RESEARCH PAPER

Phytochemical Profile and Hepatoprotective Potential of *Pergularia Daemia:* A Review

Gandepalli Pratap Kumar[1], Kabesh A[2], Mageshwara P T[3], Ponnudhurai R[4], Gangadharan R[5], Karthikeyan P[6], Dhivakaran N P[7], Anis Kumar M[8*]

[1]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
gandepallipratap@gmail.com
[2]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
kabesh0101@gmail.com
[3]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
mageshwaramageshwara630@gmail.com
[4]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
dhurairaja2005@gmail.com
[5]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
gangadharanr50@gmail.com
[6]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
karthiperumal508@gmail.com
[7]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
dhivakaran2920@gmail.com.
[8]Department of Biotechnology, V.S.B. Engineering College, Karur, Tamil Nadu, India
aniskumarmani@gmail.com.

***Corresponding Author ;** Dr M. Anis Kumar
*Professor and Head, Department of Biotechnology, V.S.B. Engineering College, Karudayampalayam, Karur, Tamilnadu, India – 639111. E-mail Id: aniskumarmani@gmail.com ORCiD: 0009-0003-9951-7201

ABSTRACT
Liver cirrhosis is a chronic and progressive liver disorder characterized by hepatocyte injury, excessive deposition of fibrous tissue, and compromised liver function. The etiology of cirrhosis includes prolonged exposure to hepatotoxins, oxidative stress, viral infections, and metabolic disturbances, leading to progressive hepatocyte degeneration and impaired liver homeostasis. *Pergularia daemia*, a medicinal plant traditionally used in the management of liver disorders and jaundice, is rich in bioactive compounds such as saponins, flavonoids, and alkaloids, which exhibit antioxidant, anti-inflammatory, and cytoprotective properties.The present study investigates the in-vitro hepatoprotective potential of *Pergularia daemia* leaf extract against toxin-induced hepatocyte injury, using diosgenin as a standard reference. Human hepatocyte cell lines (HepG2) were exposed to hepatotoxic agents to induce oxidative stress-mediated damage. Assessment parameters included cell viability (MTT assay), leakage of hepatic enzymes (ALT, AST, ALP), and oxidative stress markers such as reactive oxygen species (ROS), malondialdehyde (MDA), superoxide dismutase (SOD), and reduced glutathione (GSH). Morphological changes in hepatocytes were examined microscopically to assess cytotoxicity and structural integrity. The findings indicate that *Pergularia daemia* extract significantly enhanced hepatocyte viability, reduced liver enzyme leakage, and restored antioxidant balance in toxin-exposed hepatocytes, with effects comparable to diosgenin. These results suggest that *Pergularia daemia* exerts potent hepatoprotective effects through antioxidant and cytoprotective mechanisms. The study highlights its potential as a natural therapeutic agent for the management of liver cirrhosis. However, further in-vivo studies and clinical validation are required to establish its efficacy and safety for therapeutic applications.

Keywords: *Pergularia daemia*, hepatoprotective activity, diosgenin, liver cirrhosis, HepG2 cells
How To Cite This Article: Gandepalli Pratap Kumar, Kabesh A, Mageshwara Pt, Ponnudhurai R, Gangadharan R, Karthikeyan P, Dhivakaran Np, Anis Kumar M. Phytochemical Profile And Hepatoprotective Potential Of Pergularia Daemia: A Review. Int J Drug Deliv Technol. 2026;16(27s):645-653. Doi: 10.25258/ijddt.16.27s.74

1. INTRODUCTION

Liver cirrhosis refers to chronic, progressive and in most cases irreversible liver disease, which is characterized by massive fibrosis, nodular regeneration, and distortion of the normal liver architecture resulting in impaired liver functioning and higher mortality. Figure.1 shows a architectural design of an protective activity of *Pergularia daemia*. It is a terminal phase of different chronic liver diseases, such as non-alcoholic fatty liver disease (NAFLD), alcoholic liver disease, viral hepatitis, and metabolic disorders. The pathogenesis of cirrhosis is complicated and includes sustained oxidative stress, prolonged inflammation, hepatic stellate cells activation, and over-level of extracellular matrix components [1, 2, 3].

*Author for Correspondence: aniskumarmani@gmail.com

Such pathological processes break the integrity of hepatocytes and affect the key liver processes including detoxification, protein production and stability of metabolic activities.

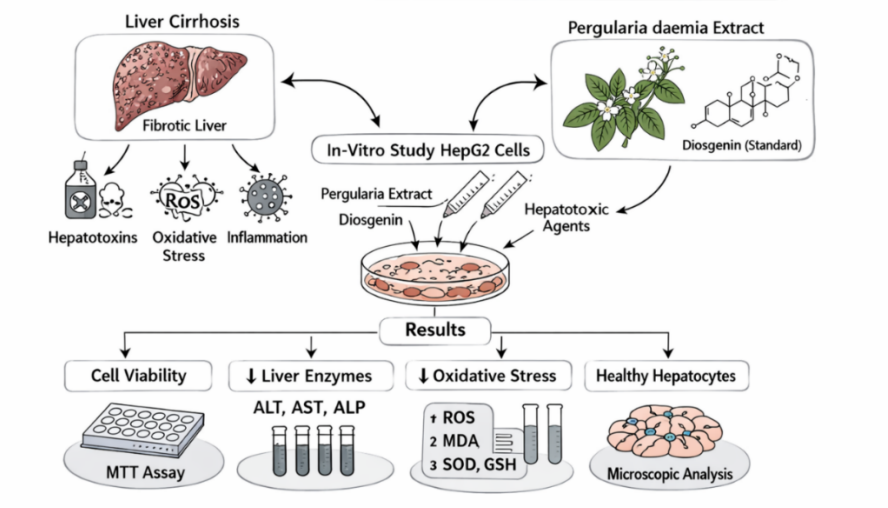

Figure.1 Hepatoprotective activity of *Pergularia daemia* in liver Cirrhosis

The burden of liver diseases has in the recent years significantly risen in the world because of the change in lifestyle, the dietary habit, and environmental factors. The traditional pharmacological interventions are not effective enough to reverse liver damage and have been linked to adverse side effects and thus, there is the need to develop safer and more effective therapeutic alternatives [4, 5, 6]. This has seen an increasing interest in natural products and phytochemicals that are associated with multi-targeted therapeutic effects and reduced toxicity profiles. Natural herbs and plant-based extracts have shown significant promise in the ability of controlling the major pathobiological mechanisms that lead to liver damage, such as oxidative stress, inflammation, and apoptosis [7, 8, 9, 10]. Steroidal saponins, as one of the natural bioactive compounds, have received especial interest due to their hepatoprotective property. Diosgenin is a naturally occurring steroidal sapogenin that has been widely researched in terms of its pharmacological properties, which are antioxidant, anti-inflammatory, anti-fibrotic and lipid-regulating effects. It is very important to suppress hepatic injury by regulating a variety of molecular signaling pathways including Nrf2, mTOR, and inflammatory cascades [1, 2, 11]. These characteristics render diosgenin a perfect standard compound to determine the hepatoprotective activity in experimental tests. *Pergularia daemia* is a commonly found medicinal plant in the tropical and subtropical areas that has long been involved in ethnomedicine as a remedy to numerous disorders, liver disorders, inflammation, and digestive problems. This plant contains a large amount of various phytochemicals including flavonoids, alkaloids, glycosides and terpenoids that have been reported to possess antioxidant and cytoprotective properties [12, 13, 14]. These methods are necessary to screen first prior to in-vivo and clinical research. Thus, this review will critically evaluate the hepatoprotective efficacy of *Pergularia daemia* with the use of diosgenin as a reference compound in a test-tube model of liver cirrhosis. The research incorporates available resources on phytochemicals-based hepatoprotection, molecular pathways of liver damage, and experimental research to give a holistic view on its treatment potentials.

1.1 Hepatoprotective role of diosgenin

A naturally occurring steroidal sapogenin, Diosgenin, has turned out to be an effective hepatoprotective agent because of its multi-faceted pharmacological activity. It is mostly obtained by plants like Dioscorea species and it has been significantly explored in regard to its use in alleviating liver-related diseases. The other important processes involved in its hepatoprotective activity are that it can control oxidative stress which is one of the biggest contributors to hepatocellular injury and liver cirrhosis progression. Research has shown that diosgenin increases the antioxidant defense system by stimulating the nuclear factor erythroid 2 related factor 2 (Nrf2) and thus increases the expression of detoxifying enzymes and decreases the reactive oxygen species (ROS) [1, 15]. Besides being an antioxidant, diosgenin is also essential in regulation of lipid metabolism especially in non-alcoholic fatty liver disease (NAFLD) which precedes cirrhosis. It is reported to have a great effect in curbing hepatic lipid accumulation through the regulation of major metabolic pathways and lipid synthetic/degradation enzymes. Moreover, the diosgenin modulates ferroptosis-mediating pathways, which inhibits lipid peroxidation and cell injury in hepatocytes [16, 17]. These results focus on its therapeutic value in eliminating fatty liver development into the hepatic diseases. Another such vital condition in the development of liver diseases is inflammation whereby diosgenin has demonstrated powerful anti-inflammatory properties by blocking several signalling pathways. It is important to note that it inhibits the NLRP3 inflammasome activation leading to the secretion of pro-inflammatory cytokines and ensuing liver damage [18]. In addition, the recent findings have also stated that diosgenin is capable of blocking STING-mediated

inflammatory signals, which ultimately suppress immune-mediated hepatic injuries [19]. These are the anti-inflammatory processes that play vital roles in the prevention of chronic liver injury and fibrosis. In addition to these effects, diosgenin also has anti-fibrotic and cytoprotective effects. It is demonstrated to mitigate chemically induced liver damage, including carbon tetrachloride (CCl4)-induced hepatotoxicity, and suppress cellular apoptosis and improve the survivability of hepatocytes [20]. Moreover, its engagement in the regulation of lipid metabolism and inflammatory genes expression also suggests that it can be used as a thorough hepatoprotective factor [11, 21]. Together, the studies provide diosgenin as a commonplace of reference in assessing the hepatoprotective activity using experimental models.

1.2 *In-vitro* hepatocyte models

The *In-vitro* hepatocyte models have proven to be important in the assessment of hepatoprotective activity because they are reproducible, cost-effective, and allow mechanistic understanding under controlled experimental conditions. These carcinoma hepatocyte cells are derived of human origin and have many biochemical features of normal hepatocytes such as enzyme activity involving detoxification and lipid metabolism and can be used to screen hepatoprotective agents [22, 23]. HepG2 cells have been used in several studies to determine 4stress. In most cases, hepatotoxic conditions are brought about by the use of hydrogen peroxide (H_2O_2) or carbon tetrachloride (CCl_4) which produce reactive oxygen species and are similar to the pathological liver injury. The activity of test compounds as protection is then tested in regard to parameters of cell viability, intracellular ROS, lipid peroxidation, and antioxidant enzyme activity [24, 25]. These tests give important clues on the cytoprotective nature of the phytochemicals.

Besides the HepG2 models, primary hepatocyte cultures, and liver slice models have also been considered to be *In-vitro* investigated. An example is the culture systems of goat liver slices which have been employed in the evaluation of the hepatoprotective activity of plant extracts in systems that are closely similar to the in-vivo conditions [24]. These models can be used to assess the tissue-level response, enzyme leakage, and structural integrity, and this will provide a more complete picture of the hepatoprotection. Also, more sophisticated *In-vitro* methods use a molecular-level analysis to determine which signaling pathways can be found in hepatocyte protection. Natural compounds have been shown to alter pathways that include Nrf2-mediated antioxidant response and apoptosis in oxidatively-stressed hepatocytes [22, 26]. These results demonstrate the significance of *In-vitro* models in closing the gap between traditional medicine and pharmacological validation so that systematic assessment of compounds such as *Pergularia daemia* can be compared with other modern agents such as diosgenin.

1.3 Oxidative stress and Molecular pathways

Oxidative stress is a key factor in the pathogenesis of liver diseases such as liver cirrhosis, where the system to maintain a balance between reactive oxygen species (ROS) development and antioxidant defense system is broken. Overproduction of ROS causes lipid peroxidation, oxidation of proteins, DNA damage and eventual apoptosis or necrosis of hepatocytes. This oxidative disequilibrium is deemed as a leading cause of the instigation of inflammatory and fibrotic pathways in the liver [8, 27]. Thus, the oxidative stress deficiency has become a major treatment approach in hepatoprotection. The activation of the Nrf2 signaling pathway that regulates the expression of the antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione peroxidase is one of the most important mechanisms. Nrf2 activation increases resistance of cells to oxidative stress and hepatocyte survival in stress [15, 28]. Oxidative stress is also related closely to inflammatory signaling pathways in liver diseases. The NLRP3 inflammasome is very important in mediating inflammatory responses by facilitating the release of pro-inflammatory cytokines like interleukin-1 2. Similar hepatoprotective effects demonstrated by the oxidative stress effect have also been observed in other natural compounds. As an example, phytochemicals and flavonoids of pharmaceutical plants could increase antioxidant activity and decrease ROS levels in hepatocyte models [22, 29]. Plant compounds, including ginsenosides and other molecules derived by plants have demonstrated efficacy in lowering inflammation and oxidation damage through mechanisms like SIRT1 activation [30]. Additionally, MAPK and autophagy related signaling pathway oxidative stress-mediated signaling pathways have also been implicated in liver injury and their modulation has been found to promote hepatoprotection [31].

1.4 Natural Compounds in Liver Protection

The use of natural compounds of medicinal plants has received great interest in the hepatoprotective capacity of these products because of their varied bioactivity components and multi-target-effected activities. Such compounds as flavonoids, saponins, polyphenols, and alkaloids have powerful antioxidant, anti-inflammatory, and anti-fibrotic effects, which are effective in reducing liver damage and inhibiting the development of the disease [12, 13]. A number of experimental studies have indicated the effectiveness of plant extracts in hepatocyte defense against the effects of toxicity caused by chemicals. An example is that the extract of Rosmarinus officinalis and mulberry leaves have demonstrated a substantial decrease in the oxidative stress markers and an enhancement of antioxidant enzyme activity in hepatotoxic models [22, 32]. Likewise, *In-vitro* systems (liver slice cultures or HepG2 cells) were used to evaluate the protective effects of methanolic extracts of medicinal plants in CCl_4 and hydrogen peroxide-induced damage and found that they preserved cell viability and reduced lipid peroxidation [23, 24]. One group of naturally occurring glycosides specifically saponins has also been identified in the

treatment of liver diseases. These are compounds known to control the cholesterol level, lower lipid levels, and enhance the hepatic functions by controlling the metabolic routes [7, 33]. Moreover, it has been shown that natural compounds have an effect on major signaling pathways in liver regeneration and repair, such as TGF-B signaling and apoptosis-related pathways [3, 34]. These mechanisms play a very important role in the prevention of fibrosis and recovery of hepatocytes.

In addition, recent studies have also pointed to the ability of herbal formulations and bioactive molecules to have an anti-inflammatory and anti-oxidative effect. Other compounds like ginsenosides and alantolactone have been promising in terms of alleviation of hepatic inflammation and oxidative injury by stimulating pathways such as SIRT1 and inhibiting cytokines [27, 30]. Plant-based extracts and polysaccharides are also hepatoprotective with important antioxidant-defense system effects and cellular integrity [26, 35]. These results justify a further study of the medicinal plants like *Pergularia daemia* as a viable source of liver disease treatment.

2. METHODOLOGY

2.1 Experimental models for hepatotoxicity assessment

Testing of the hepatoprotective activity is based on the effective experimental models that precisely reflect the conditions of hepatoprotection upon liver injury. Among them, *In-vitro* hepatocyte models are widely used because of the possibility to be reproducible, scalable, and able to offer mechanistic insights. Human hepatocellular carcinoma cell lines are most popular and mostly HepG2 cell lines are used because of their preservation of liver-specific functions including albumin production, enzyme activity, and lipid metabolism [22, 23, 25]. These models can be used to monitor controlled exposure to toxic agents and treatment compounds, which allow the accurate determination of cytotoxicity and cytoprotection. In addition, in-vivo models that are induced with the hepatotoxin carbon tetrachloride (CCl_4) and diethylnitrosamine are commonly employed to confirm *In-vitro* studies by assessing histopathological changes and systemic biochemical changes [20, 36]. These models are combined to make sure that the hepatoprotective activity is fully assessed at various levels of nature.

2.2 Induction of oxidative stress and Liver injury

An essential methodological aspect to hepatoprotective investigations is oxidative stress induction, which is a replication of the pathological process of liver diseases. To produce intracellular reactive oxygen species (ROS), which cause oxidative damage, mitochondrial dysfunction and apoptosis, chemical agents are often employed, including hydrogen peroxide (H_2O_2) [22, 26]. In the same manner, carbon tetrachloride (CCl_4) is also metabolized by the hepatic cytochrome P450 enzymes into extremely reactive trichloromethyl radicals, which trigger lipid peroxidation and rupture cellular membranes [20]. Ethanol models of hepatotoxicity are also common to model alcohol induced liver damage, with oxidative stress and inflammatory reactions being the dominant players [37]. The biochemical parameters to determine the degree of induced hepatotoxicity are the high levels of ROS, high levels of malondialdehyde (MDA), and loss of endogenous antioxidant systems like glutathione (GSH), superoxide dismutase (SOD), and catalase [28]. These markers act as essential endpoints of the evaluation of oxidative injury and intervention.

2.3 Evaluation of hepatoprotective activity

The evaluation of hepatoprotective effects is done through cell based, biochemical and enzymatic testing. The protective effect of the test compounds against induced toxicity has been widely used through the cell viability assays, including MTT, XTT and trypan blue exclusion [22, 23]. These assays are used to determine the activity and integrity of the mitochondria of the cell, which helps in revealing the survival and proliferation of cell. Lactate dehydrogenase (LDH) leakage tests are used to determine the extent of cellular damage with a higher LDH release indicating cellular harm and lower LDH release indicating shield action. Furthermore, lipid peroxidation tests which determine the amount of MDA are applied in the quantification of oxidative injury to cellular membrane [28, 35]. The antioxidant enzyme enzyme assays such as the SOD, catalase, and glutathione peroxidase enzyme assays are performed to determine the capability of compounds to restore redox balance. Tumor necrosis factor-alpha (TNF-alpha), interleukins, and other cytokines are also assessed to determine the anti-inflammatory effects [30].

2.4 Molecular and Signaling pathway analysis

Contemporary methodological styles focus on investigating molecular pathways of signaling to comprehend the pathways involved in hepatoprotection. Investigations of the regulation of major pathways that mediate oxidative stress, inflammation, and apoptosis are conducted by gene expression studies by use of methods like RT-PCR and Western blotting [28, 31]. The Nrf2 signaling pathway is one of the most important pathways as it controls the expression of antioxidant and detoxification enzymes. On the same note, the MAPK pathway is an important mediator of cellular responses to stress and inflammation and the inhibition of the pathway is linked to attenuated liver injury [31]. The interference with the apoptotic proteins, such as Bcl-2 and caspases, are also analyzed in order to evaluate the anti-apoptotic properties of therapeutic agents. These molecular studies would give greater insight into the mechanism of action of bioactive compounds on the cellular level, and offer protection.

2.5 Role of Natural Compounds in Experimental Validation

The above methodologies are used to evaluate the hepatoprotective potential of natural compounds and the plant-derived extracts systematically. Many phytochemicals such as flavonoids, polysaccharides and saponins have been shown to have a great protective

potential by increasing antioxidant defense systems and decreasing oxidative stress [26, 35]. The compounds also regulate inflammatory responses and enhance the cellular resistance to toxic attacks. Diosgenin can be used as a reference because it has been well-documented that it is an antioxidant and anti-inflammatory, and researchers can use this as a benchmark to determine the efficacy of new plant extracts like *Pergularia daemia*. These are needed in order to translate traditional medicinal knowledge into scientifically testified therapeutic interventions in the treatment of liver cirrhosis.

3. Current research on *P. daemia*

The current review offers good evidence on how natural compounds, especially diosgenin, have a high potential of hepatoprotection and how medicinal plants like *Pergularia daemia* offer a new perspective on the treatment of liver cirrhosis in the light of medicinal plants. These pathological processes have also been reported to be consistently targeted by diosgenin in a variety of molecular mechanisms, which makes it an effective standard of comparative assessment [15, 16, 17]. The recent developments in the development of drugs have delved in the modification and delivery of diosgenin to increase the therapeutic effects. As an example, the formation of diosgenin-laden nanoparticles has shown enhanced bioavailability and delivery of drugs to the liver target, with enhanced effects of hepatoprotection [38]. Likewise, synthetic analogs of diosgenin have demonstrated enhanced antioxidant activity and enhanced pharmacokinetic characteristics, implying that the analogs can be used in the future in clinical settings [39]. These developments point to the translationalism of diosgenin-based treatment in management of liver disease.

Diosgenin has also been studied to prevent hepatocellular carcinoma and other metabolic diseases, in addition to hepatoprotection. This property of balancing the signalling pathway that is associated with cell proliferation, apoptosis, and inflammation adds to its anti-cancer property [40, 41]. Also, its connection to other pathways like PI3K/Akt and the ERK also promotes its activities in promoting cell survival and alleviating apoptosis caused by oxidative stress [42]. Natural compounds that are found in foods and drugs still become increasingly important because of the safety and multi-targeted activity. Research on plant-based bioactive compounds has shown that they can be used to control metabolic dysfunctions and liver health with the approaches of network pharmacology [43]. In this regard, *Pergularia daemia* turns out to be a promising subject of hepatoprotective research.

3.1 Comparative Analysis

The comparative analysis of hepatoprotective agents shows the high therapeutic value of diosgenin and suggests the investigation of the use of *Pergularia daemia* as an alternative. Interrelated processes such as oxidative stress, inflammation, lipid dysregulation, and apoptosis cause liver cirrhosis. Diosgenin has proven to be extremely effective in all of these mechanisms and as such, it is the best model in comparison with the plant-based hepatoprotective compounds [15, 16, 17]. These processes play a vital role in regulating the process of fibrosis in liver cirrhosis. Another important issue in the management of liver diseases is the regulation of lipid metabolism. Diosgenin has also been used to decrease the hepatic lipid deposition as it alters the pathways of cholesterol transport and fatty acid metabolism [21, 11]. The given effect is especially significant in the prevention of the shift between fatty liver disease and cirrhosis. Moreover, saponins also have lipid-lowering effects, supporting the medical relevance of compounds of plant contributions [33].

Table 1: Mechanisms of hepatoprotection by diosgenin and Natural compounds

Mechanism	Key Effect	Outcome in Hepatocytes	References
Oxidative Stress Reduction	Activation of Nrf2 pathway, increased antioxidant enzymes	Reduced ROS, improved cell viability	8, 15, 16, 17
Anti-inflammatory Action	Inhibition of NLRP3 inflammasome, STING pathway	Decreased cytokine production	18, 19, 9
Lipid Regulation	Modulation of lipid metabolism pathways	Reduced lipid accumulation	11, 21, 33
Anti-apoptotic Effect	Regulation of apoptosis-related proteins	Increased hepatocyte survival	41, 42

Table 1, summarizes the major hepatoprotective mechanisms of diosgenin and related natural compounds. It clearly demonstrates that hepatoprotection is not mediated by a single pathway but involves a coordinated regulation of oxidative stress, inflammation, lipid metabolism, and apoptosis. Recent advancements have also focused on improving the therapeutic efficiency of diosgenin through novel delivery systems and structural modifications. For instance, diosgenin-loaded nanoparticles have shown enhanced bioavailability and targeted action, leading to improved hepatoprotective outcomes [38]. Similarly, synthesized derivatives of diosgenin exhibit increased antioxidant potential and better pharmacokinetic properties [39]. These developments indicate a shift towards translational applications of phytochemicals in modern medicine.

Table 2: Comparison of experimental models used in hepatoprotective studies

Model Type	Inducing Agent	Parameters Measured	Advantages	References
HepG2 Cell Line	H_2O_2, ethanol	Cell viability, ROS levels	High reproducibility	22, 25
Liver Slice Culture	CCl_4	Enzyme leakage, tissue integrity	Mimics *in-vivo* condition	24
Animal Models	CCl_4, DEN	Histopathology, biochemical markers	System-level validation	20, 36

Table 2, provides a comparative overview of commonly used experimental models in hepatoprotective research. *In-vitro* models such as HepG2 cells offer simplicity and mechanistic insights, while ex-vivo and in-vivo models provide physiological relevance. Its ability to modulate signaling pathways like PI3K/Akt and ERK contributes to reduced apoptosis and improved cellular survival [42]. Additionally, its potential role in preventing hepatocellular carcinoma highlights its importance beyond basic hepatoprotection [40]. In comparison, *Pergularia daemia* possesses a diverse phytochemical profile that suggests similar biological activities, including antioxidant and anti-inflammatory effects. However, unlike diosgenin, its mechanisms are not yet fully elucidated through advanced molecular studies. This creates a research gap that can be addressed through *In-vitro* investigations using standardized methodologies and comparative analysis with diosgenin. Overall, the findings indicate that hepatoprotective activity is governed by complex, interconnected pathways. The integration of biochemical, cellular, and molecular analyses is essential for developing effective and scientifically validated treatments for liver cirrhosis. The quantitative evidence presented by different experimental studies points to the fact that hepatoprotection is closely associated with decreasing the levels of oxidative stress, recovery of the levels of antioxidant enzymes, and blockage of the production of inflammatory mediators. The parameters give quantifiable goals on how effective compounds like diosgenin and the plant extracts like *Pergularia daemia* [15, 16, 17]. Intracellular reactive oxygen species (ROS) levels reduction is one of the most important hepatocyte protection indicators.

Table 3: Quantitative comparison of antioxidant and Cytoprotective effects

Parameter	Control (Toxic Condition)	Diosgenin Treatment	Natural Extracts (Average)	References
ROS Levels (%)	100% (baseline damage)	35–60%	55–80%	8, 15, 16
SOD Activity (U/mg protein)	20–30	45–65	35–50	17, 28
Catalase Activity (U/mg protein)	15–25	40–55	30–45	15, 35
Cell Viability (%)	40–50%	75–90%	60–75%	22, 25

Diosgenin has been depicted to inhibit ROS formation by about 40 65 per the conditions of an experiment, and has been demonstrated to augment antioxidant enzyme activities including superoxide dismutase (SOD) and catalase by 30-55 percent [15, 16]. Comparatively, general plant extracts are found to exhibit the moderate to antioxidant effect; usually, this is the markers of oxidative stress which lie between 20-45% reduction [8, 9]. This quantitative variation shows the significance of diosgenin as a standard sample in the assessment of new hepatoprotective agents The quantitative comparison of antioxidant activities and cytoprotective activities is presented in Table 3.

Besides the reduction of oxidative stress, the regulation of inflammatory mechanisms is another essential factor of hepatoprotective activity. Diosgenin has demonstrated the ability to decrease pro-inflammatory cytokines including TNF- and IL-6 by about 45-70 percent, whereas other natural products usually reduce by 30-55 percent [18, 19]. This is added anti-inflammatory effect that leads to its preventing effects of chronic liver injury and progression of fibrosis. Diosgenin also plays an important role in lipid metabolism especially in diseases like non-alcoholic fatty liver disease. Quantitative analyses show that hepatic lipid deposition decreased by 35-60 percent after diosgenin treatment as opposed to 20-40 percent when only general phytochemicals are used [21, 11]. This shows that it is better at controlling lipid homeostasis and steatosis prevention.

Table 4: Comparative analysis of anti-inflammatory and Lipid-regulating effects

Parameter	Control (Disease State)	Diosgenin Treatment	Natural Compounds (Average)	References
TNF-α Levels (%)	100%	30–55%	45–70%	18, 19
IL-6 Levels (%)	100%	35–60%	50–75%	8, 9
Lipid Accumulation (%)	100%	40–65%	60–80%	11, 21
Apoptotic Cells (%)	100%	25–50%	40–65%	41, 42

A more in-depth comparison between anti-inflammatory and lipid-regulating effects is shown in Table 4. Diosgenin has exhibited more inflammatory cytokine and lipid accumulation reduction than general natural compounds. The other observation that is significant is the increase in efficiency of the therapeutic using developed formulations. Nanoparticle delivery systems have demonstrated 2-to-3-fold increase in bioavailability leading to an increase in hepatoprotective effects [38]. Likewise, structural alterations of diosgenin have resulted in derivatives that are more antioxidant active and whose pharmacokinetic properties are enhanced [39]. These developments are signs that it is possible to optimize natural compounds to use them clinically. Diosgenin has a variety of effects on signaling pathways, such as Nrf2, mTOR, and inflammasome-mediated pathways, with a holistic protective action on liver damage [17, 43]. Contrastingly, most of the natural compounds act on a few pathways, potentially decreasing the general effectiveness of the compound. With regard to *Pergularia daemia*, its phytochemical profile may propose that it has hepatoprotective action, but quantitative and mechanistic confirmation is scarce.

4. Future perspectives

The hepatoprotective agents in future research must be directed towards the gap that exists between research and clinical practice, especially with references to natural compounds like diosgenin and medicinal plants like *Pergularia daemia*. Recent research indicates that the absorption and tissue-specific action of it can be improved by using nanoparticle-based formulations, liposomal encapsulation, and targeted delivery systems to achieve better hepatoprotective results [38]. On the same note, synthesis and structural alteration of diosgenin derivatives have demonstrated good prospects in increasing antioxidant ability and stability and new prospects of drugs development have been opened [39].

Thus, further research must be conducted to discover a compound capable of acting on several pathways such as Nrf2, mTOR, and inflammatory cascades at once [43]. Using network pharmacology and systems biology one will be able to study the synergistic interactions between phytochemicals and develop combination therapies as a strategy to enhance their efficacy and improve their effectiveness [41]. Also, artificial intelligence and computational modelling can be used to predict drug-target interactions and compound design optimization.

To conclude, the future studies need to focus on improved drug delivery methods, multi-targeted delivery, mechanistic validation of medical plants and clinical translation in order to come up with effective and safe hepatoprotective remedies of liver cirrhosis.

5. Conclusion

Liver cirrhosis is one of the most vital worldwide health issues with progressive hepatic injury which is induced by oxidative stress, inflammation, lipid dysregulation, and apoptosis. The shortcomings of the conventional therapies have increased a struggle to find alternatives to them that are safer and more effective, especially natural. In this regard, bioactive agents like diosgenin have proven to produce a great amount of hepatoprotection by acting via their multi-target effects, which are antioxidant activity, anti-inflammatory activity, and metabolic regulation. This review has indicated the critical role of *In-vitro* models of the hepatocytes in assessing the protective potential of the natural compounds and given a comparative insight into their effectiveness. Diosgenin is also a reliable standard with the virtue of a strong pharmacological profile and a steady performance in a variety of experimental parameters. Simultaneously, *Pergularia daemia* as one of the medicinal plants possesses promising potential due to the high content of phytochemicals and traditional application in liver-related diseases. Nonetheless, though the results were promising, the hepatoprotective effects of *Pergularia daemia* are to be further scientifically demonstrated with the help of the advanced molecular and experimental research. In general, the combination of traditional knowledge with the use of modern research possibilities can lead to the development of the new, effective, and safe therapeutic approaches in the management of liver cirrhosis and other hepatic disorders.

References

[1] Mohseni-Moghaddam, P., Khanmohammadi, M., and Roghani, M., "Literature review on hepatoprotective effects of diosgenin: possible mechanisms of action," *Frontiers in Pharmacology*, vol. 14, p. 1226548, Sep. 2023.

[2] Kumar, A., et al., "Role of diosgenin in gastrointestinal cancers: recent trends and future perspectives," *Medical Oncology*, vol. 42, no. 9, p. 397, Aug. 2025.

[3] Tian, C., et al., "Pharmacological and therapeutic effects of natural products on liver regeneration—a comprehensive research," *Chinese Medicine*, vol. 20, no. 1, p. 57, May 2025.

[4] Oh, K.K., et al., "The convergent application of metabolites from *Avena sativa* and gut microbiota to ameliorate non-alcoholic fatty liver disease: a network pharmacology study," *Journal of Translational Medicine*, vol. 21, no. 1, p. 263, Apr. 2023.

[5] Antwi, M.B., et al., "Unlocking therapeutic potential: exploring cross-talk among emerging nuclear receptors to combat metabolic dysfunction in steatotic liver disease," *npj Metabolic Health and Disease*, vol. 2, no. 1, p. 13, Jul. 2024.

[6] Wang, Y., Wu, J., and Shi, A., "Literature review on the use of herbal extracts in the treatment of non-alcoholic fatty liver disease," *Endocrine, Metabolic & Immune Disorders - Drug Targets*, vol. 22, no. 11, pp. 1123–1145, Sep. 2022.

[7] Xue, S., et al., "Research progress and prospects of saponins in the treatment of NAFLD: a narrative review," *Molecules*, vol. 30, no. 21, p. 4247, Oct. 2025.

[8] Fang, X., et al., "Molecular mechanism pathways of natural compounds for the treatment of non-

alcoholic fatty liver disease," *Molecules*, vol. 28, no. 15, p. 5645, Jul. 2023.

[9] Song, Z., et al., "The active components of traditional Chinese medicines regulate the multi-target signaling pathways of metabolic dysfunction-associated fatty liver disease," *Drug Design, Development and Therapy*, pp. 2693–2715, Dec. 2025.

[10] Banerjee, T., et al., "Herbal medicines for the treatment of liver cirrhosis," in *Role of Herbal Medicines: Management of Lifestyle Diseases*, Singapore: Springer, 2024, pp. 185–209.

[11] Khateeb, S., Albalawi, A., and Alkhedaide, A., "Regulatory effect of diosgenin on lipogenic genes expression in high-fat diet-induced obesity in mice," *Saudi Journal of Biological Sciences*, vol. 28, no. 1, pp. 1026–1032, Jan. 2021.

[12] Venmathi Maran, B.A., et al., "Hepatoprotective potential of Malaysian medicinal plants: a review on phytochemicals, oxidative stress, and antioxidant mechanisms," *Molecules*, vol. 27, no. 5, p. 1533, Feb. 2022.

[13] Zhou, Z., et al., "Application of herbs and active ingredients ameliorate non-alcoholic fatty liver disease under the guidance of traditional Chinese medicine," *Frontiers in Endocrinology*, vol. 13, p. 1000727, Sep. 2022.

[14] Meng, Y.F., Wu, Q.Y., and Zheng, Z., "Research progress on traditional medicine treatment for metabolic-associated fatty liver disease."

[15] Zhang, X., et al., "Diosgenin ameliorating non-alcoholic fatty liver disease via Nrf2-mediated regulation of oxidative stress and ferroptosis," *Diabetes, Obesity and Metabolism*, vol. 26, no. 12, pp. 5745–5756, Dec. 2024.

[16] Wang, L., et al., "Diosgenin alleviates lipid accumulation in NAFLD through the pathways of ferroptosis defensive and executive system," *The Journal of Nutritional Biochemistry*, vol. 140, p. 109886, Jun. 2025.

[17] Yin, ., et al., "Diosgenin attenuates nonalcoholic fatty liver disease through mTOR-mediated inhibition of lipid accumulation and inflammation," *Chemico-Biological Interactions*, vol. 405, p. 111306, Jan. 2025.

[18] Yu, W., et al., "Diosgenin attenuates metabolic-associated fatty liver disease through the hepatic NLRP3 inflammasome-dependent signaling pathway," *International Immunopharmacology*, vol. 138, p. 112581, Sep. 2024.

[19] Song, C., et al., "Protective effects of diosgenin against non-alcoholic fatty liver disease through inhibiting the STING-dependent inflammatory pathway," *European Journal of Medical Research*, Mar. 2026.

[20] Ghosian-Moghaddam, M., Mohseni-Moghaddam, P., and Roghani, M., "Therapeutic potential of diosgenin in amelioration of carbon tetrachloride-induced murine liver injury," *Drug Research*, vol. 74, no. 4, pp. 156–163, Apr. 2024.

[21] Yan, M., et al., "Diosgenin as a substitute for cholesterol alleviates NAFLD by affecting CYP7A1 and NPC1L1-related pathway," *Phytomedicine*, vol. 125, p. 155299, Mar. 2024.

[22] Zheng, Q., et al., "Investigating the hepatoprotective properties of mulberry leaf flavonoids against oxidative stress in HepG2 cells," *Molecules*, vol. 29, no. 11, p. 2597, May 2024.

[23] Chiangsom, A., et al., "Protective effect of Phikud Navakot extract against hydrogen peroxide-induced oxidative stress in HepG2 cells," *The Thai Journal of Pharmaceutical Sciences*, vol. 43, no. 4, 2025.

[24] Nambiar, ZM.K., and Varghese, V., "In vitro hepatoprotective activity of methanolic leaf extract of *Acalypha indica* against CCl4 induced hepatotoxicity in goat liver slice culture," *Trends in Sciences*, vol. 20, no. 4, p. 4562, Jan. 2023.

[25] Yang, D.K., et al., "Bulbils of aerial yam attenuate ethanol-induced hepatotoxicity in HepG2 cells through inhibition of oxidative stress by activation of the nuclear factor erythroid-2-related factor 2 signaling pathway," *Nutrients*, vol. 16, no. 4, p. 542, Feb. 2024.

[26] Abdul, N.S., and Marnewick, J.L., "Green rooibos extract attenuates high glucose induced oxidative stress in a human derived (HepG2) liver cell line," *South African Journal of Botany*, vol. 151, pp. 852–865, Dec. 2022.

[27] Wang, J., et al., "Alantolactone attenuates high-fat diet-induced inflammation and oxidative stress in non-alcoholic fatty liver disease," *Nutrition & Diabetes*, vol. 14, no. 1, p. 41, Jun. 2024.

[28] Y. H. Lu et al., "Rosmarinic acid exerts anti-inflammatory effect and relieves oxidative stress via Nrf2 activation in carbon tetrachloride-induced liver damage," *Food & Nutrition Research*, vol. 66, 2022.

[29] Mohammad, M., et al., "Amelioration of hepatic injury through oxidative stress management employing methanolic extract of crepe-ginger (*Cheilocostus speciosus*) flower," *Chemistry & Biodiversity*, vol. 22, no. 8, p. e202500261, Aug. 2025.

[30] Gao, Q., et al., "Ginsenoside Rg1 alleviates ANIT-induced cholestatic liver injury by inhibiting hepatic inflammation and oxidative stress via SIRT1 activation," *Journal of Ethnopharmacology*, vol. 319, p. 117089, Jan. 2024.

[31] Azzam, S.M., et al., "Revealing how phenytoin triggers liver damage and the potential protective effects of *Balanites aegyptiaca* fruit extracts: exploring Nrf2/MAPK/Beclin-1 signaling pathways," *Biomedicine & Pharmacotherapy*, vol. 165, p. 115265, Sep. 2023.

[32] Ielciu, I., et al., "Evaluation of hepatoprotective activity and oxidative stress reduction of *Rosmarinus officinalis* L. shoots tincture in rats

with experimentally induced hepatotoxicity," *Molecules*, vol. 26, no. 6, p. 1737, Mar. 2021.

[33] Xiao, M.Y., et al., "Natural saponins on cholesterol-related diseases: treatment and mechanism," *Phytotherapy Research*, vol. 39, no. 3, pp. 1292–1318, Mar. 2025.

[34] Asoka, A.S., et al., "Role of culinary Indian spices in the regulation of TGF-β signaling pathway in inflammation-induced liver cancer," *Molecular Nutrition & Food Research*, vol. 68, no. 11, p. 2300793, Jun. 2024.

[35] Li, Y., et al., "Structural characterization and in vitro hepatoprotective activity of an acidic polysaccharide from *Dendrobium nobile* Lindl. flower," *International Journal of Biological Macromolecules*, vol. 284, p. 138100, Jan. 2025.

[36] Liu, R.J., et al., "Effectiveness of Yigan Xiaozheng formula against diethylnitrosamine-induced liver cirrhosis in rats: JAK2/STAT3 pathway modulation and hepatocellular apoptosis reduction," *Traditional Medicine Research*, vol. 10, no. 10, p. 61, 2025

[37] Wu, Q., et al., "Pueraria extract ameliorates alcoholic liver disease via the liver–gut–brain axis: focus on restoring the intestinal barrier and inhibiting alcohol metabolism," *Journal of Agricultural and Food Chemistry*, vol. 72, no. 44, pp. 24449–24462, Oct. 2024.

[38] Mohamed, R., et al., "Diosgenin-loaded silver nanoparticles mitigate obesity-related metabolic dysfunction: an integrative analysis of biochemical, transcriptional, and molecular docking evidence," *Journal of Pharmaceutical Innovation*, vol. 21, no. 2, p. 116, Apr. 2026.

[39] Michalak, O., et al., "Antioxidant activity of novel diosgenin derivatives: synthesis, biological evaluation, and in silico ADME prediction," *Steroids*, vol. 188, p. 109115, Dec. 2022.

[40] Vittal, M., Menegassi, B., and Vinciguerra, M., "Risks, benefits, and molecular targets of fenugreek administration in the treatment of hepatocellular carcinoma," *Cancers*, vol. 18, no. 3, p. 458, Jan. 2026.

[41] Kumar, P., et al., "Network pharmacology-based study on apigenin present in the methanolic fraction of leaves extract of *Cestrum nocturnum* L. to uncover mechanism of action on hepatocellular carcinoma," *Medical Oncology*, vol. 39, no. 10, p. 155, Jul. 2022.

[42] Chen , M.Y., et al., "Diosgenin attenuates myocardial cell apoptosis triggered by oxidative stress through estrogen receptor to activate the PI3K/Akt and ERK axes," *The American Journal of Chinese Medicine*, vol. 51, no. 5, pp. 1211–1232, Jun. 2023.

[43] Prabha, S., et al., "Phytochemicals as chemosensitizers in the management of hepatocellular carcinoma," in *Liver Cancer and Phytomedicine: Chemoprevention, Chemo Sensitization and Chemotherapy Strategies*, 2025, pp. 241–305.