



Redox Healing Property of Herbal Formulation in Curing Liver Diseases

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Submission: April 13, 2023; Published: May 16, 2023

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Abstract

When an organ sustains repeated, protracted injury or inflammation that results in excessive scar tissue formation. In the case of liver, it develops fibrosis. The majority of chronic liver diseases have the potential to progress to fibrosis. Reactive oxygen species (ROS) production is crucial in causing liver damage and triggering hepatic fibrogenesis. Oxidative stress (OS) causes lipid, protein, and DNA disruption, causes hepatocytes to necrotize and apoptosis and intensifies the inflammatory response. For liver fibrosis and the difficulties that go along with it, herbs and herbal formulations are highly helpful. Due to synergistic action herbal formulations based on Indian medicinal plants are capable to reduced oxidative stress and prevent free radical generation. Our formulation is cheap, non-toxic and optimum effective with potent antioxidant property that has no side effects. This review focused on common medicinal plants that are used in our herbal formulation and their redox healing properties against liver fibrinogenesis.

Keywords: Liver fibrosis; Oxidative stress; Medicinal Plants; Herbal formulation; Antioxidant potential

Introduction

Oxidative stress, which is defined as an imbalance between pro-oxidants and antioxidant capacity within a cell, is crucial to the development of chronic liver disease that is inflammatory, metabolic, and proliferative. Cirrhosis, fibrosis, cholestasis, and necrosis are all signs of chronic liver damage (CLD) [1,2]. The last stage of many kinds of CLD is liver cirrhosis, which fibrosis precedes. Although underrated, the burden of liver disease is increasing globally [3,4]. The main causes of liver cirrhosis, which was reported to be the 11th most common cause of mortality worldwide, are ethanol consumption and chronic infections caused by hepatitis B virus (HBV) and/or hepatitis C virus (HCV). Due to the modification of the major biological components DNA, proteins, and lipids, oxidative stress damages the liver [5]. Their involvement in the modification of signaling pathways linked to gene transcription, protein expression, apoptosis, and the activation of hepatic stellate cells, DNA, protein, and lipid peroxidation products are known to play a role in the development and progression of liver fibrosis [6,7]. Inflammation, which appears as the invasion of inflammatory cells to combat numerous aggressive stimuli, is a crucial stage in the immune response.

Steatosis, or fatty deposits in the liver, fibrosis, or scarring of the liver, hepatitis, or inflammation of the liver, cirrhosis, in which scarring, and inflammation spread throughout the liver and irreversibly disrupt its shape or function, resulting in permanent cell damage and eventually liver failure, and liver cancer, which ultimately results in death, are all considered forms of hepatotoxicity [8-10]. Numerous toxicants, including paracetamol, some chemotherapy drugs, carbon tetrachloride, thioacetamide, persistent alcohol use, and microorganisms, can cause liver poisoning [11,12]. The majority of people on the planet have liver disease. There are 20,000 deaths every year attributed to liver problems [13]. Hepatotoxic male to female ratio was reported to be 1.4:1 at age 39. Numerous chemicals, including viruses, can be hazardous to the liver. (Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D), obesity, alcoholism that is ongoing or prolonged, genetic abnormalities (Haemochromatosis), a number of medications, including PCM, aspirin, ibuprofen, amiodarone, isoniazid, methotrexate, valproic acid, rifampin, etc. CCl₄, trichloroethylene, other poisons and Herbs like cascara, mahuang, kava, etc., hormones like birth control pills, anabolic steroids, and autoimmune disorders [14,15] can cause liver disease.

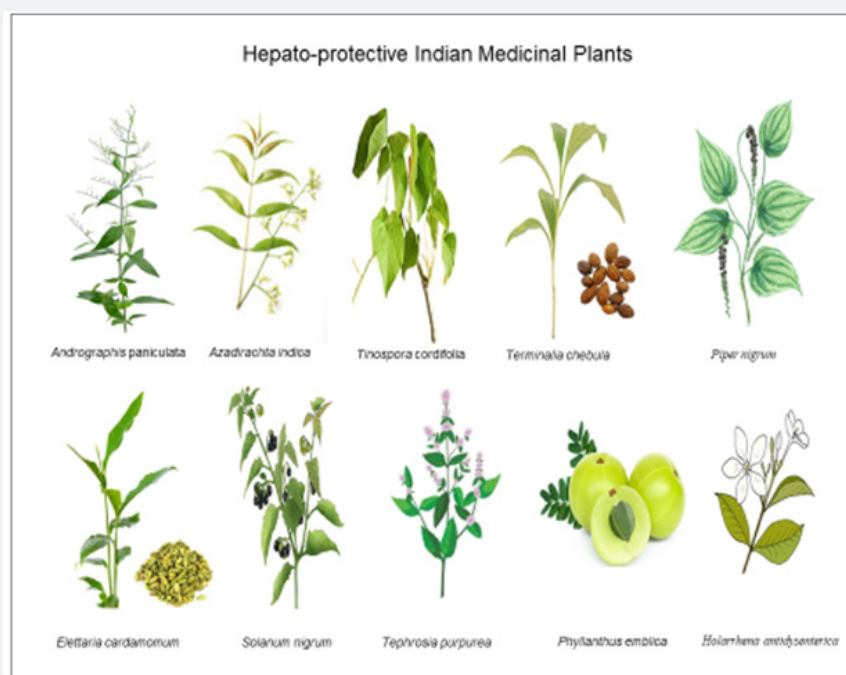


Figure 1: Hepato-protective Indian medical plant.

There are various treatments used to treat the symptoms of hepatotoxicity, but there are no particular allopathic medications used as hepatoprotectives. Leading pharmaceutical companies have spread awareness of herbal-based treatments for liver illnesses throughout the world and have been using them for a long time in India [16]. Beginning with Ayurvedic medicine and expanding to the Chinese, European, and other traditional medical systems, the use of natural treatments has a long history. By carefully combining the benefits of traditional medical systems with the contemporary idea of evidence-based medicinal evaluation, standardization, and randomized placebo controlled clinical trials, the 21st century has seen a paradigm shift towards therapeutic evaluation of herbal products in liver disease models. Different herbal formulations are well known for their Hepatoprotective effect [20]. In recent years, there has been growing interest in polyherbal formulation for the treatment of various diseases and it has enormously increased worldwide. In the traditional system of Indian medicine, plant formulation and combined extract of plants are used as a drug of choice rather than individual drug.

Concept of PHF

Ayurvedic medication formulation is based on two principles: using more than one drug in a formulation (PHF) and using more than one drug separately. This important traditional therapeutic herbal approach, also known as polypharmacy or polyherbalism, makes use of the interaction between various therapeutic plants to increase therapeutic efficacy [21]. Even though the

active phytochemical components of specific plants have a well-established history, they are typically only found in trace amounts and are seldom enough to produce the desired therapeutic effects [22]. Because of this, research has shown that combining these different plants with differing potencies could conceivably result in a better outcome than using them separately or adding up their unique effects. Synergism is the term used to describe this beneficial herb-herb interaction phenomena [23]. Certain pharmacological effects of herbal products' active ingredients are notable only when amplified by those of other plants; they are not noticeable when used alone.

Polyherbalism gives various benefits do not present in a single herbal preparation due to synergism. It is obvious that a single multi-component formulation can produce a higher therapeutic impact [24]. In order to accomplish the desired pharmacological activity for this, a lesser dose of the herbal preparation would be required, lowering the possibility of negative side effects. PHFs also improve patient convenience by removing the need to take multiple herbal formulations at once, which indirectly improves compliance and has a positive therapeutic impact [25]. When compared to a single herbal formulation, all these advantages have led to PHF's market appeal.

Reason of Using PHF

As previously noted, PHF has just lately begun to acquire popularity on a global scale since it offers some benefits that allopathic medicines do not.

a) First off, PHFs have a reputation for being highly efficient against a variety of disorders. As stated above, herbal medicines' therapeutic benefits are mediated by a variety of phytoconstituents, and the effects are amplified when related herbs are combined in PHFs.

b) Second, PHFs typically have a broad therapeutic window. The majority of them have a better risk to benefit ratio since they are safe at large doses and yet effective at low doses [26,27].

When properly made and utilized, PHFs frequently have fewer negative effects than allopathic medications. Even though most current allopathic medications are made to produce effective therapeutic results, taking them can have undesirable side effects include impotence, disorientation, convulsions, vomiting, weariness, dry mouth, and diarrhoea. Non-steroidal anti-inflammatory drug (NSAID) for rheumatoid arthritis (RA) treatment has side effects include dyspepsia, stomach ulcers, salt and fluid retention, as well as hypertension [28]. These effects are mostly gastrointestinal and renal in nature. They may choose an Ayurvedic remedy for this, which has few or no side effects. Ayurvedic treatment for one year utilizing internal herbal remedies has been demonstrated in studies to have favorable outcomes.

Herbal Remedies for Liver Fibrosis

One of the most significant organs, the liver, is essential to our body's many physiological processes including release of toxic materials safely. In the human body, the liver is where hormone and plasma protein production, glycogen storage management, RBC breakdown, and detoxification occur. Since the liver is crucial in the detoxification and transformation of substances, it is indirectly exposed to their negative effects, which makes it more prone to illness. Fibrosis, among other liver conditions, has become a significant public health issue [29-31]. It results from a persistent wound healing response to a chronic liver injury caused by a number of conditions, including autoimmune, viral, drug-induced, cholestatic, and metabolic illnesses. Extracellular matrix synthesis and deposition are excessive in hepatic fibrosis (ECM). The primary collagen-producing cells have been identified as activated hepatic stellate cells (HSCs), portal fibroblasts, and myofibroblasts of bone marrow origin. Fibrosis can progress into cirrhosis, which can then become incurable hepatocellular cancer, if it is not treated.

The level of concern is further increased by mortality figures, which show that cirrhosis caused 1.2 million deaths in 2013 as opposed to 0.8 million fatalities in 1990. More than 1 million people die each year from hepatocellular carcinoma (HCC), the fifth most prevalent malignancy worldwide. In most of the affluent western world, hepatocellular carcinoma is less common, but it seems to be sharply rising in Asian nations [32]. Therefore, it is crucial to look into the causes and treatments of hepatic fibrosis in order to restore normal liver function. Although it is utilized

in medical treatment, complementary and alternative medicine (CAM) is not a part of conventional medicine. Since it helps patients manage their chronic illness and prevents the malaise frequently associated with traditional health care, the usage of CAM is highlighted among those with chronic conditions. The National Center for Complementary and Alternative Medicine (NCCAM), USA, divides complementary and alternative medicine into five categories: entire medical system, mind-body medicine, manipulative and body-based techniques, nutrition, and herbal remedies [33,34].

Oxidative Stress and Liver Health

Different substances are metabolized by the liver to create reactive oxygen radicals. (ROS). Prooxidants are ROS that can harm tissue and the liver [35]. Stress levels may be raised by specific medications, infections, outside exposures, tissue damage, and other factors. Oxidative stress arises from a rise in prooxidant production, a fall in antioxidant levels, or both. The liver system's signaling, regulation, and redox balance are biased by molecular redox switches, oxygen detection by the thiol redox proteome, NAD/NADP, and phosphorylation/dephosphorylation systems [36].

All cellular macromolecules interact with ROS without difficulty. The phosphodiester bonds that keep the bases in RNA and DNA together are cleaved by ROS, causing RNA and DNA to lose their chain structure. In a process known as lipid peroxidation, polyunsaturated fatty acids are another important target for oxidation by ROS [37]. This process disturbs the normal structure of the membrane and results in necrosis [38]. Additionally, as cysteine is necessary for the action of enzymes, ROS, particularly the hydroxyl radical, oxidise cysteine residues in proteins to form disulfides, sulfoxides, or sulfonic acids [39,40]. Additionally, oxidative stress promotes fibrogenesis by raising toxic cytokines such tumor necrosis factor (TNF), interleukin-6 (IL-6), and transforming growth factor (TGF-).

Role of Antioxidant in Prevention of Liver Oxidative Stress

A substance that can prevent other molecules from oxidizing is known as an antioxidant. The chemical process of oxidation involves the transfer of electrons from a material to an oxidizing agent. Free radicals can be produced through oxidation processes [41]. These radicals can then trigger a series of events that harm cells. Antioxidant breaks these chains of events by scavenging free radicals and preventing other oxidation processes. Antioxidants, such as thiols, ascorbic acid, or polyphenols, frequently function as reducing agents since they prevent oxidation by themselves. Numerous studies have shown that phenolic content in plants and their antioxidant properties are connected. Polyphenol molecules, which are found in plants, have antioxidant properties [42-44]. The most frequent method for creating free radicals in food, medication, and even living systems is through the oxidative

process [45]. Oxygen radicals make up the majority of free radicals that harm biological systems. Additionally, antioxidants function as hydrogen donors, electron donors, singlet oxygen quenchers, peroxide decomposers, enzyme inhibitors, and metal chelating agents [46]. Natural antioxidants (safe and nontoxic) are needed more than synthetic antioxidants because of the impact on the immune system. The topical application of herbal treatments is among the most pronounced and the most basic traditions of health care because plants contain various elements that have a local physical impact on bodily tissues.

Summary & Conclusion

Though in India a traditional medicine named 'Ayurveda' has been practiced since several thousand years back it is not well known and popularized in the world forum due to several reasons. It is a very rich kind of holistic medicinal therapy considering the mind body relationship in health and diseases. Thousands of Indian herbs, extracts of animal origin, metal ash, and spices are being used to maintain good health and treat mostly all kind of diseases in this system of medicine with mental and physical exercises called 'Yoga'. The components are used singly or in tandem as a formulation for synergistic effects. Here the effects of some of the most potent herbs in maintenance of liver health and to treat liver diseases are presented in the light of modern medicine. Recent knowledge on etiology of step-by-step progression of liver diseases with detailed mechanism of actions, rolls of different agents in the signaling pathways are also discussed. It is well established that the bodily balance, more precisely the balance in the liver tissue and different kind of cells, oxidants and antioxidants is most important in maintaining the liver health. There are many regulatory molecules which actually maintain this balance. In case of any disturbance in this redox balance due to health and food habits, environmental and toxicological poisoning, viral and other types of infections liver diseases start and progress. If it is diagnosed early and treated with herbal formulations, then a remedy is possible.

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DOI: [10.19080/ARGH.2023.19.556016](https://doi.org/10.19080/ARGH.2023.19.556016)

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