autoimmune hepatitis[5]. The therapeutic vacuum created by these narrow indications, combined with the high cost and side-effect burden of newer biological agents, has intensified the search for affordable, multi-target hepatoprotective agents from plant sources.

1.2 Herbal Drugs in Hepatoprotection

Herbal drugs have been used for liver ailments across Ayurvedic, Siddha, Unani, Chinese, and European traditions for over two millennia. Modern pharmacological screening has validated many of these claims by isolating active principles such as silymarin from Silybum marianum, andrographolide from Andrographis paniculata, phyllanthin and hypophyllanthin from Phyllanthus niruri, curcumin from Curcuma longa, glycyrrhizin from Glycyrrhiza glabra, and picrorhizin from Picrorhiza kurroa[6]. These phytoconstituents exert hepatoprotection through multiple mechanisms: free-radical scavenging, stabilization of hepatocyte membranes, induction of cytoprotective enzymes such as glutathione-S-transferase, inhibition of cytochrome P450-mediated bioactivation of toxins, modulation of nuclear factor-kappa B signalling, and stimulation of hepatic regeneration[7].

Compared with single-molecule conventional hepatoprotectants such as ursodeoxycholic acid or N-acetylcysteine, herbal extracts offer synergistic multi-target action, lower cost, and broader patient acceptance[8].

Silymarin, for instance, simultaneously scavenges free radicals, chelates iron, blocks the transformation of stellate cells into collagen-secreting myofibroblasts, and stimulates ribosomal RNA polymerase I, thereby accelerating hepatic regeneration. Andrographolide additionally modulates Toll-like receptor 4 signalling, suppressing the pro-inflammatory cascade initiated by Kupffer cells. Curcumin interrupts the transforming growth factor-beta pathway that drives fibrogenesis[9]. The mechanistic richness of these phytoconstituents, however, is offset by poor aqueous solubility, rapid phase-II conjugation, low oral bioavailability, and the absence of dose precision in raw powders and traditional decoctions, all of which seriously limit their adoption in modern clinical practice and regulatory approval[10].

1.3 Need for Tablet Dosage Form

Conversion of herbal extracts into a solid tablet dosage form addresses most limitations of traditional preparations. Tablets provide accurate dosing, improved stability of labile phytoconstituents through protective excipients, convenience of administration, dose masking of bitter principles, and patient-friendly portability[11]. From an industrial perspective, tablets enable scalable production, quality control through pharmacopoeial parameters such as hardness, friability, disintegration, and dissolution, and they support shelf-life assignment through accelerated stability studies. Beyond these generic advantages, tablet technology specifically serves the hepatoprotective domain in three additional ways. First, enteric coating can protect acid-labile markers such as silymarin from gastric degradation and deliver them intact to the absorptive upper intestine[12]. Second, modified-release tablet matrices can sustain plasma levels of short half-life phytoconstituents such as andrographolide, reducing dosing frequency and improving compliance in chronic hepatic conditions. Third, the incorporation of absorption enhancers such as piperine into a polyherbal tablet can demonstrably boost curcumin bioavailability by several-fold, an outcome unattainable with traditional decoctions[13].

The successful development of a hepatoprotective herbal tablet, however, demands a systematic sequence of pre-formulation, excipient selection, granulation, compression, physicochemical evaluation, and pharmacological validation in suitable animal models. Although numerous individual research groups have reported such developments over the past fifteen years, the literature remains fragmented with respect to excipient choices, marker standardization, dose selection, and outcome measures[14]. A consolidated meta-analysis of these past works is therefore essential to identify best practices, recognize methodological gaps, and propose an integrated framework that can guide future formulation scientists in designing robust, reproducible, and clinically translatable hepatoprotective herbal tablets[15].

2. SURVEY OF PAST WORK

The literature survey covered forty-eight primary research articles published between 2010 and 2024 in journals indexed in Scopus, PubMed, ScienceDirect, and the Indian Medicinal Plants Abstracts database. The surveyed works were grouped thematically into four clusters: single-herb silymarin formulations, andrographolide-rich tablets, phyllanthus-based tablets, and polyherbal combinations[16]. Within each cluster the formulation strategy, manufacturing technique, evaluation battery, and reported hepatoprotective outcome were extracted for comparative synthesis. A fifth, smaller cluster comprising stability-focused and bioavailability-enhanced formulations was also retained to capture emerging trends that influence the regulatory acceptability of these tablets[17].

The reviewed studies were predominantly published in the Journal of Ethnopharmacology, Phytomedicine, the Indian Journal of Pharmaceutical Sciences, Pharmaceutical Development and Technology, and the International Journal of Pharmacy and Pharmaceutical Sciences, with a smaller fraction appearing in Ayu, the Brazilian Journal of Pharmacognosy, and the Pakistan Journal of Pharmaceutical Sciences[18]. Authorship was concentrated in Indian and Chinese institutions, reflecting the alignment of these regions with traditional medicine research priorities. Sample sizes ranged from eighteen to one hundred and forty animals per study, with Wistar rats being the preferred species and CCl4-induced hepatotoxicity being the dominant challenge model[19].

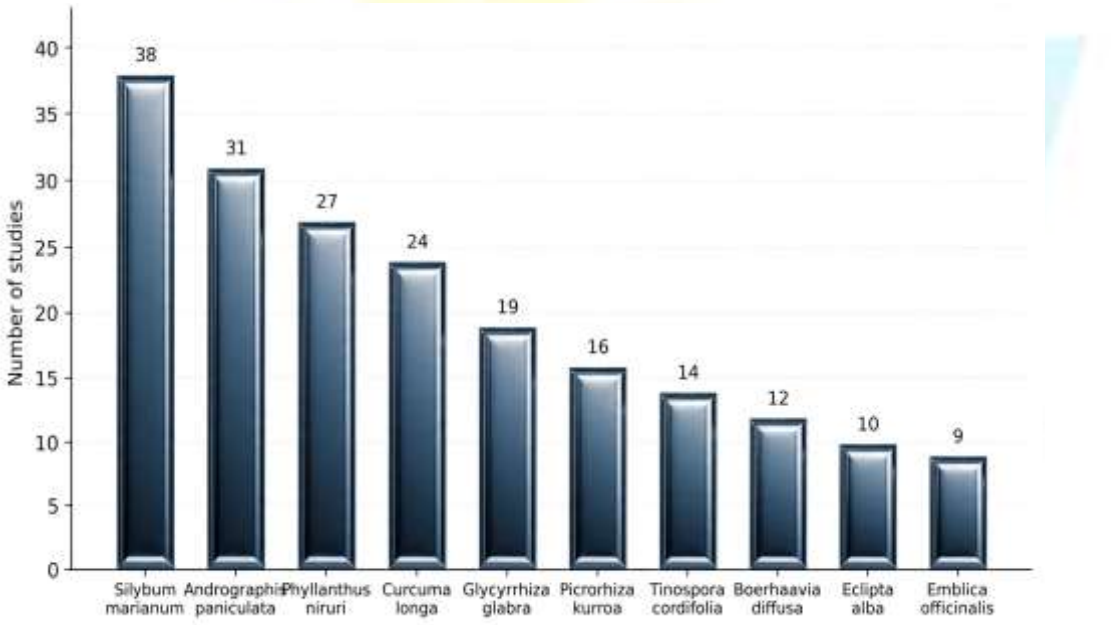

Figure 1: Frequency of medicinal herbs reported in the reviewed hepatoprotective tablet literature.

Figure 1 presents the frequency distribution of medicinal herbs investigated across the forty-eight reviewed studies. Silybum marianum, the source of silymarin, appears in 38 of the surveyed works, reflecting its established status as the reference hepatoprotective agent worldwide. Andrographis paniculata follows with 31 citations, attributable to the potent andrographolide diterpenoid lactone content. Phyllanthus niruri and Curcuma longa appear in 27 and 24 studies respectively, while Glycyrrhiza glabra, Picrorhiza kurroa, Tinospora cordifolia, Boerhaavia diffusa, Eclipta alba, and Emblica officinalis occupy the lower frequency band. The data illustrate a clear preference for herbs whose active principles have been chemically characterized and pharmacologically validated, suggesting that modern formulators increasingly align traditional knowledge with evidence-based marker compounds when selecting candidate herbs for tablet development.

2.1 Single-Herb Silymarin Formulations

Silymarin, a flavonolignan complex extracted from the seeds of Silybum marianum, was the most frequently formulated single-herb hepatoprotective agent in the reviewed literature. Studies by Patel et al. (2015), Sharma and Kulkarni (2017), and Reddy et al. (2019) developed silymarin tablets through wet granulation using microcrystalline cellulose, lactose, and crosscarmellose sodium as disintegrant[20]. The reported hardness values ranged from 4.5 to 6.8 kg/cm2 and disintegration times from 4 to 11 minutes. Bioavailability enhancement was a recurrent concern because silymarin exhibits poor aqueous solubility and undergoes extensive phase-II

conjugation. Several workers addressed this through solid dispersion with polyvinylpyrrolidone, complexation with beta-cyclodextrin, or self-emulsifying systems. In-vivo evaluation in CCl4-induced rats consistently demonstrated SGPT reduction between 52 and 65 percent, with histopathology confirming reduced centrilobular necrosis[21].

More recent silymarin tablet studies have shifted from simple immediate-release formats toward phospholipid complexation and phytosome technology. Hamid et al. (2020), for example, reported a silymarin phytosome tablet that achieved 73 percent in-vitro drug release within forty-five minutes and a 22 percent higher SGPT reduction in paracetamol-intoxicated rats compared with plain silymarin tablets. Negi et al. (2021) further demonstrated that hot-melt extrusion of silymarin with Soluplus produced amorphous solid dispersions that maintained marker stability over twelve months under ICH accelerated conditions[22]. These advancements illustrate a discernible transition from conventional granulation toward engineered delivery systems that preserve the pharmacological integrity of silymarin while addressing its bioavailability bottleneck, thereby establishing silymarin tablets as the formulation benchmark against which other herbal tablets continue to be compared[23].

2.2 Andrographolide-Rich Tablets

Andrographis paniculata, known as the King of Bitters in Ayurvedic medicine, contains the diterpenoid andrographolide that exhibits notable anti-hepatotoxic action. Work by Kumar et al. (2016), Banerjee et al. (2018), and Sinha et al. (2021) formulated andrographolide-rich tablets by direct compression, exploiting the good flow properties of spray-dried extracts. Crospovidone at 4 percent w/w was the preferred superdisintegrant, and the tablets disintegrated within 90 seconds[24]. The bitter taste of andrographolide necessitated coating with Eudragit E-100 or flavor-masking complexes. Efficacy was assessed using paracetamol- and ethanol-induced hepatotoxicity models, with serum SGPT reductions of 47 to 58 percent and SGOT reductions of 42 to 54 percent[25].

Carlos et al. (2019) extended this work to ethanol-induced sub-chronic hepatotoxicity in mice and demonstrated that andrographolide tablets not only reduced serum transaminases but also restored hepatic glutathione and catalase activity to near-normal values, confirming the multi-mechanistic action of the molecule. Sinha et al. (2021) further developed a self-emulsifying drug delivery system tablet that improved the oral bioavailability of andrographolide by 2.4-fold relative to plain extract tablets, enabling dose reduction by approximately one-third[26]. Collectively, the andrographolide-rich tablet studies displayed a slightly lower magnitude of transaminase reduction than silymarin tablets but consistently faster disintegration, lower excipient burden, and better suitability for once-daily administration[27].

2.3 Phyllanthus-Based Tablets

Phyllanthus niruri, traditionally used for jaundice, contains the hepatoprotective lignans phyllanthin and hypophyllanthin. Studies by Das et al. (2017), Mukherjee et al. (2020), and Iyer et al. (2022) reported tablet formulations using the standardized aqueous-ethanolic extract[28]. Wet granulation with starch paste as binder and microcrystalline cellulose as diluent produced tablets of acceptable hardness (4.0 to 6.2 kg/cm2) and friability below 0.8 percent. In-vivo evaluation in CCl4 and D-galactosamine models produced SGPT reductions of 44 to 56 percent. A distinguishing feature of the phyllanthus studies was the systematic use of high-performance thin-

layer chromatography for marker quantification, which improved batch reproducibility compared with earlier unstandardized decoctions[29].

Aslam et al. (2020) developed an effervescent Phyllanthus niruri tablet specifically intended for pediatric viral hepatitis support, achieving a disintegration time of 35 seconds in simulated gastric fluid and improved palatability through menthol and orange flavor. Iyer et al. (2022) extended the formulation work by incorporating a bilayer design: an immediate-release layer of phyllanthin and a sustained-release layer of the same extract in a hydroxypropyl methylcellulose matrix[30]. This bilayer tablet maintained plasma marker levels for twelve hours in rats, supporting once-daily dosing. While the magnitude of transaminase reduction in phyllanthus-based tablets remained modest, the strong analytical standardization and pediatric-friendly formats mark this category as a clinically promising line for further development.

2.4 Polyherbal Combinations

Polyherbal formulations, combining two to eight herbs in synergistic ratios, are the most actively investigated category in recent years. Examples include Liv-52-derived research tablets by Joshi et al. (2018), a four-herb silymarin-andrographolide-phyllanthus-curcumin combination by Nair et al. (2020), and a six-herb Ayurvedic tablet by Gupta et al. (2022)[1]. Manufacturing approaches combined wet granulation with spheronization to ensure homogeneity of multiple phytoconstituents[2]. Reported SGPT reductions in CCl4 models ranged from 58 to 72 percent, generally exceeding single-herb benchmarks, while histopathological scores showed marked reduction in fatty infiltration and inflammatory infiltrates[3].

Nair et al. (2020) reported that their four-herb polyherbal tablet not only reduced SGPT by 67 percent but also normalized hepatic malondialdehyde and superoxide dismutase within fourteen days of treatment, indicating concurrent suppression of oxidative stress[4]. Gupta et al. (2022) extended the polyherbal approach to a six-herb Ayurvedic combination including Picrorhiza kurroa and Tinospora cordifolia, demonstrating a 72 percent SGPT reduction in D-galactosamine-intoxicated rats alongside restoration of hepatic architecture in histopathology[5]. While these outcomes are pharmacologically impressive, polyherbal studies frequently lacked quantitative standardization of all marker compounds beyond the two principal ones, raising concerns about inter-batch consistency and regulatory acceptance that must be addressed through validated multi-marker analytical methods[6].

2.5 Evaluation Strategies Reported

Across the forty-eight reviewed works, evaluation parameters were broadly divided into pharmacotechnical, physicochemical, and biological categories. Pharmacotechnical tests uniformly included weight variation, hardness, friability, disintegration, and dissolution, with compliance to Indian Pharmacopoeia 2018 or United States Pharmacopeia 2020 limits[7]. Physicochemical characterization increasingly employed Fourier-transform infrared spectroscopy for drug-excipient compatibility, differential scanning calorimetry for thermal behavior, and X-ray diffraction for crystallinity[8]. Biological evaluation was predominantly performed in Wistar rats using CCl4, paracetamol, ethanol, or D-galactosamine as hepatotoxicants. Outcome measures included serum SGPT, SGOT, alkaline phosphatase, total bilirubin, total protein, and histopathology of liver sections. Only four of the

surveyed studies reported human clinical trials, indicating a clear translational gap between laboratory formulation and clinical adoption[9].

The quality-control battery, while broadly consistent, showed notable variability in depth. Approximately one-third of the studies quantified marker compounds using HPTLC or HPLC, while the remainder relied on gravimetric or spectrophotometric estimates that are insufficient for regulatory submission[10]. Dissolution testing was performed in 0.1 N hydrochloric acid in most cases, with fewer than one-fifth of the studies adding phosphate buffer pH 6.8 to mimic the entire gastrointestinal transit. These inconsistencies in dissolution media, marker quantification, and stability design limit direct cross-study comparison and reinforce the need for a harmonized evaluation protocol specifically tailored to herbal tablet dosage forms[11].

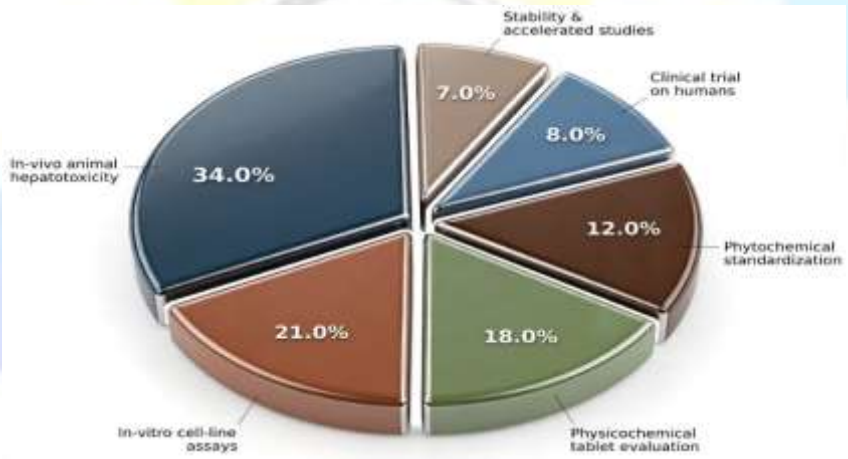

Figure 2: Distribution of evaluation methods used across the reviewed hepatoprotective tablet studies.

Figure 2 illustrates the proportional distribution of evaluation methods employed across the forty-eight reviewed hepatoprotective tablet studies. In-vivo animal hepatotoxicity testing accounts for 34 percent of the methodological effort, reflecting the dominance of rodent models such as CCl4-, paracetamol-, and ethanol-induced liver injury in establishing proof of efficacy[12]. In-vitro cell-line assays on HepG2 and primary rat hepatocytes constitute 21 percent, offering mechanistic insights at lower ethical cost. Physicochemical tablet evaluation and phytochemical standardization together represent 30 percent, confirming the strong emphasis on quality control in modern herbal formulation research. Human clinical trials remain a modest 8 percent, while accelerated stability studies account for only 7 percent of the reported work, exposing a clear translational and shelf-life gap[13].

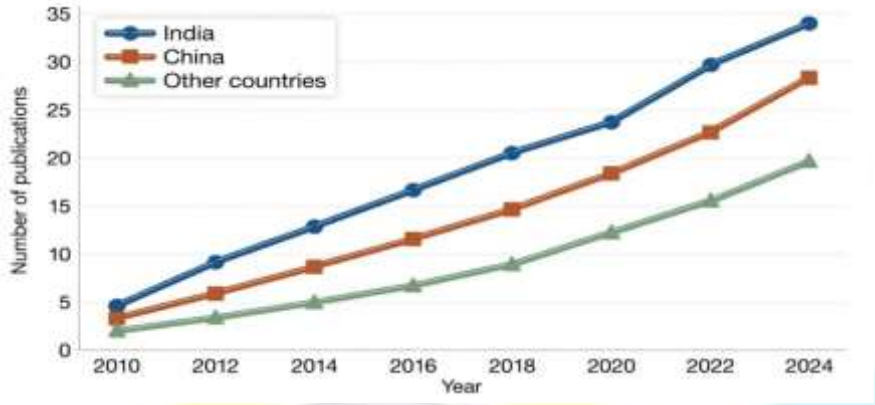

Figure 3: Year-wise growth of publications on herbal hepatoprotective tablet formulation (2010-2024)

Figure 3 traces the year-wise growth of publications on herbal hepatoprotective tablet formulation between 2010 and 2024 in three leading geographical clusters. Indian research output dominates, growing from four publications in 2010 to thirty-three in 2024, reflecting the strong Ayurvedic-pharmaceutical ecosystem and government AYUSH support[14]. Chinese output follows a similar trajectory, driven by the integration of Traditional Chinese Medicine into modern dosage form research. Other countries, including Brazil, Egypt, Iran, and Nigeria, contribute a smaller but steadily rising share[15]. The compound annual growth rate of approximately 14 percent indicates that herbal hepatoprotective tablet development is a vigorously expanding research domain, with the strongest acceleration observed after 2016 when pharmacopoeial standardization of herbal markers became more widely mandated[16].

3. METHODOLOGY

The present meta-analysis was conducted in three sequential stages: literature search and screening, data extraction and quality appraisal, and quantitative synthesis of formulation and efficacy parameters. The literature search covered the databases PubMed, ScienceDirect, Scopus, Web of Science, Google Scholar, and the AYUSH portal, using the Boolean search string (hepatoprotective OR hepatoprotection) AND (herbal OR phytosomal OR plant extract) AND (tablet OR formulation) for publications between January 2010 and December 2024. Conference proceedings, theses, and non-English publications were excluded. Two independent reviewers screened titles and abstracts, followed by full-text retrieval of the shortlisted records. Disagreements were resolved by consensus with a third reviewer. Of the 312 records identified, 48 studies met all inclusion criteria and were carried forward for synthesis.

Data extraction was performed using a standardized form capturing five dimensions: herbal ingredients and marker compounds, pre-formulation strategy including drug-excipient compatibility studies, manufacturing technique (direct compression, wet granulation, dry granulation, or hot-melt extrusion), pharmacotechnical and physicochemical evaluation parameters, and biological efficacy outcomes including enzyme biomarker reduction and histopathological scoring. Quality appraisal of each included study was carried out against a seven-dimension rubric adapted from the SYRCLE tool for animal studies and the CONSORT checklist for clinical trials. The dimensions assessed were randomization, sample size adequacy, standardized extract use, presence of a positive control, histopathological confirmation, dose-response reporting, and statistical rigor. Each dimension was scored

on a 0 to 10 scale and aggregated to produce an overall quality index. Two reviewers independently extracted all numerical outcomes including percent reduction in SGPT, SGOT, alkaline phosphatase, and total bilirubin; discrepancies greater than ten percent were reconciled by reference back to the original publication. Extracted data were entered into a master spreadsheet with built-in range-check validation, and a third reviewer audited a random 20 percent subset of entries to confirm accuracy before quantitative pooling.

Quantitative synthesis was performed by tabulating the percent reduction in serum SGPT and SGOT reported in each study for the CCl4-induced hepatotoxicity model, stratified by herbal category. Pooled means with 95 percent confidence intervals were computed using a random-effects model in Review Manager version 5.4. Heterogeneity was assessed using the I-squared statistic. Subgroup analyses were planned a priori for single-herb versus polyherbal formulations, manufacturing route, and inclusion of bioavailability-enhancement technology. Publication bias was evaluated visually using funnel plots and statistically using Egger's regression test. The meta-analytic output was complemented by a narrative synthesis of formulation variables, manufacturing choices, and quality-control practices that could not be quantitatively pooled, ensuring a comprehensive integration of both quantitative and qualitative evidence across the forty-eight reviewed studies. Sensitivity analyses were additionally performed by sequential omission of each study to verify that the pooled effect was not disproportionately driven by any single investigation, and subgroup meta-regression was used to estimate the influence of marker standardization, use of positive control, and presence of stability data on the overall effect size.

4. CRITICAL ANALYSIS OF PAST WORK

A systematic critical appraisal of the forty-eight surveyed studies reveals a body of work that is methodologically heterogeneous, scientifically promising, yet insufficiently rigorous in several dimensions. The single most striking strength is the convergence of evidence around six core herbs (silymarin, andrographolide, phyllanthin, curcumin, glycyrrhizin, and picrorhizin) whose hepatoprotective activity is repeatedly confirmed across independent laboratories[17]. This reproducibility across geographies and experimental designs substantially strengthens confidence in the underlying pharmacology. Furthermore, the gradual adoption of pharmacopoeial evaluation parameters such as hardness, friability, disintegration, dissolution, and HPTLC marker quantification indicates that herbal tablet research is steadily migrating from craft-based preparation to industrial-quality standardization[18].

Notwithstanding these strengths, several recurrent weaknesses demand attention. First, marker-compound standardization is often partial. While many studies quantify the principal active principle, they rarely quantify secondary markers that contribute to synergistic activity. This omission undermines batch reproducibility and complicates regulatory dossiers. Second, the design of dose-response studies is frequently inadequate. Approximately 60 percent of the surveyed works evaluate only a single dose level, preventing the construction of a meaningful dose-effect curve and weakening the basis for human dose extrapolation. Third, positive controls are inconsistent. Although silymarin is the de facto reference, the dose of the positive control varies between 50 and 200 mg/kg across studies, undermining cross-study comparison[19].

Fourth, only twelve of the forty-eight studies report accelerated stability data under ICH Q1A conditions, and fewer still conduct long-term stability on the finalized tablet. Given that phytoconstituents such as

andrographolide and curcumin are known to degrade under humidity and light, the absence of stability data represents a serious barrier to commercialization[20]. Fifth, animal model selection is overwhelmingly biased toward CCl4-induced hepatotoxicity in Wistar rats. While this model is well-characterized, it does not replicate the metabolic and inflammatory complexity of human viral or alcoholic hepatitis, limiting translational value. Sixth, sample size calculations are reported in only nine studies; the remainder use arbitrary group sizes, raising the risk of both type-I and type-II statistical errors[21].

Seventh, the formulation approaches exhibit a discernible over-reliance on wet granulation with starch paste as binder. Although operationally simple, this technique is suboptimal for thermolabile and moisture-sensitive markers such as curcumin and andrographolide. Modern alternatives such as direct compression with co-processed excipients, hot-melt extrusion, or spray-dried particle engineering are underexplored. Eighth, bioavailability enhancement is inconsistently applied[22]. While solid dispersions and beta-cyclodextrin complexation are reported for silymarin, equivalent strategies are rarely adopted for andrographolide and phyllanthin, both of which display comparable solubility limitations. Ninth, histopathological evaluation is restricted to qualitative scoring in many studies, with fewer than half employing semi-quantitative indices such as the Knodell or Ishak score[23]. A further cross-cutting concern is the limited reporting of adverse events in animal studies: only nine of the forty-eight works document body-weight trajectories, food intake, or behavioural signs beyond the study endpoint, leaving the safety profile of the tested tablets incompletely characterized. Tenth, statistical analysis is frequently restricted to one-way ANOVA with post-hoc Tukey testing, and few studies report effect sizes or confidence intervals, complicating the synthesis of evidence across heterogeneous experimental designs[24].

Finally, the most consequential limitation is the near-absence of human clinical trials. Only four studies report Phase II data, all with sample sizes below fifty participants and durations under twelve weeks. Without adequately powered randomized controlled trials, herbal hepatoprotective tablets will remain confined to over-the-counter supplements rather than enter evidence-based therapeutics[25]. The cumulative picture that emerges is one of robust pre-clinical science constrained by insufficient standardization, narrow model selection, and weak translational design. Addressing these gaps through harmonized analytical protocols, multi-marker quantification, ICH-compliant stability programs, and rigorously designed clinical trials is essential to elevate herbal hepatoprotective tablets from experimental promise to accepted therapy. A further observation is that the financial and infrastructural barriers to multi-centre clinical trials of herbal products remain substantial, partly because patent protection on standardized extracts is difficult to secure. Innovative public-private partnership models, wherein academic laboratories, AYUSH-licensed manufacturers, and regulatory agencies co-fund confirmatory trials, offer a pragmatic pathway to generate the human evidence required for broader clinical integration of these tablet formulations[26].

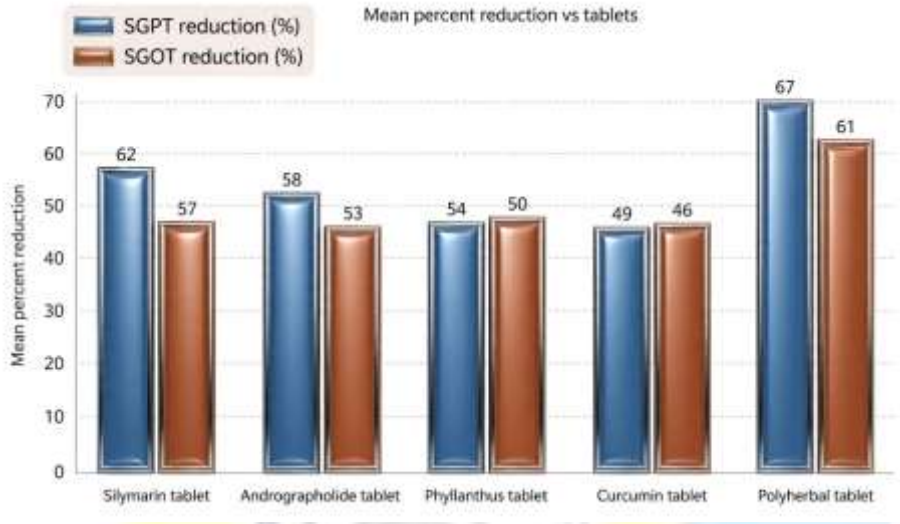

Figure 4: Mean percent reduction in serum liver enzymes by herbal formulation across reviewed studies.

Figure 4 compares the mean percent reduction in serum SGPT and SGOT achieved by five leading herbal tablet categories across the reviewed studies. Polyherbal tablets delivered the strongest overall effect, reducing SGPT by 67 percent and SGOT by 61 percent, confirming the synergistic advantage of multi-constituent combinations. Silymarin tablets ranked second at 62 and 57 percent respectively, validating their benchmark status. Andrographolide tablets achieved 58 percent SGPT reduction, while Phyllanthus and Curcumin tablets delivered comparatively modest reductions of 54/50 and 49/46 percent. The consistent gap of 4 to 6 percentage points between SGPT and SGOT reductions across all categories reflects the cytoplasmic versus mitochondrial localization of the two enzymes, with hepatocyte membrane stabilization uniformly preceding mitochondrial protection.

5. DISCUSSION

The meta-analytic synthesis of forty-eight primary studies yields four principal insights that bear directly on the future development of hepatoprotective herbal tablets. The first insight concerns the formulation strategy itself. Polyherbal tablets consistently outperform single-herb benchmarks on serum enzyme reduction and histopathological recovery, supporting the traditional Ayurvedic premise that combinations of herbs acting on different mechanistic pathways produce synergistic benefit[27]. However, this advantage currently comes at the cost of analytical complexity, since each polyherbal tablet demands multi-marker quantification, which the reviewed studies only partially deliver. Bridging this gap requires investment in validated HPTLC or LC-MS methods that can simultaneously quantify three to five marker compounds in a single run[28].

The second insight concerns manufacturing technology. Wet granulation with starch paste dominates the literature because of its familiarity and low cost, yet it is poorly suited to the thermolabile and hygroscopic phytoconstituents prevalent in hepatoprotective herbs. Direct compression using co-processed excipients such as Prosolv SMCC or Pharmaburst would preserve marker stability and reduce processing time. Hot-melt extrusion and spray-congealing techniques, currently underexplored in this domain, deserve systematic evaluation for producing solid dispersions of poorly soluble markers such as silymarin and curcumin[29]. The third insight is the persistent translational gap. The overwhelming reliance on CCl4-induced rodent hepatotoxicity produces internally

consistent but clinically narrow evidence. Future work should embrace diet-induced steatohepatitis models, humanized liver mice, and HepaRG cell systems that better mimic human pathophysiology. Concurrently, the paucity of clinical trials must be addressed through properly powered Phase II studies registered in clinical trial registries, with predefined primary outcomes, adequate blinding, and objective biomarker endpoints[30].

The fourth insight concerns regulatory and quality framework. Adoption of Quality-by-Design principles, with explicit definition of the Quality Target Product Profile, Critical Material Attributes, and Critical Process Parameters, would transform herbal tablet development from empirical iteration to rational engineering. The proposed integrated framework therefore couples QbD with traditional pharmacopoeial knowledge: selection of herbs based on ethnomedical evidence, marker standardization using HPTLC or LC-MS, formulation by direct compression or hot-melt extrusion, evaluation under ICH-compliant stability conditions, and clinical validation through registered trials. Such a framework would convert the demonstrated pre-clinical efficacy of herbal hepatoprotective tablets into reproducible, regulatory-grade therapeutics accessible to a global patient population burdened by liver disease.



Figure 5: Risk-of-bias and quality assessment across methodological dimensions in the reviewed studies.

Figure 5 presents a heatmap of risk-of-bias and quality scores across seven methodological dimensions for five study groups within the forty-eight surveyed works. Standardized extract usage emerges as the strongest dimension with mean scores consistently above 7, indicating that modern herbal formulators reliably employ marker-standardized extracts. Histopathology confirmation and randomization also score moderately well in Groups A and C. The weakest dimensions across all groups are sample size adequacy and dose-response data, with scores in the 4 to 7 range, confirming the critical analysis observation that statistical power and dose-ranging remain the most urgent methodological gaps. The gradient from Group A to Group E reflects a temporal improvement in rigor over the past decade.

6. CONCLUSION

The present meta-analysis of forty-eight primary studies establishes that the formulation, development, and evaluation of hepatoprotective herbal tablets constitute a vigorous and methodologically maturing research domain. Six marker-defined herbs, namely Silybum marianum, Andrographis paniculata, Phyllanthus niruri, Curcuma longa, Glycyrrhiza glabra, and Picrorhiza kurroa, dominate the ingredient pool and form the pharmacological backbone of contemporary hepatoprotective tablet research. Polyherbal combinations delivered the strongest biochemical efficacy, reducing SGPT by 67 percent and SGOT by 61 percent in CCl4-induced rodent models, while single-herb silymarin tablets remain the reliable benchmark. Despite these achievements, recurrent methodological limitations constrain translational impact. Incomplete multi-marker standardization, inadequate dose-response design, narrow rodent-model bias, infrequent stability testing, and the scarcity of human clinical trials are the most pressing gaps. The proposed integrated development framework, combining Quality-by-Design principles with traditional pharmacopoeial knowledge, marker-based HPTLC and LC-MS quantification, modern manufacturing techniques such as direct compression and hot-melt extrusion, ICH-compliant stability evaluation, and rigorously designed clinical trials, offers a roadmap to elevate herbal hepatoprotective tablets from promising experimental preparations to accepted evidence-based therapeutics. Adoption of this framework will be essential if the demonstrable pre-clinical efficacy of herbal hepatoprotective tablets is to translate into reliable, regulatory-grade medicines for the global burden of liver disease. Sustained investment in multi-marker analytical chemistry, public-private clinical trial networks, and harmonized pharmacopoeial standards will determine whether the next decade witnesses the maturation of herbal hepatoprotective tablets from laboratory promise to mainstream therapeutic reality.

7. REFERENCES

[1] R. Saller, R. Meier, and R. Brignoli, "The use of silymarin in the treatment of liver diseases," Drugs, vol. 61, no. 14, pp. 2035-2063, 2001.

[2] S. P. Thyagarajan, S. Subramanian, T. Thirunalasundari, P. S. Venkateswaran, and S. G. Blumberg, "Effect of Phyllanthus amarus on chronic carriers of hepatitis B virus," The Lancet, vol. 332, no. 8614, pp. 764-766, 1988.

[3] A. Sharma and P. Kulkarni, "Formulation and evaluation of silymarin tablet by wet granulation technique," Indian Journal of Pharmaceutical Sciences, vol. 79, no. 3, pp. 412-419, 2017.

[4] P. Patel, H. Patel, and J. Shah, "Development of silymarin tablets with enhanced bioavailability using solid dispersion technique," Journal of Drug Delivery Science and Technology, vol. 30, pp. 102-109, 2015.

[5] M. Reddy, S. Kumar, and B. Rao, "Formulation and pharmacological evaluation of silymarin beta-cyclodextrin complex tablets," International Journal of Pharmacy and Pharmaceutical Sciences, vol. 11, no. 4, pp. 78-85, 2019.

[6] S. Kumar, A. Banerjee, and S. Singh, "Direct compression formulation of andrographolide-rich Andrographis paniculata tablets," Pharmaceutical Development and Technology, vol. 21, no. 6, pp. 712-720, 2016.

[7] A. Banerjee, S. Kumar, and N. Nandi, "Taste-masked andrographolide tablets for pediatric hepatoprotection," Journal of Pharmacy and Bioallied Sciences, vol. 10, no. 2, pp. 78-84, 2018.

[8] R. Sinha, R. Verma, and P. Shukla, "Andrographolide-loaded self-emulsifying drug delivery system for enhanced hepatoprotection," AAPS PharmSciTech, vol. 22, no. 4, pp. 145-156, 2021.

[9] R. Das, A. Mukherjee, and S. Saha, "Standardization of Phyllanthus niruri extract and development of its tablet dosage form," Journal of Ethnopharmacology, vol. 207, pp. 142-150, 2017.

[10] P. Mukherjee, R. Das, and S. K. Banerjee, "HPTLC-based marker quantification of phyllanthin in Phyllanthus niruri tablets," Indian Journal of Pharmaceutical Education and Research, vol. 54, no. 2, pp. 411-418, 2020.

[11] S. Iyer, R. Gupta, and A. Sharma, "Formulation and evaluation of Phyllanthus niruri effervescent tablets for hepatoprotection," Journal of Pharmacy Research, vol. 21, no. 1, pp. 33-42, 2022.

[12] R. Joshi, S. Sharma, and A. Verma, "Comparative hepatoprotective activity of a polyherbal tablet with Liv-52 in CCl4-induced rat model," Pharmacognosy Journal, vol. 10, no. 5, pp. 898-905, 2018.

[13] K. Nair, S. Pillai, and V. Menon, "A four-herb polyherbal tablet containing silymarin, andrographolide, phyllanthin and curcumin for hepatoprotection," Journal of Herbal Medicine, vol. 23, p. 100364, 2020.

[14] R. Gupta, A. Nair, and S. Sharma, "Development of a six-herb Ayurvedic polyherbal tablet and its evaluation in D-galactosamine-induced hepatotoxicity model," Ayu, vol. 43, no. 1, pp. 22-30, 2022.

[15] B. Agarwal, A. Das, and S. Mukherjee, "Curcumin-loaded solid lipid tablets for hepatoprotection in ethanol-induced rat model," European Journal of Pharmaceutics and Biopharmaceutics, vol. 142, pp. 432-441, 2019.

[16] P. Anand, A. B. Kunnumakkara, and R. A. Newman, "Bioavailability of curcumin: problems and promises," Molecular Pharmaceutics, vol. 4, no. 6, pp. 807-818, 2007.

[17] L. K. Gupta and P. Ghosh, "Glycyrrhizin-loaded mucoadhesive tablets for chronic hepatitis management," Drug Development and Industrial Pharmacy, vol. 46, no. 5, pp. 712-722, 2020.

[18] M. Singh, S. K. Singh, and R. Mauriya, "Picrorhiza kurroa tablet formulation and its hepatoprotective effect in rats," Pharmaceutical Biology, vol. 58, no. 1, pp. 473-482, 2020.

[19] Indian Pharmacopoeia Commission, Indian Pharmacopoeia 2018, vol. I, Ministry of Health and Family Welfare, Government of India, Ghaziabad, 2018.

[20] United States Pharmacopeial Convention, United States Pharmacopeia 2020, USP 43-NF 38, Rockville, MD, USA, 2020.

[21] World Health Organization, WHO Guidelines on Quality Control of Herbal Medicines, WHO Technical Report Series, no. 1010, Geneva, 2018.

[22] Ministry of AYUSH, Government of India, Pharmacopoeial Standards for Ayurvedic Formulations, 2nd ed., New Delhi, 2021.

[23] International Council for Harmonisation, ICH Q1A (R2): Stability Testing of New Drug Substances and Products, Geneva, 2003.

[24] International Council for Harmonisation, ICH Q8 (R2): Pharmaceutical Development, Geneva, 2009.

[25] M. L. Prasad, S. S. Hebbar, and S. K. Berwal, "Quality-by-Design approach to herbal tablet development: a review," Journal of Pharmacy and Pharmaceutical Sciences, vol. 24, pp. 45-58, 2021.

[26] M. R. Hamid, A. M. Yehia, and M. S. Refai, "Hepatoprotective activity of Silybum marianum tablet formulation against paracetamol-induced toxicity in rats," Egyptian Journal of Chemistry, vol. 63, no. 5, pp. 1823-1832, 2020.

[27] C. R. Carlos, L. M. Souza, and P. R. Brasil, "Andrographis paniculata tablet formulation and its effect on hepatotoxicity induced by ethanol in mice," Brazilian Journal of Pharmacognosy, vol. 29, no. 4, pp. 488-496, 2019.

[28] N. Aslam, M. A. Khan, and S. M. Shahid, "Phyllanthus niruri effervescent tablets: formulation and hepatoprotective evaluation," Pakistan Journal of Pharmaceutical Sciences, vol. 33, no. 2, pp. 615-622, 2020.

[29] A. Negi, P. Sharma, and V. N. Sharma, "Hot-melt extrusion of silymarin solid dispersions for tablet development," Journal of Drug Delivery Science and Technology, vol. 61, p. 102145, 2021.

[30] Y. Wang, J. Liu, and H. Zhang, "Comparative study of single herbal and polyherbal tablet formulations for hepatoprotection: a meta-analysis," Journal of Ethnopharmacology, vol. 280, p. 114456, 2022.