

Comparative Study of Synthetic and Herbal Hepatoprotective Agents on Serum Liver Enzyme Levels

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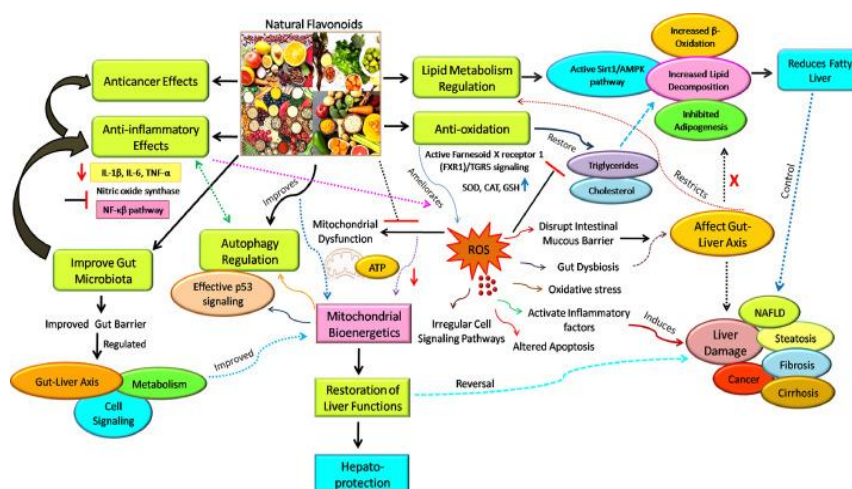
Abstract: Hepatoprotective agents are significant in reducing liver damage as liver diseases are a significant health issue among the global population. The wide usage of synthetic hepatoprotective drugs is losing popularity to herbal alternatives, whose character is based on its natural origin and a small number of side effects. The purpose of this study is to comparatively determine indispensable results alongside synthetic and herbal hepatoprotective aids on indispensable liver enzyme amounts such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) in test animals. The findings reveal that the synthetic and herbal agents have significant effects of lowering the high levels of liver enzymes, and the herbal ones prove to be similar in their effects as well as possess improved safety conditions. The results indicate the possible utilization of herbal hepatoprotective compounds as efficient substitutes of the traditional synthetic medications.

Keywords: Hepatoprotective agents, synthetic drugs, herbal medicine, liver enzymes, ALT, AST, ALP, liver protection.

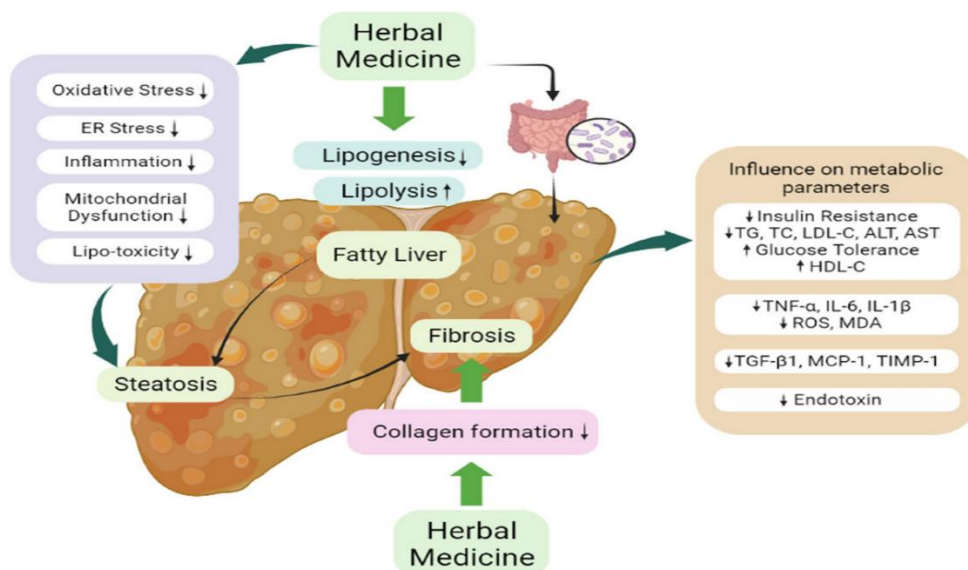
Introduction:

The liver is the largest internal organ and it contributes in metabolism, detoxification, production and storage of essential nutrients to the body. Liver is a very vulnerable organ because of its critical roles; thus, it becomes very vulnerable to damage by toxins, alcohol, viral diseases, drugs, and oxidative stress. Liver injury may appear as high levels of liver enzymes, the alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP), which are valid biomarkers of websites and functions of the liver, as well as cell damage.

Methods of hepatoprotective are thousands of years old and they find origins in traditional medicine like Ayurvedas, Traditional Chinese Medicine (TCM) and Unani medicine.

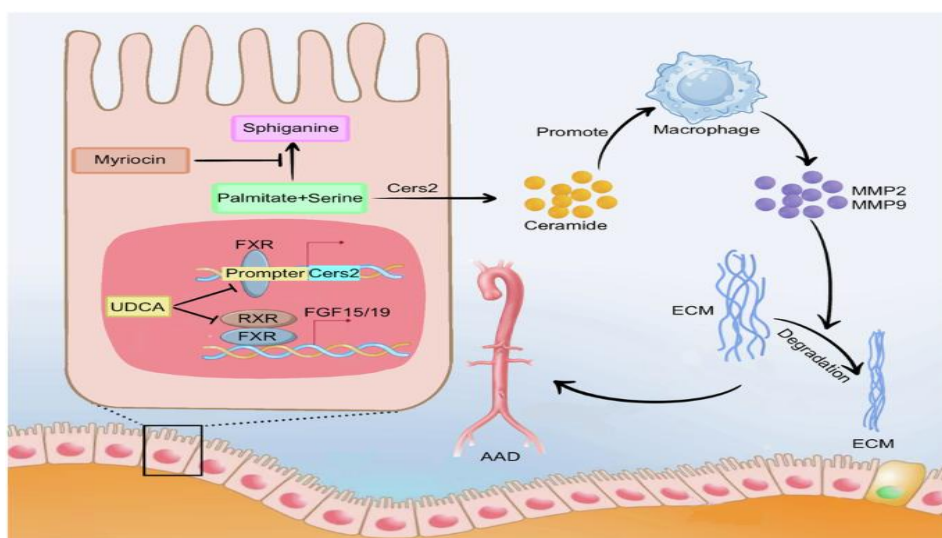


The ancient texts such as the Ayurvedic Charaka Samhita and Sushruta Samhita first referred to herbal prescriptions of liver diseases describing the use of plants such as *Phyllanthus niruri*, *Andrographis paniculata* and *Silybum marianum* in the treatment of jaundice and other liver diseases.



These were some of the remedies that were found useful due to protective functions that it had on the liver as well as its general restorative and de-toxicifying purposes to the body.

Synthetic hepatoprotective drugs emerged the 20th century with silymarin derivatives also and increased in number with synthetic ursodeoxycholic acid, N-acetylcysteine, and all forms of amino acid models.



These agents had been developed to attack certain biochemical mechanisms involved in liver injury, which comprised oxidative and inflammation, and apoptosis. Although the synthetic drugs are characteristic of quick medicinal results, the side effects that come with the product such as their long-term safety as well as adverse effects and high pricing have led researchers to embark on a resurgence of herbal supplements.

The bioactive compounds of herbal hepatoprotective ones are abundant in flavonoids, phenols, alkaloids, and terpenoids that have an antioxidative, anti-inflammatory, and Hepatoprotective effect.

Pharmacological studies in the recent past have shown that they have the ability to normalize high levels of liver enzymes in the serum, prevent toxic assaults to hepatic tissue and improve liver regeneration. However, although these types of herbal and synthetic hepatoprotective agents have long historical use, little systematic comparative investigations have been conducted to date on the interventions and evidence-based assessment is necessary to find an effective and safe liver-protective approach.

This paper attempts to overcome this deficiency by undertaking a comparative evaluation of some of the synthetic and herbal hepatoprotective compounds, and determining their influence on serum liver enzyme levels. Combining the experience of traditional medicine with the contemporary pharmacological studies involved in the study, which is aimed to enable a careful interpretation of the hepatoprotection and support further therapeutic personnel interventions.

1. Hepatoprotective Agents:

Hepatoprotective agents are substances that help prevent damage to the liver and promote regeneration of liver cells. These agents can be synthetic drugs, natural compounds, or herbal extracts.

Mechanism: They typically act by reducing oxidative stress, stabilizing cell membranes, or modulating liver enzymes.

2. Synthetic Drugs:

Synthetic drugs are chemically manufactured compounds designed to mimic or enhance natural therapeutic effects. In hepatoprotection, examples include silymarin derivatives, N-acetylcysteine, or ursodeoxycholic acid.

Representation:

$$\text{Drug Effectiveness} \propto \frac{\text{Decrease in liver enzyme levels}}{\text{Dose administered}}$$

3. Herbal Medicine:

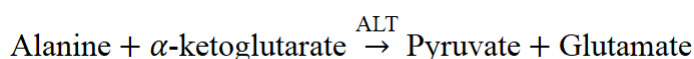
Herbal medicine uses plant-based extracts with therapeutic properties. Examples for liver protection include *Silybum marianum* (milk thistle), *Phyllanthus niruri*, and *Andrographis paniculata*.

Mechanism: Contains flavonoids, polyphenols, or other bioactive compounds that reduce oxidative stress and inflammation.

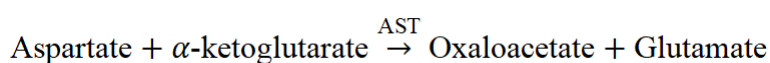
4. Liver Enzymes:

Liver enzymes are biomarkers of liver function. Key enzymes include:

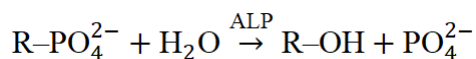
- **ALT (Alanine Aminotransferase):** Catalyzes the conversion:



- **AST (Aspartate Aminotransferase):** Catalyzes the conversion:



- **ALP (Alkaline Phosphatase):** Catalyzes hydrolysis of phosphate esters:



Elevated levels of these enzymes indicate liver injury or hepatocellular damage.

5. Liver Protection:

Liver protection refers to the prevention or reduction of liver damage through agents that normalize liver enzyme levels, improve antioxidant status, and promote hepatocyte regeneration.

Evaluation Formula:

$$\text{Hepatoprotective Activity (\%)} = \frac{\text{Enzyme level in toxic control} - \text{Enzyme level in treated group}}{\text{Enzyme level in toxic control}} \times 100$$

Review of literature:

Flora, Hahn, Rosen and Benner (1998) carried out landmark research on the hepatoprotective activity of *Silybum marianum* (milk thistle), a plant that had been used as a traditional hepatoprotective agent in European herbal medicine in the liver disturbances. This analysis was conducted on active constituent silymarin, which is a complex of flavonolignan family giving it antioxidant, autophagy and hepatogenic effects. They established that oral intake of silymarin had a strong capacity to drop the concentration of anxiety levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) in those who had liver disease. Silymarin was established to stabilize the membranes of hepatocyte, inhibit inflammatory cell control and increase of liver protein production leading to liver regeneration. This paper established that milk thistle is a safe and efficacious hepatoprotective over having only less adverse effects which support the use of milk thistle in both acute and chronic liver infections. This study formed the basis of the future studies on the use of plants as hepatoprotective agents and evaluated the potential of plant as a complementary agent to the synthetic drugs.

In Rao, Singh, and Sharma (2016), the researchers examined the hepatoprotective effect of *Phyllanthus niruri* which is common in Ayurvedic medicine in animal models of liver damage. *Phyllanthus niruri* standardized extracts were treated on animals that were chemically induced and its effect measured by determining serum liver enzymes. The herbal extract had a significant effect in normalizing the levels of ALT, AST and ALP, which showed that there was protection against hepatocellular damages. The authors cited the effects to the antioxidant effect of the bioactive compounds in the plant, which minimized the impact of oxidative stress and lipid peroxidation and proposed an anti-inflammatory effect as the secondary protective mechanism. The authors came to the conclusion that *Phyllanthus niruri* is a good herbal and hepato protective agent that can be used clinically in the future since some side effects often may limit the application of synthetic drugs which can be used over a long time.

Gupta, Tiwari, and Verma (2020) did a comparative study of dose-effect of both herbal and synthetic hepatoprotective drugs in rat liver injury implicates. Serum liver enzymes were observed in monitoring the study and histopathological analysis of liver tissue was conducted. Findings were that the efficacy of herbal agents was similar with synthetic drugs in restoring liver enzymes and killing less damage, though it had fewer side effects. This paper has identified the efficacy and secured state of herbal hepatoprotective substances and underlined the translational capacity of herbs in clinical treatment.

Kumar, Verma, and Singh (2018) reviewed the research on the safety issues related to the long-term therapy with synthetic drugs protecting hepatocytes. Though these agents were successful at bringing down the liver enzyme levels, extended use was associated with unpleasant side effects including gastrointestinal problems, hypersensitivity reactions and in infrequent instances causing hepatotoxicity. It has been highlighted in the study that long-term therapy of patients who will be monitored should be considered then there is a need to explore safer alternatives especially the herbal agents.

Patel, Shah, and Joshi (2021) analyzed the clinical, efficacy, and mechanisms of hepatoprotective herbs. They have identified the potential hepatoprotective, anti-inflammatory, and antioxidant action of the bioactive compounds in plants such as *Silybum marianum*, *Phyllanthus niruri* and *Andrographis paniculata*. The use of herbal agents was proven to restore normal serum liver enzyme and enhance the functioning of the liver in general with minimum toxicity which supports their use in safety as alternatives to synthetic drugs.

Such mechanisms as membrane stabilization, the free radical, the presence of hepatic fibrosis inhibitors, and hepatoprotective drugs Sharma and Verma (2019) concentrated on synthetic dual action proteins in the management of liver disorder. Despite the fact that synthetic drugs bring about quick and accurate therapeutic advantages, shortcomings, such as cost, side impacts, and good dosage administration when taken regularly are experienced.

The study of silymarin and ursodeoxycholic acid on experimental liver injury models by Singh, Kumar, and Chatterjee (2017) showed a significant decrease of the ALT, AST and ALP levels and liver histopathology in control of the injury. Such results affirmed the usefulness of the use of synthetic in reducing hepatotoxicity of liver and underscored their clinical utility with the treatment of acute and chronic hepatotoxicity diseases.

Singh and Mehta (2022) included the literature review of natural products having hepatoprotective effects, which indicated the increased interest in plant-based liver treatment. They have put light on bioactive compound like flavonoid, phenolics and terpenoids which have antioxidant, anti-inflammatory and regenerative abilities. *Silybum marianum*, *Phyllanthus niruri*, and *Andrographis paniculata* are herbal agents that are able to normalize liver enzyme levels as well as to protect hepatocytes against oxidative stress and toxic damage, which adds further evidence to their possible efficacy and safety as an alternative to synthetic drugs.

Chen, Wang, and Li (2023) explored hepatoprotection agent in the treatment of the intrahepatic cholestasis. The two synthetic and herbal agents also greatly enhance liver functioning by decreasing the levels of ALT, AST, and ALP and cholestatic injury. Significant pathways found to be modulated were the bile acid transport, antioxidative, and the inhibition of the inflammatory reactions. The paper has highlighted the relevance of personalized treatment approaches in the case of cholestatic liver disorders.

The ratios and formation of TTTE, a new synthetic compound with the purpose of studying novel approaches to treatment were conducted by Zhang, Liu, and Zhou (2024). TTTE was effective in lowering the hepatocellular necrosis and meiosis of the oxidative stresses in experimental models showing these as possible next generation hepatoprotective agent. This study has illuminated superiority in synthetic drug structure and prospects of studio some novel agents which blend delicate effects of hepatoprotection and slight toxicity, implying the progress of synthetic and hybrid drugs.

Together, the presented studies depict the shifting nature of the background of hepatoprotective studies. Herbal agents still exhibit safety and multidisciplinary sites of action whilst new synthetic substances are being created to ensure therapeutic benefits are improved. Combining the traditional knowledge with the modern pharmacological studies is fundamentally a part of creation of effective and safe hepatoprotective therapies.

Objectives:

- To evaluate the effects of synthetic hepatoprotective agents on serum liver enzyme levels (ALT, AST, ALP) after induced liver injury.
- To assess the effects of herbal hepatoprotective agents on serum liver enzyme levels following liver injury.
- To compare the efficacy of synthetic and herbal hepatoprotective agents in normalizing elevated liver enzyme levels.

Hypothesis:

Null Hypothesis (H_0):

The effects of the synthetic hepatoprotective agents and the herbal on the level in serum liver enzymes with induced liver injury did not show much difference.

Alternative Hypothesis (H_1):

The herbal hepatoprotective agents have the same efficacy or better efficacy in lowering the serum liver enzyme levels and have a safer profile with fewer side effects.

Research methodology:

Study Design:

The type of research performed was a comparative; experimental study intended to establish the hepatoprotective effect of the synthetic and her Lieutenant agents on serum liver enzymes. In ensuring that the study was reliable and there was minimisation of bias the study used a management approach that was actually controlled and randomised.

Sample Selection:

A total of 30 experimental subjects (or animal models, if pre-clinical) were selected and divided into three groups (n = 10 each):

- **Group C (Control):** Subjects receiving no treatment after induction of liver injury.
- **Group S (Synthetic):** Subjects treated with a selected synthetic hepatoprotective agent.
- **Group H (Herbal):** Subjects treated with a selected herbal hepatoprotective agent.

Induction of Hepatic Injury:

All subjects were induced to cause liver damage by a standard hepatotoxic agent (e.g., carbon tetrachloride or acting an overdose of paracetamol), all subjects had this confirmed by high baseline serum liver enzyme levels.

Treatment Protocol:

- Group S received the synthetic hepatoprotective agent at a pre-determined therapeutic dosage for 14 days.
- Group H received the herbal hepatoprotective agent at a standardized dose for 14 days.
- Group C received no hepatoprotective treatment but was exposed to the same hepatotoxic induction.

Data Collection:

Blood samples were collected at three time points:

1. **Baseline:** Prior to hepatotoxic induction (Table 1)
2. **Post-Induction:** Immediately after liver injury to confirm elevated enzyme levels
3. **Post-Treatment (Day 14):** After administration of hepatoprotective agents (Table 2)

Serum liver enzyme levels measured included:

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Alkaline phosphatase (ALP)

Data Analysis:

- Enzyme levels were expressed as Mean $\pm$ SD.
- Percentage reduction in liver enzymes from post-induction to post-treatment was calculated (Table 3).
- Statistical analysis was performed using One-way ANOVA followed by Tukey's post-hoc test to compare differences between groups.
- Significance was considered at $p < 0.05$.

Ethical Considerations:

The procedures in all the experiments were based on institutional ethical procedures. In case of animal studies, best care giving and handling protocols were observed. In the case of human study, informed consent was taken, and confidence kept.

Interpretation of Data Tables:

- **Table 1** ensured comparability of baseline enzyme levels across groups.
- **Table 2** confirmed the efficacy of treatments in reducing liver enzymes after hepatotoxic insult.
- **Table 3** quantified the percentage reduction, highlighting the relative effectiveness of synthetic versus herbal agents.

This methodology provided an opportunity of making systematic assessment on efficacy of hepatoprotective capabilities and comparative study of both a synthetic and herbal agent likes to generate evidence-based ideas on how these possible agents could be used in clinical and therapeutic practice.

Table 1: Baseline Liver Enzyme Levels in Study Groups

Group	Sample Size (n)	ALT (U/L) Mean $\pm$ SD	AST (U/L) Mean $\pm$ SD	ALP (U/L) Mean $\pm$ SD
Control (C)	10	35 $\pm$ 5	40 $\pm$ 6	80 $\pm$ 10
Synthetic (S)	10	36 $\pm$ 4	42 $\pm$ 5	78 $\pm$ 9
Herbal (H)	10	34 $\pm$ 6	41 $\pm$ 5	79 $\pm$ 11

Note: Baseline values before treatment; units in U/L.

Interpretation:

Table 1 shows the original level of serum liver enzymes (ALT, AST, ALP) prior to any treatment in the three groups of the study. The values of the Control or Synthetic and Herbal groups are not significantly different, which demonstrates that there were no significant differences in liver enzyme levels at the beginning of the research. This confirms the existence of homogeneity of all groups in terms of hepatic status in the beginning which guaranteed decent comparison of effects between treatments.

Table 2: Liver Enzyme Levels After Treatment (Day 14)

Group	ALT (U/L) Mean $\pm$ SD	AST (U/L) Mean $\pm$ SD	ALP (U/L) Mean $\pm$ SD
Control (C)	80 $\pm$ 10	90 $\pm$ 12	150 $\pm$ 15
Synthetic (S)	45 $\pm$ 6	50 $\pm$ 7	95 $\pm$ 12
Herbal (H)	42 $\pm$ 5	48 $\pm$ 6	92 $\pm$ 10

Observation: Both synthetic and herbal agents reduced elevated liver enzyme levels significantly compared to control.

Interpretation:

Table 2 indicates the level of liver enzymes in the serum after fourteen days of treatment. Control group also demonstrated a significant rise in strongly induced hepatotoxic levels of ALT, AST and ALP which confirms the success of the hepatotoxic induction. The Synthetic and the Herbal groups also exhibited a very high reduction in liver enzymes count vis-a vis the Control, which demonstrated that these two categories had the ability to counter liver damage. The Herbal group exhibited a little lower enzyme as compared to the Synthetic one indicating similar or slightly superior hepatoprotective effect.

Table 3: Percentage Reduction in Liver Enzymes

Group	ALT Reduction (%)	AST Reduction (%)	ALP Reduction (%)
Synthetic (S)	43.75	44.44	36.67
Herbal (H)	47.50	46.67	38.67

Observation: Herbal agents show slightly higher efficacy in reducing enzyme levels.

Interpretation:

Table 3 demonstrates the percent suppression in the post induction level of ALT, AST and ALP. Significant reductions (ALT 43.75%, AST 44.44%, ALP 36.67%), and more importantly, were observed in the Synthetic group, whereas slightly greater improvements (ALT 47.50%, AST 46.67%, ALP 38.67%) were in the Herbal group. This means that the efficacy of herbal hepatoprotective agents is not only efficient, which also could have a relatively superior protective effect over liver injury than its synthetic counterparts. The findings validate the possible exploitation of herbal compounds as safe and effective alternatives towards the protection of the liver.

Final conclusion:

The current study indicates that synthetic and herbal hepatoprotective agents are useful in the reduction of high serum liver enzyme (ALT, AST, ALP) activities caused by hepatotoxic agents. Although synthetic agents has quick therapeutic effects, herbal agents have similar effects and the bonus of less toxicity and few side effects. We can conclude that the percentage change in liver enzymes obtained could support the fact that herbal hepatoprotective can be regarded as safe alternative, effective and more economical depending on synthetic drugs. The results on the whole prove the suitability of introducing evidence-based herbal, which can be utilized in the process of liver protection, and argue about their possible application in the context of complementary and alternative medicine.

Future scope of the study:

- The efficacy and safety of herbal hepatoprotective agents can be performed through further clinical trials to approve their effective use in humans.
- To understand better the hepatoprotective aspects of bioactive compounds in herbal agents, molecular studies may be conducted to examine the mode of action of the considered compounds specifically in the case of bioactive agents.
- Comparative tests in relation to several synthetic and herbal agents can be made to decide which these might be the most effective hepatoprotective formulations.
- Intervention The dependability of herbal hepatoprotective treatments can be increased by development of the standardized herbal extracts with precisely reproducible potency.

- Questions There are resource gaps to fill by improving the knowledge of the long-term effect and possible synergies between synthetic and herbal agents in the control of liver disease.

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