

# AMELIORATIVE EFFECT OF POLYHERBAL FORMULATION FOR RESTORING LIVER HEALTH: A SYSTEMATIC REVIEW

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# ABSTRACT

Herbal medicines have been used for a wide range of ailments since ancient times. Two methods are used in Ayurvedic medicine formulation: one involves employing a single herbal preparation, or multiple combinations of them. Polyherbal formulation is the term for the later. Combining different herbs and plants to treat different medical diseases or to enhance general health is known as polyherbal medicine. Many civilizations all over the world have been using this kind of traditional medicine for centuries, and it is still commonly used today. Due to the active phytoconstituents found in single herbs, which are typically present in minute amounts and occasionally insufficient to produce the desired therapeutic effects, multi herb formulations have a well-established track record. According to scientific research, combining these plants with different potencies may theoretically result in a greater effect than using each plant alone or the sum of their individual effects. Positive interactions between herbs can therefore produce synergistic effect, which may take the form of pharmacokinetic or pharmacodynamic synergism. The great efficacy of polyherbal formulations in treating a wide range of illnesses accounts for their popularity. The growing demand of polyherbal formulations necessitates further scientific investigation in this area.

**Keywords:** Ayurveda, Polyherbal Formulation, Traditional Medical System, Liver Illnesses, Hepatoprotective, Liver Tonic

### **1. INTRODUCTION**

Raw herbs gave way to synthetic pharmaceuticals in the first part of 19th century when scientists started to extract and alter the key ingredients in herbal remedies. Yet, despite their potent pharmacological action, synthetic medications are shown to be comparatively not only costly but also have multitude of unwanted

side effects. Since, herbal medications come from nature and are seen to be safer, hence people are turning back to them these days Polyherb. Parasuraman et al. (2014)

Today approximately 80% of people in underdeveloped nations still receive their primary healthcare from traditional medicine, which is primarily based on various plant species. Approximately 500 plants are known to have therapeutic properties in ancient literature, and 800 species are employed in traditional indigenous medical systems. India, a country well-known for its biodiversity, is home to some 40,000 plant species, 15,000 of which are thought to offer therapeutic benefits. In India, communities use 7,000–7,500 plants to treat a range of illnesses Kotmire et al. (2024), Ali & Datusalia (2024), Singh et al. (2024). Numerous plant species are used in the many native medical systems, including Ayurveda, Siddha, and Unani, to cure various illnesses Sane (2002), Farnsworth et al. (1985), Abraham & Paridhavi (2013), Kunwar et al. (2010). Due to consumer demand, the \$1.5 billion annual market for herbal medicines is expanding in available widely. Using plants or plant material, either raw or processed, to cure disease is known as traditional herbal medicine, currently very popular throughout the globe Ngo et al. (2014).

Owing to the wide range of secondary metabolites that are functionally significant in medicinal plant species, natural products and their associated structures are major sources of newly developed medications Ingawale et al. (2015). Multi-herbal medicines, the blending of several herbs and plant components together to treat different medical issues or to enhance general health is the need of the hour. Throughout history, numerous nations have employed this kind of traditional medicine, which is still commonly used today. When many herbs are combined in a recipe, the synergistic effect occurs, in which the various components cooperate to maximize the beneficial effects and minimize any possible negative consequences Iroanya et al. (2014). Herbal remedies come in a variety of formats, such as tinctures, pills, and topical preparations. They are frequently tailored to the specific needs and symptoms of the patient Saleem et al. (2020). These formulations have long been utilized to treat liver illnesses throughout cultures, and new research has demonstrated encouraging outcomes in their hepatoprotective properties with few adverse effects.

Liver, which is the largest glandular organ in the body and performs myraid of function to an extent more functions than any other human organ. Liver plays a crucial function in human metabolism; the entirety of a person's blood supply flows through it many times each day Alvari et al. (2012). Liver is responsible for the production and secretion of bile, as well as the production of blood clotting proteins prothrombin and fibrinogen, as well as the mucopolysaccharide sulfuric acid ester heparin, which aids in preventing blood clots in the bloodstream. Sugar is transformed into glycogen by the liver Parveen et al. (2022). Liver illnesses are now one of the leading global causes of morbidity and death in both humans and animals. Liver illnesses, which include cirrhosis, hepatitis, liver failure, and related consequences, represent a significant global public health concern. Since, these conditions have an impact on human health Ali & Kumar (2015), liver protection becomes crucial. Hepatoprotective substances are essential for reducing the harm that chemicals, medications, and poisons can do to the liver. Liver disorders have long been treated with plant medicines in India's traditional medical system Shaik et al. (2012). Combining botanical elements from conventional medicine with herbal formulations offers a viable way to treat liver diseases. Their multi-targeted approach to treating complicated disorders has contributed to their appeal, indicating a shift in emphasis toward these formulations Vargas-Pozada & Muriel (2020). This review focused on the potential and reach of polyherbal medicines both

locally and globally, while also emphasizing the significance of Ayurveda and polyherbal formulations (PHF).

## 2. BENEFITS OF POLYHERBAL FORMULATION OVER SINGLE HERB

Plants which are used to make herbal medicines are called botanicals, and each plant has a variety of components which when combined proportionately can produce the required result. The demand for Ayurvedic Darbar et al. (2010), Bhope et al. (2011), Darbar & Chattopadhyay (2010), Benzie & Wachtel-Galor (2011) formulations is rising at a great pace because of growing interest in plant-based formulations. Phytomedicines derived from plants, which vary in species, growing environments, and physiologically active components, are safe and frequently used in combination Spinella (2002).

The pharmacological substances found in polyherbal formulations are derived from plants and have the ability to potential to show various effects such as anatgonistic, synergistic, agonistic and potentiative (Figure 1) because of their various active principles Darbar et al. (2009). Together, these pharmacological principles result in optimum treatment efficacy and minimal side effects. There are two ways by which synergism functions, namely pharmacodynamics and pharmacokinetics, depending on the type of interaction Darbar et al. (2020). When it comes to pharmacokinetic synergism, the components collectively must help in ADME (absorption, distribution, metabolism, and elimination). Alternatively, pharmacodynamic synergism examines the synergistic effect that results from targeting a similar receptor or physiological system with active ingredients that have similar therapeutic action. Apart from that, the majority of times, diseases are thought to be caused by a multitude of factors, which leads to apparent as well as unforseen symptoms. Here, a blend of herbal remedies may work on various areas concurrently to offer total relief from the ailment Chorgade (2007), Parasuraman et al. (2014), Sarwar et al. (2011), Karole et al. (2019).





The synergistic effects of polyherbalism provide several advantages not found in single-herb formulations. Clearly, a single multi-constituent formulation can have a better therapeutic impact. Because of this, a lower amount of the natural product would be required to provide the desired pharmacological action, reducing the potential for negative side effects (Table 1). Furthermore, polyherbal formulations contain a variety of compounds that combat illness complications; hence, distinct molecules treat diseases through various mechanisms, offering a comprehensive therapeutic approach for a given disease state Ramaiah et al. (2013), Rastogi et al. (2012), Darbar et al. (2018).

Table 1

Table 1 Popular Indian Medicinal Plants Used in Herbal Formulation						
S. No	Scientific Name	Common Name	Family	Parts Used in formulation		
1	Azadirachta indica	Neem	Meliaceae	Leaves		
2	Andrographis paniculata	Kalmegh	Acanthaceae	Leaves		
3	Zingiber officinale	Ginger	Zingiberaceae	Root		
4	Picrorhiza kurroa	Kutki	Scrofulariaceae	leaf, bark, and underground parts		
5	Terminalia chebula	Haritaki	Combretaceae	Seeds		
6	Asparagus racemosus	Shatamull	Liliaceae	dried roots		
7	Eugenia Jambolana	Jamun	Myrtaceae	Fruit & Seeds		
8	Trigonella graeceium	Methi	Fabaceae	leaves and seeds		
9	Piper nigrum	Morich	Piperaceae	Seeds		
10	Ocimum sanctum	tulsi	Lamiaceae	Leaves, Roots, Seeds		
11	Curcuma longa	Haldi	Zingiberaceae	rhizomes		
12	Berberis vulgaris	Barberry	Berberidaceae	fruit		
13	Moringa olifera	Soanjina	Moringaceae	roots, leaves, barks, seeds, flowers, fruits		
14	Phyllanthus niruri	Bhumyamalaki	Euphorbiaceae	roots, leaves, fruits		
15	Solanum nigrum	Kakamachi	Solanaceae	leaves, roots, bark, and flowers		

## **3. LIMITATIONS OF POLYHERBAL FORMULATION**

Combining plants that contain these elements may result in combinations that exhibit more activity than each extract taken alone. Alternatively, the coexistence of several components could result in chemical incompatibility, causing instability Stickel & Schuppan (2007). In India, the majority of Ayurvedic PHFs are produced and exported, however despite the Drugs and Cosmetic Act's establishment to regulate production and quality control, the manufacturing of Ayurvedic herbal preparations is subject to slightly lesser regulations (Table 2). Toxicity studies and clinical trials on herbal formulations are not required, per good clinical standards, in order for the maker of Ayurvedic herbal formulations to apply for patents and be granted manufacturing licenses Girish & Pradhan (2017), Darbar et al. (2000).

### Table 2

Table 2 Advantages and Disadvantages of Herbal Formulation					
Advantages	Disadvantages				
Better patients tolerance as well as acceptance	Adverse Interactions with Pharmaceuticals				
Safe and effective	Lack of Regulation				

No adverse drug reaction	Unknown Side-effects
Easily available and found in large variety and	Slower Healing than Pharmaceuticals
quantity	

### 4. HERBAL FORMULATION FOR HEPATIC DYSFUNCTIONS

Herbal drugs have become increasingly popular and their use is widespread. These polyherbal preparations are marketed as tonics with a variety of purposes, including growth promoters and appetite stimulants, gastrointestinal and hepatic regulators, liver tonics and stimulants, and treatments for hepatic dysfunction and regeneration Darbar et al. (2010). Biologically active chemicals from plants, such as silymarin, picroliv, ellagic acid, curcumin, andrographolide, and glycyrrhizin, can be used as appropriate building blocks for hepatoprotective medications that are both efficacious and targeted Darbar et al. (2020). To obtain the intended antioxidant, antifibrotic, antiviral, immunomodulatory, and anti-inflammatory effects, hepatoprotective herbals may also be combined Sharma et al. (2015). These medications will enhance biliary functions, support hepatic regeneration, and stop liver cell deterioration or necrosis brought on by narcotics, poisons, and viruses. Additionally, the bioavailability, stability, and effectiveness of these active compounds may be enhanced by the use of derivatives Padmanabhan & Jangle (2014), Sivakumar et al. (2014).

#### 5. MODE OF ACTION OF POLYHERBAL COMPOUNDS Figure 2



Figure 2 Liver Detoxifying Pathway by Herbal Formulation

PHFs have a complex range of hepatoprotective properties that work together to protect hepatocytes against the harmful effects of several hepato-toxins. These mixtures show amazing effectiveness in mitigating harm from substances like CCl<sub>4</sub>, alcohol, medications, and pollutants found in the environment, enabling the return of healthy liver function Darbar et al. (2021). The presence of several

phytoconstituents in herbal preparations is responsible for their antioxidant capabilities. Bioactive constituents likes flavonoids, alkaloids, terpenoids, phenolic acids, and tannins actively play a critical part in reducing free radicals and decrease the load of oxidative stress on hepatocytes. Considering that oxidative stress is a key factor in the development of hepatic pathophysiology, this role is crucial Darbar et al. (2021). These formulations are essential for preventing hepatocyte damage and apoptosis because they suppress lipid peroxidation and reduce ROS (Figure 2). Their anti-inflammatory and antifibrotic qualities are also quite important. Hepatic dysfunction progresses due in part to chronic inflammation and fibrosis Belapurkar et al. (2014). Through modulating proinflammatory cytokines such as IL-1 $\beta$  and TNF- $\alpha$  and blocking key signaling pathways like NF- $\kappa$ B and MAPK, these formulations function as strong anti-inflammatory drugs Hamid et al. (2021). Moreover, they lessen fibrosis by preventing the buildup of extracellular matrix proteins including collagen Rajanna et al. (2021).

The methods by which these PHFs produce hepatoprotection also heavily involve immunomodulatory actions Saha & Ghosh (2012), Yadav et al. (2016). Livina, VLS, Clearliv, BV-7310, Amlycure DS, Livomyn, PNK, Livergen, Syrup, Livactine, and Livshis are among the formulations that contain plants having immunomodulating capacity like *Tinospora cordifolia* and *Andrographis paniculata*, which work together to regulate immune cell activity and cytokine production. In order to maintain immunological homeostasis and reduce immune-mediated liver injury, these benefits fortify immune responses against harm caused by toxins Ghosh et al. (2011), Akbarzadeh et al. (2015).

The hepatoprotective activities of these formulations are mostly attributed to the promotion of cellular activity and liver regeneration. Both the recovery from injury and the restoration of normal hepatic function are guaranteed by the stimulation of hepatocyte proliferation and the manufacture of proteins unique to the liver. Increasing the liver's ability for detoxification is a key component of PHFs' mode of action. By boosting the activity of phase I and phase II detoxification enzymes such cytochrome P450, GSH S-transferase, and uridine diphosphate glucuronosyltransferases, these formulations enhance the liver's capacity to neutralize and remove toxins. Thus, the load on the liver is lessened, reducing the possibility of toxic agent-induced liver damage Pingale et al. (2008). In summary, PHFs have hepatoprotective action because of the intricate interactions between their immunomodulatory, regenerative, antifibrotic, antioxidant, and detoxification-enhancing qualities. As therapeutic approaches, these compositions hold great promise for averting liver injury and preserving general hepatic function.

## 6. LIVER TONIC

One of the main organs in the human body is the liver. It aids in both the breakdown of food and the majority of micronutrient absorption Siddiqui et al. (2017), Aladejana (2023). Global concern over chronic liver disease (CLD) is growing. Infection, alcohol misuse, exposure to hepatotoxic medications, autoimmune conditions, and metabolic diseases are among the common etiological factors. Cirrhosis of the liver and its associated consequences are the outcome of the chronic liver disease Kantharia et al. (2023), Gaurav et al. (2023). For this reason, maintaining a healthy liver is essential. Ayurvedic liver tonics is recommended to maintain optimal liver health Khan et al. (2024). However, it has been shown that practically every commercially available liver tonic has antioxidant, antibacterial, and anti-inflammatory qualities Shakya et al. (2022), Abbas et al. (2023). Studies revealed that the well-known liver tonic Liv-52 significantly protected rats' livers

against the hepatotoxic effects of carbon tetrachloride (CCl<sub>4</sub>). Lakshmi et al. (2023), Singh et al. (2023). An ideal replacement for allopathic liver medications is an Ayurvedic liver tonic. Due to their natural qualities, liver tonics (Table 3) can help to maintain healthy liver function and offer quick relief from liver problems. Table 3

Table 3 Popular Polyherbal Liver Tonic in India					
S. No.	Popular Liver Tonic in India	Key Highlights			
1	LIV 52	Protects the liver.			
2	Dizicure Tonic	Treats liver and its related issues			
3	Livray Liver Tonic	Easily available			
4	Livncid Ayurvedic Liver Tonic	Free from side effects.			
5	Hepano Liver Syrup	Good for liver health.			
6	Unilivzyme Syrup	Promotes fast healing.			
7	Livray-Ds Ayurvedic Liver Tonic	Improves liver health.			
8	Regliv Ayurvedic Liver Tonic	Improves digestion.			
9	Hepazyme	Treats fatty liver.			
10	Livina	Hepatoprotective			

With the greatest Ayurvedic characteristics, India have compiled an exclusive assortment of herbal syrups (Figure 3). Quality, composition, safety, and popularity are the factors that determine the ranking of these products. Figure 3



### **Popular Polyherbal Liver Tonic in India**

#### Figure 3 Ten Popular Marketed Liver Tonic

### 7. PREFERENCE OF HERBAL DRUGS IN MODERN SOCIETIES

In the western world, interest in plants as medications has grown in recent years. In the global setting, herbal remedies are widely used as the preferred therapeutic approach worldwide. The increased popularity of natural products among consumers has led to an increase in demand for herbal medications in recent years.



On the other hand, the increasing demand for herbal medicines has led to the systematic large-scale production in a variety of forms, including pills, capsules, ointments, nasal sprays, ophthalmic preparations, oral suspensions, powders, transdermal patches, and more (Figure 4). Among these, herbal products related to liver have the largest global commercial market Bramhankar et al. (2021). Thus, even in affluent countries, the public's use of plant-based crude extracts for self-medication is increasing and is currently being accepted as an alternative to traditional medicine Chaudhary & Kumari (2022).

It is projected that the global market for herbal drugs will grow significantly between 2024 and 2031. The market is anticipated to expand beyond the estimated horizon in 2022 due to the constant growth rate and increasing adoption of tactics by major players. Herbal liver medications are currently in high demand and have a promising future Debnath et al. (2024).

### 8. SUMMARY AND CONCLUSION

Developing nations are facing challenges in various areas like controlling population growth, rising poverty and pollution. The rising cost of medications and their side effects add to the burden which has resulted in popularity of PHFs as these formulations are aligned with the Ayurvedic Principles such as Tridoshas and Panchamahabhutas. Moreover, with advancement in scientific knowledge the phytoconstituents have been identified and formulated in synergistic combination thereby enhancing the efficacy and working as an acceptable alternative. The issue of antibiotic resistance has also led to the exploration of alternative or replacement therapy and PHFs have been able to fill-up the gap. PHFs simultaneously can help in boosting immunity as well as providing antimicrobial, antioxidative, and antiinflammatory action. Although, PHFs are efficacious and safe but with responsible and well-informed approach they can provide life support and well-being at global level. Public awareness, responsible manufacturing and stringent regulatory control can ensure that formulations meet international standard and can work as adjuvant therapy to mitigate the health problems of mankind.

### **CONFLICT OF INTERESTS**

None.

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